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2024 ESC Guidelines for the management of peripheral arterial and aortic diseases

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Authors/Task Force Members: Lucia Mazzolai *†, (Chairperson) (Switzerland), Gisela Teixido-Tura ‡, (Task Force Co-ordinator) (Spain), Stefano Lanzi ‡, (Task Force Co-ordinator) (Switzerland), Vinko Boc (Slovenia), Eduardo Bossone (Italy), Marianne Brodmann [1] (Austria), Alessandra Bura-Rivière (France), Julie De Backer [2] (Belgium), Sebastien Deglise (Switzerland), Alessandro Della Corte (Italy), Christian Heiss (United Kingdom), Marta Kałużna-Oleksy (Poland), Donata Kurpas (Poland), Carmel M. McEniery (United Kingdom), Tristan Mirault (France), Agnes A. Pasquet (Belgium), Alex Pitcher (United Kingdom), Hannah A.I. Schaubroeck (Belgium), Oliver Schlager (Austria), Per Anton Sirnes (Norway), Muriel G. Sprynger (Belgium), Eugenio Stabile (Italy), Françoise Steinbach (France), Matthias Thielmann (Germany), Roland R.J. van Kimmenade (Netherlands), Maarit Venermo (Finland), Jose F. Rodriguez-Palomares *†, (Chairperson) (Spain), and ESC Scientific Document Group

* Corresponding authors: Lucia Mazzolai, Department of Angiology, Lausanne University Hospital (CHUV), and Medical School, Lausanne University (UNIL) Lausanne, Switzerland. Tel: +41 (0)21 314 0750. Email: Lucia.Mazzolai@chuv.ch; and Jose F. Rodriguez-Palomares, Cardiovascular Imaging Section and Aortic Diseases Unit (VASCERN), Department of Cardiology, Vall d'Hebron Hospital Universitari, Vall d'Hebron Barcelona Hospital Campus, Vall d'Hebron Institut de Recerca (VHIR), Barcelona, Spain, and Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares, Instituto de Salud Carlos III, Madrid, Spain, and Department of Medicine, Universitat Autònoma de Barcelona, Spain. Tel: +34 93 882 3881. Email: josefernando.rodriguez@vallhebron.cat

† The two Chairpersons contributed equally to the document and are joint corresponding authors.

‡ The two Task Force Co-ordinators contributed equally to the document.

Author/Task Force Member affiliations are listed in author information.

[1] Representing the European Society of Vascular Medicine (ESVM)

[2] Representing the European Reference Network on Rare Multisystemic Vascular Diseases (VASCERN)

ESC Clinical Practice Guidelines (CPG) Committee: listed in the Appendix.

ESC subspecialty communities having participated in the development of this document:

Associations: Association for Acute CardioVascular Care (ACVC), Association of Cardiovascular Nursing & Allied Professions (ACNAP), European Association of Cardiovascular Imaging (EACVI), European Association of Preventive Cardiology (EAPC), European Association of Percutaneous Cardiovascular Interventions (EAPCI), Heart Failure Association (HFA).

Councils: Council for Cardiology Practice, Council on Hypertension.

Working Groups: Adult Congenital Heart Disease, Aorta and Peripheral Vascular Diseases, Cardiovascular Surgery, Thrombosis.

Patient Forum

Document Reviewers: Alessia Gimelli, (CPG Review Co-ordinator) (Italy), Jean-Baptiste Ricco, (CPG Review Co-ordinator) (France), Elena Arbelo (Spain), Christian-Alexander Behrendt (Germany), Michael Böhm (Germany), Michael A. Borger (Germany), Margarita Brida (Croatia), Sergio Buccheri (Sweden), Gill Louise Buchanan (United Kingdom), Christina Christersson (Sweden), Gert J. de Borst (Netherlands), Marco De Carlo (Italy), Roman Gottardi (Austria), Lydia Hanna (United Kingdom), Lynne Hinterbuchner (Austria), Borja Ibanez (Spain), Ignatios Ikonomidis (Greece), Stefan James (Sweden), Thomas Kahan (Sweden), Klaus Kallenbach[2] (Luxemburg), Lars Køber (Denmark), Konstantinos C. Koskinas (Switzerland), Juraj Madaric[1] (Slovakia), Blandine Maurel (France), John William McEvoy (Ireland), Gil Meltzer (Israel), Borislava Mihaylova (United Kingdom), Richard Mindham (United Kingdom), Ioana Mozos (Romania), Jens Cosedis Nielsen (Denmark), Eva Prescott (Denmark), Amina Rakisheva (Kazakhstan), Barbara Rantner (Germany), Bianca Rocca (Italy), Xavier Rossello (Spain), Jean Paul Schmid (Switzerland), Daniel Staub (Switzerland), Sabine Steiner (Germany), Isabella Sudano (Switzerland), Martin Teraa (Netherlands), Ilonca Vaartjes (Netherlands), Rafael Vidal-Perez (Spain), Christiaan Vrints (Belgium), and Katja Zeppenfeld (Netherlands)

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Abbreviations and acronyms

^{18}F–NaF	Fluorine-18–sodium fluoride
6MWD	Six-minute walking distance
6MWT	Six-minute walk test
AA	Abdominal aorta
AAA	Abdominal aortic aneurysm
AAD	Acute aortic dissection
AAE	Aortic adverse events
AAL	Ascending aortic length
AAS	Acute aortic syndrome
ABI	Ankle–brachial index
ACAS	Asymptomatic Carotid Atherosclerosis Study
ACB	Asymptomatic Cervical Bruit Study
ACC/AHA	American College of Cardiology and American Heart Association
ACEI	Angiotensin-converting enzyme inhibitor
ACS	Acute coronary syndrome
ACST	Asymptomatic Carotid Surgery Trial
ACTA2	Alpha-actin gene
AD	Aortic dissection
ADAM	American Aneurysm Detection and Management
ADD-RS	Aortic dissection detection-risk score
AF	Atrial fibrillation
AHI	Aortic height index
ALI	Acute limb ischaemia
AMI	Acute mesenteric ischaemia
AP	Antero-posterior
ARB	Angiotensin receptor blocker
ARR	Absolute risk reduction
ASCVD	Atherosclerotic cardiovascular disease
ASE	American Society of Echocardiography

ASI	Aortic size index
BASIL	Bypass versus Angioplasty in Severe Ischaemia of the Leg trial
BAV	Bicuspid aortic valve
BB	Beta-blocker
BEST-CLI	Best Endovascular versus Best Surgical Therapy for Patients with Critical Limb Ischemia trial
b.i.d.	Bis in die (twice daily)
BMI	Body mass index
BP	Blood pressure
b.p.m.	Beats per minute
BSA	Body surface area
BTK	Below-the-knee
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CANTOS	Canakinumab Anti-Inflammatory Thrombosis Outcomes Study
CANVAS	Canagliflozin Cardiovascular Assessment Study
CAS	Carotid artery stenting
CCA	Common carotid artery
CCB	Calcium channel blocker
CCT	Cardiovascular computed tomography
CDT	Catheter-based thrombectomy
cdTLR	Clinically driven target lesion revascularization
CEA	Carotid endarterectomy
CEUS	Contrast-enhanced ultrasound
CHA_2DS_2-VASc	Congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 and sex category (female)
CI	Confidence interval
cIMT	Carotid intima media thickness
CK	Creatinine kinase
CKD	Chronic kidney disease
CLTI	Chronic limb-threatening ischaemia
CMI	Chronic mesenteric ischaemia
CMR	Cardiovascular magnetic resonance
CoA	Coarctation of the aorta
COMPASS	Cardiovascular Outcomes for People Using Anticoagulation Strategies
COPD	Chronic obstructive pulmonary disease
CP	Carotid plaque
CREDENCE	Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation
CREST-2	Carotid Revascularization Endarterectomy vs. Stenting Trial 2
CRP	C-reactive protein
CS	Carotid artery stenosis
CSA/h	Cross-sectional area-to-height ratio
CT	Computed tomography
CTA	Computed tomography angiography
CV	Cardiovascular
CVD	Cardiovascular disease
CVRF	Cardiovascular risk factor
DAPT	Dual antiplatelet therapy
DBP	Diastolic blood pressure
DD	D-dimer
DISSECT	Duration, Intimal tear, Size, Segmental Extent, Clinical complications, Thrombosis
DPI	Dual pathway inhibition
DSA	Digital subtraction angiography
DTA	Descending thoracic aorta
DUS	Duplex ultrasound
DWI	Diffusion-weighted imaging
ECG	Electrocardiogram
ECST	European Carotid Surgery Trial
eGFR	Estimated glomerular filtration rate
EMPA-REG OUTCOME	(Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients
ESC	European Society of Cardiology
ESH	European Society of Hypertension
ESRD	End-stage renal disease
EUCLID	Examining Use of tiCagreLor In peripheral artery Disease
FDA	(United States) Food and Drug Administration
FDG	Fluorodeoxyglucose
FDR	First-degree relative
FET	Frozen elephant trunk
FID	Focal intimal disruption
FL	False lumen
GERAADA	German Registry of Acute Aortic Dissection Type A
GFR	Glomerular filtration rate
GLP-1RA	Glucagon-like peptide-1 receptor agonist
GSV	Great saphenous vein
HADS	Hospital anxiety and depression score
HbA1c	Glycated haemoglobin
HBET	Home-based exercise training
HF	Heart failure
HITS	High-intensity transient signal
HOME	Hyperinsulinaemia: the Outcomes of its Metabolic Effects
HR	Hazard ratio
HRQoL	Health-related quality of life
hs-CRP	High-sensitivity C-reactive protein
HSR	High surgical risk
HTAD	Heritable thoracic aortic disease
IC	Intermittent claudication
ICA	Internal carotid artery
ID	Intimal disruption
IL	Interleukin
ILT	Intensive lipid-lowering therapy
IMA	Inferior mesenteric artery
IMH	Intramural haematoma
IMPROVE-AD	The Improving outcomes in vascular disease—aortic dissection trial
IMPROVE-IT	IMProved Reduction of Outcomes: Vytorin Efficacy International Trial
IPE	Icosapent ethyl
IRAD	International Registry of Acute Aortic Dissection
ISTH	International Society on Thrombosis and Haemostasis
i.v.	Intravenous
IVUS	Intravascular ultrasound
LDL-C	Low-density lipoprotein cholesterol
LEADER	Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results trial
LSA	Left subclavian artery
LV	Left ventricular
MACE	Major adverse cardiac event

MAD	Multisite artery disease
MALE	Major adverse limb event
MAP	Mean arterial pressure
MESA	Multi-Ethnic Study of Atherosclerosis
MFS	Marfan syndrome
MHV	Mechanical heart valve
MI	Myocardial infarction
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
MWD	Maximal walking distance
NASCET	North American Symptomatic Carotid Endarterectomy Trial
OAC	Oral anticoagulation
o.d.	Once daily
OMT	Optimal medical treatment
OR	Odds ratio
PAAD	Peripheral arterial and aortic diseases
PA	Popliteal aneurysm
PAD	Peripheral arterial disease
PAU	Penetrating atherosclerotic ulcer
PC-AKI	Post-contrast acute kidney injury
PCSK9	Proprotein convertase subtilisin/kexin type 9
PET	Positron emission tomography
PET-CT	PET-computed tomography
PFWD	Pain-free walking distance
PROM	Patient-reported outcome measure
PSV	Peak systolic velocity
PSVr	Peak systolic velocity ratio
PVD	Polyvascular disease
QoL	Quality of life
RAR	Renal-aortic peak flow velocity ratio
RAS	Renal artery stenosis
RCT	Randomized controlled trial
REACH	The REduction of Atherothrombosis for Continued Health
REDUCE-IT	Reduction of Cardiovascular Events With Icosapent Ethyl–Intervention Trial
ROMS	Retrograde open mesenteric stenting
ROPAC	Registry Of Pregnancy And Cardiac disease
RPE	Rate of perceived exertion
RR	Relative risk
SAMMPRIS	Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis trial
SAPPHIRE	Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy trial
SAPT	Single antiplatelet therapy
SBP	Systolic blood pressure
SCI	Spinal cord ischaemia
SCS	Spinal cord stimulation
SET	Supervised exercise training
SF-36	Short-form 36-item health questionnaire
SGLT2i	Sodium-glucose co-transporter-2 inhibitor
SMA	Superior mesenteric artery
SMART	Secondary Manifestation of ARTerial disease
SOCRATES	Acute Stroke or Transient Ischaemic Attack Treated with Aspirin or Ticagrelor and Patient Outcomes trial
SCORE2	Systematic Coronary Risk Evaluation 2
SCORE2-Diabetes	Systematic Coronary Risk Evaluation 2 - diabetes
SCORE2-OP	Systematic Coronary Risk Evaluation 2–Older Persons
SPACE-2	Stent Protected Angioplasty versus Carotid Endarterectomy study
SPPB	Short physical performance battery
SRUCC	Society of Radiologists in Ultrasound
SS	Subclavian stenosis
SSFP	Steady-state free precession
STJ	Sinotubular junction
STS/AATS	Society of Thoracic Surgeons/American Association for Thoracic Surgery
SUSTAIN-6	Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes
SVS	Society for Vascular Surgery
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
TAA	Thoracic aortic aneurysm
TAAA	Thoracoabdominal aortic aneurysm
TAAD	Type A aortic dissection
TAD	Thoracic aortic disease
TAI	Traumatic aortic injury
TAV	Tricuspid aortic valve
TAVI	Transcatheter aortic valve implantation
TBAD	Type B aortic dissection
TBI	Toe–brachial index
TCAR	Transcarotid artery revascularization
$TcPO_2$	Transcutaneous oxygen pressure
TOE	Transoesophageal echocardiography
TEM	Type entry malperfusion classification
TEVAR/EVAR	Thoracic endovascular aortic aneurysm repair
TFCAS	Transfemoral carotid artery stenting
THALES	Acute Stroke or Transient Ischaemic Attack Treated with Ticagrelor and acetylsalicylic acid for Prevention of Stroke and Death trial
TIA	Transient ischaemic attack
TIMI	Thrombolysis in myocardial infarction
TP	Toe pressure
TS	Turner syndrome
TTE	Transthoracic echocardiography
UEAD	Upper-limb artery disease
UKPDS	United Kingdom Prospective Diabetes Study: clinical and therapeutic implications for type 2 diabetes
uTBAD	Uncomplicated type B aortic dissection
VascuQoL	Vascular quality of life questionnaire
VAST	Vertebral Artery Stenting Trial
vEDS	Vascular Ehlers–Danlos syndrome
VIST	Vertebral Artery Ischaemia Stenting Trial
VKA	Vitamin K antagonist
WELCH	Walking Estimated Limitation Calculated by History
WIfI	Wound, Ischaemia, foot Infection classification
WIQ	Walking Impairment Questionnaire

1. Preamble

Guidelines evaluate and summarize available evidence with the aim of assisting health professionals in proposing the best diagnostic or therapeutic approach for an individual patient with a given condition. Guidelines are intended for use by health professionals and the European Society of Cardiology (ESC) makes its guidelines freely available.

ESC Guidelines do not override the individual responsibility of health professionals to make appropriate and accurate decisions in consideration of each patient's health condition and in consultation with that patient or the patient's caregiver where appropriate and/or necessary. It is also the health professional's responsibility to verify the rules and regulations applicable in each country to drugs and devices at the time of prescription and to respect the ethical rules of their profession.

ESC Guidelines represent the official position of the ESC on a given topic and are regularly updated when warranted by new evidence. ESC Policies and Procedures for formulating and issuing ESC Guidelines can be found on the ESC website (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Guidelines-development/Writing-ESC-Guidelines). This guideline updates and replaces the previous peripheral arterial disease and aortic disease guidelines from 2017 and 2014, respectively.

The Members of this task force were selected by the ESC to include professionals involved with the medical care of patients with this pathology as well as patient representatives and methodologists. The selection procedure included an open call for authors and aimed to include members from across the whole of the ESC region and from relevant ESC Subspecialty Communities. Consideration was given to diversity and inclusion, notably with respect to gender and country of origin.

The task force performed a critical review and evaluation of the published literature on diagnostic and therapeutic approaches including assessment of the risk–benefit ratio. The strength of every recommendation and the level of evidence supporting them were weighed and scored according to pre-defined scales as outlined in *Tables 1* and *2* below. Patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs) were also evaluated as the basis for recommendations and/or discussion in these guidelines. The task force followed ESC voting procedures and all approved recommendations were subject to a vote and achieved at least 75% agreement among voting members. Members of the task force with declared interests on specific topics were asked to abstain from voting on related recommendations.

The experts of the writing and reviewing panels provided declaration of interest forms for all relationships that might be perceived as real or potential sources of conflicts of interest. Their declarations of interest were reviewed according to the ESC declaration of interest rules which can be found on the ESC website (http://www.escardio.org/guidelines) and have been compiled in a report published in a supplementary document with the guidelines. Funding for the development of ESC Guidelines is derived entirely from the ESC with no involvement of the healthcare industry.

The ESC Clinical Practice Guidelines (CPG) Committee supervises and co-ordinates the preparation of new guidelines and is responsible for the approval process. In addition to review by the CPG Committee, ESC Guidelines undergo multiple rounds of double-blind peer review by external experts, including members from across the whole of the ESC region, all National Cardiac Societies of the ESC and from relevant ESC Subspecialty Communities. After appropriate

Table 1 Classes of recommendations

Classes of recommendations	Definition	Wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

Table 2 Levels of evidence

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

revisions, the guidelines are signed off by all the experts in the task force. The finalized document is signed off by the CPG Committee for publication in the *European Heart Journal*.

ESC Guidelines are based on analyses of published evidence, chiefly on clinical trials and meta-analyses of trials, but potentially including other types of studies. Evidence tables summarizing key information from relevant studies are generated early in the guideline development process to facilitate the formulation of recommendations, to enhance comprehension of recommendations after publication, and reinforce transparency in the guidelines development process. The tables are published in their own section of ESC Guidelines and reference specific recommendation tables.

Off-label use of medication may be presented in this guideline if a sufficient level of evidence shows that it can be considered medically appropriate for a given condition. However, the final decisions concerning an individual patient must be made by the responsible health professional giving special consideration to:

- The specific situation of the patient. Unless otherwise provided for by national regulations, off-label use of medication should be limited to situations where it is in the patient's interest with regard to the quality, safety, and efficacy of care, and only after the patient has been informed and has provided consent.
- Country-specific health regulations, indications by governmental drug regulatory agencies, and the ethical rules to which health professionals are subject, where applicable.

2. Introduction

Peripheral arterial and aortic diseases (PAAD) are highly prevalent and significantly increase cardiovascular (CV) mortality and morbidity in the general population,[1,2] consequently, intensive preventive strategies are needed. However, patients with PAAD are generally underdiagnosed and undertreated[3,4] compared with patients with coronary artery disease (CAD).[5] Common risk factors in PAAD often coexist, requiring a multidisciplinary approach for effective management.[5] Early diagnosis is crucial for better outcomes. These guidelines address PAAD, updating and merging the 2017 peripheral arterial diseases and 2014 aortic diseases guidelines. The focus is primarily on atherosclerotic arterial diseases, but they also address some non-atherosclerotic genetic conditions. While not exhaustive, these 2024 guidelines offer guidance on diagnosis, surveillance, and treatment. A number of new and revised recommendations are summarized in *Tables 3* and *4*, respectively. Readers should consider non-atherosclerotic conditions and refer to specific documents.[6–9]

A general approach to PAAD is provided in the central illustration (*Figure 1*).

In the management of PAAD, the following aspects must be highlighted:

- ***Shared decision-making*** to involve patients, explore treatment options, assess patient values, and reach decisions collaboratively.
- ***Multidisciplinary approach (Figure 1) in expert and high-volume PAAD centres for complex patients or procedures***. These centres provide diverse services, including diagnosis, treatment planning, minimally invasive procedures, open surgery, post-operative and outpatient care, and ideally, research and innovation. They should provide continuous clinical service (24/7) and have access to digital imaging. These guidelines recognize variations in healthcare systems, population sizes, and needs, impacting the definition of 'high volume' in PAAD care across countries.

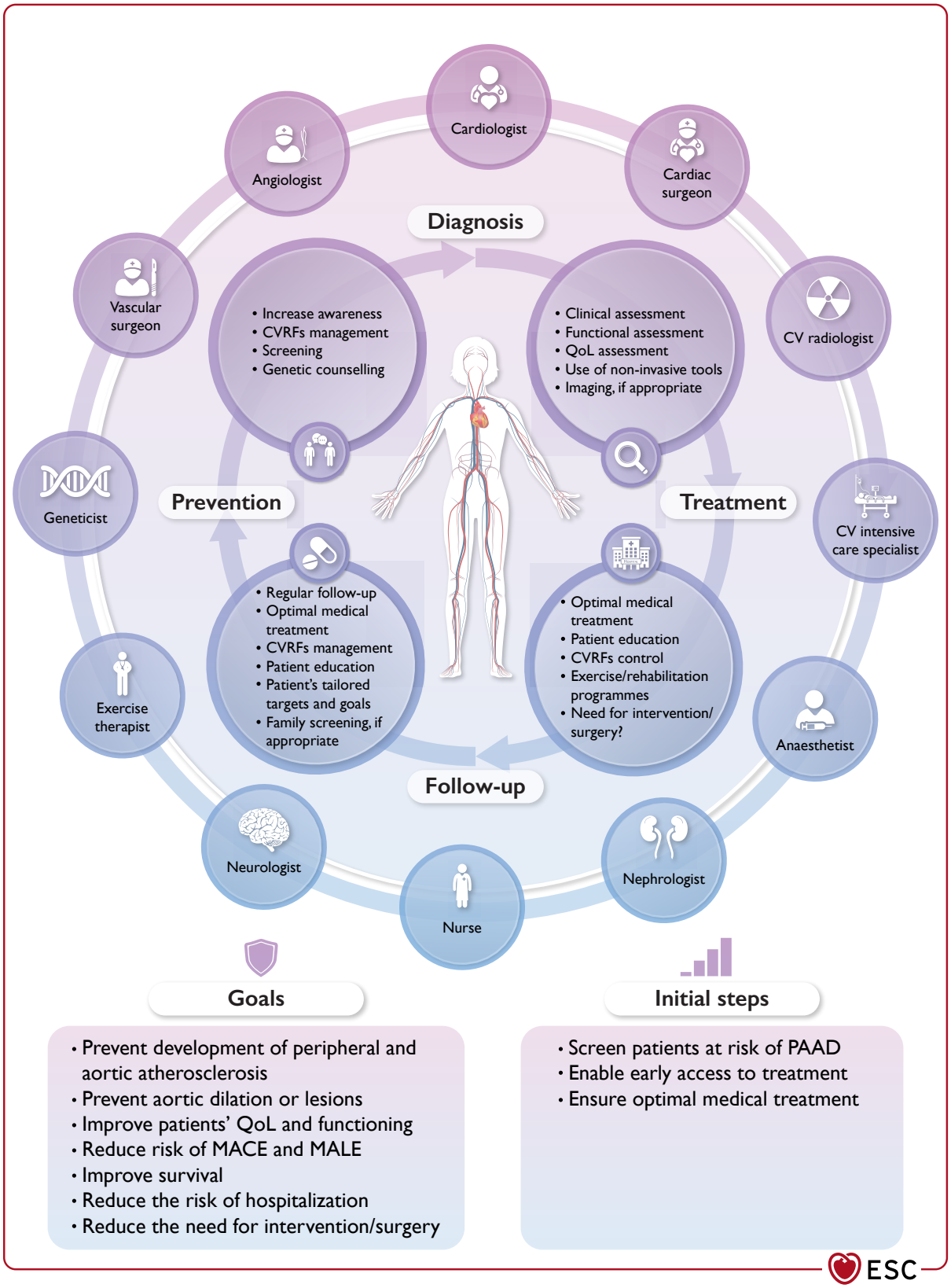

Figure 1 Central illustration: from diagnosis to treatment, a holistic multidisciplinary peripheral arterial and aortic diseases approach. CV, cardiovascular; CVRFs, cardiovascular risk factors; MACE, major adverse cardiac event; MALE, major adverse limb event; PAAD, peripheral arterial and aortic diseases; QoL, quality of life.

3. What is new

Table 3 New recommendations

Recommendations	Class	Level
Recommendations for clinical and laboratory, and for functional quality of life, assessment in patients with peripheral arterial and aortic disease		
When managing PAAD, it is recommended to adopt a comprehensive approach that addresses the entirety of arterial circulation.	I	B
Recommendations for peripheral arterial disease screening		
In patients with AAA, femoro-popliteal aneurysm screening with DUS should be considered.	IIa	C
In patients needing intervention with transfemoral access, screening for iliofemoral artery disease may be considered.	IIb	C
In patients with two or more CVRFs, screening for asymptomatic CS may be considered.	IIb	C
Recommendations for abdominal aortic aneurysm screening		
Opportunistic AAA screening with DUS should be considered in symptomatic/asymptomatic PAD patients.	IIa	B
Recommendations for lifestyle, physical activity, and patient education		
Use of web- or app-based secondary prevention risk calculators should be considered in the shared decision-making to improve patient adherence to treatment and lifestyle changes.	IIa	C
E-cigarettes may be considered as an aid to quitting tobacco smoking, but it is advisable to limit their use and avoid simultaneous use with conventional cigarettes due to unknown long-term effects.	IIb	C
Recommendations for lipid-lowering therapy in patients with peripheral arterial and aortic diseases		
In patients with atherosclerotic PAAD, lipid-lowering therapy is recommended.	I	A
An ultimate LDL-C goal of <1.4 mmol/L (55 mg/dL) and a >50% reduction in LDL-C vs. baseline are recommended in patients with atherosclerotic PAAD.	I	A
If the target LDL-C level is not achieved on maximally tolerated statins and ezetimibe, treatment with a PCSK9 inhibitor is recommended in patients with atherosclerotic PAAD, to achieve target values.	I	A
If the target LDL-C level is not achieved, a combination of statins and ezetimibe is indicated in patients with atherosclerotic PAAD, to achieve the given target values.	I	B
For statin-intolerant patients with atherosclerotic PAAD, at high CV risk, who do not achieve their LDL-C goal on ezetimibe, it is recommended to add bempedoic acid either alone or in combination with a PCSK9 inhibitor.	I	B
Statins for the reduction of growth and rupture of AAA should be considered.	IIa	B
Statins for the reduction of growth and rupture of TAA may be considered.	IIb	B
In high-risk patients with PAAD and triglycerides >1.5 mmol/L despite lifestyle measures and statin therapy, icosapent ethyl 2 g b.i.d. may be considered in addition to a statin.	IIb	B
Fibrates are not recommended for cholesterol lowering.	III	B
Recommendations for exercise therapy in patients with peripheral arterial disease		
In patients with symptomatic PAD, SET is recommended.	I	A
In those patients undergoing endovascular revascularization, SET is recommended as an adjuvant therapy.	I	A
When SET is not available or feasible, a structured and monitored (calls, logbooks, connected devices) HBET programme should be considered.	IIa	A
Walking should be considered as the first-line training modality. When walking exercise is not an option, alternative exercise modes (strength training, arm cranking, cycling, and combinations of different training modes) should also be considered.	IIa	A
Walking training performed at high intensity (77%–95% of maximal heart rate or 14–17 self-perceived exertion on Borg's scale) should be considered to improve walking performance, and high-intensity exercise training (various aerobic training modes) should be considered to improve cardiorespiratory fitness.	IIa	A
Training frequency of at least three times per week, training session duration of at least 30 min, and training programme duration of at least 12 weeks should be considered.	IIa	B
In patients with PAD, exercise training to moderate-severe claudication pain may be considered to improve walking performance. However, improvements are also achievable with lesser claudication pain severities (low-mild pain or pain-free).	IIb	B
Based on patient's tolerance, a progressive increase (every 1–2 weeks) in exercise training load may be considered.	IIb	C

Continued

Recommendations for antithrombotic therapy in patients with peripheral arterial disease		
Treatment with combination rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered for patients with PAD and high ischaemic risk, and non-high bleeding risk.	IIa	A
Treatment with combination rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered for patients with PAD and non-high bleeding risk following lower-limb revascularization.	IIa	B
Aspirin (75–100 mg) for primary prevention may be considered in patients with asymptomatic PAD and DM, in the absence of contraindications.	IIb	A
Recommendations for interventional treatment of asymptomatic and symptomatic peripheral arterial disease (general)		
In patients with symptomatic PAD, after a 3 month period of OMT and exercise therapy, PAD-related QoL assessment is recommended.	I	B
It is recommended to adapt the mode and type of revascularization options to anatomical lesion location, lesion morphology, and general patient condition.	I	C
In patients with symptomatic PAD and impaired PAD-related QoL after a 3 month period of OMT and exercise therapy, revascularization may be considered.	IIb	B
In patients with PAD, revascularization is not recommended if the reason is to solely prevent progression to CLTI.	III	B
In patients with asymptomatic PAD, revascularization is not recommended.	III	C
Recommendations for interventional treatment of patients with symptomatic peripheral arterial disease (per arterial bed)		
In femoro-popliteal lesions, drug-eluting treatment should be considered as the first-choice strategy.	IIa	A
In femoro-popliteal lesions, if revascularization is indicated, an open surgical approach should be considered when an autologous vein (e.g. GSV) is available in patients with low surgical risk.	IIa	C
In patients with severe IC undergoing endovascular femoro-popliteal revascularization, treatment of BTK arteries may be considered in the same intervention.	IIb	C
Recommendations in patients with peripheral arterial disease: follow-up of patients with peripheral arterial disease		
It is recommended to regularly, at least once a year, follow-up patients with PAD, assessing clinical and functional status, medication adherence, limb symptoms, and CVRFs, with DUS assessment as needed.	I	C
Recommendations for the management of chronic limb-threatening ischaemia		
Early recognition of CLTI and referral to the vascular team are recommended for limb salvage.	I	C
Recommendations for medical treatment in patients with chronic limb-threatening ischaemia		
It is recommended that patients with CLTI are managed by a vascular team.	I	C
In patients with CLTI and ulcers, offloading mechanical tissue stress is indicated to allow wound healing.	I	C
Lower-limb exercise training is not recommended in patients with CLTI and wounds.	III	C
Recommendations for interventional treatment of chronic limb-threatening ischaemia		
In CLTI patients, it is recommended to perform revascularization as soon as possible.	I	B
In CLTI, it is recommended to use autologous veins as the preferred conduit for infra-inguinal bypass surgery.	I	B
In multilevel vascular disease, it is recommended to eliminate inflow obstructions when treating downstream lesions.	I	C
In CLTI patients with good autologous veins and low surgical risk (<5% peri-operative mortality, >50% 2 year survival), infra-inguinal bypass may be considered.	IIb	B
In CLTI patients, endovascular treatment may be considered as first-line therapy, especially in patients with increased surgical risk or inadequate autologous veins.	IIb	B
Recommendations for follow-up in patients with chronic limb-threatening ischaemia		
In patients with CLTI, following revascularization it is recommended to follow-up patients on a regular basis.	I	C
At follow-up, it is recommended to assess clinical, haemodynamic and functional status, limb symptoms, treatment adherence, and CVRFs.	I	C
Recommendations for carotid artery stenosis assessment		
It is recommended to use the NASCET method or its non-invasive equivalent to assess ICA stenosis.	I	B
It is not recommended to use the ECST method for ICA stenosis assessment.	III	C
Recommendations for the management of subclavian artery stenosis		
Bilateral arm BP measurement is recommended for all patients with PAAD.	I	B
Endovascular revascularization may be considered over surgery, despite similar long-term outcomes, due to lower complication rates.	IIb	B
Routine revascularization in patients with atherosclerotic subclavian artery disease is not recommended.	III	C
Recommendations for diagnostic strategies for renal artery disease		
DUS is recommended as the first-line imaging modality in patients with suspicion of RAS.	I	B

Continued

Recommendations for treatment strategies for renal artery disease		
Revascularization		
In patients with atherosclerotic unilateral >70% RAS, concomitant high-risk features, and signs of kidney viability, renal artery revascularization should be considered after OMT has been established.	IIa	B
In patients with atherosclerotic bilateral (>70%) RAS or RAS in a solitary kidney, concomitant high risk features, and signs of kidney viability, renal artery revascularization should be considered.	IIa	B
In patients with hypertension and/or signs of renal dysfunction due to RAS caused by fibromuscular dysplasia, concomitant high-risk features, and signs of kidney viability, revascularization with primary balloon angioplasty and bailout stenting should be considered.	IIa	B
In patients with an indication for renal artery revascularization and complex anatomy, or after failed endovascular revascularization, open surgical revascularization should be considered.	IIa	B
In patients with atherosclerotic unilateral RAS, routine revascularization is not recommended.	III	A
Recommendations in patients with visceral artery stenosis		
In patients with acute or chronic mesenteric ischaemia, assessment by a vascular team is recommended.	I	C
Revascularization of asymptomatic atherosclerotic visceral artery stenosis is not recommended.	III	C
Recommendations for surgery in aortic root and ascending aorta dilatation associated with tricuspid aortic valve		
In patients with dilatation of the tubular ascending aorta who can be offered surgery with low predicted risk, ascending aortic replacement should be considered at a maximum diameter >52 mm.	IIa	B
In patients undergoing surgery for tricuspid aortic valve disease who have concomitant dilatation of the aortic root or ascending tubular aorta, and low predicted surgical risk, ascending aorta or root replacement should be considered at a maximum diameter ≥45 mm, otherwise ≥50 mm.	IIa	B
SAPT with low-dose aspirin (75–100 mg/day) should be considered for the first 3 months after valve-sparing aortic surgery when there are no other baseline indications for OAC.	IIa	C
In patients undergoing non-aortic-valve cardiac surgery who have concomitant dilatation of the ascending aorta or aortic root with a maximum diameter ≥50 mm, concomitant aortic surgery should be considered.	IIa	C
Recommendations for surgery in aortic arch aneurysms		
In patients with low or intermediate operative risk with an aortic arch aneurysm and recurrent episodes of chest pain not attributable to non-aortic causes, open surgical replacement of the arch is recommended.	I	C
In patients undergoing open surgical repair of an aortic arch aneurysm, an elephant trunk or frozen elephant trunk procedure should be considered if the aneurysmal disease extends into the proximal descending thoracic aorta.	IIa	C
Recommendations for follow-up after treatment of aortic aneurysms		
After open repair of TAA, an early CCT is recommended within 1 month, and then yearly CCT follow-up for the first 2 post-operative years and every 5 years thereafter is recommended if findings are stable.	I	B
After 5 post-operative years without complications, continuing long-term follow-up of TEVAR by CCT every 5 years should be considered.	IIa	B
If growth of the excluded aneurysm is observed, without evidence of type I or III endoleak, repeating CCT every 6–12 months, depending on the growth rate observed, should be considered.	IIa	C
In low-risk patients, from 1 year post-operatively after EVAR, repeating DUS/CEUS every 2 years should be considered.	IIa	B
If any abnormality during DUS/CEUS is found, confirmation should be considered using additional CCT or CMR (based on potential artefacts).	IIa	B
Recommendations for diagnostic work-up of acute aortic syndrome		
CCT from neck to pelvis is recommended as the first-line imaging technique in patients with suspected AAS since it is widely available, accurate, and provides information about the entry tear, extension, and possible complications (malperfusion, dilatation, or rupture).	I	C
In patients with suspected AAS, TOE is recommended to guide peri-operative management and detect complications.	I	C
Recommendations for medical treatment in acute aortic syndromes		
In patients with AAS who can be managed conservatively and who achieved haemodynamic targets with i.v. anti-impulse therapy, switching to oral BBs and, if necessary, up-titration of other BP-lowering agents is recommended after 24 h if gastrointestinal transit is preserved.	I	B
If the patient has a contraindication for BBs, a non-dihydropyridine calcium blocker should be considered.	IIa	B
Recommendations for intervention in type A acute aortic dissection		
In patients with acute TAAD who have extensive destruction of the aortic root, a root aneurysm, or a known genetic aortic disorder, aortic root replacement is recommended with a mechanical or biological valved conduit.	I	B
In patients presenting with acute TAAD, transfer from a low- to a high-volume aortic centre with the presence of a multidisciplinary team should be considered to improve survival if transfer can be accomplished without significant delay in surgery.	IIa	B
In selected patients, a valve-sparing root repair may be considered, when performed by experienced surgeons.	IIb	B

Continued

Recommendations for aortic repair strategies in type A acute aortic dissection		
In patients with acute TAAD and a partially dissected aortic root but no significant aortic valve leaflet pathology, aortic valve resuspension is recommended over valve replacement.	I	B
In patients with acute TAAD undergoing aortic repair, an open distal anastomosis is recommended to improve survival and increase FL thrombosis rates.	I	B
In patients with acute TAAD without an intimal tear in the arch or a significant arch aneurysm, hemi-arch repair is recommended over more extensive arch replacement.	I	B
In patients with acute TAAD and a secondary intimal tear in the arch or proximal DTA, extended aortic repair with stenting of the proximal DTA (e.g. by the frozen elephant technique) may be considered to reduce late distal aortic complications (e.g. aneurysm evolution of the remaining dissected descending aorta).	IIb	C
Recommendations for the management of malperfusion in the setting of acute aortic dissection		
In patients with acute TAAD presenting with malperfusion (cerebral, mesenteric, lower limb, or renal), immediate aortic surgery is recommended.	I	B
In patients with acute TAAD presenting with cerebral malperfusion or non-haemorrhagic stroke, immediate aortic surgery should be considered to improve neurological outcome and reduce mortality.	IIa	B
In patients with acute TAAD presenting with clinically significant mesenteric malperfusion syndrome, immediate invasive angiographic diagnostics to evaluate percutaneous malperfusion repair before or directly after aortic surgery, in aortic centres with expertise, should be considered.	IIa	C
Recommendations for the management of patients presenting with acute type B aortic dissection		
In patients with uncomplicated acute TBAD, TEVAR in the subacute phase (between 14 and 90 days) should be considered in selected patients with high-risk features to prevent aortic complications.	IIa	B
Recommendations for the management of patients presenting with chronic type B aortic dissection		
In chronic TBAD and with a descending thoracic aortic diameter ≥60 mm, treatment is recommended in patients at reasonable surgical risk.	I	B
In patients with chronic TBAD and a descending thoracic aortic diameter ≥55 mm, an indication for intervention should be considered in patients with low procedural risk.	IIa	C
In patients with chronic post-dissection thoracoabdominal aortic aneurysms, the use of fenestrated/branched stent grafts may be considered, when treatment is indicated.	IIb	C
Recommendations for the management of penetrating atherosclerotic ulcer		
In uncomplicated type B PAU with high-risk imaging features, endovascular treatment should be considered.	IIa	C
Recommendations for traumatic aortic injury		
In cases of severe aortic injury (grade 4), immediate repair is recommended.	I	A
In minimal aortic injury (grades 1 or 2), initial medical therapy under careful clinical and imaging surveillance should be considered.	IIa	C
In cases of progression of the IMH (grade 2), semi-elective repair (within 24–72 h) should be considered.	IIa	C
Recommendations for follow-up after treatment of acute aortic syndrome		
In medically treated type B AAS or IMH, follow-up imaging is recommended at 1, 3, 6, and 12 months after onset, then yearly if imaging findings are stable.	I	C
In medically treated PAU, follow-up imaging is recommended at 1 month after diagnosis, then every 6 months if imaging findings are stable.	I	C
After open surgery for AAS, follow-up imaging by CCT and TTE within 6 months, then CCT at 12 months and then yearly if findings are stable, should be considered.	IIa	B
If no complications occur within the first 5 years, CCT every 2 years thereafter should be considered.	IIa	B
If no residual patent FL is documented for 3 post-operative years, subsequent surveillance by CCT every 2–3 years should be considered.	IIa	C
In the follow-up of medically treated PAU, after 2 years of imaging stability, larger intervals should be considered in low-risk patients.	IIa	C
Recommendations for the management of patients with heritable thoracic aortic disease		
It is recommended that medical management of patients with HTAD is individualized and based on shared decision-making.	I	C
It is recommended that patients with known or suspected syndromic or non-syndromic HTAD are evaluated in a centre with experience in the care of this patient group.	I	C
Recommendations for genetic testing and aortic screening in aortic disease		
In patients with HTAD, guidance of clinical management by the underlying gene/variant, when known, should be considered.	IIa	B

Continued

Recommendations for imaging in women with Turner syndrome		
To take the smaller body size of women (≥15 years) with TS into account, the use of the ascending ASI (ratio of aortic diameter [mm] to BSA [m^2]), AHI (ratio of aortic diameter [mm] to height [m]), or aortic z-score is recommended to define the degree of aortic dilatation and assess the risk of aortic dissection.	I	C
It is recommended to define imaging and clinical surveillance intervals according to the estimated risk for dissection, based on the ascending ASI and concomitant lesions.	I	C
Recommendations for aortic surgery in women with Turner syndrome		
Elective surgery for aneurysms of the aortic root and/or ascending aorta should be considered in women with TS who are ≥15 years of age, have an ascending ASI >23 mm/m^2, an AHI >23 mm/m, a z-score >3.5, and have associated risk factors for aortic dissection or are planning pregnancy.	IIa	C
Elective surgery for aneurysms of the aortic root and/or ascending aorta may be considered for women with TS who are ≥15 years of age, have an ascending ASI >25 mm/m^2, an AHI >25 mm/m, a z-score >4, and who do not have associated risk factors for aortic dissection.	IIb	C
Recommendations for medical treatment in patients with vascular Ehlers–Danlos syndrome		
In patients with vEDS, regular vascular surveillance of the aorta and peripheral arteries by DUS, CCT, or CMR is recommended.	I	C
Treatment with celiprolol should be considered in patients with vEDS.	IIa	B
Recommendations for vascular imaging in Marfan syndrome		
In patients with MFS, TTE is recommended: • At least annually in patients with an aortic root diameter <45 mm in the absence of additional risk factors • At least every 6 months in patients with an aortic root diameter <45 mm in the presence of additional risk factors • At least every 6–12 months in patients with an aortic root diameter ≥45 mm in the absence of additional risk factors	I	C
In patients without previous aortic surgery, complete peripheral vascular and thoracoabdominal aortic imaging by CMR or CCT and DUS is recommended at the first evaluation, and subsequently every 3–5 years if stable.	I	C
Recommendations for medical treatment in Marfan syndrome		
In patients with MFS, treatment with either a BB or an ARB, in maximally tolerated doses (unless contraindicated), is recommended to reduce the rate of aortic dilatation.	I	A
In patients with MFS, the use of both a BB and an ARB, in maximally tolerated doses (unless contraindicated), should be considered to reduce the rate of aortic dilatation.	IIa	A
Recommendations for pregnancy in women with Marfan syndrome		
It is recommended that all women with MFS: • Have a pre-conception evaluation to address the risks of maternal CV and other complications • Have follow-up in a centre with access to a pregnancy heart and vessel team	I	C
It is recommended that couples in which a partner has or is at risk of HTAD be offered pre-conception genetic counselling.	I	C
Imaging of the whole aorta (by CMR/CCT) is recommended prior to pregnancy.	I	C
Follow-up during pregnancy is recommended with a frequency determined by aortic diameter and growth.	I	C
Intake of BBs during pregnancy is recommended.	I	C
Prophylactic aortic root surgery is recommended in women desiring pregnancy with aortic diameters >45 mm.	I	C
Prophylactic aortic root surgery may be considered in women desiring pregnancy with aortic diameters of 40–45 mm.	IIb	C
Recommendations for physical exercise in patients with Marfan syndrome		
It is recommended to individualize physical activity in patients with MFS based on aortic diameter, family history of aortic dissection, and pre-existing fitness.	I	C
Regular moderate aerobic exercise with a level of intensity informed by aortic diameter is recommended in most patients with MFS.	I	C
For patients who present with aortic dissection and/or have undergone aortic surgery, post-operative cardiac rehabilitation aiming at improving both physical and mental health should be considered.	IIa	B
Recommendations for imaging follow-up in Loeys–Dietz syndrome		
In patients with Loeys–Dietz syndrome, TTE at baseline and subsequently every 6–12 months, depending on aortic diameter and growth, is recommended.	I	C
In patients with Loeys–Dietz syndrome, a baseline arterial imaging study from head to pelvis with CMR or CCT and subsequent surveillance with CMR or CCT or DUS every 1–3 years is recommended.	I	C
Recommendations for imaging and surgery in *ACTA2*-related heritable thoracic aortic disease		
Annual monitoring of the aortic root/ascending aorta with TTE to evaluate for aortic root/ascending aorta enlargement is recommended.	I	C
Imaging of the aorta with CMR/CCT every 3–5 years is recommended.	I	C
Prophylactic aortic root surgery should be considered with a diameter ≥45 mm, or lower in cases with other risk factors.	IIa	C

Continued

Recommendations for bicuspid aortic valve-associated aortopathy management		
Surgery for bicuspid aortopathy of the root phenotype is recommended when the maximum aortic diameter is ≥50 mm.	I	B
Screening by TTE in FDRs of BAV patients with root phenotype aortopathy and/or isolated aortic regurgitation is recommended.	I	C
In patients with low surgical risk, surgery for bicuspid aortopathy of ascending phenotype should be considered when the maximum aortic diameter is >52 mm.	IIa	B
Recommendations for evaluation and medical treatment of patients with coarctation of the aorta		
In patients with native or repaired coarctation, lifelong follow-up is recommended, including regular imaging of the aorta with CCT/CMR every 3–5 years (adapted to clinical status and previous imaging findings).	I	B
Recommendations for screening and management of polyvascular disease and peripheral arterial disease with cardiac diseases		
In patients with PVD, an LDL-C reduction by ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.	I	A
In patients with stable PVD who are symptomatic in at least one territory and without high bleeding risk, treatment with a combination of rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered.	IIa	A

AAA, abdominal aortic aneurysm; AAD, acute aortic dissection; AAS, acute aortic syndrome; AHI, aortic height index; ARB, angiotensin receptor blocker; ASI, aortic size index; BAV, bicuspid aortic valve; BB, beta-blocker; b.i.d., twice daily; BP, blood pressure; BTK, below-the-knee; BSA, body surface area; CCT, cardiovascular computed tomography; CEUS, contrast-enhanced ultrasound; CLTI, chronic limb-threatening ischaemia; CMR, cardiovascular magnetic resonance; CS, carotid artery stenosis; CV, cardiovascular; CVRFs, cardiovascular risk factors; DM, diabetes mellitus; DTA, descending thoracic aorta; DUS, duplex ultrasound; ECST, European Carotid Surgery Trial; FDR, first-degree relative; FL, false lumen; GSV, great saphenous vein; HBET, home-based exercise training; HTAD, heritable thoracic aortic disease; ICA, internal carotid artery; IMH, intramural haematoma; IC, intermittent claudication; i.v., intravenous; LDL-C, low-density lipoprotein cholesterol; MFS, Marfan syndrome; NASCET, North American Symptomatic Carotid Endarterectomy Trial; OAC, oral anticoagulation; o.d., once daily; OMT, optimal medical treatment; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease; PAU, penetrating atherosclerotic ulcer; PVD, polyvascular disease; QoL, quality of life; RAS, renal artery stenosis; SAPT, single antiplatelet therapy; SET, supervised exercise training; TAA, thoracic aortic aneurysm; TAAD, type A aortic dissection; TBAD, type B aortic dissection; TOE, transoesophageal echocardiography; TEVAR/EVAR, thoracic endovascular aortic aneurysm repair; TS, Turner syndrome; TTE, transthoracic echocardiography; vEDS, vascular Ehlers–Danlos syndrome.

Table 4 Revised recommendations

Recommendations in 2017 (PAD) and 2014 (Aortic)	Class	Level	Recommendations in 2024	Class	Level
Recommendations for abdominal aortic aneurysm screening					
Screening for AAA with DUS					
Is recommended in all men >65 years of age.	I	A	Is recommended in men aged ≥65 years with a history of smoking to reduce the risk of death from ruptured AAA.	I	A
(i) May be considered in women >65 years of age with history of current/past smoking.	IIb	C	May be considered in men aged ≥75 years (irrespective of smoking history) or in women aged ≥75 years who are current smokers, hypertensive, or both.	IIb	C
(ii) Is not recommended in female non-smokers without familial history.	III	C			
Family AAA screening with DUS					
Targeted screening for AAA with ultrasound should be considered in first-degree siblings of a patient with AAA.	IIa	B	Is recommended for FDRs of patients with AAA aged ≥50, unless an acquired cause can be clearly identified.	I	C
Opportunistic AAA screening with DUS					
Targeted screening for AAA with ultrasound should be considered in first-degree siblings of patients with AAA.	IIa	B	Should be considered in men ≥65 years and in women aged ≥75 years during TTE.	IIa	B
Recommendations for antihypertensive therapy in patients with peripheral and aortic disease					
In patients with PAD and hypertension, it is recommended to control blood pressure at <140/90 mmHg	I	A	In patients with PAAD and hypertension an SBP target towards 120–129 mmHg, if tolerated, is recommended.	I	A
ACEIs or ARBs should be considered as first-line therapy in patients with PAD and hypertension.	IIa	B	ACEIs/ARBs may be considered in all patients with PAD, regardless of BP levels, in the absence of contraindications.	IIb	B
Recommendations for lipid-lowering therapy for patients with peripheral arterial and aortic diseases					
In patients with PAD, it is recommended to reduce LDL-C to <1.8 mmol/L (70 mg/dL) or decrease it by >50% if baseline values are 1.8–3.5 mmol/L (70–135 mg/dL).	I	C	An ultimate LDL-C goal of <1.4 mmol/L (55 mg/dL) and a >50% reduction in LDL-C vs. baseline are recommended in patients with atherosclerotic PAAD.	I	A
Recommendations for carotid artery stenosis assessment					
DUS (as first-line imaging), CTA, and/or MRA are recommended for evaluating the extent and severity of extracranial carotid stenosis.	I	B	It is recommended to use DUS as first-line imaging to diagnose ICA stenosis.	I	C

Continued

Recommendations in patients with visceral artery stenosis					
In patients with acute embolic occlusion of the SMA, both endovascular and open surgery therapy should be considered.	IIa	B	In patients with acute mesenteric ischaemia due to acute occlusion of the SMA, endovascular revascularization is recommended.	I	B
Recommendations for surveillance of patients with abdominal aorta aneurysm					
In patients with small (30–55 mm) AAA, the following time interval should be considered: • Every 3 years for AAA of 30–39 mm diameter • Every 2 years for AAA of 40–44 mm diameter • Every year for AAA >45 mm diameter.	IIa	B	DUS surveillance should be considered annually in women with AAA of 40–45 mm and in men with AAA of 40–49 mm.	IIa	B
Recommendations for surgery in aortic root and ascending aorta dilatation associated with tricuspid aortic valve					
Surgery should be considered in patients who have isolated aortic arch aneurysm with a maximal diameter ≥55 mm.	IIa	C	Surgery is recommended in patients with dilatation of the aortic root or ascending aorta with a tricuspid aortic valve and a maximum diameter of ≥55 mm.	I	B
Aortic valve repair using the reimplantation technique or remodelling with aortic annuloplasty is recommended in young patients with aortic root dilation and tricuspid aortic valves.	I	C	Valve-sparing aortic root replacement is recommended in patients with aortic root dilatation if performed in experienced centres and durable results are expected.	I	B
Lower thresholds for intervention may be considered according to BSA in patients with small stature or in the case of rapid progression, aortic valve regurgitation, planned pregnancy, and patient's preference.	IIb	C	Ascending aortic or root replacement may be considered at a maximum diameter of ≥50 mm in patients with proximal aorta dilatation who can be offered surgery with low predicted risk and present with any of the following: • Growth of the aortic diameter ≥3 mm per year • Resistant hypertension • Short stature (<1.69 m) • Root phenotype • Aortic length >11 cm • Age <50 years • Desire for pregnancy • Aortic coarctation.	IIb	B
Recommendations for surgery in aortic arch aneurysms					
Aortic arch repair may be considered in patients with aortic arch aneurysm who already have an indication for surgery of an adjacent aneurysm located in the ascending or descending aorta.	IIb	C	In patients undergoing open surgical repair of an ascending aortic aneurysm, concomitant hemi-arch replacement should be considered if the dilatation extends into the proximal aortic arch (>50 mm).	IIa	C
Recommendations for follow-up after treatment of aortic aneurysms					
After TEVAR or EVAR, surveillance is recommended after 1, 6, and 12 months and then yearly. Shorter intervals can be proposed in the event of abnormal findings requiring closer surveillance.	I	C	After TEVAR, follow-up imaging is recommended at 1 and 12 months post-operatively, then yearly until the fifth post-operative year if no abnormalities are documented.	I	B
Long-term surveillance of open abdominal aortic repair may be considered at loose (5 year) intervals using colour DUS or CCT imaging.	IIb	C	After open repair of AAA, first follow-up imaging is recommended within 1 post-operative year, and every 5 years thereafter if findings are stable.	I	A
If neither endoleak nor AAA sac enlargement is documented during first year after EVAR, then colour DUS, with or without contrast agents, should be considered for annual post-operative surveillance, with non-contrast CT imaging every 5 years.	IIa	C	After EVAR, follow-up imaging is recommended with CCT (or CMR) and DUS/CEUS at 1 month and 12 months post-operatively, then, if no abnormalities are documented, DUS/CEUS is recommended every year, repeating CCT or CMR (based on potential artefacts) every 5 years.	I	A
Recommendations for diagnostic work-up of acute aortic syndrome					
TTE is recommended as an initial imaging investigation. In stable patients with a suspicion of AAS, the following imaging modalities are recommended (or should be considered according to local availability and expertise):	I	C	In patients with suspected AAS, focused TTE (with use of contrast if feasible) is recommended during the initial evaluation.	I	C
MRI	I	C	In patients with suspected AAS, CMR should be considered as an alternative imaging technique if CCT is not available.	IIa	C

Continued

TOE	IIa	C	In patients with suspected AAS, TOE is recommended to guide peri-operative management and detect complications.	I	C
Recommendations for medical treatment in acute aortic syndromes					
In all patients with AD, medical therapy, including pain relief and blood pressure control, is recommended.	I	C	Invasive monitoring with an arterial line and continuous three-lead ECG recording, as well as admission to an intensive care unit, is recommended.	I	B
Recommendations for the management of patients presenting with acute type B aortic dissection					
In complicated TBAD, TEVAR is recommended.	I	C	In patients with complicated acute TBAD, emergency intervention is recommended.	I	B
In complicated TBAD, surgery may be considered.	IIb	C			
In complicated TBAD, TEVAR may be recommended.	IIb	C	In patients with complicated acute TBAD, TEVAR is recommended as the first-line therapy.	I	B
In complicated TBAD, surgery may be considered.	IIb	C			
Recommendations for the management of intramural haematoma					
In complicated type B IMH, TEVAR should be considered.	IIa	C	In complicated type B IMH, TEVAR is recommended.	I	C
Recommendations for the management of penetrating atherosclerotic ulcer					
In the case of type A PAU, surgery should be considered.	IIa	C	In the case of type A PAU, surgery is recommended.	I	C
In complicated type B PAU, TEVAR should be considered.	IIa	C	In complicated type B PAU, endovascular treatment is recommended.	I	C
Recommendations for traumatic aortic injury					
In cases of TAI with suitable anatomy requiring intervention, TEVAR should be preferred to surgery.	IIa	C	In cases of TAI with suitable anatomy requiring intervention, TEVAR is recommended over open surgery.	I	A
Recommendations for genetic testing and aortic screening in aortic disease					
It is recommended to investigate FDRs (siblings and parents) of a subject with TAAD to identify a familial form in which relatives all have a 50% chance of carrying the family mutation/disease.	I	C	Imaging screening of family members of patients with TAD with risk factors for HTAD in whom no (likely) pathogenic variant is identified should be considered starting at age 25, or 10 years below the youngest case, whichever is younger. If the initial screening is normal, continued screening every 5 years until the age of 60 should be considered.	IIa	C
Recommendations for bicuspid aortic valve-associated aortopathy management					
Cardiac MRI or CT is indicated in patients with BAV when the morphology of the aortic root and the ascending aorta cannot be accurately assessed by TTE.	I	C	CCT or CMR of the entire thoracic aorta is recommended at first diagnosis and when important discrepancies in measurements are found between subsequent TTE controls during surveillance, or when the diameter of the aorta exceeds 45 mm.	I	C
In the case of aortic diameter >50 mm or an increase of >3 mm per year measured by echocardiography, confirmation of the measurement is indicated, using another imaging modality (CT or MRI).	I	C			
In the case of a diameter of the aortic root or the ascending aorta >45 mm or an increase of >3 mm per year measured by echocardiography, annual measurement of aortic diameter is indicated.	I	C	Surveillance serial imaging by TTE is recommended in BAV patients with a maximum aortic diameter >40 mm, either with no indication for surgery or after isolated aortic valve surgery, after 1 year, then if stability is observed, every 2–3 years.	I	C
In cases of BAV, surgery of the ascending aorta is indicated in the case of: • Aortic root or ascending aortic diameter >50 mm in the presence of other risk factors (coarctation of the aorta, systemic hypertension, family history of dissection, or increase in aortic diameter of >3 mm per year).	I	C	In patients with low surgical risk and ascending phenotype bicuspid aortopathy, surgery should be considered at a maximum diameter ≥50 mm if any of the following is the case: • Age <50 years • Short stature • Ascending aortic length ≥11 cm • Aortic diameter growth rate >3 mm per year • Family history of acute aortic syndrome • Aortic coarctation • Resistant hypertension • Concomitant non-aortic-valve cardiac surgery • Desire for pregnancy	IIa	C

Continued

In cases of BAV, surgery of the ascending aorta is indicated in the case of: • Aortic root or ascending aortic diameter >45 mm when surgical aortic valve replacement is scheduled.	I	C	Surgery for bicuspid aortopathy in patients undergoing aortic valve surgery should be considered at a root or ascending diameter ≥45 mm.	IIa	C
Recommendations for screening and management of polyvascular disease and peripheral arterial disease with cardiac diseases					
In patients undergoing CABG, DUS is recommended in patients with a recent (<6 months) history of TIA/stroke.	I	B	Carotid DUS should be considered for stable patients scheduled for CABG with TIA/stroke within the past 6 months without carotid revascularization.	IIa	B

AAA, abdominal aortic aneurysm; AAS, acute aortic syndrome; ACEI, angiotensin-converting enzyme inhibitor; AD, aortic dissection; ARB, angiotensin receptor blocker; BAV, bicuspid aortic valve; BP, blood pressure; BSA, body surface area; CABG, coronary artery bypass grafting; CCT, cardiovascular computed tomography; CEUS, contrast-enhanced ultrasound; CMR, cardiovascular magnetic resonance; CT, computed tomography; CTA, computed tomography angiography; DUS, duplex ultrasound; ECG, electrocardiogram; FDR, first-degree relative; HTAD, heritable thoracic aortic disease; ICA, internal carotid artery; IMH, intramural haematoma; LDL-C, low-density lipoprotein cholesterol; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease; PAU, penetrating atherosclerotic ulcer; SBP, systolic blood pressure; SMA, superior mesenteric artery; TAAD, type A aortic dissection; TAD, thoracic aortic disease; TAI, traumatic aortic injury; TBAD, type B aortic dissection; TOE, transoesophageal echocardiography; TEVAR/EVAR, thoracic endovascular aortic aneurysm repair; TIA, transient ischaemic attack; TTE, transthoracic echocardiography.

4. Epidemiology and risk factors

4.1. Epidemiology

Peripheral arterial disease (PAD) is prevalent worldwide and affects 113 million people aged 40 and older, of which 42.6% are in countries with a low-to-middle sociodemographic index. Global prevalence is 1.52%, increases with age (14.91% in those aged 80–84 years), and is higher in females than in males (18.03% vs. 10.56%, in the same age group).[10–13]

PAD prevalence rose by 72% from 1990 to 2019, considering a 45% growth rate in the world population.[10,11,14] The overall global age-standardized prevalence is about 1470 per 100 000 persons (*Figure 2*).[14]

Ischaemic cerebral disease, mainly linked to carotid stenosis (65% of cases), has a prevalence of 77.19 million, marking a 95% increase from 1990 to 2019.[15]

The overall prevalence of aortic disease including aneurysm and dissections is estimated at around 1% to 3% in the general population, with up to 10% prevalence in older age groups. European studies show a decrease in abdominal aortic aneurysm (AAA) prevalence in screened men >65 years of age, at 1.3%–3.3%,[16,17] contrasting with the United States of America's 5% found in screened male smokers.[16,17] Globally, in 2019, there were 172 000 aortic aneurysm-related deaths (82.1% increase from 1990).[10]

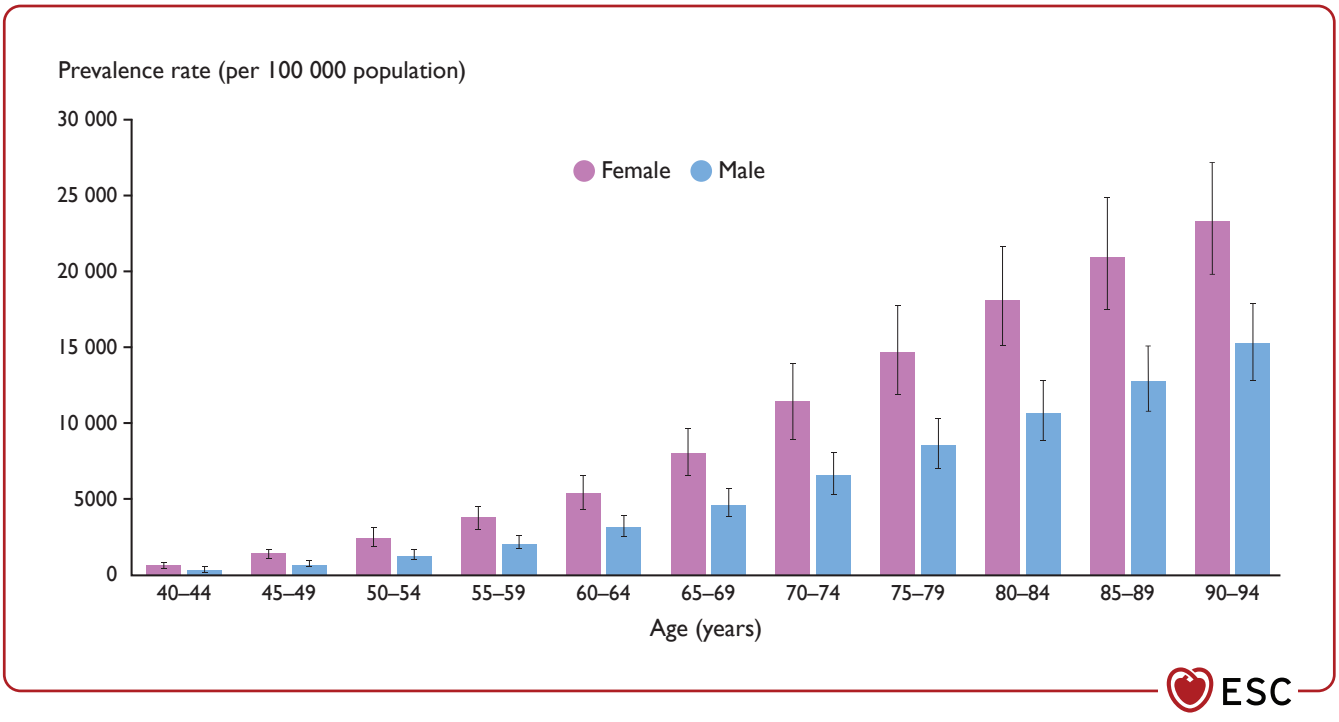

Figure 2 Estimated specific prevalence of peripheral arterial disease, by sex, in people aged 40 years and older. Adapted from[12] under the terms of the Open access Creative Commons CC-BY license.

4.2. Risk factors

Main PAAD risk factors are summarized in *Figure 3*. Traditional risk factors in tools like Framingham, Reynolds, Atherosclerotic Cardiovascular Disease (ASCVD) risk estimator Plus (United States of America), SCORE2 (Systematic Coronary Risk Evaluation 2, age 40–69 years), SCORE2-Diabetes (Systematic Coronary Risk Evaluation 2 - diabetes), and SCORE2-OP (Systematic Coronary Risk Evaluation 2–Older Persons) (Europe)[18] also contribute to PAAD's pathophysiology and development. More details are available in Supplementary data online, *Section 1.1*, and the *2021 ESC Guidelines on CV disease prevention in clinical practice*.[19]

Low-density lipoprotein cholesterol (LDL-C) is a pivotal factor in atherosclerosis,[19] with diabetes and tobacco exposure significantly

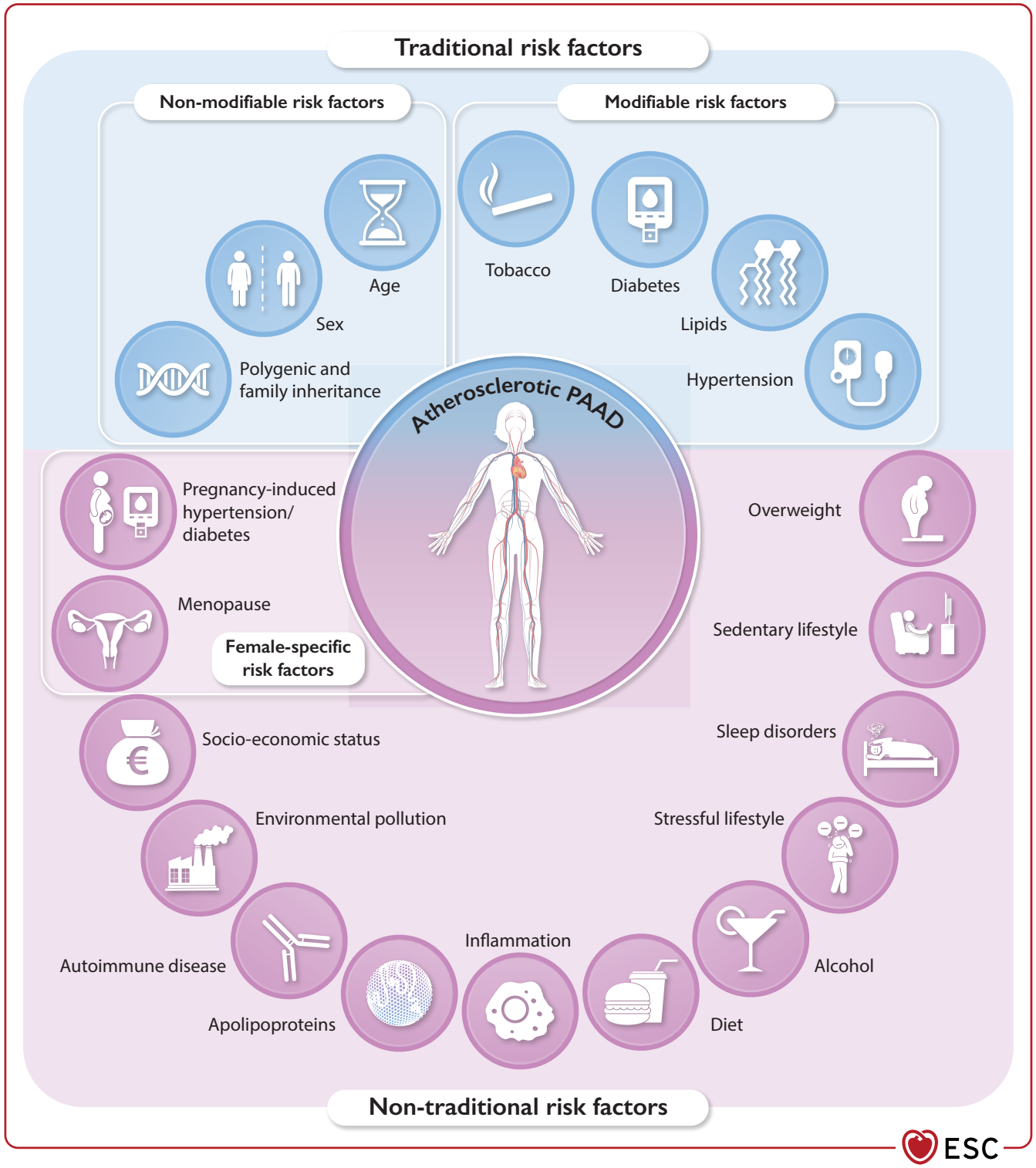

Figure 3 Main risk factors associated with atherosclerosis in peripheral arterial and aortic diseases. PAAD, peripheral arterial and aortic diseases.

amplifying PAD risk by 2–4 times each.[20] Both men and women face a similar risk of PAD, but women have distinct risk factors (*Figure 3*).[21] Hypertension and male sex are major risk factors for AAA, whereas diabetes mellitus lowers its incidence by 25%.[22–24] Thoracic aortic aneurysm (TAA) or dissection share atherosclerotic risk factors, yet monogenic or polygenic diseases like Marfan syndrome (MFS), more prevalent in younger individuals, also contribute.[24,25] Inflammation as a risk factor can be observed in PAAD[26] and the potential for inflammation to be a modifiable risk factor is indicated by research related to colchicine and the effects demonstrated by canakinumab (a monoclonal antibody that reduces inflammation by inhibiting interleukin-1 beta).[27,28]

5. Evaluation of peripheral arteries and aorta

To be consistent with existing literature, the term PAD is used to refer to lower-extremity atherosclerotic arterial disease.

5.1. Clinical history and examination, and laboratory assessment, in patients with peripheral arterial and aortic diseases

Clinical evaluation encompassing history (including family history), review of symptoms, and physical examination are the first steps in diagnosing and assessing patients with PAAD. Pulse palpation, femoral, carotid, and abdominal bruit auscultation, heart auscultation, and observation of the legs and feet need to be part of the vascular examination.

Clinical signs, beyond aiding diagnosis, offer prognostic insights. Carotid bruits double the risk of myocardial infarction (MI) and CV death,[29,30] while a brachial systolic blood pressure (SBP) difference of more than 15 mmHg raises CV death risk by 50%.[31] Hence, bilateral arm blood pressure (BP) measurement is recommended.[32] Lab assessments should include lipid profile (including lipoprotein[a] at least once in a lifetime),[33] fasting glycaemia, glycated haemoglobin (HbA1c), renal function, blood count, coagulation studies, liver function, electrolytes, and inflammatory markers (C-reactive protein [CRP] and erythrocyte sedimentation rate). Additional evaluations, like thyroid function tests, are advised as needed.

5.2. Functional and quality of life assessment in patients with peripheral arterial and aortic diseases

Patients with PAD have decreased walking performance and self-reported physical and mental health-related quality of life (HRQoL).[34–40] Muscle strength and balance are also impaired,[41–45] leading to a faster decline in functional (physical functioning) performance in both symptomatic and asymptomatic patients.[46,47] Depression is associated with greater impairment in functional performance.[48,49] Impaired functional status is related to decreased self-reported HRQoL,[50,51] and predicts further mobility loss and CV mortality.[52,53] Very poor HRQoL has been found in patients with chronic limb-threatening ischaemia (CLTI).[54]

Different questionnaires are available assessing different facets (functional, mental, and social status) of patient-reported outcome measures (PROMs).[34–36,38] The Short-form 36-item health questionnaire (SF-36) (including physical- and mental health-related items) is the most used generic questionnaire in PAD.[35,36,38] The Edinburgh Claudication Questionnaire is a modified version of the initially developed Rose questionnaire and has a sensitivity of 91% and a specificity of 99% in comparison with a physician-based diagnosis.[55,56] The Walking Impairment Questionnaire (WIQ), the Walking Estimated Limitation Calculated by History (WELCH), and the Vascular quality of life (VascuQoL) questionnaire are the most used PAD-specific questionnaires.[34–36,38]

Treadmill testing, using standardized criteria, is the gold standard to assess walking performance.[37,57–62] Patients are asked to walk until maximal pain levels, defining the maximal walking distance (MWD). Patients are also asked to indicate the point at which pain begins, defining the pain-free walking distance (PFWD). Constant-load protocols have poorer reliability than graded protocols.[60–64] Additionally, the six-minute walk test (6MWT) should be performed to assess functional walking performance.[62,65] For muscular lower-limb strength assessment,[66] isokinetic dynamometry has good test–retest reliability.[67] Alternatively, the Short physical performance battery (SPPB) test should be used.[62,64,68,69] The SPPB has good test–retest reliability.[64]

Few data exist on HRQoL, functional assessment, and exercise capacity in patients with aortic diseases.[70,71] Those with acute aortic dissection (AAD), as well as patients who had aortic valve or thoracic aortic surgery, may present with depression and anxiety, leading to mental health issues[72,73] that can also be assessed with the SF-36 questionnaire or the hospital anxiety and depression score (HADS).[72] Patients with MFS have reduced HRQoL and a significant decline over time in physical HRQoL.[74,75] Assessing HRQoL in aortic disease patients is crucial for understanding well-being, disease impact, and treatment effects. This involves PROMs, including surveys, symptom assessment, functional evaluation, psychological well-being (HADS), social and occupational function, and medication/treatment side effects. It also covers healthcare utilization and patient satisfaction, informing care and enhancing aortic disease management.

Recommendation Table 1 — Recommendations for clinical and laboratory, and for functional and quality of life, assessment in patients with peripheral arterial and aortic disease (see also Evidence Table 1)

Recommendations	Class[a]	Level[b]
When managing PAAD, it is recommended to adopt a comprehensive approach that addresses the entirety of the arterial circulation.[76]	I	B
To assess PAAD, it is recommended to perform thorough clinical, vascular, and CVRFs laboratory evaluation.[77]	I	C
Overall evaluation of functional (physical functioning) performance with objective tests should be considered in patients with symptomatic and asymptomatic chronic PAD.[57,61,63]	IIa	B
Overall evaluation of self-reported (i.e. by questionnaire) physical and mental/social HRQoL should be considered in patients with PAAD.[34–36,38,72]	IIa	B

CVRFs, cardiovascular risk factors; HRQoL, health-related quality of life; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease.
[a]Class of recommendation.
[b]Level of evidence.

5.3. Vascular examination of peripheral arteries

The ankle-brachial index (ABI)[78,79] is a low-cost, easy, and largely used tool, used both at rest or after exercise[80–84] for PAD diagnosis and surveillance (*Figure 4*). Both oscillometric and Doppler methods have shown good concordance.[78]

Resting ABI has a 68%–84% sensitivity and an 84%–99% specificity for PAD diagnosis (*Figure 4*).[79] An ABI ≤0.90 confirms PAD diagnosis.[79,85–87] For values >1.40, the term 'non-compressible arteries' should be used.

Ankle–brachial index >1.40, seen in arterial stiffness (diabetes, severe kidney failure, or advanced age), correlates with increased CV events and mortality risk.[88,89] For ABI >1.40, assessing resting toe–brachial index (TBI) is recommended.[79,90–95]

Toe–brachial index addresses medium-calibre artery rigidity[96] measuring pressure on the hallux, second, or third toe using laser Doppler probe or plethysmography.[97,98] Sensitivity and specificity for PAD diagnosis

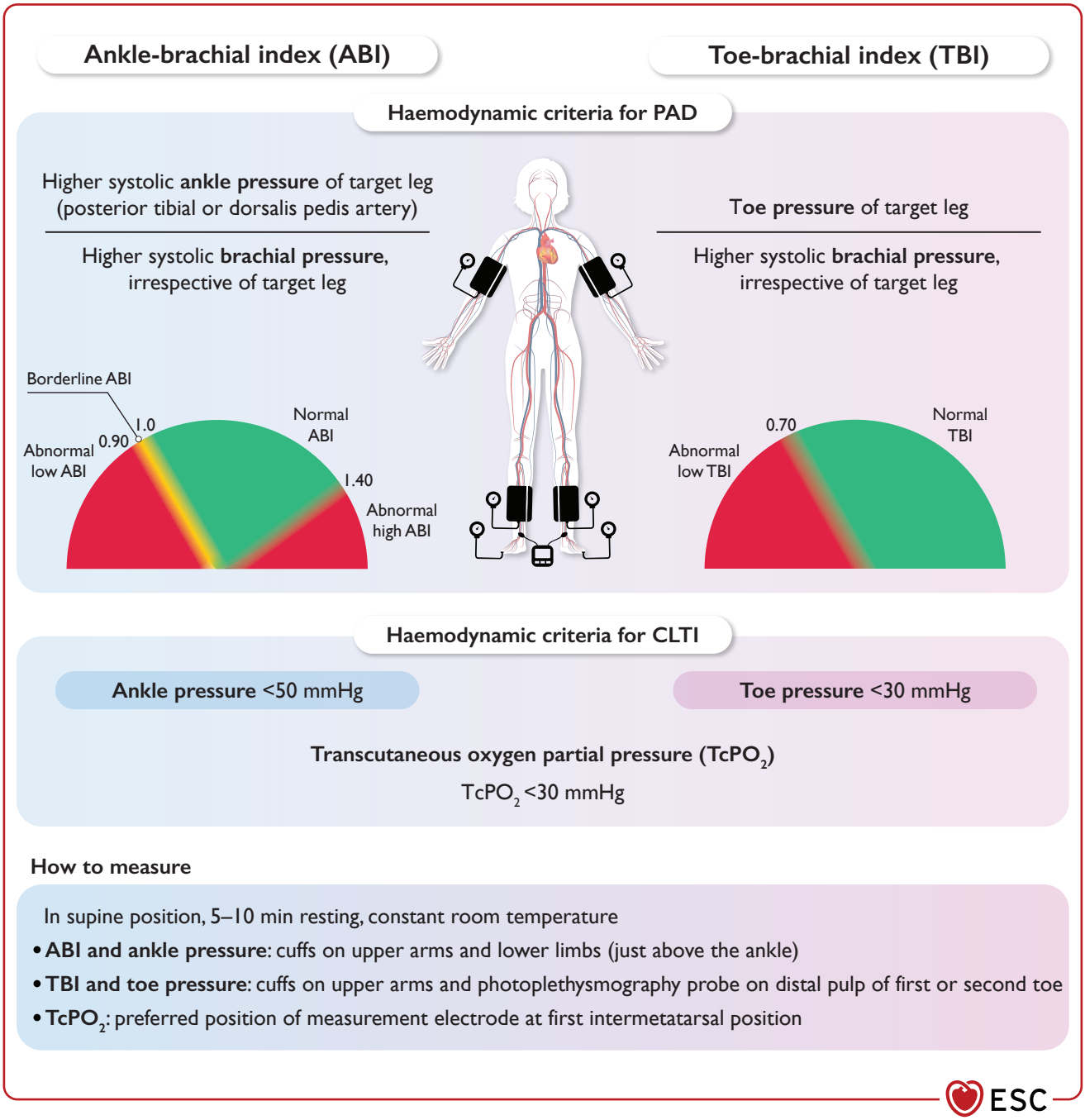

Figure 4 Haemodynamic assessment of peripheral arterial disease. ABI, ankle–brachial index; CLTI, chronic limb-threatening ischaemia; PAD, peripheral arterial disease; TBI, toe–brachial index; $TcPO_2$, transcutaneous oxygen pressure.

range from 45% to 100% and 17% to 100%, respectively.[91] The usual pathological threshold for TBI is ≤0.70 (*Figure 4*).[99]

Used within the Framingham risk score, ABI enables the upgrading of risk estimation in 'low-risk' women and men,[77,88] it allows CV risk assessment in diverse ethnic groups independently of risk factors,[77,89] and is inexpensive and minimally time-consuming.[100] Trained physicians have better reproducibility than inexperienced ones.[101,102]

In patients with exertional limb pain relieved by rest and a resting ABI >0.90, exercise testing with post-exercise ABI measurements or exercise oximetry has been proposed to diagnose lower-limb arterial stenoses.[103–105]

The post-exercise ABI is determined 1 min after the cessation of a standardized treadmill exercise.[106] The physician measures bilateral ankle BP, starting with the symptomatic leg, using the ankle artery used for the reference resting ABI measurement. Brachial SBP should simultaneously be measured to enable calculation of the post-exercise ABI.[104]

Discrepancies in PAD diagnosis exist between exercise criteria, such as a fall in absolute ankle BP >30 mmHg or a drop of >20% in the post-exercise ABI.[104] Recent studies identified numerous false positives in a healthy population when using a post-exercise ABI drop of >20% as the diagnostic threshold, as commonly proposed.[103]

Measurement of transcutaneous oxygen pressure ($TcPO_2$) is a means of evaluating tissue viability and is proposed as a diagnostic criterion of CLTI (*Figure 4*).[107] $TcPO_2$ is affected by local and general factors such as skin thickness, probe temperature, inflammation, and oedema,[108,109] resulting in misleading values.

Resting $TcPO_2$ >30 mmHg is a favourable indicator of wound healing;[110–112] however, resting $TcPO_2$ <10 mmHg is associated with bad prognosis for wound healing and amputation in CLTI patients treated with bone marrow-derived stem cells.[107] When performed at successive levels on an ischaemic limb, $TcPO_2$ measurement may help to determine amputation level.[113–115]

Exercise transcutaneous oximetry has also been proposed.[116,117] This seems of interest to detect proximal (buttock) claudication[105] or unsuspected exercise-induced hypoxaemia[118] in patients with intermittent claudication (IC).[117]

5.3.1. Duplex ultrasound

Duplex ultrasound (DUS) is a first step in the vascular work-up for PAD screening and diagnosis, allowing a dynamic, non-invasive, radiation- and contrast-free examination. It localizes vascular lesions and quantifies their extent and severity through velocity criteria.[119–121] In combination with ABI or TBI, DUS permits determining the haemodynamic relevance of arterial lesions[122,123] and estimation of ABI.[124] DUS has a sensitivity of 88% and specificity of 95% for >50% stenosis detection.[125] Post-exercise DUS can reveal borderline arterial lesions if initial findings are inconclusive.[122,126,127]

Duplex ultrasound distinguishes atherosclerotic (even subclinical disease) from non-atherosclerotic lesions, but its reliability relies on the sonographer's expertise.[122] Cross-sectional imaging is advisable for revascularization planning. ABI and DUS are recommended for PAD patient follow-up post-revascularization.[128]

More recent techniques, such as flow imaging, 3D echography, ultrafast ultrasound, and shear wave elastography, as well as the use of contrast-enhanced ultrasound (CEUS), could further improve DUS performance.[129]

5.3.2. Digital subtraction angiography, computed tomography angiography, and magnetic resonance angiography

Detailed information about these techniques can be found in the Supplementary data online, *Section 1.2* (*Table S1*). Digital subtraction angiography (DSA) remains mostly limited to revascularization procedures. Computed tomography angiography (CTA) offers better spatial resolution than magnetic resonance angiography (MRA) and better calcification visualization; however, it can also overestimate stenosis severity due to the blooming effect. MRA allows arterial wall and lumen assessment as well as tissue and organ perfusion distal to or surrounding the explored arterial territory.

Recommendation Table 2 — Recommendations for diagnostic tests in patients with peripheral arterial disease

Recommendations	Class[a]	Level[b]
Measurement of the ABI is recommended as the first-line non-invasive test for screening and diagnosis of PAD, using an ABI ≤0.90 as a diagnostic criterion.[79,90,130,131]	I	B
In the case of non-compressible ankle arteries or ABI >1.40, additional methods such as TP, TBI or Doppler waveform analysis are recommended.[90,91,124,132,133]	I	B

ABI, ankle–brachial index; PAD, peripheral arterial disease; TBI, toe–brachial index; TP, toe pressure.
[a]Class of recommendation.
[b]Level of evidence.

5.4. Evaluation of the aorta

The aorta can be divided into different anatomical regions (from proximal to distal) for reporting purposes. The main anatomical aortic regions are the aortic root, ascending aorta, aortic arch, descending thoracic aorta (DTA), abdominal aorta (AA), infrarenal aorta, and the iliac arteries (*Figure 5*).[134,135]

5.4.1. Aortic measurements

The main imaging techniques used for aortic evaluation are illustrated in *Table 5*.

Evaluating aortic dilation and progression depends on standardized measurements. In echocardiography, aortic diameters should be measured using the leading-to-leading edge method during end-diastole (as systole sees about a 2 mm aortic expansion) in all segments (*Figure 6*).[137,138]

Most studies supporting prophylactic surgery have used this approach. Furthermore, better agreement exists between echo's leading-to-leading edge and cardiovascular computed tomography (CCT)/cardiovascular magnetic resonance (CMR)'s inner-to-inner edge during end-diastole.[137,139,140] However, when the aortic wall thickens (e.g. atheroma, thrombus, intramural haematoma [IMH], or aortitis) or in cases of aortic dissection (AD), also report the outer-to-outer diameter (*Figure 6*).

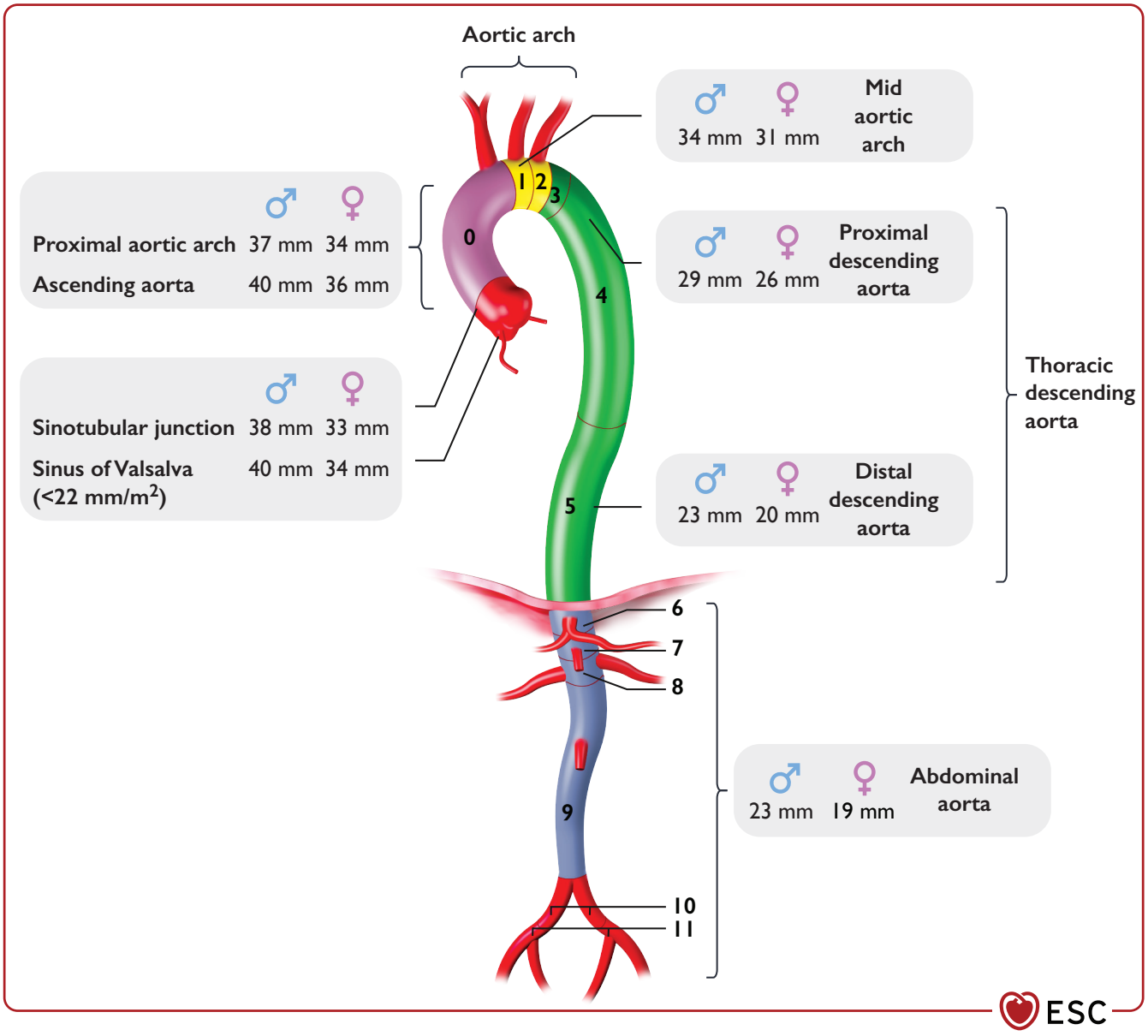

Figure 5 Anatomy and aortic segments and upper normal values for aortic dimensions. Numbers represent the 11 aortic segments based on the Society for Vascular Surgery/Society of Thoracic Surgeons (SVS/STS) classification for surgical and endovascular purposes.[136] Z-scores can be calculated for aortic root and ascending aorta. Calculation of z-scores can be performed following these links: https://www.marfan.fr/accueil/z-score-calculus/ or https://marfan.org/dx/z-score-adults.

Table 5 Main aortic imaging techniques

	TTE/DUS	TOE	CCT	CMR
Availability	++++	+++	++	+
Cost	+	++	+++	++++
Time requirement	+	+++	+++	++++
Radiation	0	0	+++	0
Spatial resolution	1 mm	1 mm	0.6 mm	1–2 mm
Temporal resolution	20 msec	20 msec	80 msec	30 msec
Nephrotoxicity	0	0	+++	+
Accuracy	++	++++	++++	++++
Serial examination	++++	++	++	++++
Aortic wall visualization	++	+++	++++	++++
Aortic valve function	+++	++++	+	++++
RV/LV function	+++	+++	+++[a]	++++
Aortic root assessment	+++	+++	++++	++++
Aortic arch assessment	++	+++	++++	++++
Thoracic aorta assessment	+	++	++++	++++
Abdominal aorta assessment	+++	-	++++	++++

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; LV, left ventricle; RV right ventricle; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography.
[a]CCT can be used to evaluate left and right ventricular function only if retrospective gating is used.

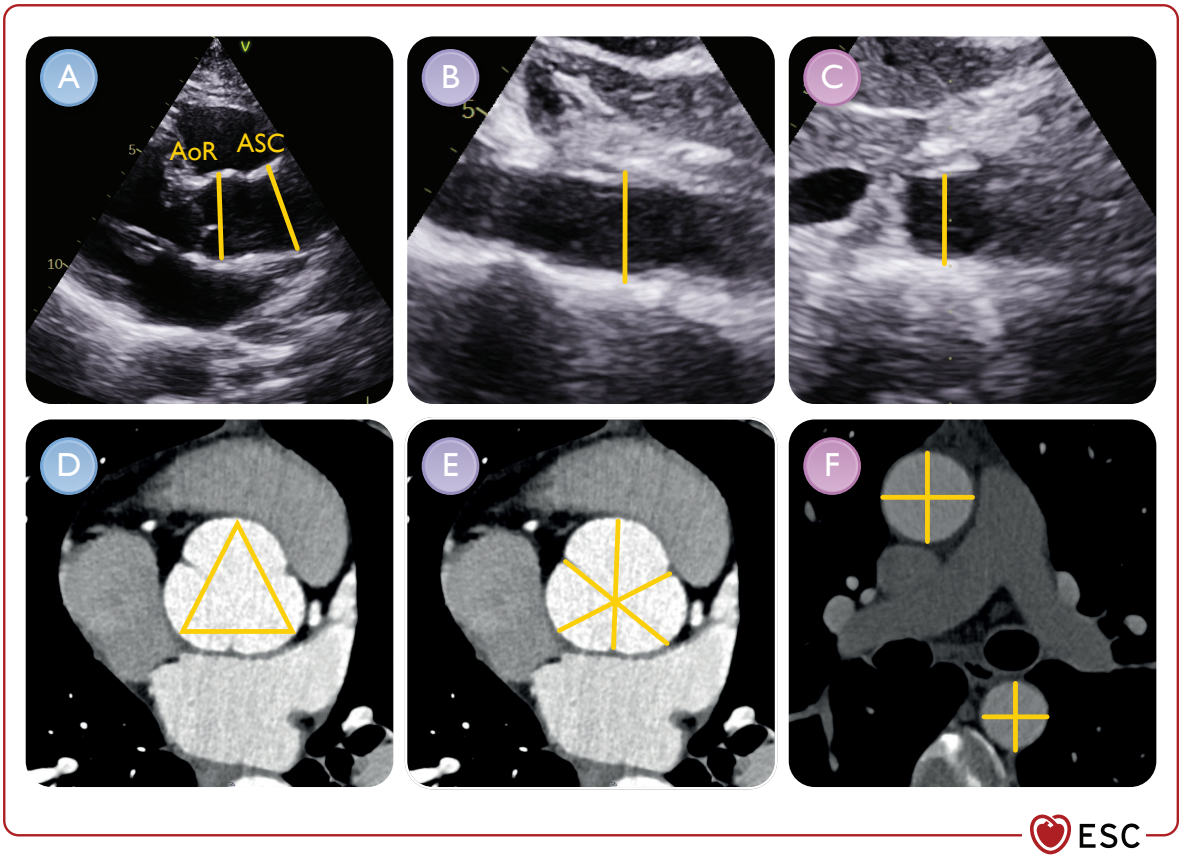

Figure 6 Conventional measurements of the aorta at different levels by echocardiography or duplex ultrasound (*A*, *B*, *C*), cardiovascular computed tomography or cardiovascular magnetic resonance (*D*, *E*, *F*). (*A*) Echocardiographic measurements of the aortic root and ascending aorta using the leading-to-leading edge methodology. (*B*) The outer-to-outer convention in the abdominal aorta in cases with aortic wall disease in a longitudinal view. This method can be used in a non-circular section as an alternative. (*C*) The outer-to-outer antero-posterior diameter of the abdominal aorta in a cross-sectional view. Evaluation of the aortic root using the cusp-to-cusp diameter (*D*) and the cusp-to-commissure convention (*E*); (*F*) measurement of the ascending aorta and the descending aorta with the double-oblique technique. AoR, aortic root; ASC, proximal ascending aorta.

Given the high incidence of atherosclerotic plaques/thrombi in the AA, the outer-to-outer convention should be preferred (also presenting the best agreement with CCT and CMR) (*Figure 6*).[141,142]

Regarding CCT and CMR, measurements must be performed using the inner-to-inner edge method (*Figure 6*) in end-diastole (fewer motion artefacts).[137,143,144]

The aortic root is measured in the parasternal long axis by transthoracic echocardiography (TTE),[137,139,140,145] since the short axis underestimates the diameter due to possible plane obliquity. By CMR or CCT, the cusp-to-cusp diameter best correlates with echocardiography (*Figure 6*). A diameter difference >5 mm (among root diameters within the same imaging modality) indicates root asymmetry, frequent in bicuspid aortic valve (BAV) or genetic aortopathies, which is important to be determined since it generates underestimations.[146] While 3D echocardiography is a potential surveillance alternative in these cases (especially if CMR/CCT is limited for serial follow-up), validation studies are lacking.[147]

In end-diastole, measure the ascending aorta by moving the transducer 1–2 intercostal spaces up in the parasternal long axis. Echocardiography provides information on aortic arch or DTA enlargement, but diagnostic certainty (precise measurement of the diameters) is lacking. CCT or CMR uses the double-oblique technique to measure aortic diameters, reporting antero-posterior and perpendicular dimensions for accurate assessment.[148] It is recommended to report aortic measurements by specific segments based on anatomical landmarks and to relate the largest diameter to a nearby anatomical structure for reference.

Changes in aortic diameter require a ≥3 mm increase in echocardiography, which should be confirmed with CCT/CMR and compared with baseline measurements. For accurate assessment, stick to the same imaging technique, centre, methodology, and side-by-side comparisons.[137,140]

5.4.2. Normal aortic values

When evaluating aortic dimensions and clinical relevance, consider factors like aortic region, anthropometric measurements, patient history, and underlying medical conditions. Factors influencing aortic and peripheral artery size in the normal population include age, sex, ethnicity, body surface area (BSA), and, particularly, height.[149]

Body surface area is the most used method to normalize aortic dimensions based on an individual's body size, thus an ascending thoracic aorta >22 mm/m^2 or a DTA >16 mm/m^2 is considered aortic dilatation.[150–152] However, extremes of low or high body weight pose limitations. In such cases, surgical thresholds may involve indexing aortic diameter by height (an aorta height index >32.1 mm/m is associated with a 12% yearly risk of aortic adverse events [AAE]),[153] aortic cross-sectional area to patient height (a ratio ≥10 cm^2/m implies reduced long-term survival),[154] or aortic length (from the aortic annulus to the innominate artery, considering a length >11 cm a threshold for surgery).[155]

To correlate measured diameter with the expected one based on age, sex, and body surface, use nomograms or z-score calculation formulas, especially in heritable thoracic aortic disease (HTAD). Supplementary data online, *Figure S1* and *Table S2*, presents nomograms developed for echocardiography, applicable also to CCT and CMR.[156,157] Calculation of z-scores can be performed following these links: https://www.marfan.fr/accueil/z-score-calculus/ or https://marfan.org/dx/z-score-adults/; reference values used for their estimation may vary depending on age and other factors. However, z-scores are limited by the fact that not all ethnic groups are equally represented (mostly white) and over- or underweight can lead to an over- or underestimation.[158]

Moreover, with ageing and loss of elastic properties, the aorta tends to enlarge. Aortic growth in adults is about 0.9 mm per 10 years in males and 0.7 mm per 10 years in females, which may be influenced by BP, physical activity, and genetic factors.

Recommendation Table 3 — Recommendations for imaging of the aorta (see also Evidence Table 2)

Recommendations	Class[a]	Level[b]
It is recommended that aortic diameters are measured at pre-specified anatomical landmarks, and the largest diameter of the section be perpendicular to the longitudinal axis.[134,135]	I	C
It is recommended in cases of serial imaging of the aorta over time to use the same imaging modality with the same measurement method.[159]	I	C
It is recommended to consider renal function, pregnancy, age, and history of allergy to contrast media to select the optimal imaging modality with minimal radiation exposure and lowest iatrogenic risk, except for emergency cases.[159–161]	I	C
Indexing aortic diameters to BSA, along with the use of nomograms, z-scores, or other indexing methods, should be considered for more accurate assessment of aortic size, especially for body sizes at the lower end of the normal distribution.[156–158]	IIa	B

BSA, body surface area.
[a]Class of recommendation.
[b]Level of evidence.

5.4.3. Chest X-ray and electrocardiogram

Chest X-ray obtained for other indications in asymptomatic patients or in cases of acute aortic syndrome (AAS) suspicion may detect abnormalities of aortic size/contour that need to be confirmed by another imaging technique. It presents limited sensitivity (64%) and specificity (86%) in the diagnosis of aortic diseases;[162] thus, a normal chest X-ray may not rule out the diagnosis of AAS.[162–164] On the contrary, chest X-ray may identify other causes of chest pain (e.g. pleural effusion or pneumothorax).

Electrocardiogram (ECG) might be useful to rule out other causes of chest pain (e.g. MI) or AAS complications (coronary occlusion/dissection) but it is not useful for AAS diagnosis.

5.4.4. Echocardiography

It is considered the first-line imaging technique in the evaluation of aortic disease, assessing all echocardiographic windows and the aortic valve. It provides key anatomic information (i.e. dilatation, atherosclerotic lesions, or dissection) for the ascending aorta, arch, and AA; however, it is not useful to assess the exact diameters of the aortic arch and DTA (requiring confirmation with CCT/CMR). Also, the distal ascending aorta and proximal arch (blind spot) are inadequately visualized due to left mainstem bronchus interposition.

Transthoracic echocardiography can identify AAS complications (e.g. aortic regurgitation, tamponade, or wall motion abnormalities), but its diagnostic accuracy for AAS is limited (sensitivity: 78%–100% for type A, 31%–55% for type B). Contrast enhancement improves diagnosis.[165]

Transoesophageal echocardiography (TOE) is highly accurate (sensitivity: up to 99%, specificity: 89% for AAS), except with absolute contraindications like oesophageal issues, bleeding, recent gastro-oesophageal surgery, or respiratory distress. TOE is convenient for bedside and intraoperative use but less suitable for long-term surveillance, which requires evaluation with CCT/CMR.

Recommendation Table 4 — Recommendations for thoracic aortic measurements

Recommendations	Class[a]	Level[b]
TTE is recommended as the first-line imaging technique in evaluating thoracic aortic diseases.[159,165]	I	B
It is recommended to report aortic diameters using the leading-to-leading edge convention in end-diastole by echocardiography.[137,139,140,159]	I	C
It is recommended to report aortic diameters using the inner-to-inner edge convention in end-diastole by CCT or CMR.[137,143,144,159]	I	C
It is recommended to report aortic diameters from images obtained with the double-oblique technique (not axial images) by CCT or CMR.[148]	I	C
ECG-triggered CCT is recommended for comprehensive diagnosis, follow-up, and pre-invasive treatment assessment of the entire aorta, particularly the root and ascending aorta.[159]	I	C
CMR is recommended for diagnosis and follow-up of thoracic aortic diseases, especially when chronic follow-up is required.[166–168]	I	C
The aortic root should be measured using the cusp-to-cusp distance. Also, the presence of asymmetry (>5 mm) among distances should be reported.[137,146]	IIa	C
If an increase of ≥3 mm per year in aortic diameters by TTE is observed, confirmation by CCT/CMR should be considered.[137,159]	IIa	C
Chest X-ray may be considered in cases of low clinical probability of AAS; however, a negative exploration should not delay dedicated aortic imaging in high-risk patients.[162–164]	IIb	C

AAS, acute aortic syndrome; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; ECG, electrocardiogram; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.

5.4.5. Duplex ultrasound imaging of the abdominal aorta

After scanning both transversally and longitudinally, the antero-posterior (AP) diameter in a cross-sectional view of the AA should be measured. Ensure the DUS beam is perpendicular to the AA axis, forming a circular vessel section. If the AA is sinuous or dilated, achieving equal AP and transverse diameters may be challenging. In such instances, calculate the mean ellipse diameter or measure the AA diameter in a clear longitudinal view with a perpendicular diameter (*Figure 6*).[122] The outer-to-outer (*Figure 6*) method is the one recommended by the American Institute of Ultrasound in Medicine, the American College of Cardiology/American Heart Association (ACC/AHA), and the European Society of Cardiology (ESC), since it is more reliable in cases of atherosclerotic plaque or intravascular thrombus and best correlates with CCT and CMR. However, the most effective methodology is under debate and further studies are needed to determine the best convention.[169]

Normal diameters of the AA are reported in *Figure 5* and Supplementary data online, *Section 1.3*.

5.4.6. Cardiovascular computed tomography

Cardiovascular computed tomography, due to its quick acquisition, wide availability, high reproducibility, and suitability for emergency departments, is the primary imaging method for aortic disease diagnosis, prognosis, and therapy planning (sensitivity 100%, specificity 98% for AAS).[170–172] 'Double or triple rule-out' protocols concurrently assess the aorta, pulmonary, and coronary arteries.[173,174]

Electrocardiogram triggering is crucial to prevent motion artefacts (especially in the aortic root and ascending aorta), which can distort measurements or resemble dissection flaps, facilitating coronary artery assessment. The standard protocol comprises non-enhanced scans (for calcification, IMH, or surgical material), contrast-enhanced CCT angiography, and a late scan (to visualize contrast leakage or aortic wall late enhancement suggestive of inflammation or infection).[175]

Iodinated contrast agents carry potential allergic reactions and post-contrast acute kidney injury (PC-AKI) risks.[176] In these cases, opt for contrast-free CCT for accurate aortic diameter measurement (also for CMR-intolerant patients). Moreover, excessive radiation caution is crucial, particularly in young females, when performing CCT for monitoring chronic aortic diseases.[177]

5.4.7. Cardiovascular magnetic resonance

Cardiovascular magnetic resonance comprehensively evaluates the aorta, including shape, diameter, tissue characteristics (inflammation, infection, atheroma, bleeding),[178] lesion extent, side branches, adjacent structures, and mural thrombus. It assesses ventricular and valve function, quantifies flow, and employs cine steady-state free precession (SSFP) or ECG-gated angio-CMR for the aortic root, while non-gated sequences suffice for the rest. Recently, 4D flow sequences[179] have been developed to evaluate complex intravascular flows,[180,181] complex flow parameters (wall shear stress, pulse wave velocity, or kinetic energy), or flow quantification at different levels in one unique acquisition (useful in AD or congenital diseases).[182,183]

Cardiovascular magnetic resonance obviates ionizing radiation and iodinated contrast (3D contrast CMR), making it ideal for young patients, women, and pregnancy. Caution is warranted, especially with non-macrocyclic gadolinium, for estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 (Supplementary data online, *Section 1.2*). CMR is increasingly used in patients with intracardiac devices (pacemakers/implantable cardioverter defibrillators, CMR- and non-CMR-compatible devices) with proper monitoring, but not for those with cochlear implants or intracranial clips.[184,185]

In the acute setting, CMR use is limited because of low availability, difficulties in monitoring unstable patients, and longer acquisition times.[166,186]

5.4.8. Positron emission tomography

Positron emission tomography (PET) usually uses ^{18}F-fluorodeoxyglucose (FDG), allowing non-invasive assessments of metabolic activity

(inflammation/infection) and treatment response.[187,188] Although different tracers have been tested to identify calcification, fibrosis and/or thrombus formation, most PET studies have focused on vasculitis.

The relationship between FDG-PET images and AAA progression is controversial. However, fluorine-18–sodium fluoride (^{18}F–NaF) PET-computed tomography (PET-CT), a marker of active vascular calcification and high-risk plaques, has shown a correlation between increased tracer uptake, AAA growth, and CV events.[189]

PET-CT has shown better diagnostic accuracy in identifying lesions and detecting graft infection or infectious aortic diseases.[190–193] High radiation exposure, high costs, and limited availability are the main limitations of PET.

5.4.9. Intravascular ultrasound

Intravascular ultrasound (IVUS) provides high-resolution imaging for artery and vein diseases, aiding complex aortic disease management by distinguishing true and false lumens and guiding stent placement. It is operator-dependent, costly, and less accessible, but seems to provide better measurements for acute aortic syndromes.[194]

5.4.10. Digital subtraction aortography

Non-invasive imaging modalities have replaced DSA in first-line diagnostic testing, both in suspected AAS or known chronic AD; however, DSA might be useful if findings in non-invasive techniques are ambiguous or incomplete. It is primarily used for the percutaneous treatment of CAD, aortic visceral branches, or for monitoring thoracic endovascular aortic aneurysm repair (TEVAR/EVAR) implantation.

6. Screening for carotid, peripheral arterial, and aortic diseases

6.1. Screening for carotid and peripheral arterial diseases

6.1.1. Lower-extremity peripheral arterial disease

Due to elevated CV risk in chronic PAD, early diagnosis, prevention, and robust cardiovascular risk factor (CVRF) control are essential, even in asymptomatic cases. 'Intermediary CV risk' individuals may be reclassified as 'high or very high risk', prompting adapted prevention. ABI is the preferred first-line test for asymptomatic individuals aged ≥65 years,[14,195] especially women.[196] Screening might also be beneficial at a younger age in case of CVRFs, but data are still lacking. Clinical examination, functional status, and walking capacity assessment are recommended to detect 'masked PAD'.[77]

In diabetes, early PAD (and foot neuropathy) diagnosis is crucial. Effective CVRF management and treatment can prevent CV disease, foot wounds, and amputation.[197] In patients with diabetes and normal resting ABI, TBI measurement should be considered.

The prevalence of popliteal aneurysms (PAs) is high in patients with AAA and subaneurysmal aortic dilatation, warranting screening. PAs are correlated with iliac and femoral artery diameters.[76] In patients needing transfemoral access, screening for iliofemoral artery disease may be considered.[198]

6.1.2. Carotid artery stenosis

Due to the low prevalence of ≥70% asymptomatic carotid artery stenosis (CS) in the general population (0%–3.1%), widespread screening is not recommended since it does not reduce stroke risk and might lead to inappropriate stress and invasive procedures.[199,200] Conversely, screening for significant CS in a highly selected population might be cost-effective, especially if prevalence is ≥20% (*Table 6*).[201] When the degree of asymptomatic CS is ≥70%, the 5 year ipsilateral stroke risk is significantly increased (14.6%) and revascularization may be beneficial.[202] Selective screening aims to prevent CV events, rather than identifying candidates for an intervention.[203]

Table 6 High-risk populations for carotid artery stenosis

Population	Prevalence of carotid stenosis (%)
>60 years + CVRFs (hypertension, CAD, current smoking, first-degree family history of stroke)[210]	Two CVRFs: 14% Three CVRFs: 16% Four CVRFs: 67%
Hypertension + cardiac disease[211]	22%
HD[212]	• In HD patients, prevalence of carotid stenosis is high, and is associated with high peri-operative and long-term stroke or death rates • Carotid stenosis is a predictor of death in patients with long-term dialysis and aged ≥70 years at time of surgery • Lower risk if previous renal transplant.
PAD[213]	23.2%
Severe CAD (before CABG)	• Almost 20%[214] • Carotid bruit and T2DM: increased predictive value[215] • Carotid stenosis = risk factors for peri-operative stroke.[215]
Carotid bruit[216]	31%
Previous neck irradiation[217]	21.7% (70%–99% stenosis)

CABG, coronary artery bypass grafting; CAD, coronary artery disease; CVRFs, cardiovascular risk factors; HD, haemodialysis; PAD, peripheral arterial disease; T2DM, type 2 diabetes mellitus.

6.1.3. Multisite artery disease

Multisite artery disease (MAD) is defined as the presence of atherosclerosis in two or more vascular beds.[204] This is a common condition in patients with atherosclerotic diseases. Although associated with worse clinical outcomes, screening for asymptomatic disease in additional vascular sites did not seem to improve outcomes.[77] More recently, screening for coronary calcifications (coronary artery calcium [CAC] score) and screening for carotid and femoral plaques have

been shown to be of potential assistance in CV risk reclassification of 'presumed moderate-risk patients' into a higher-risk category, leading to more aggressive prevention strategies.[205–209]

Recommendation Table 5 — Recommendations for peripheral arterial disease screening (see also Evidence Table 3)

Recommendations	Class[a]	Level[b]
In patients with diabetes or chronic kidney disease, and normal resting ABI, TBI measurement should be considered.	IIa	B
In patients ≥65 years of age with CVRFs, screening for PAD by ABI or TBI should be considered.[77,218,219]	IIa	C
In patients with AAA, femoro-popliteal aneurysm screening with DUS should be considered.[76]	IIa	C
In patients ≥65 years without CVRFs, screening for PAD by ABI or TBI may be considered.[220]	IIb	C
In patients needing intervention with transfemoral access, screening for iliofemoral artery disease may be considered.[198]	IIb	C
In patients with two or more CVRFs, screening for CS may be considered.[201,203,210]	IIb	C

AAA, abdominal aortic aneurysm; ABI, ankle–brachial index; CS, carotid artery stenosis; CVRFs, cardiovascular risk factors; DUS, duplex ultrasound; PAD, peripheral arterial disease; TBI, toe–brachial index.
[a]Class of recommendation.
[b]Level of evidence.

Recommendation Table 6 — Recommendations for abdominal aortic aneurysm screening

Recommendations	Class[a]	Level[b]
Screening for AAA with DUS:		
Is recommended in men aged ≥65 years with a history of smoking to reduce the risk of death from ruptured AAA.[221–224,234]	I	A
May be considered in men aged ≥75 years (irrespective of smoking history) or in women aged ≥75 years who are current smokers, hypertensive, or both.[227,228,235–237]	IIb	C
Family AAA screening with DUS:		
Is recommended for FDRs of patients with AAA aged ≥50, unless an acquired cause can be clearly identified.[231]	I	C
Opportunistic AAA screening with DUS:		
Should be considered in symptomatic/asymptomatic PAD patients.[233]	IIa	B
Should be considered in men aged ≥65 years and in women aged ≥75 years during TTE.[232]	IIa	B

AAA, abdominal aortic aneurysm; FDR, first-degree relative; DUS, duplex ultrasound; PAD, peripheral arterial disease; TTE, transthoracic echocardiography.
Smoking is defined as lifetime smoking of >100 cigarettes or equivalent. This threshold is used to distinguish between substantial exposure and occasional use.
[a]Class of recommendation.
[b]Level of evidence.

6.2. Screening for aortic diseases

6.2.1. Screening for abdominal aortic aneurysm

Abdominal aortic aneurysm screening by DUS is effective in reducing rupture-related mortality in populations with high AAA prevalence (especially male smokers aged ≥65 years).[221–224] However, no such effect has been found in a single large study in which AAA prevalence was low (current or former smoking women aged 65–74 years, or with a history of CAD).[225]

Screening for AAA by non-contrast computed tomography (CT) was not found to be effective over 5 years in males aged 65–74 years in a Danish trial.[226] Longer-term follow-up is planned, and as the technique involves ionizing radiation, no recommendation is made in relation to CT at present.

Screening may be considered in populations at intermediate risk, such as men aged >75 years, or women aged >75 years who are hypertensive, smokers, or both, since almost all women in a contemporary population-based study who had ruptured AAA and were aged >75 years were either smokers or hypertensive.[227,228]

Screening for AAA is recommended in first-degree relatives (FDRs) of patients with AAA (especially siblings), as they are at increased risk of AAA when >50 years of age.[229] The risk associated with family history is uncertain, but a population-based study estimated a relative risk of around 2.[230] Screening should be repeated periodically if initial assessment is reassuring and performed at a relatively young age.[231]

Opportunistic screening (during TTE) identified AAA in about 2% of subjects, thus it may be considered in high-prevalence populations (males ≥65 or women ≥75 years of age).[232] Additionally, opportunistic screening detects AAA in patients with symptomatic/asymptomatic PAD (with a 12% cumulative incidence in symptomatic PAD), making it worthwhile in this population.[233]

6.2.2. Screening for thoracic aortic aneurysm

Screening for TAA is described in detail in *Section 10.1* and *Section 10.2*.

7. Optimal medical treatment

Optimal medical treatment (OMT), including lifestyle measures and pharmacological treatment, is recommended for all patients with PAAD (*Figure 7*).

7.1. Lifestyle, exercise, patient education

Apart from genetic-related TAA, hypertension and ASCVD are the main causative factors for PAAD. As lifestyle factors are strongly related to ASCVD,[11] patients with PAAD should strive to maintain a healthy lifestyle. The *2021 ESC Guidelines on cardiovascular prevention*[19] give comprehensive guidance on risk factors for ASCVD and their treatment.

7.1.1. Diet

A Mediterranean diet rich in legumes, dietary fibre, nuts, fruits, and vegetables proves crucial and efficacious for primary and CV prevention in PAAD.[238] It has demonstrated notable reductions in cholesterol and BP,[239–247] and holds potential protective benefits against PAAD development.[248,249] In a large cohort with 17.5 years of follow-up, adherence to a Mediterranean diet was associated with reduced AAA risk in current and ex-smokers.[249,250] Malnutrition and metabolic disorders can complicate post-invasive procedure recovery and nutritional support may improve nutritional status and HRQoL.[251]

7.1.2. Physical activity

Few patients with chronic symptomatic PAD meet the physical activity guidelines[252] for reducing the risk of major adverse cardiac events (MACE).[253,254] Better ambulation, HRQoL, and vascular outcomes have been observed in patients meeting the physical activity time-intensity guidelines.[19,255] Regular physical activity is also relevant in patients with aortic diseases[70,71,256–259] and lowers resting heart rate and BP, thus decreasing the risk of aortic complications.[256,259] Few data exist on the practice of exercise and sports in patients with aortic diseases.[70,71,256–259] Recommendations should be individualized and based on risk stratification.[71]

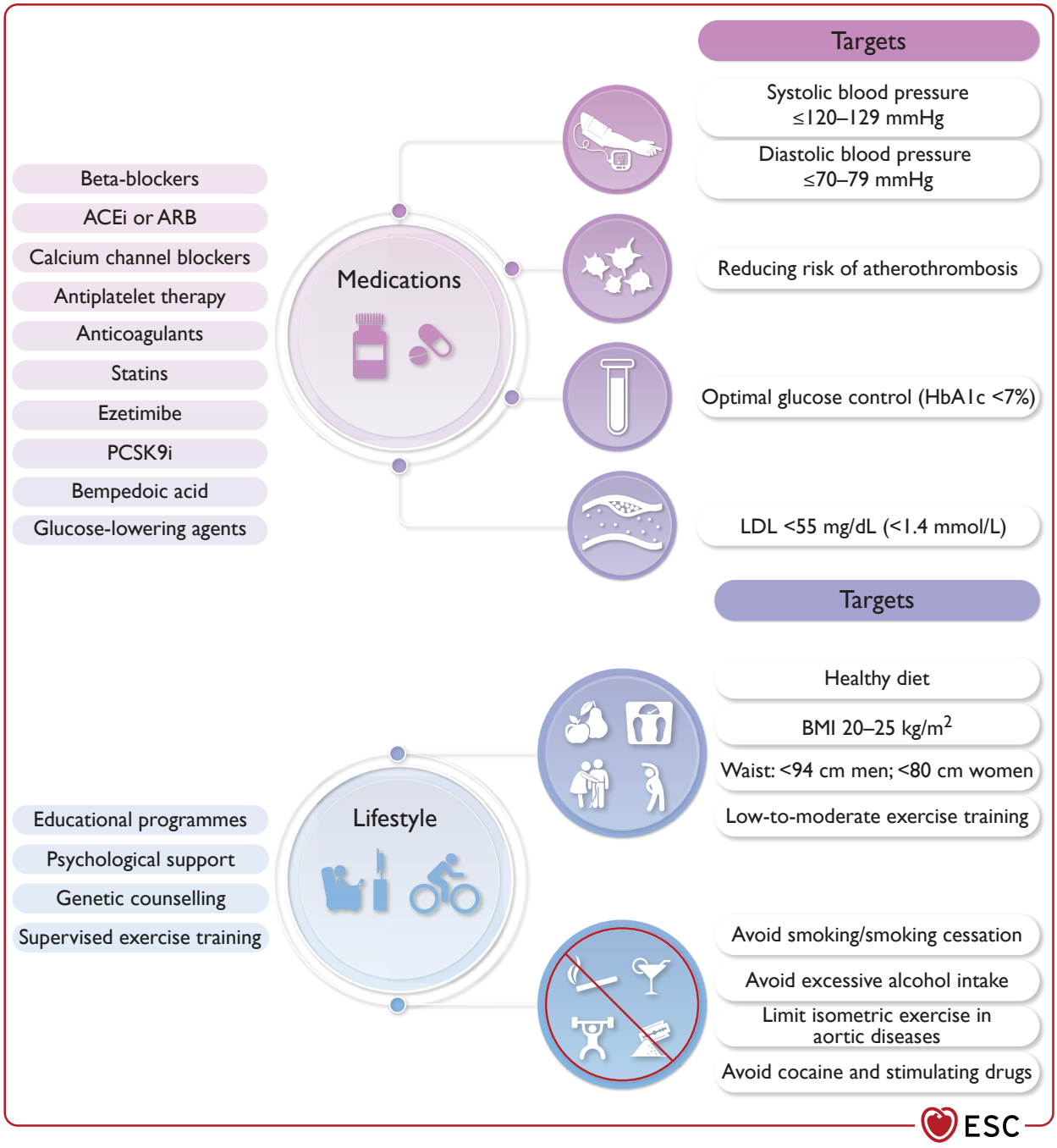

Figure 7 Cardiovascular risk modification and healthy lifestyle interventions and targets in patients with peripheral arterial and aortic diseases. ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; BMI, body mass index; LDL, low-density lipoprotein; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; HbA1c, glycated haemoglobin.

7.1.3. Smoking

Patients with PAAD who smoke should strongly be advised to quit (see Supplementary data online, *Section 1.1.5*). Complete smoking cessation and avoiding second-hand smoke or environmental particle air pollution are crucial in patients with PAAD to reduce the risk of death, AD, acute mesenteric ischaemia (AMI), AAA, and PAD.[119,260–267] Smokers should be offered structural follow-up support, including nicotine replacement therapy, varenicline, and bupropion, individually or in combination.[19,268,269] Smoking avoidance also includes cannabis, associated with premature ASCVD.[266]

Vaping and e-cigarette use has surged in the past decade, viewed by some as a healthier option than smoked tobacco, though long-term health effects remain unknown.[270] E-cigarettes may be considered as an aid to quit tobacco smoking, as a recent Cochrane review found that they increase quit rates as compared with nicotine replacement therapy,[271] but their use has been associated with adverse effects on CV, respiratory, immunological, and periodontal health compared with non-users, but with a milder impact than smoked cigarettes.[272–274] However, their use should be brief and preferably not concurrent with traditional cigarettes.[271,275]

The main limitation of the evidence base remains imprecision due to the small number of randomized controlled trials (RCTs), often with low event rates and follow-up limited to 2 years.

7.1.4. Patient education

While detailed explanations of CVRFs might not always inspire lifestyle changes,[276] providing plain language and visual aids is essential for patient understanding.[277] Structured programmes, incorporating psychological and behavioural aspects, are pivotal in fostering desired changes.[276] Engaging patients' families, friends, and support networks significantly contributes to perpetuating these changes (particularly in self-care),[276] and increases treatment compliance and self-efficacy, reducing hospitalization risk and enriching patient HRQoL.[278,279] When caregivers disconnect from healthcare professionals, they should be recognised to receive better support systems.[280,281] Psychosocial interventions are crucial to navigating complexities with resilience.[282]

Advocating active involvement, education, clear communication, and shared decision-making is key for achieving optimal patient outcomes.[276–283]

7.1.5. Risk scoring models in secondary prevention

Recent ESC CV prevention guidelines discuss risk models for developing vascular disease in healthy individuals and ASCVD patients.[19] Several registries enabling risk prediction in ASCVD have been developed: REACH (The REduction of Atherothrombosis for Continued Health)[284] and SMART (Secondary Manifestation of ARTerial disease)[285] which use clinical parameters such as medical history, SBP, and common biomarkers. Addition of carotid ultrasound did not improve the model.[286] A new algorithm combining the SMART and REACH models[287] enables calculation of lifetime risk and treatment effects. The SMART model has recently been updated and validated[288,289] with the SMART-2 algorithm. These tools are available online as clinical risk calculators (see www.u-preveotnt.com) and smartphone apps on the ESC website (https://www.escardio.org/Education/ESC-Prevention-of-CVD-Programme/Risk-assessment/SMART-Risk-Score).

Recommendation Table 7 — Recommendations for lifestyle, physical activity, and patient education (see also Evidence Table 4)

Recommendations	Class[a]	Level[b]
In patients with PAAD, cessation and abstinence from smoking of any kind is recommended to reduce the risk of AD, MI, death, and limb ischaemia.[119,261–267]	I	A
A healthy diet rich in legumes, dietary fibre, nuts, fruits, and vegetables, with a high flavonoid intake (Mediterranean diet), is recommended for CV disease prevention in patients with PAAD.[239–241,249,290–293]	I	A
Low- to moderate-intensity (or high if tolerated)[c] aerobic activities are recommended in patients with PAD to increase overall and pain-free walking distance.[37,294]	I	A
In patients with PAAD, behavioural counselling to promote healthy diet, smoking cessation, and physical activity is recommended to improve the CV risk profile.[241,249,253,295]	I	B
It is recommended to promote patient and caregivers' education and empowerment through tailored guidance on lifestyle adjustments and the importance of regular physical activity.[276,277,283]	I	C
In patients with PAAD, avoidance of exposure to second-hand smoke and air pollution should be considered.[261]	IIa	C
Physical exercise and sports activities should be considered in patients with aortic diseases based on prior risk stratification (based on the extent of the aneurysm, risk of dissection, and BP control).[71]	IIa	C
Use of web- or app-based secondary prevention risk calculators should be considered in the shared decision-making to improve patient adherence to treatment and lifestyle changes.[288,289]	IIa	C
E-cigarettes may be considered as an aid to quit tobacco smoking, but it is advisable to limit their use and avoid simultaneous use with conventional cigarettes due to unknown long-term effects.[119,271,296,297]	IIb	C

AD, aortic dissection; BP, blood pressure; CV, cardiovascular; MI, myocardial infarction; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease.
[a]Class of recommendation.
[b]Level of evidence.
[c]Low intensity refers to an exercising heart rate (HR) of 57%–63% HRmax or a rate of perceived exertion (RPE) on the Borg's scale of 9–11. Moderate intensity refers to an exercising heart rate of 64%–76% HRmax or RPE of 12–13. Vigorous intensity refers to an exercising heart rate of 77%–95% HRmax or RPE of 14–17.[298]

7.2. Principles of pharmacological medical therapy

7.2.1. Antithrombotic therapy

Antithrombotic therapy is crucial for patients with symptomatic PAAD at high CV risk. While trials are fewer than in CAD, recent evidence should guide practice. In the absence of specific indications for chronic oral anticoagulation (OAC) in concomitant CV disease, a single antiplatelet agent is the primary long-term treatment for patients with symptomatic PAAD. Combining it with another antiplatelet agent or low-dose anticoagulants depends on the patient's ischaemic and bleeding risk, as well as therapeutic paths (e.g. endovascular therapy). Recent guidelines[299] propose a tool for bleeding risk assessment in PAD patients (OAC^3 PAD score).

Antithrombotic strategy is detailed in *Sections 8* and *9* for each arterial territory.

7.2.2. Antihypertensive therapy

New 2024 ESC Guidelines on hypertension are currently published and should be reviewed for further details.[300] Patients with hypertension and PAAD are considered to have target organ damage and are at high CV risk.[300]

Different meta-analyses showed that systolic BP treatments reduce CV risk in all ages up to 85 years down to a level of 120–129 mmHg.[301,302] There is no need to increase the BP target in healthy patients up to the age of 85 years.[303,304] To reduce cardiovascular disease (CVD) risk, it is recommended that treated SBP values in most adults be targeted to 120–129 mmHg, provided the treatment is well tolerated. However, in cases where BP-lowering treatment is poorly tolerated and achieving an SBP of 120–129 mmHg is not possible, it is recommended to target an SBP level that is 'as low as reasonably achievable' (ALARA principle).[301,302,305] To avoid overtreatment, out-of-office BP measurements may be helpful when pursuing this target.

If on-treatment SBP is on target, but diastolic blood pressure (DBP) is ≥80 mmHg, intensified treatment may be considered to further reduce the CV risk.[306]

Because the CVD benefit of an on-treatment BP target of 120–129 mmHg may not generalize to some groups, setting personalized and more lenient BP targets (e.g. <140/90 mmHg) has to be considered in patients with pre-treatment orthostatic hypotension, age ≥85 years, clinically significant frailty at any age, or a limited lifespan (<3 years).[301]

Patients with both PAAD and hypertension face a high or very high CV risk. Antihypertensive medications such as diuretics, beta-blockers (BBs), calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin receptor blockers (ARBs) are all appropriate options for managing hypertension in PAAD. These agents can be used as monotherapy or in various combinations (excluding ARBs+ACEIs), considering individual patients' conditions. It is often necessary to implement combination therapy, preferably in the form of a single pill, to effectively achieve the recommended treatment goals. However, ACEIs or ARBs should be considered as first-line antihypertensive therapy to reduce CV events.[300,307–312]

Regardless of BP levels and in the absence of contraindications, ACEIs/ARBs may be considered in all patients with PAD to reduce cardiovascular events.[312,313] A meta-analysis suggests that antihypertensive treatment may improve mean walking distance in patients with PAD.[310]

Beta-blockers can be prescribed, if necessary, to patients with intermittent claudication, since they do not worsen walking capacity or limb events.[314] There is some evidence suggesting a higher amputation rate[315] or increased rate of re-intervention[316] in patients with CLTI treated with ACEIs, although in one smaller study no effect on limb-related outcomes was observed.[317] Thus, they remain a treatment option in hypertensive patients with PAD, especially in those with concomitant CAD.[318] BBs were not associated with worsened clinical outcomes in a retrospective study[319] on CLTI patients, but it seems prudent to avoid excessively low heart rates in these patients.

7.2.2.1. Renovascular hypertension

Angiotensin-converting enzyme inhibitors and ARBs effectively manage unilateral renal artery stenosis (RAS) by blocking the renin–angiotensin system, potentially reducing renal capillary perfusion pressure.[320–322] This transiently lowers glomerular filtration rate (GFR) and raises serum creatinine. For bilateral RAS, regular follow-up assessments of renal function and kidney perfusion are advised.

Angiotensin-converting enzyme inhibitors and ARBs additionally (combined with hydrochlorothiazide and/or CCBs if needed) contribute to CV risk reduction in patients with atherosclerotic disease and reduced eGFR.[307,323,324]

Recommendation Table 8 — Recommendations for antihypertensive therapy in patients with peripheral and aortic disease

Recommendations	Class[a]	Level[b]
In patients with PAAD and hypertension an SBP target towards 120–129 mmHg, if tolerated, is recommended.[301–305,325]	I	A
In unilateral RAS patients, it is recommended that antihypertensive medication include ACEIs/ARBs.[307,320–323]	I	B
In patients with PAAD and hypertension, ACEIs or ARBs should be considered as first-line antihypertensive therapy.[307,312]	IIa	B
In RAS-related hypertension, the combination of ACEIs/ARBs with diuretics and/or calcium channel blockers should be considered.[324]	IIa	B
An individualized, more lenient BP goal (e.g. <140/90 mmHg) should be considered in:[301] • Age ≥85 years • Residential care • Symptomatic orthostatic hypotension	IIa	C
An individualized, more lenient BP goal (e.g. <140/90 mmHg) may be considered in:[301] • Clinically severe frailty at any age • Limited life expectancy (<3 years)	IIb	C
In patients with bilateral RAS, antihypertensive medication including ACEIs/ARBs may be considered if close patient monitoring (renal function) is feasible.[321]	IIb	B
ACEIs/ARBs may be considered in all patients with PAD, regardless of BP levels, in the absence of contraindications.[312,313]	IIb	B

Continued

In cases where on-treatment SBP is at or below target (120–129 mmHg) but DBP is not at target (≥80 mmHg), intensifying BP-lowering treatment to achieve an on-treatment DBP of 70–79 mmHg may be considered to reduce CVD risk.[306]	IIb	C

ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; BP, blood pressure; CVD, cardiovascular disease; DBP, diastolic blood pressure; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease; RAS, renal artery stenosis; SBP, systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.

7.2.3. Lipid-lowering therapy

Patients with symptomatic PAAD are at very high CV risk but are usually inadequately managed compared with patients with CAD.[5,247,326–332] Both LDL-C reduction by ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended to obtain a reduction in CV death, MI, and stroke, and to improve walking distance.[242,333–336]

7.2.3.1. Statins

Statins demonstrate mortality and CV event reduction in RCTs for PAD, CS, and severe aortic arch plaques.[243–245] Even in advanced disease stages, they are linked to lower MACE and mortality.[246]

Statins significantly improve CV outcomes in patients with PAD, reducing major adverse limb events (MALE).[244,327–329,337,338] Meta-analyses show enhanced walking distances.[244,338,339]

For CS, statin pre-treatment lowers recurrent stroke risk post-transient ischaemic attack (TIA).[19,340–343] While lacking RCTs in renovascular or visceral artery disease, statins benefit cardiorenal events and post-RAS stenting prognosis.[344–346]

Mixed evidence suggests statins may mitigate AAA and TAA growth.[347–352] However, since most patients with AAA or TAA present with associated CVRFs, liberal use of lipid-lowering treatment[19] should be considered, using an individualized approach with shared decision-making and considering residual CV risk.[353] Pre-operative statin use links to increased 5 year survival after TEVAR.[19]

Statin use was associated with a mean AAA growth rate reduction and a lower rupture risk.[347–349,352,354]

Some evidence suggests that statins may reduce TAA growth rate and risk of rupture.[350,351,355]

No benefit on AAA or TAA growth rate was shown with fenofibrate therapy.[356,357]

7.2.3.2. Ezetimibe

Ezetimibe combined with statins benefits selected patients with PAAD, particularly when the target LDL-C level is not met.[335] In an IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) subanalysis, involving acute coronary syndrome (ACS) patients with PAD, ezetimibe consistently reduced CV risk, especially in high-risk subgroups.[247,331]

7.2.3.3. Proprotein convertase subtilisin/kexin type 9 inhibitors

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, in addition to statins, reduce CV events in symptomatic atherosclerotic disease patients with LDL-C ≥1.8 mmol/L.[336] Adding them to statins further reduces MACE and MALE risk in patients with PAD and improves walking distance;[333] however, their potential in TAA/AAA is an emerging area of research.[247]

Inclisiran, administered semi-annually, has proved a notable 26% MACE risk reduction in a pooled phase III analysis,[358] but its role in PAAD is not firmly established and ongoing RCTs including PAD participants (e.g. ClinicalTrials.gov NCT05030428) aim to provide insights.

7.2.3.4. Bempedoic acid

Bempedoic acid, acting upstream of statins in cholesterol metabolism, has been shown to reduce cholesterol levels by 17%–28%[359,360] and demonstrated a decrease in the incidence of MACE in statin-intolerant PAD patients.[361] However, its impact on aortic diseases and AAA still requires further research.

7.2.3.5. Hypertriglyceridaemia

Beyond LDL-C, evidence shows insulin resistance, elevated triglycerides, and remnant lipoproteins are associated with ASCVD, particularly in PAD.[362–365] However, in a meta-analysis and an RCT, fibrates showed no benefit over placebo in reducing MACE in patients with PAD for a composite outcome of non-fatal stroke, non-fatal MI, and vascular death.[366] Fibrates showed no benefit over placebo in reducing coronary and cerebrovascular events in patients with PAD in an RCT.[367] While the relationship between triglycerides and aortic diseases is complex and not fully understood, some evidence suggests that triglyceride levels may contribute to the development and progression of aortic diseases.

In contrast, icosapent ethyl (IPE) demonstrated a reduction in mortality and morbidity among individuals with hypertriglyceridaemia in the Reduction of Cardiovascular Events With Icosapent Ethyl–Intervention Trial (REDUCE-IT).[368] Its impact on patients with PAAD is unexplored,[369] although a small pilot RCT suggested an improved ABI in hyperglycaemic haemodialysis patients.[370]

Recommendation Table 9 — Recommendations for lipid-lowering therapy in patients with peripheral arterial and aortic diseases

Recommendations	Class[a]	Level[b]
In patients with atherosclerotic PAAD, lipid-lowering therapy is recommended.[242,334–336]	I	A
An ultimate LDL-C goal of <1.4 mmol/L (55 mg/dL) and a >50% reduction in LDL-C vs. baseline are recommended in patients with atherosclerotic PAAD.[19,242,246,300,335]	I	A
Statins are recommended in all patients with PAD.[328,329,337,371]	I	A
If the target LDL-C level is not achieved on maximally tolerated statins and ezetimibe, treatment with a PCSK9 inhibitor is recommended in patients with atherosclerotic PAAD, to achieve target values.[372,373]	I	A
If the target LDL-C level is not achieved, a combination of statins and ezetimibe is indicated in patients with atherosclerotic PAAD, to achieve the given target values.[247]	I	B
For statin-intolerant patients with atherosclerotic PAAD, at high CV risk, who do not achieve their LDL-C goal on ezetimibe, it is recommended to add bempedoic acid either alone or in combination with a PCSK9 inhibitor.[361]	I	B
Statins for the reduction of growth and rupture of AAA should be considered.[347–349,352,354]	IIa	B

Continued

Statins for the reduction of growth and rupture of TAA may be considered.[350,351,355]	IIb	B
In high-risk patients with PAAD and triglycerides >1.5 mmol/L despite lifestyle measures and statin therapy, icosapent ethyl 2 g b.i.d. may be considered in addition to a statin.[368]	IIb	B
Fibrates are not recommended for cholesterol lowering.[367]	III	B

AAA, abdominal aortic aneurysm; b.i.d., twice daily; CV, cardiovascular; LDL-C, low-density lipoprotein cholesterol; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease; PCSK9, proprotein convertase subtilisin/kexin type 9; TAA, thoracic aortic aneurysm.
[a]Class of recommendation.
[b]Level of evidence.

7.2.4. Diabetes and pre-diabetes conditions

Screening for diabetes or pre-diabetes is recommended in PAAD. Recent ESC Guidelines on diabetes and CVD[374] provide detailed diagnostic criteria and underscore the importance of diagnosing diabetes in ASCVD patients and vice versa. Both Type 1 (T1DM) and Type 2 (T2DM) diabetes mellitus imply significantly increased risk of PAD, carotid stenosis, and polyvascular disease, depending on disease duration and the status of other CVRFs. Diabetes is present in 30% of patients with IC and 50%–70% of those with CLTI.[375,376] Although the prevalence of PAD in patients with diabetes is 20%–30%, only half of them are symptomatic because of peripheral neuropathy with decreased pain sensitivity.[377] As already detailed in *Section 4*, diabetes implies reduced risk of TAA, AAA, or aortic dissection. However, patients with T2DM and PAAD are in the very high-risk group for stroke, MI, and CV death,[374] and for T1DM, an online risk prediction tool has recently been developed.[377–380]

For non-pregnant PAAD patients, aiming for an HbA1c level of <53 mmol/mol (7%) to avoid significant hypoglycaemia is appropriate. Consider a higher threshold (<69 mmol/mol [8.5%]) for limited life expectancy or when treatment risks outweigh benefits.[374]

In PAAD, it is recommended to aim for tight glycaemic control, preferably with agents with proven CV benefits such as sodium-glucose co-transporter-2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1RA), adding metformin and other glucose-lowering agents as necessary.[374,381–384]

The Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) trial and Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes (SUSTAIN-6) investigated subcutaneous GLP-1RAs liraglutide (≤1.8 mg/day) and semaglutide (0.5 or 1.0 mg/week), respectively, vs. placebo in T2DM patients with high CV risk. Overall, 12.7% of patients in LEADER and 14.0% in SUSTAIN-6 presented with PAD at baseline. Although non-statistically significant due to a lack of power, the effects on MACE showed a consistently beneficial trend in PAD: liraglutide (hazard ratio (HR), 0.77; 95% confidence interval (CI), 0.58–1.01) and semaglutide (HR, 0.61; 95% CI, 0.33–1.13).[381]

The (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME) investigated the SGLT2i empagliflozin (10 mg or 25 mg per day) vs. placebo in patients with T2DM and high CV risk. Overall, 20.8% of patients presented with PAD at baseline. In these patients, empagliflozin reduced CV death (HR, 0.57; 95% CI, 0.37–0.88) and all-cause mortality (HR, 0.62; 95% CI, 0.44–0.88), and there was a non-significant reduction in limb amputation: 5.5% with empagliflozin vs. 6.3% with placebo (HR, 0.84; 95% CI, 0.54–1.32).[382] In the Canagliflozin Cardiovascular Assessment Study (CANVAS)[385] investigating canagliflozin, there was an increased risk of amputation, but this was not confirmed in the Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) trial investigating canagliflozin in patients with T2DM and chronic kidney disease (CKD).[386] Still, the use of other SLGT2is seems reasonable in PAD patients.

Patients with carotid stenosis were included in trials testing GLP-1RA and SGLT2i, but no analysis on this subpopulation was performed. A meta-analysis of eight trials investigating GLP-1RAs vs. placebo in patients with T2DM reported a reduction in all strokes (HR, 0.84; 95% CI, 0.75–0.93).[387] Among patients with T2DM and prior history of MI or non-fatal stroke, GLP-1RAs reduced the incidence of recurrent MACE (HR, 0.86; 95% CI, 0.8–0.92).[388] SGLT2is do not appear to reduce stroke in patients with T2DM, but patients with a stroke history experienced similar cardiorenal benefits as the rest of the population.[389]

Before the era of GLP-1RAs and SGLT2is, different studies (United Kingdom Prospective Diabetes Study [UKPDS] 34[390] and Hyperinsulinaemia: the Outcomes of its Metabolic Effects [HOME] trials[391]) showed that metformin reduced the risk of MALE and MACE in patients with PAD.[391,392] But a recent study with GLP-1RA dulaglutide found the same risk reduction in MACE between patients with and without baseline metformin, calling into question its add-on value.[384,393] However, there are studies suggesting that metformin may reduce AAA growth (see *Section 9.2.4*).

Recommendation Table 10 — Recommendations for the medical management of patients with peripheral arterial and aortic diseases and diabetes

Recommendations	Class[a]	Level[b]
It is recommended to apply tight glycaemic control (HbA1c <53 mmol/mol [7%]) to reduce microvascular complications in patients with PAAD.[374,394–397]	I	A
SGLT2i with proven CV benefit are recommended in patients with T2DM and PAAD to reduce CV events, independent of baseline or target HbA1c and concomitant glucose-lowering medication.[382,386,398–402]	I	A
GLP-1RAs with proven CV benefit are recommended in patients with T2DM and PAAD to reduce CV events, independent of baseline or target HbA1c and concomitant glucose-lowering medication.[381,403–407]	I	A
It is recommended to avoid hypoglycaemia in patients with PAAD.[374,408–412]	I	B
It is recommended to individualize HbA1c targets according to comorbidities, diabetes duration, and life expectancy.[408,411]	I	C
It is recommended to prioritize the use of glucose-lowering agents with proven CV benefits,[c,d] followed by agents with proven CV safety,[e] over agents without proven CV benefit or safety.[374]	I	C
If additional glucose control is needed, metformin should be considered in patients with T2DM and PAAD.[374,384,393]	IIa	B

CV, cardiovascular; GLP-1RAs, glucagon-like peptide-1 receptor agonists; HbA1c, glycated haemoglobin; PAAD, peripheral arterial and aortic diseases; SGLT2i, sodium-glucose co-transporter-2 inhibitors; T2DM, type 2 diabetes mellitus.
[a]Class of recommendation.
[b]Level of evidence.
[c]Empagliflozin, canagliflozin, dapagliflozin, sotagliflozin.
[d]Liraglutide, semaglutide subcutaneous, dulaglutide, efpeglenatide.
[e]Metformin, pioglitazone, dipeptidyl peptidase 4 (DPP-4) inhibitor (sitagliptin, alogliptin, linagliptin), glimepiride, gliclazide, insulin glargine, insulin degludec, ertugliflozin, lixisenatide, exenatide (extended release), oral semaglutide.

7.2.5. Other pharmacological therapy

Increased attention is focused on inflammation in ASCVD,[413] supported by the Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS),[414] which showed that canakinumab, a monoclonal antibody targeting interleukin (IL)-1β, reduced MACE in high-risk patients with previous MI and increased high-sensitivity (hs)-CRP. Data for patients with PAAD are not reported. Furthermore, low-dose colchicine (0.5 mg/day) has been shown to reduce MACE among those with stable atherosclerosis after recent MI.[415] However, the effect of colchicine and other anti-inflammatory drugs in PAAD remains unproven.[416]

8. Peripheral arterial disease

8.1. Lower-extremity peripheral arterial disease

8.1.1. Peripheral arterial disease syndromes

8.1.1.1. Clinical presentation and diagnosis

Atheromatous lower-extremity PAD is a chronic disease with different clinical manifestations. PAD may be symptomatic or asymptomatic and may or may not be associated with limb wounds. Wound healing and amputation risk may be affected by the concomitant presence of PAD, diabetes, and/or infection;[417] therefore, amputation risk assessment should be systematically performed using the Wound, Ischaemia, and foot Infection (WIfI) classification.

PAD presents as:

- Asymptomatic PAD: suspected by lower-limb pulse abolition or imaging studies performed for other purposes and detected by pathological ABI or TBI.[418,419] These patients do not present with IC or atypical effort-related symptoms. However, attention should be paid to those with wounds, with masked effort-related symptoms due to reduced walking capacity (for reasons other than PAD), or reduced pain sensitivity. 'Masked PAD' is defined as PAD without provoked leg pain because of reduced walking capacity for other reasons or reduced pain sensitivity.[420]
- Symptomatic (effort-related) PAD: patients with pathological ABI or TBI, presenting with IC, atypical effort-related symptoms, or chronic lower-limb wounds (diabetic foot or non-healing ulceration/gangrene ≥2 weeks) without critically reduced limb perfusion.[417,421] In these patients, IC is characterized by exertional muscle pain and dysfunction in the supply area of the obstructed arterial segment, which is relieved at rest.[422] Some patients may present with atypical symptoms or with 'masked PAD'.[420,423] In women, the prevalence of IC is lower than in men, while atypical symptoms are more common.[424]
- CLTI represents the more severe chronic PAD presentation and underlies poor limb outcomes without intervention. In addition to common signs of chronic PAD, patients with CLTI present with a critical haemodynamic status (ankle pressure <50 mmHg, toe pressure [TP] <30 mmHg, or $TcPO_2$ <30 mmHg) responsible for ischaemic rest pain, non-healing chronic (>2 weeks of duration) ulceration, or foot gangrene.[425,426]

PAD syndromes can be categorized according to their clinical presentation (*Table 7*).

The 5 year cumulative incidence of clinical deterioration from asymptomatic PAD to IC is 7%, and 21% from IC to CLTI.[427] All patients with PAD are at high risk of MACE, cerebrovascular disease, and MALE (*Figure 8*).[428–430] The 5 year cumulative incidence of CV mortality is 9% in asymptomatic PAD and 13% in symptomatic patients. In comparison with symptomatic PAD, CLTI further increases all-cause mortality risk (relative risk [RR] 2.26) and the risk of MACE (RR 1.73).[431] Health insurance data reveal a major amputation rate of 9% in patients with CLTI and 1% in patients with IC, while considerably higher amputation rates were reported in trials and registries data focusing on patients with CLTI.[432–435] Among patients with PAD, development of MALE is associated with poor prognosis, with a three-fold increase in death and a 200-fold increase in subsequent lower-extremity amputation.[429]

Prevention of MALE is crucial, and the risk of MACE/MALE increases with the increased number of arterial beds involved.

Table 7 Peripheral arterial disease categorized according to clinical presentation

Clinical characteristics of PAD	Rutherford classification		Fontaine classification	
	Category	Signs and symptoms	Stage	Signs and symptoms
Asymptomatic PAD	**0**	Asymptomatic	**I**	Asymptomatic
Symptomatic (effort-related) PAD	**1**	Mild claudication	**IIa**	Non-disabling intermittent claudication
	2	Moderate claudication	**IIb**	Disabling intermittent claudication
	3	Severe claudication		
Chronic limb-threatening Ischaemia	**4**	Ischaemic rest pain	**III**	Ischaemic rest pain
	5	Minor tissue loss	**IV**	Ischaemic ulceration or gangrene
	6	Major tissue loss		

PAD, peripheral arterial disease.

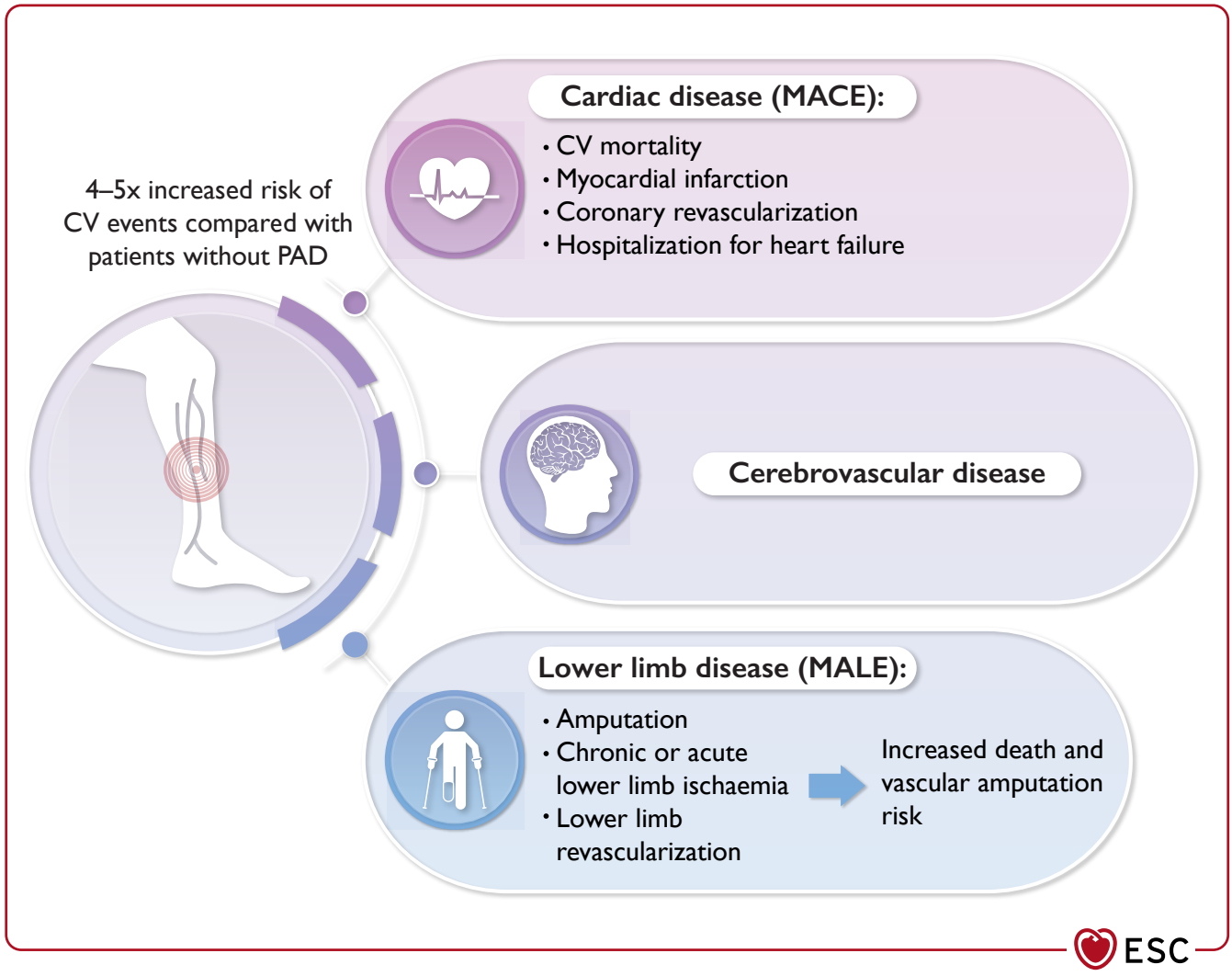

Figure 8 Cardiovascular risk in patients with peripheral arterial disease. CV, cardiovascular; MACE, major adverse cardiac event; MALE, major adverse limb event; PAD, peripheral arterial disease.

8.1.1.1.1. Diagnostic tests. Vascular assessment: ABI, TBI, $TcPO_2$ measurements (refer to *Section 5.3*)

Ankle–brachial index is the proposed initial non-invasive diagnostic test to confirm lower-limb decreased perfusion status[90,436,437] and needs to be reported separately for each leg (see Recommendation Table 2). An ABI ≤0.90 confirms PAD diagnosis.[90,436,437] In cases of an ABI >0.90 and clinical suspicion of PAD, post-exercise ABI measurements should be considered, along with imaging studies (preferably by treadmill). A post-exercise ABI decrease of >20% may serve as a PAD diagnostic criterion.[438,439]

In cases of abnormally high ABI values (ABI >1.4; see Recommendation Table 2) and patients with CLTI and diabetes[440] (see Recommendation Table 11), TP measurements, the calculation of TBI and $TcPO_2$, as well as pulse volume recordings or analysis of distal arterial Doppler waveforms, should be considered,[90,91,132,133,441] and ABI can be estimated from distal Doppler waveforms independent of diabetes and media sclerosis.[124]

Apart from the assessment of limb perfusion, ABI serves as a surrogate marker for CV and all-cause mortality.[88,442,443] A diagnostic PAD algorithm is depicted in *Figure 9*.

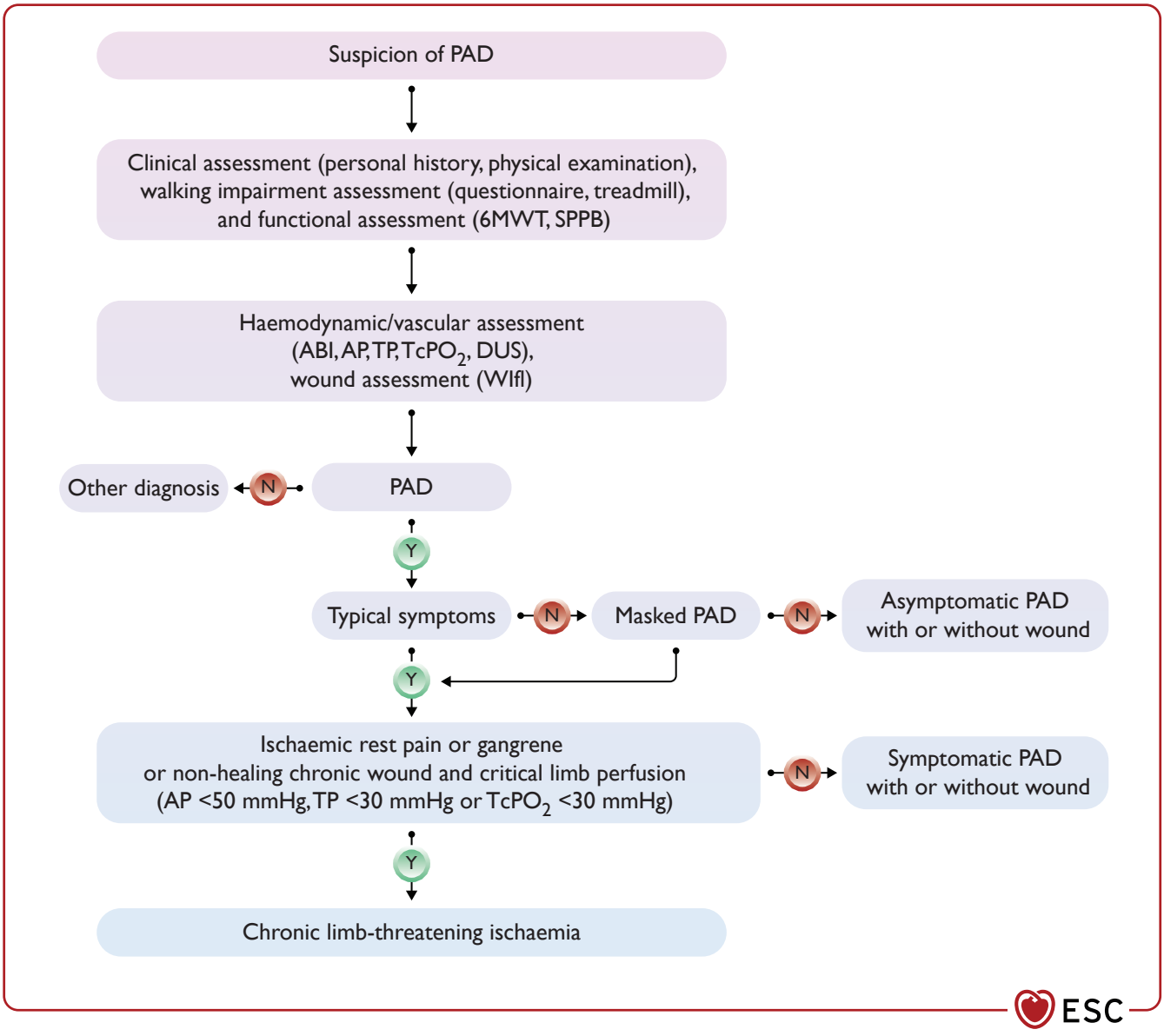

Figure 9 Diagnostic algorithm for peripheral arterial disease. 6MWT, six-minute walk test; ABI, ankle–brachial index; AP, ankle pressure; DUS, duplex ultrasound; PAD, peripheral arterial disease; SPPB, short physical performance battery; $TcPO_2$, transcutaneous oxygen pressure; TP, toe pressure; WIfI, Wound, Ischaemia, and foot Infection classification.

Walking impairment questionnaires, assessment of functional and walking capacity

Determining walking impairment, capacity, and functional status in all patients with PAD is mandatory (refer to *Section 5.2*).

Assessment of amputation risk

In patients with PAD and chronic lower-limb wounds (diabetic foot ulcer, non-healing lower-limb ulceration, or gangrene of ≥2 weeks of duration), even without haemodynamic parameters of critical limb perfusion, the additional presence of comorbidities such as diabetes and/or wound infection may contribute to an increased risk of amputation. The WIfI classification system takes the patients' limb perfusion, wound size, and the extent of foot infection into account to determine the amputation risk (*Table 8*).[417,444–446]

8.1.1.1.2. Imaging methods. Duplex ultrasound is recommended as the first-line imaging method for PAD screening and diagnosis. CTA and/or MRA are recommended as adjuvant imaging. For details refer to Supplementary data online, *Section 1.4*.

Table 8 Assessment of the risk of amputation: the Wound, Ischaemia, and foot Infection classification

Component	Score	Description		
W (Wound)	0	No ulcer (ischaemic rest pain)		
	1	Small, shallow ulcer on distal leg or foot without gangrene		
	2	Deeper ulcer with exposed bone, joint or tendon ± gangrenous changes limited to toes		
	3	Extensive deep ulcer, full thickness heel ulcer ± calcaneal involvement ± extensive gangrene		
I (Ischaemia)		ABI	Ankle pressure (mmHg)	Toe pressure or $TcPO_2$
	0	≥0.80	>100	≥60
	1	0.60–0.79	70–100	40–59
	2	0.40–0.59	50–70	30–39
	3	<0.40	<50	<30
fI (foot infection)	0	No symptoms/signs of infection		
	1	Local infection involving only skin and subcutaneous tissue		
	2	Local infection involving deeper than skin/subcutaneous tissue		
	3	Systemic inflammatory response syndrome		

	Ischaemia – 0				Ischaemia – 1				Ischaemia – 2				Ischaemia – 3			
W–0	VL	VL	VL	VL	VL	L	L	M	L	L	M	M	M	H	H	H
W–1	VL	VL	VL	VL	L	M	M	M	M	H	H	H	H	H	H	H
W–2	VL	VL	VL	VL	M	M	H	H	H	H	H	H	H	H	H	H
W–3	VL	VL	VL	VL	M	M	M	H	H	H	H	H	H	H	H	H
	fI–0	fI–1	fI–2	fI–3	fI–0	fI–1	fI–2	fI–3	fI–0	fI–1	fI–2	fI–3	fI–0	fI–1	fI–2	fI–3

Very low (green) = VL = clinical stage 1; low (yellow) = L = clinical stage 2; moderate (orange) = M = clinical stage 3; high (red) = H = clinical stage 4.
ABI, ankle–brachial index; $TcPO_2$, transcutaneous oxygen pressure.
The **W**ound, **I**schaemia and foot **I**nfection (WIfI) classification allows the assessment of the individual risk of amputation in PAD patients: it comprises scores for wound size (**W**), degree of ischaemia (**I**), as assessed by the ABI, ankle pressure, and toe pressure or $TcPO_2$, and extent of foot infection (**fI**) as depicted in the respective table. The combination of all three components results in the amputation risk stratification (***VL*** = very low, ***L*** = low, ***M*** = moderate, ***H*** = high). Table reproduced with permission from.[417]

Recommendation Table 11 — Recommendations for diagnostic tests in patients with peripheral arterial disease and diabetes, renal failure, and wounds

Recommendations	Class[a]	Level[b]
Measuring TP or TBI is recommended in patients with diabetes or renal failure if resting ABI is normal.[90,91,94,440]	I	C
In patients with PAD and chronic wounds, the WIfI classification system should be considered to estimate individual risk of amputation.[417,444–446]	IIa	C

ABI, ankle–brachial index; PAD, peripheral arterial disease; TBI, toe–brachial index; TP, toe pressure; WIfI, Wound, Ischaemia, and foot Infection classification.
[a]Class of recommendation.
[b]Level of evidence.

Recommendation Table 12 — Recommendations for imaging in patients with peripheral arterial disease

Recommendations	Class[a]	Level[b]
DUS is recommended as the first-line imaging method to confirm PAD lesions.[122,123,447]	I	C
In symptomatic patients with aorto-iliac or multisegmental/complex disease, CTA and/or MRA are recommended as adjuvant imaging techniques for preparation of revascularization procedures.[448,449]	I	C
Analysis of anatomical imaging tests in conjunction with symptoms and haemodynamic tests prior to an invasive procedure is recommended.[426]	I	C

CTA, computed tomography angiography; DUS, duplex ultrasound; MRA, magnetic resonance angiography; PAD, peripheral arterial disease.
[a]Class of recommendation.
[b]Level of evidence.

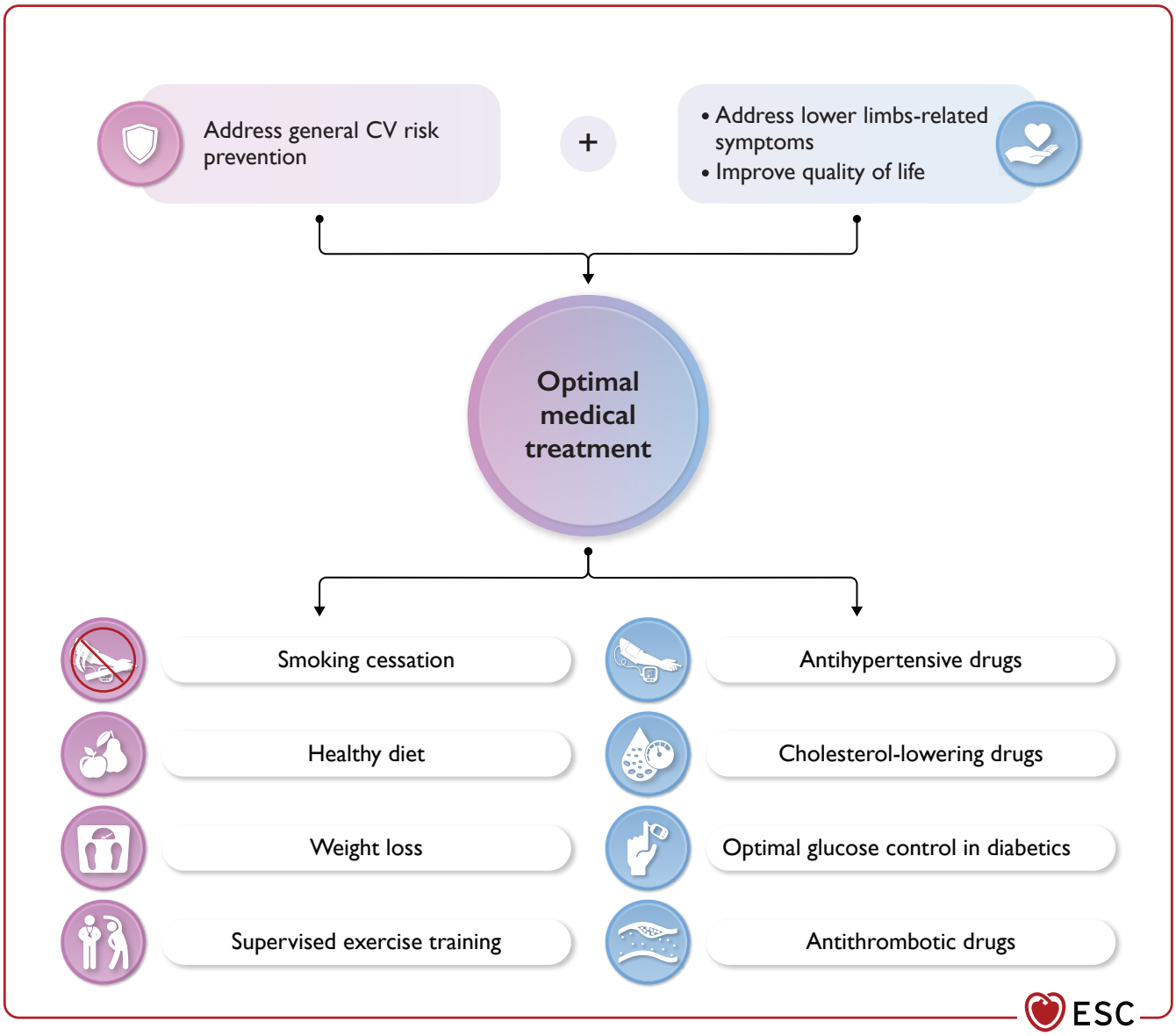

Figure 10 Optimal medical treatment in patients with peripheral arterial disease. CV, cardiovascular.

8.1.1.2. Medical treatment

Patients with PAD should receive comprehensive OMT, including supervised exercise training and lifestyle modification (*Figures 10–12*). A personalized programme of guidelines-guided pharmacotherapy to reduce MACE and MALE should be prescribed and tightly followed.

Patients with PAD are less likely to receive OMT than patients with CAD.[450–452] For general lifestyle and pharmacological therapy see *Section 7*.

8.1.1.2.1. Exercise therapy. A consensus document on exercise and PAD has been published recently.[62] Symptomatic patients should be medically screened before any supervised exercise training (SET) programme initiation.[37,62] In patients with symptomatic PAD, SET is safe and improves treadmill PFWD, MWD, functional walking as measured by six-minute walking distance (6MWD), HRQoL, and cardiorespiratory fitness (*Figure 13*).[294,453–463] Exercise has not been found to improve ABI.[457,458] Ideally, SET should be co-ordinated by vascular physicians, and training sessions supervised by clinical exercise physiologists or physiotherapists.[62] In Europe, SET is usually underused.[464,465]

When SET is not available, home-based exercise training (HBET) should be proposed (*Figure 13*), although it is inferior with regard to improving walking performance.[466–469] HBET is safe and its inferiority is reduced if monitoring is implemented.[469,470] Compared with no exercise, HBET improves walking performance.[471] SET training frequency should be at least three times per week, for 30–60 min, and the programme last for at least 12 weeks.[37,58,59,454,472,473] Patients should exercise to moderate-severe claudication pain to improve walking performance.[37,294,453,454,456–458,474] However, prescribing high-pain exercise may hinder programme uptake and adherence. Additionally, it has been reported that improvements in walking performance may be obtained with less severe claudication pain.[455,460] Therefore, a flexible approach is recommended, considering the patient's needs

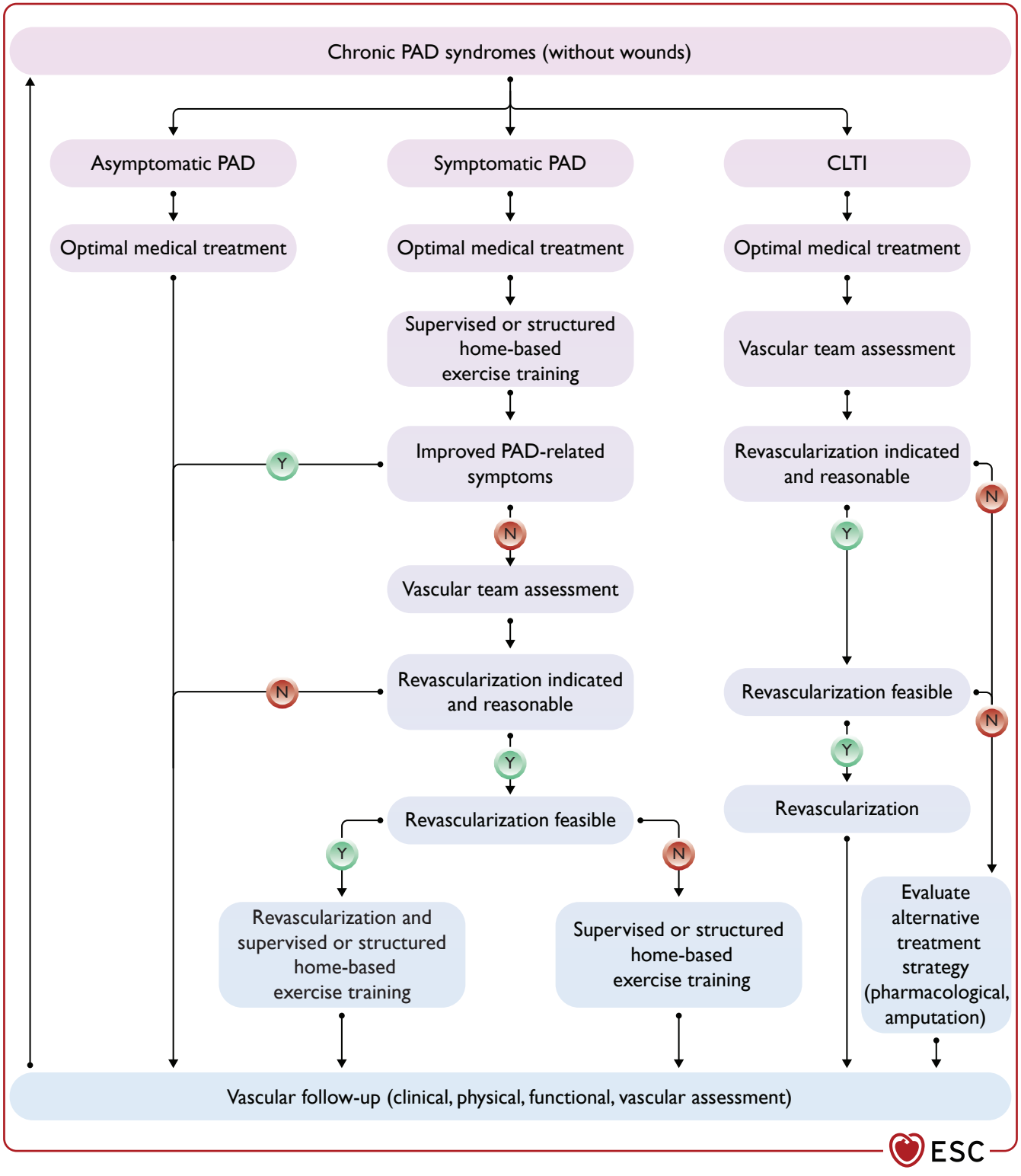

Figure 11 Treatment algorithm in peripheral arterial disease without wounds. CLTI, chronic limb-threatening ischaemia; PAD, peripheral arterial disease.

and preferences.[62] Alternative training modalities, such as strength training, arm cranking, cycling, and combinations of different modes, have proven effective in improving walking performance compared with traditional walking training, with limited evidence for HRQoL.[475] However, this evidence is low due to small sample size and risk of bias.[475] Vigorous intensity exercise training (77%–95% of maximal heart rate or 14–17 on the rate of perceived exertion on Borg's scale) has been shown to induce the best walking and cardiorespiratory fitness improvements.[294,457] Training programmes should begin at low-to-moderate intensity, gradually advancing to vigorous exercise if well tolerated.[62] This approach assesses patient response and minimizes complications.[37,62]

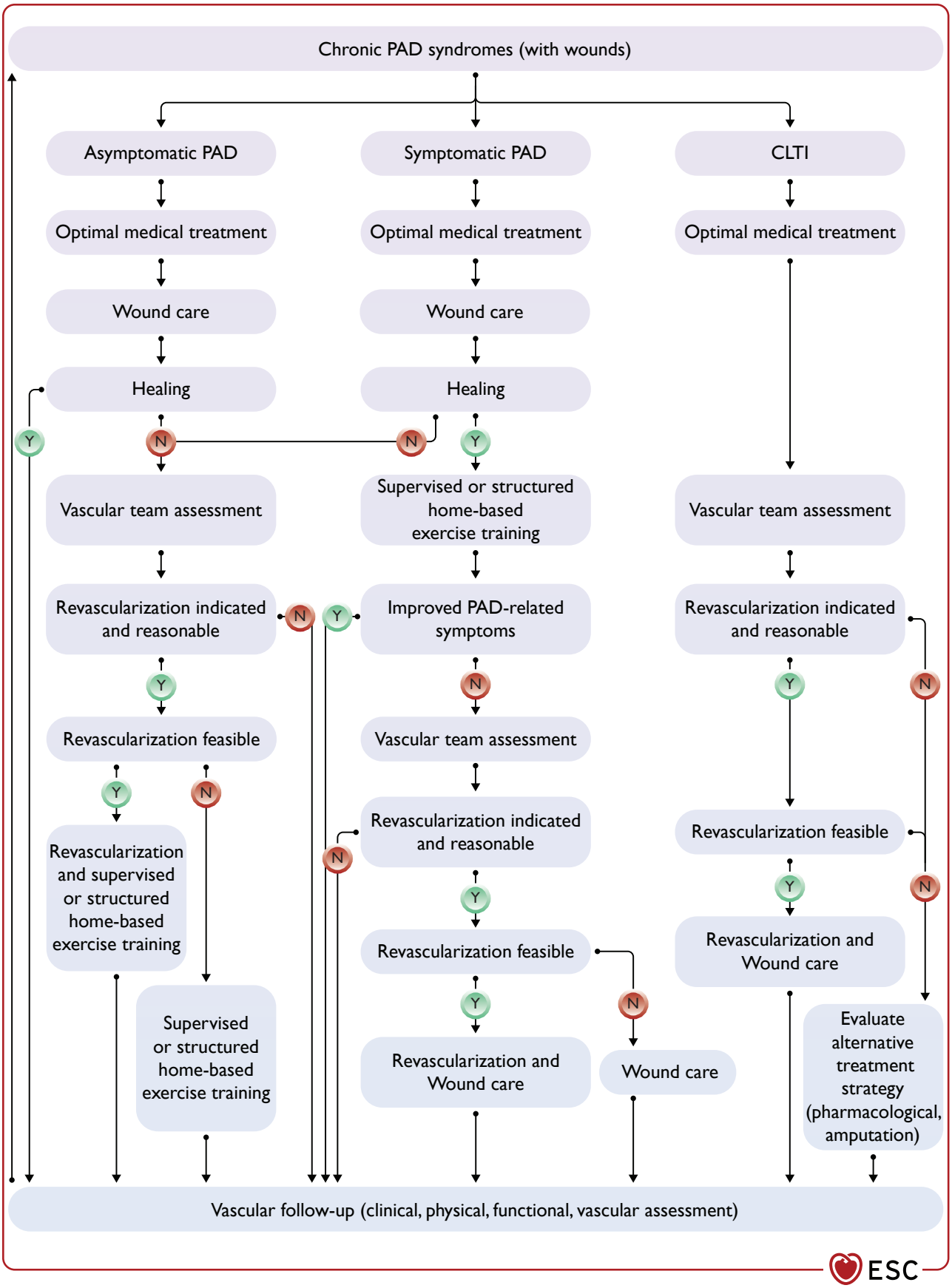

Figure 12 Treatment algorithm in peripheral arterial disease with wounds. CLTI, chronic limb-threatening ischaemia; PAD, peripheral arterial disease.

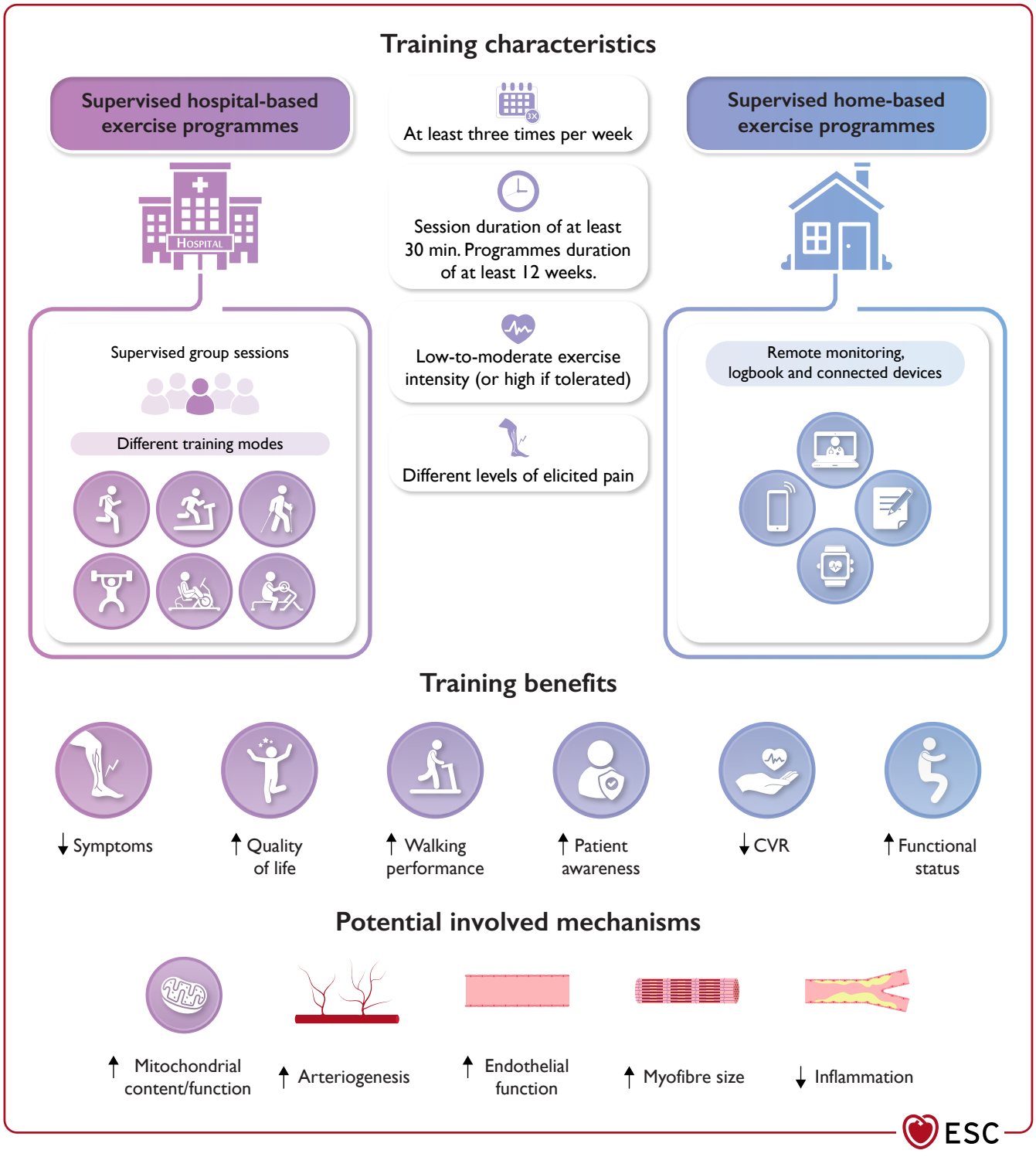

Figure 13 Exercise training characteristics and benefits in patients with peripheral arterial disease. CVR, cardiovascular risk.

Data on the efficacy of exercise therapy in women compared with men are scarce. Women may respond less well than men,[476,477] although discrepancies among studies exist.[478–481]

SET combined with endovascular revascularization significantly improves walking performance, HRQoL, and reduces future revascularization.[482,483]

An exercise therapy algorithm in PAD has been recently described.[62]

Recommendation Table 13 — Recommendations for exercise therapy in patients with peripheral arterial disease (see also Evidence Table 5)

Recommendations	Class[a]	Level[b]
In patients with symptomatic PAD, SET is recommended.[294,453,456–458,462]	I	A
In those patients undergoing endovascular revascularization, SET is recommended as an adjuvant therapy.[482,483]	I	A
When SET is not available or feasible, a structured and monitored (calls, logbooks, connected devices) HBET programme should be considered.[468,469,471]	IIa	A
Walking should be considered as a first-line training modality. When walking exercise is not an option, alternative exercise modes (strength training, arm cranking, cycling, and combinations of different training modes) should also be considered.[475]	IIa	A
Walking training performed at high intensity (77%–95% of maximal heart rate or 14–17 self-perceived exertion on Borg's scale) should be considered to improve walking performance,[294] and high-intensity exercise training (various aerobic training modes) should be considered to improve cardiorespiratory fitness.[294,457]	IIa	A
Training frequency of at least three times per week, training session duration of at least 30 min, and training programme duration of at least 12 weeks should be considered.[472]	IIa	B
In patients with PAD, exercise training to moderate-severe claudication pain may be considered to improve walking performance.[37,454,456,458] However, improvements are also achievable with lesser claudication pain severities (low-mild pain or pain-free).[455,460]	IIb	B
Based on patient's tolerance, a progressive increase (every 1–2 weeks) in exercise training load may be considered.[37,62]	IIb	C

HBET, home-based exercise training; PAD, peripheral arterial disease; SET, supervised exercise training.
[a]Class of recommendation.
[b]Level of evidence.

8.1.1.2.2. Pharmacological treatment. Antithrombotic therapy

Asymptomatic PAD

Although patients with PAD are at very high CV risk,[404,484] a trial evaluating the effect of antiplatelet agents in asymptomatic patients with an ABI ≤0.95 did not show an effect on MACE or revascularization.[485] Another trial on patients with an ABI ≤0.99 and diabetes also failed to show any difference in MACE or amputation.[486] However, these data were not powered to analyse subgroups and do not rule out the possibility that aspirin could provide a benefit in subjects at increased risk of CV events. In a randomized trial evaluating aspirin in the prevention of cancer and CVD in patients with diabetes without known arterial disease, MACE occurred in a significantly lower percentage of participants in the aspirin group than in the placebo group, with more major bleeding events in the aspirin group.[487] The effect of antithrombotics in patients with higher-risk PAD (i.e. ABI <0.90 and other CV risk factors) has not been evaluated in randomized trials. Antithrombotic therapy should not be systematically administered in patients with asymptomatic PAD.

Symptomatic PAD

In patients with symptomatic PAD, antithrombotic therapy improves CV prognosis.[488–492] Clopidogrel may have a modest advantage over aspirin (*Figure 14*).[493,494] In the Examining Use of tiCagreLor In peripheral artery Disease (EUCLID) trial, single antiplatelet therapy (SAPT) with ticagrelor showed no superior benefit in the reduction of MACE or major bleeding compared with clopidogrel.[495–497]

Dual antithrombotic therapy with aspirin and vascular-dose rivaroxaban (2.5 mg b.i.d.) in patients with PAD is more effective than aspirin alone, reducing MACE, MALE, and preventing acute limb ischaemia (ALI), but with increased major bleeding risk.[429,430,498,499] Patients with high-risk limb presentation (CLTI, previous amputation, or revascularization) or high-risk comorbidities (heart failure [HF], diabetes, or polyvascular disease [PVD]) benefit the most.[498]

After endovascular therapy, dual antiplatelet therapy (DAPT) for 1–3 months is supported by rare randomized studies.[500,501] DAPT is not associated with reduced CV mortality or MACE,[501] but seems to improve patency without increasing bleeding (*Figure 15*).[502–504] The combination of aspirin 100 mg and vascular-dose rivaroxaban (2.5 mg b.i.d.), started post-revascularization, showed a moderate but significantly lower incidence of MALE and MACE compared with aspirin alone,[490,505] without an increase in thrombolysis in myocardial infarction (TIMI) major bleedings, but with an increase in International Society on Thrombosis and Haemostasis (ISTH) major bleedings, especially when clopidogrel was given for >1 month.[506]

Patients with CLTI are at high risk of MACE and MALE.[429,431,507] Among CLTI patients, there is no robust evidence favouring a specific antithrombotic strategy for vein graft maintenance. DAPT with clopidogrel and aspirin is not superior to aspirin alone in below-the-knee (BTK) bypass grafts.[508–510] Vitamin K antagonists (VKAs) may be considered for high-risk conduits with low bleeding risk.[509]

Dual antiplatelet therapy could confer benefit for prosthetic conduit (occlusion, revascularization, amputation, or death), without increasing major bleeding.[510] VKAs with an international normalized ratio (INR) of 3–4.5 are slightly beneficial in venous conduits, but with a 1.9-fold and 1.3-fold increase in major and fatal bleedings, respectively.[509] A study suggested that VKAs could be associated with prolonged patency of at-risk prosthetic grafts due to poor run-off.[511]

In patients with another indication for OAC (such as atrial fibrillation [AF] or mechanic valve replacement) and PAD, anticoagulation is warranted.[512] Additional SAPT post-endovascular therapy should be brief.

Recommendation Table 14 — Recommendations for antithrombotic therapy in patients with peripheral arterial disease (see also Evidence Table 6)

Recommendations	Class[a]	Level[b]
Use of antiplatelet therapy with aspirin alone (range 75–160 mg o.d.) or clopidogrel alone (75 mg o.d.) is recommended for the reduction of MACE in patients with symptomatic PAD.[488–490]	I	A
Treatment with combination rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered for patients with PAD, high ischaemic risk,[c] and non-high bleeding risk.[d,429,498,499]	IIa	A

Continued

Treatment with combination rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered for patients with PAD and non-high bleeding risk following lower-limb revascularization.[490,505]	IIa	B
Use of antiplatelet therapy with clopidogrel alone (75 mg o.d.) may be considered over aspirin to reduce MI, stroke, and vascular death.[493,494]	IIb	B
Aspirin (75–100 mg) for primary prevention may be considered in patients with asymptomatic PAD and DM, in the absence of contraindications.[419,487]	IIb	A
DAPT for at least 1 month after revascularization may be considered to reduce limb events.[500,501,503,513,514]	IIb	B
Long-term DAPT in patients with PAD is not recommended.[489]	III	A
Oral anticoagulant monotherapy for PAD (unless for another indication) is not recommended.[515]	III	A
The routine use of ticagrelor in patients with PAD is not recommended.[495]	III	A
It is not recommended to systematically treat patients with asymptomatic PAD without any sign of clinically relevant ASCVD with antiplatelet drugs.[485]	III	B

ASCVD, atherosclerotic cardiovascular disease; DAPT, dual antiplatelet therapy; DM, diabetes mellitus; MACE, major adverse cardiovascular events; MI, myocardial infarction; o.d., once daily; PAD, peripheral arterial disease.
[a]Class of recommendation.
[b]Level of evidence.
[c]High ischaemic risk: previous amputation, critical limb threatening ischaemia, previous revascularization, high-risk comorbidities (heart failure, diabetes, vascular disease in two or more vascular beds), eGFR <60 mL/min/1.73 m^2.[498]
[d]High bleeding risk: dialysis or renal impairment GFR <15 mL/min/1.73 m^2, acute coronary syndrome <30 days, history of intracranial haemorrhage, stroke or TIA, active or clinically significant bleeding.

Pharmacotherapy to decrease walking impairment

Verapamil,[516] statins,[517,518] antiplatelet agents, and prostanoids (prostaglandins I_2 and E_1)[519] can alleviate walking impairment in patients with symptomatic PAD. However, drugs like cilostazol, naftidrofuryl, pentoxifylline, buflomedil, carnitine, and propionyl-L-carnitine are suggested to increase walking distance in patients with IC without impacting CV health.[339,520] Their objective benefit is generally limited, ranging from mild to moderate, with considerable variability.[339] The additional benefit of these drugs alongside antithrombotics, antihypertensives, and statins remains unknown.

Cilostazol, a phosphodiesterase type III inhibitor, improved MWD compared with placebo and pentoxifylline.[520–522] In a Cochrane analysis, 100 mg twice daily increased MWD by 76%,[521] while another review reported a 25% average improvement.[520] Cilostazol also has antiplatelet effects, requiring cautious combination with other anticoagulant and antiplatelet treatments.[522] Notably, it increases bleeding complications.[523]

Naftidrofuryl oxalate, tested for IC,[524] demonstrated a 74% average increase in MWD and improved HRQoL.[524,525] In a systematic review, the average MWD improvement was 60% compared with placebo.[520] However, inconsistent results for other medications, such as prostanoids, pentoxifylline, L-arginine, buflomedil, or *Gingko biloba*, preclude their recommendation for patients with IC.[519,526,527]

8.1.1.2.3. Aorto-iliac lesion revascularization. Aorto-iliac lesions can be treated by either an endovascular or a surgical approach according to the lesion morphology and patient risk. Long-term patency with a low risk of complications can be achieved by balloon angioplasty with or without stenting in external iliac arteries or primary stenting in common iliac arteries.[528] A meta-analysis evaluated outcomes of open surgery vs. an endovascular approach in aorto-iliac lesions (TASC II C-D) and found that short-term morbidity and mortality favours the endovascular approach, but early and mid-term primary patency favours open surgery; however, secondary patency is comparable in all groups.

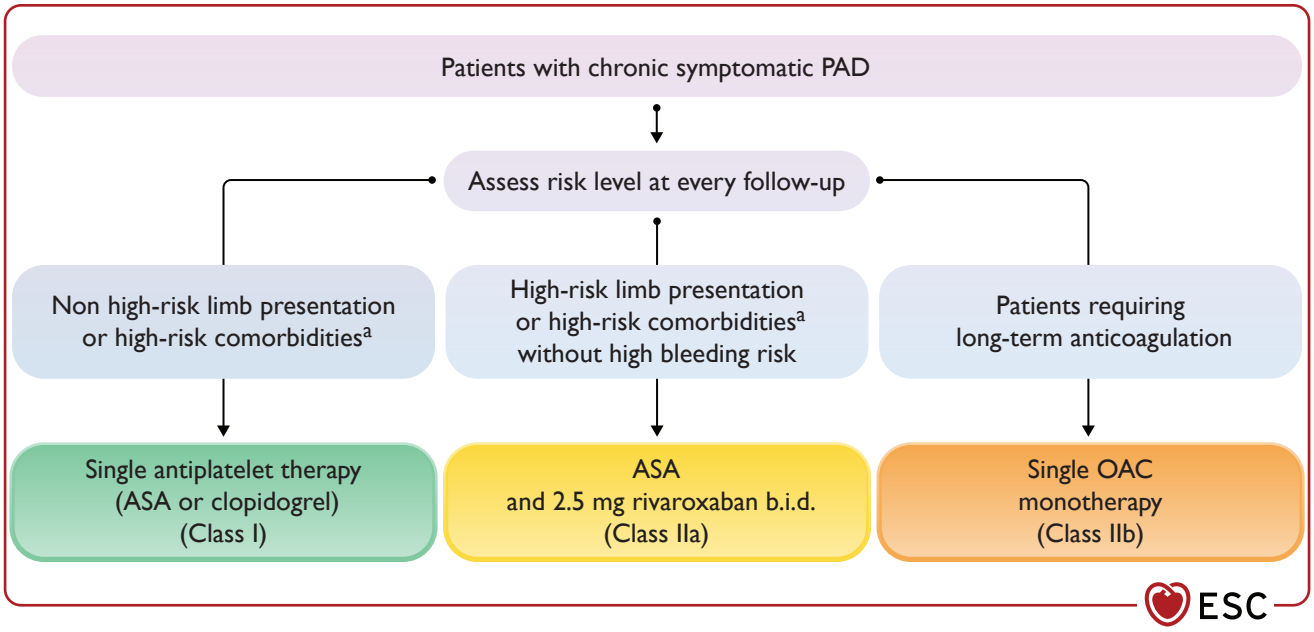

Figure 14 Long-term antithrombotic therapy in patients with symptomatic peripheral arterial disease. b.i.d., twice daily; OAC, oral anticoagulant; PAD, peripheral arterial disease; ASA, aspirin [a]High-risk limb presentation: previous amputation, chronic limb-threatening ischaemia, previous revascularization, high-risk comorbidities: heart failure, diabetes, vascular disease in two or more vascular beds, moderate kidney dysfunction; eGFR <60 mL/min/1.73 m^2.

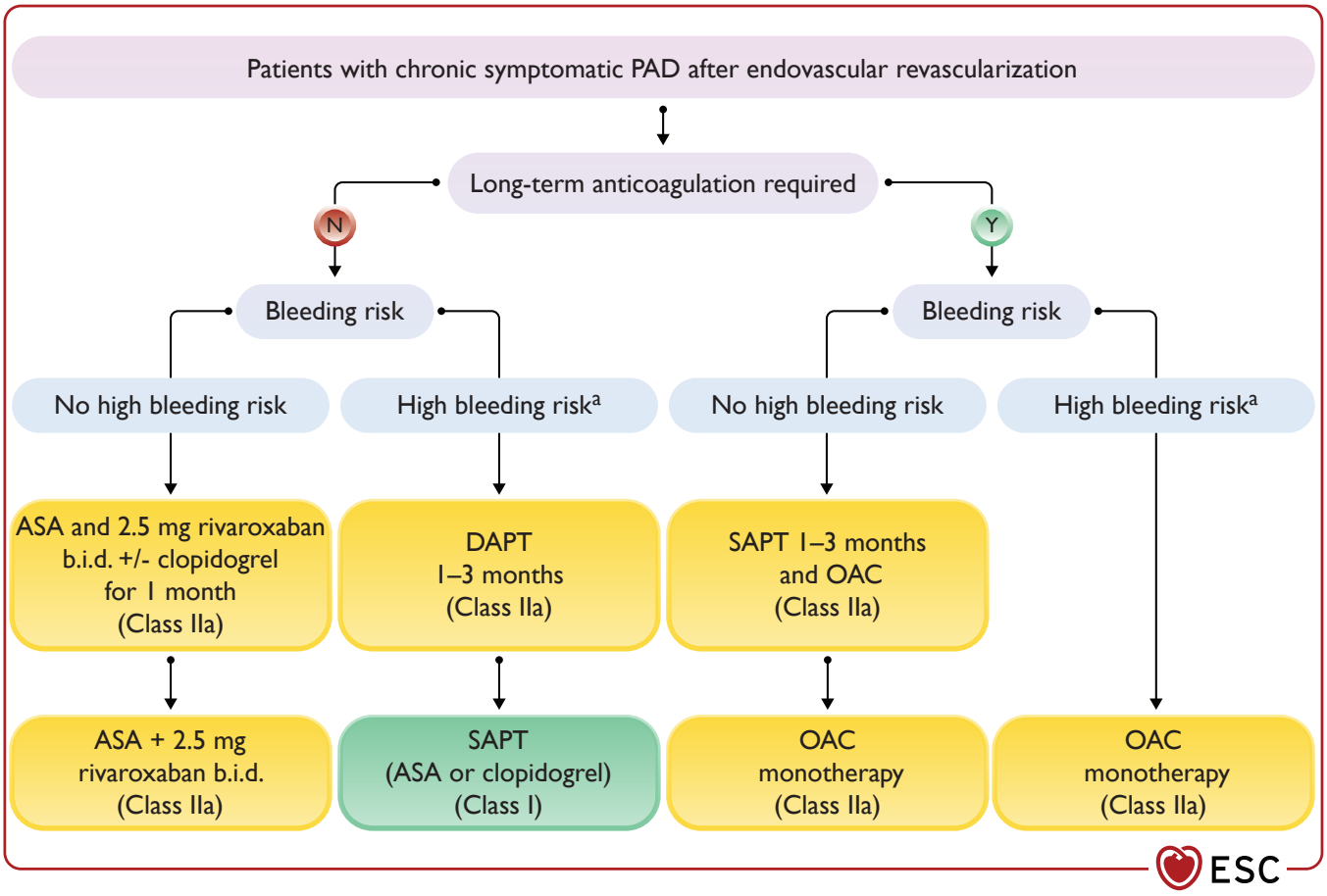

Figure 15 Patients with chronic symptomatic PAD after endovascular revascularization. b.i.d., twice daily; DAPT, dual antiplatelet therapy; OAC, oral anticoagulant; PAD, peripheral arterial disease; ASA, aspirin; SAPT, single antiplatelet therapy [a]High bleeding risk: dialysis or a renal impairment glomerular filtration rate <15 mL/min/1.73 m^2, acute coronary syndrome <30 days, history of intracranial haemorrhage, stroke or TIA, active or clinically significant bleeding.

8.1.1.2.4. Femoro-popliteal lesion revascularization. If revascularization is indicated, endovascular therapy should be the first choice even for complex lesions, especially in surgical high-risk patients.[119,529–531]

Endovascular therapy faces the challenge of sustaining long-term patency and durability in the femoro-popliteal region, particularly post-stent placement in a highly mobile artery. Drug-eluting balloons have improved long-term patency in complex patient cohorts and lesions.[532] With regard to paclitaxel-coated devices, a meta-analysis caused a decline in their usage, especially as the United States Food and Drug Administration (FDA) reacted and restricted their use.[533] Consequently, data from large national databases were evaluated and the mortality signal could not be confirmed. The FDA revised its position, and drug-eluting treatment is now deemed to be a safe and efficient treatment strategy for femoro-popliteal lesions.[534–538]

An open surgical approach in femoro-popliteal lesions should be considered when an autologous vein (e.g. great saphenous vein [GSV]) is available and the patient shows low surgical risk, and in complex lesions after an interdisciplinary team discussion.

8.1.1.2.5. Below-the-knee artery revascularization. In patients with severe IC in whom endovascular femoro-popliteal treatment is performed, BTK arteries can be treated in the same intervention if there is substantially impaired outflow.[539]

Recommendation Table 15 — Recommendations for interventional treatment of asymptomatic and symptomatic peripheral arterial disease (general)

Recommendations	Class[a]	Level[b]
In patients with symptomatic PAD, after a 3 month period of OMT and exercise therapy, PAD-related QoL assessment is recommended.[119]	I	B
It is recommended to adapt the mode and type of revascularization options to anatomical lesion location, lesion morphology, and general patient condition.[119]	I	C
In patients with symptomatic PAD and impaired PAD-related quality of life after a 3 month period of OMT and exercise therapy, revascularization may be considered.[465,540]	IIb	B
In patients with PAD, revascularization is not recommended if the reason is to solely prevent progression to CLTI.[541–544]	III	B
In patients with asymptomatic PAD, revascularization is not recommended.[119,529]	III	C

CLTI, chronic limb-threatening ischaemia; OMT, optimal medical treatment; PAD, peripheral arterial disease; QoL, quality of life.
[a]Class of recommendation.
[b]Level of evidence.

Recommendation Table 16 — Recommendations for interventional treatment of patients with symptomatic peripheral arterial disease (per arterial bed)

Recommendations	Class[a]	Level[b]
In femoro-popliteal lesions, drug-eluting treatment should be considered as the first-choice strategy.[534–537]	IIa	A
In iliac lesions, balloon angioplasty with or without stenting in external iliac arteries, or primary stenting in common iliac arteries, should be considered.[545–548]	IIa	B
In femoro-popliteal lesions, if revascularization is indicated, endovascular therapy should be considered.[119,529–531]	IIa	B
In femoro-popliteal lesions, if revascularization is indicated, an open surgical approach should be considered when an autologous vein (e.g. GSV) is available in patients with low surgical risk.[119,529]	IIa	C
In patients with severe IC undergoing endovascular femoro-popliteal revascularization, treatment of BTK arteries may be considered in the same intervention.[549,550]	IIb	C

BTK, below-the-knee; GSV, great saphenous vein; IC, intermittent claudication.
[a]Class of recommendation.
[b]Level of evidence.

8.1.1.3. Follow-up

Asymptomatic and symptomatic PAD are at increased risk of leg symptom worsening[427] and of CV mortality and morbidity.[419,431,551] Follow-up post-revascularization is crucial to ensure perfusion improvement, address CVRFs, optimize pharmacological treatment adherence, identify disease progression, and evaluate mental health and functional capacity. Experienced vascular care physicians should conduct follow-up, although specific protocols are currently undefined.[128,552] Data on asymptomatic PAD follow-up are limited.[553] For symptomatic PAD or post-intervention, annual follow-up are advised, including ABI/TBI measurement and DUS for new or worsening symptoms.

Recommendation Table 17 — Recommendations in patients with peripheral arterial disease: follow-up of patients with peripheral arterial disease

Recommendations	Class[a]	Level[b]
It is recommended to regularly, at least once a year, follow up patients with PAD, assessing clinical and functional status, medication adherence, limb symptoms, and CVRFs, with DUS assessment as needed.[553,554]	I	C

CVRFs, cardiovascular risk factors; DUS, duplex ultrasound; PAD, peripheral arterial disease.
[a]Class of recommendation.
[b]Level of evidence.

8.1.2. Chronic limb-threatening ischaemia

8.1.2.1. Clinical presentation and diagnosis

Chronic limb-thretening ischaemia describes chronic lower-limb hypoperfusion responsible for ischaemic rest pain, or non-healing ulceration or gangrene (typically in distal segments).[555,556] Ischaemic rest pain primarily affects the patient's forefoot and aggravates in a supine position, while lowering of the affected leg eases ischaemic symptoms.

8.1.2.1.1. Definition. Chronic limb-thretening ischaemia should be considered in the presence of one of the following lower-limb clinical signs or symptoms:

- Ischaemic rest pain
- Non-healing lower-limb wound of ≥2 weeks' duration
- Lower-limb gangrene

The following haemodynamic criteria may be used to guide diagnosis in patients with suspicion of CLTI:

- Ankle pressure <50 mmHg
- TP <30 mmHg
- $TcPO_2$ <30 mmHg

8.1.2.1.2. Initial assessment and risk of amputation. For patients with CLTI, initial diagnostic steps involve clinical examination and limb perfusion assessment through haemodynamic measurements. Regarding haemodynamic assessment in CLTI, standard ABI may be normal or falsely elevated due to non-compressible arteries related to medial sclerosis (common in diabetes or CKD),[557] which can be overcome by estimation of ABI based on Doppler waveforms.[124] Therefore, standard ankle pressure alone may not be reliable in estimating limb loss risk.[441,558] In addition, a large proportion of patients with ulcers may have below-the-ankle lesions.[440] In patients with CLTI, TP, TBI, or $TcPO_2$ should additionally be obtained.[90,441,559]

Particularly in patients with CLTI, the WIfI classification system should be applied. In addition to patients' limb perfusion, the WIfI classification considers the wound size and the extent of foot infection to determine the individual risk of amputation.[417,444–446]

8.1.2.1.3. Imaging. In all patients with CLTI, comprehensive vascular imaging is mandatory to evaluate revascularization options. CLTI commonly affects more than one arterial segment of the lower limbs, involving infra-popliteal arteries (BTK and below-the-ankle arteries) in most cases. While non-invasive imaging (DUS, CTA, MRA) provides reliable results for above-the-knee arteries, imaging of BTK arteries, especially below the ankle, may be hampered by severe calcification.[448,560,561] Therefore, in CLTI additional DSA with dedicated views of the foot should be considered for the assessment of BTK arteries.[560] Even in patients who are not candidates for revascularization, DSA should be obtained to prevent unnecessary amputation or to minimize amputation extent.[560,562]

8.1.2.1.4. Mortality risk assessment. All-cause mortality and event rates of MI are more than two-fold higher in CLTI patients than in unselected patients with an ABI ≤0.90.[431]

In CLTI patients undergoing revascularization, the post-revascularization period is particularly associated with an increased risk of MALE and MACE.[563] The management of patients with CLTI should therefore include an individual peri-procedural risk assessment. Referring to the peri-procedural risk patients can be categorized as average procedural risk (peri-procedural mortality <5% and 2 year survival >50%) or high procedural risk (peri-procedural mortality ≥5% and 2 year survival ≤50%).[564,565]

Besides revascularization, it also needs to be considered that lower-limb amputation is associated with 30 day mortality rates of up to 22%.[566]

Recommendation Table 18 — Recommendations for the management of chronic limb-threatening ischaemia

Recommendations	Class[a]	Level[b]
For limb salvage in patients with CLTI, revascularization is recommended.[564,567]	I	B
Early recognition of CLTI and referral to the vascular team are recommended for limb salvage.[417,560]	I	C
In patients with CLTI, imaging of the entire affected limb should be considered.[560]	IIa	C

CLTI, chronic limb-threatening ischaemia.
[a]Class of recommendation.
[b]Level of evidence.

8.1.2.2. Medical treatment

Chronic limb-thretening ischaemia is associated with a high risk of ischaemic events,[429,431] thus management of patients with CLTI must include OMT.

In addition, rest pain, optimal wound care, and infection control should be managed. A vascular team, including at least a vascular physician, a vascular surgeon, and a radiologist, should be involved to prevent amputation.[568] Lower-limb exercise training is contraindicated until ulcers are healed and aggressive offloading should be ensured to allow healing. Depending on infection extent, oral antibiotics may suffice, however, if extensive with systemic signs of inflammation, admission for intravenous (i.v.) antibiotic administration may be required.[569,570]

Good-quality evidence on the advantages of one type of wound dressing over others is lacking, while in selected patients individualized treatments with antimicrobial dressing,[571] silver dressing,[572] collagen dressing,[573] honey- or iodine-based dressings,[574] platelet-rich plasma, or negative pressure therapy[575,576] may accelerate wound healing, shorten hospital stay, and prevent amputations. If deep-seated infection is suspected, X-ray or MRA are required to diagnose osteomyelitis, in which case a longer course of antibiotics may be necessary.[577] Antibiotics for osteomyelitis treatment may be empirical, however, they should be adapted according to (preferably tissue) cultures.[578–581]

Ulcers require assessment of venous aetiology and potential for endovenous therapy, while mixed ulcers require compression therapy after revascularization.[582]

Recommendation Table 19 — Recommendations for medical treatment in patients with chronic limb-threatening ischaemia (see also Evidence Table 7)

Recommendations	Class[a]	Level[b]
It is recommended that patients with CLTI are managed by a vascular team.[568]	I	C
In patients with CLTI and ulcers, offloading mechanical tissue stress is recommended to allow wound healing.[583,584]	I	C
It is recommended to treat infection with antibiotics.[569,570]	I	C
Lower-limb exercise training is not recommended in patients with CLTI and wounds.[584]	III	C

CLTI, chronic limb-threatening ischaemia.
[a]Class of recommendation.
[b]Level of evidence.

8.1.2.3. Interventional treatment

8.1.2.3.1. Revascularization. In CLTI, revascularization should be attempted to rapidly restore an inline direct blood flow to the foot.[585–588] Three RCTs compared endovascular therapy with open surgery in infra-inguinal arteries. In the Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial, no significant difference was found regarding mortality or amputation-free survival at 2 years.[589] However, surgery was associated with a significantly reduced risk of amputation, death, or both after 2 years.[564,589] In the Best Endovascular versus Best Surgical Therapy for Patients with Critical Limb Ischemia (BEST-CLI) trial (median follow-up of 2.7 years), the incidence of MALE or death was lower in patients in which one segment of the GSV was available for surgical revascularization than in patients who underwent endovascular revascularization. In the same trial, outcomes of patients for whom an alternative bypass conduit was needed for surgical revascularization were similar to those of patients who underwent endovascular revascularization.[567]

In the BASIL-2 trial, which included patients requiring infra-popliteal, with or without additional further proximal infra-inguinal, revascularization procedures, endovascular revascularization was associated with better amputation-free survival than surgical revascularization, which was primarily due to fewer deaths in this group.[590] It is important to consider[591] both revascularization options individually in each patient, considering the complexity of the diseased anatomical region.

Multilevel disease

Patients with CLTI commonly present with multilevel disease.[592] Especially for complex lesions, comprehensive patient assessment, including the individual patient's clinical presentation, the lesion morphology, and the peri-procedural risk, needs to be undertaken by a multidisciplinary vascular team to weigh the risks against the benefits of the respective methods of revascularization (endovascular vs. surgical).[590,593–596] A structured approach is essential to achieve rapid and durable restoration of an inline flow to the foot. When possible, the angiosome concept can be considered, targeting the most affected ischaemic area.[597] When CLTI leaves no viable revascularization options, transcatheter arterialization of deep veins may be considered.[598]

Aorto-iliac disease

An endovascular approach is the first choice, commonly employing bare metal or covered stents.[599–603] Surgery is reserved for extensive obstructions and lesions treated unsuccessfully with an endovascular procedure.[604] Hybrid revascularization should be considered in occlusion of the common femoral artery or profunda femoris artery requiring endarterectomy, in addition to inflow and/or outflow disease amenable to endovascular therapy. Hybrid procedures should be encouraged in a one-step modality.[605]

Femoro-popliteal disease

Chronic limb-threatening ischaemia is unlikely to be related to isolated superficial femoral artery lesions; femoro-popliteal involvement in combination with aorto-iliac or infra-popliteal disease is frequently found. In 40% of cases, inflow treatment of femoro-popliteal disease is necessary.[606] The revascularization strategy should be selected according to lesion complexity.[422] If endovascular therapy is chosen, landing zones for potential bypass grafts should be preserved. When bypass surgery is decided, the bypass should be as short as possible, using the saphenous veins.[567]

Infra-popliteal disease

Extended infra-popliteal disease is mainly seen in patients with diabetes[607–610] and CKD,[611,612] often being associated with superficial femoral artery lesions. In short infra-popliteal lesions, endovascular

therapy is the first choice.[593] Drug-eluting balloons[607] and bare metal stent implantation[613] have shown no superiority over plain balloon angioplasty, although drug-eluting stents may be used for relatively short proximal lesions.[614–616]

8.1.2.3.2. Spinal cord stimulation. Spinal cord stimulation (SCS) may be considered in treating patients with CLTI and no viable revascularization options. SCS offers modest pain relief and an 11% reduction in amputation rate compared with conservative management at 1 year. No effect was seen in ulcer healing and benefits should be weighed against the high cost and possible complications.[617] Recent technological advances in neuromodulation may improve the treatment value of this modality.[618]

8.1.2.3.3. Amputation. Minor amputation, usually up to the forefoot, is often needed for necrotic tissue removal with minor impact on patient mobility. Pre-amputation revascularization enhances wound healing. In cases of extensive necrosis or infectious gangrene, primary major amputation without revascularization may be preferable to avoid complications. Secondary amputation is indicated when revascularization fails, re-intervention is not possible, or limb deterioration persists despite a patent graft and optimal management. BTK amputation allows better mobility with a prosthesis. For bedridden patients, above-the-knee amputation may be the preferred choice.

Recommendation Table 20 — Recommendations for interventional treatment of chronic limb-threatening ischaemia

Recommendation	Class[a]	Level[b]
In CLTI patients, it is recommended to perform revascularization as soon as possible.[564]	I	B
In CLTI, it is recommended to use autologous veins as the preferred conduit for infra-inguinal bypass surgery.[567,593]	I	B
In multilevel vascular disease, it is recommended to eliminate inflow obstructions when treating downstream lesions.	I	C
An individual risk assessment (weighing the patient's individual procedural risk of endovascular vs. surgical revascularization) by a multidisciplinary vascular team is recommended.	I	C
In CLTI patients with good autologous veins and low surgical risk (<5% peri-operative mortality, >50% 2 year survival), infra-inguinal bypass may be considered.[564,567,590]	IIb	B
In CLTI patients, endovascular treatment may be considered as first-line therapy, especially in patients with increased surgical risk or inadequate autologous veins.[564,567,590]	IIb	B

CLTI, chronic limb-threatening ischaemia.
[a]Class of recommendation.
[b]Level of evidence.

8.1.2.4. Follow-up

In patients with CLTI, the incidence of CV events is increased.[619,620] Follow-up should focus on general clinical CV condition, prevention of revascularization failure, wound healing, and contralateral limb status. After revascularization, at least an annual appointment with a vascular physician expert in CLTI management is warranted. Due to the lack of evidence, recommendations are largely based on consensus and expert opinions.[128]

First-year incidence of vein graft stenosis is 20%;[621] however, if uneventful for 12 months, late issues are scarce.[622] Clinical examination, ABI (or TBI) measurement, and DUS should be performed within 4–6 weeks and thereafter at 3, 6, 12, and 24 months after bypass surgery.[128]

After endovascular treatment, restenosis and occlusion ranges from 5% in the pelvic region to >50% in the infra-popliteal arteries.[623,624] Unlike after surgery, no plateau phase is seen, and the failure rate is constant for at least 5 years. Surveillance includes clinical assessment looking for recurrent symptoms or signs, ABI measurement, and DUS based on the first check-up: if normal, DUS is recommended if symptoms reappear; if abnormal, initial DUS, re-intervention, or closer DUS follow-up on a case-by-case basis are recommended.[128] Post-procedural ankle duplex-based estimated ABI of <0.90 predicts suboptimal wound healing, clinically driven target lesion revascularization (cdTLR), and MALE.[625]

After revascularization, closer follow-up and wound care are recommended until healing. Thereafter, annual appointments with vascular physicians with expertise in CLTI management should be scheduled to check for symptoms, foot condition, ABI, and CVRFs, including availability for TP and $TcPO_2$ if needed. Recurrence of symptoms may also be due to the progression of atherosclerotic disease above or below the bypass or angioplasty site.[427]

Recommendation Table 21 — Recommendations for follow-up in patients with chronic limb-threatening ischaemia

Recommendations	Class[a]	Level[b]
In patients with CLTI, following revascularization it is recommended to follow up patients on a regular basis.[552,626,627]	I	C
At follow-up, it is recommended to assess clinical, haemodynamic and functional status, limb symptoms, treatment adherence, and CVRFs.[552,625–628]	I	C

CLTI, chronic limb-threatening ischaemia; CVRFs, cardiovascular risk factors.
[a]Class of recommendation.
[b]Level of evidence.

8.1.3. Acute limb ischaemia

8.1.3.1. Clinical presentation and diagnosis

Acute limb ischaemia is caused by an abrupt decrease in arterial limb perfusion. Potential causes are PAD progression, cardiac/aortic embolization, AD, graft thrombosis, aneurysm thrombosis, popliteal artery entrapment syndrome, trauma, phlegmasia cerulea dolens, ergotism, hypercoagulable states, and iatrogenic complications related to vascular procedures. ALI is a medical emergency and timely recognition is crucial to successful treatment.[629–632] Patients should be rapidly evaluated by a vascular specialist[633] or rapidly transferred to a facility with such resources.

The time constraint is due to the period that skeletal muscle and nerves will tolerate ischaemia—roughly 4–6 h.[634] Lower-extremity symptoms can include both pain and loss of function. The longer and the stronger these symptoms are, the less likely the possibility of limb salvage.

Table 9 Clinical categories of acute limb ischaemia

Grade	Category	Sensory loss	Motor deficit	Arterial Doppler signal	Venous Doppler signal	Capillary refill	Biomarkers	Prognosis
I	Viable	None	None	Yes	Yes	Yes	Not elevated	No immediate threat
IIA	Marginally threatened	None or minimal (toes)	None	No	Yes			Salvageable if promptly treated
IIB	Immediately threatened	More than toes	Mild-moderate	No	Yes			Salvageable if promptly revascularized
III	Irreversible	Profound, anaesthetic	Profound paralysis (rigor)	No	No	No	Massively elevated	Major tissue loss, permanent nerve damage inevitable

Adapted with permission from.[641]

8.1.3.1.1. Clinical examination. The emergency level and the choice of therapeutic strategy depend on the clinical presentation, mainly according to neurological deficits. Clinical assessment must include symptom duration as well as sensory and motor deficit severity to distinguish a threatened from a non-viable extremity. Neurological deficits (sensory loss or especially motor deficit) are signs of limb threat and require emergency imaging and revascularization.[635] Severe sensory deficit and paralysis suggest the limb may be unsalvageable. Clinical ALI categories are presented in *Table 9*.

8.1.3.1.2. Imaging and functional tests. The imaging method depends on availability and aims to diagnose clot presence and assess haemodynamic severity. DSA, CTA, DUS, and contrast-enhanced (CE)-MRA are options based on local expertise, availability, and preference.[636] DUS helps determine treatment urgency when assessing neurological deficit is challenging. Loss of arterial signal suggests limb threat, while a present signal may indicate the limb is not immediately threatened, allowing for ABI measurement. The absence of both arterial and venous Doppler signals, coupled with extensive motor deficit, suggests the limb may be irreversibly damaged (non-salvageable).[637] In addition, biomarkers of muscle damage such as creatinine kinase (CK) or myoglobin may be useful as high levels indicate rhabdomyolysis, risk of amputation,[638] kidney failure, and mortality.[639] In limb ischaemia, CK and myoglobin elevations may be lower in chronic cases, possibly due to ischaemic pre-conditioning and collateral development.[640]

8.1.3.2. Medical treatment

Upon clinical diagnosis, initiate analgesia, anticoagulation, and i.v. fluids. Addressing acidosis and hyperkalaemia may be necessary. Administer i.v. unfractionated heparin (bolus 5000 IU or 70–100 IU per kg body weight, followed by continuous infusion with dose adjustment based on patient response, monitored by activated clotting time or activated partial thromboplastin time) or subcutaneous low molecular weight heparin (e.g. enoxaparin 1 mg per kg twice daily) to prevent further embolization and thrombus propagation.

8.1.3.3. Surgical and interventional treatment

For a salvageable limb, urgent revascularization is essential. Diagnostic imaging, if it will not delay treatment, is recommended to guide therapy. If the limb is deemed unsalvageable, primary amputation or comfort care is indicated.

Different revascularization modalities can be applied, including percutaneous catheter-directed thrombolytic therapy, percutaneous mechanical thrombus extraction or thrombo-aspiration (with or without thrombolytic therapy), or surgical thrombectomy, bypass, and/or arterial repair.[642] Moreover, these modalities can be combined, with the strategy determined by factors such as neurological deficit, ischaemia duration, localization, size, aetiology, comorbidities, type of conduit (artery or graft), and therapy-related risks and outcomes. Current endovascular approaches to ALI boast high technical success rates.[626] To reduce morbidity and mortality, an endovascular-first approach is often preferred, especially in patients with severe comorbidities. Thrombus extraction, thrombo-aspiration, and surgical thrombectomy are indicated in cases of neurological deficit, while catheter-directed thrombolytic therapy is more appropriate in less severe cases without neurological deficit. Modern catheter-based thrombectomy (CDT) is associated with 12-month amputation rates of <10% in Rutherford IIB.[643] A meta-analysis showed that although CDT in the treatment of not immediately threatening ALI showed high angiographic success, the long-term outcomes were relatively poor, with low patency and a substantial risk of major amputation.[644] Systemic thrombolysis has no role in the treatment of patients with ALI.

A meta-analysis showed that CDT and surgery have similar limb salvage rates.[645] Recent analyses indicate benefits of endovascular approaches in terms of mortality at similar amputation rates.[646,647]

A comparison of percutaneous thrombectomy vs. ultrasound-accelerated thrombolysis for the initial management of ALI showed no difference in terms of amputation, bleeding, clinical success, and adverse events, with primary patency at 30 days of 82% and 71%, respectively.[629,648,649]

After thrombus removal, in cases of pre-existing arterial lesions, these should be treated by endovascular therapy or open surgery. If surgical treatment is required, it should be ideally performed in a hybrid room with capacity to allow sufficient completion angiographic imaging and initiation of local lysis if any remaining clot is visualized. Lower-extremity four-compartment fasciotomies should be performed in patients with long-lasting ischaemia to prevent post-reperfusion compartment syndrome.[637] The management of ALI is summarized in *Figure 16*.

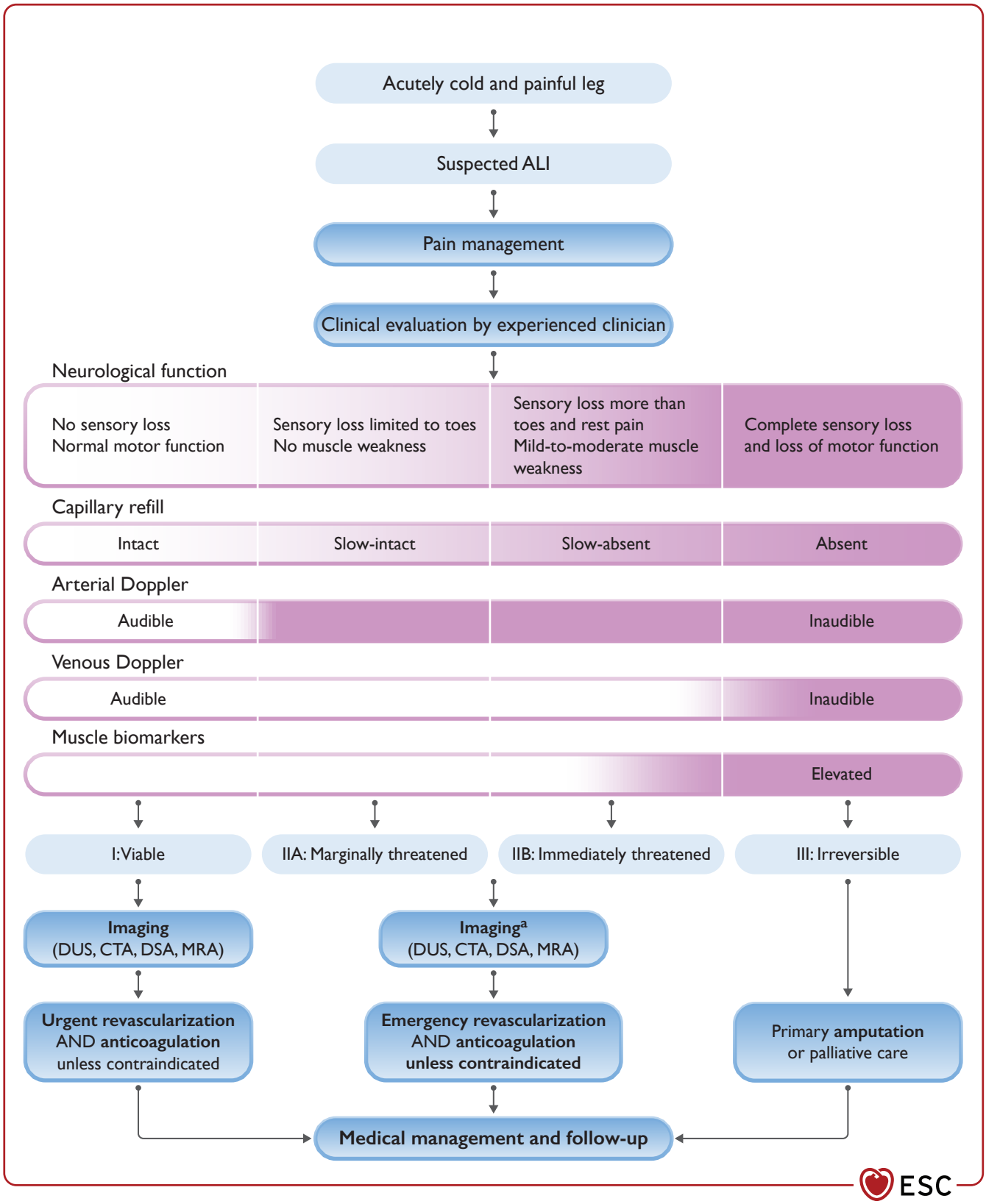

Figure 16 Management of acute limb ischaemia. ALI, acute limb ischaemia; CTA, computed tomography angiography; DSA, digital subtraction angiography; DUS, duplex ultrasound; MRA, magnetic resonance angiography. [a]Should not delay treatment.

8.1.3.4. Follow-up

After revascularization or amputation, haemodynamic success should be established, aetiology of ALI investigated, and OMT ensured. Statins improve outcomes after revascularization.[552,630] Since ALI is frequently caused by thrombo-embolism, Holter-ECG, echocardiogram, and aortic imaging are useful to allow initiation of appropriate therapy, in particular anticoagulation.[650] Additionally, consider other prothrombotic syndromes, such as antiphospholipid syndromes and vasculitis, if clinically suspected. While there is only sparse evidence, the inclusion of PAD patients after revascularization into structured follow-up may improve their functional outcomes.[627]

Recommendation Table 22 — Recommendations for the management of patients presenting with acute limb ischaemia (see also Evidence Table 8)

Recommendations	Class[a]	Level[b]
In patients with ALI, it is recommended that an urgent evaluation is performed by a vascular clinician with sufficient experience to assess limb viability and implement appropriate therapy.[635]	I	C
In cases of neurological deficit, urgent revascularization is recommended; diagnostic imaging is recommended to guide treatment, provided it does not delay treatment, or if the need for primary amputation is obvious.[422,635,651,652]	I	C
In the absence of severe neurological deficit, revascularization is recommended within hours of initial imaging in a case-by-case decision.[422,635,652]	I	C
Treatment with analgesics is recommended as soon as possible for pain control.	I	C
It is recommended to monitor for compartment syndrome after revascularization and treat (fasciotomy).[637,652]	I	C
It is recommended to assess clinical and haemodynamic success following revascularization.[627]	I	C
In patients with ALI, it is recommended to obtain a comprehensive medical history and determine the cause of thrombosis and/or embolization.[650]	I	C
In patients with ALI, following revascularization if not on anticoagulation for other reasons, DAPT or rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered.[514,653]	IIa	C
Upon confirmation of ALI diagnosis, treatment with heparin may be considered.[635,654–656]	IIb	C

ALI, acute limb ischaemia; b.i.d., twice daily; DAPT, dual antiplatelet therapy; DPI, dual pathway inhibition; o.d., once daily.
[a]Class of recommendation.
[b]Level of evidence.

8.2. Extracranial carotid and vertebral artery disease

8.2.1. Clinical presentation and diagnosis

8.2.1.1. Clinical presentation

Atherosclerotic CS represents one of the major causes of acute ischaemic stroke (20%).[657]

CS may be revealed by a cervical bruit, but also by a TIA or stroke.

8.2.1.2. Diagnosis

Atherosclerotic lesions are primarily located in specific arterial segments, including the carotid bifurcation, siphon, M1 segment of the middle cerebral artery, brachiocephalic trunk, subclavian artery, first and fourth segments of the vertebral artery, or first segment of the basilar artery. Carotid plaques (CP), originating in the intima, offer a better representation of the atherosclerotic process than carotid intima-media thickness (cIMT). CP may be diffuse or focal (protuberant). According to the Mannheim carotid plaque consensus, a CP is defined as a focal structure encroaching into the arterial lumen by ≥0.5 mm or ≥50% of the surrounding vessel.[658] The American Society of Echocardiography (ASE) recently proposed a definition that includes any focal thickening considered atherosclerotic in origin and encroaching into the lumen of any carotid artery segment (protuberant-type plaque) or, in the case of diffuse vessel wall atherosclerosis, when cIMT measures ≥1.5 mm in any carotid artery segment.[659] Plaques can progress to CS, defined as ≥50% narrowing of the extracranial internal carotid artery (ICA), with stenosis severity estimated using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method or its non-invasive equivalent assessed by DUS (*Figure 17*).[122,660] Other methods are described in the Supplementary data online, *Section 1.5*. The European Carotid Surgery Trial (ECST) and the area methods overestimate the severity of the CS and are not recommended.[77]

Carotid DUS is safe, accurate, and reliable if performed by a skilled vascular specialist. It is the first-line imaging modality for screening, diagnosis, and surveillance of extracranial carotid arteries.[77] The degree of stenosis is mostly based on Doppler analysis of blood flow in the common carotid artery (CCA), ICA, and external carotid artery (*Table 10*).[661,662] Vertebral and subclavian arteries must also be checked. In some cases, indirect signs of severe stenosis have to be evaluated by transcranial and/or ophthalmic artery Doppler. Severe arterial calcification can decrease DUS accuracy.[122]

Recommendation Table 23 — Recommendations for carotid artery stenosis assessment

Recommendations	Class[a]	Level[b]
It is recommended to use the NASCET method or its non-invasive equivalent to assess ICA stenosis.[77,122,660]	I	B
It is recommended to use DUS as first-line imaging to diagnose ICA stenosis.[77,663]	I	C
It is not recommended to use the ECST method for ICA stenosis assessment.[77,122,660]	III	C

DUS, duplex ultrasound; ECST, European Carotid Surgery Trial; ICA, internal carotid artery; NASCET, North American Symptomatic Carotid Endarterectomy Trial.
[a]Class of recommendation.
[b]Level of evidence.

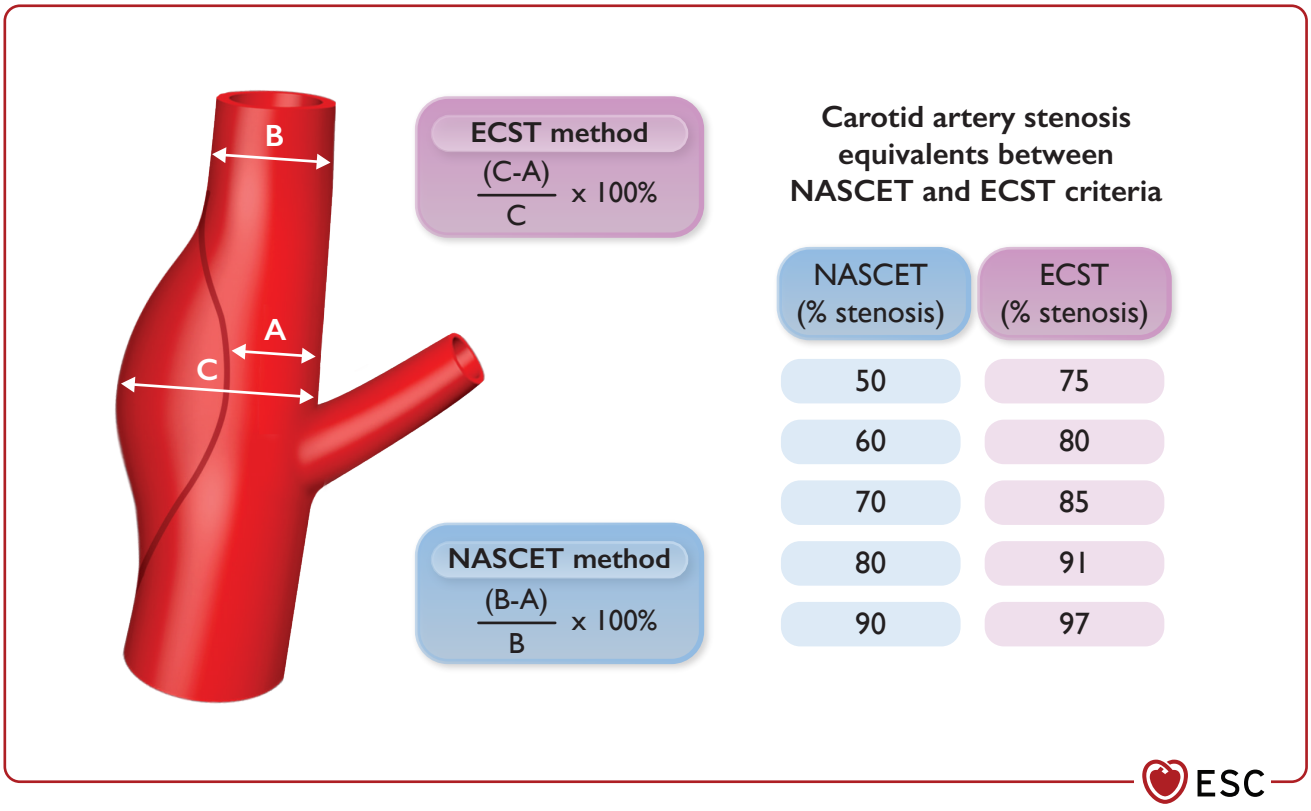

Figure 17 North American Symptomatic Carotid Endarterectomy Trial/European Carotid Surgery Trial methods. ECST, European Carotid Surgery Trial; NASCET, North American Symptomatic Carotid Endarterectomy trial.

Table 10 Peak systolic velocity criteria for grading internal carotid artery stenosis

% stenosis	Reference	50%–69% (moderate stenosis)	≥70% (severe stenosis)
PSV threshold	SRUCC[662] --- Gornik *et al.*[661]	125–230 cm/s --- ≥180 cm/s or ≥125 cm/s + PSV ICA/CCA ≥2	>230 cm/s --- Overestimation with SRUCC criteria but no consensus

CCA, common carotid artery; ICA, internal carotid artery; PSV, peak systolic velocity; SRUCC, Society of Radiologists in Ultrasound.

8.2.2. Asymptomatic carotid artery stenosis

8.2.2.1. Medical treatment

Optimal medical treatment is based on CVRF correction through lifestyle intervention and pharmacological treatment, with the goal of reducing cerebrovascular and global CV events.[19] Concerning hypertension, similar target values as those presented in the general section are recommended for patients with asymptomatic CS.

8.2.2.1.1. Lipid-lowering therapy. See *Section 7*.

8.2.2.1.2. Antihypertensive therapy. See *Section 7*.

8.2.2.1.3. Glucose-lowering therapy. See *Section 7*.

8.2.2.1.4. Antithrombotic therapy. The clinical benefit of antithrombotic treatment in patients with asymptomatic CS remains unproven.[664] The only RCT (the Asymptomatic Cervical Bruit Study [ACB]) addressing the issue enrolled only 188 patients per arm, and failed to show superiority of aspirin vs. placebo in reducing TIA, stroke, MI, or death.[665] In observational studies, SAPT (mainly low-dose aspirin) was associated with reduced risk of MACE, although data were conflicting for moderate stenosis (i.e. 50%–75%);[664] DAPT, combining aspirin and clopidogrel, has no benefit over SAPT.[496,497]

The Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial reported a non-significant decrease in MACE in patients with either history of carotid revascularization or asymptomatic patients with >50% CS and CVRFs allocated to dual antithrombotic therapy (aspirin 100 mg o.d. and rivaroxaban 2.5 mg b.i.d.)

vs. aspirin alone or rivaroxaban 5 mg b.i.d. alone. However, specific data on asymptomatic CS were not reported.

Since these patients present a two times higher risk of MI,[30] lifelong low-dose aspirin should be considered in asymptomatic CS patients at increased risk for CV events (i.e. diabetic patients) and low bleeding risk[497] to reduce stroke and CV risk.[19,299,488,666]

Recommendation Table 24 — Recommendations for antithrombotic treatment in patients with carotid stenosis

Recommendations	Class[a]	Level[b]
Carotid artery disease		
In patients with symptomatic CS, not undergoing carotid endarterectomy or stenting, DAPT with low-dose aspirin and clopidogrel (75 mg) is recommended for the first 21 days or longer, followed by clopidogrel 75 mg or long-term aspirin to reduce the risk of stroke.[667–669]	I	A
In patients with asymptomatic >50% CS, long-term antiplatelet therapy (commonly low-dose aspirin) should be considered if bleeding risk is low.[488,497,670,671]	IIa	C

CS, carotid artery stenosis; DAPT, dual antiplatelet therapy.
[a]Class of recommendation.
[b]Level of evidence.

8.2.2.2. Interventional treatment

8.2.2.2.1. Open surgery vs. medical therapy. The rationale for carotid endarterectomy (CEA) in asymptomatic CS stems from two trials that were published some time ago. The Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Asymptomatic Carotid Surgery Trial 1 (ACST-1) compared CEA with medical therapy in asymptomatic patients with 60%–99% CS.[672–674] In ACAS, 5 year rates of ipsilateral stroke/death under CEA vs. medical therapy were 5.1% vs. 11.0%. ACST-1 reported 5 year rates of any stroke of 6.4% vs. 11.8%, respectively. In a combined analysis of both trials, CEA conferred less benefit in women at 5 years.[675] At 10 years, however, ACST-1[674] reported that females benefit following CEA (absolute risk reduction [ARR] 5.8%) to the same extent as men (ARR 5.5%).

Medical treatment has advanced following the recruitment of patients in these trials.[672–676] A 60%–70% decline in annual stroke rates was also observed in medically treated patients in both trials over 1995 to 2010.[676] This reduction was attributed to better medical treatment and lower smoking incidence. The Stent Protected Angioplasty versus Carotid Endarterectomy study (SPACE-2) compared OMT alone against OMT plus CEA/carotid artery stenting (CAS) in asymptomatic patients with CS ≥70% according to ECST criteria. Due to slow recruitment, the study was underpowered. The 1 year rate of the major secondary endpoint was 2.5% after CEA, 3.0% after CAS, and 0.9% after OMT.[677] Incidence of any stroke or death from any cause within 30 days or any ipsilateral ischaemic stroke within 5 years (primary efficacy endpoint) was 2.5% with CEA plus OMT, 4.4% with CAS plus OMT, and 3.1% with OMT alone. Results from the Carotid Revascularization Endartectomy vs. Stenting Trial 2 (CREST-2) are awaited to clarify whether intervention is beneficial in the treatment of asymptomatic CS compared with modern OMT.

Table 11 High-risk features associated with increased risk of stroke in patients with asymptomatic internal carotid artery stenosis on optimal medical treatment

Clinical[a]	Contralateral TIA/stroke[681,682]
Cerebral imaging	Ipsilateral silent infarction[683–685]
Ultrasound/CT imaging	Stenosis progression (>20%)[340,684,685] Spontaneous embolization on transcranial Doppler (HITS)[341,686] Impaired cerebral vascular reserve[687,688] Large plaques[689,690] Echolucent plaques[136,691] Increased juxta-luminal black (hypoechogenic) area[689,690]
MRA[b]	Intraplaque haemorrhage[692,693] Lipid-rich necrotic core[694,695]

CT, computed tomography; HITS, high-intensity transient signal; MRA, magnetic resonance angiography; TIA, transient ischaemic attack.
[a]Age is not a predictor of poorer outcome.
[b]More than 40 mm^2 on digital analysis.

The ARR in stroke favouring surgery over OMT was only 4.6% at 10 years in ACST-1, indicating that 95% of asymptomatic patients ultimately underwent unnecessary interventions.[674,678]

A recent meta-analysis confirmed the role of modern OMT in reducing major stroke, combined stroke, and mortality in asymptomatic patients, suggesting that OMT has the potential to reduce the requirement for surgical intervention in patients with asymptomatic carotis stenosis.[679]

In conclusion, for invasive treatment of asymptomatic carotid stenosis, the overall risk reduction is low compared with OMT. Current data are not available to assess subgroups that may still benefit from intervention. However, there is a need to target revascularization in a subgroup of patients with clinical and/or imaging features that increase the risk for stroke on OMT (*Table 11*).[678,680]

Importantly, ACST-1 found no evidence that age >75 years at baseline was associated with any ipsilateral stroke reduction at 5–10 years.[676–678,696] Neither the ACAS nor ACST-1 studies found any evidence that stenosis severity or contralateral occlusion increased late stroke risk.[672,674,697] In a recent meta-analysis, increasing stenosis was associated with late ipsilateral stroke only in the presence of concomitant high-risk features.[698] The general algorithm of CS management is presented in *Figure 18*.[552]

8.2.2.2.2. Carotid revascularization: surgery vs. stenting. In a recent meta-analysis update on RCTs in asymptomatic patients comparing CEA vs. CAS, including altogether 7092 patients, CAS was associated with significantly higher rates of 30 day 'any' stroke and 30 day death/any stroke, while CEA was associated with significantly higher rates of 30 day MI. No significant differences were seen in 30 day death, 30 day disabling stroke, 30 day death/disabling stroke, or 30 day death/any stroke/MI when CAS was compared with CEA.[699] In the largest RCT, ACST-2, post-operative death and major stroke were similar (1.0%) between groups.[700,701]

No significant difference was found in the 5 and 10 year incidence of ipsilateral stroke and any stroke between CEA and CAS.[696,702,703] The 5 year non-procedural stroke rate in ACST-2 was 2.5% in each group for fatal/disabling stroke, and 5.3% with CAS vs. 4.5% with CEA for any stroke.[700,701]

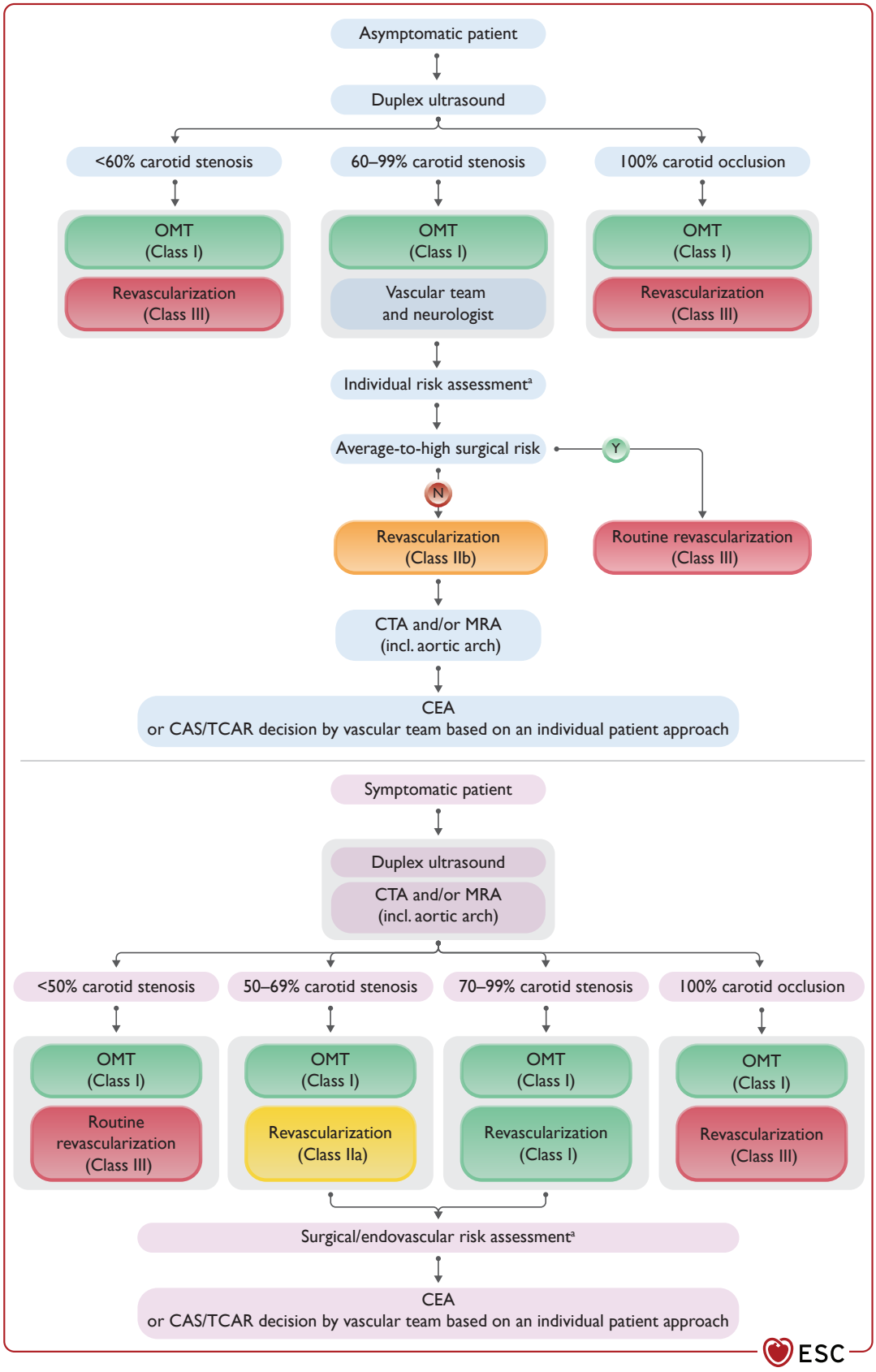

Figure 18 Algorithm of carotid artery stenosis management. CAS, carotid artery stenting; CEA, carotid endarterectomy; CTA, computed tomography angiography; MRA, magnetic resonance angiography; OMT, optimal medical treatment; TCAR, transcarotid artery revascularization; TIA, transient ischaemic attack. [a]Assess presence of high-risk features according to *Table 11*. If surgery/revascularization is considered, assess the overall risk related to surgery according to *Table 12*.

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial randomized symptomatic and asymptomatic patients deemed 'high-risk for surgery' to either CEA or CAS (using embolic protection devices).[704] Overall, 71% of SAPPHIRE patients were asymptomatic, and in these patients the 30 day rate of death/stroke after CAS was 5.8% vs. 6.1% after CEA[704]—both beyond the recommended 3%. If these procedural risk levels reflect contemporary practice, most 'high-risk for surgery' asymptomatic patients would be better treated medically.

A small sample size RCT has provided evidence that the use of a double-layer mesh stent can reduce the occurrence of peri-procedural diffusion-weighted imaging (DWI)-detected ischaemic lesion after carotid stents, when compared with conventional stents. At 1 year follow-up the use of a double-layer mesh stent was associated with a significant reduction in the composite endpoint of MACE and in-stent restenosis or occlusion. The clinical benefit of these findings has to be proven.[705,706]

Transcarotid artery revascularization (TCAR) has been introduced recently. Although no RCTs are available, large registry-based analyses report a 99.7% technical success rate and low 30 day complication rates (<3% in 30 day stroke/death and <1% MI).[681]

In a large-scale registry the 1 year rate of stroke or death was 6.4% for TCAR, 5.2% for CEA, and 9.7% for transfemoral carotid artery stenting (TFCAS).[707]

Properly conducted RCTs comparing TCAR with CEA in asymptomatic patients are required to establish the true place of TCAR in carotid revascularization.[708]

Recommendation Table 25 — Recommendations for interventional treatment in patients with asymptomatic carotid artery stenosis

Recommendations	Class[a]	Level[b]
When ICA revascularization is considered, documented peri-operative stroke/death rates should be <3% and the patient's life expectancy should be considered >5 years after careful consideration of the risks and benefits by a vascular team. [674,709]	IIa	B
In 'average surgical risk' patients over 75 years of age with a CS of 60%–99%, in the presence of high-risk features, CEA, in addition to OMT, should be considered.[674,709]	IIa	B
In 'high surgical risk' patients with a CS of 60%–99%, in the presence of high-risk features, CAS, in addition to OMT, may be considered.[699,701,704]	IIb	B
In 'average surgical risk' patients with a CS of 60%–99%, in the presence of high-risk features, CAS, in addition to OMT, may be considered as an alternative to CEA.[696,701,702,710]	IIb	B
In asymptomatic patients with ICA stenosis, in the absence of high-risk features and with a life expectancy <5 years, routine revascularization is not recommended.[674]	III	A

CAS, carotid artery stenting; CEA, carotid endarterectomy; CS, carotid artery stenosis; ICA, internal carotid artery; OMT, optimal medical treatment.
[a]Class of recommendation.
[b]Level of evidence.

8.2.3. Symptomatic carotid artery stenosis

8.2.3.1. Medical treatment

8.2.3.1.1. Lipid-lowering therapy. See *Section 7*.

8.2.3.1.2. Antihypertensive therapy. See *Section 7*.

8.2.3.1.3. Glucose-lowering therapy. See *Section 7*.

8.2.3.1.4. Antithrombotic therapy. Symptomatic CS is associated with a high risk of early recurrence of cerebrovascular ischaemic events.[667–669,683] DAPT with low-dose aspirin and clopidogrel is recommended for all patients with symptomatic CS for at least 3 months.[669] Those undergoing surgical revascularization can stop clopidogrel after surgery.[711] Those undergoing endovascular revascularization should continue DAPT with clopidogrel and low-dose aspirin for 4 weeks after the procedure.[488,666,711,712] In patients with stroke related to extracranial arterial disease, aspirin was more effective than VKAs in reducing recurrencies.[687,713] Subgroup analysis from the Acute Stroke or Transient Ischaemic Attack Treated with Aspirin or Ticagrelor and Patient Outcomes (SOCRATES) trial suggested a lower rate of MACE in patients receiving ticagrelor vs. aspirin;[689] however, this analysis was underpowered to make any conclusions regarding the benefit of ticagrelor.

A combination of aspirin and clopidogrel in the early phase of symptomatic carotid stenosis reduces asymptomatic cerebral embolization and stroke.[692,694,714] It also reduces stroke recurrence after a minor stroke/TIA.[667,668]

Recently, the Acute Stroke or Transient Ischaemic Attack Treated with Ticagrelor and acetylsalicylic acid for Prevention of Stroke and Death (THALES) trial showed a 17% reduction in the risk of death or stroke when using ticagrelor and aspirin vs. aspirin alone in patients with minor stroke or high-risk TIA;[715] however, bleeding events occurred more frequently in the ticagrelor plus aspirin group.[700,716] Of note, COMPASS data cannot be applied to symptomatic carotid stenosis since these patients were excluded because of intracranial bleeding risk.[499]

Recommendation Table 26 — Recommendations for evaluation and medical treatment in patients with symptomatic carotid artery stenosis

Recommendations	Class[a]	Level[b]
DAPT is recommended in the early phase of minor strokes in patients with ICA stenosis, if not revascularized, for at least 21 days, considering the bleeding risk.[667,668]	I	A
It is recommended that symptomatic ICA stenosis patients are assessed by a vascular team including a neurologist.[667,668]	I	C
Long-term treatment with SAPT should be considered following ICA revascularization.[667,668]	IIa	C
DAPT may be considered in the early phase of minor stroke in patients with ICA stenosis for up to 90 days, considering the bleeding risk.[667,668]	IIb	B

DAPT, dual antiplatelet therapy (aspirin and clopidogrel); ICA, internal carotid artery; SAPT, single antiplatelet therapy.
[a]Class of recommendation.
[b]Level of evidence.

8.2.3.2. Interventional treatment

8.2.3.2.1. Open surgery. Optimal medical treatment is recommended for all symptomatic patients with CS. In recently symptomatic patients with <50% stenosis, CEA (plus OMT) did not prevent stroke. However, surgery reduced stroke risk in patients with moderate (50%–69%) and severe (70%–99%) stenosis. The benefit from surgery increased with increasing severity of stenosis, except for 'near-occlusion' lesions (95%–99% stenosis with distal ICA collapse or a narrow calibre lumen with 'trickle flow').[660,717–720]

Some features are associated with a higher increase of stroke in symptomatic patients (50%–99% stenosis) medically treated: age (>75 years), symptoms within 14 days, male sex, hemispheric (vs. retinal) symptoms, cortical (vs. lacunar) stroke, increasing comorbidities, irregular stenosis, stenosis severity, contralateral occlusion, tandem intracranial stenosis, and failure to recruit intracranial collaterals.[721]

Large-scale registries suggest that CEA can be performed safely in the first 7 days after TIA/minor stroke.[722–724] However, not all patients benefit from urgent revascularization, and controversy exists over the safety of performing CEA within the first 48 h after symptom onset due to an increased risk of haemorrhagic transformation. Higher-risk patients include those with acute carotid occlusion, a persisting major neurological deficit, an area of middle cerebral artery infarction exceeding one-third, evidence of pre-existing parenchymal haemorrhage, and signs of impaired consciousness.[724,725]

The choice to perform carotid revascularization within 48 h from symptom onset is still debatable.[726]

Table 12 High-risk peri-operative features for carotid endarterectomy

Clinical
Congestive heart failure (NYHA functional class III/IV)
Unstable angina (CCS III/IV)
CAD with LM or >1 vessel with 70% stenosis
Recent MI (<30 days)
Planned open heart surgery (<30 days)
LVEF <30%
Severe pulmonary disease
Severe renal disease
Anatomical
Surgically inaccessible lesions • At or above C2 • Below the clavicle
Ipsilateral neck irradiation
Spinal immobility of the neck
Contralateral carotid artery occlusion (increases risk for stroke)
Contralateral laryngeal palsy
Tracheostomy

CAD, coronary artery disease; CCS, Canadian Cardiovascular Society; LM, left main; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association.

8.2.3.2.2. Endovascular therapy vs. open surgery. Contemporary RCTs comparing CEA with CAS in symptomatic patients reported a significantly higher risk of 30 day 'any stroke' and 'death/stroke' following CAS. This is mainly due to higher rates of minor stroke, which were non-disabling and resolved within 6 months.[711,727]

However, the occurrence of a peri-operative stroke is associated with three-fold poorer long-term survival,[727] similar to a post-procedural MI (which was more frequent after CEA).[728]

In CAS patients, the risk increased in those aged >60 years, especially for those aged >80 years, who are four times more likely to experience a procedural stroke/death. When comparing CAS with CEA, the age-related effect became apparent in patients aged 60–65 years, and CEA is superior to CAS in patients aged >70 years.[729,730]

Elderly CAS patients may experience more peri-operative strokes, mainly minor ipsilateral strokes, possibly due to a higher burden of aortic arch disease. In these cases, operator/institution experience may play a role in determining peri-procedural outcomes. CAS is associated with significantly lower risks for MI, transient cranial nerve injury, and haematoma.[731,732]

Beyond the 30 day peri-operative period, long-term data suggest that outcomes after CAS are similar to those with CEA.[703,733] The predicted magnitude of 30 day risk (according to clinical/anatomical characteristics and operator/centre experience) will thus largely determine whether CEA or CAS is preferable in individual patients.

Post-hoc trial analysis revealed enhanced benefits of CEA when performed within 2 weeks of the ischaemic event,[734] with reduced complications compared with CAS performed within 1 week of stroke/TIA. The Carotid Stenosis Trialists' Collaboration found a higher stroke/death rate (8.3% with CAS vs. 1.3% with CEA) for CAS in patients treated within 1 week of the last symptomatic event.[735] These findings support a preference for early CEA in symptomatic patients. However, these trials, initiated over 30 years ago, lack evaluation of current OMT. Initially designed as an alternative for high surgical risk (HSR) patients,[704,736] carotid stenting's efficacy needs consideration in contemporary practice (*Table 12*).[735]

In conclusion, CEA is still the treatment choice for patients with symptomatic carotid stenosis. However, in patients eligible for carotid revascularization but deemed high surgical risk by a multidisciplinary team, CAS may be preferred over CEA—the patient must be a suitable candidate for CAS, and the complication rate should not surpass 6%.

At present, TCAR results have been analysed in registries only. In these studies, in-hospital stroke/death has been significantly lower after TCAR compared with transfemoral CAS.[707,737] Similar to the previous results established for CEA, symptomatic patients undergoing TCAR demonstrate similar outcomes if the procedure is performed >48 h after the neurological event.[738] However, TCAR has not yet been evaluated in RCTs and has not been compared with CEA or OMT.

8.2.3.2.3. Vertebral arteries. The evidence on the use of lifestyle modifications and medical therapy in cases of symptomatic vertebral artery stenosis is lacking, but their use is reasonable given the overall CV risk in these patients.

Evidence on the use of preventive strategies and antithrombotic agents is lacking, but their use is reasonable in the presence of other CVRFs.

Surgery on extracranial vertebral stenosis (with transposition to CCA, trans-subclavian vertebral endarterectomy, distal venous bypass) can be performed with low stroke/death rates in experienced centres.[739,740] However, with limited expertise in complex vertebral artery reconstructions, open surgery has been mostly replaced by endovascular interventions.

In a combined analysis of the the Vertebral Artery Ischaemia Stenting Trial (VIST), the Vertebral Artery Stenting Trial (VAST), and the Stenting and Aggressive Medical Management for Preventing

Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial,[741] no clear benefit was shown for extracranial vertebral artery stenting.

Randomized controlled trials have not assessed surgical techniques like vertebral artery endarterectomy or transposition. While case series exist, they often lack a control group following a consistent medical treatment protocol.[742] As a result, the effectiveness of these procedures remains uncertain.

Recommendation Table 27 — Recommendations for interventions in patients with symptomatic carotid artery stenosis

Recommendations	Class[a]	Level[b]
It is recommended to perform CEA of symptomatic 70%–99% ICA stenosis provided a documented 30 day risk of procedural death/stroke is <6%.[660,719]	I	A
If indicated, it is recommended to perform CEA within 14 days in symptomatic ICA stenosis patients.[734]	I	B
OMT is recommended for all symptomatic ICA stenosis patients.[19]	I	A
CEA of symptomatic 50%–69% ICA stenosis should be considered provided a documented 30 day risk of procedural death/stroke is <6%.[660,719]	IIa	A
For symptomatic patients at high risk for CEA with a 70%–99% ICA stenosis, CAS should be considered provided a documented 30 day risk of procedural death/stroke is <6%.[703]	IIa	B
For symptomatic patients <70 years of age with a 70%–99% ICA stenosis, CAS may be considered provided a documented 30 day risk of procedural death/stroke is <6%.[703]	IIb	A
Revascularization is not recommended in patients with ICA lesions <50%.[660,719]	III	A

CAS, carotid artery stenting; CEA, carotid endarterectomy; ICA, internal carotid artery; OMT, optimal medical treatment.
[a]Class of recommendation.
[b]Level of evidence.

8.2.3.3. Follow-up

Peri-operative and post-procedural medical management after carotid revascularization should include OMT. Post-operative hypertension is a risk factor for stroke and TIAs, wound bleeding, and intracranial haemorrhage.[743] Therefore, proper pharmacological BP control is important in optimizing outcomes.[744]

Fluctuations of hypertension and hypotension are not uncommon and should be treated promptly.[744,745]

An intensive lipid-lowering therapy (ILT) aiming at >50% LDL-C reduction and LDL-C <1.4 mmol/L (55 mg/dL) is also recommended.[19]

Antiplatelet therapy should be tailored according to type of intervention. In CEA, the reduction in peri-procedural and long-term ischaemic events under low-dose aspirin has been demonstrated.[746,747] After carotid stenting, DAPT (aspirin and clopidogrel) is recommended, while optimal duration is debated.[748] In the peri-operative period after CAS, DAPT should be prescribed and continued for at least 30 days post-procedure.[77,749,750] Ticagrelor, when included in DAPT following CAS/TCAR, presents a drawback due to its elevated bleeding risk compared with clopidogrel.[751–753]

Duplex ultrasound is the first-line technique to evaluate patients after CEA or CAS. CTA and MRA are alternative methods for determining restenosis.[749,754]

After CEA or CAS, DUS is recommended at baseline (<3 months) and annually thereafter until the patient is stable (i.e. until no restenosis is observed in two consecutive annual scans). Regular surveillance (e.g. every 2 years) can be performed based on the stenosis of the contralateral ICA, risk profile, and patient's life expectancy.[749,754]

For patients combining multiple CVRFs after the procedure, DUS may be beneficial every 6 months until a stable clinical pattern is established, and annually thereafter.[749,754]

Early surveillance, especially within 1–3 months and particularly in cases where intraoperative completion imaging is absent (e.g. after CEA), aids in detecting technical errors and setting a baseline for future comparisons.

Follow-up enables the identification of ipsilateral carotid restenosis and contralateral disease progression, offering a chance for timely intervention to minimize the risk of stroke. Nevertheless, this concept is facing growing challenges due to a reduced and selective role for intervention in asymptomatic patients. A surveillance protocol holds significance when anticipated outcomes are expected to cost-effectively influence a medical or interventional treatment plan.[749,754]

Recommendation Table 28 — Recommendations for follow-up in patients with carotid artery stenosis

Recommendations	Class[a]	Level[b]
Once-yearly follow-up is recommended to check for CVRFs and treatment compliance.[754]	I	A
After ICA stent implantation, DAPT with aspirin and clopidogrel is recommended for at least 1 month.[77,749,750]	I	A
After ICA revascularization, long-term aspirin or clopidogrel is recommended.[746,747]	I	B
During follow-up, it is recommended to assess neurological symptoms, CVRFs, and treatment adherence at least yearly in patients with CS.[754]	I	C
After ICA revascularization, surveillance with DUS is recommended within the first month.[749,754]	I	C

CS, carotid artery stenosis; CVRFs, cardiovascular risk factors; DAPT, dual antiplatelet therapy; DUS, duplex ultrasound; ICA, internal carotid artery.
[a]Class of recommendation.
[b]Level of evidence.

8.3. Other arterial locations

8.3.1. Subclavian artery disease

8.3.1.1. Clinical presentation and diagnosis

Atherosclerotic upper-limb artery disease (UEAD) is most frequently located in the subclavian artery.[755,756] Digital ischaemia is most frequently caused by non-atherosclerotic aetiologies, including thromboembolism, systemic sclerosis, idiopathic, thromboangiitis obliterans, iatrogenic, or cancer.[757] Isolated subclavian stenosis (SS) is often asymptomatic and may be suspected because of an absolute inter-arm SBP difference >10–15 mmHg.[758] In the Multi-Ethnic Study of Atherosclerosis (MESA), prevalence of asymptomatic SS was approximately 4.5% (male: 5.1%, female: 3.9%) in adults and more frequent in patients with PAD (11.4%).[759] In patients attending CV clinics, a

>25 mmHg SBP difference doubles prevalence and independently predicts mortality.[32,758] As obstructive disease progresses, particularly affecting vertebral vessels, the risk of ischaemia or steal symptoms significantly rises. Visual disturbances, syncope, ataxia, vertigo, dysphasia, dysarthria, and facial sensory deficits during arm movements may indicate subclavian steal syndrome, correlating with inter-arm BP difference.[760] Brachiocephalic occlusive disease can lead to stroke or TIA in carotid and vertebral territories, manifesting as exercise-induced fatigue, pain, and arm claudication. Severe cases, especially with distal disease, may result in rest pain and digital ischaemia with necrosis.

Duplex ultrasound assessment of subclavian arteries enables the detection of SS via intrastenotic high-velocity flows (50% stenosis: peak systolic velocity [PSV] ≥230 cm/s, PSV ratio [PSVr] ≥2.2; 70% stenosis PSV ≥340 cm/s and PSVr ≥3.0) or monophasic post-stenotic waveforms.[761] The majority of patients (>90%) with at least 50% proximal SS have either intermittent or continuous flow reversal in the vertebral artery, though not all will be symptomatic.[760,762] When subclavian steal syndrome is suspected, flow reversal should be assessed in the ipsilateral extracranial vertebral artery by hyperaemia testing and if available transcranial Doppler.[762] Severe stenosis or occlusion of the right brachiocephalic trunk is associated with reduced flow velocities in the ipsilateral subclavian artery and the CCA. Abnormal or doubtful DUS should lead to anatomic imaging (CTA/MRA).[763] CTA is excellent for supra-aortic lesions and can provide extravascular information, especially when thoracic outlet syndrome is a differential diagnosis. MRA provides both functional and morphological information useful to distinguish antegrade from retrograde perfusion and to estimate stenosis severity.[764] DSA is performed if endovascular therapy is indicated. PET is useful for the diagnosis of arteritis but not for assessment of atherosclerotic lesions in clinical practice.

8.3.1.2. Treatment strategy (medical and interventional)

Optimal medical treatment is recommended in all patients with symptomatic UEAD to reduce CV risk.[32] Revascularization is indicated in symptomatic patients with TIA/stroke, coronary subclavian steal syndrome, ipsilateral haemodialysis access dysfunction, or impaired HRQoL. Revascularization should be considered in asymptomatic patients with planned coronary artery bypass grafting (CABG) using the internal mammary artery and those with ipsilateral haemodialysis access, as well as asymptomatic patients with significant bilateral SS/occlusion for adequate BP surveillance. For revascularization, both endovascular and surgical procedures are available. There are no RCTs comparing endovascular vs. open repair but individual studies, including the Danish Vascular Registry, indicate similar long-term symptom resolution but higher general complication rates and hospital length of stay for open surgery.[765] The risk of severe complications, including vertebrobasilar stroke, is low with both approaches. The post-procedural stroke rate is reported at 1.3% for endovascular therapy[765] and 0.9%–2.4% after open surgery.[765–767]

Percutaneous angioplasty for subclavian arterial stenosis is often used with stenting. There is no conclusive evidence to determine whether stenting is more effective than balloon angioplasty.[768] Similar results were reported for endovascular therapy of the innominate artery.[769] In heavily calcified ostial lesions, balloon-expandable stents give more radial force than nitinol stents. An endovascular approach is often the default strategy. However, in selected patients with low operative risk, with subclavian artery occlusion or after endovascular therapy failure, surgical subclavian–carotid transposition is safe with excellent long-term patency results (5 year patency 96%).[766] Carotid–subclavian bypass surgery with a prosthetic graft showed long-term benefit with low operative mortality and morbidity, especially in patients with extensive disease or re-occlusion after stenting (5 year patency 97%).[770] Other options are extrathoracic extra-anatomic bypass procedures (axillo-axillary, carotid–axillary, or carotid–carotid bypass);[771,772] however, axillo-axillary bypasses may occlude at 1 year in 14% of cases.[773] The transthoracic approach is an option in patients with multivessel disease involving the aortic arch and several supra-aortic vessels.[767]

While critical hand ischaemia owing to below-the-elbow atherosclerotic occlusive disease is relatively uncommon, interventions are associated with a high rate of success, major amputations are rare, and many can be treated non-operatively.[756] In appropriately selected patients, both endovascular and open interventions have a high rate of success.[755,756]

In symptomatic patients with contraindications for endovascular therapy or open surgery, prostanoid infusion or thoracic sympathectomy may be considered.[774]

8.3.1.3. Follow-up

Patients with UEAD should be followed up to ensure optimal CV prevention. Tighter follow-up is required in symptomatic patients to reassess indication for revascularization as a large proportion of symptoms resolve spontaneously.[775] After revascularization, patients should be followed up to allow early detection and treatment of impending late procedural failure.

Recommendation Table 29 — Recommendations for the management of subclavian artery stenosis (see also Evidence Table 9)

Recommendations	Class[a]	Level[b]
Bilateral arm BP measurement is recommended for all patients with PAAD.[32,758]	I	B
In symptomatic patients with atherosclerotic subclavian artery disease (TIA/stroke, coronary subclavian steal syndrome, ipsilateral haemodialysis access dysfunction, severe ischaemia), both revascularization options (endovascular ± stenting or surgery) should be considered and discussed case by case by a vascular team.[776]	IIa	B
Endovascular revascularization may be considered over surgery, despite similar long-term outcomes, due to lower complication rates.[765]	IIb	B
In patients with atherosclerotic subclavian artery disease, revascularization:		
Should be considered in cases of proximal stenosis in patients undergoing CABG using the ipsilateral internal mammary artery.[777–781]	IIa	C
Should be considered in cases of proximal stenosis in patients who already have the ipsilateral internal mammary artery grafted to coronary arteries with evidence of myocardial ischaemia.[777,778,780]	IIa	C
Should be considered in cases of ipsilateral haemodialysis arteriovenous access.[778]	IIa	C
Routine revascularization in patients with atherosclerotic subclavian artery disease is not recommended.[776]	III	C

BP, blood pressure; CABG, coronary artery bypass grafting; PAAD, peripheral arterial and aortic diseases; TIA, transient ischaemic attack.
[a]Class of recommendation.
[b]Level of evidence.

8.3.2. Renal artery disease

8.3.2.1. Clinical presentation and diagnosis

8.3.2.1.1. Epidemiology. In >90% of cases, RAS is caused by atherosclerosis and typically involves the ostial renal arterial segment (*Table 13*).[782] Above 65 years of age, overall prevalence of ≥60% RAS is 6.8%, with a higher prevalence in men (9.1%) than in women (5.5%).[783] In patients with PAD, RAS prevalence ranges between 7% and 42%, influenced by diagnostic criteria.[784]

8.3.2.1.2. Clinical presentation. Clinical presentation comprises renovascular hypertension, renal function impairment and eventually, flash pulmonary oedema (*Table 13*). RAS reduces the filtration capacity of the affected kidney, which activates the renin–angiotensin–aldosterone pathway, potentially resulting in renovascular hypertension.[782,785] In unilateral RAS, the functioning contralateral kidney may increase sodium excretion to prevent sodium retention and volume overload. In high-grade bilateral RAS or in unilateral RAS without a functioning second kidney, the risk of cardiorenal deterioration is higher than in unilateral disease.[786]

8.3.2.1.3. Diagnosis of renal artery disease. First diagnostic steps include laboratory tests to examine renal function, analysis of office and out-of-office BP recordings (ambulatory BP monitoring or home BP monitoring, as recommended by [upcoming] ESC/European Society of Hypertension [ESH] Guidelines for arterial hypertension), and non-invasive haemodynamic assessment of renal arteries by DUS.[787]

Renal artery PSV >200 cm/s measured by DUS allows the diagnosis of a >50% RAS (sensitivity 95%, specificity 90%).[788] A renal-aortic peak flow velocity ratio (RAR = renal artery PSV/aortic PSV) >3.5 has 84%–91% sensitivity and 95%–97% specificity for the detection of ≥60% RAS.[789] A side-to-side difference of the intrarenal resistance index ≥0.5 between both kidneys may serve as an additional haemodynamic criterion for haemodynamically relevant RAS.[787,790] Other DUS criteria (acceleration time, acceleration index) have lower diagnostic accuracy.[791]

Sensitivity and specificity of contrast-enhanced MRA in the diagnosis of RAS is 88% and 100%, respectively;[789] however, MRA overestimates the degree of RAS by 26%–32%.[789] The advantages of MRA are the possibility of assessing renal parenchymal blood flow and freedom from radiation and iodinated contrast agents.

Spiral multidetector CTA allows renal artery diameter measurements and provides information on vessel wall calcification and mural plaques. RAS diagnosis by CTA presents 64%–100% sensitivity and 92%–98% specificity.[789] CTA drawbacks include radiation exposure, the need for contrast media in patients with impaired renal function, and limited haemodynamic assessment of RAS.

Catheter angiography is the gold standard for diagnosing RAS, enabling additional haemodynamic measures (*Figure 19*).[792] Considering the potential risks of invasive procedures, DUS and other non-invasive modalities (CTA or MRA) should precede catheter angiography and invasive haemodynamic measurements (*Figure 19*).

Renal scintigraphy, plasma renin measurements before and after ACEI provocation, and venous renin measurements are not considered for RAS evaluation.

8.3.2.1.4. Prognosis. Atherosclerotic RAS progresses with respect to the degree of stenosis, while total renal artery occlusions occur less frequently.[793] The presence of significant RAS is a strong predictor for mortality[794] and renovascular disease is an important risk factor for the development of end-stage renal disease (ESRD).[795] The risk of RAS-related ESRD is higher in men than in women and increases with age.[795]

Table 13 Clinical signs suggestive of renal artery disease

Hypertension onset before 30 years of age
Severe hypertension after the age of 55 years, when associated with CKD or heart failure
Hypertension and abdominal bruit
Rapid and persistent worsening of previously controlled hypertension
Resistant hypertension • Three antihypertensive drugs including a diuretic agent or • ≥4 antihypertensive drugs and • Other secondary form unlikely
Hypertensive crisis (i.e. acute renal failure, acute heart failure, hypertensive encephalopathy, or grade 3–4 retinopathy)
New azotaemia or worsening of renal function after treatment with RAAS blockers
Unexplained atrophic kidney or discrepancy in kidney size, or unexplained renal failure
Flash pulmonary oedema

CKD, chronic kidney disease; RAAS, renin–angiotensin–aldosterone system.

8.3.2.2. Treatment strategy (medical and interventional)

8.3.2.2.1. Medical therapy. Optimal medical treatment is recommended in RAS patients.[785] Data on antithrombotic therapy in patients with atherosclerotic RAS are scarce and retrospective.[796] However, the use of an antiplatelet agent is reasonable in atherosclerotic RAS.

No prospective study has specifically examined antithrombotic therapy post-RAS stenting, and information from existing RAS stenting trials is limited.[797] Following the antithrombotic treatment approach in non-coronary arterial beds, it is suggested to use DAPT for at least 1 month after RAS stent implantation.[666]

8.3.2.2.2. Revascularization. Revascularization in atherosclerotic RAS

Prospective RCTs comparing endovascular revascularization with OMT in atherosclerotic RAS favoured renal artery stenting over balloon angioplasty.[792]

However, renal artery stenting showed no superiority over OMT in reducing BP, CV events, renal events, or mortality in unilateral atherosclerotic RAS.[788,798,799] A trial suggested a potential benefit of renal artery angioplasty for BP in bilateral RAS, but subsequent RCTs did not confirm this.[800–802] Data on the benefit of renal artery stenting in sparing antihypertensive drugs are inconsistent.[324,800,801,803,804]

In specific circumstances or RAS aetiologies, revascularization should be considered (*Figure 19*). Open surgical renal artery revascularization appears comparable to endovascular treatment regarding BP and renal function.[805,806] Thus, open surgery can be an alternative approach in cases with a revascularization indication and complex anatomy or failed endovascular repair.

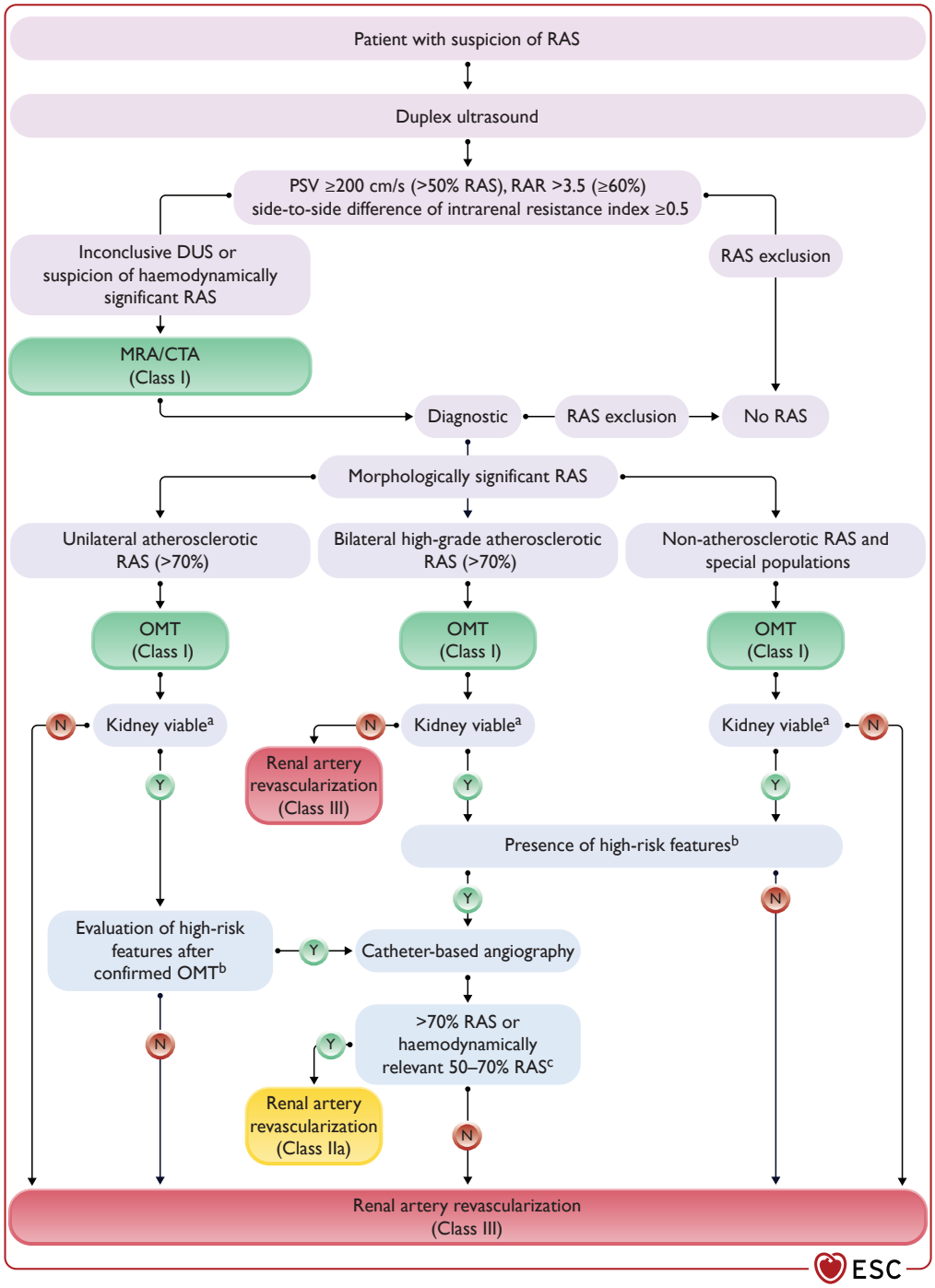

Figure 19 Diagnostic and treatment algorithm for renal artery stenosis. CTA, computed tomography angiography; MRA, magnetic resonance angiography; OMT, optimal medical treatment; Pd/Pa, distal coronary pressure to aortic pressure ratio; PSV, peak systolic velocity; RAR, renal-aortic peak flow velocity ratio; RAS, renal artery stenosis.
[a]see table below

[a]Kidney viability in RAS		
	Signs of viability	Signs of non-viability
Renal size	>8 cm	<7 cm
Renal cortex	Distinct cortex (>0.5 cm)	Loss of corticomedullar differentiation
Proteinuria	Albumin-creatinine ratio <20 mg/mmol	Albumin-creatinine ratio >30 mg/mmol
Renal resistance index	<0.8	>0.8

[b]Rapidly progressive, treatment-resistant arterial hypertension; rapidly declining renal function; flash pulmonary oedema; solitary kidney.
[c]Resting mean pressure gradient >10 mmHg; systolic hyperaemic pressure gradient >20 mmHg; renal PdPa ≤ 0.9 (or 0.8).

8.3.2.3. Follow-up

Following the diagnosis of significant RAS and the implementation of OMT and/or renal artery revascularization, regular follow-up exams are crucial. Monitoring should encompass laboratory tests to assess renal function, analysis of office and out-of-office BP recordings (ambulatory or home BP monitoring per upcoming ESC/ESH Guidelines for arterial hypertension), and renal artery DUS. DUS, comprising renal PSV, RAR, side-to-side difference of the resistance index, and kidney size, is the preferred imaging modality during follow-up.[787]

In conservatively managed RAS patients, follow-up assessment should re-evaluate potential indications for renal artery revascularization (*Figure 19*).

After renal artery stenting, the initial follow-up is recommended at 1 month and subsequently every 12 months or when new signs or symptoms arise.[807] Re-intervention may be considered for in-stent restenosis ≥60% detected by DUS, recurrent signs and symptoms (diastolic BP >90 mmHg on >3 antihypertensive drugs, or a >20% increase in serum creatinine).[787,808]

Recommendation Table 30 — Recommendations for diagnostic strategies for renal artery disease

Recommendations	Class[a]	Level[b]
DUS is recommended as the first-line imaging modality in patients with suspicion of RAS.[787,789–791]	I	B
In cases of DUS-based suspicion of RAS or inconclusive DUS, MRA, or CTA are recommended.[789,791]	I	B
In patients with atherosclerotic RAS, it is recommended to assess clinical high-risk features and kidney viability when evaluating renal artery revascularization.[809,810]	I	B

CTA, computed tomography angiography; DUS, duplex ultrasound; MRA, magnetic resonance angiography; RAS, renal artery stenosis.
[a]Class of recommendation.
[b]Level of evidence.

Recommendation Table 31 — Recommendations for treatment strategies for renal artery disease (see also Evidence Table 10)

Recommendations	Class[a]	Level[b]
Medical therapy		
In patients with atherosclerotic RAS the use of low-dose aspirin may be considered.[811]	IIb	C
Revascularization		
In patients with atherosclerotic unilateral >70% RAS, concomitant high-risk features, and signs of kidney viability, renal artery revascularization should be considered after OMT has been established.[798,809,810]	IIa	B
In patients with atherosclerotic bilateral (>70%) RAS or RAS in a solitary kidney, concomitant high risk features, and signs of kidney viability, renal artery revascularization should be considered.[800–802]	IIa	B
In patients with hypertension and/or signs of renal dysfunction due to RAS caused by fibromuscular dysplasia, concomitant high-risk features, and signs of kidney viability, revascularization with primary balloon angioplasty and bailout stenting should be considered.[812,813]	IIa	B
In patients with an indication for renal artery revascularization and complex anatomy, or after failed endovascular revascularization, open surgical revascularization should be considered.[805,806]	IIa	B
In patients with atherosclerotic unilateral RAS, routine revascularization is not recommended.[324,800–804,814]	III	A

Continued

RAS, renal artery stenosis.
[a]Class of recommendation.
[b]Level of evidence.

8.3.3. Visceral artery disease

8.3.3.1. Acute mesenteric ischaemia

Acute mesenteric ischaemia can be caused by arterial embolism or thrombosis *in situ*, non-occlusive mesenteric ischaemia (usually due to superior mesenteric artery [SMA] vasoconstriction), and venous thrombosis. In recent decades, embolism decreased from 46% to 35%, while arterial thrombosis increased from 20% to 35%.[815–817] Acute thrombo-embolic occlusion most frequently affects the SMA. Due to extensive collaterals, it infrequently leads to intestinal infarction.

8.3.3.1.1. Clinical presentation and diagnosis. Clinical examination

Early diagnosis of AMI is based on high clinical suspicion. Embolic AMI typically manifests as sudden onset intense abdominal pain, accompanied by minimal physical findings, bowel emptying (vomiting, diarrhoea), and a common embolic source (primarily AF).[818–820] Emboli may also lodge in other locations, aiding diagnosis. Acute arterial thrombosis tends to occur in areas with pre-existing atherosclerotic disease, resulting in a less dramatic clinical presentation. Patients may have previous symptoms of chronic mesenteric ischaemia (CMI) or other atherosclerotic manifestations.[821]

Laboratory tests are unreliable for the diagnosis of AMI, although elevated levels of l-lactate, leucocytosis, and D-dimer (DD) may exist.[822–825]

Imaging

Computed tomography angiography is the gold standard for diagnosis,[826,827] allowing the detection of thrombi and/or emboli in the SMA trunk or its branches together with the recognition of intestinal ischaemic signs. A plain abdominal X-ray lacks specificity. A normal result does not rule out the diagnosis.[828]

8.3.3.1.2. Treatment strategy. Most patients require immediate revascularization to survive. There are no RCTs comparing surgical vs. endovascular intervention in AMI. Two meta-analyses found endovascular revascularization to be superior to surgical intervention in terms of in-hospital mortality and rates of bowel resection.[829,830] An open surgical approach is most appropriate in centres where endovascular interventions are less available and in patients with peritonitis.[831] Retrograde open mesenteric stenting (ROMS) is an alternative that offers shorter operative time; the SMA is punctured in the open abdomen, followed by stenting.[832]

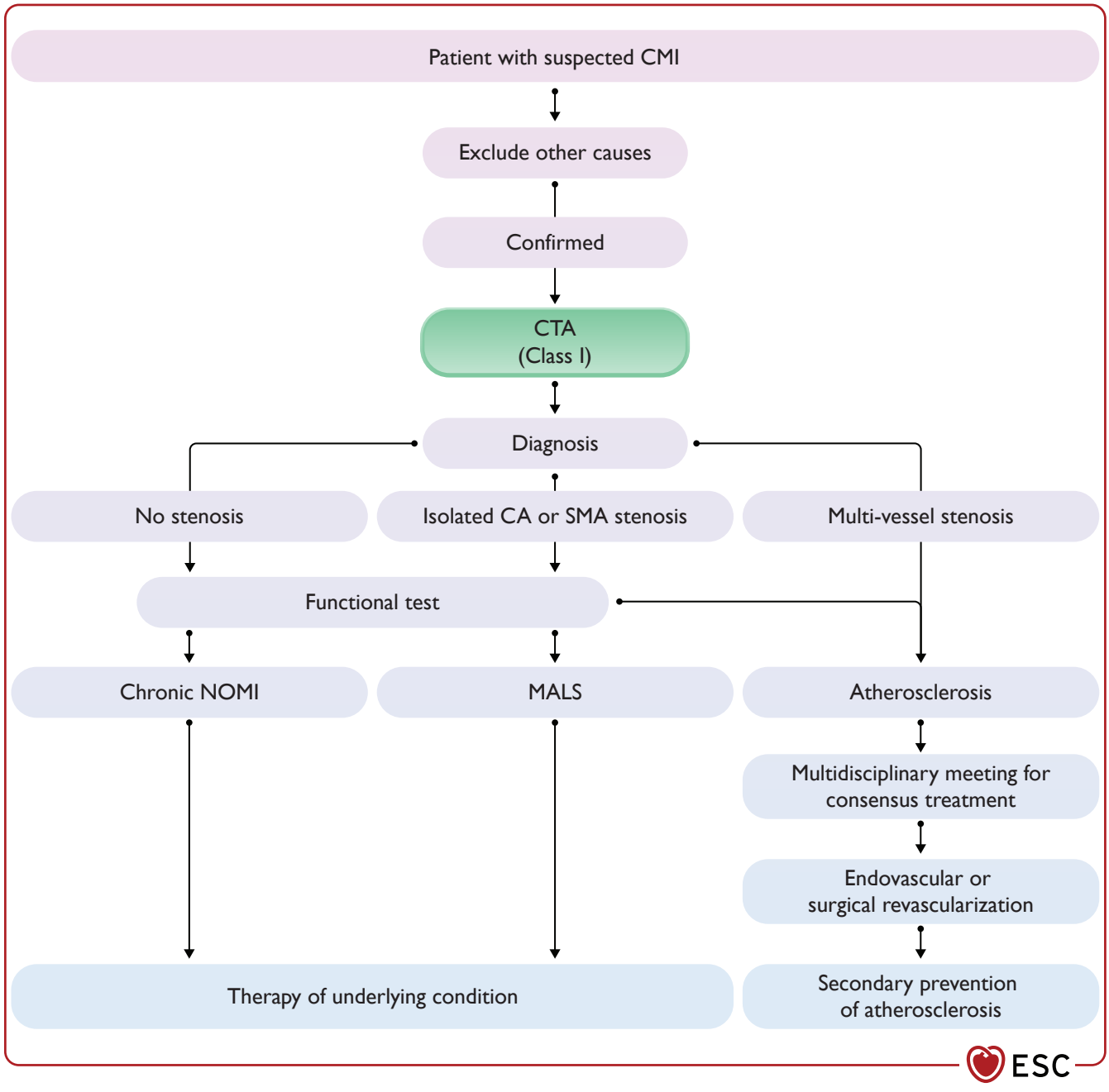

Figure 20 Algorithm of chronic mesenteric ischaemia management. CA, coeliac artery; CMI, chronic mesenteric ischaemia; CTA, computed tomography angiography; MALS, median arcuate ligament syndrome; NOMI, non-occlusive mesenteric ischaemia; SMA, superior mesenteric artery.

8.3.3.1.3. Follow-up. Most patients treated for AMI require lifelong anticoagulant/antiplatelet therapy to prevent recurrence. Patients undergoing revascularization should have surveillance with CTA or DUS within 6 months,[833] as recurrent AMI after mesenteric revascularization accounts for 6%–8% of late deaths.[834] Current Society for Vascular Surgery (SVS) Guidelines recommend DUS at 1, 6, and 12 months after the intervention, and then annually thereafter.[754]

8.3.3.2. Chronic mesenteric artery disease

Occlusive CMI is mostly caused by atherosclerosis and more frequently affects females (65%–72%).[835,836] Symptoms typically manifest when at least two mesenteric vessels are involved due to extensive collaterals. Prevalence of asymptomatic coeliac artery and/or SMA stenosis is 3% in patients under 65 years of age and 18% in those aged >65.[837] However, inadequate anastomoses can result in symptomatic ischaemia even with a single-vessel atherosclerotic occlusion.[838,839]

8.3.3.2.1. Clinical presentation and diagnosis. Clinical examination

Like AMI, early diagnosis of CMI relies on clinical suspicion. Classic symptoms include post-prandial abdominal pain, weight loss, and gastrointestinal disturbances like diarrhoea or constipation. Patients may develop food aversion to avoid pain, but their appetite remains

unaffected, distinguishing them from individuals with malignancies. An abdominal examination might reveal a bruit.

Lactate, lactate dehydrogenase, and/or leucocyte count are unhelpful in CMI diagnosis.[840,841] Functional testing (tonometry, visible light spectroscopy) is applicable in patients with symptomatic mesenteric stenosis and single-vessel disease.[842]

Imaging

Duplex ultrasound is valuable due to its low costs, absence of the need for contrast agents, and no radiation. However, skilled investigators in specialized centres are required for the examination. Despite suggested diagnostic criteria, consensus is lacking.[843,844] Anatomical mapping for treatment planning typically involves CTA or MRA,[845,846] with DSA reserved only for therapeutic purposes (*Figure 20*).

8.3.3.2.2. Treatment strategy. Optimal medical treatment is the basis of CMI management. Prophylactic revascularization is not recommended for asymptomatic CMI. In symptomatic cases, a meta-analysis favoured endovascular over open surgery due to fewer complications and a trend towards lower 30 day mortality.[835] However, open surgery showed superior long-term results, with fewer symptom recurrences and higher 1 and 5 year primary patency rates in two additional meta-analyses.[847,848] Despite the growing use of endovascular therapy, open surgery remains indicated after failed endovascular therapy without the option for repeat intervention, and in cases with extensive occlusions, calcifications, or technical challenges.

8.3.3.2.3. Follow-up. Following CMI revascularization, lifelong medical treatment, including lifestyle changes and OMT for atherosclerosis, is recommended. SVS guidelines propose mesenteric DUS surveillance for recurrent stenosis. A potential follow-up schedule involves controls within 1 month post-procedure, biannually for the first 2 years, and annually thereafter.[849]

Recommendation Table 32 — Recommendations in patients with visceral artery stenosis

Recommendations	Class[a]	Level[b]
In patients with acute mesenteric ischaemia due to acute occlusion of the SMA, endovascular revascularization is recommended.[829–831]	I	B
In patients with suspected acute or chronic mesenteric ischaemia, CTA is recommended.[826,827,845,846]	I	C
In patients with acute or chronic mesenteric ischaemia, assessment by a vascular team is recommended.	I	C
Revascularization of asymptomatic atherosclerotic visceral artery stenosis is not recommended.	III	C

CTA, computed tomography angiography; SMA, superior mesenteric artery.
[a]Class of recommendation.
[b]Level of evidence.

9. Aorta

9.1. Atheromatous disease of the aorta

9.1.1. General concepts

Atheromatous disease of the aorta has an estimated incidence of 40%–51.3%, being complicated in 7.6% of cases.[850–853] Earlier stages of atherosclerosis, presenting as plaque inflammation, can be present in 48% of asymptomatic individuals.[850] Atherosclerotic plaque classification is based on plaque thickness and the presence of ulceration or mobile components (*Table 14*).[159,171,854] This classification is crucial because severe or complex atherosclerotic plaques in the aortic arch or ascending aorta are strongly linked to cerebrovascular events (odds ratio [OR] 4–9.1 for plaques ≥4 mm).[855–860] Additionally, the annual incidence of stroke recurrence remains high (up to 16%) despite antiplatelet or anticoagulant therapy.[855,861]

9.1.2. Treatment

9.1.2.1. Primary prevention

Asymptomatic non-severe/non-complex aortic plaques (*Table 14*) should not mandate antiplatelet therapy. Nonetheless, in severe/complex plaques, statins should be indicated to decrease plaque progression or CV events,[862] and SAPT with clopidogrel or low-dose aspirin should be considered after risk/benefit evaluation.[493,666,861,863] However, in this scenario, anticoagulation[861] or DAPT (low-dose aspirin and clopidogrel) are not indicated.[666,863] Floating aortic thrombi and complex mobile plaques are rare, with limited large-scale trials on their management. Guidance relies on case reports, observational studies, and expert opinions, yet there is evidence favouring anticoagulation, particularly for symptomatic cases.[864]

9.1.2.2. Secondary prevention

Secondary prevention with antiplatelet therapy after an embolic event is recommended to prevent recurrences.[666,865,866] While the value of DAPT vs. SAPT remains uncertain, recent studies indicate that prolonged DAPT raises bleeding risk without added antithrombotic benefits.[667,863,867] Treatment duration is unclear and must strike a balance between early benefit (notably within 7 days post-emboli) and steady bleeding risk. Statins (LDL target below 1.4 mmol/L [55 mg/dL]) prove effective in preventing strokes regardless of the aetiology.[862,865,868] Additionally, a healthy lifestyle is crucial for improving CV health and reducing complications.

Recommendation Table 33 — Recommendations for primary and secondary prevention in aortic atheromatous plaques

Recommendations	Class[a]	Level[b]
Primary prevention		
In patients with severe/complex aortic atheromatous plaques, statins should be considered to decrease progression and risk of CV events.[862]	IIa	C
SAPT with clopidogrel or low-dose aspirin should be considered in severe/complex plaques.[493,666,861,863]	IIa	C
Anticoagulation[861] or DAPT[863] are not recommended in aortic plaques since they present no benefit and increase bleeding risk.[666]	III	C
Secondary prevention after an embolic event related to aortic atherosclerosis		
In patients with an embolic event and evidence of an aortic arch atheroma, intensive lipid management to an LDL-C target <1.4 mmol/L (<55 mg/dL) is recommended to prevent recurrences.[242,862,865,868]	I	A
In patients with an embolic event and evidence of an aortic arch atheroma, SAPT is recommended to prevent recurrences.[666,865,866]	I	C

CV, cardiovascular; DAPT, dual antiplatelet therapy; LDL-C, low-density lipoprotein cholesterol; SAPT, single antiplatelet therapy.
[a]Class of recommendation.
[b]Level of evidence.

Table 14 Grading of atherosclerotic aortic plaques

Grade	Severity (atheroma thickness)	Description
1	Normal	Intimal thickness <2 mm
2	Mild	Intimal thickening of 2 to <3 mm
3	Moderate	Atheroma ≥3 to <4 mm (no mobile/ulcerated components)
4	Severe	Atheroma ≥4 mm (no mobile/ulcerated components)
5	Complex	Grade 2, 3, or 4 atheroma plus mobile/ulcerated components

9.2. Aortic aneurysms

9.2.1. General concepts

9.2.1.1. Definitions

Aortic dilatation, the second most frequent aortic disease after atherosclerosis, is defined as an aortic diameter >2 standard deviations of the predicted mean diameter depending on age, sex, and body size (z-score >2). However, in clinical practice, aortic root dilatation can be suspected in male adults when aortic diameter is >40 mm and in females at >36 mm,[138,149,869] or with an indexed diameter/BSA (aortic size index [ASI]) >22 mm/m^2. In extreme BSA and age values, use of z-scores is recommended (see *Section 5.4* for their calculation).

Arterial aneurysm is defined as a diameter >1.5 times (>50%) larger than the predicted one. This definition, as well as the use of z-scores, introduces the need for normal values and correction for age, sex, and body size. However, correcting for BSA can lead to underestimation in overweight patients,[870] therefore a correction for height (aortic height index [AHI]) is becoming more popular.[153] In terms of clinical risk, both ASI and AHI have been shown to improve risk stratification for AAE.[153,871] Since in many cases of aortic dilatation the surgical indication is established before achieving this aneurysmal diameter, we strongly recommend the use of *significant aortic dilation* specifying the diameter or the indexed diameter value rather than the term 'aneurysm'.

Thoracic aortic aneurysms (TAAs) are more prevalent in men than in women (ratio 4:1);[872] however, the growth rate is greater in women (0.96 ± 1.00 mm per year) than in men (0.45 ± 0.58 mm per year), and thus the risk of AAE.[873]

Aneurysms can be fusiform or saccular based on morphology. Saccular aneurysms relate to infection, penetrating atherosclerotic ulcer (PAU), trauma, or inflammatory diseases, while fusiform aneurysms connect with degenerative and connective tissue conditions. Although evidence about their natural course is limited, saccular aneurysms are considered more malignant in terms of AAE. Based on location, aortic aneurysms are classified into TAA and abdominal aortic aneurysm (AAA) (*Figure 21*). They differ in treating specialists, causes, age at onset, risk factors, and complications. However, this binary classification is artificial due to the prevalence of thoracoabdominal aortic aneurysms (TAAA) and tandem lesions (20%–30% of AAA patients also have TAA),[874,875] emphasizing the importance of comprehensive aortic and vascular assessments at diagnosis. When detecting an aortic aneurysm at any site, it is advisable to conduct a thorough evaluation of the entire aorta initially and during subsequent follow-ups. Specifically, when diagnosing a TAA, it is crucial to assess the aortic valve, particularly in cases of BAV. Data on peripheral aneurysms in TAA, particularly in femoro-popliteal segments, is less clear compared with AAA. However, cerebral aneurysms, notably prevalent in women and those with HTAD, warrant thorough screening, particularly in symptomatic cases.[876–878]

Recommendation Table 34 — Recommendations for initial evaluation of thoracic aortic aneurysm and abdominal aortic aneurysm

Recommendations	Class[a]	Level[b]
When an aortic aneurysm is identified at any location, assessment of the entire aorta is recommended at baseline and during follow-up.[874,875]	I	C
When a TAA is identified, assessment of the aortic valve (especially for BAV) is recommended.[879,880]	I	C
When an AAA is identified, evaluation of the presence of aneurysm in the femoro-popliteal arterial segment should be considered.[876–878,881]	IIa	C
Patients with aortic aneurysm are at increased risk of CVD, thus general CV prevention should be considered.[26,882,883]	IIa	C

AAA, abdominal aortic aneurysm; BAV, bicuspid aortic valve; CV, cardiovascular; CVD, cardiovascular disease; TAA, thoracic aortic aneurysm.
[a]Class of recommendation.
[b]Level of evidence.

9.2.2. Thoracic aortic aneurysms

9.2.2.1. Aetiology, risk factors, and natural history

Thoracic aortic aneurysms occur in 5–10/100 000 person-years,[884] with an approximate predominance of root and/or ascending aorta of ~60%, arch of ~10%, and descending aorta of ~30%.[885,886]

Hypertension is the main risk factor (80%); however, genetics may be involved in 20% of cases.[887] The decision to refer patients for genetic evaluation should consider age, family history, and presence of syndromic features,[25,888] as reported in more detail in *Section 10.1*.

9.2.2.2. Ascending thoracic aorta and arch aneurysms

(1) **Aortic root aneurysms** (including sinuses of Valsalva: annuloaortic ectasia). They can be idiopathic, associated with HTAD (syndromic/non-syndromic), or found in 20%–30% of BAV patients (see *Section 10*).[879,880] Patients are usually younger (30–50 years of age), with aortic regurgitation, and with a 1:1 sex ratio.

(2) **Supra-coronary aortic aneurysms** (above sinuses of Valsalva). Caused by atherosclerosis in relation to hypertension affecting older patients (59–69 years) and males (ratio 3:1),[880] or related to medial degeneration (isolated or associated with aortic valve disease, including BAV) (see *Section 10*). Primary bacterial infection or syphilis are uncommon. Arteritis is rare, but Takayasu's and giant cell arteritis can lead to aneurysm formation.

(3) **Aortic arch aneurysms.** Often accompanying adjacent ascending or descending aorta aneurysms, aortic arch aneurysms present surgical challenges due to potential neurological and CV risks. They are typically linked to atherosclerosis, with cystic medial degeneration primarily affecting ascending aorta-related arch aneurysms. Deceleration injuries or coarctation may extend into the aortic arch.[889]

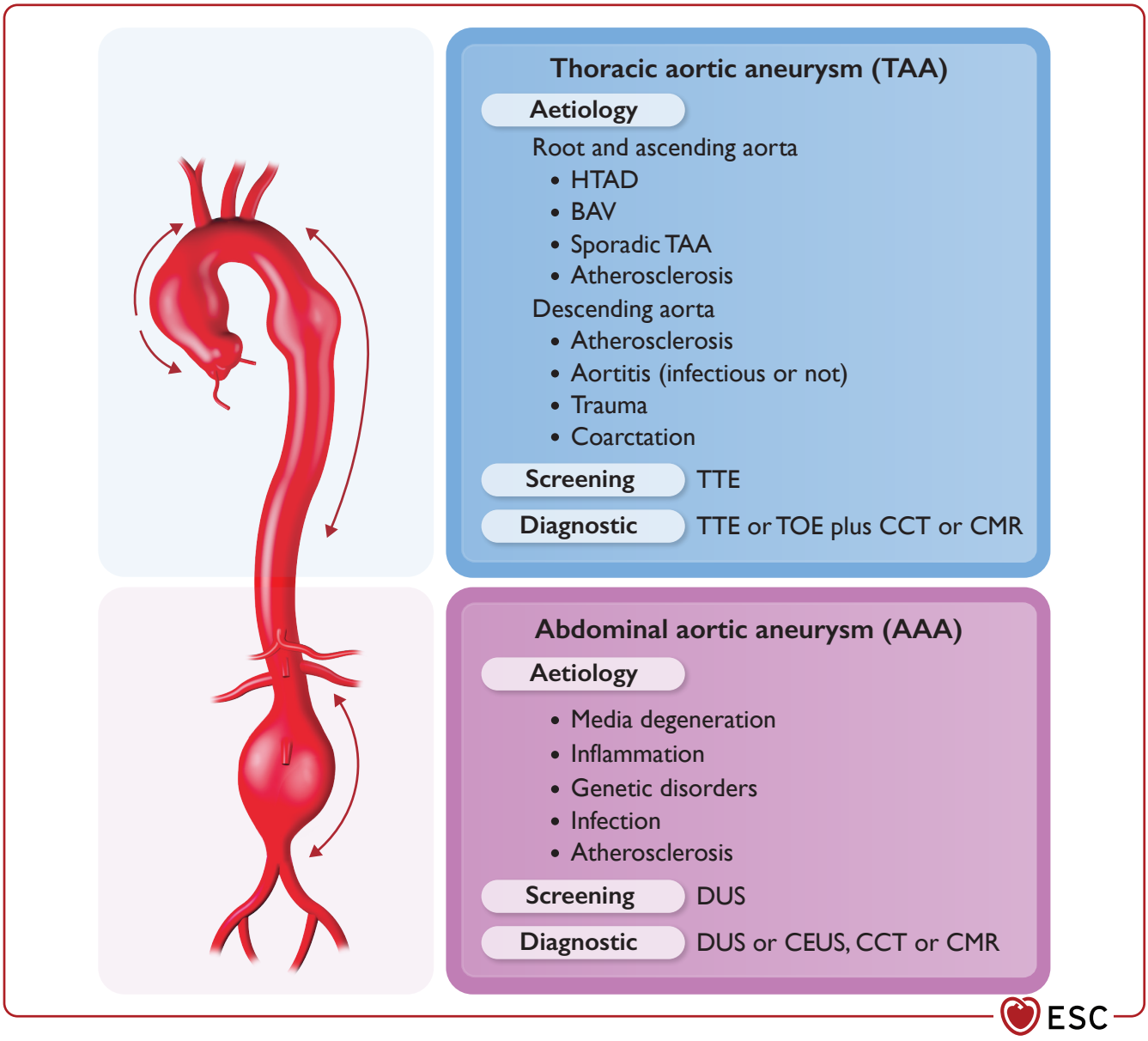

Figure 21 Thoracic and abdominal aortic aneurysms: aetiology, screening and diagnostic methods. AAA, abdominal aortic aneurysm; BAV, bicuspid aortic valve; CCT, cardiovascular computed tomography; CEUS, contrast-enhanced Doppler ultrasound; CMR, cardiovascular magnetic resonance; DUS, Doppler ultrasound; HTAD, heritable thoracic aortic disease; TAA, thoracic aortic aneurysm; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography.

Thoracic aortic aneurysm patients are usually asymptomatic, diagnosed incidentally during unrelated imaging or screenings. Symptoms such as chest pain, aortic regurgitation, and compression-related issues may occur.[890] Patients with aortic root involvement (as seen in HTAD) are more prone to suffer from AAE.[891,892]

Thoracic aortic aneurysm growth rate is variable, associated with aetiology, location, and baseline aortic diameter.[893–895] Degenerative TAAs grow faster in women than men and are associated with a three-fold higher risk of AAE.[24,873,896] When the aorta reaches 57.5 mm in size, reported yearly rates of rupture, dissection, and death are 3.6%, 3.7%, and 10.8%, respectively.[897–899]

9.2.2.3. Descending thoracic aorta and thoracoabdominal aorta aneurysms

They can involve different parts of the DTA and may extend to the AA: TAAA. TAAAs are divided into five groups[900] according to the modified TAAA classification scheme (*Figure 22*), which is crucial for risk stratification. By classifying aneurysm extent, surgeons can anticipate procedure complexity, select suitable techniques, and reduce risks during surgical planning.

Most DTA aneurysms and TAAA are degenerative with calcification, although other causes include trauma, infection, inflammation, or genetic factors[901,902] (*Figure 21*). Patients with HTAD rarely develop

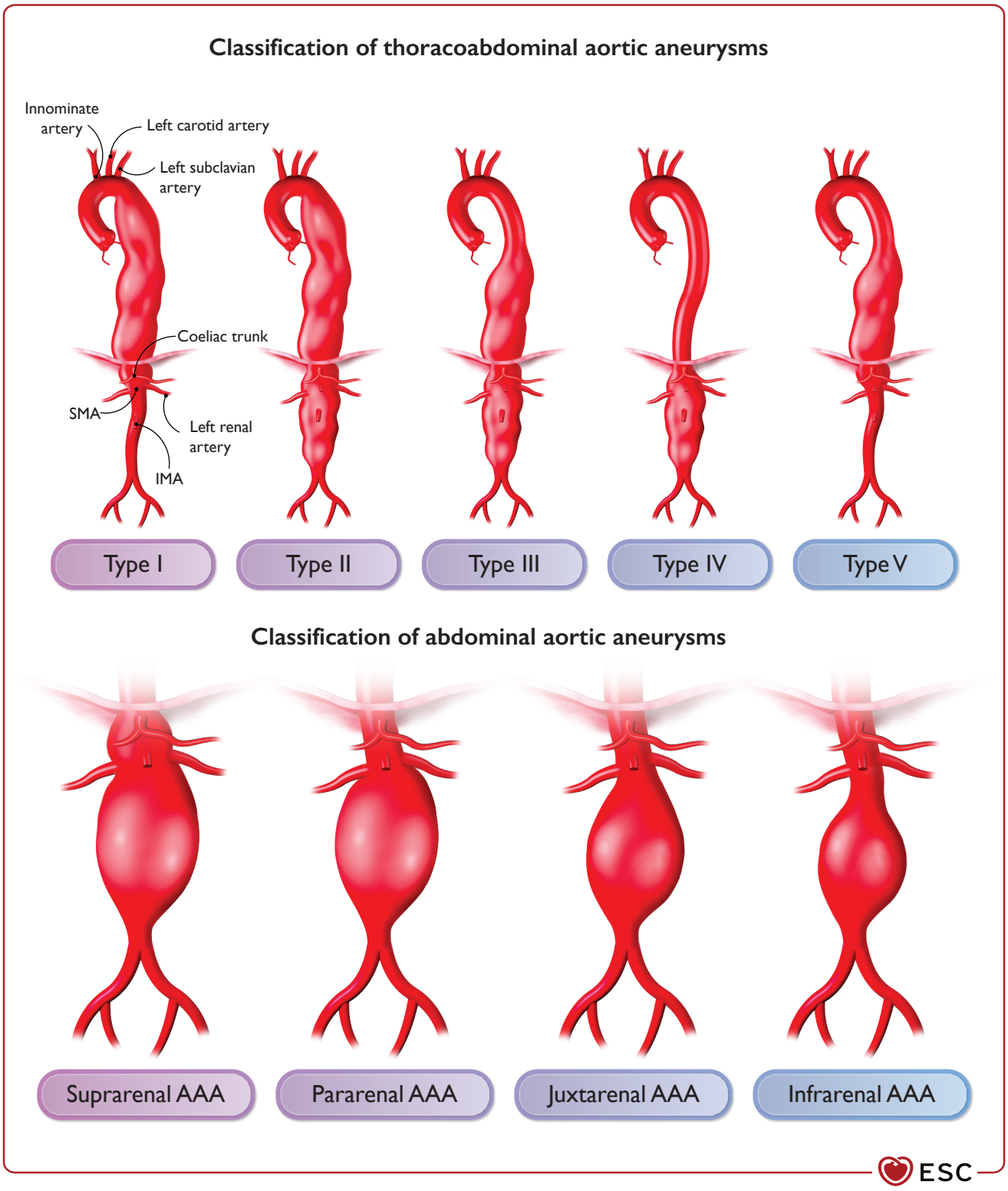

Figure 22 Classification of thoracoabdominal[900] and abdominal aortic aneurysms. AAA, abdominal aortic aneurysm; IMA, inferior mesenteric artery; SMA, superior mesenteric artery.

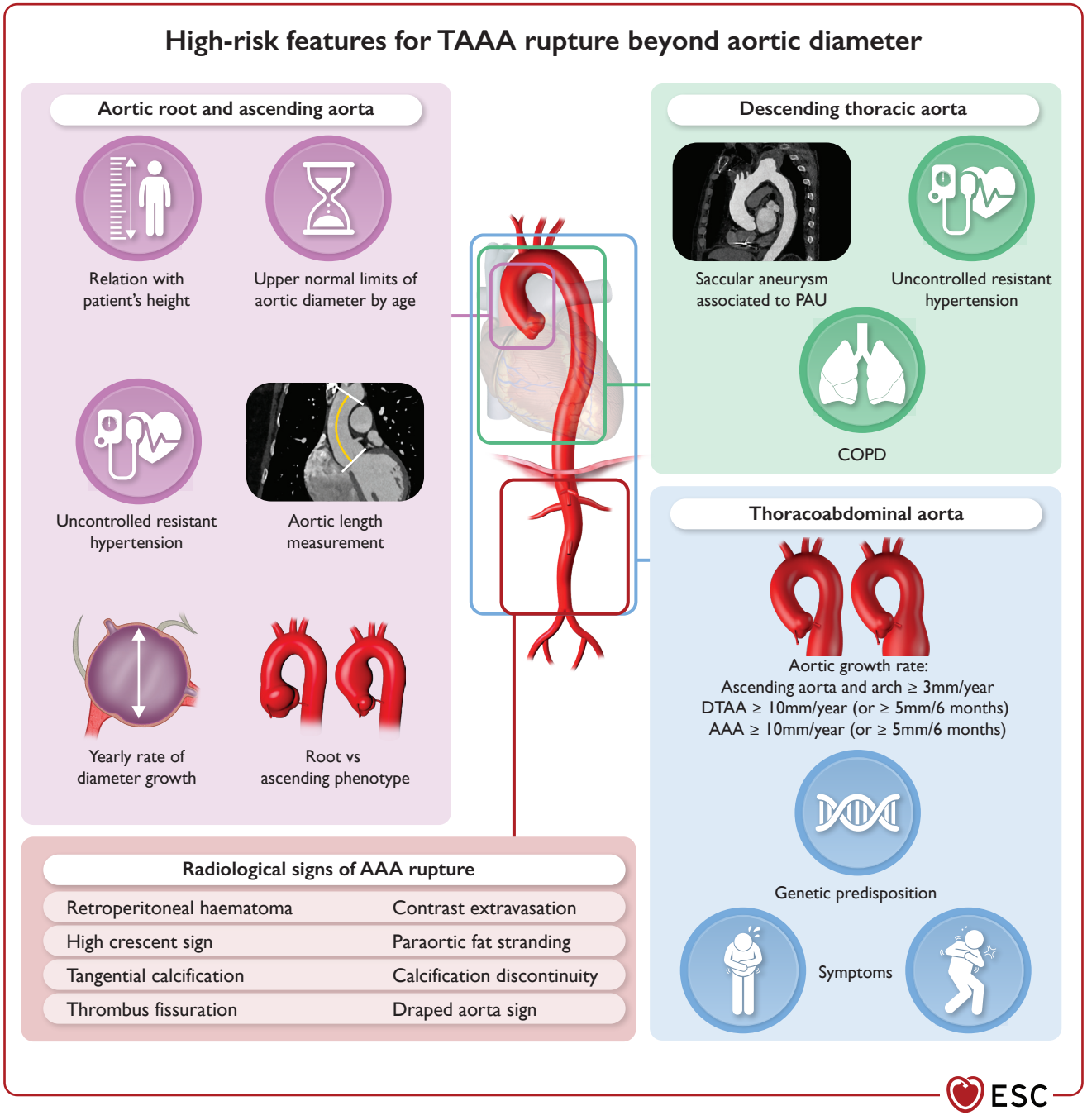

Figure 23 Risk factors for thoracic and abdominal aneurysm rupture. AAA, abdominal aortic aneurysm; COPD, chronic obstructive pulmonary disease; DTAA, descending thoracic aorta aneurysm; PAU, penetrating atherosclerotic ulcer; TAAA, thoracoabdominal aortic aneurysm.[905–908]

thoracoabdominal aortic aneurysms without dissection. Mean age at diagnosis is 59–69, with a male predominance of 2–4:1. Aneurysm growth rate is 1.9–3.4 mm per year,[902,903] but tends to increase notably with diameters over 50 mm or post-proximal aorta surgery in patients with MFS. In this population, debate continues as to whether this reflects a more vulnerable aorta associated to the genetic disease or haemodynamic changes post-surgery.

For untreated DTA aneurysm patients, 5 year survival is about 54%, with aortic rupture as the leading cause of death.[904] Rupture risk factors include HTAD, a diameter over 50 mm, hypertension, smoking, chronic obstructive pulmonary disease (COPD), symptoms, chronic aortic dissection, and age. A significant rise in AAE risk occurs at a 60 mm diameter. Although dissection can occur in smaller aortas, the individual risk is low.[899] High-risk features for rupture are represented in *Figure 23*.

9.2.2.4. Surveillance

Patients with TAA who do not meet surgical criteria require chronic follow-up that includes clinical evaluation and imaging techniques. The best imaging modality depends on aneurysm location: TTE, CCT, or CMR when affecting the aortic root and the ascending aorta; CMR and CCT when involving the distal ascending aorta, the aortic arch, or the DTA.[159,171] Follow-up should be conducted with the same imaging technique and in the same centre.[909] If a TAA is only moderate in size and remains relatively stable over time, CMR rather than CCT is reasonable to minimize radiation exposure.[172,910] Follow-up for aortic aneurysms associated with HTAD is described in *Section 10.1.3.2*.

Figure 24 proposes a follow-up algorithm for patients with TAA. In cases of aortic root or proximal ascending aorta dilatation, after initial diagnosis by TTE the basal diameter and extension must be confirmed by CMR or CCT. If there is agreement between techniques, TTE can be used for follow-up; however, if there is a difference of ≥3 mm, surveillance must be performed by CMR or CCT. After the initial diagnosis, imaging is required at 6–12 months, depending on aetiology and baseline diameter (*Figure 24*); see *Sections 5.4.2* and *9.2.1* about indexed values of aortic dimensions, to ensure stability.[159,911] Subsequently, imaging can be performed annually if there is no expansion/extension or customized according to the underlying condition. If the aorta shows rapid expansion (≥3 mm per year) or approaches the surgery/endovascular repair threshold, a closer evaluation is recommended every 6 months. In contrast, stability in aortic diameters over years could lengthen these intervals (especially in non-genetic aneurysms and those <45 mm). In cases of dilatation of aortic arch or DTA, diameters obtained by TTE are deemed less precise and need confirmation by CMR or CCT. In those types of aneurysms, follow-up frequency will depend on the baseline diameter and aetiology and will follow the same criteria established in the algorithm in *Figure 24* for the 40–49 mm range. However, for the 50–55 mm range, the aorta should be re-imaged every 6 months until the threshold for intervention is reached (see *Sections 9.2.5.3* and *9.2.5.4*).

Recommendation Table 35 — Recommendation for the surveillance of patients with thoracic aortic aneurysms (non-heritable thoracic aortic disease)

Recommendations	Class[a]	Level[b]
In thoracic aortic dilatation, TTE is recommended at diagnosis to assess aortic valve anatomy and function, aortic root, and ascending aorta diameters. Additionally, a global aortic evaluation using all echocardiographic views is recommended.[159]	I	C
CMR or CCT is recommended for surveillance of patients with aneurysm at the distal ascending aorta, aortic arch, DTA, or TAAA.[70,159,172,912–915]	I	C
In thoracic aortic dilatation, CCT or CMR is recommended to confirm TTE measurements, rule out aortic asymmetry, and determine baseline diameters for follow-up.[137,143,144]	I	C
Follow-up imaging with TTE, CCT, or CMR (based on aneurysm location) should be considered annually if there is no expansion/extension or customized according to baseline aortic diameter and the underlying condition.[70,159,172]	IIa	C
TTE is not recommended for the surveillance of aneurysms in the distal ascending aorta, aortic arch, or DTA.[159,171]	III	C

Continued

CCT, Cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DTA, descending thoracic aorta; TAAA, thoracoabdominal aortic aneurysm; TTE, transthoracic echocardiography.
See proposed algorithm in *Figure 24*.
[a]Class of recommendation.
[b]Level of evidence.

9.2.3. Abdominal aortic aneurysms

9.2.3.1. General concepts

An AAA is defined as a focal dilation at least 1.5 times its normal diameter, generally ≥30 mm. Most AAAs are fusiform, and many are lined with laminated thrombi.[916] Their prevalence increases with age, with a 4:1 male/female ratio.[872] They are commonly classified based on their relation to renal arteries (*Figure 22*) because of the complexity of surgical treatment. AAA extends to the common iliac arteries in 25% of cases and in up to 20% of patients is associated with peripheral femoral and/or popliteal artery aneurysm.[876–878]

9.2.3.2. Aetiology, risk factors, and natural history

Smoking, age, male sex, and familial history of aneurysmal disease are major risk factors,[917–921] whereas diabetes is associated with a decreased risk[922,923] and slower growth rate[924] (*Figure 21*, see also *Section 5*). Other aetiologies include inflammation (5%–10% of all AAA),[925] genetic disorders, and infection. The mean growth rate is around 3 mm per year (1–6 mm)[906,926] and depends on sac diameter, presence of genetic disorders, continuous smoking, metabolism (presence of inflammation), and aortic wall calcification.[927–929] Risk of rupture rises exponentially depending on diameter, being higher in women.[930,931]

AAAs are asymptomatic in two-thirds of cases and if they become symptomatic, rupture is the main manifestation. They often represent incidental imaging findings, as the sensitivity of clinical examination—especially palpation of an abdominal mass—is generally poor. Symptoms may include acute abdominal or back pain, and in some cases, hypovolaemic shock. However, contained rupture may present with atypical low flank or abdominal pain (see *Figure 23* for high-risk factors and radiological signs or AAA rupture).[932–935] Independently of risk of rupture, patients with AAA have impaired survival: the 5 year mortality rate is higher (×4 in women, ×2 in men) despite AAA repair, likely due to the presence of cardiovascular disease in other areas.[936]

9.2.3.3. Surveillance

Those with an aortic diameter <25 mm present low risk of developing large AAA in 10 years, whereas a diameter of 25–29 mm deserves reassessment after 4 years.[937,938] DUS is the standard imaging technique for surveillance; however, CCT provides superior visualization of the AA and its branches, especially for pre-operative planning. CMR is reasonable in selected patients (young and female) when a long follow-up is considered, to avoid radiation.

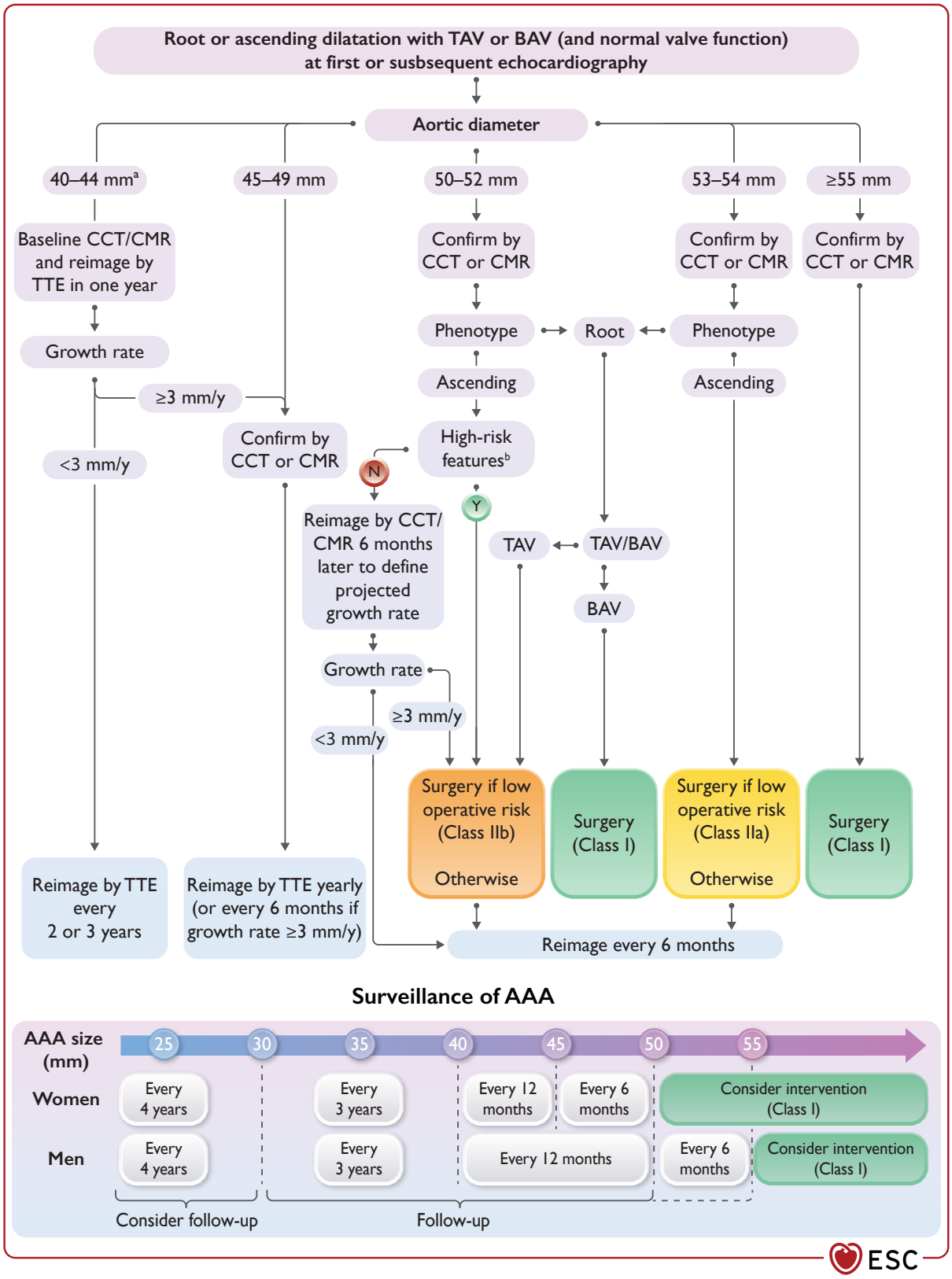

Figure 24 Surveillance of patients with **non-heritable** thoracic aortic disease and abdominal aortic aneurysms. AAA, abdominal aortic aneurysm, BAV, bicuspid aortic valve; CCT, cardiovascular computed tomography; HTAD, heritable thoracic aortic disease; CMR, cardiovascular magnetic resonance; TAV, tricuspid aortic valve; TTE, transthoracic echocardiography. [a]36–44 mm in women. [b]For TAV and BAV: age <50 years; height <1.69 m; ascending length >11 cm; uncontrolled hypertension; and, for BAV: coarctation; family history of acute aortic events.

A meta-analysis advises follow-up intervals for AAAs based on size: 3 years for 30–39 mm, 1 year for 40–44 mm, and 6 months for 45–54 mm in men, with <1% rupture risk.[938] Women have similar growth rates but a four-fold higher rupture risk.[938] A proposed follow-up algorithm is displayed in *Figure 24*. Consider shorter intervals for rapid growth (≥10 mm per year or ≥5 mm per 6 months), in which case repair may be considered.

Recommendation Table 36 — Recommendations for surveillance of patients with abdominal aortic aneurysm

Recommendations	Class[a]	Level[b]
DUS surveillance is recommended every 6 months in men with AAA of 50–55 mm and in women with AAA of 45–50 mm.[938]	I	B
CCT or CMR is recommended if DUS does not allow adequate measurement of AAA diameter.[148,939–942]	I	B
DUS is recommended for AAA surveillance.[943]	I	C
DUS surveillance every 3 years should be considered in patients with AAA of 30–<40 mm.[938]	IIa	B
DUS surveillance should be considered annually in women with AAA of 40–<45 mm and in men with AAA of 40–<50 mm.[938]	IIa	B
DUS surveillance should be considered every 4 years in patients with aortic diameter ≥25 mm and <30 mm and life expectancy >2 years.[937,938]	IIa	C

AAA, abdominal aortic aneurysm; CCT, Cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DUS, duplex ultrasound.
[a]Class of recommendation.
[b]Level of evidence.

9.2.4. Optimal medical treatment of aortic aneurysms

In patients with aortic aneurysms, the role of antithrombotic therapy is uncertain. In complicated aortic atherosclerotic plaques, concomitant CAD is common (OR 2.99) and SAPT should be considered (see Section 9.1). In patients with AAA, results of observational studies are conflicting in relation to aneurysm growth. Low-dose aspirin is not associated with a higher risk of AAA rupture but could worsen prognosis in cases of rupture.[944] In an RCT of patients with AAA (35–44 mm), ticagrelor did not reduce growth rate.[945]

Optimal medical treatment for aortic aneurysms aims to lower CV morbidity, slow growth rate, delay surgery, reduce peri-operative risk, and prevent AAE. Aneurysm patients face elevated CV risk due to common CVRFs, and the 10 year CV event mortality risk (heart attacks or strokes) is 15 times higher than AAE risk, even after repair.[882,883] According to the SMART risk score algorithm, optimal implementation of risk management guidelines would reduce the 10 year risk of MACE from 43% to 14% in patients with AAA.[936] Thus, lifestyle modification, exercise, smoking cessation, and treatment of risk factors are crucial (see *Section 7*).

Risk factors and possible drug treatment to reduce AAA growth and/or the risk of rupture have been thoroughly discussed in a recent review paper.[946] Their meta-analysis suggested a possible effect of ACEIs (but not ARBs) on the risk of rupture, whereas another meta-analysis[947] did not indicate an effect of ACEIs on AAA growth. A reduction of AAA growth by statins is indicated in a recent meta-analysis.[352] Furthermore, reduced AAA growth by the antidiabetic drug metformin has been suggested in several meta-analyses[352,948,949] and there are several ongoing RCTs to explore this. For BP, follow general hypertension guidelines. Aim for BP below 140/90 mmHg, with a target of 120/80 mmHg, if tolerated.[300,302,305] Data on the specific positive effects of beta-blockers and ARBs in TAA and AAA are limited (mostly derived from MFS populations). However, it is reasonable to use BBs and/or ARBs as first-line antihypertensive drugs in TAA and AAA.

Consider moderate/high-intensity statins in TAA patients but skip for those with low CV risk and non-atherosclerotic (HTAD). In AAA, consider statins to reduce aneurysm risks, including growth, rupture, and peri-operative mortality.[330,347,348] Low-dose aspirin is debated but may be reasonable given elevated CV risk factors in TAA and AAA patients.[666,950] Additionally, apply all CVD secondary prevention measures to these patients (see *Section 7*).

Some evidence suggests that fluoroquinolones could be associated with an increased risk for aneurysm progression and dissection,[951–956] but conflicting analyses do not support this association. The cautious use of fluoroquinolones should not be discouraged when there is a clinical indication, even considering concerns regarding aortic aneurysm and dissection (AA/AD). Note that AA/AD risk (both thoracic and abdominal) may increase due to infection itself, regardless of the antibiotic chosen. Infectious disease specialists discourage routine fluoroquinolone use as a first-line antibiotic if equally effective alternatives exist. Hence, do not withhold this therapy in aortic disease cases when clinically necessary. All medical and lifestyle recommendations are summarized in *Figure 7*.

Recommendation Table 37 — Recommendations for medical treatment in patients with thoracic aorta or abdominal aortic aneurysms

Recommendations	Class[a]	Level[b]
In patients with aortic aneurysm (TAA and/or AAA), optimal implementation of CV risk management and medical treatment (see detailed recommendations in dedicated Tables of Recommendations[c]) are recommended to reduce MACE.[936]	I	C
Fluoroquinolones, while generally discouraged for patients with aortic aneurysms, may be considered if there is a compelling clinical indication and no other reasonable alternative.[951–960]	IIb	B

AAA, abdominal aortic aneurysm; CV, cardiovascular; MACE, major adverse cardiovascular events; TAA, thoracic aortic aneurysm.
[a]Class of recommendation.
[b]Level of evidence.
[c]see Tables of Recommendations 7 to 10.

9.2.5. Surgical management of aortic aneurysms

9.2.5.1. Surgical treatment of aortic root and ascending aorta

In isolated dilatation of the ascending tubular (supra-coronary) aorta, a supra-commissural tubular graft is inserted with the distal anastomosis just before the aortic arch. For aneurysms extending proximally below the sinotubular junction (STJ) with involvement of aortic sinuses, the surgical approach depends on the aortic annulus and valve condition. If the aortic valve cusps are pliable, experienced centres may recommend aortic valve-sparing techniques,[961–965] such as David's procedure (reimplantation) or the Yacoub technique (remodelling).[890,966–968]

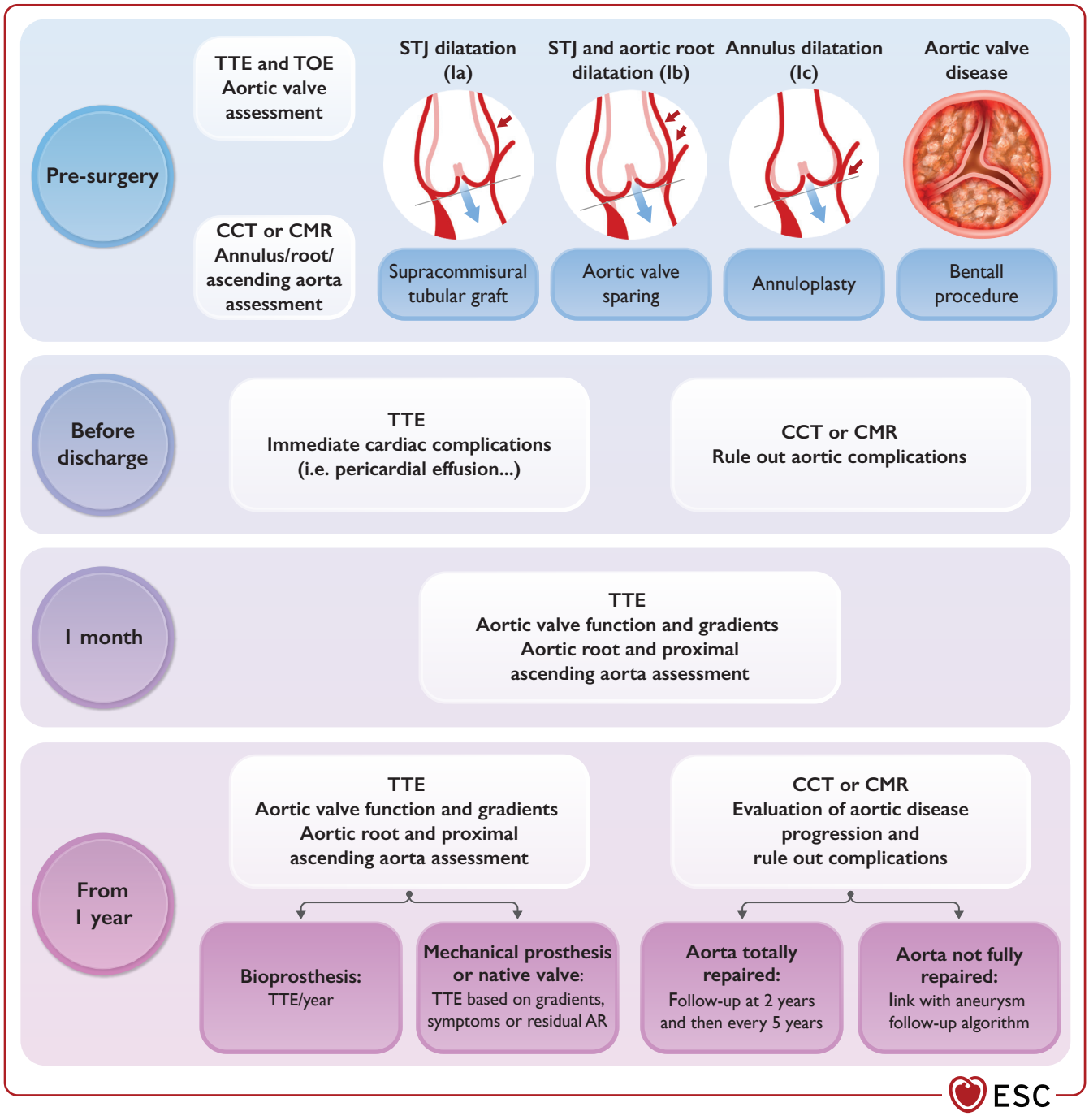

Figure 25 Peri-operative algorithm for the management of patients with surgically treated aortic root and ascending aortic aneurysm. AR, aortic regurgitation; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; STJ, sinotubular junction; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography.

Otherwise, composite replacement of the aortic root and valve with the Bentall procedure is indicated.

Pre-operative evaluation[890] and initial follow-up of patients is defined in *Figure 25*. Patients with a bioprosthetic valve should be monitored by TTE annually. However, in patients with mechanical prosthesis or native aortic valve, clinical evaluation and TTE should be performed as soon as possible if new heart symptoms develop.[969] SAPT with low-dose aspirin (75–100 mg per day) should be considered for the first 3 months after conservative aortic valve surgery if there are no indications for OAC. Lifelong OAC with a VKA is recommended for all patients with a Bentall mechanical prosthesis.[970,971] However, in patients with no baseline indications for OAC, low-dose aspirin (75–100 mg/day) or OAC using a VKA should be considered for the first 3 months after Bentall surgery with a bioprosthesis.[972,973]

Although many risk factors associated with AAE have been described (such as elongation, angulation, and unfavourable biomechanics), aortic diameter is still the main determinant of aortic complications and death.[974–976] AAE rates decreased with prophylactic aortic surgery over a decade,[977] and additionally, surgical risk for ascending aortic/aortic root surgery dropped significantly.[978–980] Now, experienced cardiac surgery centres report <1% mortality with elective surgery.[980,981]

Most acute type A aortic dissections (acute TAAD) occur at diameters below 55 mm. However, the risk exceeds 1% between 50 and 54 mm,[982] with a critical point at 52–53 mm.[153,981,983] Pre-dissection aortic diameter at the tubular level is 25%–30% smaller than post-dissection. Over 60% of non-MFS, non-BAV acute TAAD patients have a non-dilated ascending aorta before dissection.[984,985] Additionally, the 'root phenotype' has been reported to be more malignant than those with ascending phenotype, with higher velocity of progression and AAE risk.[154,891,892,986]

Novel parameters, like ascending aortic length (AAL) and the ascending-arch angle, correlate with acute TAAD risk.[155,976] AAL ≥13 cm links to nearly five-fold higher yearly AAE rates compared with AAL <9 cm, with a threshold of >11 cm as a risk indicator.[155] Indexing aortic diameters to anthropometric parameters has been suggested and a proportional increase in the risk of AAE has been retrospectively demonstrated for increasing diameter indexed to BSA,[904] diameter indexed to patient height,[153] or cross-sectional area indexed to patient height.[154] However, these diameter-based indexing methods share the same limitations in risk prediction as the absolute diameter in the general population,[984,985] whereas they can be advantageous in patients with small body size.[153,154] These additional risk factors (beyond the diameter) are summarized in *Figure 23*.

Recommendation Table 38 — Recommendations for surgery in aortic root and ascending aorta dilatation associated with tricuspid aortic valve (see also Evidence Table 11)

Recommendations	Class[a]	Level[b]
Surgery is recommended in patients with dilatation of the aortic root or ascending aorta with a tricuspid aortic valve and a maximum diameter of ≥55 mm.[172,894,899,904]	I	B
Valve-sparing aortic root replacement is recommended in patients with aortic root dilatation if performed in experienced centres and durable results are expected.[961–965]	I	B
VKAs are recommended lifelong for all patients with a Bentall procedure with an MHV prosthesis.[970,971]	I	B
In patients with dilatation of the tubular ascending aorta who can be offered surgery with low predicted risk,[c] ascending aortic replacement should be considered at a maximum diameter >52 mm.[153,981,983]	IIa	B
In patients undergoing surgery for tricuspid aortic valve disease who have concomitant dilatation of the aortic root or ascending tubular aorta, and low predicted surgical risk, ascending aorta or root replacement should be considered at a maximum diameter ≥45 mm, otherwise ≥50 mm.[70,987–989]	IIa	B
SAPT with low-dose aspirin (75–100 mg per day) should be considered for the first 3 months after valve-sparing aortic surgery when there are no other baseline indications for OAC.	IIa	C
In patients undergoing non-aortic-valve cardiac surgery who have concomitant dilatation of the ascending aorta or aortic root with a maximum diameter ≥50 mm, concomitant aortic surgery should be considered.[70,990,991]	IIa	C
Ascending aortic or root replacement may be considered at a maximum diameter of ≥50 mm in patients with proximal aorta dilatation who can be offered surgery with low predicted risk[c] and present with any of the following:[153–155,891,892] • Growth of the aortic diameter ≥3 mm per year • Resistant hypertension[d] • Short stature <1.69 m • Root phenotype • Aortic length[e] >11 cm • Age <50 years • Desire for pregnancy • Aortic coarctation	IIb	B

MHV, mechanical heart valve; OAC, oral anticoagulation; SAPT, single antiplatelet therapy; VKA, vitamin K antagonist.
For heritable thoracic aortic disease and bicuspid aortic valve-related thoracic aortic aneurysm refer to *Section 10*.
[a]Class of recommendation.
[b]Level of evidence.
[c]Individual patient's risk <3%.
[d]Hypertension that cannot be adequately controlled despite use of three or more agents recommended by a physician with expertise in the management of hypertension.
[e]Curvilinear distance at aortic centreline between the ventriculo-aortic junction and the origin of the innominate artery.

9.2.5.2. Surgical treatment of aortic arch aneurysms

Surgery for arch aneurysms is challenging, primarily due to risks like hypothermic circulatory arrest and the need for brain protection, resulting in higher mortality and stroke rates. Isolated aortic arch surgery is appropriate for asymptomatic degenerative aortic arch aneurysms ≥55 mm in diameter or symptoms or signs of local compression. Hemi-arch or total arch replacement are frequently required in patients who have an indication for surgery on an adjacent aneurysm of the ascending aorta. In specific cases, supra-aortic vessel transposition via off-pump debranching followed by TEVAR of the arch can be an alternative to traditional surgery, particularly when avoiding hypothermic circulatory arrest is a concern.[992–996] When the disease involves the proximal descending aorta or future need for treatment of the descending aorta is anticipated, the frozen elephant trunk (FET) technique is a good option.[997] Assessment of patency and morphology of the circle of Willis is recommended when treatment involves the aortic arch.[998,999]

Recommendation Table 39 — Recommendations for surgery in aortic arch aneurysms

Recommendations	Class[a]	Level[b]
In patients with low or intermediate operative risk with an aortic arch aneurysm and recurrent episodes of chest pain not attributable to non-aortic causes, open surgical replacement of the arch is recommended.[70,172]	I	C

Continued

In patients with an isolated aortic arch aneurysm who are asymptomatic and have low operative risk, open surgical replacement should be considered at an arch diameter of ≥55 mm.[70,172,899]	IIa	B
In patients undergoing open surgical repair of an ascending aortic aneurysm, concomitant hemi-arch replacement should be considered if the dilatation extends into the proximal aortic arch (>50 mm).[70,172,1000]	IIa	C
In patients undergoing open surgical repair of an aortic arch aneurysm, an elephant trunk or frozen elephant trunk procedure should be considered if the aneurysmal disease extends into the proximal descending thoracic aorta.[70,172,997,1001]	IIa	C
In patients undergoing open surgical repair of an ascending aortic aneurysm, concomitant hemi-arch or arch replacement may be considered in experienced centres if the dilatation extends into the aortic arch (>45 mm).[70,172,1001]	IIb	C
In patients with an aortic arch aneurysm who meet criteria for intervention but have high surgical risk, a hybrid or endovascular approach may be considered.[70,172]	IIb	C

For heritable thoracic aortic disease refer to *Section 10*.
[a]Class of recommendation.
[b]Level of evidence.

9.2.5.3. Surgical treatment of the thoracic descending aorta

9.2.5.3.1. General considerations. At 60 mm diameter, a DTA aneurysm has a 10% annual rupture risk, justifying intervention at ≥55 mm.[902,1002] Intervention at a diameter <55 mm may not bring any further survival benefit except for women,[904,1003] patients with connective tissue disorders,[904] or rapid growth (≥10 mm per year or ≥5 mm every 6 months),[1004] (for high-risk factors see *Figure 23*). This threshold may be increased in high surgical risk patients.[1005] It is advisable to centralize complex procedures in centres with expertise in aortic diseases and a multidisciplinary team for effective patient management.

9.2.5.3.2. Open repair. Thoracic endovascular aortic aneurysm repair is recommended as first-choice intervention for DTA aneurysms,[1006–1010] thus open repair is limited to patients with unsuitable anatomy for TEVAR[1011] or connective tissue disorders.[1012] The early mortality benefit of TEVAR seems to decrease after 1 year, and thereafter long-term survival (10 years) seems better with open repair.[1013] Therefore, open repair is advisable for young, healthy patients with unsuitable TEVAR anatomy and prolonged life expectancy, particularly when symptoms from aneurysm rupture or compression arise.

However, open repair involves significant post-operative risks, necessitating thorough pre-operative evaluations for cardiac, pulmonary, renal function, carotid, and peripheral arterial diseases. Risks include stroke, mesenteric and renal ischaemia due to clamping duration,[1014,1015] and paraplegia tied to the extent of aneurysmal disease.[1016,1017] Outside experienced centres, outcomes have shown minimal improvement in recent years, with mortality rates around 10% and spinal cord ischaemia rates at 11%–15%.[1016,1018]

9.2.5.3.3. Endovascular repair. Comparative studies favour TEVAR over open repair, showing lower mortality (6%) and morbidity.[1006,1019,1020] However, TEVAR's survival advantage is balanced by an increased risk of follow-up re-intervention. It reduces spinal cord injury risk (3%).[1021–1024] Left subclavian artery (LSA) coverage during TEVAR for proximal sealing is required in up to 50% of cases.[1025] This is associated with an increased risk of cerebrovascular events, spinal cord ischaemia (SCI), and upper-limb ischaemia,[1026,1027] justifying previous surgical or concomitant endovascular (with branched or fenestrated grafts) revascularization of the LSA in an elective setting.[1026,1028,1029] In cases of inadequate distal zone sealing, safe coverage of the coeliac artery has been proposed when sufficient collateral circulation exists,[1030,1031] but results are controversial.[1032]

9.2.5.4. Surgical treatment of thoracoabdominal aorta aneurysms

9.2.5.4.1. General considerations. Since AAEs increase when TAAA diameter exceeds 60 mm,[902,1002,1033] and there are more technical surgical challenges in TAAA repair (compared with DTA aneurysm or AAA), TAAA repair, in low-moderate surgical risk patients, is proposed if the aortic diameter is ≥60 mm. However, surgical repair should be considered at diameters ≥55 mm if patients present with high-risk features (*Figure 24*) or are at very low risk and under the care of experienced surgeons in a multidisciplinary aorta team.[1004,1033,1034] HTAD, distal location, chronic dissection, and BAV[903] are associated with rapid growth rate and will require closer follow-up.

9.2.5.4.2. Open repair. Open TAAA repair is a complex aortic procedure. Post-operative mortality risk increases with left ventricular (LV) dysfunction, renal insufficiency, and advanced age.[1035–1037] Since organs and tissues distal to the aortic clamp will suffer from prolonged ischaemia, extracorporeal circulation is mandatory to reduce complications,[1011,1038] especially SCI (2.5%–15%).[1011,1039–1044] The mortality rate after open TAAA repair varies between 6% and 8% in high-volume centres[1006,1011,1039] vs. 30% in less experienced centres,[1045,1046] raising the recommendation to perform these complex procedures only in specialized institutions.

9.2.5.4.3. Endovascular repair. Endovascular repair is a promising alternative for treating challenging aortic anatomy like juxta-renal AAA (*Figure 22*).[1047,1048] The use of fenestrated and branched endografts has shown excellent results, allowing perfusion of visceral vessels.[1049–1053] While direct comparison studies with open TAAA repair are lacking,[1054] the increasing adoption of endovascular procedures is notable, especially for high-risk patients, with low post-operative mortality rates (<10%).[1051,1052,1055–1058] A recent meta-analysis confirms these excellent outcomes, endorsing endovascular repair for TAAA.[1059] The incidence of post-operative SCI (around 5%) is similar between endovascular and open repair.[1052,1057,1060,1061] Thus, at mid-term follow-up, endovascular repair is durable with acceptable secondary re-intervention rates, which remain one of the major limitations.[1052,1057,1058,1060,1061] Factors favouring endovascular vs. open repair in TAAA are presented in *Table 15*.

Recommendation Table 40 — Recommendations for the management of patients presenting with descending thoracic aortic and thoracoabdominal aortic aneurysms

Recommendations	Class[a]	Level[b]
In patients with unruptured DTA aneurysm (without HTAD), elective repair is recommended if diameter ≥55 mm.[902,1002]	I	B
In patients without HTAD with unruptured DTA aneurysm, when elective repair is indicated and anatomy is suitable, TEVAR is recommended over open repair.[1006,1019,1020]	I	B
In patients with DTA aneurysm who undergo TEVAR with planned LSA coverage, it is recommended to revascularize the LSA before TEVAR to reduce the risk of SCI and stroke.[1026,1028,1029]	I	B
In patients with unruptured degenerative TAAA, elective repair is recommended when the diameter is ≥60 mm.[902,1002,1033]	I	B
In patients without significant comorbidities and with unruptured DTA aneurysm, when elective repair is indicated and anatomy is unsuitable for TEVAR, open repair should be considered if life expectancy exceeds 2 years.[1013]	IIa	B
In TAAA, surgical repair should be considered at diameters ≥55 mm if patients present with high-risk features, are at very low risk, and are under the care of experienced surgeons in a multidisciplinary aorta team.[1004,1033,1034]	IIa	B
In patients with unruptured degenerative TAAA and suitable anatomy, when elective repair is indicated, endovascular repair using fenestrated and/or branched endografts should be considered in experienced centres.[1051,1052,1055–1059]	IIa	B
In patients with unruptured DTA aneurysm (without HTAD) and high-risk features,[c] elective repair may be considered if the diameter is <55 mm.[904,1003,1004,1033,1034]	IIb	B

Continued

DTA, descending thoracic aorta; HTAD, heritable thoracic aortic disease; LSA, left subclavian artery; SCI, spinal cord ischaemia; TAAA, thoracoabdominal aortic aneurysm; TEVAR, thoracic endovascular aortic aneurysm repair.
For heritable thoracic aortic disease refer to *Section 10*.
[a]Class of recommendation.
[b]Level of evidence.
[c]See *Figure 23* for high-risk features.

9.2.5.5. Surgical treatment of abdominal aorta aneurysms

9.2.5.5.1. General considerations. Rupture remains the most feared AAA complication, and is associated with the maximum diameter,[1063] as well as other risk factors (*Figure 23*). Different studies[1064–1071] (including the United Kingdom Small Aneurysm Trial [UKSAT] and American Aneurysm Detection and Management [ADAM] trial) reported no benefits from open or endovascular interventions (despite lower peri-operative complication rates) in asymptomatic AAA patients with a maximal diameter <55 mm in men and <50 mm in women. Evidence that women are more likely to rupture under surveillance and at a smaller aortic diameter justified a lower (50 mm) threshold. Another interesting method to quantify the risk of rupture based on body size, which seems a better predictor in women, has been proposed.[1072] However, in the absence of recent studies, thresholds for intervention have not changed in recent years. Considering the complexity of patient management, it is advisable to centralize complex procedures in centres with a high level of expertise in aortic diseases and a multidisciplinary team.

9.2.5.5.2. Pre-operative cardiovascular evaluation and choice of treatment. Coronary artery disease is the leading cause of early mortality after AAA repair,[937,1073] and is associated with a 5%–10% rate of peri-operative CV complications such as death, MI, or stroke.[1074,1075] Since endovascular repair is associated with lower mortality (<1%) and CV complications,[1076–1079] the need for pre-operative cardiac

Table 15 Overview of factors favouring open vs. endovascular repair in thoracoabdominal aortic aneurysm

Characteristic	Favours open repair	Favours endovascular repair
Biological age and life expectancy	• Younger age • Considerable life expectancy with acceptable quality of life	• Older age • Limited life expectancy
Anatomical considerations	• If aortic and branch anatomy preclude endovascular approach • Poor vascular access	• Suitable proximal and distal landing zones • Favourable visceral and renal configuration • Vascular access obtainable
Pathological	• Chronic dissection	• Acute dissection
Background/causal factor	• Hereditary aortic disease	• Degenerative aortic disease
Cardiopulmonary condition	• Good cardiopulmonary reserve	• Poor cardiopulmonary reserve
Fitness	• No significant comorbidities • Successful rehabilitation likely	• Severe organ impairment (renal, kidney, pulmonary) • Obesity • Limited mobility, unlikely to rehabilitate successfully
Urgency	• Elective repair • Emergency repair without a viable endovascular solution	• Elective repair • Emergency repair with time for custom-made graft or suitable for standard grafts

Adapted from Ouzounian *et al.* with permission.[1062]

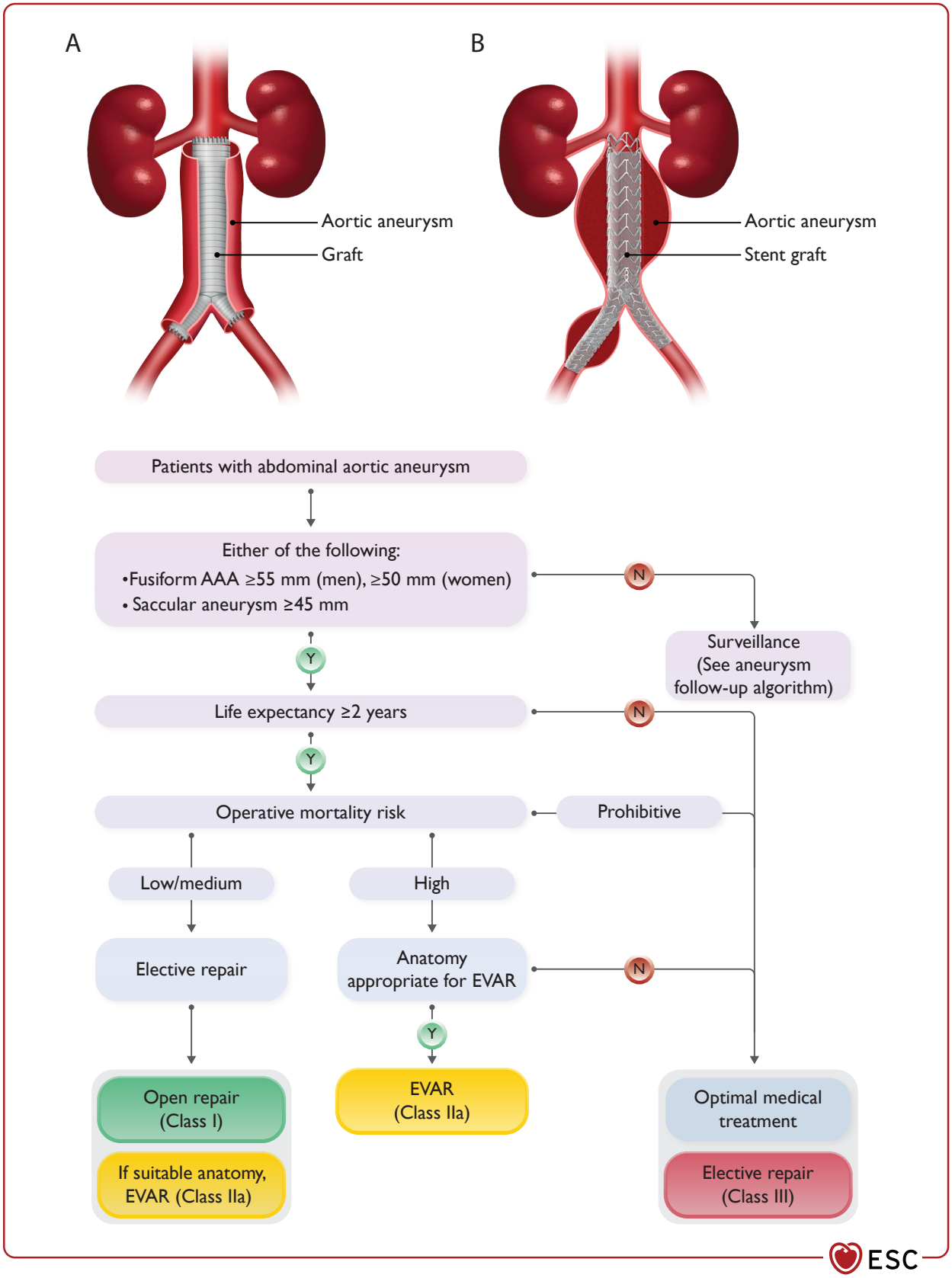

Figure 26 Algorithm for individual decision-making process in the treatment of patients with abdominal aortic aneurysm. (*A*) Illustration of open repair (graft). (*B*) Illustration of endovascular treatment (EVAR). AAA, abdominal aortic aneurysm; EVAR, endovascular aortic aneurysm repair.

work-up will depend on procedure risk, symptoms, and patient-specific CVRFs (see *Sections 4* and *12*, and the *2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery*).[1080] Coronary revascularization before elective aortic surgery in patients with stable cardiac symptoms cannot be recommended, since there is evidence that this strategy does not improve outcomes or reduce the 30 day MI rate.[1080,1081]

A complete vascular evaluation (that includes not only the AA but also the entire aorta: ascending, arch, and descending aorta) is mandatory to determine the best strategy in AAA management, CCT being, by consensus, the optimal pre-operative imaging modality.[1082,1083] When CCT is contraindicated, consider CMR, though calcification assessment is challenging. Pre-operative planning should determine EVAR feasibility by sizing the aorto-iliac system, yet adherence to device-specific instructions remains uncertain.[1084–1090] DUS assessment of the femoro-popliteal segment is advocated since femoro-popliteal aneurysms are commonly associated with AAA.[1091,1092] Additionally, the technique of choice should be discussed between the treating physician and the patient based on the patient's life expectancy and preferences, operator and hospital volumes, and surveillance compliance.[910,1093–1097] Elective AAA repair is not recommended in frail patients or those with life expectancy <2 years.[1098,1099] The individual decision-making process in AAA patients is displayed in *Figure 26*.

Different studies have demonstrated a significant short-term survival benefit for EVAR, but with similar long-term outcomes compared with open repair (up to 15 years)[1100–1103] also reported in females.[1104] However, loss of early benefit is associated with an increased rate of late complications occurring after 8 years, especially late ruptures.[1079] These trials used earlier-generation EVAR devices, so the durability of the latest-generation devices remains uncertain. Recent data, however, suggest a reduced risk of late complications and fewer re-interventions.[1105–1108]

9.2.5.5.3. Open abdominal aorta aneurysm repair. Open AAA repair through mid-line laparotomy (with <30 min clamping time) with a Dacron graft has been the preferred choice for years, despite notable CV morbidity[1078,1100,1109–1113] and a 2%–5% mortality rate.[1110,1111,1113,1114] In ruptured AAA, open repair results are worse than those of elective surgery, with an unchanged complication rate of around 48%.[1115] Thus, endovascular repair is recommended to reduce peri-operative morbidity and mortality.[1116–1118]

Open AAA repair raises incisional hernia risk, particularly in obese patients, suggesting prophylactic mesh use in high-risk cases.[1119–1121]

9.2.5.5.4. Endovascular abdominal aorta aneurysm repair. Endovascular abdominal aorta aneurysm repair reduces peri-operative mortality to <1%, although it implies higher risk of re-intervention in the long term.[1122–1124] Current devices offer features like active fixation, repositioning ability, low-profile design, and polymer-filled rings for improved sealing.[1106,1125–1128] New devices demonstrate similar long-term outcomes with reduced re-intervention risk,[1090] expanding treatment possibilities to 60%–70% of infrarenal AAA cases.[1129,1130]

In cases of juxta- or para-renal AAA (*Figure 22*), both open and endovascular treatment can be proposed in high-volume centres, with similar short- and long-term results. The choice between open surgical repair and endovascular repair depends on various factors, including the patient's anatomy, overall health, and the extent of the aneurysm (see *Table 15*). In cases of complex endovascular treatment, a fenestrated or branch stent endograft should be considered.[1096,1131]

A percutaneous femoral approach is suitable since it provides quicker access, reduced invasiveness, and allows local anaesthesia. Some evidence supports the use of ultrasound-guided percutaneous access for EVAR due to a lower rate of access-related complications and a shorter operation time.[1132–1135]

As patients treated by EVAR are more prone to late complications (endoleaks, migration, or rupture) and re-interventions, lifelong surveillance is currently mandatory.[1096,1136–1140]

Recommendation Table 41 — Recommendations for the management of patients presenting with abdominal aortic aneurysm

Recommendations	Class[a]	Level[b]
Elective repair is recommended if AAA diameter is ≥55 mm in men or ≥50 mm in women.[1064–1067]	I	A
In ruptured AAA with suitable anatomy, endovascular repair is recommended over open repair to reduce peri-operative morbidity and mortality.[1116–1118]	I	B
Prior to AAA repair, DUS assessment of the femoro-popliteal segment, to detect concomitant aneurysms, should be considered.[1091,1092]	IIa	B
In patients with AAA with suitable anatomy and reasonable life expectancy (>2 years), EVAR should be considered as the preferred therapy, based on shared decision-making.[910,1096,1141–1143]	IIa	B
In patients with unruptured AAA and aneurysm growth ≥5 mm in 6 months or ≥10 mm per year, repair may be considered.[1064,1065]	IIb	C
Elective repair for patients presenting with a saccular aneurysm ≥45 mm may be considered.[1144]	IIb	C
In patients with AAA and limited life expectancy (<2 years), elective AAA repair is not recommended.[1098,1099]	III	B
Prior to AAA repair, routine evaluation with coronary angiography and systematic revascularization in patients with chronic coronary syndromes is not recommended.[1080,1081]	III	C

AAA, abdominal aortic aneurysm; DUS, duplex ultrasound; EVAR, endovascular aortic aneurysm repair; TAA, thoracic aortic aneurysm.
See also *Figure 23*.
[a]Class of recommendation.
[b]Level of evidence.

9.2.6. Endoleaks

Endoleaks are defined as the persistence of blood flow outside the graft but inside the aneurysm sac, preventing complete thrombosis (*Figure 27*). They are the most common complication, with an incidence up to one-third of either early or late procedures (those appearing after 1 year).[1145] Chronic anticoagulation constitutes a risk factor for re-intervention, late conversion surgery, or mortality.[1146] Endoleaks exposing the aneurysm sac to systemic pressure and expansion will require re-intervention to prevent rupture.

Five types of endoleaks have been described, as detailed in *Figure 27*. Type I and type III require correction with a new (endovascular) procedure. Type II is present in about 25% of patients but may seal

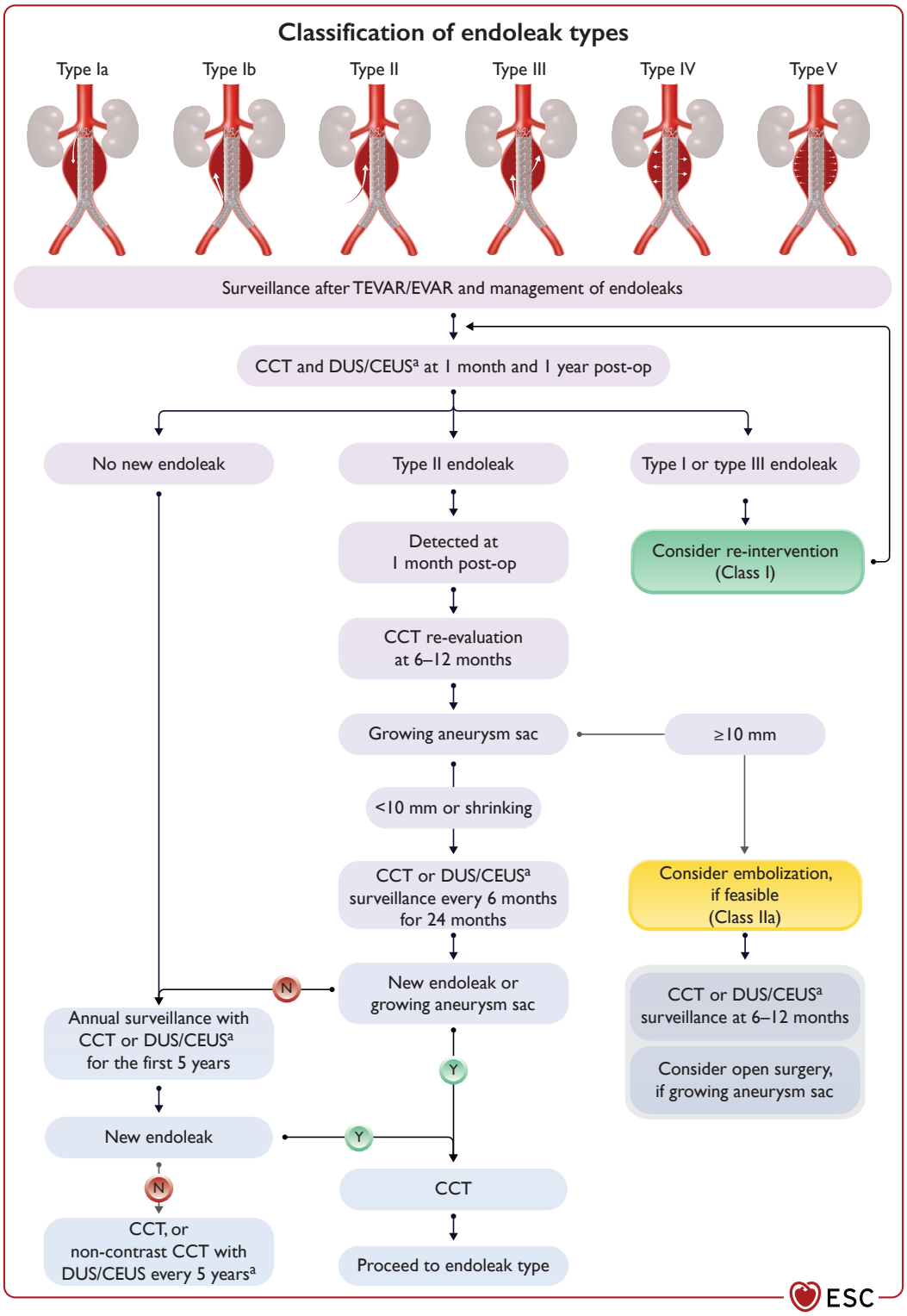

Figure 27 Algorithm for follow-up after thoracic endovascular aortic aneurysm repair, and management of endoleaks and their classification. CEUS, contrast-enhanced ultrasound; CCT, cardiovascular computed tomography; DUS, duplex ultrasound; TEVAR, thoracic endovascular aortic aneurysm repair; EVAR: Endovascular aortic repair. [a]In cases of TEVAR, CCT is the preferred imaging technique since DUS/CEUS does not permit the correct evaluation of the thoracic aorta. In cases of renal failure, non-contrast CCT is a good alternative to monitor aneurysm sac growing and is associated to DUS/CEUS for EVAR monitoring. Endoleaks are classified into five types: Type Ia, proximal attachment site endoleak; Type Ib, distal attachment site endoleak; Type II, backfilling of the aneurysm sac through branch vessels of the aorta; Type III, graft defect or component misalignment; Type IV, leakage through the graft wall attributable to endograft porosity; and Type V; caused by 'endotension', possibly resulting from aortic pressure transmitted through the graft/thrombus to the aneurysm sac. Adapted from Rokosh *et al.* with permission.[1147]

spontaneously in approximately 50% of cases. Risk factors for type II endoleaks include patent collaterals, presence of accessory arteries, and anticoagulation. In cases of significant sac expansion (≥10 mm), re-intervention should be considered, preferably by vessel or sac embolization. Type IV, attributed to device porosity, is rare with modern devices and no intervention is needed. Type V induces sac expansion without any visible endoleak. Treatment may be considered for significant sac growth (≥10 mm) and consists of stent graft relining or definitive endograft explant and open surgical repair.

Cardiovascular computed tomography with(out) contrast, and DUS and/or CEUS, are the main imaging modalities for TEVAR/EVAR follow-up. Imaging within the first 30 days is recommended to assess treatment success and/or complications. For TEVAR, contrast-enhanced CCT is the preferred imaging technique for follow-up and should be performed regularly (shorter or longer intervals are based on the expansion rate). In renally impaired patients, combined follow-up using DUS and non-contrast enhanced CCT is a suitable alternative (see follow-up algorithm, *Figure 27*). For EVAR, CCT and DUS/CEUS are recommended at 1 month following repair. Thereafter, surveillance should be based on the risk of late complications and includes DUS and/or CEUS (*Figure 27*).

Recommendation Table 42 — Recommendations for the management of patients presenting with endoleaks

Recommendations	Class[a]	Level[b]
It is recommended to perform 30 day imaging after TEVAR/EVAR, by CCT and DUS/CEUS, to assess the success of intervention.[1096]	I	B
It is recommended to re-intervene to achieve a seal in patients with type I endoleak after TEVAR/EVAR.[1137,1148]	I	B
It is recommended to re-intervene, principally by endovascular means, to achieve a seal in patients with type III endoleak after TEVAR/EVAR.[1139]	I	B
Re-intervention, principally with an endovascular approach or embolization, should be considered in patients with type II or V endoleak and significant sac expansion ≥10 mm or significantly decreasing proximal or distal seal.[1096,1149]	IIa	C

CCT, cardiovascular computed tomography; CEUS, contrast-enhanced ultrasound; DUS, Duplex ultrasound; TEVAR/EVAR, thoracic endovascular aortic aneurysm repair.
[a]Class of recommendation.
[b]Level of evidence.

9.2.7. Long-term follow-up after aortic repair

Long-term success in the management of aortic aneurysms depends also on strict post-treatment surveillance, for both secondary prevention of the aortic disease and early identification of post-repair complications.

In endovascularly treated patients, surveillance aims to detect endoleaks, aneurysmal sac dilatation, and graft structural failure or migration.[1150] Surgical treatments, while carrying higher operative risks, often yield more durable results with rarer late complications mostly related to laparotomy.[1151]

After intervention on the thoracic aorta, TTE, TOE, CCT, and CMR are used for follow-up, CCT being the most used and available method for both endovascular and surgical treatments.[1150–1152] After intervention on the AA, CCT, CMR, and DUS/CEUS are used. DUS/CEUS can detect the most common drawbacks of EVAR, except for graft structural issues. For chronic and periodic monitoring, the use of CMR, especially in young women, should be considered (to reduce radiation exposure). However, the choice between these modalities should consider patient factors, potential artefacts, and local imaging expertise and availability. Both for the thoracic and abdominal aorta, due to the lack of studies systematically comparing different surveillance time intervals, recommendations are mostly based on consensus or evidence from single-centre observational studies.[70,1153]

9.2.7.1. Follow-up after thoracic aortic aneurysm treatment

Complications after ascending aorta graft replacement, though rare, include pseudo-aneurysms and graft infections. Pseudo-aneurysms, occurring in roughly 5% of cases, are most common within the first 2 post-operative years, linked to aortic dissection surgery, HTAD, and synthetic glues.[1154] CMR studies systematically following peri-anastomotic haematomas have reported higher rates (15%).[1155] Graft infections can occur in 0.5%–6% of surgical patients with high morbidity and mortality rates, requiring rapid diagnosis. Treatment typically involves surgery and antibiotics, tailored to factors like overall health, infection severity, and underlying conditions.[1156] Residual aortic disease progression depends on the underlying condition, such as HTAD, and requires individualized surveillance.

After TEVAR for DTA aneurysm, late complications are higher than with surgery (up to 38%), leading to re-operation in 24% of cases.[1150] However, over 80% of TEVAR complications arise within the initial post-operative years.[1157] Notably, FET results in fewer stent graft-related complications: 2% stent-induced intimal tear, 3% endoleak, and 7% need for additional TEVAR.[1158]

After surgical treatment of TAAs, the protocol is a first CCT scan at discharge or 1 month, then another in the first post-operative year (at 6, 9, or 12 months), followed by a 2 year scan, and if no issues arise, scans every 5 years thereafter (*Figure 25*).[1062,1159] Stricter lifelong surveillance is recommended after TEVAR: after first imaging at 1 month, yearly controls are recommended for at least the first 5 post-operative years, then less frequently if no complications are detected (*Figure 27*).

Cardiovascular risk profile modification, cardiac rehabilitation, and lifestyle adjustments are an integral part of post-aneurysm repair follow-up (*Figure 7*).[24]

9.2.7.2. Follow-up after abdominal aortic aneurysm treatment

Evidence for follow-up after AAA is more robust than after TAA repair.[70,1096] Post-surgery, anastomotic or para-anastomotic complications are rare (2%–4%).[1160] In contrast, EVAR has higher complication rates (16%–30%), necessitating lifelong surveillance.[1079,1150] EVAR's survival advantage over surgery diminishes after 8 years, with higher aneurysm-related mortality risk for EVAR.[1079] However, most failures are detectable early, and complications seldom occur later in patients with normal early controls.[1161,1162] CCT effectively detects early EVAR abnormalities,[1163] but DUS/CEUS surveillance proves accurate, reducing the need for radiation and nephrotoxic agents, and lowering costs (*Figure 27*).[1164–1167]

Interestingly, a meta-analysis found low compliance of patients to post-operative surveillance without differences in all-cause mortality, aneurysm-related mortality, and re-intervention between compliant and non-compliant patients.[1168] Altogether, the above-mentioned evidence supports stratified methods of surveillance,[1096] with

identification of high-risk situations (e.g. older patients, inadequate sealing, type II endoleaks, no early post-procedural shrinkage of the aneurysmal sac) for which more frequent evaluation should be planned.[1161,1169,1170]

Follow-up of OMT is highly important in AAA patients (*Figure 7*).[24] Statin use after AAA repair (surgical or EVAR) is associated with decreased short- and long-term mortality.[1171] In addition, surveillance for aneurysm development in other arterial locations is recommended.

Recommendation Table 43 — Recommendations for follow-up after treatment of aortic aneurysms (see also Evidence Table 12)

Recommendations	Class[a]	Level[b]
Thoracic aortic aneurysm		
After open repair of TAA, an early CCT is recommended within 1 month, and then yearly CCT follow-up for the first 2 post-operative years and every 5 years thereafter is recommended if findings are stable.[c,70,1153,1159]	I	B
After TEVAR, follow-up imaging is recommended at 1 and 12 months post-operatively, then yearly until the fifth post-operative year if no abnormalities[d] are documented.[70,1153,1158]	I	B
After 5 post-operative years without complications, continuing long-term follow-up of TEVAR by CCT every 5 years should be considered.[70,1153,1158]	IIa	B
If growth of the excluded aneurysm is observed, without evidence of type I or III endoleak, repeating CCT every 6–12 months, depending on the growth rate observed, should be considered.[1150]	IIa	C
When frequent controls are required in TAA patients treated either by open or endovascular repair, CMR should be considered instead of CCT after the first year of follow-up. However, the choice between these imaging modalities should be based on individual patient factors, the potential for artefacts, and the local availability and expertise in specific imaging techniques.[1155]	IIa	C
Abdominal aortic aneurysm		
After open repair of AAA, first follow-up imaging is recommended within 1 post-operative year, and every 5 years thereafter if findings are stable.[1079,1096]	I	A
After EVAR, follow-up imaging is recommended with CCT (or CMR) and DUS/CEUS at 1 month and 12 months post-operatively, then, if no abnormalities[d] are documented, DUS/CEUS is recommended every year, repeating CCT or CMR (based on potential artefacts) every 5 years.[70,1079,1100,1163–1165,1167]	I	A
In higher-risk patients, i.e. with inadequate sealing or type II endoleak at first CCT control, more frequent DUS/CEUS imaging should be considered.[e,1096,1161,1164,1165,1167]	IIa	B
In low-risk[f] patients, from 1 year post-operatively after EVAR, repeating DUS/CEUS every 2 years should be considered.[1096]	IIa	B
If any abnormality during DUS/CEUS is found, confirmation should be considered using additional CCT or CMR (based on potential artefacts).[1163,1166]	IIa	B
In post-treatment surveillance, administration of OMT (see 8.1.2.2 and 8.2.4) and assessment of aneurysm development/growth in other arterial segments should be considered.	IIa	C

Continued

AAA, abdominal aortic aneurysm; CCT, cardiovascular computed tomography; CEUS, contrast-enhanced ultrasound; CMR, cardiovascular magnetic resonance; DUS, Duplex ultrasound; EVAR, endovascular aortic repair; OMT, optimal medical treatment; TAA, thoracic aortic aneurysm; TEVAR, thoracic endovascular aortic repair.
[a]Class of recommendation.
[b]Level of evidence.
[c]Both at the level of the treated segment and in the residual native aorta.
[d]Including: endoleak (any type), enlargement of the excluded aneurysm, and stent graft migration/separation/fracture.
[e]e.g. imaging every 6 months during the first year, thereafter every 2–3 years.
[f]Low-risk: early sac shrinkage >10 mm, relatively younger age (<70 years), proximal and distal sealing >10 mm, no endoleak.

9.3. Acute thoracic aortic syndromes

9.3.1. General concepts

Acute aortic syndromes are life-threatening emergencies, including classic AAD, IMH, PAU, aortic pseudo-aneurysm, and traumatic aortic injuries (TAI). They involve aortic wall damage and share a dynamic, overlapping pathophysiology, clinical presentation, and diagnostic and therapeutic approaches.[24,172,174,910] AAS may also be iatrogenic following open or endovascular/percutaneous procedures, or cardiac surgery.[1172]

To guide AAS management, several anatomical classifications have been developed, the Stanford and the DeBakey systems being the most widely used. The Stanford system classifies AAS according to whether the ascending aorta is involved (type A or DeBakey type I and type II) or not (type B or DeBakey type IIIa and type IIIb) regardless of the site of origin of the intimal tear.[172,174,910,1173] This classification considers not only anatomical and treatment aspects, but also prognostic implications, since patients with DeBakey type II AAS will probably be left without structural aortic wall lesions after surgery (*Figure 28*).

Furthermore, if time elapsed from symptom onset to diagnosis is considered, AAS can be divided into hyperacute (<24 h), acute (1–14 days), subacute (15–90 days), and chronic (>90 days) (*Figure 28*).[1174–1176]

A new classification considers the intimal tear's entry site and dissection extension (*Figure 29*).[136] Subscript P describes the proximal involved aorta, and subscript D indicates the distal zone. This classification guides treatment decisions for sealing the entry tear. AADs limited to the aortic arch or originating as retrograde dissections from the descending aorta that extend into the arch and stop before the ascending aorta are termed as ***non-A non-B AD***.[1177–1179]

Recently, a European update of the Stanford classification—Type Entry Malperfusion (TEM) classification—has been proposed.[1180] This combines information about the type of dissection, its extent, and the presence of complications (malperfusion), thus providing greater prognostic insights (*Figure 29*). This classification is recommended by the European Association for Cardio-Thoracic Surgery. The TEM and other classifications are described in the Supplementary data online, *Section 1.6*.

9.3.1.1. Epidemiology and risk factors

Classic AAD (comprising 80%–90% of AAS; incidence of 2.6–3.5 cases per 100 000 person-years)[24,1181] is characterized by the presence of an intimal flap separating the true from the false lumen (FL).[24,172,910]

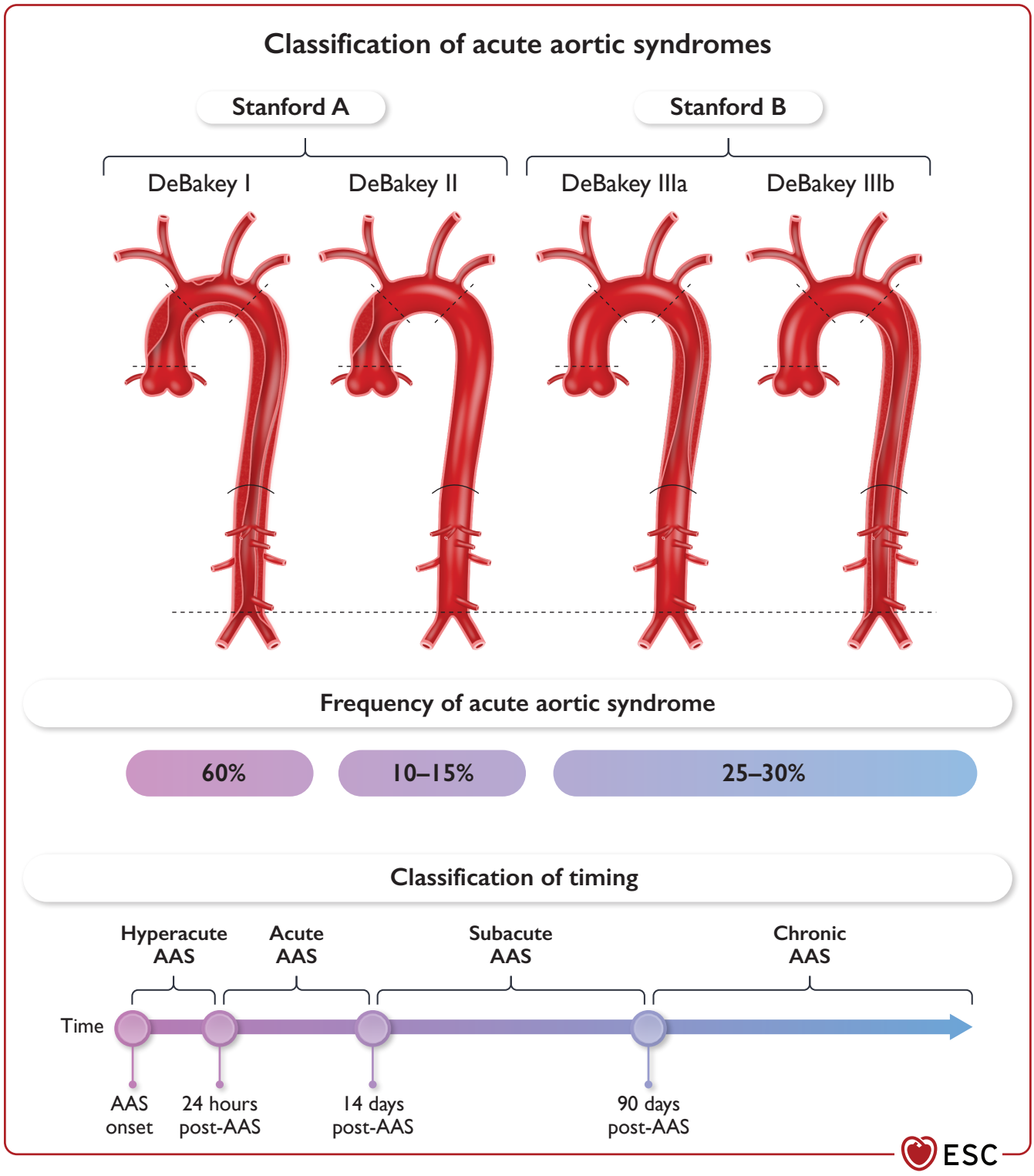

Figure 28 Anatomical and temporal classification of acute aortic syndrome. AAS, acute aortic syndrome.

Acute aortic dissection occurs mostly in males (~65%) and in the seventh decade of life (~63 years).[1175,1182] Multiple risk factors often coexist directly linked to factors like wall stress (with systemic hypertension being the most common) and/or aortic media abnormalities, including syndromic and non-syndromic genetic diseases. HTAD, BAV, prior aortic surgery, and larger aortic dimensions are more frequent among young patients (<40 years).[24,1182,1183] Systemic hypertension and cocaine abuse are more common among African-American

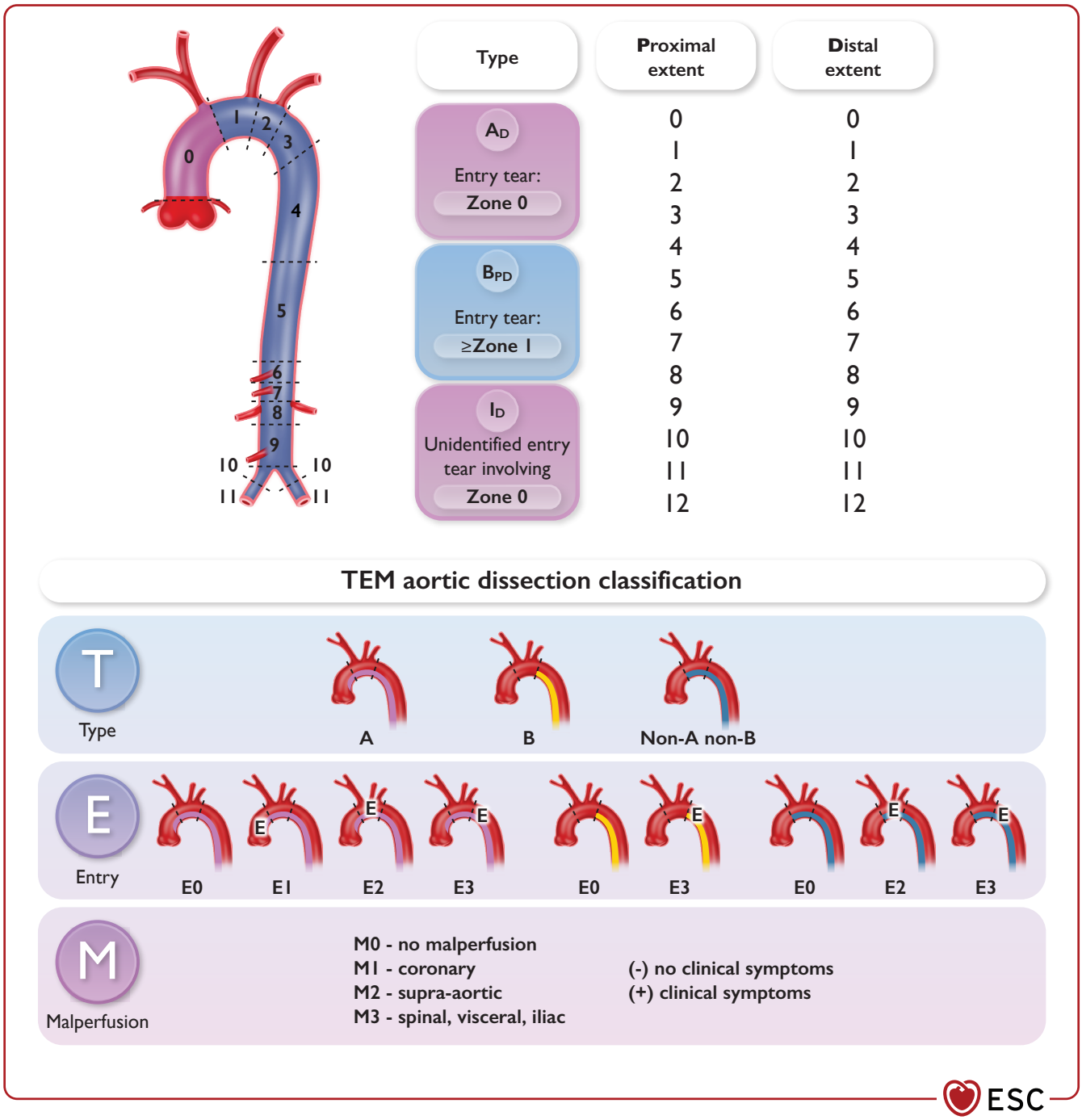

Figure 29 Aortic dissection classification system based on the 2020 Society for Vascular Surgery/Society of Thoracic Surgeons Reporting Standards and the European update of the Stanford classification—Type Entry Malperfusion classification. A, type A aortic dissection; B, type B aortic dissection; non-A, non-B, aortic dissection limited to the aortic arch or retrograde dissection extending into the arch (but not in the ascending aorta). Upper panel: Classification of AAD considering the intimal tear's entry site and dissection extension. Subscript P describes the proximal involved aorta, and subscript D indicates the distal zone. Lower panel: The TEM classification is the European update of the Stanford classification combining information about the Type of dissection (T), the Entry site (E), and the presence of Malperfusion (M). Also refer to Supplementary data online, *Section 1.6*. Society for Vascular Surgery/Society of Thoracic Surgeons (SVS/STS). Reproduced with permission from.[136,1180]

than among white patients.[1184,1185] Of note, the incidence of iatrogenic AD during cardiac catheterization is very low (around 0.01%–0.02%) and during cardiac surgery is 0.06%–0.23%, with favourable in-hospital and long-term prognosis.[1186,1187]

9.3.1.1.1. Sex differences. A specific female sex phenotype appears to be evident in acute TAAD. At admission, acute TAAD female patients are usually older but have lower body mass index (BMI), BSA, and creatinine plasma levels. They present less frequently with active smoking,

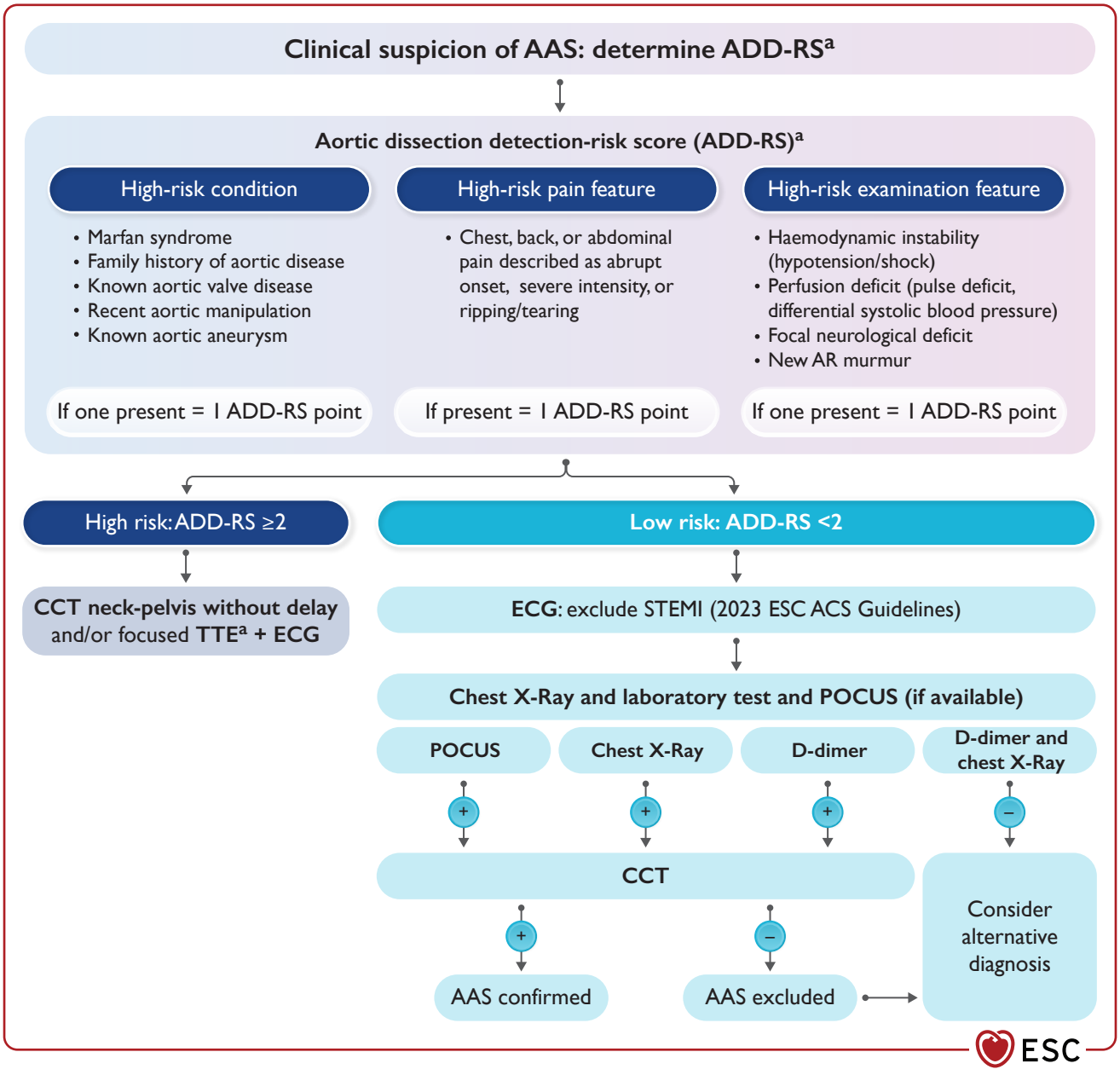

Figure 30 Multiparametric diagnostic work-up of acute aortic syndrome. AAS, acute aortic syndrome; ADD-RS, aortic dissection detection-risk score; CCT, cardiovascular computed tomography; ECG, electrocardiogram; POCUS, point-of-care ultrasound; STEMI, ST elevation myocardial infarction; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography; +, findings compatible with AAS. [a]In haemodynamically unstable patients: consider TTE and/or TOE as first-line imaging technique depending on local expertise and availability.

BAV, and previous cardiac surgery,[1188] but diabetes mellitus is more common in women than in men. In-hospital surgical mortality does not differ between sexes, although 10 year survival appears to be higher in men. Among only medically treated acute TAAD patients, prohibitive high in-hospital mortality has been equally registered for both sexes (men 58.6% vs. women 53.8%).[1188] However, further studies are needed to explore AAD sex differences to design appropriate diagnostic and therapeutic interventions and preventive strategies.[1189]

Pregnancy increases the risk of AAS, more often in the last trimester (50%) or post-partum (33%).[1190]

9.3.1.1.2. Chronobiology. Acute aortic dissection presents chronobiological patterns, with a higher incidence in morning hours (peak between 8 am and 9 am) and winter (peak in January in the Northern Hemisphere).[24,1175]

9.3.1.1.3. Outcomes. For acute TAAD, in-hospital mortality has decreased from 31% to 22% due to better surgical outcomes; for acute type B aortic dissection (acute TBAD), in-hospital mortality has remained stable over the years (14%).[1175,1182] Including deaths before admission, 30 day mortality for AAD ranges from 23% to 55.8% in Western Europe.[1181]

Non-A, non-B dissection patients tend to be younger (median age 59 years) and have a lower mortality than acute TAAD patients.[1180,1191] The 30 day mortality in patients medically treated is around 14%,[1179] and 4.4% for those successfully treated surgically.[1177]

9.3.1.2. Clinical presentation

Acute TAAD typically presents with sudden, severe chest/back pain, often described as 'sharp', alongside a history of arterial hypertension. However, around 6.4% of patients do not experience pain.[1182,1192,1193] Hypotension and shock are frequent. Unique clinical features specific to acute TAAD include pericardial effusion, aortic regurgitation, and coronary artery involvement leading to ACS (particularly the right coronary artery).[1194] Stroke may occur when supra-aortic branches are involved. Additional complications encompass paraplegia (resulting from spinal ischaemia), acute kidney injury, intestinal ischaemia, or limb ischaemia. Isolated abdominal aortic dissection occurs in about 1.3% of acute TBAD cases when the intimal flap originates below or at the renal arteries.[1195]

A complete clinical evaluation is mandatory, consisting of a central neurological evaluation, heart and lung auscultation (aortic diastolic murmur, pericardial rubbing, etc.), abdominal palpation (tenderness, etc.), and assessment of peripheral pulsations as well as mobility and sensibility in upper and lower limbs. SBP differences (pulse deficit) should be sought.

9.3.1.3. Diagnostic work-up

Early diagnosis is still a major pitfall in managing AAD patients, therefore, a diagnostic multiparametric algorithm is proposed (*Figure 30*). It combines the aortic dissection detection-risk score (ADD-RS) with D-dimer (DD) and has been validated with an excellent capacity to rule out AAS.[1196–1200]

In patients presenting with chest pain, a routine chest radiography and ECG are recommended to exclude other aetiologies; however, the absence of these findings should not delay further investigations.[163] Laboratory tests should be obtained, but awaiting results should not delay imaging if there is a high probability of AAD. The most common finding is an increase in DD level, which is the case in several other conditions such as pulmonary embolism or infections. When DD levels are below 500 ng/mL, AAD is unlikely.[172,1201]

A focused TTE at the emergency department, if available, is recommended[1202,1203] to assess pericardial effusion, wall motion abnormalities, aortic regurgitation, and aortic diameters. Sometimes a dissection flap can be visualized, especially when using contrast.[165]

When AAD is suspected, ECG-gated CCT from neck to pelvis is the preferred imaging technique, with 100% sensitivity and 98% specificity, and should be performed as soon as possible to confirm diagnosis, localize entry tear, extension (type A vs. type B), and malperfusion.[170,172,1182,1204] When ACS or pulmonary embolism are still in the differential diagnosis, a triple rule-out ECG-gated CCT scan protocol can be performed be performed to avoid motion artefacts mimicking acute TAAD.[170,1205,1206] However, this strategy is associated with higher contrast and radiation doses, might be less accurate for AAS, and does not reduce the need for additional imaging tests.[170,1207] If CCT is not available or in haemodynamically unstable patients, TOE can confirm diagnosis. TOE is especially useful pre-, intra, and postoperatively to monitor changes in the anatomical AAD configuration or surgical complications. CMR could be a valuable alternative for CCT, however, it is less available, requires a longer examination time, relies on patient collaboration, and consequently, is less frequently used in the acute setting. CCT, CMR, and TOE all provide good diagnostic accuracy[172,1204] (See Supplementary data online, *Table S4*).

Recommendation Table 44 — Recommendations for diagnostic work-up of acute aortic syndromes

Recommendations	Class[a]	Level[b]
In unstable patients who cannot be transferred to CCT, TOE is recommended for diagnosis[1204,1208,1209] and evaluation of the coeliac trunk and mesenteric artery.[1210]	I	B
In patients presenting with clinical features compatible with possible AAS, a multiparametric algorithm for ruling in or out AAS using the ADD-RS is recommended.[1196–1200]	I	B
ECG-gated CCT from neck to pelvis is recommended as the first-line imaging technique in patients with a suspected AAS since it is widely available, accurate, and provides information about the entry tear, extension, and possible complications (malperfusion, dilatation, or rupture).[170]	I	C
In patients with suspected AAS, focused TTE (with use of contrast if feasible) is recommended during the initial evaluation.[170]	I	C
In patients with suspected AAS, TOE is recommended to guide peri-operative management and detect complications.[170]	I	C
In patients with suspected AAS, CMR should be considered as an alternative imaging technique if CCT is not available.[170]	IIa	C

AAS, acute aortic syndrome; ADD-RS, aortic dissection detection-risk score; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; ECG, electrocardiogram; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography.
See also *Figure 30*.
[a]Class of recommendation.
[b]Level of evidence.

9.3.1.4. Therapeutic intervention in acute aortic dissection

9.3.1.4.1. Initial treatment. Acute aortic syndrome care should be centralized in experienced centres and managed by aorta teams.[1211] The cornerstone in AAS is initial reduction of the pulse pressure by lowering SBP below 120 mmHg and heart rhythm ≤60 beats per minute (b.p.m.). The aim is to decrease aortic wall stress to avoid further extension of dissection with possible rupture or malperfusion.[174,1212–1216] Intravenous beta blockade (labetalol as a first choice due to its alpha- and beta-blocking properties) is generally accepted as the best option. Also, esmolol, an ultra-short-acting beta-blocker, can be titrated quickly and easily, making it particularly useful in the acute setting. If contraindicated, i.v. non-dihydropyridine CCBs could be used for heart rate control. If the BP target is not reached after initiating beta-blockers, i.v. vasodilators such as nitrates or dihydropyridine CCBs (e.g. nicardipine) can be administered concomitantly with rate-controlling agents first to avoid reflex tachycardia. In cases of malperfusion, higher BP could be tolerated to optimize perfusion to the threatened region. Early placement of an arterial line to monitor BP invasively is mandatory and admission to an intensive care unit is advisable (including ECG and urine output monitoring).[1205,1217,1218] Antihypertensive treatment can be gradually switched to oral therapy once BP and heart rate targets are reached and the patient has normal gastrointestinal transit. Adequate pain control is necessary to help reach these haemodynamic goals. Intravenous morphine can be cautiously titrated to induce pain relief (*Figure 31*).

In-hospital mortality, reaching 60%, correlates with AAS type, location, patient comorbidities, and treatment. Risk rises with complications like pericardial tamponade, coronary involvement, or malperfusion. *Figure 32* describes the main signs and symptoms of complications and the mortality rate associated with them.[1219–1223]

Recommendation Table 45 — Recommendation for medical treatment in acute aortic syndromes

Recommendations	Class[a]	Level[b]
In patients with AAS, immediate anti-impulse treatment targeting SBP <120 mmHg and heart rate ≤60 b.p.m. is recommended. In cases of spinal ischaemia or concomitant brain injury, maintaining higher MAP is recommended.[1214–1216]	I	B
Intravenous BBs (e.g. labetalol or esmolol) are recommended as first-line agents. If necessary, i.v. vasodilators (e.g. dihydropyridine calcium blockers or nitrates) could be added.[174,1224]	I	B
Invasive monitoring with an arterial line and continuous three-lead ECG recording, as well as admission to an intensive care unit, is recommended.[1205,1217,1218,1225]	I	B
In patients with AAS who can be managed conservatively and who achieved haemodynamic targets with i.v. anti-impulse therapy, switching to oral BBs and, if necessary, up-titration of other BP-lowering agents, is recommended after 24 h if gastrointestinal transit is preserved.[174,1216]	I	B
Adequate pain control to achieve haemodynamic targets is recommended.[174]	I	C
If the patient has a contraindication for BBs, a non-dihydropyridine calcium blocker should be considered.[174,1224]	IIa	B

AAS, acute aortic syndrome; BB, beta-blocker; BP, blood pressure; b.p.m., beats per minute; ECG, electrocardiogram; i.v., intravenous; MAP, mean arterial pressure; SBP, systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.

Interventional treatment in acute TAAD and acute TBAD is described in the next sections and summarized in *Figure 33*.

9.3.1.4.2. Type A aortic dissection interventional treatment. Immediate surgical repair is recommended for acute TAAD, however, a high mortality rate (~50% and 1%–2% per hour) within the first 48 h is described if managed medically only.[1232] Despite advances in surgical and anaesthetic techniques, there is still a high risk of perioperative mortality (17%–25%) and neurological complications (18%).[1233] In recent reports from the International Registry of Acute Aortic Dissection (IRAD), medically managed patients had a 23.7% mortality rate (0.5% per hour) compared with 4.4% (0.09% per hour) for those undergoing surgery.[1234] Analyses of pre- and post-July 2007 IRAD data showed no difference in 48 h mortality for medically treated patients, but surgical mortality decreased (from 5.5% to 3.9%).[1234] As surgical techniques have improved, data have shown improved post-operative survival rates.[1235] The use of the GERAADA (German Registry of Acute Aortic Dissection Type A) score[1236] should be considered in patients undergoing surgery to determine 30 day mortality (https://www.dgthg.de/de/GERAADA_Score).

Surgical intervention surpasses conservative therapy in long-term follow-up,[1237] even for challenging cases. Thus, all acute TAAD patients should receive surgical treatment; however, cardiogenic shock secondary to pericardial tamponade, malperfusion of coronary arteries, mesenteric circulation, lower extremities, kidneys, or brain, and/or coma are major predictors for post-operative mortality (*Figure 32*).[1234,1238] Among octogenarians, in-hospital mortality was lower after surgery than with conservative treatment (37.9% vs. 55.2%), but with a non-significant difference due to small sample size.[1239] While some have reported excellent surgical and quality of life (QoL) outcomes in elderly patients,[1239] others found

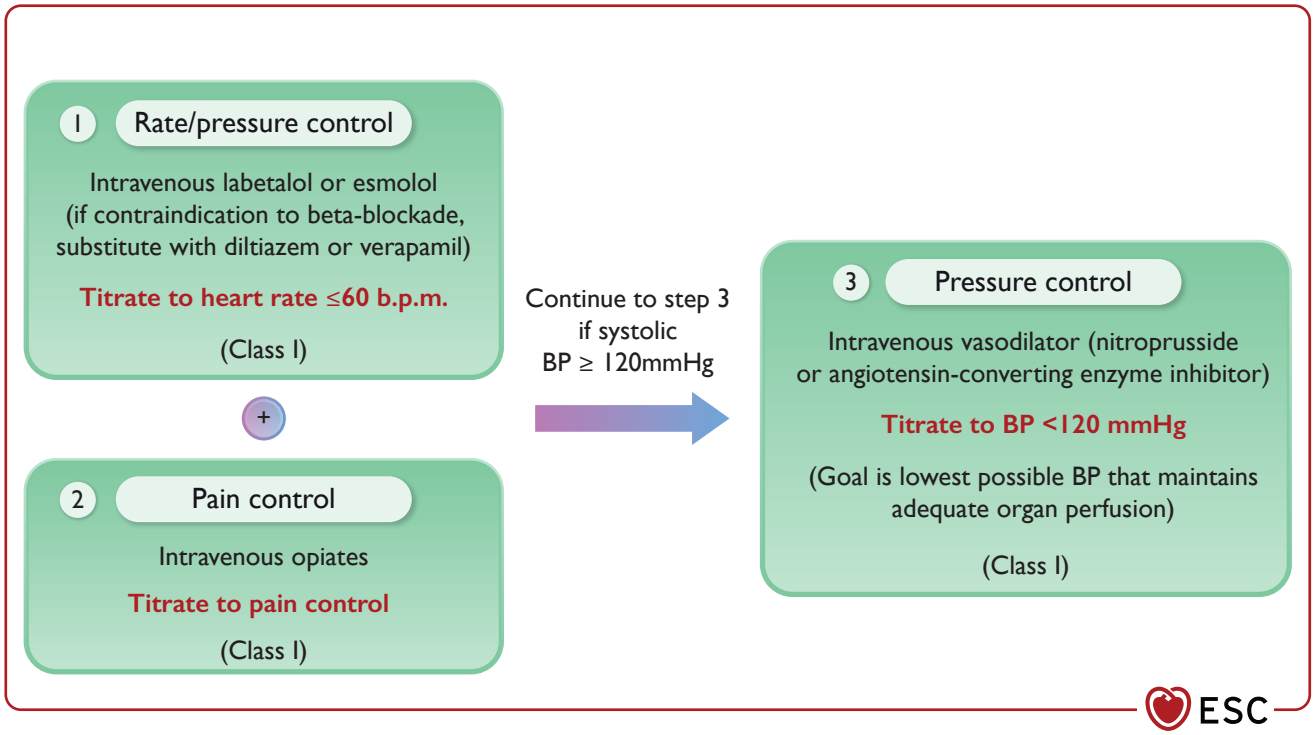

Figure 31 Medical management of acute aortic syndrome. BP, blood pressure; b.p.m: beats per minute.

a higher rate of post-operative neurological complications.[1240] Based on the current evidence, age per se should not be considered an exclusion criterion for surgery.

For optimal repair of acute TAAD regarding long-term outcomes, including risk of late death and late re-operation, the following points need to be addressed. First, in most cases of aortic regurgitation associated with acute TAAD, the aortic valve is essentially normal and can be preserved.[1241–1243] Alternatively, valve replacement can be performed in cases of pre-existent structural valve disease. The decision whether to replace the aortic root is based on the presence of tears in the sinuses, extensive dissection of sinuses/coronary ostia, or significant dilatation of the root. The risk of late dilatation of the aortic sinuses when spared should be considered.[1242,1244] Additionally, the distal extent of aortic repair is a topic of debate. Ascending aortic replacement or hemi-arch replacement alone is technically easier and effectively closes the entry site but leaves a large part of the diseased aorta untreated. In acute TAAD with visceral or renal malperfusion, the primary entry tear is often in the descending aorta. Consider extended therapies like FET repair for these patients, offering a complete repair with a low chance of late re-intervention despite increased technical complexity.[1245–1247]

For potential cardiac arrest from pericardial tamponade, consider an emergency pericardial puncture as a temporary life-saving measure before transferring to the operating room.[1248,1249]

Recommendation Table 46 — Recommendations for intervention in type A acute aortic dissection

Recommendations	Class[a]	Level[b]
In patients with acute TAAD, emergency surgical consultation and evaluation and immediate surgical intervention is recommended.[1182,1250]	I	B
In patients with acute TAAD who have extensive destruction of the aortic root, a root aneurysm, or a known genetic aortic disorder, aortic root replacement is recommended with a mechanical or biological valved conduit.[1251–1255]	I	B
In patients presenting with acute TAAD, transfer from a low- to a high-volume aortic centre with the presence of a multidisciplinary team should be considered to improve survival if transfer can be accomplished without significant delay in surgery.[1256,1257]	IIa	B
In selected patients, a valve-sparing root repair may be considered, when performed by experienced surgeons.[1251,1258,1259]	IIb	B

TAAD, type A aortic dissection.
[a]Class of recommendation.
[b]Level of evidence.

The frozen elephant trunk technique

The FET technique addresses complex aortic and aortic arch issues in a single operation,[1260–1263] creating a secure landing zone for future interventions. Recent advances involve 'proximalization'—placing the FET in the aortic arch's zone 0 or 1, treating proximal arch aortic issues, and enhancing the landing zone for downstream procedures—which surpasses the standard elephant trunk technique.[1264,1265]

Recommendation Table 47 — Recommendations for aortic repair strategies in type A acute aortic dissection

Recommendations	Class[a]	Level[b]
In patients with acute TAAD and a partially dissected aortic root but no significant aortic valve leaflet pathology, aortic valve resuspension is recommended over valve replacement.[1251–1255]	I	B
In patients with acute TAAD undergoing aortic repair, an open distal anastomosis is recommended to improve survival and increase FL thrombosis rates.[1266–1269]	I	B
In patients with acute TAAD without an intimal tear in the arch or a significant arch aneurysm, hemi-arch repair is recommended over more extensive arch replacement.[1270–1272]	I	B
In patients with acute TAAD and a secondary intimal tear in the arch or proximal DTA, an extended aortic repair with stenting of the proximal DTA (e.g. by using the frozen elephant trunk technique) may be considered to reduce late distal aortic complications (e.g. aneurysm evolution of the remaining dissected descending aorta).[1273,1274]	IIb	C

DTA, descending thoracic aorta; FL, false lumen; TAAD, type A aortic dissection.
[a]Class of recommendation.
[b]Level of evidence.

Malperfusion in type A aortic dissection

In acute TAAD with malperfusion, operative mortality correlates with the number of affected organs. Around 30% of patients develop malperfusion syndrome due to elevated pressure in the FL caused by substantial proximal inflow and insufficient distal outflow, leading to visceral organ and limb ischaemia.[1175] The intimal flap may extend into peripheral arteries, causing a static 'stenosis-like' blockage. Malperfusion typically combines dynamic and static obstructions, necessitating surgical and hybrid interventions for affected patients (*Figure 34*).

Mesenteric malperfusion, a life-threatening complication with a mortality rate of 65%–95%, leads to diverse treatment approaches. Some centres prefer early direct reperfusion before aortic surgery,

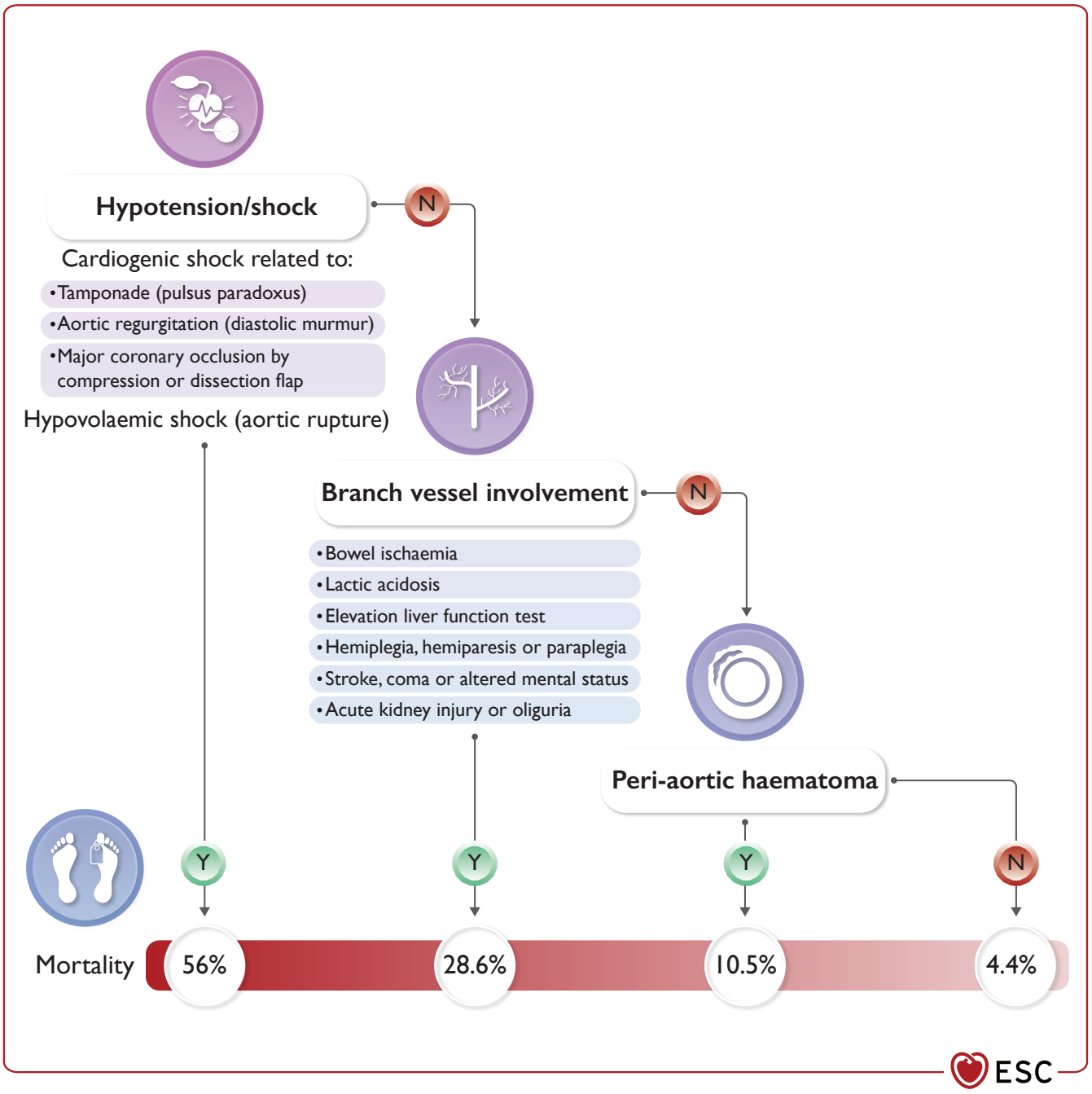

Figure 32 Complications in acute aortic syndromes, clinical evidence associated with malperfusion syndrome, and in-hospital mortality associated with these complications.

while others favour conventional central aortic repair.[1275] The IRAD registry highlights the superiority of a surgical and hybrid approach over medical or endovascular therapy alone. Central aortic repair effectively restores perfusion, showing promising results for renal malperfusion, extremity malperfusion, uncomplicated mesenteric malperfusion, or combinations.

Cerebral malperfusion, equally grave, triggers treatment debates necessitating a multidisciplinary strategy. Evidence supports surgical

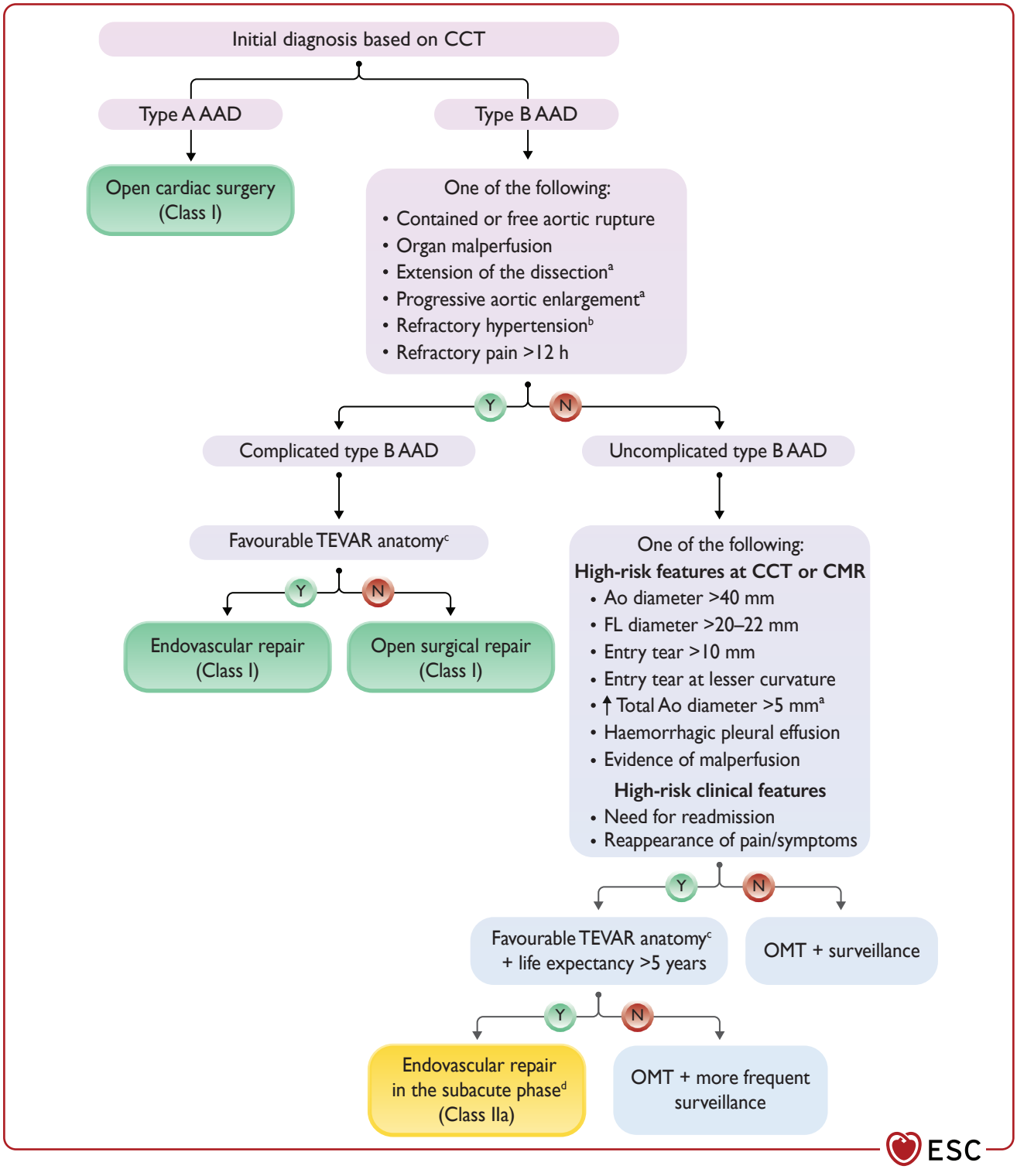

Figure 33 Interventional treatment algorithm in acute aortic dissection. AAD, acute aortic dissection; Ao, aorta; CCT, cardiovascular computed tomography; OMT, optimal medical treatment; TEVAR, thoracic endovascular aortic repair. [a]On serial imaging in the acute phase during the hospital stay. [b]Ongoing hypertension despite more than three classes of antihypertensive drugs. [c]Defined as the presence of adequate proximal and distal landing zones for the prosthesis and adequate iliac/femoral vessels for vascular access. [d]Between 14 and 90 days after dissection onset.[172,1226–1231]

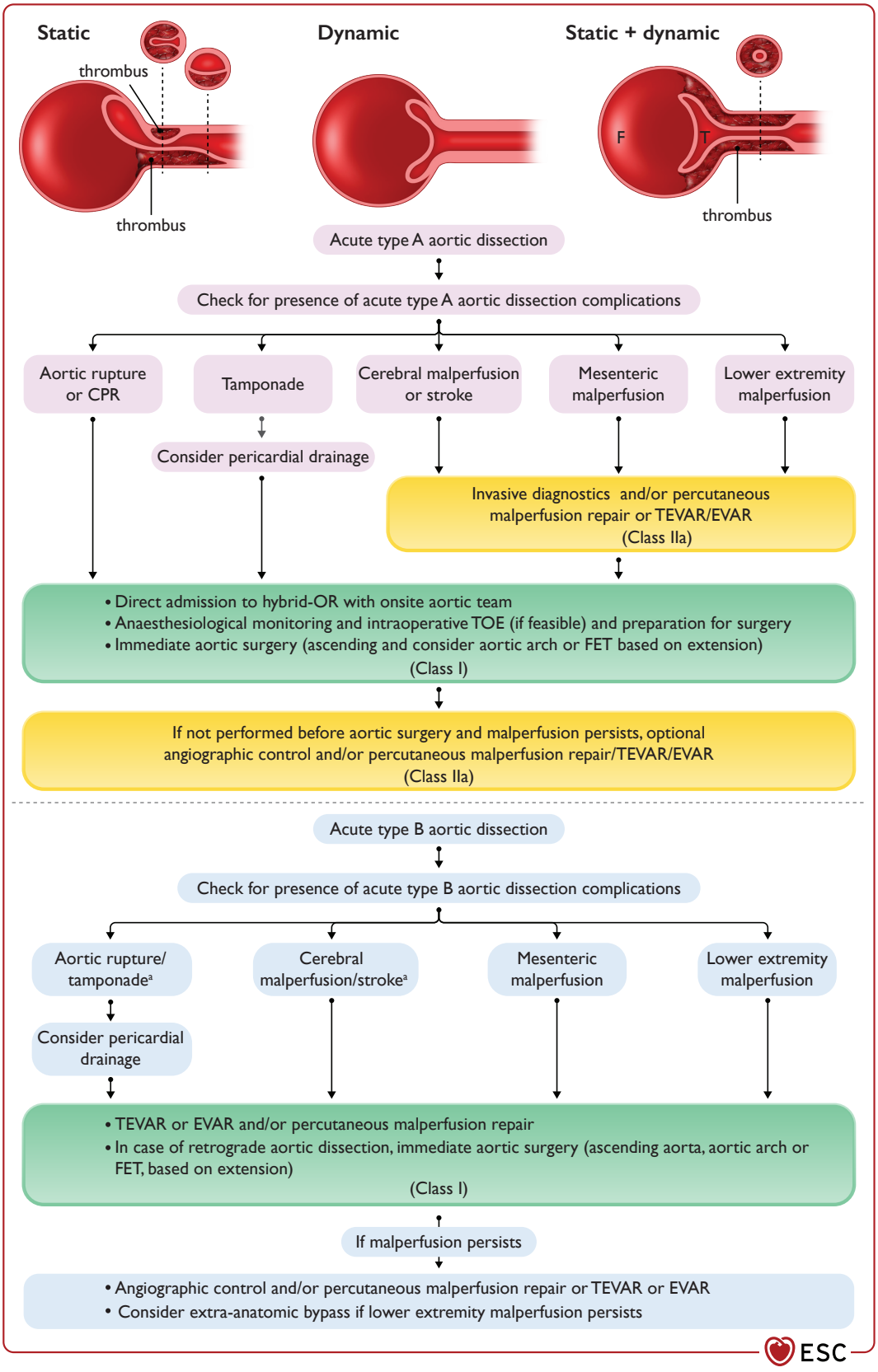

Figure 34 Mechanisms and clinical management of aortic branch obstruction in acute aortic dissection. CPR, cardiopulmonary resuscitation; F, false lumen; FET, frozen elephant trunk; OR, operating room; T, true lumen; TOE, transoesophageal echocardiography; TEVAR/EVAR, thoracic endovascular aortic aneurysm repair. [a]Develops only in retrograde type A dissection.

intervention, reducing mortality rates to 25%–27%, compared with 76% with medical management alone.[1255,1276] Close monitoring and rapid intervention are essential to achieve optimal outcomes and minimize the risk of permanent neurological damage. A recommended algorithm for malperfusion management is displayed in *Figure 34*.

Recommendation Table 48 — Recommendations for the management of malperfusion in the setting of acute aortic dissection

Recommendations	Class[a]	Level[b]
In patients with acute TAAD presenting with malperfusion (cerebral, mesenteric, lower limb, or renal), immediate aortic surgery is recommended.[1275,1277]	I	B
In patients with acute TAAD presenting with cerebral malperfusion or non-haemorrhagic stroke, immediate aortic surgery should be considered to improve neurological outcome and reduce mortality.[1255,1276,1278]	IIa	B
In patients with acute TAAD presenting with clinically significant mesenteric malperfusion syndrome, immediate invasive angiographic diagnostics to evaluate percutaneous malperfusion repair before or directly after aortic surgery, in aortic centres with expertise, should be considered.[1278–1280]	IIa	C

TAAD, type A aortic dissection.
[a]Class of recommendation.
[b]Level of evidence.

Endovascular treatment in type A aortic dissection

Endovascular therapy alone has been attempted in highly selected cases and the concept of a single endovascular valve-carrying conduit was suggested recently but has not yet been validated.[1281,1282]

Treatment in non-A non-B aortic dissection

Conservative management leads to high mortality (malperfusion, aortic rupture); thus, surgery or endovascular therapy is favoured within 14 days of symptom onset. For complicated non-A non-B aortic dissection with an arch tear, consider FET repair, though if feasible, stent-graft implantation for primary tear coverage is an alternative.[1179,1283]

9.3.1.4.3. Acute type B aortic dissection interventional treatment. Acute TBAD presents without complications (uncomplicated) in around 50% of cases.[1250] Complicated acute TBAD includes aortic rupture, malperfusion-related issues, rapid aortic expansion, paraplegia/paraparesis, aortic haematoma, refractory pain, and hypertension despite optimal therapy, which associates with an approximately 50% mortality risk with conservative treatment.[1193,1250,1284,1285]

Open surgery used to be the sole option for complicated acute TBAD but carried a mortality rate of 25%–50%. Consequently, medical management, now considered the standard for uncomplicated cases, significantly reduces mortality. Goals include lowering SBP and heart rate with BBs (see *Section 9.3.1.4.1*). However, adherence is the main limitation of chronic medical treatment, with a rate below 50%.[1286,1287] Compliance increases with previous aortic surgery, severity of hypertension, and understanding of the disease process. Thus, surveillance and disease awareness are imperative for these patients.

Endovascular therapy for complicated acute TBAD is now the first-line treatment, provided there is favourable anatomy, due to positive short- and long-term outcomes.[1288–1294] Open surgery is reserved for unsuitable cases, and fenestration could be considered as an ultima ratio. In selected instances, correcting side branch compression before proximal sealing may be considered.[136]

In recent years, the ADSORB (Acute Dissection Stentgraft OR Best Medical Treatment) and INSTEAD-XL (Investigation of Stent Grafts in Aortic Dissection with extended length of follow-up) trials[1219,1226,1295] have reported that early intervention for uncomplicated acute and subacute TBAD is beneficial compared with medical management, and there is important debate on whether to treat patients with uncomplicated acute TBAD to improve their life expectancy.[1296–1298] Intervention is considered early within 90 days after onset of symptoms and may be safer when performed in the subacute phase (>14 days after onset of symptoms), but data are scarce.[1298–1300] The Society of Thoracic Surgeons/American Association for Thoracic Surgery (STS/AATS) 2022 guidelines[1294] state that prophylactic TEVAR may be considered also in patients with suitable anatomy and high-risk features (*Figure 33*) to reduce late aortic-related adverse events. However, this matter is not entirely settled, and the Improving outcomes in vascular disease—aortic dissection (IMPROVE-AD trial) is currently underway. This trial aims to evaluate clinical outcomes in patients with subacute (from 48 h to 6 weeks) uncomplicated type B aortic dissection (uTBAD), comparing upfront TEVAR plus medical therapy against medical therapy with surveillance for deterioration.

Aortic characteristics change over time, and endovascular treatment in the chronic phase offers limited potential for aortic remodelling. Identifying specific characteristics at the time of acute TBAD diagnosis that predict a complicated course has been attempted. Independent predictors of TBAD outcomes include a primary entry tear >10 mm located at the inner aortic curvature,[1301] initial aortic diameter >40 mm,[1301,1302] initial FL diameter >20 mm,[1301] number/size of fenestrations between the true lumen and FL,[1303] stent graft-induced new entry tear,[1304,1305] and partial FL thrombosis.[1306,1307] These parameters are summarized in a new system for the categorization of AD, DISSECT (**D**uration from onset of symptoms, **I**ntimal tear location, **S**ize of the aorta based on maximum trans-aortic diameter, **S**egmental Extent, **C**linical complications related to the dissection, **T**hrombosis of the FL),[1308] which serves as a guide to support a therapeutic decision (*Figure 33*).[1308] A recent meta-analysis found TEVAR to be superior to best medical therapy in uncomplicated acute TBAD. Early outcomes were similar, but TEVAR was associated with fewer long-term events and better aortic remodelling.[1297,1298,1309] Thus, in stable TBAD with suitable anatomy and high-risk features, pre-emptive TEVAR to improve the late outcome should be considered.

Accurate endograft sizing is vital for TEVAR success, as errors may lead to complications. Disease-specific factors, such as acute thoracic aortic syndromes, pose challenges due to fluctuations in aorta diameter from haemorrhagic shock and resuscitation. Sizing decisions must account for these changes. Measuring the thoracic aorta based on admission CCT may be imprecise, even with proper centreline measurements. Real-time imaging, especially IVUS, enhances accuracy, particularly in hypovolaemic cases. However, further research is required to clarify the role of intraoperative imaging methods (e.g. IVUS, TOE, 3D CCT) in endograft sizing and long-term outcomes for optimal patient care.[194]

Recommendation Table 49 — Recommendations for the management of patients presenting with acute type B aortic dissection

Recommendations	Class[a]	Level[b]
Medical therapy including pain relief and blood pressure control is recommended in all patients with acute TBAD.[1215,1219,1310,1311]	I	B
In patients with complicated acute TBAD, emergency intervention is recommended.[1193,1250,1284,1285,1288,1289,1291–1293]	I	B
In patients with complicated acute TBAD, TEVAR is recommended as the first-line therapy.[c,910,1288–1293]	I	B
In patients with acute TBAD, BBs should be considered as the first-line medical therapy.[1216,1312]	IIa	B
In patients with uncomplicated acute TBAD, TEVAR in the subacute phase (between 14 and 90 days) should be considered in selected patients with high-risk features[d] to prevent aortic complications.[1219,1226,1295,1297,1298,1308,1309]	IIa	B

BBs, beta-blockers; HTAD, heritable thoracic aortic disease; TBAD, type B aortic dissection; TEVAR, thoracic endovascular aortic repair.
See also *Figure 33*.
[a]Class of recommendation.
[b]Level of evidence.
[c]Except in patients with known or suspected HTAD.
[d]For high-risk features see *Figure 33*.

9.3.1.4.4. Chronic type B aortic dissection interventional treatment. Type B aortic dissection is considered as chronic 3 months after the onset of symptoms, but it also includes residual type B dissection after repair of TAAD. Aortic complications, especially aneurysmal degeneration, will occur in up to 50% of these patients.[1302,1313] Therefore, in chronic TBAD, indications for treatment include the onset of new aortic symptoms such as rapid expansion, malperfusion, or rupture.[1314] In asymptomatic patients, aneurysmal dilatation is the most important risk factor for rupture, reaching 20% when the diameter exceeds 55 mm.[1302,1315] Risk of rupture increases with diameter; it has been reported a risk of 15.3% and 18.8% between 50–55 mm and 54–56 mm, respectively, thus suggesting 50–55 mm as a threshold for elective surgery.[1316] However, smaller diameters should be considered in patients with HTAD. According to several studies, mortality in the chronic phase is high (40%–70%) and it is mainly related to patients' comorbidities, such as heart disease and stroke.

Open repair

Despite the lack of data comparing open repair vs. TEVAR in chronic TBAD, open surgery remains the first-line treatment in low-risk patients or those with HTAD. The STS/AATS guidelines[1294] state that open repair should be considered in chronic TBAD patients with indication for intervention, unless comorbidities are prohibitive or anatomy is not suitable for TEVAR. The surgical technique for chronic TBAD is like those for degenerative aneurysms, but repair is more complex due to the dissection flap.[1317] Surgical mortality rates between 6% and 11% and SCI rates between 3% and 11% have been reported.[1317–1321] Patients treated in low-volume centres present higher mortality rates (up to 20%), which reinforces the recommendation for centralization in experienced centres.

Endovascular repair

Thoracic endovascular aortic aneurysm repair (TEVAR) is the preferred treatment for eligible chronic TBAD patients, offering low early mortality (<5%), with stroke and SCI rates below 3%. It is also suitable for high-risk patients who are not candidates for open repair. The primary goal is to close the entry tear, induce FL thrombosis, and promote aortic remodelling to mitigate growth and rupture risk.[1322,1323] A systematic review showed 90% immediate technical success and 86% complete FL thrombosis. However, FL thrombosis usually occurs above the coeliac trunk, necessitating lifelong distal FL surveillance.[1324] Coverage of the LSA is often necessary and should be associated with revascularization. In a recent meta-analysis[1325] comparing TEVAR to open repair in chronic TBAD, TEVAR showed lower early mortality, stroke rates, SCI, and respiratory complications but a higher re-intervention rate. Long-term survival rates were similar, but open repair offered greater durability.[1326]

Adequate distal sealing poses a challenge due to the dissection extending to the iliac artery, with additional re-entries, allowing retrograde flow into the thoracic aneurysm. In chronic TBAD patients with AA enlargement, insufficient distal landing, or large re-entry tears, TEVAR alone is discouraged. Instead, a comprehensive repair involving the visceral aorta, infra-renal aorta, and iliac artery is needed. Recent studies have shown favourable results using custom or improvized fenestrated/branched endografts with careful patient selection.[1062,1327–1329] A multidisciplinary team-based approach in experienced centres is necessary for good outcomes.[1330]

Recommendation Table 50 — Recommendations for the management of patients presenting with chronic type B aortic dissection

Recommendations	Class[a]	Level[b]
Antihypertensive therapy is recommended in all patients with chronic TBAD.[1331–1333]	I	B
In chronic TBAD with acute symptoms of malperfusion, rupture, or progression of disease, emergency intervention is recommended.[1302,1313,1314]	I	C
In patients with chronic TBAD and a descending thoracic aortic diameter ≥60 mm, treatment is recommended in patients at reasonable surgical risk.[1302,1315,1334]	I	B
In patients with chronic TBAD and a descending thoracic aortic diameter ≥55 mm, an indication for intervention should be considered in patients with low procedural risk.[1302,1316]	IIa	C
In patients with chronic post-dissection thoracoabdominal aortic aneurysms, the use of fenestrated/branched stent grafts may be considered, when treatment is indicated.[1062,1327–1329]	IIb	C

TBAD, type B aortic dissection.
[a]Class of recommendation.
[b]Level of evidence.

9.3.1.4.5. Management during pregnancy. Management of AD during pregnancy requires a multidisciplinary team and specialized centres. Initial care should consider general medical recommendations (as previously described), using drugs with the lowest teratogenic impact.

In cases of type A dissection, if the foetus is viable, caesarean delivery will be performed before aortic repair. If the foetus is not viable, surgery will be done with the foetus in place.[1335,1336] In uncomplicated type B

dissections, strict control of the pregnant patient and foetus with conservative medical management is recommended.[1224,1335] Although limited to selected cases, successful TEVAR has been described in complicated TBAD.[1227] More information is detailed in the *2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy*.[1337]

9.3.2. Intramural haematoma

Intramural haematoma, constituting 5%–25% of AAS cases, involves vasa vasorum haemorrhage within the aortic media, with or without intimal disruption (ID).[70,172,1338] Most cases (60%–70%) involve the DTA (ascending aorta ~30%, aortic arch ~10%).[70,172,1192] Although it usually occurs at an older age than AAD, risk factors and symptoms are similar;[70,172,1192,1338] however, aortic regurgitation, malperfusion syndrome, and pulse deficits are less frequent in type A IMH than in TAAD.[70,172]

9.3.2.1. Diagnostic work-up

Diagnostic IMH work-up should be similar to that proposed for AAS (*Figure 30*), but with different morphological features in the imaging techniques.

CCT and CMR (followed by TOE) are the leading techniques for diagnosis.[70,159,171–173] Unenhanced followed by contrast-enhanced CCT represents the most used tool in the acute setting (hyperintense signal of aortic wall before contrast administration).[70,171,172] The IMH diagnostic hallmark consists of crescentic or circular aortic wall thickening in the absence of an intimal flap or aortic wall enhancement following contrast administration.[70,171,172] CMR is an excellent imaging technique to detect small IMHs and for the differentiation of IMH (hyperenhanced images in T1-weighted images) from atherosclerotic thickening of the aorta, thrombus, or thrombosed dissection.[172] TTE yields low sensitivity (<40% for IMH cut-off limit of 5 mm).[171]

9.3.2.2. Clinical outcomes

Intramural haematoma may evolve into AAD (12% of patients), saccular (8%) or fusiform aneurysm (22%), and/or ID (54%).[1192,1339–1342] Partial or total regression is reported in 34% of patients.[70,1192,1343] Outcomes are comparable to those in AAD. In-hospital mortality for type A IMH is 26.6% (surgical 24.1% and medical 40.0%). In this regard, higher mortality for IMH involving the aortic valvular complex has been observed.[1175] In-hospital mortality for type B IMH is 4.4% but worsens once surgery is indicated (surgical 20.0% vs. medical 3.8%).[1175,1344]

9.3.2.3. Geographical variations

Reports from South Korea and Japan reveal notable disparities with Western nations in IMH incidence (28.9% vs. 5.7% of overall AAD as reported by IRAD), treatment strategies, and outcomes. In Eastern regions, the majority (80.8%) of type A IMH patients received medical treatment, resulting in significantly improved clinical outcomes (in-hospital mortality 6.6% [5.9% for medical and 9.4% for surgical]).[1345] These results may be partially explained by the detection of early-stage IMH (mild, uncomplicated cases) at primary centres.[1345–1347]

Table 16 High-risk features of intramural haematoma type A and B

Ascending aorta involvement
Difficult BP control
Persistent/recurrent pain despite aggressive BP control
Maximum aortic diameter: • Type A: >45–50 mm • Type B: >47–50 mm
Progression to aortic dissection
Focal intimal disruption with ulcer-like projection
Haematoma thickness >10 mm (type A) or >13 mm (type B)
Enlarging haematoma thickness
Enlarging aortic diameter
Pericardial effusion at admission (type A)
Recurrent pleural effusion
Detection of organ malperfusion

BP, blood pressure.
Adapted with permission from.[172]

9.3.2.4. Management

Current IMH therapeutic interventions are similar to AAD, with the first step consisting mainly of pain and BP control regardless of the anatomopathological features (*Figure 31*).

9.3.2.4.1. Type A intramural haematoma. As in AAD, type A IMH involves the ascending aorta. Surgery (emergency or urgent depending on clinical status) is recommended. In selected patients with increased operative risk (i.e. multiple comorbidities) and uncomplicated type A IMH without high-risk imaging features (*Table 16*) a 'wait-and-see strategy' in a reference/experienced centre may be reasonable.[70,172,1348,1349]

9.3.2.4.2. Type B intramural haematoma. In type B IMH, the disease is in the descending aorta, distal to the left subclavian artery. For uncomplicated type B IMH, initial management involves medical treatment and thorough clinical and imaging monitoring.[70,172] If uncomplicated type B IMH presents high-risk imaging characteristics (see *Table 16*), the multidisciplinary team should consider endovascular repair as an option. In contrast, complicated type B IMH warrants consideration of TEVAR.[1350,1351] However, in unfavourable anatomy, open surgery remains an alternative.

ID has been described in 54% of type B IMH cases.[1192,1339–1342] Approximately 28% of them are tiny intimal disruptions (≤3 mm) that are not related to AAEs. However, 14% of them evolve into focal intimal disruptions (FID) (>3 mm), with prognostic implications; thus, all patients with ID require close follow-up with imaging techniques. In the acute phase, FID has a poor prognosis owing to the high risk of aortic rupture and should be treated early and invasively, especially large FID (≥10 mm length and ≥5 mm depth).[1342,1352] However, in the chronic phase, most FIDs evolve with slow aortic dilatation and without complications, and they can be managed with medical treatment and close imaging surveillance.[1352]

Recommendation Table 51 — Recommendations for the management of intramural haematoma

Recommendations	Class[a]	Level[b]
In patients with IMH, medical therapy including pain relief and blood pressure control is recommended.[24,172]	I	C
In type A IMH, urgent surgery is recommended.[172,1175,1192]	I	C
In type B IMH, initial medical therapy under careful surveillance is recommended.[1175,1192,1347,1350,1353]	I	C
In uncomplicated[c] type B IMH, repetitive imaging (CCT or CMR) is indicated.[1175,1192,1347,1350,1353]	I	C
In complicated[c] type B IMH, TEVAR is recommended.[1175,1192,1347,1350,1353]	I	C
In uncomplicated[c] type B IMH but with high-risk imaging features[d], TEVAR should be considered.[1347,1350]	IIa	C
In complicated[c] type B IMH, surgery may be considered in patients with anatomy unfavourable for TEVAR.[1175,1192,1347,1350,1353]	IIb	C
In selected patients with increased operative risk and uncomplicated[c] type A IMH without high-risk imaging features[d], a 'wait and see' strategy may be considered.[1348,1354–1356]	IIb	C

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; IMH, intramural haematoma; TEVAR, thoracic endovascular aortic repair.
[a]Class of recommendation.
[b]Level of evidence.
[c]Uncomplicated/complicated IMH refers to the absence or presence of recurrent pain, expansion of the IMH, periaortic haematoma, and intimal disruption.
[d]High-risk features of intramural hematoma type A and B are described in *Table 16*.

9.3.3. Penetrating atherosclerotic ulcer

Penetrating atherosclerotic ulcer (2%–7% of all AAS cases) is characterized by localized ulceration of an aortic atherosclerotic plaque penetrating through the internal elastic lamina into the media, frequently associated with IMH and diffuse atherosclerosis.[70,172,174,910,1338,1343]

Often, multiple PAUs are present, ranging from 5 to 25 mm in diameter and 4 to 30 mm in depth.[70,172,174,1338] They occur mostly in the middle and lower DTA, with the aortic arch and AA less involved. The ascending aorta is rarely affected,[70,172,910,1192] but when this occurs, especially complicated with IMH, the risk of rupture is 33%–75% and progression to dissection is associated with a high mortality rate.

Most patients are older males, smokers, aged >65, with multiple comorbidities like systemic hypertension, CAD, COPD, renal insufficiency, and concurrent abdominal aneurysm.[24,172,910,1357]

Symptoms are like those in AAD and may manifest in older age after a long asymptomatic phase (often PAU is diagnosed as an incidental finding during an imaging examination).[24,172,910,1357] It should be highlighted that symptom onset may indicate PAU expansion (tunica adventitia involvement); thus, urgent imaging (CCT or CMR) and appropriate therapeutic intervention are needed to prevent aortic rupture.[70,171,172,174]

9.3.3.1. Diagnosis

Diagnostic work-up is described in *Figure 30*. CCT represents the technique of choice for diagnosis. TOE and CMR represent possible valid alternatives considering availability and local expertise.[70,159,171–173] Of note, ^{18}FDG-PET-CT is a promising technique since it can detect increased glucose uptake in PAUs as a marker of increased metabolic activity and inflammation, which has been associated with major adverse events.[1358,1359] This information may be used to guide treatment decisions, such as the selection of patients who may benefit from endovascular or surgical intervention.[1360]

9.3.3.2. Treatment

Medical treatment as described for AD is recommended (*Figure 31*). Management of incidental cases is not clearly defined.[174] Small series suggest that isolated, asymptomatic, small PAUs may be safely managed conservatively with regular surveillance.[1361,1362]

Surgery is recommended in type A PAU with the option of a 'wait-and-see strategy' in highly selected high-risk patients with no high-risk features (*Figure 35*). However, in uncomplicated type B PAU, medical treatment along with careful clinical and imaging surveillance is recommended.[174,1350] When intervention is needed, endovascular treatment (early and 3 year aortic mortality 7.2% and 10.4%, respectively)[1350] should be preferred to open surgery (early and 3 year aortic mortality of 15.9% and 25.0%, respectively).[174,1350] In cases of uncomplicated PAU with high-risk imaging features[1363–1365] (*Figure 35*), endovascular treatment should also be considered. The natural history of PAU of the abdominal aorta (AA) with associated IMH is less known. In a review of PAU of the AA, endovascular stenting was the preferred treatment of choice (62%), followed by open surgical repair (35%) and conservative therapy (3%).[1366]

Recommendation Table 52 — Recommendations for the management of penetrating atherosclerotic ulcer

Recommendations	Class[a]	Level[b]
In all patients with PAU, medical therapy including pain relief and blood pressure control is recommended.[24,172]	I	C
In cases of type A PAU, surgery is recommended.[172]	I	C
In cases of type B PAU, initial medical therapy under careful surveillance is recommended.[1347,1350]	I	C
In uncomplicated type B PAU, repetitive imaging (CMR, CCT, or TOE) is recommended.[1347,1350]	I	C
In complicated type B PAU, endovascular treatment (TEVAR) is recommended.[1347,1350,1357]	I	C
In uncomplicated type B PAU with high-risk imaging features,[c] endovascular treatment should be considered.[1347,1350]	IIa	C
In selected patients with increased operative risk and uncomplicated type A PAU without high-risk imaging features,[c] a 'wait-and-see' strategy may be considered.[1367]	IIb	C
In complicated type B PAU, surgery may be considered based on anatomy and medical comorbidities.[1347,1350]	IIb	C
In isolated, asymptomatic, small PAUs with no high-risk features,[c] conservative management with regular surveillance and medical treatment may be considered.[24,1361]	IIb	C

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; PAU, penetrating atherosclerotic ulcer; TOE, transoesophageal echocardiography; TEVAR, thoracic endovascular aortic repair.
[a]Class of recommendation.
[b]Level of evidence.
[c]See *Figure 35* for high-risk imaging features of PAU.

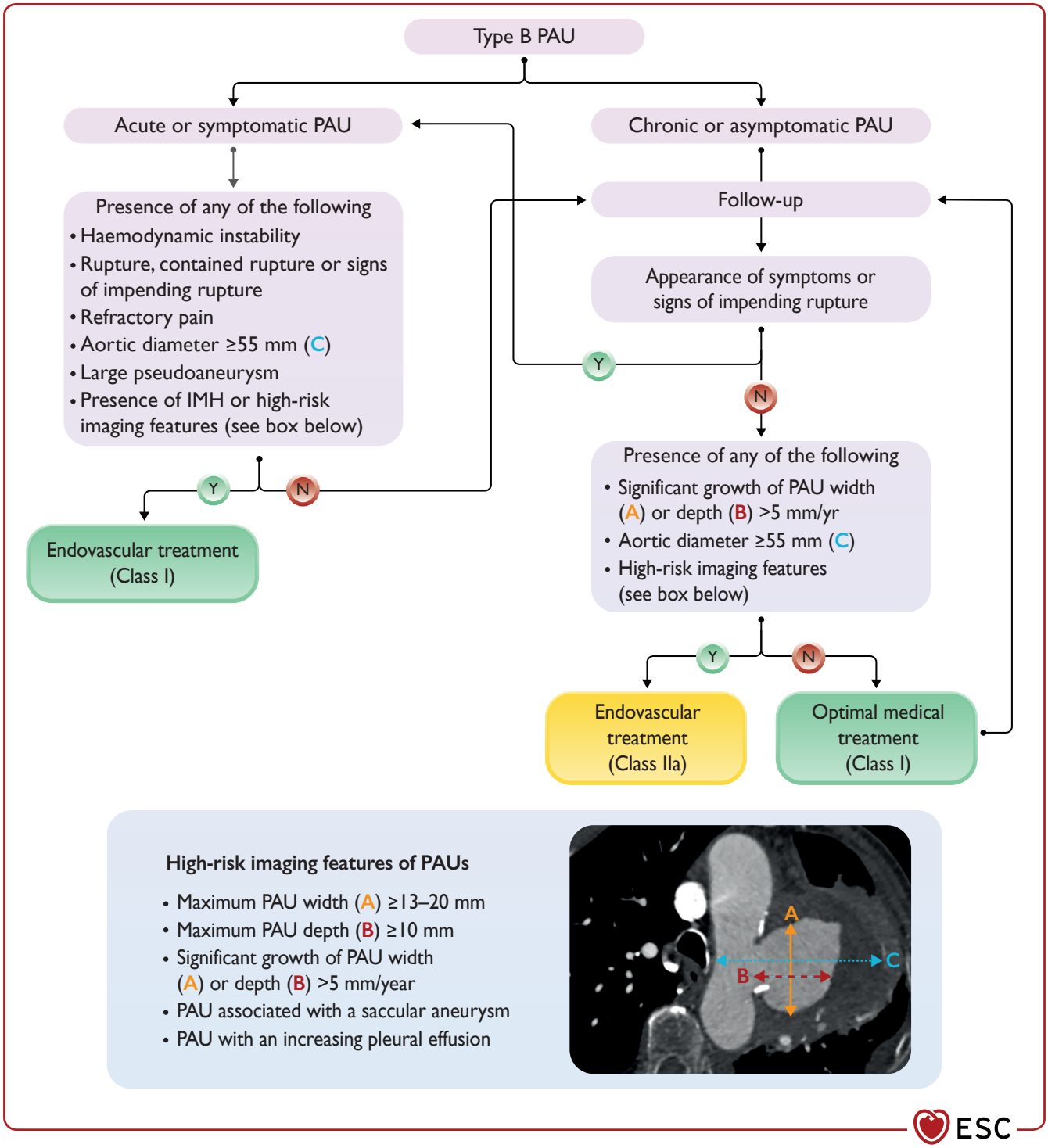

Figure 35 High-risk features in penetrating atherosclerotic ulcer and management of patients with type B penetrating atherosclerotic ulcer. IMH, intramural haematoma; PAU, penetrating atherosclerotic ulcer; TEVAR, thoracic endovascular aortic repair. (*A*) Maximum PAU width. (*B*) Maximum PAU depth; (*C*) Maximal aortic diameter at the site of the PAU.[910]

9.3.4. Aortic pseudo-aneurysm

Aortic pseudo-aneurysms, or false aneurysms, result from aortic wall disruption, typically caused by factors like trauma,[1368] surgery, or infections. They are often symptomless, detected incidentally during post-aortic procedure imaging. Symptoms may include chest pain, compression, and if untreated, they can lead to fatal rupture or other severe complications.[1369,1370]

Pseudo-aneurysm repair seems always indicated regardless of size or position to prevent progression and rupture. Nevertheless, in some circumstances and under close follow-up, patients could be monitored by CCT, CMR, or TOE and intervention could be postponed unless size expansion, symptoms, or compression of surrounding structures occur.[1371] Pseudo-aneurysms could be treated by open surgery or endovascular treatment (occluders, stent grafts, or coils). There is no randomized study comparing open surgery vs. TEVAR; however, treatment of choice is commonly based on anatomical features, clinical presentation, and the patient's comorbidities and decided by a multidisciplinary team in specialized centres.[1045,1371]

9.3.5. Traumatic aortic injury

Traumatic aortic injury (TAI), commonly from high-speed motor accidents or falls, involves partial or complete aorta transection. It results from rapid deceleration causing torsion and shearing forces, often affecting relatively immobile aorta segments like the aortic isthmus (90%), aortic root (5%), or diaphragmatic hiatus (5%).[24,70,172]

Traumatic aortic injury is classified based on the degree of lesion in the aortic wall (*Figure 36*): grade I (intimal tear), grade II (IMH), grade III (pseudo-aneurysm), and grade IV (aortic rupture). In the Crash Injury Study, 130/613 deaths (21%) were associated with TAI (mortality associated with aortic rupture 91%; at-scene survival 9%).[1372]

9.3.5.1. Diagnosis and therapeutic interventions

Due to non-specific symptoms and signs (often obscured by concomitant multiple organ injury) a timely diagnosis relies on a high level of clinical suspicion.[70,172] CCT (accuracy close to 100%) represents the technique of choice, acting as a 'one-stop shop' to rapidly assess the entire skeletal system and internal organs.[70,171,172] TOE may be an alternative, although limited by availability, local expertise, and potentially a patient's multiple traumas.[24,70,172] Therapeutic interventions are dependent on the extent of aorta lesion and patient clinical status as assessed by a multidisciplinary team. Generally, aggressive fluid administration should be avoided because it may exacerbate bleeding, coagulopathy, and hypertension. To reduce risk of rupture, mean BP should not exceed 80 mmHg.[172] Minimal aortic injury (grades 1 and 2) may be managed medically along with strict clinical and imaging surveillance; moderate aortic injury (grade 3) with semi-elective repair (within 24–72 h) to allow patient stabilization (though in some patients urgent repair is needed);[24,1373] and severe aortic injury (grade 4) with immediate repair.[1374] If there is progression of the IMH (grade 2), semi-elective repair (within 24–72 h) may be considered. TEVAR is preferred (if feasible) to open surgery (in-hospital mortality 7.9% vs. 20% and 1 year mortality 8.7% vs. 17%). In semi-elective repair, if the LSA needs to be covered, prior LSA revascularization before TEVAR is suggested to reduce the risk of paraplegia [172,1373,1374]

9.3.5.2. Long-term surveillance in traumatic aortic injury

In addition to clinical assessment, CCT is the imaging choice for follow-up.[70,171,172] Cumulative exposure to radiation and iodinated contrast medium remains the major limitation in young patients, especially in women. A combination of a chest X-ray and CMR (if no graft artefacts) would be a valid alternative.[24,171,172]

Recommendation Table 53 — Recommendations for traumatic aortic injury

Recommendations	Class[a]	Level[b]
In cases of severe aortic injury (grade 4), immediate repair is recommended.[24,1373,1374]	I	A
In cases of TAI with suitable anatomy requiring intervention, TEVAR is recommended over open surgery.[24,1373,1374]	I	A
In all TAI patients, medical therapy including pain relief, and blood pressure and heart rate control, is recommended.[24,172]	I	C
In cases of TAI suspicion, CCT is recommended.[159,172]	I	C
In cases of moderate aortic injury (grade 3), repair is recommended.[24,1373]	I	C
If CCT is not available, TOE should be considered.[159,172]	IIa	C
In minimal aortic injury (grades 1 or 2), initial medical therapy under careful clinical and imaging surveillance should be considered.[24,1374]	IIa	C
In cases of progression of the IMH (grade 2), semi-elective repair (within 24–72 h) should be considered.[24,1374]	IIa	C

CCT, cardiovascular computed tomography; IMH, intramural haematoma; TAI, traumatic aortic injury; TOE, transoesophageal echocardiography; TEVAR, thoracic endovascular aortic repair.
[a]Class of recommendation.
[b]Level of evidence.

9.3.6. Iatrogenic aortic injuries

Iatrogenic aortic lesions are those associated with invasive procedures (cardiac surgery, most commonly dissection type A, or coronary angiography, with a similar proportion of type A and B dissections) (see *Section 9.3.2.1*). Incidence is low and ADs are the most common lesions. Main risk factors are advanced age, presence of CVRFs, atherosclerosis, aortic aneurysms, or PAD (*Figure 37*). Patients with iatrogenic AAS are often painless with correspondingly less chest or back pain.[1375]

While historically associated with high mortality,[1375] recent registries like the German GERAADA indicate a mortality rate similar to that for spontaneous dissections.[1186]

Clinical management is based on the underlying lesion (AAD, IMH) and location; however, conservative management has been described with good results in type A iatrogenic dissection if the coronary flow is preserved and the dissection is small.[1376] Iatrogenic lesion classification is depicted in *Figure 37*.[1377] Although scarce, data support a conservative approach based on evolution in type 1 and 2 lesions (Dunning classification), and surgery in type 3.[1377] In cases of coronary involvement, stent implantation sealing the flap may be proposed.[1376,1377]

9.3.7. Long-term follow-up of acute aortic syndrome

Imaging modalities and time intervals for surveillance vary according to lesion location (ascending/descending aorta), type of treatment (medical, endovascular, surgical), and underlying disease (HTAD).[70,1062,1153] Compared with the chronic disease setting, follow-up of AAS patients is characterized by a higher risk of complications and need for re-operation.[1378] Patients receiving TEVAR for AAS involving the descending aorta are more prone

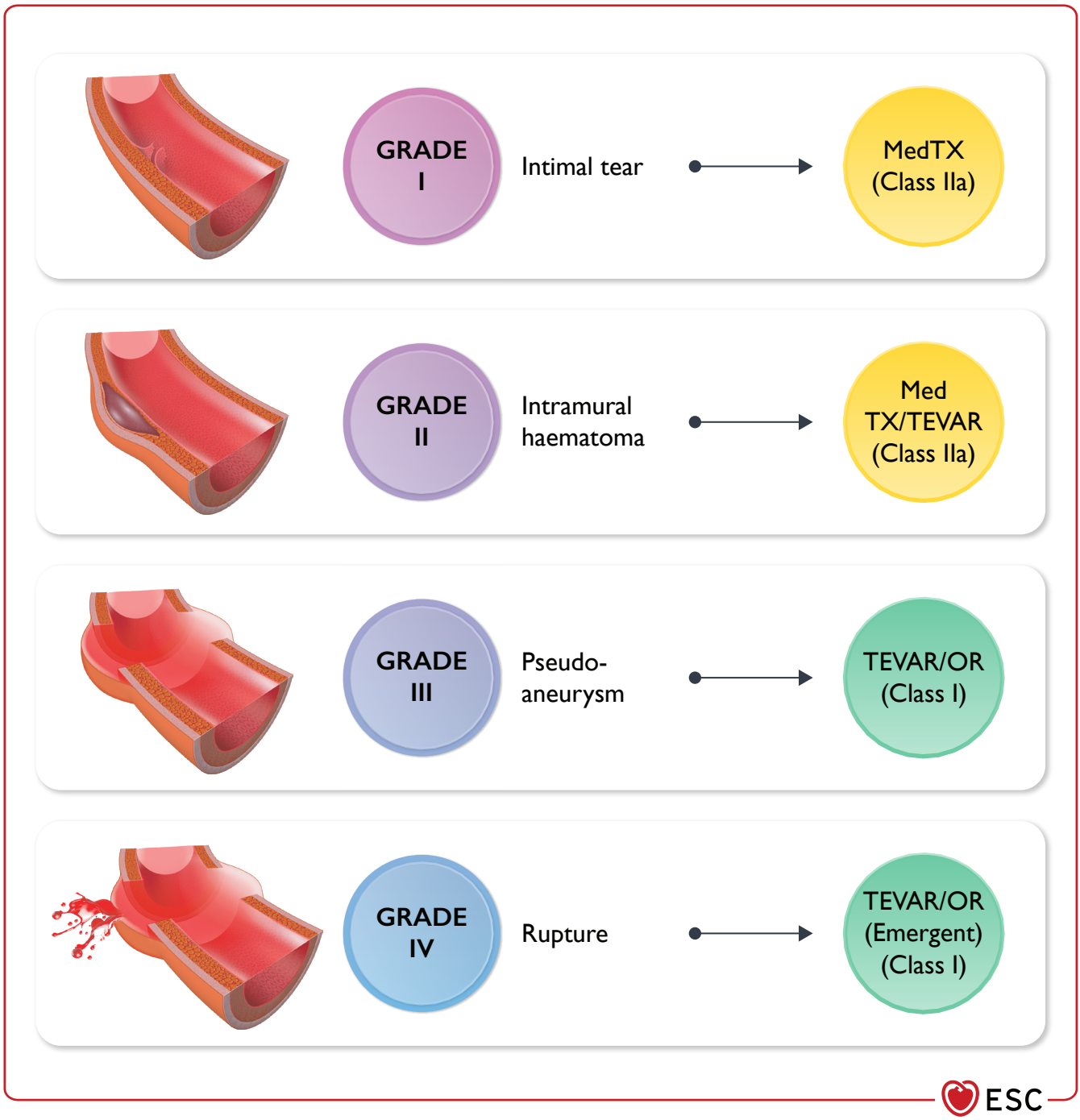

Figure 36 Classification and treatment of traumatic aortic injuries. Med, medical; OR, open surgery repair; TEVAR, thoracic endovascular aortic repair; Tx, treatment.

(27%–49%) to requiring a second intervention than patients undergoing surgical repair.[1379,1380] However, need for re-intervention at follow-up (after initial treatment of AAD) seems to have a significant impact on survival for TAAD[1381] but not for TBAD.[1380]

9.3.7.1. Follow-up after invasive treatment

Following surgery for AAS, imaging surveillance will focus on persistence/obliteration of the FL, anastomotic dehiscence, progressive dilatation of residual native aorta (with or without residual dissection), or graft infection. CCT is the most used modality, but in patients requiring frequent examinations CMR can be considered to reduce radiation.

Compared with outcomes of open surgery for aortic aneurysms, time to re-intervention in patients developing complications is significantly shorter,[1159] also due to the faster average growth of the dissected aorta (about 1 mm per year).[70] Considering the reported incidence rates (around 10%) of complications requiring re-operation, it is reasonable to follow patients every 6 months in the first year (including an early—within 1 month—echocardiography to follow native or prosthetic aortic valve function), then yearly up to the third post-operative

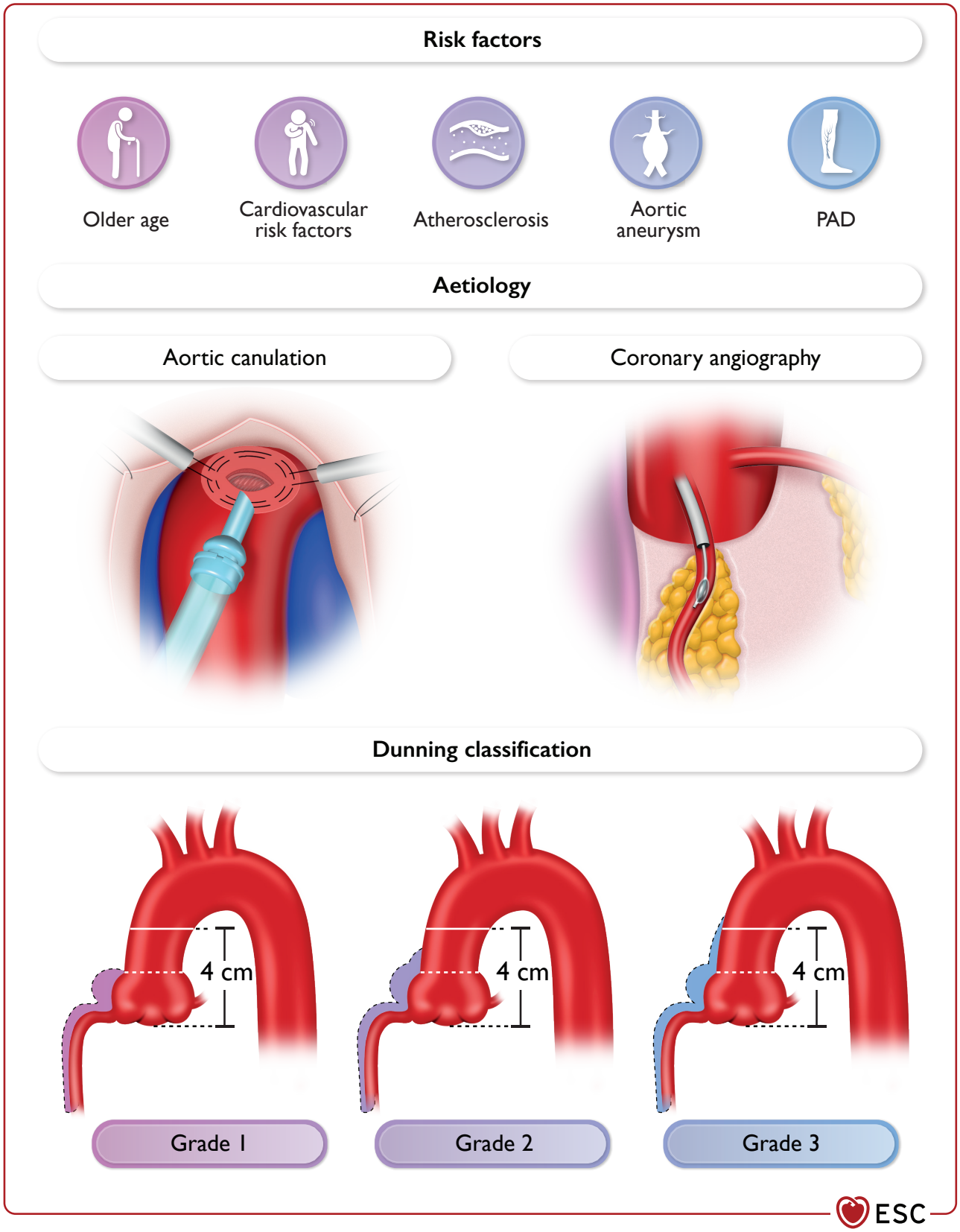

Figure 37 Aetiology, risk factors, and classification of iatrogenic aortic injuries. PAD, peripheral arterial disease. Dunning classification of iatrogenic aortic dissection:[1377]: type 1, dissection limited to the sinuses of Valsalva; type 2, dissection of the ascending aorta outside the sinuses but < 40 mm from the aortic annulus. type 3, dissection > 40 mm from the annulus.

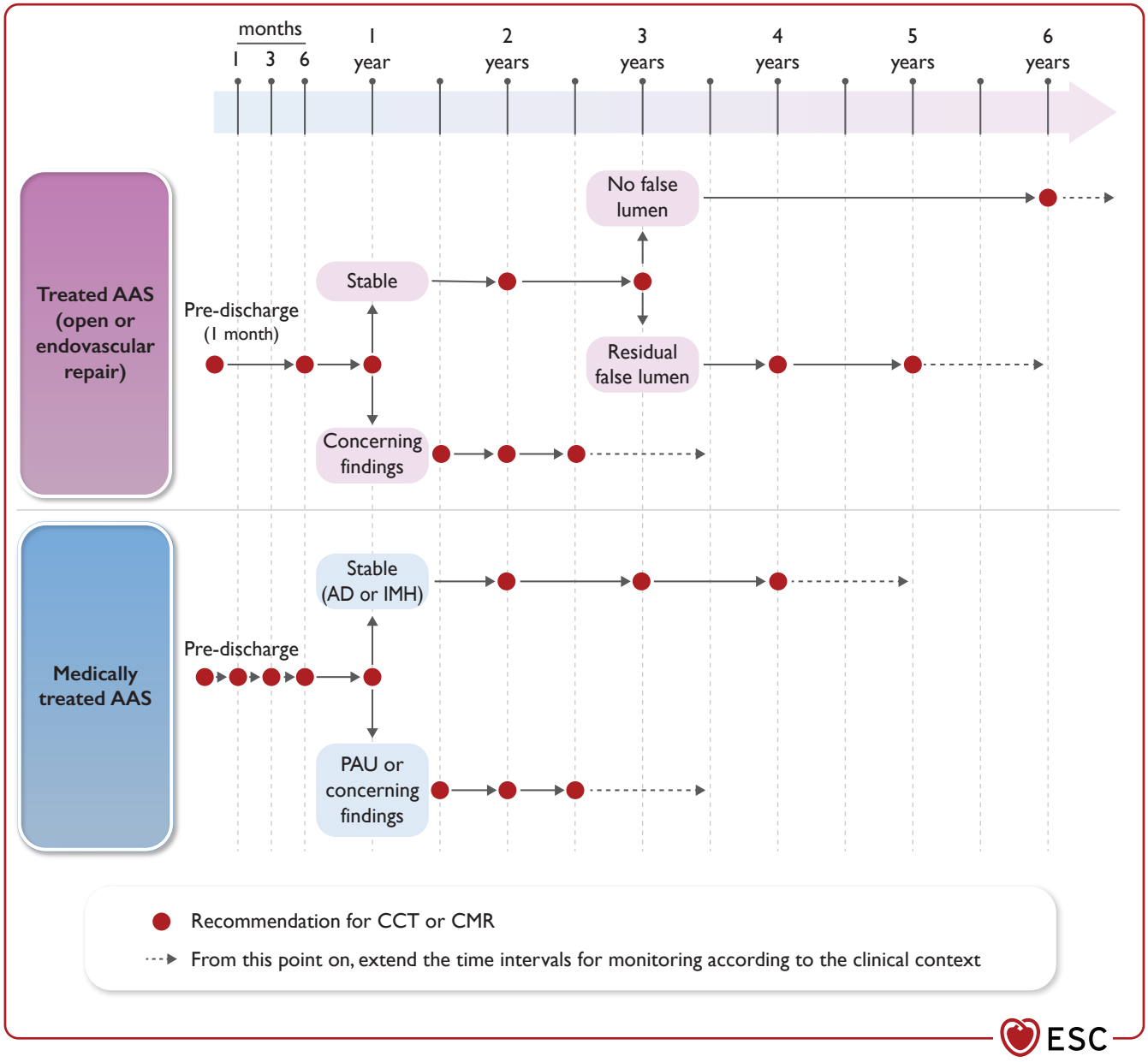

Figure 38 Algorithm for follow-up after acute aortic syndrome. AAS, acute aortic syndrome; AD, aortic dissection; CMR, cardiovascular magnetic resonance; CCT, cardiovascular computed tomography IMH, intramural haematoma; PAU, penetrating atherosclerotic ulcer.

year and then every 2–3 years if there are no complications (*Figure 38*).[1153,1159]

TEVAR implies a higher risk for late re-interventions,[1159,1378] and a sequence of imaging intervals at 1, 6, 12, 24, 36, 48, and 60 months is recommended if no abnormality is detected (shorter intervals should be considered in high-risk patients). Thereafter, controls can be performed every 2–3 years. Compared with the time points after surgery, an adjunctive early control at 1 month is necessary to exclude asymptomatic retrograde type A dissection induced by TEVAR (70% of cases occurring within 30 post-operative days).[1382]

Besides imaging surveillance, clinical follow-up is aimed at achieving strict BP control, limiting the burden of CVRFs, and providing patients with counselling for lifestyle modifications and prescriptions for sport activity.[24] There is evidence that statin treatment may improve survival in AAS patients under medical treatment, whereas BBs may improve survival in surgically treated patients.[1333]

9.3.7.2. Follow-up under medical treatment (chronic type B aortic dissection, intramural haematoma, penetrating atherosclerotic ulcer)

Around 70% of TBAD patients survive the hyperacute phase. If there is no malperfusion, uncontrolled hypertension, or impending rupture, initiate anti-impulse therapy alongside surveillance.

Chronic aortic dilatation, reaching 55 mm, is the leading cause (about 40%) of intervention, while acute complications necessitating immediate treatment are rare.[1301,1383] Imaging controls should be performed at least at 1, 6, and 12 months after discharge and yearly thereafter; however, one additional earlier scan, e.g. within 3 months, may reveal important changes occurring in the subacute phase, when the dissected aorta remains successfully amenable to early TEVAR.[1383] During surveillance, late complications may be predicted by imaging features, including the number and location of the entry tear(s), and dimensions of the FL, total (true + false) lumen, or entry tear.[1383] This might help in risk stratification to modulate the stringency of surveillance in the individual patient (*Figure 33*).[1213]

Type B IMH and PAU are usually conservatively treated with antihypertensive therapy and watchful monitoring. Most of the medically treated IMHs have a favourable course, whereas PAUs are less predictable in terms of risk of acute TBAD or rupture.[1350] Therefore, for IMH the same surveillance criteria as for medically treated uncomplicated TBAD can be employed; for PAU more frequent controls are advisable, i.e. one every 6 months instead of every year. Selectively, in asymptomatic patients with 2 year growth-rate stabilization and no high-risk features, intervals between controls can be longer (every 1–2 years) (*Figures 35* and *38*).[70,1384]

Recommendation Table 54 — Recommendations for follow-up after treatment of acute aortic syndrome

Recommendations	Class[a]	Level[b]
After TEVAR for AAS, follow-up imaging is recommended at 1, 6, and 12 months post-operatively, then yearly until the fifth post-operative year if no abnormalities[c] are documented.[1159,1378,1382]	I	B
In medically treated type B AAS or IMH, follow-up imaging is recommended at 1, 3, 6, and 12 months after onset, then yearly if imaging findings are stable.[1301,1383]	I	C
In medically treated PAU, follow-up imaging is recommended at 1 month after diagnosis, then every 6 months if imaging findings are stable.[70,1350,1384]	I	C
After open surgery for AAS, follow-up imaging by CCT and TTE within 6 months, then CCT at 12 months and then yearly if findings are stable,[d] should be considered.[1153,1159,1383]	IIa	B
If no complications[c] occur within the first 5 years, CCT every 2 years thereafter should be considered.[1159,1378]	IIa	B
If no residual patent FL is documented for 3 post-operative years, subsequent surveillance by CCT every 2–3 years should be considered.[1153,1159,1383]	IIa	C
If abnormalities[c] are documented at any time of follow-up after TEVAR for AAS, then CCT should be considered every 3–6 months.[1159,1378,1382]	IIa	C
When frequent controls are required in AAS patients treated either by open or endovascular repair, CMR should be considered instead of CCT after the first-year follow-up.[70,1153]	IIa	C
In the follow-up of medically treated PAU, after 2 years of imaging stability, larger intervals should be considered in low-risk patients[e].[70,1350,1384]	IIa	C

AAS, acute aortic syndrome; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; FL, false lumen; IMH, intramural haematoma; PAU, penetrating atherosclerotic ulcer; TEVAR, thoracic endovascular aortic repair; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]Including: pseudo-aneurysm, graft infection, endoleak (any type), enlargement of the excluded aneurysm, and stent graft migration/separation/fracture.
[d]Both in terms of extent of residual FL and of aortic diameters at any level.
[e]Low-risk: based on width and depth of PAU (See *Figure 35* for high-risk features).

10. Genetic and congenital diseases of the aorta

10.1. Genetic and chromosomal diseases

This section discusses genetic and congenital aortic diseases. Aortic root and ascending aortic disease is commonly linked to congenital or hereditary factors, while descending aortic problems, especially in the AA, often result from atherosclerosis.[1385] Unless noted otherwise, recommendations provided herein are intended for adults.

Genetic diseases affecting the thoracic aorta are grouped under the broader term of HTAD. HTAD comprises a clinically and genetically heterogeneous group of disorders sharing the common denominator of aneurysm or dissection of the thoracic aorta. Familial forms (thoracic aortic disease [TAD] affecting ≥2 individuals in one family) or confirmed genetic entities (familial or sporadic) as well as syndromes conferring a risk for TAD fall under the definition of HTAD.[70] Due to the rarity of these conditions, robust evidence for many scenarios, such as intervention thresholds, surgical methods, open surgery vs. endovascular approaches, and pregnancy planning, is lacking. Thus, a multidisciplinary and individualized approach is advisable.[70,1386,1387]

Recommendation Table 55 — Recommendations for the management of patients with heritable thoracic aortic disease

Recommendations	Class[a]	Level[b]
It is recommended that medical management of patients with HTAD is individualized and based on shared decision-making.[1386]	I	C
It is recommended that patients with known or suspected syndromic or non-syndromic HTAD are evaluated in a centre with experience in the care of this patient group.[888]	I	C

HTAD, heritable thoracic aortic disease.
[a]Class of recommendation.
[b]Level of evidence.

Clinically, HTADs can manifest as either syndromic or non-syndromic entities. The genes identified to date may underly both entities and predominantly show autosomal dominant inheritance patterns. While TAD is the primary feature in HTAD, extra-aortic features (skeletal/ocular) may be key to diagnosing certain syndromic cases. In some cases, the presence of extra-aortic manifestations may aid in risk stratification and hence in defining optimal management.[1388–1390] The main clinical and genetic data on syndromic and non-syndromic HTADs are summarized in the Supplementary data online, *Table S5*.

Numerous underlying gene defects have been discovered in both syndromic and non-syndromic cases, leading to the constitution of three major molecular groups: genes encoding components of: (i) the extracellular matrix; (ii) the transforming growth factor-beta (TGF-ß) signalling pathway; and (iii) the smooth muscle cell contractile apparatus. Clinical and CV outcomes vary between these groups and will

help pave the way to precision medicine in HTAD.[1391] Extensive clinical and imaging studies in HTAD revealed arterial vasculature involvement beyond the thoracic aorta. Patients may develop aneurysms and/or dissections beyond the aorta in diseases such as MFS, Loeys–Dietz or vascular Ehlers–Danlos syndrome (vEDS),[1390,1392,1393] or can be prone to occlusive vascular disease in the setting of alpha-actin gene (*ACTA2*) variants.[1394] Large clinical variability is observed within families carrying an identical variant and instances of incomplete penetrance (a 'skipped generation') are observed. All HTAD entities display cystic medial degeneration, hindering precise diagnosis using pathology.

Both genetic testing and imaging (mainly by TTE, but also consider CMR or CCT if the aortic root/ascending aorta are not properly visualized) in patients and family members are important in the diagnosis of HTAD. In those patients in whom no genetic cause is identified, but in whom there is a high suspicion of an underlying genetic defect, genetic re-evaluation needs to be considered after 3–5 years. Genetic testing should always be accompanied with appropriate counselling. Furthermore, appropriate assessment of HRQoL and psychological support should be offered to patients and families.[1395] Indications for genetic testing and aortic screening in HTAD are illustrated in the algorithm in *Figure 39*.

Although isolated AAA is less frequently associated with a genetic basis, patients with high-risk features (syndromic features, early onset of disease, absence of CVRFs, and/or family history of TAD or AAA) should be evaluated in centres with experience in HTAD to evaluate the need for genetic testing and specific surveillance, including active clinical screening in family members.

Recommendation Table 56 — Recommendations for genetic testing and aortic screening in aortic disease

Recommendations	Class[a]	Level[b]
Genetic testing		
In patients with aortic root/ascending aneurysms or thoracic aortic dissection, gathering family history information for at least three generations about TAD, unexplained sudden deaths, and peripheral and intracranial aneurysms is recommended.[880,1396–1402]	I	B
In patients with aortic root/ascending aortic aneurysms or thoracic aortic dissection and risk factors for HTAD,[c] genetic counselling at an expert centre and subsequent testing, if indicated, is recommended.[1399,1403–1408]	I	B
In patients with HTAD who have a pathogenic/likely pathogenic variant, genetic testing of at-risk biological relatives (i.e. cascade testing) is recommended, irrespective of age.[70,1407,1409]	I	C
In patients with HTAD, guidance of clinical management by the underlying gene/variant, when known, should be considered.[70,1391,1410–1416]	IIa	B
Aortic imaging screening		
In patients with TAD with risk factors for HTAD,[c] with a negative family history of TAD and in whom no (likely) pathogenic variant is identified, TTE[d] screening aortic imaging of FDRs[e] is recommended.[1396,1402]	I	B
Imaging screening of family members of patients with TAD with risk factors for HTAD[c] in whom no (likely) pathogenic variant is identified should be considered starting at age 25, or 10 years below the youngest case, whichever is younger. If the initial screening is normal, continued screening every 5 years until the age of 60 should be considered.[25]	IIa	C

Continued

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; FDR, first-degree relative; HTAD, heritable thoracic aortic disease; TAD, thoracic aortic disease; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]See *Figure 39*.
[d]CMR/CCT may be indicated if the aortic root/ascending aorta cannot be visualized adequately.
[e]Parents, siblings, children.

10.1.1. Turner syndrome

10.1.1.1. Diagnosis, clinical presentation, and natural history

Turner syndrome (TS), resulting from partial or complete monosomy of the X-chromosome, affects 1 in 2500 live-born females.

About 50% of patients experience CV issues like ascending aortic dilatation, BAV, aortic coarctation, elongated aortic arch, and partial abnormal pulmonary venous return.[1417–1419] All women present with generalized arteriopathy and TS itself is an independent risk factor for thoracic aortic dilatation. AD risk (type A in 85% and type B in 15%) is elevated in this population,[1420–1422] although recent studies indicate that this risk may be lower with proper treatment guidelines.[1423–1426] Risk factors include aortic dilatation, BAV, coarctation, and arterial hypertension. Defining aortic dilatation in TS requires adjustment for anthropometric parameters and aortic growth data for dissection risk estimation.[1427] Z-scores used in the general population are equivalent to Turner-specific z-scores.[1428]

Imaging surveillance

In newly diagnosed TS, TTE and CMR are recommended at baseline for the evaluation of congenital heart defects and aortic anatomy/diameters. For women aged 15 years and older with TS, adjusting for their smaller body size is essential when assessing aortic dimensions. Utilize metrics like the ascending aortic size index (ASI), aortic height index (AHI), or aortic z-scores to gauge aortic dilation and dissection risk. Further follow-up is dictated by baseline aortic diameters, age, and risk factors (*Figure 40*).

Recommendation Table 57 — Recommendations for imaging in women with Turner syndrome

Recommendations	Class[a]	Level[b]
To take the smaller body size of women (≥15 years) with TS into account, the use of the ascending ASI (ratio of aortic diameter [mm] to BSA [m^2]), AHI (ratio of aortic diameter [mm] to height [m]), or aortic z-score is recommended to define the degree of aortic dilatation and assess the risk of aortic dissection.[153,1417,1421,1423,1428,1429]	I	C
It is recommended to define imaging and clinical surveillance intervals according to the estimated risk for dissection, based on the ascending ASI and concomitant lesions.[c,1420,1421]	I	C

AHI, aortic height index; ASI, aortic size index; BSA, body surface area; TS, Turner syndrome.
[a]Class of recommendation.
[b]Level of evidence.
[c]Concomitant lesions: hypertension, aortic coarctation, bicuspid aortic valve (*Figure 40*).

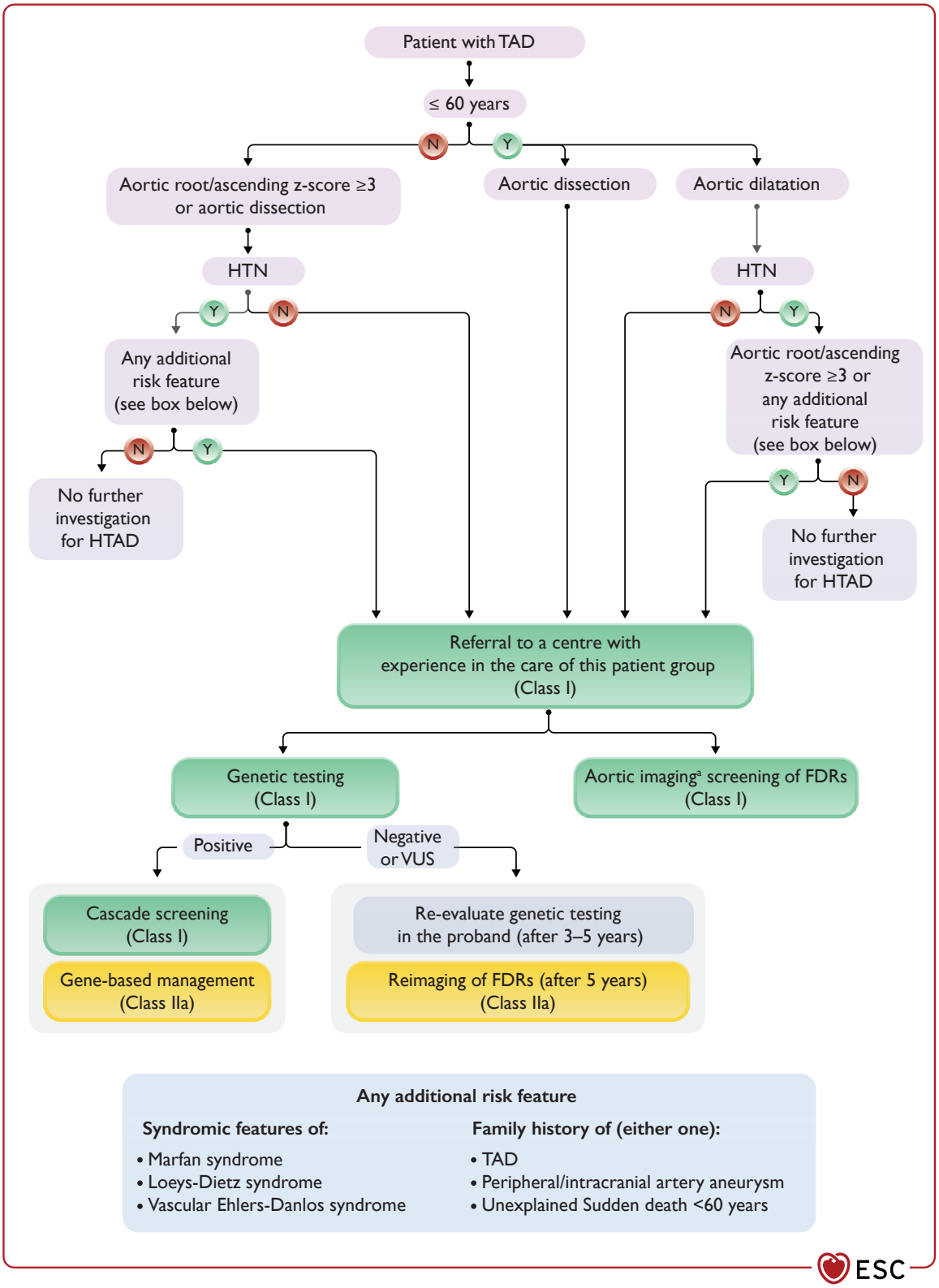

Figure 39 Algorithm for genetic and imaging screening in patients with thoracic aortic disease. CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; FDR, first-degree relative; HTAD, heritable thoracic aortic disease; HTN, arterial hypertension; TAD, thoracic aortic disease; TTE, transthoracic echocardiography; VUS, variant of uncertain significance. [a]mainly by TTE, but also consider CMR or CCT if the aortic root/ascending aorta are not properly visualized.

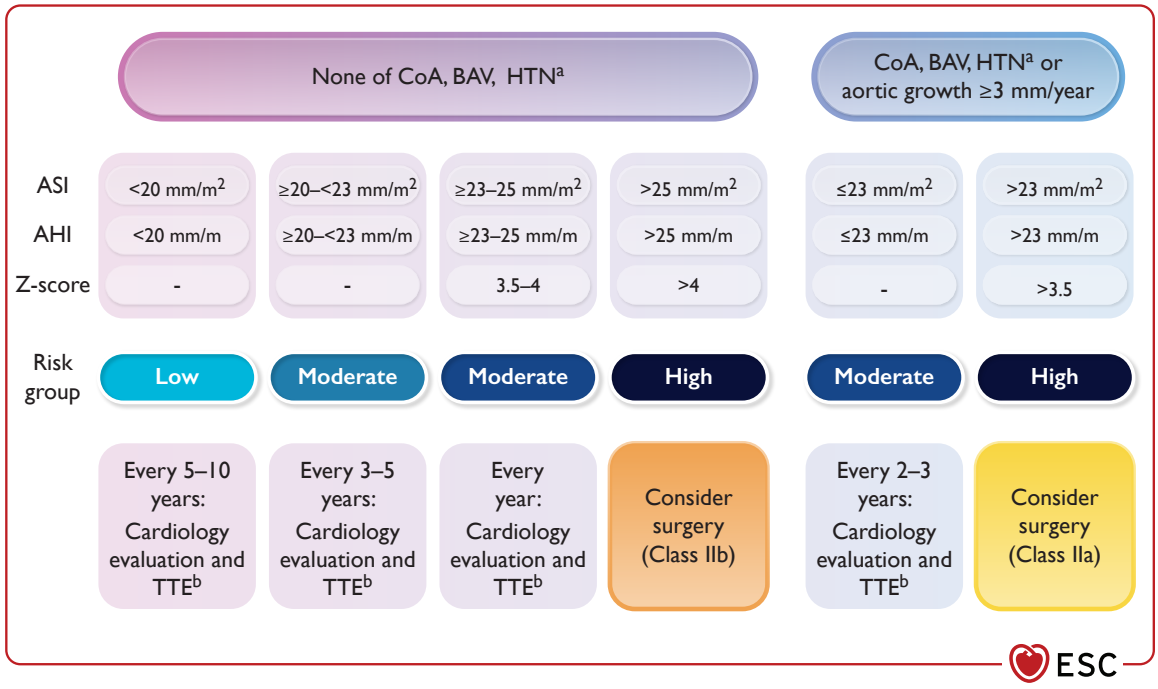

Figure 40 Algorithm for surveillance in women (≥15 years) with Turner syndrome. AHI, aortic height index (ratio of aortic diameter [mm] to height [m]); ASI, aortic size index (ratio of aortic diameter [mm] to BSA [m^2]); BAV, bicuspid aortic valve; BSA, body surface area; CCT, Cardiovascular Computed Tomography; CMR, cardiovascular magnetic resonance; CoA, coarctation of the aorta; HTN, arterial hypertension; TTE, transthoracic echocardiography. [a]HTN: arterial hypertension, not under control despite more than three classes of antihypertensive drugs. [b]CMR (preferably) or CCT if inadequate visualization of the ascending aorta.

10.1.1.2. Medical treatment

In the absence of clinical trials, a pragmatic approach in a shared-decision model is adopted regarding TS medical treatment. Adoption of the strategy for inhibition of aortic growth with BBs and/or ARBs as in MFS may be considered. Hypertension should be treated according to general guidelines.[300]

Hormonal treatment with growth hormone (in childhood), sex (oestrogen and/or progesterone), and thyroid hormones needs to be discussed in a multidisciplinary team with the paediatrician and endocrinologist.[1430–1434]

10.1.1.3. Surgery of aortic aneurysms

Aortic aneurysm surgery in TS should be informed, individualized, and consider factors beyond aortic diameter (indexed). These include BAV, coarctation, uncontrolled hypertension (despite more than three classes of antihypertensive drugs), rapid aortic growth (≥3 mm per year) and planned pregnancy.

Recommendation Table 58 — Recommendations for aortic surgery in women with Turner syndrome

Recommendations	Class[a]	Level[b]
Elective surgery for aneurysms of the aortic root and/or ascending aorta should be considered in women with TS who are ≥15 years of age, have an ascending ASI >23 mm/m^2, an AHI >23 mm/m, a z-score >3.5, and have associated risk factors for aortic dissection[c] or are planning pregnancy.[70,1417,1421]	IIa	C
Elective surgery for aneurysms of the aortic root and/or ascending aorta may be considered for women with TS who are ≥15 years of age, have an ascending ASI >25 mm/m^2, an AHI >25 mm/m, a z-score >4, and who do not have associated risk factors for aortic dissection[c].[70,1417,1421]	IIb	C

AHI, aortic height index (ratio of aortic diameter [mm] to height [m]); ASI, aortic size index (ratio of aortic diameter [mm] to BSA [m^2]); TS, Turner syndrome.
[a]Class of recommendation.
[b]Level of evidence.
[c]Bicuspid aortic valve, elongation of the transverse aorta, coarctation of the aorta, and/or uncontrolled hypertension (despite more than three classes of antihypertensive drugs). See *Figure 40*.

10.1.1.4. Pregnancy and physical exercise

Turner syndrome often involves fertility challenges, but assisted reproductive therapy has increased pregnancy rates. However, pregnancy in TS can elevate the risk of AD, particularly with additional risk factors (*Figure 40*). Recent studies suggest improved pregnancy outcomes due to better guideline adherence.[1435,1436] Prophylactic aortic root surgery in women with TS contemplating pregnancy is recommended when the ASI reaches 25 mm/m^2.[1337] These decisions should be made by an expert team in a shared-decision process.

Physical exercise has a beneficial impact on CVD risk and HRQoL in TS.[1437] Structural congenital heart defects and aortic diameters (ASI, AHI and z-score) (*Figure 40*) need to be considered in the recommendations on the level of sports practice.[1418]

10.1.2. Vascular Ehlers–Danlos syndrome

10.1.2.1. Diagnosis, clinical presentation, and natural history

Vascular Ehlers–Danlos syndrome is a rare (prevalence of 1/50 000 to 1/200 000) autosomal dominant disease caused by pathogenic variants in the *COL3A1* gene, which encodes the pro-alpha1 chains of type III procollagen. The most common *COL3A1* variants provoke a disruption in the assembly of type III collagen fibrils, causing an important loss of mechanical strength of arteries and other hollow organs, especially the bowel and uterus.[1438] Identification of a causal *COL3A1* variant is a requirement for the diagnosis of vEDS.[1439]

vEDS is the most severe form of Ehlers–Danlos syndrome because of its clinical life-threatening vascular complications, making early identification and a thorough family inquiry particularly crucial.

Clinical complications may start during adolescence and repeat at unpredictable time intervals. The most common complications involve medium-sized arteries: dissections, aneurysms, arterial ruptures, and arteriovenous fistulas. AD (both type A and B) occurs in up to 10% of patients.[1440]

Prognosis depends on the type of *COL3A1* variant, with null variants (no gene product or absence of function) showing a better outcome.[1441] The rate of recurrence of organic complications in patients with vEDS is 1.6 events per 5 year period. Life expectancy is reduced to an average of 51 years.[1442]

10.1.2.2. Surveillance and imaging

Management of vEDS is complex and requires a multidisciplinary approach. Recommendations include: lifestyle modification to minimize injury and risk of vessel/organ rupture, identification of a care team, individualized emergency care plans, maintaining BP in the normal range, aggressive hypertension treatment, and annual surveillance of the vascular tree by DUS, CCT (low radiation alternatives), or CMR (if feasible).[1439] A recent survey among European expert centres indicated that arterial monitoring is standard clinical practice and that frequency of follow-up should be adapted individually.[1443] The prognosis improves when patients are properly managed.[1441]

10.1.2.3. Medical treatment

Medical management is based on optimal BP control. Celiprolol, a BB with vasodilatory properties, has been shown to reduce vascular morbidity in two retrospective studies[1441,1444] and one randomized, open-label trial.[1445] There is no consensus about the age at which to start treatment, but starting after 10 years of age is considered reasonable by many experts.

Recommendation Table 59 — Recommendations for medical treatment in patients with vascular Ehlers–Danlos syndrome (see also Evidence Table 13)

Recommendations	Class[a]	Level[b]
In patients with vEDS, regular vascular surveillance of the aorta and peripheral arteries by DUS, CCT, or CMR is recommended.[1439,1443]	I	C
Treatment with celiprolol should be considered in patients with vEDS.[1441,1444,1445]	IIa	B

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DUS, duplex ultrasound; vEDS, vascular Ehlers–Danlos syndrome.
[a]Class of recommendation.
[b]Level of evidence.

10.1.2.4. Surgical treatment

Acute, unexplained pain requires urgent imaging to exclude arterial rupture. Acute arterial complications usually require hospitalization and a conservative approach in most cases. Interventional vascular or intestinal procedures are limited to vital risk. Procedures requiring organ inflation should be avoided or performed with extreme caution. There are no clear recommendations regarding aortic/arterial diameters at which to intervene in patients with vEDS. Thus, decisions need to be made on a case-by-case basis.

10.1.2.5. Pregnancy

Pregnancy in vEDS incurs a risk of (fatal) arterial and uterine complications. Pregnancy does not appear to affect overall mortality compared with nulliparous vEDS women.[1446] However, patients need to be engaged in a shared-decision process, informed by vascular status and underlying variant type.

10.1.3. Marfan syndrome

10.1.3.1. Diagnosis, clinical presentation, and natural history

Marfan syndrome, the most common syndromic HTAD condition (prevalence of 1/5000–1/10 000), arises from pathogenic fibrillin-1 gene (*FBN1*) variants. Beyond the CV system, multiple organ systems are often affected, including the eyes and skeleton. Diagnosis relies on recognizing clinical features in line with the revised Ghent nosology, which includes genetic testing.[1447]

Aortic aneurysm and dissection involving the aortic root are a hallmark of the disease. Less commonly, the descending thoracic and abdominal aorta may be involved. With increasing survival and age in MFS, the prevalence of TBAD seems to be increasing, exceeding type A dissection rates in recent reports.[1448,1449] TBAD will often occur at diameters below surgical thresholds. Previous aortic root replacement, mitral valve surgery, and a longer life span are associated with TBAD. Additional CV features include mitral valve prolapse, extra-aortic arterial involvement, myocardial dysfunction, and arrhythmias.[1393,1450–1452] Thanks to improved diagnosis in earlier stages, proper management including surveillance, medical treatment, and timely prophylactic aortic surgery, life expectancy in MFS patients is now approaching that of the general population.[1416,1453]

The major determinant of TAAD is the aortic root diameter, with increased risk of rupture when it exceeds 50 mm.[1454] Other risk factors include family history of AAS at low diameter, aortic root growth rate (annualized growth rate ≥3 mm or more in adults), pregnancy, and hypertension (hypertension persisting notwithstanding three or more antihypertensive medications prescribed by a physician with experience in hypertension treatment). Increasing evidence for variant-based differences in aortic risk is emerging and may be considered.[1413,1416]

10.1.3.2. Imaging surveillance

Transthoracic echocardiography is the appropriate imaging modality for initial evaluation and follow-up of the aortic root in most patients and allows evaluation of the distal segments of the aorta in many. Also, TTE is useful for assessing mitral and aortic valve regurgitation, mitral valve prolapse with/out annular disjunction, and LV dysfunction. In some cases (especially when pectus abnormalities are present) TTE windows may be suboptimal, and CMR (preferably)/CCT may be preferred. Periodical evaluation of the global aorta and peripheral arteries with CMR/CCT and DUS (every 3–5 years based on the patient's evolution) is indicated since they also present a higher incidence of

peripheral aneurysms,[1455] which are associated with more aggressive forms of the disease.[1393] CMR is preferred over CCT to avoid radiation exposure; however, its use should be adapted to local availability/expertise. Additionally, CMR allows evaluation of biomechanical and haemodynamic parameters that can be useful in risk stratification.[181,1456,1457] Given its superior spatial resolution, CCT may be recommended for pre-operative planning and in cases of measurement inconsistency. Imaging of intracerebral vessels is indicated in cases of symptoms and/or clinical manifestations of aneurysms/rupture. Recommendations for imaging surveillance are illustrated in *Figure 41* and should be adjusted to the individual patient, taking the history and presence of abnormalities during preceding studies into account.

Recommendation Table 60 — Recommendations for vascular imaging in Marfan syndrome

Recommendations	Class[a]	Level[b]
In patients with MFS, TTE is recommended:[70,171,1458,1459] • At least annually in patients with an aortic root diameter <45 mm in the absence of additional risk factors[c] • At least every 6 months in patients with an aortic root diameter <45 mm in the presence of additional risk factors[c] • At least every 6–12 months in patients with an aortic root diameter ≥45 mm in the absence of additional risk factors[c]	I	C
In patients without previous aortic surgery, complete peripheral vascular and thoracoabdominal aorta imaging by CMR or CCT and DUS is recommended at the first evaluation, and subsequently every 3–5 years if stable.[70,1455,1459]	I	C
In patients with MFS who have undergone aortic root replacement, surveillance imaging of the thoracic aorta by CMR (or CCT) is recommended at least every 3 years.[70,1458]	I	C

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DUS, duplex ultrasound; MFS, Marfan syndrome; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]Risk factors: aortic root diameter >40 to ≤45 mm and family history of aortic dissection at small aortic dimensions (i.e. <50 mm); resistant hypertension (hypertension persisting notwithstanding three or more antihypertensive medications prescribed by a physician with experience in hypertension treatment); and rapid growth of the aorta (annualized growth rate ≥3 mm or more in adults).

10.1.3.3. Medical treatment

Medical treatment is described in Recommendation Table 61. Some caution may be warranted with the use of CCBs: these have shown an increased aortic risk in a mouse model and in retrospective case control studies,[1460] and alternatives are preferred for hypertension treatment.

Recommendation Table 61 — Recommendations for medical treatment in Marfan syndrome (see also Evidence Table 14)

Recommendations	Class[a]	Level[b]
In patients with MFS, treatment with either a BB or an ARB, in maximally tolerated doses (unless contraindicated), is recommended to reduce the rate of aortic dilatation.[1461,1462]	I	A
In patients with MFS, the use of both a BB and an ARB, in maximally tolerated doses (unless contraindicated), should be considered to reduce the rate of aortic dilatation.[1463,1464]	IIa	A

ARB, angiotensin receptor blocker; BB, beta-blocker; MFS, Marfan syndrome.
[a]Class of recommendation.
[b]Level of evidence.

10.1.3.4. Aortic surgery

Open surgery is preferred over endovascular procedures in patients with MFS. Endovascular procedures may be considered in selected cases in emergency settings and/or in centres with a high level of expertise.[1465] The thresholds for aortic root surgery need to take additional risk factors, as well as the expertise of the team, into account.[1466]

Recommendation Table 62 — Recommendations for aortic surgery in Marfan syndrome

Recommendations	Class[a]	Level[b]
Surgery is indicated in patients with MFS who have aortic root disease with a maximal aortic sinus diameter ≥50 mm.[70,172,1466–1468]	I	B
Surgery to replace the aortic root and ascending aorta, using the valve-sparing surgery technique, is recommended in patients with MFS or related HTAD with aortic root dilatation when anatomical features of the valve allow its preservation and the surgeon has specific expertise.[70,1466,1469]	I	B
Surgery should be considered in patients with MFS who have an aortic root aneurysm with a maximal aortic sinus diameter ≥45 mm and additional risk factors.[c,1467,1469]	IIa	C
In patients with MFS and an aneurysm of the ascending aorta, aortic arch, descending thoracic aorta, or abdominal aorta of ≥50 mm, surgical replacement of the aneurysmal segment by a surgeon with specific expertise should be considered.[1467,1469]	IIa	C

HTAD, heritable thoracic aortic disease; MFS, Marfan syndrome.
[a]Class of recommendation.
[b]Level of evidence.
[c]Family history of aortic dissection at small aortic dimensions (i.e. <50 mm); resistant hypertension (hypertension persisting notwithstanding three or more antihypertensive medications prescribed by a physician with experience in hypertension treatment); and rapid growth of the aorta (annualized growth rate ≥3 mm or more in adults).

10.1.3.5. Pregnancy and physical exercise

In pregnant MFS women, the risk of AD increases up to eight times relative to the general population.[1470] The risk for TAAD is determined by the aortic diameter, but type B dissections tend to occur even more commonly and may occur without prior dilatation.[1470,1471] Patients should be aware of the persisting risk of TBAD after aortic root replacement.[1471] Women unaware of the diagnosis are at the highest risk of dissection.[1470–1472]

The Registry Of Pregnancy And Cardiac disease (ROPAC) indicates that women managed according to guidelines are at low risk of pregnancy-related complications and major effects of BBs on foetal growth were not shown, although this needs to be carefully monitored.[70,1337,1435,1471,1472]

Recommendation Table 63 — Recommendations for pregnancy in women with Marfan syndrome

Recommendations	Class[a]	Level[b]
It is recommended that all women with MFS: • Have a pre-conception evaluation to address the risks of maternal CV and other complications • Have follow-up in a centre with access to a pregnancy heart and vessel team.[1473]	I	C
It is recommended that couples in which a partner has or is at risk for HTAD be offered pre-conception genetic counselling.	I	C
Imaging of the whole aorta (by CMR/CCT) is recommended prior to pregnancy.	I	C
Follow-up during pregnancy is recommended with a frequency determined by aortic diameter and growth.[1337,1474,1475]	I	C
Intake of BBs during pregnancy is recommended.[1476]	I	C
Prophylactic aortic root surgery is recommended in women desiring pregnancy with aortic diameters >45 mm.[1435,1472]	I	C
Prophylactic aortic root surgery may be considered in women desiring pregnancy with aortic diameters of 40–45 mm.[1472,1475,1477]	IIb	C
ARBs are not recommended during pregnancy.[1478–1480]	III	B

ARBs, angiotensin receptor blockers; BBs, beta-blockers; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; CV, cardiovascular; HTAD, heritable thoracic aortic disease; MFS, Marfan syndrome.
[a]Class of recommendation.
[b]Level of evidence.

Exercise is potentially associated with an increased risk of aortic dilatation and AAD. It is recommended to individualize physical activity in MFS based on aortic diameter, family history of dissection or sudden death, and pre-existing fitness status.[71] Although competitive sports are contraindicated, moderate aerobic exercise is recommended with a level of intensity based on aortic diameters.[71]

Two studies[1481,1482] showed that mild-moderate dynamic exercise improved aortic wall structure and function and reduced aortic growth rate in MFS mouse models. Recent data in MFS children and young adults indicate that adhering to daily physical exercise (10 000 steps a day) had a beneficial effect on aortic root growth.[1483] Although a limited number of clinical studies have evaluated physical activity rehabilitation programmes, two studies[1484,1485] evidenced that physical activity, up to a moderate specific intensity, may be recommended. Thus, although physical activity poses a dilemma, individualized adapted programmes are most likely successful in encouraging exercise in MFS.

Recommendation Table 64 — Recommendations for physical exercise in patients with Marfan syndrome

Recommendations	Class[a]	Level[b]
It is recommended to individualize physical activity in patients with MFS based on aortic diameter, family history of aortic dissection, and pre-existing fitness.	I	C
Regular moderate aerobic exercise with a level of intensity informed by aortic diameter is recommended in most patients with MFS.	I	C
For patients who present with aortic dissection and/or have undergone aortic surgery, post-operative cardiac rehabilitation aiming at improving both physical and mental health should be considered.[73,1483,1484,1486]	IIa	B

MFS, Marfan syndrome.
[a]Class of recommendation.
[b]Level of evidence.

10.1.4. Other syndromic and non-syndromic heritable thoracic aortic diseases and/or arterial disorders

Main clinical and genetic data of known syndromic and non-syndromic HTAD entities are summarized in the Supplementary data online, *Table S5*. The two most prevalent diseases for each entity include Loeys–Dietz syndrome and *ACTA2*-related HTAD, respectively. Given the rarity of these entities, specific recommendations regarding surveillance and treatment are lacking and largely adopted from the recommendations for MFS. Some disease-specific recommendations are mentioned below.

10.1.4.1. Loeys–Dietz syndrome

10.1.4.1.1. Diagnosis, clinical presentation, and natural evolution. The spectrum of clinical presentations in Loeys–Dietz syndrome is very wide. Some patients fulfil criteria for MFS,[1447] while some features such as bifid uvula and hypertelorism are very specific to the disease. Clinical manifestations are listed in the Supplementary data online, *Table S5*. There is a tendency for AD and rupture at lower vessel dimensions than is typically seen in other similar conditions.[1390,1487] Pathogenic variants in six genes (*TGFBR1* and *TGFBR2, TGFB2* and *TGFB3, SMAD2* and *SMAD3*), all encoding components of the TGF-ß signalling pathway, cause Loeys–Dietz syndrome. Differences in clinical manifestations and aortic outcome according to the underlying gene and the extent of extra-aortic features have been reported and need to be considered in surveillance and defining thresholds for surgery.[1388,1390,1391]

Surveillance in Loeys–Dietz syndrome is described in Recommendation Table 65 and *Figure 41*. Although the indication for surgery must be considered according to the underlying genetic defect and the presence of risk factors (Recommendation Table 66 and *Figure 42*), a 45 mm aortic diameter threshold should be considered (≥40 mm in cases of associated high-risk features).

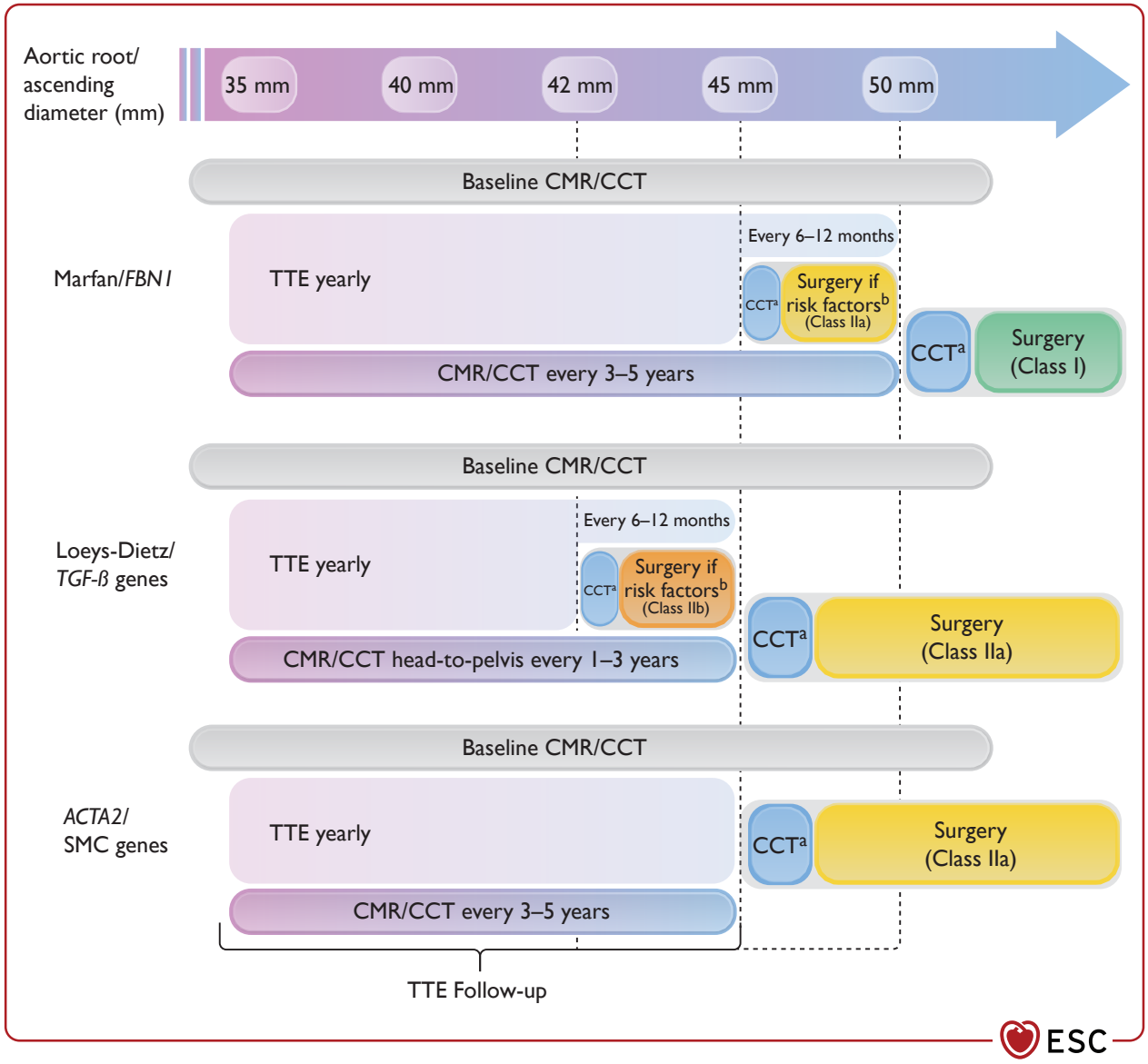

Figure 41 Algorithm for imaging surveillance in patients with syndromic and non-syndromic heritable thoracic aortic disease. CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DUS, duplex ultrasound; HTAD, heritable thoracic aortic disease; SMC, smoth muscle cell; TTE, transthoracic echocardiography. [a]Pre-surgical CCT. [b]See respective tables of recommendations for aortic surgery in Marfan (Table 62) and Loeys-Dietz syndrome (Table 66).

Recommendation Table 65 — Recommendations for imaging follow-up in Loeys–Dietz syndrome

Recommendations	Class[a]	Level[b]
In patients with Loeys–Dietz syndrome, TTE at baseline and subsequently every 6–12 months, depending on aortic diameter and growth,[c] is recommended.[70,1390,1488]	I	C
In patients with Loeys–Dietz syndrome, a baseline arterial imaging study from head to pelvis with CMR or CCT and subsequent surveillance with CMR or CCT or DUS every 1–3 years is recommended.[70,1488]	I	C

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; DUS, duplex ultrasound; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]More frequent imaging if aortic root/ascending diameter >42 mm and aortic growth rate ≥3 mm per year.

Recommendation Table 66 — Recommendations for aortic root surgery in Loeys–Dietz syndrome

Recommendations	Class[a]	Level[b]
Aortic root replacement should be considered for patients with Loeys–Dietz syndrome if the aortic root diameter exceeds 45 mm.[1388,1390,1489–1492]	IIa	C
It may be considered to adjust the threshold for surgery according to the underlying gene, taking associated risk features[c] into account.[1391]	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
[c]High-risk features include certain specific pathogenic variants; women with *TGFBR2* variants and small body size; severe extra-aortic features; family history of aortic dissection (especially at young age or relatively small aortic diameter); and aortic growth rate ≥3 mm per year.

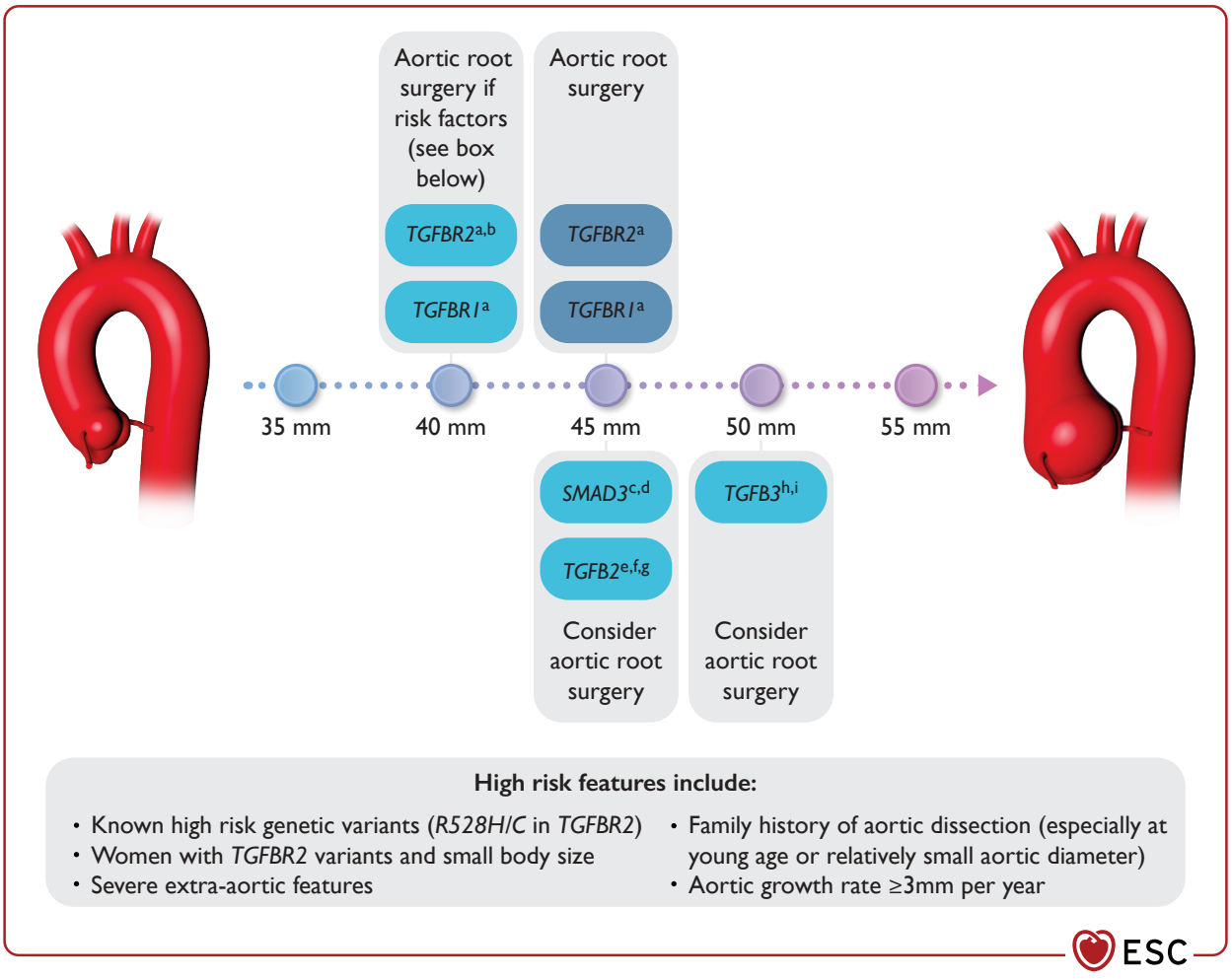

Figure 42 Suggested thresholds for prophylactic aortic root/ascending replacement in Loeys–Dietz syndrome. From a[1388], b[1391], c[1492], d[1491], e[1490], f[1489], g[1493], h[1494], i[1495].

10.1.4.2. ACTA2-related heritable thoracic aortic disease

Pathogenic variants in the *ACTA2* gene, encoding for smooth muscle-specific alpha-actin (a critical component of the vascular smooth muscle cell contractile apparatus), lead to aortic aneurysms and dissections in non-syndromic patients.[1496] Patients primarily present with type A or B aortic dissection, and with aneurysms that involve the root and/or ascending aorta. A subset of pathogenic variants predisposes to occlusive vascular diseases.[1497] Surveillance is summarized in Recommendation Table 67 and *Figure 41*. TAAD may occur at aortic diameters <45 mm, and consideration of surgery at diameters <45 mm should be informed by the presence of additional clinical and genetic risk factors.[1410] Genetic and imaging cascade screening of first-degree family members is an essential element of care, as treatable disease may otherwise be missed in family members—with fatal consequences.

Recommendation Table 67 — Recommendations for imaging and surgery in *ACTA2*-related heritable thoracic aortic disease (see also Evidence Table 11)

Recommendations	Class[a]	Level[b]
Annual monitoring of the aortic root/ascending aorta with TTE to evaluate aortic root/ascending aorta enlargement is recommended.[1498]	I	C
Imaging of the aorta with CMR/CCT every 3–5 years is recommended.[1498]	I	C
Prophylactic aortic root surgery should be considered with an aortic diameter ≥45 mm, or lower in cases with other risk factors.[c,1499]	IIa	C

CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]Risk factors for aortic dissection: family history of dissection with no or minimal dilatation or young age; rapid growth ≥3 mm per year.

10.2. Aortic disease associated with bicuspid aortic valves

Bicuspid aortic valves, the most common congenital heart defect (0.5%–2% of live births), besides being a risk factor for aortic valve disease, is associated with a peculiar form of aortopathy, characterized by morphological and clinical heterogeneity (bicuspid valvulo-aortopathy). Its inheritance is high, with autosomal dominant transmission of BAV in a minority of cases, but no single-gene model clearly explaining BAV inheritance.[1500–1502] Several genes, generally implicated in embryogenesis and cell differentiation, have been associated with BAV/BAV-related aortopathy, but each of them explained <5% of cases.[1503–1507] Therefore,

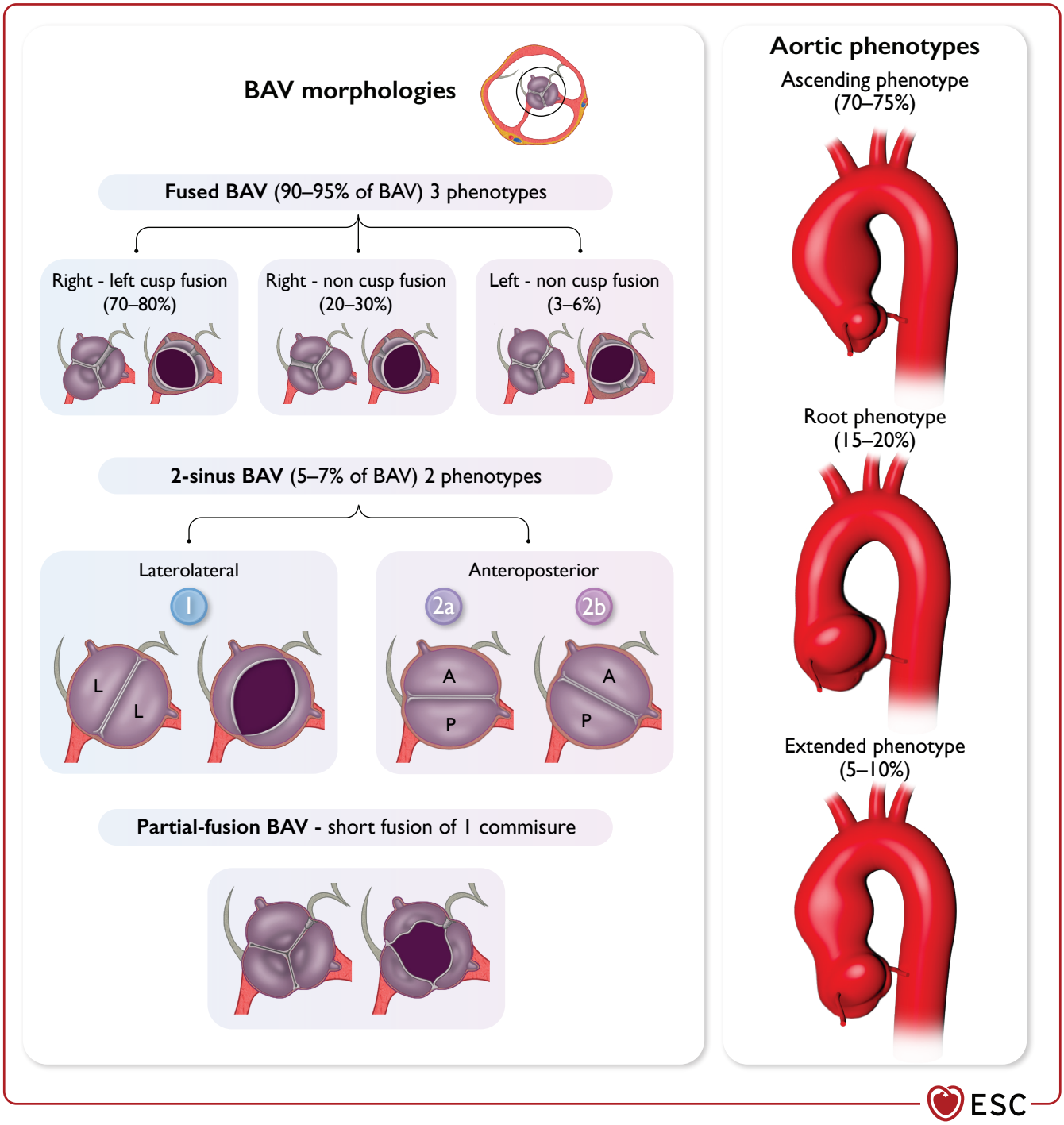

Figure 43 Bicuspid aortic valve, valvulo-aortopathy nomenclature. Modified from Michelena *et al.*[1510] A, anterior; BAV, bicuspid aortic valve; L, lateral; P, posterior. Although preferential associations exist, each of the three valve types—'fused BAV', '2-sinus BAV', and 'partial-fusion BAV'—can be variably associated with dilatation predominantly located at the sinuses of Valsalva ('root phenotype', 15%–20%) or at the tubular (supra-coronary) tract ('ascending phenotype', 70%–75%). A minor proportion of patients present with equal dilatation of the sinusal and tubular segments or ascending dilatation extending into the proximal arch ('extended phenotype', 5%–10%).

genetic testing is not indicated for isolated BAV disease, but reserved for patients with syndromic features, family history of aortic disease, or aneurysms/dissections of medium-sized arteries other than the thoracic aorta, and may be considered in patients with the root phenotype.[1389,1508,1509]

We recommend adopting a new international consensus nomenclature and classification, established by a panel of experts, to replace the previous various concurrent nomenclatures used[1510] (*Figure 43*). Aneurysm prevalence reaches 40% in clinical series and 0.85 per 100 patient-years in population studies. AAEs are rare, but 8- to 10-fold more frequent than in the general population.[1001,1511] The longest available follow-up of BAV subjects was recently reported,[1512] showing a total lifetime morbidity burden as high as 86%, a predominant part of which was driven by valve-related complications (aortic stenosis, endocarditis, HF).

When a BAV is first detected, a complete study of the thoracic aorta is necessary; vice versa, in every patient with ascending aortic dilatation, valve morphology should be ascertained.[70,969] When TTE detects BAV-associated aortic dilatation, CCT or CMR is recommended to confirm measurements, exclude coarctation, and record baseline diameters at different levels for subsequent periodic assessments.[137,1001] Surveillance by TTE becomes necessary when the maximum diameter exceeds 40 mm. In mixed tricuspid aortic valve (TAV) and BAV series, AAEs occurred in 2/10 000 patient-years with a diameter >40 mm (vs. 0.1–0.3/10 000 patient-years in the general population)[894] (*Figure 43*). Considering average aortic diameter growth of 0.2–0.6 mm per year,[893,1513] once fast progression is excluded, follow-up can be scheduled every 2–3 years (according to risk profile). In 5%–15% of cases, BAV patients have at least one FDR with either BAV or ascending aortic dilatation; root phenotype and aortic regurgitation in the proband predict ascending dilatation in FDRs.[1514] FDR screening is considered cost-effective, but the age at which relatives should undergo TTE remains to be determined.[1515,1516]

A diameter exceeding 55 mm at any level mandates surgery.[70,969,1001] However, the historically known relation between diameter and acute complications has been recently reappraised. Both in large mixed[153] and purely BAV series,[981] an ascending diameter of about 52 mm already marked an AAE risk increase from ~1% to 4%–5%. Additionally, early post-operative mortality for elective surgery of the proximal aorta ranges today between 0.25% and 2%.[980,981] Therefore, aortic surgery in low surgical risk (<3%) patients with an ascending diameter >52 mm implies a lower risk than observed in the natural history of the disease. For aortic root dilatation in BAV patients, the 'hinge point' was at 50 mm;[981] this phenotype is associated with faster growth rate,[893] higher risk of events following isolated aortic valve replacement,[1517] worse survival if not operated,[1518] and higher risk of acute TAAD.[976,1519]

Surgery should be considered when the diameter is ≥50 mm in selected ascending phenotype patients (*Figures 23, 24* and *43*).[70,1001] Among those factors, family history of AAEs, poorly controlled hypertension, aortic coarctation, and rapid (≥3 mm per year) diameter growth should be noted. Surgery at >50 mm may also be considered in a shared decision with the patient, taking lifestyle and psychological factors into consideration,[70,1001] since 50 mm should correspond to an approximately 10-fold increase in the risk of AAEs.[894] In a study of patients with aortic diameter ≥40 mm, those with diameters of 50 mm faced a 1% risk of AAEs within 5 years, compared with 0.1% for those with 40 mm diameters, explaining the 10-fold difference; however, this study did not exclusively involve BAV patients.[894] Another recent study[1520] specifically focused on BAV patients found a 0.4% incidence of AAEs per patient-year for diameters above 50 mm, in contrast to the general BAV population's 0.03% incidence.[1521] Previous guidelines also suggested aortic repair for a cross-sectional area-to-height ratio (CSA/h) >10 cm^2/m;[70] nevertheless, more recently, it has been suggested that the CSA/h threshold for the ascending tract in BAV should be 13 cm^2/m.[981] For the average height of male and female Europeans (1.8 m and 1.67 m, respectively), a CSA/h of 10 cm^2/m would correspond to a diameter of 48 mm or 46 mm, respectively, whereas 13 cm^2/m means 54 mm or 53 mm. It is reasonable to refer to the 13 cm^2/m CSA/h cut-off for ascending aortic repair, especially in individuals ≤1.69 m in height (since 13 cm^2/m corresponds to ≤52 mm diameter). Recently, besides dilatation, aortic elongation is also considered a risk factor,[974] and a curvilinear length >11.5 cm at the vessel's centreline increases the yearly risk of AAEs.[155] Age is another factor to consider: at 50 years, a 40 mm ascending aorta corresponds to the upper normal limit for patients with large body size,[149] and therefore the same diameter at a higher age could imply a lower risk of AAEs.

Recommendation Table 68 — Recommendations for bicuspid aortic valve-associated aortopathy management

Recommendations	Class[a]	Level[b]
When a BAV is first diagnosed, initial TTE to assess diameters of the aorta at several levels is recommended.[1001,1510,1522]	I	B
Surgery for bicuspid aortopathy is recommended when the maximum aortic diameter is ≥55 mm.[70,172,899,969,1001]	I	B
Surgery for bicuspid aortopathy of the root phenotype[c] is recommended when the maximum aortic diameter is ≥50 mm.[70,893,981,986,1001,1519,1523]	I	B
CCT or CMR of the entire thoracic aorta is recommended at first diagnosis and when important discrepancies in measurements are found between subsequent TTE controls during surveillance, or when the diameter of the aorta exceeds 45 mm.[1001,1510]	I	C
Screening by TTE in FDRs of BAV patients with root phenotype[c] aortopathy and/or isolated aortic regurgitation is recommended.[1001,1510,1514]	I	C
Surveillance serial imaging by TTE is recommended in BAV patients with a maximum aortic diameter >40 mm, either with no indication for surgery or after isolated aortic valve surgery, after 1 year, then if stability is observed, every 2–3 years.[70,1001]	I	C
Screening by TTE in FDRs of all BAV patients should be considered.[70,1001,1500,1510,1515]	IIa	B
In patients with low surgical risk, surgery for bicuspid aortopathy of ascending phenotype[d] should be considered when the maximum aortic diameter is >52 mm.[153,172,981]	IIa	B

Continued

In patients with low surgical risk and ascending phenotype bicuspid aortopathy, surgery should be considered at a maximum diameter ≥50 mm if any of the following is the case:[70,153,155,981,1001] • Age <50 years • Shorter stature[e] • Ascending aortic length ≥11 cm[f] • Aortic diameter growth rate ≥3 mm per year[g] • Family history of acute aortic syndrome • Aortic coarctation • Resistant hypertension[h] • Concomitant non-aortic-valve cardiac surgery • Desire for pregnancy	IIa	C
Surgery for bicuspid aortopathy in patients undergoing aortic valve surgery should be considered at a root or ascending diameter ≥45 mm.[70,172,969]	IIa	C

BAV, bicuspid aortic valve; BP, blood pressure; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; CSA/h, cross-sectional area-to-height ratio; FDRs, first-degree relatives; TTE, transthoracic echocardiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]Root phenotype = aortic dilatation with sinus diameter > tubular diameter.
[d]Ascending phenotype = aortic dilatation with tubular diameter > sinus diameter.
[e]Patient height between 1.50 and 1.69 m (yielding a CSA/h ratio >13 cm^2/m).
[f]Curvilinear distance at aortic centreline between the ventriculo-aortic junction and the origin of the innominate artery.
[g]In order to ascertain real rapid growth, side-by-side re-evaluation of images obtained with the same modality and technique should be performed.
[h]Hypertension persisting notwithstanding three or more antihypertensive medications prescribed by a physician with experience in hypertension treatment, including diuretics.

10.3. Coarctation of the aorta and aortic arch variants

10.3.1. Coarctation of the aorta

This topic is extensively discussed in the *ESC 2020 Guidelines for the management of adult congenital heart disease*.[1468] Coarctation of the aorta (CoA) manifests as a discrete stenosis or a hypoplastic segment typically located at the insertion of the ductus arteriosus. More distal locations are known as mid-aortic syndrome and require dedicated management.[1524] Associated lesions include BAV (up to 50%–85%), intracerebral aneurysms (10%), and ascending aortic aneurysms.[1525,1526] CoA may be associated with syndromes such as TS. Research indicates that up to 12.6% of females diagnosed with CoA also have TS, and coarctation is observed in 7%–18% of patients with TS.[1417,1468,1527]

10.3.1.1. Diagnostic work-up

Mild cases of CoA may only become evident in adulthood. Symptoms reflect pre-stenotic hypertension (e.g. headache, nosebleeds) and post-stenotic hypoperfusion (e.g. abdominal angina and claudication). The natural course is largely driven by hypertension-related complications, including HF, intracranial haemorrhage, premature coronary/cerebral artery disease, and aortic rupture/dissection.[1528] Presently, there is no evidence supporting screening for intracerebral aneurysms in asymptomatic patients.

A systolic non-invasive gradient between upper and lower extremities, an abnormal ABI, or an invasive peak-to-peak gradient ≥20 mmHg indicates significant CoA. In the presence of collaterals or decreased LV function, gradients or ABI may underestimate severity. A diastolic tail in the DTA or abdominal diastolic antegrade flow by TTE is suggestive of significant narrowing. Criteria to consider significant CoA are listed in *Figure 44*. TTE is also useful to detect LV hypertrophy, which is a marker of disease. CMR and CCT are the preferred imaging techniques, depicting the narrowing as well as the surrounding anatomy, necessary for interventional decision-making.

10.3.1.2. Treatment and follow-up

In native CoA and re-coarctation (*Figure 44*) covered stenting is the first-choice treatment. Interposition of a tube graft is the preferred surgical therapy if stenting is less suitable.[1529] Hypertension remains an important complication, even after successful treatment, and is more common when the initial repair is performed in adulthood.[1528] Right arm 24 h ambulatory BP measurement or exercise tests better detect hypertension.[1530,1531]

All CoA patients require lifelong follow-up.[1532] Imaging of the aorta with CMR/CCT every 3–5 years, adjusted to previous imaging findings and type of intervention, is required to document post-repair or post-interventional complications (such as re-coarctation). Patch repairs are at particular risk of repair-site para-anastomotic aneurysms or pseudo-aneurysms, the latter possibly occurring following interposition grafts as well.[1533]

Recommendation Table 69 — Recommendations for evaluation and medical treatment of patients with coarctation of the aorta

Recommendations	Class[a]	Level[b]
In patients with native or repaired coarctation, lifelong follow-up is recommended, including regular imaging of the aorta with CCT/CMR every 3–5 years (adapted to clinical status and previous imaging findings).[1534,1535]	I	B
Coarctation or re-coarctation repair (either surgical or endovascular) is indicated in patients with hypertension with an increased non-invasive gradient between the upper and lower limbs (decreased ABI) confirmed with invasive measurement (peak-to-peak >20 mmHg), with a preference for stenting when technically feasible.[1536]	I	C
In patients with coarctation, BP measurements at both arms and one lower extremity are recommended.	I	C
It is recommended to treat hypertension in patients with coarctation according to ESC hypertension guidelines.[300]	I	C
Endovascular treatment should be considered in patients with hypertension with >50% narrowing relative to the aortic diameter at the diaphragm, even if the invasive peak-to-peak gradient is <20 mmHg, when technically feasible.[1537]	IIa	C
Endovascular treatment should be considered in normotensive patients with an increased non-invasive gradient confirmed with invasive peak-to-peak gradient >20 mmHg, when technically feasible.[1468]	IIa	C

ABI, ankle–brachial index; BP, blood pressure; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; ESC, European Society of Cardiology.
[a]Class of recommendation.
[b]Level of evidence.

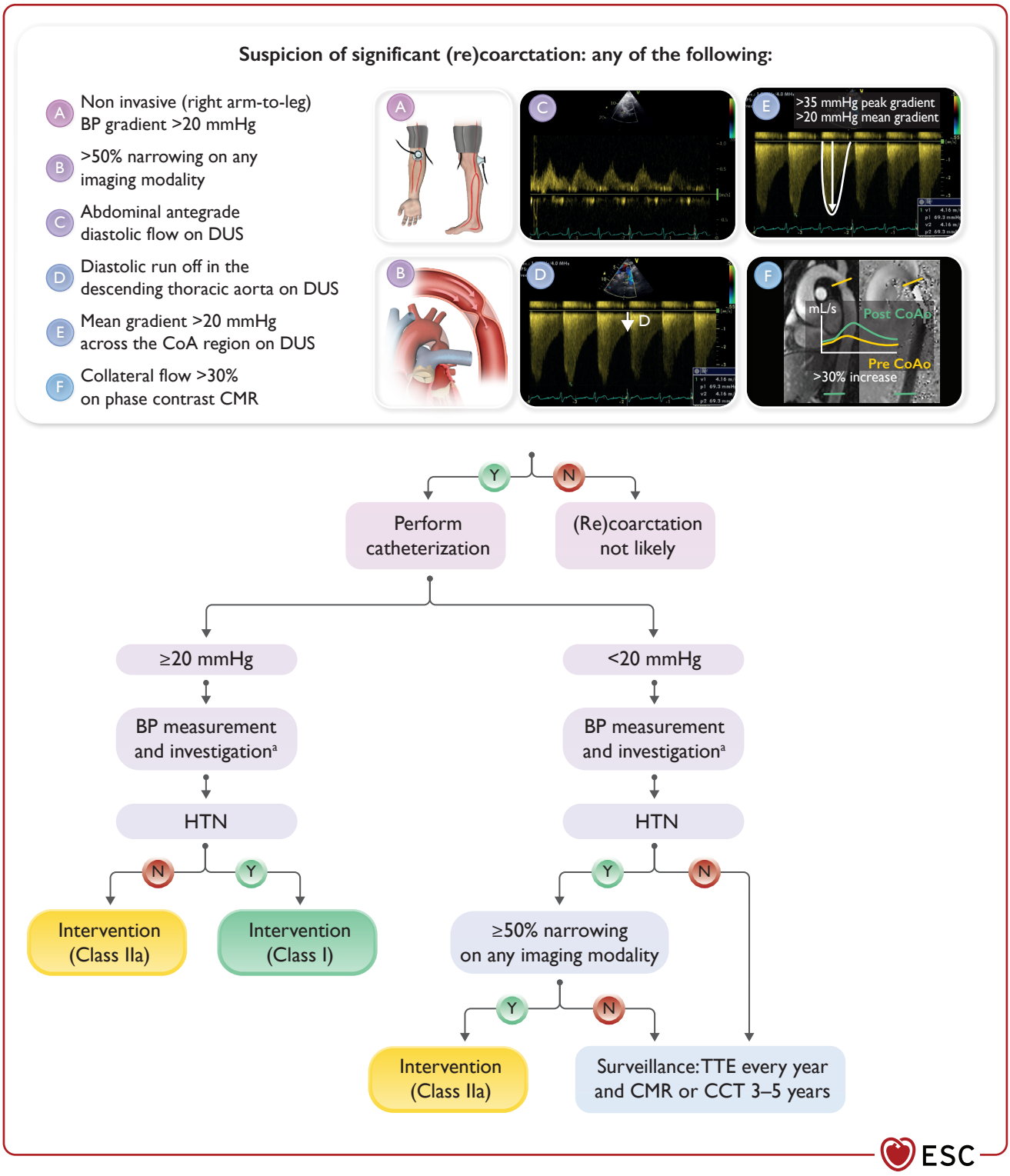

Figure 44 Criteria for significant coarctation/re-coarctation of the aorta and management algorithm. BP, blood pressure; CCT, cardiovascular computed tomography; CMR, cardiovascular magnetic resonance; CoA, coarctation of the aorta; DUS, duplex ultrasound; HTN, hypertension; TTE, transthoracic echocardiography. [a]Diagnosis of hypertension may require confirmation with ambulatory BP measurement and should also be considered in cases of exercise-induced hypertension and/or left ventricular hypertrophy on TTE.

10.3.2. Aortic arch anatomic variants

A type I arch, where the three great vessels directly arise from the aorta, is the most common form, occurring in about 70% of the population. The type II (bovine) arch is the most frequent variant: type II-A (9% of the population) has the left common carotid artery arising from the innominate artery, and type II-B (13% of the population) has both the innominate and left common carotid arteries originating from a common point on the aortic arch.[1538,1539] Limited data suggest that a bovine arch is associated with a higher risk of aortic dilation and aortic events/complications.[1540,1541] These variations are important to report as they can impact specific medical procedures and diagnostic interpretations.

10.3.3. Aberrant subclavian artery and Kommerell's diverticulum

The most common variant is the aberrant right subclavian artery, where the right subclavian artery arises as the last branch of the aortic arch, usually after the left subclavian artery, and often passes behind the oesophagus through the mediastinum, potentially causing dysphagia lusoria, respiratory symptoms, or recurrent laryngeal nerve palsy. The less common variant, the aberrant left subclavian artery, is typically associated with congenital heart defects, such as a right aortic arch. However, in adulthood, both variations are often incidental findings.[1542]

Kommerell's diverticulum is a remnant of the fourth dorsal aortic arch due to incomplete regression, found in 20%–60% of those with an aberrant subclavian artery.[1543] Surgical intervention is advised for a diverticulum orifice >30 mm or combined diverticulum and adjacent descending aorta diameter >50 mm, or both.[1544] Successful repair has been described using open, endovascular, or hybrid approaches depending on anatomy, comorbidities, and expertise.[1543]

11. Polyvascular peripheral arterial disease and peripheral arterial disease in patients with cardiac diseases

11.1. Polyvascular disease

Polyvascular disease is defined as the simultaneous presence of clinically relevant obstructive atherosclerotic lesions in at least two major arterial territories.

11.1.1. Epidemiology and prognosis

Approximately 1 in 4–6 patients with atherosclerosis have PVD (*Figure 45*).[620,1545] According to the REACH registry, patients with PAD were most likely both to have PVD at baseline and to develop PVD over the observational period.[1546,1547]

PVD independently increases major CV event risk, roughly doubling it compared with single arterial bed symptoms.[1547–1549] Event rates rise with the number of affected arterial beds.[1546,1550]

11.1.2. Screening for atherosclerosis in other arterial territories

Screening for PVD in atherosclerotic patients relies on medical history, clinical exam, and ABI measurement. If suspected, start with non-invasive DUS, followed by CTA/MRA if needed.[1557] Assessing concurrent atherosclerosis in other vascular regions is detailed in *Table 17*.

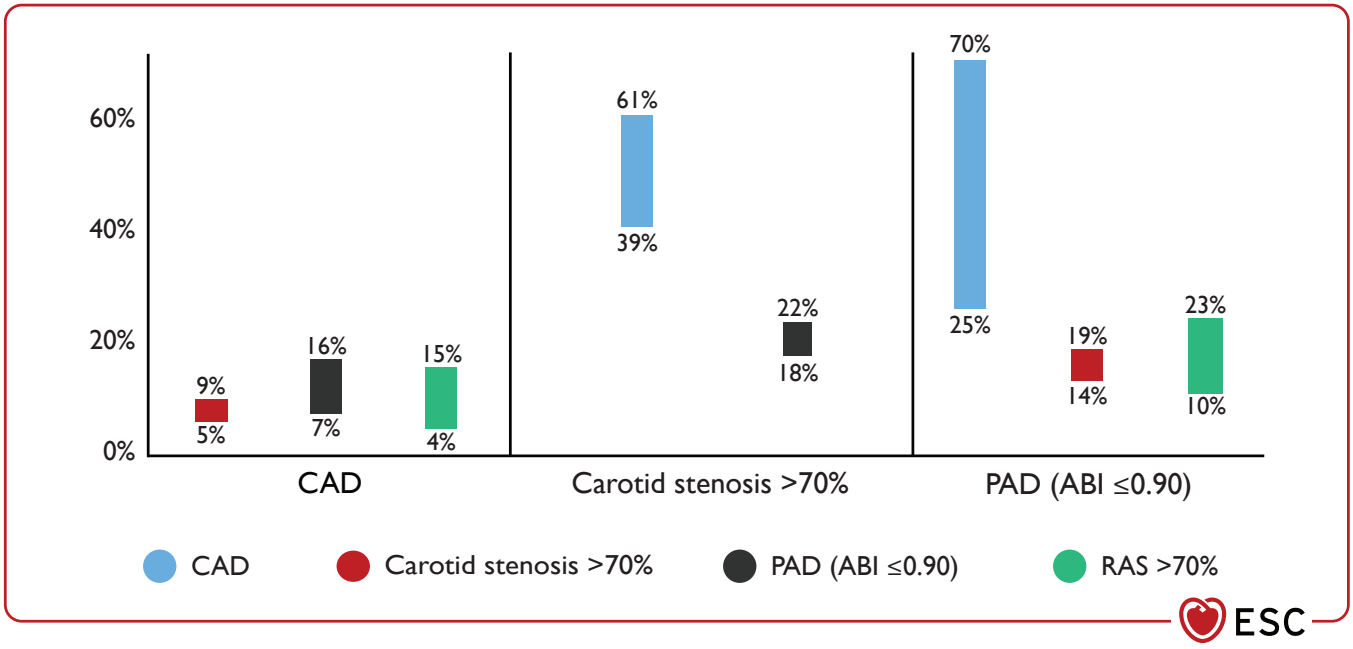

Figure 45 Reported rate ranges of other localizations of atherosclerosis in patients with a specific arterial disease. The graph reports the rates of concomitant arterial diseases in patients presenting an arterial disease in one territory (e.g. in patients with CAD, 5%–9% of cases have concomitant carotid stenosis >70%). Adapted from 2017 ESC Guidelines on PAD.[77,493,784,1549,1551–1556] ABI, ankle–brachial index; CAD, coronary artery disease; PAD, peripheral arterial disease; RAS, renal artery stenosis.

Table 17 Need for assessment of associated atherosclerotic disease in additional vascular territories in symptomatic patients with coronary artery disease, peripheral arterial disease, or carotid stenosis

	Leading disease		
Assessment in other vascular territories	**CAD**	**PAD**	**Carotid stenosis**
CAD		May be helpful to optimize medical treatment[431] and to be considered in patients scheduled for open vascular surgery with poor functional capacity or significant risk factors or symptoms. [1080]	Consider in patients scheduled for carotid endarterectomy and suspected CAD.[1558]
PAD	Potential benefits in identifying high-risk patients and guiding treatment decisions.[429,1559–1561]		
Carotid stenosis	Useful in patients undergoing elective CABG.[1555,1562]		

CABG, coronary artery bypass grafting; CAD, coronary artery disease; PAD, peripheral arterial disease.

11.1.2.1. Screening for coronary artery disease in patients with symptomatic peripheral arterial disease

The morbidity and mortality of patients with PAD is high due to CV complications. Given high CAD event rates in patients with PAD, CAD screening may be helpful to optimize medical treatment and is not intended to increase the rate of coronary interventions.[431] Evaluation can be performed by stress testing or CCT; however, there is no evidence that systematic screening for CAD in stable PAD improves outcomes. Coronary angiography is less suitable due to invasiveness. In patients requiring lower-limb revascularization, CAD management should be based on the *2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery*.[1080]

11.1.2.2. Screening for peripheral arterial disease in patients with coronary artery disease

In high-risk CAD patients with three-vessel disease or recent ACS, systematic screening for multisite atherosclerotic disease through ABI and DUS of carotids, lower-extremity, and renal arteries did not improve outcomes.[1563] However, a subgroup analysis of the COMPASS trial suggests potential benefits when adding vascular-dose rivaroxaban to aspirin in stable patients with CAD and PAD, raising the question of whether identifying PAD in stable CAD patients could be advantageous.[429,1559] In patients undergoing CABG, the presence of concomitant PAD is associated with a three-fold risk of subsequent CV events after CABG.[1560,1561] The GSV should be spared whenever possible, since the success of peripheral arterial revascularization in complex lesions is strongly associated with the availability of sufficient autologous venous segments.[567,1564]

11.1.2.3. Screening for coronary artery disease in patients with carotid stenosis

Due to the high prevalence of CAD among patients scheduled for elective CEA,[1565,1566] pre-operative CAD screening, including coronary angiography, may be considered in suspected patients.[1558] CAD requires prioritization of revascularization according to the patient's clinical status and the severity of carotid disease and CAD. Coronary revascularization should generally be performed first; the exception is recently symptomatic patients with unstable neurological symptoms in whom carotid revascularization should be prioritized.[680]

11.1.2.4. Screening for carotid stenosis in patients with coronary artery disease

Carotid artery stenosis screening may be useful in patients undergoing elective CABG. Ischaemic stroke after CABG is multifactorial,[1567] but also depends on the degree of carotid disease.[1556] Two studies suggest that limiting DUS to patients with at least one risk factor (age >65 years, history of cerebrovascular disease, presence of a carotid bruit, multivessel CAD or PAD) identifies most patients with significant (≥70%) CS.[1555,1562] Nevertheless, addition of CEA to CABG is unlikely to provide significant stroke reduction. In a study in patients with CAD with >80% CS undergoing staged or synchronous carotid procedures (two-thirds were neurologically asymptomatic and 73% had unilateral asymptomatic carotid stenosis), in-hospital stroke rates and 30 day mortality were similar in patients treated with CABG + CEA and in those treated with isolated CABG.[1568] Another study suggests that selective use of DUS should be considered before CABG in patients with a history of neurological events or PAD.[1569]

11.1.3. Management of patients with polyvascular disease

Polyvascular disease requires proactive management of all modifiable risk factors through lifestyle changes and drug therapy. Scientific evidence suggests the benefit of intensified antithrombotic therapy, with no increase in risk of bleeding.[1570] ILT offers comparable benefits for PVD patients and those with single arterial territory disease. However, the benefits of ILT in patients with PVD are not dependent on baseline LDL-C.[1571]

Revascularization should be reserved for symptomatic arterial territories, using the least invasive strategy in a multidisciplinary vascular team approach.

11.2. Peripheral arterial disease and heart failure

Left ventricular (LV) dysfunction is observed in 20%–30% of PAD patients,[1572,1573] mostly associated with CAD.[1574] High aortic stiffness

can increase LV afterload and impair coronary blood flow, resulting in hypertension, LV hypertrophy, LV diastolic dysfunction, and HF.[1575,1576] Skeletal muscle involvement and deconditioning due to PAD may aggravate HF severity.[1577,1578]

Peripheral arterial disease and HF are independently associated with poor outcomes and those with concomitant HF have a 30% higher risk of MACE and 40% higher risk of all-cause mortality.[1574] Evaluation of LV function in patients with PAD may be useful for better CV risk stratification and comprehensive management of their CV disease.[1579] This is of particular importance when an intermediate- or high-risk vascular intervention is planned. Expectedly, the presence of PAD in patients with HF is also associated with poor outcomes.[1580–1584] These patients represent a high-risk group in which intense risk-factor modification strategies and optimization of HF therapy are warranted.

11.3. Peripheral arterial disease and AF

The prevalence of AF among patients with PAD is around 12%.[1585–1590] A meta-analysis revealed that in patients with AF and PAD, risk of all-cause mortality, CV mortality, and MACE is 40%, over 60%, and over 70% higher, respectively compared with patients with AF without PAD.[1591] PAD is included in the CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 [doubled], diabetes, stroke [doubled], vascular disease, age 65 to 74 and sex category [female]) risk score, which underlies the prognostic importance of PAD in patients with AF.[1592]

11.4. Peripheral arterial disease and aortic stenosis

Peripheral arterial disease frequently accompanies symptomatic aortic stenosis, especially among patients not eligible for surgical aortic valve replacement (20%–30%).[198,1593–1595] In these patients, pre-procedural CCT/CTA or CMR[1596] of the aorta and major peripheral arteries is mandatory to evaluate the access site for transcatheter aortic valve implantation (TAVI) and plan a closure strategy for the access site. Patients with PAD have increased risk of all-cause mortality and vascular complications after TAVI,[198] thus, screening for PAD in these patients may be helpful.

Recommendation Table 70 — Recommendations for screening and management of polyvascular disease and peripheral arterial disease with cardiac diseases (see also Evidence Table 15)

Recommendations	Class[a]	Level[b]
In patients with PVD, an LDL-C reduction by ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[242,1571]	I	A
In patients with PAD and newly diagnosed AF with a CHA_2DS_2-VASc score ≥2, full oral anticoagulation is recommended.[1597]	I	C
Screening for ilio-femoral PAD is recommended in patients undergoing TAVI.[198,1598]	I	B
Carotid DUS should be considered for stable patients scheduled for CABG with TIA/stroke within the past 6 months without carotid revascularization.[1556,1569]	IIa	B
In patients with stable PVD who are symptomatic in at least one territory and without high bleeding risk,[c] treatment with a combination of rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered.[429,1559]	IIa	A
Carotid DUS may be considered for stable patients scheduled for CABG without TIA/stroke within the past 6 months.[1555,1562]	IIb	C

Continued

AF, atrial fibrillation; b.i.d., twice daily; CABG, coronary artery bypass grafting; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 and sex category (female); DUS, duplex ultrasound; eGFR, estimated glomerular filtration rate; LDL-C, low-density lipoprotein cholesterol; o.d., once daily; PAD, peripheral arterial disease; PVD, polyvascular disease; TAVI, transcatheter aortic valve implantation; TIA, transient ischaemic attack.

[a]Class of recommendation.

[b]Level of evidence.

[c]Prior history of intracerebral haemorrhage or ischaemic stroke, history of other intracranial pathology, recent gastrointestinal bleeding or anaemia due to possible gastrointestinal blood loss, other gastrointestinal pathology associated with increased bleeding risk, liver failure, bleeding diathesis or coagulopathy, extreme old age or frailty, or renal failure requiring dialysis or with eGFR <15 mL/min/1.73 m^2.

12. Key messages

Peripheral arterial and aortic diseases are highly prevalent, often asymptomatic, and linked to increased morbidity and mortality. Early diagnosis is crucial for better outcomes and management requires a multidisciplinary team. CVRF control is crucial to prevent progression and complications. Despite the benefit of medical therapy, lifestyle changes, healthy diet, abstinence from smoking, exercise/rehabilitation, and education are essential for effective management. Patient empowerment is essential to improve adherence and close/regular monitoring is essential to improve prognosis. Use of web- or app-based calculators for estimation of CV risk in the secondary prevention of ASCVD may aid patient motivation for lifestyle changes and adherence to medication.

Peripheral arteries

Atherosclerotic lower-extremity PAD is a chronic disease needing lifelong follow-up.

Assessment of walking impairment, functional status, and amputation risk is crucial in PAD management.

Ankle–brachial index should be the initial diagnostic test for screening and diagnosing PAD, and serves as a surrogate marker for CV and all-cause mortality. DUS is the first-line imaging method to confirm PAD lesions.

Supervised exercise training or, if not available, HBET, improves walking and functional performances, and reduces CV risk. Exercise training remains underused and increased awareness is warranted.

In asymptomatic PAD patient revascularization is not recommended. In symptomatic PAD patient need for interventional treatment, following a period of optimal medical treatment and exercise, should be discussed in a multidisciplinary setting.

Chronic limb-threatening ischaemia increases the risk of CV events, needs early diagnosis, rapid referral to a multidisciplinary vascular team, and revascularization for limb salvage.

Acute limb ischaemia warrants rapid clinical assessment by a vascular team and urgent revascularization.

Duplex ultrasound is the first-line diagnostic modality for carotid stenosis. Routine revascularization is not recommended if asymptomatic. In symptomatic patients multidisciplinary assessment is recommended.

Atherosclerotic UEAD is most frequently located in the subclavian artery and may be suspected because of an absolute inter-arm SBP difference >10–15 mmHg. DUS is first-line imaging and routine revascularization is not recommended.

The key to early diagnosis of acute and chronic mesenteric ischaemia is a high level of clinical suspicion—laboratory tests are unreliable for the diagnosis. Acute SMA occlusion requires immediate revascularization.

Aorta

Aortic aneurysms are managed based on size, location, and growth rate. Small aneurysms are monitored regularly (Guidelines provide disease-specific follow-up algorithms), while larger ones may require surgical/endovascular repair to prevent rupture.

In aortic root aneurysms, aortic replacement may be considered at >52 mm in low-risk patients and at experienced centres.

Aortic diameter is the primary risk factor for aortic events. However, evidence supports diameter indexation (especially in extreme BSA populations) and the use of aortic length (>11 cm), the AHI (>32.1 mm/m), growth rate (≥3 mm per year for ascending aorta and arch or >5 mm per 6 months in the thoracoabdominall aorta), and age/sex for risk assessment.

Multidisciplinary collaboration, hybrid operating rooms, and advanced stent technology have increased the adoption of hybrid approaches and endovascular therapies for different thoracoabdominal aortic diseases.

Acute aortic syndrome management involves medical treatment in critical care units and selective surgical intervention based on location and complications. The main problem in these conditions continues to be a delay in diagnosing patients or transferring them to an aortic centre. Improved diagnostic algorithms and reduced surgical complications have lowered mortality rates. Surgical/endovascular treatment in the subacute phase is advised for high-risk patients with type B aortic syndrome.

Suspected genetic aortic conditions require evaluation at experienced centres to assess both the patient and their FDRs for genetic studies. Genetic aortic conditions should be considered based on family history, syndromic features, age <60 years, and no CVRFs (Guidelines offer a screening algorithm for thoracic aorta disease). A comprehensive evaluation of the entire aorta and other vascular territories is recommended in HTAD. Recent advances in genetics are enabling personalized and patient-centred assessment. This includes using different aortic diameter thresholds to indicate surgery and implementing diverse surveillance algorithms.

13. Gaps in evidence

There are several areas where robust evidence is still lacking and which deserve to be addressed in future clinical research.

(1) Epidemiology and risk factors in PAAD:
   (a) Improve PAAD risk definition.
   (b) Provide contemporary data on PAAD prevalence in Europe.
   (c) Inflammation biomarkers, metabolomics, and proteomics may have prognostic value in PAAD.
(2) Evaluation of peripheral arteries and aorta:
   (a) Follow-up algorithms can assist PAAD patient management but have limitations and evidence on cost-effectiveness is needed.
   (b) The best methodology for aortic measurements remains to be elucidated.
(3) Screening for carotid, peripheral arterial, and aortic diseases:
   (a) Screening in specific populations: research is needed to understand the nuances of screening in particular populations and whether modifications to current guidelines are necessary.
   (b) Patient outcomes and benefits of screening: impact of screening on patient outcome should be assessed.
(4) OMT and PAAD:
   (a) Research needed on QoL and workability.
   (b) Research needed for optimal preventive strategies.
   (c) Exercise therapy and rehabilitation for PAAD should be more accessible and employed.
   (d) Anti-inflammatory therapy should be investigated.
   (e) Antithrombotic therapies in specific risk groups of PAAD and patients undergoing revascularization should be addressed.
(5) Aortic aneurysms:
   (a) Discovering novel individualized risk stratification parameters beyond well-established markers.
   (b) Assessing the safety of fluoroquinolone use in patients with aortic aneurysm.
(6) Acute aortic syndromes:
   (a) Assess the management of pregnancy-related AAS.
   (b) Identify diagnostic biomarkers other than D-dimer.
   (c) Management in uncomplicated TBAD and IMH should be assessed.
(7) Genetic aortic diseases:
   (a) Need to refine risk estimation in AD, particularly in HTAD, especially the risk of type B aortic dissection.
   (b) There is insufficient evidence to support the efficacy of any medication in reducing the risk of AD.
(8) Sex differences in PAAD:
   (a) Investigate sex and age differences.
   (b) Assess the optimal parameter or indexed parameter to guide intervention decisions in women with aortic and PAD diseases.

14. Sex differences

Sex differences have been evaluated and discussed in the specific sections.

15. 'What to do' and 'What not to do' messages from the guidelines

Table 18 'What to do' and 'What not to do'. 'What to do and What not to do' lists all Class I and Class III recommendations from the text.

Table 18 'What to do' and 'What not to do'

Recommendations	Class[a]	Level[b]
Recommendations for clinical and laboratory, and for functional and quality of life, assessment in patients with peripheral arterial and aortic disease		
When managing PAAD, it is recommended to adopt a comprehensive approach that addresses the entirety of arterial circulation.	I	B
To assess PAAD, it is recommended to perform thorough clinical, vascular, and CVRF laboratory evaluation.	I	C
Recommendations for diagnostic tests in patients with peripheral arterial disease		
Measurement of the ABI is recommended as the first-line non-invasive test for screening and diagnosis of PAD, using an ABI ≤0.90 as a diagnostic criterion.	I	B
In the case of non-compressible ankle arteries or ABI >1.40, additional methods such as TP, TBI or Doppler waveform analysis are recommended.	I	B
Recommendations for imaging of the aorta		
It is recommended that aortic diameters are measured at prespecified anatomical landmarks, and the largest diameter of the section be perpendicular to the longitudinal axis.	I	C
It is recommended in cases of serial imaging of the aorta over time to use the same imaging modality with the same measurement method.	I	C
It is recommended to consider renal function, pregnancy, age, and history of allergy to contrast media to select the optimal imaging modality with minimal radiation exposure and lowest iatrogenic risk, except for emergency cases.	I	C
Recommendations for thoracic aortic measurements		
TTE is recommended as the first-line imaging technique in evaluating thoracic aortic diseases.	I	B
It is recommended to report aortic diameters using the leading-to-leading edge convention in end-diastole by echocardiography.	I	C
It is recommended to report aortic diameters using the inner-to-inner edge convention in end-diastole by CCT or CMR.	I	C
It is recommended to report aortic diameters from images obtained with the double-oblique technique (not axial images) by CCT or CMR.	I	C
ECG-triggered CCT is recommended for comprehensive diagnosis, follow-up, and pre-invasive treatment assessment of the entire aorta, particularly the root and ascending aorta.	I	C
CMR is recommended for diagnosis and follow-up of thoracic aortic diseases, especially when chronic follow-up is required.	I	C
Recommendations for abdominal aortic aneurysm screening		
Screening is recommended in men aged ≥65 years and with a history of smoking to reduce the risk of death from ruptured AAA.	I	A
Screening is recommended in FDRs of patients with AAA aged ≥50, unless an acquired cause can be clearly identified.	I	C
Recommendations for lifestyle, physical activity, and patient education		
In patients with PAAD, cessation and abstinence from smoking of any kind is recommended to reduce the risk of AD, MI, death, and limb ischaemia.	I	A
A healthy diet rich in legumes, dietary fibre, nuts, fruits, and vegetables, with a high flavonoid intake (Mediterranean diet), is recommended for CV disease prevention in patients with PAAD.	I	A
Low- to moderate-intensity (or high if tolerated) aerobic activities are recommended in patients with PAD to increase overall and pain-free walking distance.	I	A
In patients with PAAD, behavioural counselling to promote healthy diet, smoking cessation, and physical activity is recommended to improve the CV risk profile.	I	B
It is recommended to promote patient and caregivers' education and empowerment through tailored guidance on lifestyle adjustments and the importance of regular physical activity.	I	C
Recommendations for antihypertensive therapy in patients with peripheral and aortic disease		
In patients with PAAD and hypertension an SBP target towards 120–129 mmHg, if tolerated, is recommended.	I	A
In unilateral RAS patients, it is recommended that antihypertensive medication include ACEIs/ARBs.	I	B
Recommendations for lipid-lowering therapy for patients with peripheral arterial and aortic diseases		
In patients with atherosclerotic PAAD, lipid-lowering therapy is recommended.	I	A
An ultimate LDL-C goal of <1.4 mmol/L (55 mg/dL) and a >50% reduction in LDL-C vs. baseline are recommended in patients with atherosclerotic PAAD.	I	A
Statins are recommended in all patients with PAD.	I	A
If the target LDL-C level is not achieved, a combination of statins and ezetimibe is indicated in patients with atherosclerotic PAAD, to achieve the given target values.	I	B

Continued

If the target LDL-C level is not achieved on maximally tolerated statins and ezetimibe, treatment with a PCSK9 inhibitor is recommended in patients with atherosclerotic PAAD, to achieve target values.	I	A
For statin-intolerant patients with atherosclerotic PAAD, at high CV risk, who do not achieve their LDL-C goal on ezetimibe, it is recommended to add bempedoic acid either alone or in combination with a PCSK9 inhibitor.	I	B
Fibrates are not recommended for cholesterol lowering.	III	B
Recommendations for the medical management of patients with peripheral arterial and aortic diseases and diabetes		
It is recommended to apply tight glycaemic control (HbA1c <53 mmol/mol [7%]) to reduce microvascular complications in patients with PAAD.	I	A
SGLT2i with proven CV benefit are recommended in patients with T2DM and PAAD to reduce CV events, independent of baseline or target HbA1c and concomitant glucose-lowering medication.	I	A
GLP-1RAs with proven CV benefit are recommended in patients with T2DM and PAAD to reduce CV events, independent of baseline or target HbA1c and concomitant glucose-lowering medication.	I	A
It is recommended to avoid hypoglycaemia in patients with PAAD.	I	B
It is recommended to individualize HbA1c targets according to comorbidities, diabetes duration, and life expectancy.	I	C
It is recommended to prioritize the use of glucose-lowering agents with proven CV benefits, followed by agents with proven CV safety, over agents without proven CV benefit or safety.	I	C
Recommendations for diagnostic tests in patients with peripheral arterial disease and diabetes, renal failure and wounds		
Measuring TP or TBI is recommended in patients with diabetes or renal failure if resting ABI is normal.	I	C
Recommendations for imaging in patients with peripheral arterial disease		
DUS is recommended as first-line imaging method to confirm PAD lesions.	I	C
In symptomatic patients with aorto-iliac or multisegmental/complex disease, CTA and/or MRA are recommended as adjuvant imaging techniques for preparation of revascularization procedures.	I	C
Analysis of anatomical imaging tests in conjunction with symptoms and haemodynamic tests prior to an invasive procedure is recommended.	I	C
Recommendations for exercise therapy in patients with peripheral arterial disease		
In patients with symptomatic PAD, SET is recommended.	I	A
In those patients undergoing endovascular revascularization, SET is recommended as an adjuvant therapy.	I	A
Recommendations for antithrombotic therapy in patients with peripheral arterial disease		
Use of antiplatelet therapy with aspirin alone (range 75–160 mg o.d.) or clopidogrel alone (75 mg o.d.) is recommended for the reduction of MACE in patients with symptomatic PAD.	I	A
Long-term DAPT in patients with PAD is not recommended.	III	A
Oral anticoagulant monotherapy for PAD (unless for another indication) is not recommended.	III	A
The routine use of ticagrelor in patients with PAD is not recommended.	III	A
It is not recommended to systematically treat patients with asymptomatic PAD without any sign of clinically relevant ASCVD with antiplatelet drugs.	III	B
Recommendations on interventional treatment of asymptomatic and symptomatic peripheral arterial disease (general)		
In patients with symptomatic PAD, after a 3 month period of OMT and exercise therapy, PAD-related QoL assessment is recommended.	I	B
It is recommended to adapt the mode and type of revascularization options to anatomical lesion location, lesion morphology, and general patient condition.	I	C
In patients with PAD, revascularization is not recommended if the reason is to solely prevent progression to CLTI.	III	B
In patients with asymptomatic PAD, revascularization is not recommended.	III	C
Recommendations in patients with peripheral arterial disease: follow-up of patients with peripheral arterial disease		
It is recommended to regularly, at least once a year, follow-up patients with PAD, assessing clinical and functional status, medication adherence, limb symptoms, and CVRFs, with DUS assessment as needed.	I	C
Recommendations for the management of chronic limb-threatening ischaemia		
For limb salvage in patients with CLTI, revascularization is recommended.	I	B
Early recognition of CLTI and referral to the vascular team are recommended for limb salvage.	I	C
Recommendations for medical treatment in patients with chronic limb-threatening ischaemia		
It is recommended that patients with CLTI are managed by a vascular team.	I	C
In patients with CLTI and ulcers, offloading mechanical tissue stress is recommended to allow wound healing.	I	C

Continued

It is recommended to treat infection with antibiotics.	I	C
Lower-limb exercise training is not recommended in patients with CLTI and wounds.	III	C
Recommendations for interventional treatment of chronic limb-threatening ischaemia		
In CLTI patients, it is recommended to perform revascularization as soon as possible.	I	B
In CLTI, it is recommended to use autologous veins as the preferred conduit for infra-inguinal bypass surgery.	I	B
In multilevel vascular disease, it is recommended to eliminate inflow obstructions when treating downstream lesions.	I	C
An individual risk assessment (weighing the patient's individual procedural risk of endovascular vs. surgical revascularization) by a multidisciplinary vascular team is recommended.	I	C
Recommendations for follow-up in patients with chronic limb-threatening ischaemia		
In patients with CLTI, following revascularization it is recommended to follow-up patients on a regular basis.	I	C
At follow-up, it is recommended to assess clinical, haemodynamic and functional status, limb symptoms, treatment adherence, and CVRFs.	I	C
Recommendations for the management of patients presenting with acute limb ischaemia		
In patients with ALI, it is recommended that an urgent evaluation is performed by a vascular clinician with sufficient experience to assess limb viability and implement appropriate therapy.	I	C
In cases of neurological deficit, urgent revascularization is recommended; diagnostic imaging is recommended to guide treatment, provided it does not delay treatment, or if the need for primary amputation is obvious.	I	C
In the absence of severe neurological deficit, revascularization is recommended within hours of initial imaging in a case-by-case decision.	I	C
Treatment with analgesics is recommended as soon as possible for pain control.	I	C
It is recommended to monitor for compartment syndrome after revascularization and treat (fasciotomy).	I	C
It is recommended to assess clinical and haemodynamic success following revascularization.	I	C
In patients with ALI, it is recommended to obtain a comprehensive medical history and determine the cause of thrombosis and/or embolization.	I	C
Recommendations for carotid artery stenosis assessment		
It is recommended to use the NASCET method or its non-invasive equivalent to assess ICA stenosis.	I	B
It is recommended to use DUS as first-line imaging to diagnose ICA stenosis.	I	C
It is not recommended to use the ECST method for ICA stenosis assessment.	III	C
Recommendations for antithrombotic treatment in patients with carotid stenosis		
In patients with symptomatic CS, not undergoing carotid endarterectomy or stenting, DAPT with low-dose aspirin and clopidogrel (75 mg) is recommended for the first 21 days or longer, followed by clopidogrel 75 mg or long-term aspirin to reduce the risk of stroke.	I	A
Recommendations for interventional treatment in patients with asymptomatic carotid artery stenosis		
In asymptomatic patients with ICA stenosis, in the absence of high-risk features and with a life expectancy <5 years, routine revascularization is not recommended.	III	A
Recommendations for evaluation and medical treatment in patients with symptomatic carotid artery stenosis		
DAPT is recommended in the early phase of minor strokes in patients with ICA stenosis, if not revascularized, for at least 21 days, considering the bleeding risk.	I	A
It is recommended that symptomatic ICA stenosis patients are assessed by a vascular team including a neurologist.	I	C
Recommendations for interventions in patients with symptomatic carotid artery stenosis		
It is recommended to perform CEA of symptomatic 70%–99% ICA stenosis provided a documented 30 day risk of procedural death/stroke is <6%.	I	A
If indicated, it is recommended to perform CEA within 14 days in symptomatic ICA stenosis patients.	I	B
OMT is recommended for all symptomatic ICA stenosis patients.	I	A
Revascularization is not recommended in patients with ICA lesions <50%.	III	A
Recommendations for follow-up in patients with carotid artery stenosis		
Once-yearly follow-up is recommended to check for CVRFs and treatment compliance.	I	A
After ICA stent implantation, DAPT with aspirin and clopidogrel is recommended for at least 1 month.	I	A
After ICA revascularization, long-term aspirin or clopidogrel is recommended.	I	B
During follow-up, it is recommended to assess neurological symptoms, CVRFs, and treatment adherence at least yearly in patients with CS.	I	C
After ICA revascularization, surveillance with DUS is recommended within the first month.	I	C

Continued

Recommendations for the management of subclavian artery stenosis		
Bilateral arm BP measurement is recommended for all patients with PAAD.	I	B
Routine revascularization in patients with atherosclerotic subclavian artery disease is not recommended.	III	C
Recommendations for diagnostic strategies for renal artery disease		
DUS is recommended as the first-line imaging modality in patients with suspicion of RAS.	I	B
In cases of DUS-based suspicion of RAS or in inconclusive DUS, MRA or CTA are recommended.	I	B
In patients with atherosclerotic RAS, it is recommended to assess clinical high-risk features and kidney viability when evaluating renal artery revascularization.	I	B
Recommendations for treatment strategies for renal artery disease		
In patients with atherosclerotic unilateral RAS, routine revascularization is not recommended.	III	A
Recommendations in patients with visceral artery stenosis		
In patients with acute mesenteric ischaemia due to acute occlusion of the SMA, endovascular revascularization is recommended.	I	B
In patients with suspected acute or chronic mesenteric ischaemia, CTA is recommended.	I	C
In patients with acute or chronic mesenteric ischaemia, assessment by a vascular team is recommended.	I	C
Revascularization of asymptomatic atherosclerotic visceral artery stenosis is not recommended.	III	C
Recommendations for primary and secondary prevention in aortic atheromatous plaques		
Anticoagulation or DAPT are not recommended in aortic plaques since they present no benefit and increase bleeding risk.	III	C
In patients with an embolic event and evidence of an aortic arch atheroma, intensive lipid management to an LDL-C target <1.4 mmol/L (<55 mg/dL) is recommended to prevent recurrences.	I	A
In patients with an embolic event and evidence of an aortic arch atheroma, SAPT is recommended to prevent recurrences.	I	C
Recommendations for initial evaluation of thoracic aorta aneurysm and abdominal aortic aneurysm		
When an aortic aneurysm is identified at any location, assessment of the entire aorta is recommended at baseline and during follow-up.	I	C
When a TAA is identified, assessment of the aortic valve (especially for BAV) is recommended.	I	C
Recommendation for the surveillance of patients with thoracic aortic aneurysms (non-heritable thoracic aortic disease)		
In thoracic aortic dilatation, TTE is recommended at diagnosis to assess aortic valve anatomy and function, aortic root, and ascending aorta diameters. Additionally, a global aortic evaluation using all echocardiographic views is recommended.	I	C
CMR or CCT is recommended for surveillance of patients with aneurysm at the distal ascending aorta, aortic arch, DTA, or TAAA.	I	C
In thoracic aortic dilatation, CCT or CMR is recommended to confirm TTE measurements, rule out aortic asymmetry, and determine baseline diameters for follow-up.	I	C
TTE is not recommended for the surveillance of aneurysms in the distal ascending aorta, aortic arch, or DTA.	III	C
Recommendations for surveillance of patients with abdominal aortic aneurysm		
DUS surveillance is recommended every 6 months in men with AAA of 50–55 mm and in women with AAA of 45–50 mm.	I	B
DUS is recommended for AAA surveillance.	I	C
CCT or CMR is recommended if DUS does not allow adequate measurement of AAA diameter.	I	B
Recommendations for medical treatment in patients with thoracic aorta or abdominal aortic aneurysms		
In patients with aortic aneurysm (TAA and/or AAA), optimal implementation of CV risk management and medical treatment (see detailed recommendations in dedicated Tables of Recommendations) are recommended to reduce MACE.	I	C
Recommendations for surgery in aortic root and ascending aorta dilatation associated with tricuspid aortic valve		
Surgery is recommended in patients with dilatation of the aortic root or ascending aorta with a tricuspid aortic valve and a maximum diameter of ≥55 mm.	I	B
Valve-sparing aortic root replacement is recommended in patients with aortic root dilatation if performed in experienced centres and durable results are expected.	I	B
VKAs are recommended lifelong for all patients with a Bentall procedure with an MHV prosthesis.	I	B
Recommendations for surgery in aortic arch aneurysms		
In patients with low or intermediate operative risk with an aortic arch aneurysm and recurrent episodes of chest pain not attributable to non-aortic causes, open surgical replacement of the arch is recommended.	I	C

Continued

Recommendations for the management of patients presenting with descending thoracic aortic and thoracoabdominal aortic aneurysms		
In patients with unruptured DTA aneurysm (without HTAD), elective repair is recommended if diameter ≥55 mm.	I	B
In patients without HTAD with unruptured DTA aneurysm, when elective repair is indicated and anatomy is suitable, TEVAR is recommended over open repair.	I	B
In patients with DTA aneurysm who undergo TEVAR with planned LSA coverage, it is recommended to revascularize the LSA before TEVAR to reduce the risk of SCI and stroke.	I	B
In patients with unruptured degenerative TAAA, elective repair is recommended when the diameter is ≥60 mm.	I	B
Recommendations for the management of patients presenting with abdominal aortic aneurysm		
Elective repair is recommended if AAA diameter is ≥55 mm in men or ≥50 mm in women.	I	A
In ruptured AAA with suitable anatomy, endovascular repair is recommended over open repair to reduce peri-operative morbidity and mortality.	I	B
In patients with AAA and limited life expectancy (<2 years), elective AAA repair is not recommended.	III	B
Prior to AAA repair, routine evaluation with coronary angiography and systematic revascularization in patients with chronic coronary syndromes is not recommended.	III	C
Recommendations for the management of patients presenting with endoleaks		
It is recommended to perform 30 day imaging after TEVAR/EVAR, by CCT + DUS/CEUS, to assess the success of intervention.	I	B
It is recommended to re-intervene to achieve a seal in patients with type I endoleak after TEVAR/EVAR.	I	B
It is recommended to re-intervene, principally by endovascular means, to achieve a seal in patients with type III endoleak after TEVAR/EVAR.	I	B
Recommendations for follow-up after treatment of aortic aneurysms		
After open repair of TAA, early CCT is recommended within 1 month, and then yearly CCT follow-up for the first 2 post-operative years and every 5 years thereafter is recommended if findings are stable.	I	B
After TEVAR, follow-up imaging is recommended at 1 and 12 months post-operatively, then yearly until the fifth post-operative year if no abnormalities are documented.	I	B
After open repair of AAA, first follow-up imaging is recommended within 1 post-operative year, and then every 5 years thereafter if findings are stable.	I	A
After EVAR, follow-up imaging is recommended with CCT (or CMR) and DUS/CEUS at 1 month and 12 months post-operatively, then, if no abnormalities are documented, DUS/CEUS is recommended every year, repeating CCT or CMR (based on potential artefacts) every 5 years.	I	A
Recommendations for diagnostic work-up of acute aortic syndrome		
In unstable patients who cannot be transferred to CCT, TOE is recommended for diagnosis and evaluation of the coeliac trunk and mesenteric artery.	I	B
In patients presenting with clinical features compatible with possible AAS, a multiparametric algorithm for ruling in or out AAS using the ADD-RS is recommended.	I	B
ECG-gated CCT from neck to pelvis is recommended as the first-line imaging technique in patients with a suspected AAS since it is widely available, accurate, and provides information about the entry tear, extension, and possible complications (malperfusion, dilatation, or rupture).	I	C
In patients with suspected AAS, focused TTE (with use of contrast if feasible) is recommended during the initial evaluation.	I	C
In patients with suspected AAS, TOE is recommended to guide peri-operative management and detect complications.	I	C
Recommendation for medical treatment in acute aortic syndromes		
In patients with AAS, immediate anti-impulse treatment targeting SBP <120 mmHg and heart rate ≤60 b.p.m. is recommended. In cases of spinal ischaemia or concomitant brain injury, maintaining higher MAP is recommended.	I	B
Intravenous BBs (e.g. labetalol) are recommended as first-line agents. If necessary, i.v. vasodilators (e.g. dihydropyridine calcium blockers or nitrates) could be added.	I	B
Invasive monitoring with an arterial line and continuous three-lead ECG recording, as well as admission to an intensive care unit, is recommended.	I	B
In patients with AAS who can be managed conservatively and who achieved haemodynamic targets with i.v. anti-impulse therapy, switching to oral BBs and, if necessary, up-titration of other BP-lowering agents, is recommended after 24 h if gastrointestinal transit is preserved.	I	B
Adequate pain control to achieve haemodynamic targets is recommended.	I	C

Continued

Recommendations for intervention in type A acute aortic dissection		
In patients with acute TAAD, emergency surgical consultation and evaluation and immediate surgical intervention is recommended.	I	B
In patients with acute TAAD who have extensive destruction of the aortic root, a root aneurysm, or a known genetic aortic disorder, aortic root replacement is recommended with a mechanical or biological valved conduit.	I	B
Recommendations for aortic repair strategies in type A acute aortic dissection		
In patients with acute TAAD and a partially dissected aortic root but no significant aortic valve leaflet pathology, aortic valve resuspension is recommended over valve replacement.	I	B
In patients with acute TAAD undergoing aortic repair, an open distal anastomosis is recommended to improve survival and increase FL thrombosis rates.	I	B
In patients with acute TAAD without an intimal tear in the arch or a significant arch aneurysm, hemi-arch repair is recommended over more extensive arch replacement.	I	B
Recommendations for the management of malperfusion in the setting of acute aortic dissection		
In patients with acute TAAD presenting with malperfusion (cerebral, mesenteric, lower limb, or renal), immediate aortic surgery is recommended.	I	B
Recommendations for the management of patients presenting with acute type B aortic dissection		
Medical therapy including pain relief and blood pressure control is recommended in all patients with acute TBAD.	I	B
In patients with complicated acute TBAD, emergency intervention is recommended.	I	B
In patients with complicated acute TBAD, TEVAR is recommended as the first-line therapy.	I	B
Recommendations for the management of patients presenting with chronic type B aortic dissection		
Antihypertensive therapy is recommended in all patients with chronic TBAD.	I	B
In chronic TBAD with acute symptoms of malperfusion, rupture, or progression of disease, emergency intervention is recommended.	I	C
In patients with chronic TBAD and a descending thoracic aortic diameter ≥60 mm, treatment is recommended in patients at reasonable surgical risk.	I	B
Recommendations for the management of intramural haematoma		
In patients with IMH, medical therapy including pain relief and blood pressure control is recommended.	I	C
In type A IMH, urgent surgery is recommended.	I	C
In type B IMH, initial medical therapy under careful surveillance is recommended.	I	C
In uncomplicated type B IMH, repetitive imaging (CCT or CMR) is indicated.	I	C
In complicated type B IMH, TEVAR is recommended.	I	C
Recommendations for the management of penetrating atherosclerotic ulcer		
In all patients with PAU, medical therapy including pain relief and blood pressure control is recommended.	I	C
In cases of type A PAU, surgery is recommended.	I	C
In cases of type B PAU, initial medical therapy under careful surveillance is recommended.	I	C
In uncomplicated type B PAU, repetitive imaging (CMR, CCT, or TOE) is recommended.	I	C
In complicated type B PAU, endovascular treatment (TEVAR) is recommended.	I	C
Recommendations for traumatic aortic injury		
In cases of severe aortic injury (grade 4), immediate repair is recommended.	I	A
In cases of TAI with suitable anatomy requiring intervention, TEVAR is recommended over open surgery.	I	A
In all TAI patients, medical therapy including pain relief, and blood pressure and heart rate control, is recommended.	I	C
In cases of TAI suspicion, CCT is recommended.	I	C
In cases of moderate aortic injury (grade 3), repair is recommended.	I	C
Recommendations for follow-up after treatment of acute aortic syndrome		
After TEVAR for AAS, follow-up imaging is recommended at 1, 6, and 12 months post-operatively, then yearly until the fifth post-operative year if no abnormalities are documented.	I	B
In medically treated type B AAD or IMH, follow-up imaging is recommended at 1, 3, 6, and 12 months after onset, then yearly if imaging findings are stable.	I	C
In medically treated PAU, follow-up imaging is recommended at 1 month after diagnosis, then every 6 months if imaging findings are stable.	I	C

Continued

Recommendations for the management of patients with heritable thoracic aortic disease		
It is recommended that medical management of patients with HTAD is individualized and based on shared decision-making.	I	C
It is recommended that patients with known or suspected syndromic or non-syndromic HTAD are evaluated in a centre with experience in the care of this patient group.	I	C
Recommendations for genetic testing and aortic screening in aortic disease		
In patients with aortic root/ascending aneurysms or thoracic aortic dissection, gathering family history information for at least three generations about TAD, unexplained sudden deaths, and peripheral and intracranial aneurysms is recommended.	I	B
In patients with aortic root/ascending aortic aneurysms or thoracic aortic dissection and risk factors for HTAD, genetic counselling at an expert centre and subsequent testing, if indicated, is recommended.	I	B
In patients with HTAD who have a pathogenic/likely pathogenic variant, genetic testing of at-risk biological relatives (i.e. cascade testing) is recommended, irrespective of age.	I	C
In patients with TAD with risk factors for HTAD, with a negative family history of TAD and in whom no (likely) pathogenic variant is identified, TTE screening aortic imaging of FDRs is recommended.	I	B
Recommendations for imaging in women with Turner syndrome		
To take the smaller body size of women (≥15 years) with TS into account, the use of the ascending ASI (ratio of aortic diameter [mm] to BSA [m^2]), AHI (ratio of aortic diameter [mm] to height [m]), or aortic z-score is recommended to define the degree of aortic dilatation and assess the risk of aortic dissection.	I	C
It is recommended to define imaging and clinical surveillance intervals according to the estimated risk for dissection, based on the ascending ASI and concomitant lesions.	I	C
Recommendations for medical treatment in patients with vascular Ehlers–Danlos syndrome		
In patients with vEDS, regular vascular surveillance of the aorta and peripheral arteries by DUS, CCT, or CMR is recommended.	I	C
Recommendations for vascular imaging in Marfan syndrome		
In patients with MFS, TTE is recommended: • At least annually in patients with an aortic root diameter <45 mm in the absence of additional risk factors • At least every 6 months in patients with an aortic root diameter <45 mm in the presence of additional risk factors • At least every 6–12 months in patients with an aortic root diameter ≥45 mm in the absence of additional risk factors	I	C
In patients without previous aortic surgery, complete peripheral vascular and thoracoabdominal aorta imaging by CMR or CCT and DUS is recommended at the first evaluation, and subsequently every 3–5 years if stable.	I	C
In patients with MFS who have undergone aortic root replacement, surveillance imaging of the thoracic aorta by CMR (or CCT) is recommended at least every 3 years.	I	C
Recommendations for medical treatment in Marfan syndrome		
In patients with MFS, treatment with either a BB or an ARB, in maximally tolerated doses (unless contraindicated), is recommended to reduce the rate of aortic dilatation.	I	A
Recommendations for aortic surgery in Marfan syndrome		
Surgery is indicated in patients with MFS who have aortic root disease with a maximal aortic sinus diameter ≥50 mm.	I	B
Surgery to replace the aortic root and ascending aorta, using the valve-sparing surgery technique, is recommended in patients with MFS or related HTAD with aortic root dilatation when anatomical features of the valve allow its preservation and the surgeon has specific expertise.	I	B
Recommendations for pregnancy in women with Marfan syndrome		
It is recommended that all women with MFS: • Have a pre-conception evaluation to address the risks of maternal CV and other complications • Have follow-up in a centre with access to a pregnancy heart and vessel team	I	C
It is recommended that couples in which a partner has or is at risk of HTAD be offered pre-conception genetic counselling.	I	C
Imaging of the whole aorta (by CMR/CCT) is recommended prior to pregnancy.	I	C
Follow-up during pregnancy is recommended with a frequency determined by aortic diameter and growth.	I	C
Intake of BBs during pregnancy is recommended.	I	C
Prophylactic aortic root surgery is recommended in women desiring pregnancy with aortic diameters >45 mm.	I	C
ARBs are not recommended during pregnancy.	III	B
Recommendations for physical exercise in patients with Marfan syndrome		
It is recommended to individualize physical activity in patients with MFS based on aortic diameter, family history of aortic dissection, and pre-existing fitness.	I	C
Regular moderate aerobic exercise with a level of intensity informed by aortic diameter is recommended in most patients with MFS.	I	C

Continued

Recommendations for imaging follow-up in Loeys–Dietz syndrome		
In patients with Loeys–Dietz syndrome, TTE at baseline and subsequently every 6–12 months, depending on aortic diameter and growth, is recommended.	I	C
In patients with Loeys–Dietz syndrome, a baseline arterial imaging study from head to pelvis with CMR or CCT and subsequent surveillance with CMR or CCT or DUS every 1–3 years is recommended.	I	C
Recommendations for imaging and surgery in *ACTA2*-related heritable thoracic aortic disease		
Annual monitoring of the aortic root/ascending aorta with TTE to evaluate aortic root/ascending aorta enlargement is recommended.	I	C
Imaging of the aorta with CMR/CCT every 3–5 years is recommended.	I	C
Recommendations for bicuspid aortic valve-associated aortopathy management		
When a BAV is first diagnosed, initial TTE to assess diameters of the aorta at several levels is recommended.	I	B
Surgery for bicuspid aortopathy is recommended when the maximum aortic diameter is ≥55 mm.	I	B
Surgery for bicuspid aortopathy of the root phenotype is recommended when the maximum aortic diameter is ≥50 mm.	I	B
CCT or CMR of the entire thoracic aorta is recommended at first diagnosis and when important discrepancies in measurements are found between subsequent TTE controls during surveillance, or when the diameter of the aorta exceeds 45 mm.	I	C
Screening by TTE in FDRs of BAV patients with root phenotype aortopathy and/or isolated aortic regurgitation is recommended.	I	C
Surveillance serial imaging by TTE is recommended in BAV patients with a maximum aortic diameter >40 mm, either with no indication for surgery or after isolated aortic valve surgery, after 1 year, then if stability is observed, every 2–3 years.	I	C
Recommendations for evaluation and medical treatment of patients with coarctation of the aorta		
In patients with native or repaired coarctation, lifelong follow-up is recommended, including regular imaging of the aorta with CCT/CMR every 3–5 years (adapted to clinical status and previous imaging findings).	I	B
Coarctation or re-coarctation repair (either surgical or endovascular) is indicated in patients with hypertension with an increased non-invasive gradient between the upper and lower limbs (decreased ABI) confirmed with invasive measurement (peak-to-peak >20 mmHg), with a preference for stenting when technically feasible.	I	C
In patients with coarctation, BP measurements at both arms and one lower extremity are recommended.	I	C
It is recommended to treat hypertension in patients with coarctation according to ESC hypertension guidelines.	I	C
Recommendations for screening and management of polyvascular disease and peripheral arterial disease with cardiac diseases		
In patients with PVD, an LDL-C reduction by ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.	I	A
In patients with PAD and newly diagnosed AF with a CHA_2DS_2-VASc score ≥2, full oral anticoagulation is recommended.	I	C
Screening for ilio-femoral PAD is recommended in patients undergoing TAVI.	I	B

AAA, abdominal aortic aneurysm; AAS, acute aortic syndrome; ABI, ankle–brachial index; ACEI, angiotensin-converting enzyme inhibitor; AD, aortic dissection; ADD-RS, aortic dissection detection-risk score; AF, atrial fibrillation; AHI, aortic height index; ALI, acute limb ischaemia; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; ASI, aortic size index; BAV, bicuspid aortic valve; BB, beta-blocker; BP, blood pressure; b.p.m., beats per minute; CCT, cardiovascular computed tomography; CEA, carotid endarterectomy; CEUS, contrast-enhanced ultrasound; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 and sex category (female); CLTI, chronic limb-threatening ischaemia; CMR, cardiovascular magnetic resonance; CS, carotid artery stenosis; CTA, computed tomography angiography; CV, cardiovascular; CVRF, cardiovascular risk factor; DAPT, dual antiplatelet therapy; DTA, descending thoracic aorta; DUS, duplex ultrasound; ECG, electrocardiogram; ECST, European Carotid Surgery Trial; ESC, European Society of Cardiology; FDR, first-degree relative; FL, false lumen; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated haemoglobin; HTAD, heritable thoracic aortic disease; ICA, internal carotid artery; IMH, intramural haematoma; i.v., intravenous; LDL-C, low-density lipoprotein cholesterol; LSA, left subclavian artery; MACE, major adverse cardiac event; MAP, mean arterial pressure; MFS, Marfan syndrome; MHV, mechanical heart valve; MI, myocardial infarction; MRA, magnetic resonance angiography; NASCET, North American Symptomatic Carotid Endarterectomy Trial; o.d., once daily; OMT, optimal medical treatment; PAAD, peripheral arterial and aortic diseases; PAD, peripheral arterial disease; PAU, penetrating atherosclerotic ulcer; PCSK9, proprotein convertase subtilisin/kexin type 9; PVD, polyvascular disease; RAS, renal artery stenosis; QoL, quality of life; SAPT, single antiplatelet therapy; SBP, systolic blood pressure; SCI, spinal cord ischaemia; SET, supervised exercise training; SGLT2i, sodium-glucose co-transporter-2 inhibitor; SMA, superior mesenteric artery; T2DM, type 2 diabetes mellitus; TAA, thoracic aortic aneurysm; TAAA, thoracoabdominal aortic aneurysm; TAAD, type A aortic dissection; TAD, thoracic aortic disease; TAI, traumatic aortic injury; TAVI, transcatheter aortic valve implantation; TBAD, type B aortic dissection; TBI, toe–brachial index; TOE, transoesophageal echocardiography; TEVAR/EVAR, thoracic endovascular aortic aneurysm repair; TP, toe pressure; TS, Turner syndrome; TTE, transthoracic echocardiography; vEDS, vascular Ehlers–Danlos syndrome; VKA, vitamin K antagonist.

[a]Class of recommendation.

[b]Level of evidence.

16. Evidence tables

Evidence tables are available on the *European Heart Journal* website.

17. Data availability statement

No new data were generated or analysed in support of this research.

18. Author information

Author/task force Member Affiliations: Gisela Teixido-Tura, Cardiovascular Imaging section and Aortic diseases Unit (VASCERN), Department of Cardiology, Vall d'Hebron Hospital Universitari, Vall d'Hebron Barcelona Hospital Campus, Vall d' Hebron Institut de Recerca (VHIR), Barcelona, Spain, Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares, Instituto de Salud Carlos III, Madrid, Spain; **Stefano Lanzi**, Department of Angiology, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland; **Vinko Boc**, Department of Vascular Diseases, University Medical Centre Ljubljana, Ljubljana, Slovenia; **Eduardo Bossone**, Department of Public Health, University of Naples "Federico II", Naples, Italy, Department of Translational Medical Sciences, University of Naples "Federico II", Naples, Italy; **Marianne Brodmann**, Division of Angiology, Medical

University Graz, Graz, Austria; **Alessandra Bura-Rivière**, Vascular Medicine Department, Toulouse University Hospital, Toulouse, France, Faculty of Medicine, University Toulouse 3, Toulouse, France; **Julie De Backer**, Cardiology and Center for Medical Genetics, Ghent University Hospital, Ghent, Belgium; **Sebastien Deglise**, Department of Vascular Surgery, University Hospital Lausanne (CHUV), Lausanne, Switzerland; **Alessandro Della Corte**, Department of Translational Medical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy, Unit of Cardiac Surgery, Monaldi Hospital, Naples, Italy; **Christian Heiss**, Department of Clinical and Experimental Medicine, University of Surrey, Guildford, United Kingdom, Vascular Medicine Department, Surrey and Sussex Healthcare NHS Trust, Redhill, United Kingdom; **Marta Kałużna-Oleksy**, 1st Department of Cardiology, Poznan University of Medical Sciences, Poznan, Poland; **Donata Kurpas**, Division of Research Methodology, Department of Nursing, Faculty of Nursing and Midwifery, Wroclaw Medical University, Poland; **Carmel M. McEniery**, Medicine, University of Cambridge, Cambridge, United Kingdom; **Tristan Mirault**, Vascular Medicine Department, Université Paris Cité, Paris, France, Vascular Medicine Department, Assistance Publique Hôpitaux de Paris-APHP, Hôpital Européen Georges-Pompidou, Paris, PARCC U970 team 5 Innate and Adaptative Immunity in Vascular Diseases, INSERM, Paris, France; **Agnes A. Pasquet**, Department of Cardiovascular Diseases, Cliniques Universitaires Saint Luc, Brussels, Belgium, IREC/CARD, UCLouvain, Brussels, Belgium; **Alex Pitcher**, The Heart Centre, Oxford University NHS Foundation Trust, Oxford, United Kingdom; **Hannah A.I. Schaubroeck**, Department of Intensive Care Medicine, Ghent University Hospital, Ghent, Belgium; **Oliver Schlager,** Division of Angiology, Department of Medicine II, Medical University of Vienna, Vienna, Austria; **Per Anton Sirnes**, Cardiology Practice, Kardiokonsult, Son, Norway, Cardiology section, Volvat Medical Centre, Moss, Norway; **Muriel G. Sprynger**, Cardiology, University Hospital of Liège, Liège, Belgium; **Eugenio Stabile**, Division of Cardiology, Health Science Department, Università della Basilicata, Potenza, Italy; **Françoise Steinbach** (France), ESC Patient Forum, Sophia Antipolis, France; **Matthias Thielmann**, Department of Thoracic and Cardiovascular Surgery, West-German Heart and Vascular Center, University Hospital Essen, University Duisburg-Essen, Essen, Germany; **Roland R.J. van Kimmenade**, Department of Cardiology, Radboud University Medical Center, Nijmegen, Netherlands; and **Maarit Venermo**, Department of Vascular Surgery, University of Helsinki and Helsinki University Hospital, Helsinki, Finland.

19. Appendix

ESC Scientific Document Group

Includes Document Reviewers and ESC National Cardiac Societies.

Document Reviewers:

Alessia Gimelli (CPG Review Co-ordinator) (Italy), Jean-Baptiste Ricco (CPG Review Co-ordinator) (France), Elena Arbelo (Spain), Christian-Alexander Behrendt (Germany), Michael Böhm (Germany), Michael A. Borger (Germany), Margarita Brida (Croatia), Sergio Buccheri (Sweden), Gill Louise Buchanan (United Kingdom), Christina Christersson (Sweden), Gert J. de Borst (Netherlands), Marco De Carlo (Italy), Roman Gottardi (Austria), Lydia Hanna (United Kingdom), Lynne Hinterbuchner (Austria), Borja Ibanez (Spain), Ignatios Ikonomidis (Greece), Stefan James (Sweden), Thomas Kahan (Sweden), Klaus Kallenbach[2] (Luxemburg), Lars Køber (Denmark), Konstantinos C. Koskinas (Switzerland), Juraj Madaric[1] (Slovakia), Blandine Maurel (France), John William McEvoy (Ireland), Gil Meltzer (Israel), Borislava Mihaylova (United Kingdom), Richard Mindham (United Kingdom), Ioana Mozos (Romania), Jens Cosedis Nielsen (Denmark), Eva Prescott (Denmark), Amina Rakisheva (Kazakhstan), Barbara Rantner (Germany), Bianca Rocca (Italy), Xavier Rossello (Spain), Jean Paul Schmid (Switzerland), Daniel Staub (Switzerland), Sabine Steiner (Germany), Isabella Sudano (Switzerland), Martin Teraa (Netherlands), Ilonca Vaartjes (Netherlands), Rafael Vidal-Perez (Spain), Christiaan Vrints (Belgium), and Katja Zeppenfeld (Netherlands).

ESC National Cardiac Societies actively involved in the review process of the *2024 ESC Guidelines for the management of peripheral arterial and aortic diseases*:

Algeria: Algerian Society of Cardiology, Mohammed El Amine Bouzid; **Armenia**: Armenian Cardiologists Association, Arsen A. Tsaturyan; **Austria**: Austrian Society of Cardiology, Georg Delle Karth; **Azerbaijan**: Azerbaijan Society of Cardiology, Fuad Samadov; **Belgium**: Belgian Society of Cardiology, Antoine Bondue; **Bosnia and Herzegovina**: Association of Cardiologists of Bosnia and Herzegovina, Alden Begić; **Bulgaria**: Bulgarian Society of Cardiology, Ivo Petrov; **Croatia**: Croatian Cardiac Society, Majda Vrkic Kirhmajer; **Cyprus**: Cyprus Society of Cardiology, Georgios P. Georghiou; **Czechia**: Czech Society of Cardiology, Pavel Procházka; **Denmark**: Danish Society of Cardiology, Torsten B. Rasmussen; **Egypt**: Egyptian Society of Cardiology, Yasser A. Sadek; **Estonia**: Estonian Society of Cardiology, Jaagup Truusalu; **Finland**: Finnish Cardiac Society, Petri Saari; **France**: French Society of Cardiology, Guillaume Jondeau; **Germany**: German Cardiac Society, Christiane Tiefenbacher; **Greece**: Hellenic Society of Cardiology, Kimon Stamatelopoulos; **Hungary**: Hungarian Society of Cardiology, Endre Kolossváry; **Iceland**: Icelandic Society of Cardiology, Elín Hanna Laxdal; **Ireland**: Irish Cardiac Society, Monica Monaghan; **Israel**: Israel Heart Society, Jonathan Koslowsky; **Italy**: Italian Federation of Cardiology, Ciro Indolfi; **Kazakhstan**: Association of Cardiologists of Kazakhstan, Nursultan Kospanov; **Kosovo (Republic of)**: Kosovo Society of Cardiology, Pranvera Ibrahimi; **Kyrgyzstan**: Kyrgyz Society of Cardiology, Olga Lunegova; **Latvia**: Latvian Society of Cardiology, Ainars Rudzitis; **Lithuania**: Lithuanian Society of Cardiology, Andrius Berūkštis; **Luxembourg**: Luxembourg Society of Cardiology, Katja Lottermoser; **Malta**: Maltese Cardiac Society, Maryanne Caruana; **Morocco**: Moroccan Society of Cardiology, Raissuni Zainab; **North Macedonia**: National Society of Cardiology of North Macedonia, Marijan Bosevski; **Norway**: Norwegian Society of Cardiology, Stein Samstad; **Portugal**: Portuguese Society of Cardiology, Ana Teresa Timoteo; **Romania**: Romanian Society of Cardiology, Ovidiu Dragomir Chioncel; **San Marino**: San Marino Society of Cardiology, Pier Camillo Pavesi; **Slovakia**: Slovak Society of Cardiology, Maria Rasiova; **Slovenia**: Slovenian Society of Cardiology, Borut Jug; **Spain**: Spanish Society of Cardiology, Ariana González Gomez; **Sweden**: Swedish Society of Cardiology, Stefan James; **Switzerland**: Swiss Society of Cardiology, Marc Righini; **Tunisia**: Tunisian Society of Cardiology and Cardio-Vascular Surgery, Amine Tarmiz; **Turkey**: Turkish Society of Cardiology, Eralp Tutar; and **Ukraine**: Ukrainian Association of Cardiology, Maksym Sokolov.

ESC Clinical Practice Guidelines (CPG) Committee: Eva Prescott (Chairperson) (Denmark), Stefan James (Co-Chairperson) (Sweden), Elena Arbelo (Spain), Colin Baigent (United Kingdom),

Michael A. Borger (Germany), Sergio Buccheri (Sweden), Borja Ibanez (Spain), Lars Køber (Denmark), Konstantinos C. Koskinas (Switzerland), John William McEvoy (Ireland), Borislava Mihaylova (United Kingdom), Richard Mindham (United Kingdom), Lis Neubeck (United Kingdom), Jens Cosedis Nielsen (Denmark), Agnes A. Pasquet (Belgium), Amina Rakisheva (Kazakhstan), Bianca Rocca (Italy), Xavier Rossello (Spain), Ilonca Vaartjes (Netherlands), Christiaan Vrints (Belgium), Adam Witkowski (Poland), and Katja Zeppenfeld (Netherlands).

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