



Peripartum management of hypertension: a position paper of the ESC Council on Hypertension and the European Society of Hypertension

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Received 23 November 2019; editorial decision 10 December 2019; accepted 10 December 2019; online publish-ahead-of-print 16 December 2019

Hypertensive disorders are the most common medical complications in the peripartum period associated with a substantial increase in morbidity and mortality. Hypertension in the peripartum period may be due to the continuation of pre-existing or gestational hypertension, *de novo* development of pre-eclampsia or it may be also induced by some drugs used for analgesia or suppression of postpartum haemorrhage. Women with severe hypertension and hypertensive emergencies are at high risk of life-threatening complications, therefore, despite the lack of evidence-based data, based on expert opinion, antihypertensive treatment is recommended. Labetalol intravenously and methyl dopa orally are then the two most frequently used drugs. Short-acting oral nifedipine is suggested to be used only if other drugs or iv access are not available. Induction of labour is associated with improved maternal outcome and should be advised for women with gestational hypertension or mild pre-eclampsia at 37 weeks' gestation. This position paper provides the first interdisciplinary approach to the management of hypertension in the peripartum period based on the best available evidence and expert consensus.

Keywords

Pre-existing hypertension • Gestational hypertension • Pre-eclampsia • Antihypertensive drugs • Hypertensive emergency • Low dose of acetylsalicylic acid

Hypertensive disorders in pregnancy complicate 5–10% of pregnancies and are a major cause of maternal, foetal, and neonatal morbidity and mortality.^{1,2} Women with gestational hypertension or pre-eclampsia require close management during the peripartum period,

defined in this document as the last month of gestation and the first few months after delivery. For coding and reporting purposes, the peripartum period is defined as before birth through the 28th day following birth.

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Key messages

- Hypertensive disorders in the peripartum period contribute substantially to maternal and foetal morbidity and mortality;
- Systolic blood pressure (SBP) > 160 mmHg is associated with an adverse maternal outcome (e.g. stroke, pulmonary oedema);
- Early diagnosis and adequate treatment are essential;
- Blood pressure (BP) \geq 160/110 mmHg lasting >15 min warrants immediate drug treatment;
- Labetalol i.v. and oral nifedipine are currently suggested as first-line treatment for hypertensive emergencies during pregnancy;
- Methyldopa should not be used primarily for urgent BP reduction;
- Magnesium sulfate is recommended for the prevention of eclampsia and treatment of seizures but should not be given concomitantly with calcium channel blockers (risk of hypotension due to potential synergism);
- Early maternal warning signs, e.g., SBP > 160 mmHg, tachycardia and oliguria, should be followed by proper diagnostic workup and, possibly, treatment.
- Labetalol, nifedipine, enalapril, and metoprolol are considered safe for breastfeeding mothers.

The current ESC guidelines on management of cardiovascular disease in pregnancy address the issue of peripartum hypertension within a general context.³ New aspects and advances emerged since their publication, especially in the field of hypertensive emergency/urgency.⁴ However, in most countries, it is primarily the obstetrician who manages hypertension in the peripartum period, particularly shortly before delivery and during labour. Due to the high rate and unpredictable nature of complications, all pre-eclamptic women should be hospitalized and closely monitored in obstetric care centres with adequate maternal and neonatal intensive care resources. Induction of labour should be attained after 37 weeks of gestation.⁵ Ten percent of maternal deaths due to hypertensive disorders in pregnancy occur in the postpartum period. Other complications of severe postpartum hypertension include stroke and eclampsia.⁶ Because of the lack of randomized clinical trials (which is often the case in obstetrics), most of the recommendations are based on expert consensus.⁷

The objectives of this position paper are to critically review the current literature on peripartum management of hypertension and to provide recommendations for the clinician. The position paper should also help hypertension specialists, cardiologists, intensivists, obstetricians, and anaesthesiologists to treat hypertension in the peripartum period, including hypertensive emergencies, an issue usually not covered by a majority of guidelines on hypertension in pregnancy. It could also be relevant to GPs who are responsible for immediate postpartum care in some countries.

Blood pressure changes in the peripartum period

In a normal pregnancy, blood pressure (BP) falls to a nadir at between 20 and 24 weeks of gestation. Thereafter, the BP gradually increases until term when pre-pregnancy values are achieved.

Blood pressure usually falls immediately after delivery, and then rises progressively with its peak between days 3–6 after delivery.^{8,9}

Diagnosis and classification of hypertensive disorders in the peripartum period

Blood pressure measurement

The first BP measurement should be taken in both upper arms, with subsequent measurements taken in the arm with the higher BP value, preferably in the sitting position or in the left lateral recumbent position during labour, always using a cuff of appropriate size; the arm should be supported at heart level. Korotkoff V phase should be used to designate diastolic BP (DBP). The mercury sphygmomanometer is still considered the gold standard for BP measurement in pregnancy. However, as mercury sphygmomanometers have been banned in European health care institutions, other devices for standard sphygmomanometry or automatic/semi-automatic (usually oscillometric) BP devices, validated according to standardized protocols (specifically for pregnancy and pre-eclampsia) should be used.¹⁰ It is important to note that not all automatic devices are validated for use in pregnancy and pre-eclampsia and those that are not specifically validated for this condition tend to under-estimate actual BP levels and are unreliable in severe pre-eclampsia. The best solution may be an auscultatory hybrid device with a liquid-crystal display on a vertical column simulating a mercury sphygmomanometer;¹¹ however, these devices are not yet widely used. Wrist BP monitors are not recommended.¹²

In hypertensive emergencies, BP should be also measured in both arms and in lower limbs if there is a clinical suspicion of aortic dissection.⁴

Ambulatory BP monitoring (ABPM) is superior to routine BP measurement for the prediction of pregnancy outcome.¹³ It can help to rule out white-coat hypertension, a phenomenon quite common in pregnancy,¹⁴ and may identify nocturnal hypertension, a finding frequently reported in pre-eclampsia.¹⁵

Home BP measurement (HBPM) is suitable for long-term monitoring, especially in patients on antihypertensive treatment; together with teletransmission of BP data, it may become the future solution saving repeated office visits and hospital admissions.¹⁶ Trials are currently assessing its place in pregnancy and in the postpartum period.¹⁷

Diagnosis of hypertension

Hypertension in pregnancy is diagnosed if systolic BP (SBP) \geq 140 mmHg and/or DBP \geq 90 mmHg, measured in the office or in hospital; it has to be confirmed, preferably on 2 separate occasions or at least 15 min apart in severe hypertension (i.e. \geq 160/110 mmHg in the obstetric literature).¹⁸

Classification of hypertensive disorders

Hypertension in the peripartum period may have the following causes:

- (1) continuation of hypertensive disorders in pregnancy
 - pre-existing hypertension (usually persists > 6 weeks postpartum)
 - gestational hypertension including pre-eclampsia (defined as gestational hypertension associated with significant proteinuria; should resolve within 6–12 weeks postpartum)
- (2) *de novo* pre-eclampsia (headaches, epigastric pain, visual disturbances, seizures)
- (3) iatrogenic causes
 - drugs: non-steroidal anti-inflammatory drugs (NSAIDs) for analgesia, ergot derivatives for postpartum haemorrhage, or ephedrine, used to correct hypervolaemia after regional anaesthesia
- (4) pain (inadequate analgesia)
- (5) anxiety

The above definition of pre-eclampsia is in concordance with the 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy.³ However, the International Society for the Study of Hypertension in Pregnancy introduced a new broader definition of pre-eclampsia, being now defined as gestational hypertension accompanied by one or more of the following new-onset conditions at or after 20 weeks of gestation: (i) proteinuria; (ii) evidence of other maternal organ dysfunction (including acute kidney injury, liver involvement, neurological complications, haematological complications); or (iii) uteroplacental dysfunction (e.g. foetal growth restrictions, abnormal umbilical artery Doppler wave form analysis for stillbirth).¹⁹

First-trimester screening and prevention of pre-eclampsia is recommended in all pregnant women.²⁰ All pregnant women with hypertension should be periodically assessed for proteinuria in the second half of pregnancy to screen for pre-eclampsia. Significant proteinuria as a diagnostic criterion for pre-eclampsia is defined as >0.3 g/24 h or albumin-to-creatinine ratio (ACR) \geq 30 mg/mmol. If the dipstick test is positive (\geq 1+), prompt evaluation of ACR in a single-spot urine sample or 24-h urine collection should follow. An ACR < 30 mg/mmol reliably rules out proteinuria in pregnancy.²¹ When pre-eclampsia is clinically suspected, a soluble fms-like tyrosine kinase (sFlt)-to-placental growth factor (PlGF) ratio \leq 38 can be used to exclude the development of pre-eclampsia in the next week.²²

Management of mild to moderate hypertension in the peripartum period

Mild to moderate hypertension (140–159/90–109 mmHg in obstetric literature) in the peripartum period should be treated following the current guidelines.³ As dietary and lifestyle interventions showed only minimal effects on pregnancy outcome, non-pharmacological management of hypertension in pregnancy is only of limited value.²³ Regular exercise might be continued with caution and obese women should be advised to avoid a weight gain of more than 6.8 kg.²⁴ While there is no evidence from randomized clinical trials, the current European hypertension guidelines recommend the initiation of drug treatment in all hypertensive women in pregnancy with BP persistently \geq 150/95 mmHg.^{3,25} Antihypertensive medication should be initiated at values >140/90 mmHg in the following clinical conditions:

- gestational hypertension (with or without proteinuria)
- pre-existing hypertension with the superimposition of gestational hypertension
- hypertension with subclinical organ damage or symptoms at any time during pregnancy.

The drugs of choice are methyldopa (centrally acting alpha-2 agonist), beta-blockers (most data available for labetalol, a non-selective beta-blocker which also acts as an alpha blocker in higher doses; also beta-1 selective drugs such as metoprolol and bisoprolol are widely used and considered safe, with atenolol best avoided) and dihydropyridine calcium channel blockers (most data available for nifedipine; also felodipine and isradipine can be used). ACE inhibitors, angiotensin receptor blockers, and renin inhibitors are not recommended in pregnancy.^{3,26}

Acute-onset, severe hypertension in the peripartum period

The definition of severe hypertension in pregnancy is inconsistent, varying across medical professional societies, with SBP values 160–180 mmHg and DBP \geq 110 mmHg. The 2018 Guidelines on Cardiovascular Disease in Pregnancy³ recommend considering an SBP \geq 170 or DBP \geq 110 mmHg an emergency with consequent hospitalization.

On the other hand, by a recent American College of Obstetricians and Gynaecologists (ACOG) Committee Opinion,¹⁸ an acute-onset of severe hypertension (\geq 160/110 mmHg), accurately measured by standard techniques and persisting for \geq 15 min, is considered a hypertensive emergency in pregnancy. This stricter definition of hypertensive emergency in pregnancy takes into consideration the data from the confidential enquiries into maternal deaths in the UK.¹

Women developing severe hypertension or severe postpartum hypertension are at high risk of life-threatening complications. Data on antihypertensive drugs for postpartum use are extremely limited and again based on expert opinion rather than on evidence.

Hypertensive emergencies

Hypertensive emergency is generally defined as severe hypertension (in pregnancy, SBP \geq 160 mmHg or DBP \geq 110 mmHg) with acute hypertension-mediated organ damage (HMOD) which is often life threatening (aortic dissection, acute myocardial infarction, pulmonary oedema, respiratory failure, and stroke). The majority of hypertensive emergencies occur with a DBP > 120 mmHg.^{4,25}

Hypertensive emergency in pregnancy is specifically defined as pre-eclampsia/eclampsia and SBP \geq 160 mmHg and DBP \geq 110 mmHg or markedly elevated BP (DBP > 120 mmHg) and progressive acute end-organ damage (aortic dissection, acute myocardial infarction, pulmonary oedema, and respiratory failure).

The recent ESC Council on Hypertension position document on the management of hypertensive emergencies⁴ suggested not using the term hypertensive urgency because there is no evidence that patients without acute HMOD are different from those with asymptomatic uncontrolled hypertension. Therefore, the term

Table 1 Risk factors for hypertensive emergencies in pregnancy

Pre-eclampsia
Cardiac disease
Chronic renal disease
Concomitant use of recreational drugs (e.g. cocaine, methamphetamine) and other BP raising medication (e.g. erythropoietin, anabolic steroids and some herbal remedies)
Non-compliance with antihypertensives
Use of uterocontractive drugs (e.g. ergonovine maleate, methyl ergonovine maleate) for prevention and treatment of postpartum haemorrhage caused by uterine atony
Non-Hispanic black population
Low socioeconomic status

hypertensive crisis, coined to discriminate between hypertensive urgencies and emergencies, has become obsolete.

Risk factors for hypertensive emergencies in pregnancy

Risk factors for hypertensive emergencies in pregnancy are listed in Table 1.

History, clinical presentation, and diagnostic workup

History

The physician should focus on emergency symptoms (headache, visual disturbances, chest pain, dyspnoea, neurological symptoms, abdominal pain, nausea, anorexia) and possible causes such as non-adherence/non-compliance with antihypertensive drugs, use of drugs (with special attention to those affecting BP; e.g., NSAIDs, steroids, sympathomimetics, cocaine, uterocontractive drugs, etc.), current antihypertensive medication or treatment withdrawal and secondary causes of hypertension. Hypertension-specific questions should include the duration of hypertension and previous BP control.

Physical examination

Physical examination should assess signs of complications: impending eclampsia, brisk reflexes, papilledema; the presence of hepatic tenderness suggesting hepatic swelling and risk of rupture; pulmonary oedema suggestive of heart failure and risk of peripartum cardiomyopathy (increased in the presence of pre-eclampsia).

Diagnostic tests

The basic diagnostic workup in a case of suspected hypertensive emergency is provided in Table 2. Further diagnostic tests depend on the clinical presentation and may include echocardiography, abdominal and vascular ultrasound, specific laboratory tests (troponin in patients experiencing acute chest pain; N-terminal pro B-type natriuretic peptide (NT-proBNP) in those developing heart failure; urine drug screen in suspected drug abuse.

An sFlt-1:PIGF ratio of 38 or lower can be used to predict the short-term absence of pre-eclampsia in women in whom the syndrome is clinically suspected.^{22,28}

Table 2 Diagnostic workup in suspected hypertensive emergency in pregnancy

Primary work-up
Fundoscopy
EKG
Haemoglobin, platelet count, fibrinogen
Serum creatinine, eGFR, electrolytes, LDH, haptoglobin
Urine: ACR
Urine microscopy: red cells, leukocytes, casts
Specific tests
High-sensitivity cardiac troponin (acute chest pain)
NT-proBNP (heart failure)
Plasma or urinary fractionated metanephrines (to rule out pheochromocytoma)
sFlt-1/PIGF (pre-eclampsia)
Echocardiography (aortic dissection, heart failure or ischaemia)
Brain CT or MRI
Renal ultrasound (renal parenchymal disease) and duplex renal artery Doppler (renovascular disease)
Urine drug screen (suspected methamphetamine or cocaine use)
Assessment of foetal wellbeing
Electronic foetal heart monitoring
Ultrasound examination for foetal growth
Amniotic fluid assessment
Uterine artery Doppler velocimetry (mean pulsatility index >95th percentile in the second trimester and/or bilateral notching)

ACR, albumin/creatinine ratio; CT, computed tomography; eGFR, estimated glomerular filtration rate; EKG, electrocardiography; LDH, lactate acid dehydrogenase; MRI, magnetic resonance imaging; NT-proBNP, N-terminal pro-brain natriuretic peptide; sFlt-1/PIGF, soluble fms-like tyrosine kinase 1 to placental growth factor.

Adapted from refs (25) and (27).

Plasma-free metanephrines or urinary fractionated metanephrines are the tests of first choice to rule out pheochromocytoma, a rare and usually curable cause of hypertension (the tests have a nearly maximal negative predictive value). False-positive tests (10–15%) are mostly due to inappropriate sampling, effect of medication as a confounder (e.g. labetalol and methyl dopa) or elevated sympathetic activity. In suspected cases, only magnetic resonance imaging reducing radiation exposure is suitable for reliable tumour localization (sensitivity > 90%).

Assessment of foetal wellbeing is an integral part of patient evaluation, which includes electronic foetal heart monitoring, ultrasound for foetal growth and amniotic fluid assessment. Uterine artery Doppler velocimetry may be useful; a mean pulsatility index > 95th percentile in the second trimester and/or bilateral notching may contribute to the suspicion of clinical diagnosis of pre-eclampsia.²⁷

Management of hypertensive emergencies

A retrospective cohort study conducted in 15 hospitals in California, USA, in women with acute severe intrapartum hypertension, found a significantly higher risk of severe maternal morbidity compared with those not developing severe hypertension.²⁹

Table 3 Maternal early warning criteria

Systolic blood pressure < 90 or > 160 mmHg
Diastolic blood pressure > 100 mmHg
Heart rate < 50 or > 130 b.p.m.
Oxygen saturation on room air, at sea level, < 95%
Oliguria (< 35 mL/h for 2 h or more)
Maternal agitation, confusion, or unresponsiveness (changed mental status)
Non-remitting headache in patient with hypertensive disease of pregnancy
Shortness of breath

Adapted from ref. (30).

Maternal abnormal parameters requiring immediate bedside evaluation in order to provide timely diagnostic and therapeutic interventions with the intention to improve the quality of care³⁰ are listed in Table 3.

The immediate goal is to decrease mean BP by 15–25% with the target to achieve SBP 140–150 mmHg and DBP 90–100 mmHg.

Table 4 shows the most commonly used drugs for BP exceeding 160/100 mmHg in pregnancy. Labetalol is considered safe and effective for i.v. treatment of severe pre-eclampsia. Intravenous hydralazine is still widely used, particularly in North America, despite being associated with a number of adverse effects mostly related to maternal hypotension, including a greater risk of caesarean section, more frequent placental abruption, more maternal oliguria, and foetal tachycardia, suggesting the need for close monitoring of maternal BP and foetal wellbeing during its use.³¹

Short-acting oral nifedipine is still popular with some obstetricians, although it has been shown to induce uncontrolled hypotension, particularly when combined with magnesium sulfate resulting in foetal compromise, thus its use should be avoided except in low-resource settings when other drugs are unavailable or until i.v. access can be obtained and alternative drugs administered. If immediate-release oral nifedipine is not available and i.v. access has not yet been established, either 200 mg of labetalol or 1.0–1.5 g of methyldopa can be administered orally.

A recent pooled analysis of seven trials comparing oral nifedipine with i.v. labetalol in severe hypertension during pregnancy found nifedipine as efficacious and safe as i.v. labetalol³² although this meta-analysis included four studies from developing countries and based its conclusions on only 363 women–infant pairs.

Alternatively, i.v. urapidil or nicardipine can be used. Sodium nitroprusside should be only used as the drug of last choice for extreme emergencies and for the shortest possible period of time (if BP cannot be controlled by other means) because prolonged treatment is associated with an increased risk of foetal cyanide poisoning and increased intracranial pressure in the pregnant woman (with potential worsening of cerebral oedema).

When pre-eclampsia is associated with pulmonary oedema, the drug of choice is nitroglycerine (glycerol trinitrate) in i.v. infusion (5 µg/min), gradually increased every 3–5 min to a maximum dose of 100 µg/min.

The American College of Obstetricians and Gynecologists Committee Opinion concluded that labetalol i.v., hydralazine i.v. (i.m.) and immediate-release oral nifedipine are the three most frequently used drugs in hypertensive emergencies during pregnancy and that they can be used without cardiac monitoring.¹⁸

Management of heart failure

Thirty percent of patients with pre-existing heart disease with pre-eclampsia also develop heart failure during pregnancy,³³ it typically occurs at the end of the second trimester or immediately postpartum. Pulmonary oedema may occur as a complication of pre-eclampsia without cardiac impairment.³⁴ N-terminal pro-B type natriuretic peptide levels predict cardiovascular events during pregnancy, but these are also elevated in women with pre-eclampsia without any cardiac abnormality.^{35,36} A low NT-proBNP has a strong negative predictive value, but its high levels do not have a strong positive value.³⁷

A pregnant woman presenting with heart failure should be evaluated by a multidisciplinary team, which decides on the management based on the maternal and foetal condition: if the foetus is viable, the choice is between immediate delivery or continuing the pregnancy with heart failure therapy.³⁸ In the case of severe heart failure and/or foetal distress, deliver is the only option. In mild heart failure and no foetal distress, the pregnancy should continue with heart failure management. Drug treatment of acute heart failure in pregnancy follows the guidelines for non-pregnant patients with few exceptions.³⁷ Diuretics are considered safe during pregnancy but intravascular volume depletion should be avoided and prophylactic anticoagulation considered. ACE inhibitors and angiotensin receptor blockers are contraindicated during pregnancy and can be only used in exceptional circumstances. Other afterload reducing agents such as nitrates or hydralazine may be considered for treatment of heart failure. Non-invasive positive-pressure ventilation can be considered, based on a number of case reports and lack of reported side-effects.

Use of magnesium sulfate

Intravenous magnesium sulfate is recommended for the prevention of eclampsia and for the treatment of seizures, it should not be given concomitantly with calcium channel blockers because of the risk of hypotension due to potential synergism.³⁹ Most of the guidelines agree that primary prevention of eclampsia is recommended for patients presenting with severe pre-eclampsia with the onset of persistent neurological signs (severe headache, visual disturbances, hyperactive deep-tendon reflexes) during pregnancy but, also, in the postpartum period.^{12,40} The standard dosing of magnesium sulfate is 4 g i.v. as a loading dose followed by continuous infusion of 1 g/h until delivery for a maximum of 24 h; magnesium sulfate should only be administered under close maternal monitoring.

Delivery

Induction of labour is associated with improved maternal outcome and should be advised for women with gestational hypertension or mild pre-eclampsia at 37 weeks' gestation.⁵

Optimal timing of delivery depends on foetal wellbeing, gestational age, and type of hypertensive disorder. While pre-eclampsia without

Table 4 Most commonly used drugs for treatment of hypertensive emergencies in pregnancy

Drug	Mechanism	Route	Onset of action	Duration of action	Starting dose	Titration dose	Maximum dose	Perinatal concerns	Contra-indications	Adverse effects
Labetalol	Alpha-1 and non-selective beta-blocker	iv (intermittent) iv (infusion)	5–10 min	2–6 h	10–20 mg iv (over 2 min) 1–2 mg/min	20–80 mg iv every 20–30 min Increase by 1 mg/min every 10 min	300 mg	Foetal distress secondary to abrupt maternal hypotension; neonatal bradycardia and hypoglycaemia	II or III degree AV block; systolic heart failure; asthma; bradycardia	Bronchoconstriction (CAUTION in women with asthma); foetal bradycardia; postural hypotension; sleep disturbances; rebound hypertension; masking hypoglycaemia
Hydralazine	Direct vasodilator	iv (intermittent)	10 min	12 h	5 mg/iv or im	5–10 mg iv every 20–40 min	30 mg	Foetal distress secondary to abrupt maternal hypotension; caesarian section; abruption; APGAR score <7 more common; rarely neonatal thrombocytopenia and neonatal lupus		Headache; palpitations; tachycardia; nausea/vomiting; flushing; hypotension; lupus-like syndrome; CAUTION: side effects may mimic worsening pre-eclampsia
Nifedipine short-acting formulation	Dihydropyridine calcium channel blocker	Oral	5–10 min	2–4 h	10–20 mg	Repeat in 30 min if needed	30 mg	Foetal distress secondary to abrupt maternal hypotension; increased liver clearance may require higher doses		Uncontrolled hypotension (high when combined with magnesium sulphate); stroke; MI (particularly when given sublingually); headache; flushing; reflex tachycardia
Nitroglycerine	Direct vasodilator	iv (infusion)	1–5 min	3–5 min	5 µg/min	Increase by 5 µg/min every 5 min	200 µg/min			Headache; reflex tachycardia
Esmolol	Beta-1-blocker	iv (infusion)	<1 min	15–30 min	Bolus 500 µg/kg; maintenance 50 µg/kg/min	Increase by 50 µg/kg/min every 4 min	300 µg/kg/min	Foetal bradycardia; resistant foetal beta-blockade	II or III degree AV block; systolic heart failure; asthma; bradycardia	First-degree heart block; maternal bradycardia; CHF; bronchospasm
Nicardipine	Dihydropyridine calcium channel blocker	iv (infusion)	1–5 min	4–6 h	5 mg/h	Increase by 2.5 mg/h every 5–15 min	15 mg/h		Liver failure	Tachycardia; flushing; headache
Urapidil	Alpha-1 blocker and weak central 5-hydroxytryptamine agonist	iv (infusion)	3–5 min	4–6 h	Bolus 12.5–25 mg; maintenance 5–40 mg/h		40 mg/h			
Sodium nitroprusside	Non-selective direct NO inhibitor	iv (infusion)	<1 min	2–3 min	0.25 µg/kg/min	Increase by 0.25–0.5 µg/kg/min every 2–3 min	5 µg/kg/min	Foetal cyanide and thiocyanide toxicity if used > 4 h		Nausea; vomiting

AV, atrioventricular; CHF, chronic heart failure; im, intramuscular; iv, intravenous; NO, nitric oxide.

severe features is potentially manageable by expectation, the presence of eclampsia usually requires delivery soon after maternal stabilization.

Vaginal delivery should be considered for women with any hypertensive disorders in pregnancy unless a caesarean delivery is required for obstetric indications.⁴⁰

All women with severe pre-eclampsia should be delivered promptly, either vaginally or by caesarean section, regardless of gestational age.

Legislation in most countries allows termination of pregnancy if the mother's life is at imminent threat.

Antihypertensive treatment should be continued during labour and delivery to keep SBP < 160 mmHg and DBP < 110 mmHg.

Prevention of pre-eclampsia

Women at high or moderate risk of pre-eclampsia should take low-dose (100–150 mg) acetylsalicylic acid (aspirin) daily from week 12 to weeks 36–37.⁴¹ High dose calcium supplementation (≥ 1 g/day) may reduce the risk of pre-eclampsia and pre-term birth, particularly for women with low calcium diet.⁴²

Corticosteroids for acceleration of foetal pulmonary maturity

Antenatal corticosteroid therapy should be considered for all women presenting with pre-eclampsia at ≤ 34 weeks of gestation and in women with gestational hypertension presenting at ≤ 34 weeks only if delivery is considered within the next 7 days.

A rescue dose of corticosteroids may be considered for women at ≤ 34 weeks remaining at high risk of pre-term delivery 14 days or more after an initial course of antenatal corticosteroids; repeated doses are recognized to reduce infant birthweight and head circumference.⁴³

Antenatal corticosteroids may be considered for women delivering by elective caesarean section at ≤ 38 weeks' gestation to reduce respiratory morbidity.⁴⁰

Pheochromocytoma in pregnancy

Pheochromocytoma in a pregnant woman is rare (0.002% of all pregnancies) but extremely dangerous.^{44,45} If undiagnosed, maternal and foetal mortality is around 50%. Early detection and proper treatment during pregnancy decrease maternal (<5%) and foetal (~15%) mortality. The crucial factor is early recognition of a pheochromocytoma in a pregnant woman with hypertension (see Diagnostic workup, Table 2). When pheochromocytoma is diagnosed within the first 24 weeks of gestation, laparoscopic adrenalectomy after 10–14 days of medical pre-treatment with alpha-adrenergic blockade (lowering maternal and foetal mortality) is recommended. Calcium channel blockers are an alternative option but are frequently used as complementary treatment to alpha-adrenergic blockade. If the tumour is not diagnosed until the third trimester, the patient should be managed using the same protocol as for surgical preparation until the foetus is viable. Caesarean section with tumour removal in the same session

or at a later stage is strongly preferred as vaginal delivery is associated with higher mortality. Epidural, general, or combined anaesthetic techniques can be used.

Identification of postpartum hypertension

Blood pressure should be checked within 6 h of delivery in all normotensive women without complications because of the risk of late onset pre-eclampsia. Blood pressure fluctuations postpartum are a usual finding. Transient hypertension may appear postpartum in normotensive uncomplicated pregnancies; this may be due to pain (inadequate analgesia), drugs (NSAIDs for analgesia, ergot derivatives for postpartum haemorrhage, or ephedrine), excess fluid administration (hypervolaemia after regional anaesthesia), salt and water accumulated during pregnancy moving into the intravascular compartment or restoration of non-pregnant vascular tone. A BP rise postpartum is physiological and, should mild hypertension develop (mostly on Days 3–6), it usually resolves spontaneously without the need for drug treatment.⁴⁶ As pre-eclampsia may also have late presentation, checking BP postpartum on regular basis (i.e. at least once daily) for the first 5 days after delivery is important. It is recommended to check BP every other day after discharge from hospital for up to 1 week.²⁶

De novo development of pre-eclampsia in the postpartum period should be suspected in women with hypertension associated with headaches, epigastric pain (possibly with nausea and vomiting), visual disturbances (e.g. blurred vision, flashing lights, double vision, floating spots, etc.), dyspnoea (potentially caused by pulmonary oedema), sudden swelling of the face, hands, or feet, or with seizures up to 4 weeks postpartum.

Management of postpartum hypertension

All women with hypertension in pregnancy should have their BP and urine checked at 6 weeks postpartum and persistent hypertension confirmed by 24-h ambulatory monitoring.^{47,48} It is also suggested that all women with persisting hypertension under the age of 40 are assessed for a secondary cause of hypertension. Women with persisting hypertension or proteinuria 6 weeks after delivery should be referred to a specialist.

Antihypertensive medication should be selected with respect to breastfeeding. Many guidelines still consider methyldopa the drug of choice for management of postpartum hypertension; however, it should be used with caution in women at risk of developing depression.⁴⁹

All antihypertensive agents taken by nursing mothers are transferred into breast milk; however, most of the agents are present at very low concentrations except for propranolol, atenolol, acebutolol, and nifedipine, achieving levels similar to those in maternal plasma. Beta-blockers are generally considered safe, even though some of them (propranolol, atenolol, and acebutolol) may induce signs of neonatal beta-blockade. Recommended beta-blocking drugs are

Table 5 Maternal antihypertensive medication usually compatible with breastfeeding

ACE inhibitors
Benazepril
Captopril
Enalapril
Quinapril
Calcium channel blockers
Diltiazem
Nifedipine
Verapamil
Beta-blockers
Labetalol
Metoprolol
Nadolol
Oxprenolol
Propranolol
Timolol
Diuretics
Furosemide
Hydrochlorothiazide
Spironolactone
Other
Clonidine
Hydralazine
Methyldopa
Minoxidil

labetalol and some beta-1 selective blockers of which metoprolol has both favourable pharmacokinetics and the most available data on safety. Calcium channel blockers are also generally considered safe with the dihydropyridine type calcium channel most frequently used, with felodipine and nifedipine having acceptable safety and efficacy profile. Nonetheless, the manufacturer does not recommend using nifedipine in nursing mothers; despite this, nifedipine is widely used without neonatal side effects reported. Nifedipine may be the drug of choice in black women of African or Caribbean origin.

Table 5 provides a list of antihypertensive drugs usually compatible with breastfeeding; however, this list may be updated periodically and it is advised that all prescribers should review current prescribing information. Most guidelines suggest labetalol, nifedipine and enalapril as first-line antihypertensive drugs for breastfeeding mothers.⁵⁰ While generally contraindicated in pregnancy, ACE inhibitors can be used in lactating mothers unless the neonate is premature or has renal failure. Enalapril is specifically listed in Table 5 as the most widely used ACE inhibitor in this indication (due to its safety and favourable pharmacokinetics) and may be particularly suitable for treatment of peripartum cardiomyopathy. Diuretics (furosemide, hydrochlorothiazide, and spironolactone) may reduce milk production and are generally not preferred in breastfeeding women.

Antihypertensive medication is usually continued until BP has normalized, which may be days to several weeks postpartum. Home BP monitoring is suggested.

Hypertension within gestational hypertension and pre-eclampsia will normalize within 3 months postpartum in most cases.⁵¹

Self-monitoring with self-titration of antihypertensive medication has shown promise but further trials are needed to confirm this on a wider scale.¹⁷

Transfer to the intensive care unit

The decision to transfer a patient to the intensive care unit (ICU) (either antenatal or postpartum) should be made collectively by a team of specialists based on the stability of the patient, physical examination, vital signs, laboratory values, imaging, and expected care required. There might be local differences; however, in the presence of any of the following factors, transfer to the ICU should be strongly considered:³⁰

- Need for respiratory support and possible intubation;
- Heart rate > 150 b.p.m. or < 40 b.p.m.;
- Tachypnoea > 35 min;
- Acid–base imbalance or severe electrolyte abnormalities;
- Need for pressor support or other forms of cardiovascular support;
- Need for more invasive monitoring;
- Abnormal EKG findings, e.g., requiring further intervention such as cardioversion or defibrillation;
- Need for i.v. antihypertensive medication once first-line drugs have failed.

Long-term cardiovascular consequences of gestational hypertension

Several population-based retrospective cohort studies have shown that women with gestational hypertension or pre-eclampsia in particular are at increased risk of developing hypertension, stroke, ischaemic heart disease, and thrombo-embolic disease in later adult life.⁵² In a 50-year follow-up study, an association between pre-eclampsia and cardiovascular mortality was confirmed.⁵³ Data from the National Patient Register and the National Birth Register in Denmark have shown a small but significant increased risk of cardiomyopathy in women with a history of hypertensive disorders in pregnancy (compared with normotensive women) more than 5 months after delivery.⁵⁴ A more recent analysis of the nationwide Danish register data found the risks of peripartum cardiomyopathy significantly higher in women with hypertensive disorders in pregnancy and with pre-eclampsia in particular.⁵⁵ Thus, cardiovascular risk assessment and lifestyle modifications are recommended in all women with a pregnancy-related hypertensive disorder to avoid complications in subsequent pregnancies and to reduce maternal cardiovascular risk in the future.^{56,57} As these women have an increased risk of early onset of hypertension, regular visits for checking their BP and metabolic factors are strongly recommended, preferably on an annual basis.

Gaps in evidence

There are no specific studies designed for the treatment of hypertension in the entire peripartum period. Most of the studies were

performed in women with mild to moderate hypertension in pregnancy showing efficacy and safety but no clear benefit from the treatment for mothers nor the babies (no difference in outcome of pre-eclampsia, neonatal death, pre-term birth, small-for-gestational-age babies). The only positive finding from antihypertensive treatment is halving the risk of developing severe hypertension. The current guidelines are based on expert consensus recommending thresholds to initiate treatment with antihypertensive drugs. Prospective studies, even observational, are desperately needed.

Postpartum hypertension is probably more frequent than previously thought; it can have devastating consequences including maternal stroke and death. There are only a few randomized clinical trials, mostly of short duration with no hard endpoints. No trial with a prospective design has been initiated for the prevention of postpartum hypertension. Therefore, prophylactic treatment of hypertension to prevent pre-eclampsia is not recommended. It is not clear whether drugs used for severe hypertension antepartum have the same efficacy postpartum. It is also not known which agent in treatment of acute severe hypertension postpartum is preferred.

Conflict of interest: none declared.

References

- Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, Harper A, Hulbert D, Lucas S, McClure J, Millward-Sadler H, Neilson J, Nelson-Piercy C, Norman J, O'Herlihy C, Oates M, Shakespeare J, de Swiet M, Williamson C, Beale V, Knight M, Lennox C, Miller A, Parmar D, Rogers J, Springett A. Saving mothers' lives: reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. *BJOG* 2011;**118**:1-203.
- Stevens TA, Swaim LS, Clark SL. The role of obstetrics/gynecology hospitalists in reducing maternal mortality. *Obstet Gynecol Clin North Am* 2015;**42**:463-475.
- Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cifková R, De Bonis M, Iung B, Johnson MR, Kintscher U, Kranke P, Lang IM, Morais J, Pieper PG, Presbitero P, Price S, Rosano GMC, Seeland U, Simoncini T, Swan L, Warnes CA, Deaton C, Simpson IA, Aboyans V, Agewall S, Barbato E, Calda P, Coca A, Coman IM, De Backer J, Delgado V, Di Salvo G, Fitzsimons S, Fitzsimons D, Garbi M, Gevaert S, Hindricks G, Jondeau G, Kluin J, Lionis C, McDonagh TA, Meier P, Moons P, Pantazis A, Piepoli MF, Rocca B, Roffi M, Rosenkranz S, Sarkozy A, Shlyakhto E, Silversides CK, Sliwa K, Sousa-Uva M, Tamargo J, Thorne S, Van de Velde M, Williams B, Zamorano JL, Windecker S, Aboyans V, Agewall S, Barbato E, Bueno H, Coca A, Collet J-P, Coman IM, Dean V, Delgado V, Fitzsimons D, Gaemperli O, Hindricks G, Iung B, Juni P, Katus HA, Knuuti J, Lancellotti P, Leclercq C, McDonagh TA, Piepoli MF, Ponikowski P, Richter DJ, Roffi M, Shlyakhto E, Simpson IA, Sousa-Uva M, Zamorano JL, Hammoudi N, Piruzyan A, Mascherbauer J, Samadov F, Prystrom A, Pasquet A, Caluk J, Gotcheva N, Skoric B, Heracleous H, Vejlsstrup N, Maser M, Kaaja RJ, Sribinowska-Kostovska E, Mounier-Vehier C, Vahktangadze T, Rybak K, Giannakoulas G, Kiss RG, Thrainsdottir IS, Erwin RJ, Porter A, Geraci G, Ibrahim P, Lunegova O, Mintale I, Kadri Z, Benlamin H, Barysiene J, Banu CA, Caruana M, Grati C, Haddour L, Bouma BJ, Estensen M-E, Hoffman P, Petris AO, Moiseeva O, Bertelli L, Tesic BV, Dubrava J, Koželj M, Prieto-Arévalo R, Furenäs E, Schwerzmann M, Mourali MS, Ozer N, Mitchenko O, Nelson-Piercy C; ESC Scientific Document Group. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. *Eur Heart J* 2018;**39**:3165-3241.
- van den Born BH, Lip GYH, Brguljan-Hitij J, Cremer A, Segura J, Morales E, Mahfoud F, Amraoui F, Persu A, Kahan T, Agabiti Rosei E, de Simone G, Gosse P, Williams B. ESC Council on hypertension position document on the management of hypertensive emergencies. *Eur Heart J Cardiovasc Pharmacother* 2019;**5**: 37-46.
- Koopmans CM, Bijlenga D, Groen H, Vijgen SM, Aarnoudse JG, Bekedam DJ, van den Berg PP, de Boer K, Burggraaf JM, Bloemenkamp KW, Drogtróp AP, Franx A, de Groot CJ, Huisjes AJ, Kwee A, van Loon AJ, Lub A, Papatsonis DN, van der Post JA, Roumen FJ, Scheepers HC, Willekes C, Mol BW, van Pampus MG; HYPITAT Study Group. Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial. *Lancet* 2009;**374**:979-988.
- Kuklina EV, Tong X, Bansil P, George MG, Callaghan WM. Trends in pregnancy hospitalizations that included a stroke in the United States from 1994 to 2007: reasons for concern? *Stroke* 2011;**42**:2564-2570.
- Duley L, Meher S, Jones L. Drugs for treatment of very high blood pressure during pregnancy. *Cochrane Database Syst Rev* 2013;CD001449. doi: 10.1002/14651858.CD001449.pub3.
- Robson SC, Hunter S, Boys RJ, Dunlop W. Hemodynamic changes during twin pregnancy. A Doppler and M-mode echocardiographic study. *Am J Obstet Gynecol* 1989;**161**:1273-1278.
- Podmow T, August P. Postpartum course of gestational hypertension and pre-eclampsia. *Hypertens Pregnancy* 2010;**29**:294-300.
- Stergiou GS, Palatini P, Asmar R, Ioannidis JP, Kollias A, Lacy P, McManus RJ, Myers MG, Parati G, Shennan A, Wang J, O'Brien E; European Society of Hypertension Working Group on Blood Pressure Monitoring. Recommendations and Practical Guidance for performing and reporting validation studies according to the Universal Standard for the validation of blood pressure measuring devices by the Association for the Advancement of Medical Instrumentation/European Society of Hypertension/International Organization for Standardization (AAMI/ESH/ISO). *J Hypertens* 2019;**37**:459-466.
- Davis GK, Roberts LM, Mangos GJ, Brown M. Comparisons of auscultatory hybrid and automated sphygmomanometers with mercury sphygmomanometry in hypertensive and normotensive pregnant women: parallel validation studies. *J Hypertens* 2015;**33**:499-506.
- Mounier-Vehier C, Amar J, Boivin JM, Denolle T, Fauvel JP, Plu-Bureau G, Tsatsaris V, Blacher J. Hypertension and pregnancy: expert consensus statement from the French Society of Hypertension, an affiliate of the French Society of Cardiology. *Fundam Clin Pharmacol* 2017;**31**:83-103.
- O'Brien E, Parati G, Stergiou G, Asmar R, Beilin L, Bilo G, Clement D, de la Sierra A, de Leeuw P, Dolan E, Fagard R, Graves J, Head GA, Imai Y, Kario K, Lurbe E, Mallion JM, Mancia G, Mengden T, Myers M, Ogedegbe G, Ohkubo T, Omboni S, Palatini P, Redon J, Ruilope LM, Shennan A, Staessen JA, vanMontfrans G, Verdecchia P, Waeber B, Wang J, Zanchetti A, Zhang Y; European Society of Hypertension Working Group on Blood Pressure Monitoring. European Society of Hypertension position paper on ambulatory blood pressure monitoring. *J Hypertens* 2013;**31**:1731-1768.
- Magee LA, Ramsay G, von Dadelszen P. What is the role of out-of-office BP measurement in hypertensive pregnancy? *Hypertens Pregnancy* 2008;**27**:95-101.
- Ditisheim A, Wuerzner G, Ponte B, Vial Y, Irion O, Burnier M, Boulvain M, Pechère-Bertschi A. Prevalence of hypertensive phenotypes after preeclampsia: a prospective cohort study. *Hypertension* 2018;**71**:103-109.
- Denolle T, Weber JL, Calvez C, Getin Y, Daniel JC, Lurton O, Cheve MT, Marechaud M, Bessec P, Carbonne B, Razafintsalama T. Diagnosis of white coat hypertension in pregnant women with teletransmitted home blood pressure. *Hypertens Pregnancy* 2008;**27**:305-313.
- Cairns AE, Tucker KL, Leeson P, Mackillop LH, Santos M, Velardo C, Salvi D, Mort S, Mollison J, Tarassenko L, McManus RJ; SNAP-HT Investigators. Self-management of postnatal hypertension: the SNAP-HT trial. *Hypertension* 2018;**72**: 425-432.
- ACOG Committee Opinion No. 767 summary: emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. *Obstet Gynecol* 2019;**133**:409-412.
- Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, Hall DR, Warren CE, Adoyi G, Ishaku S; International Society for the Study of Hypertension in Pregnancy (ISSHP). The hypertensive disorders of pregnancy: ISSHP classification, diagnosis & management recommendations for international practice. *Pregnancy Hypertens* 2018;**13**:291-310.
- Poon LC, Shennan A, Hyett JA, Kapur A, Hadar E, Divakar H, McAuliffe F, Silva Costa F, Dadelszen P, McIntyre HD, Kihara AB, Di Renzo GC, Romero R, D'Alton M, Berghella V, Nicolaides KH, Hod M, Hanson M, Ma R, Purandare CN, Fuchtnier C, Visser G, Morris J, Gooden R. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: a pragmatic guide for first-trimester screening and prevention. *Int J Gynaecol Obstet* 2019;**145**: 1-33.
- Chappell LC, Shennan AH. Assessment of proteinuria in pregnancy. *BMJ* 2008;**336**:968-969.
- Zeisler H, Lllurba E, Chantraine F, Vatish M, Staff AC, Sennström M, Olovsson M, Brennecke SP, Stepan H, Allegranza D, Dilba P, Schoedl M, Hund M, Verlohren S. Predictive value of the sFt-1: PlGF ratio in women with suspected preeclampsia. *N Engl J Med* 2016;**374**:13-22.
- Dodd JM, for the LIMIT Randomised Trial Group, Turnbull D, McPhee AJ, Deussen AR, Grivell RM, Yelland LN, Crowther CA, Wittert G, Owens JA, Robinson JS. Antenatal lifestyle advice for women who are overweight or obese: LIMIT randomised trial. *BMJ* 2014;**348**:g1285-g1285.
- Leddy MA, Power ML, Schulkin J. The impact of maternal obesity on maternal and fetal health. *Rev Obstet Gynecol* 2008;**1**:170-178.

25. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I; Authors/Task Force Members. 2018 ESC/ESH Guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: the Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *J Hypertens* 2018;**36**:1953–2041.
26. National Institute for Health and Clinical Excellence. Hypertension in pregnancy: diagnosis and management. NG133.2019. www.nice.org.uk/guidance/ng133.
27. Stepan H, Herraiz I, Schlembach D, Verlohren S, Brennecke S, Chantraine F, Klein E, Lapaire O, Lurba E, Ramoni A, Vatis M, Wertaschnigg D, Galindo A. Implementation of the sFlt-1/PlGF ratio for prediction and diagnosis of pre-eclampsia in singleton pregnancy: implications for clinical practice. *Ultrasound Obstet Gynecol* 2015;**45**:241–246.
28. Duhig KE, Myers J, Seed PT, Sparkes J, Lowe J, Hunter RM, Shennan AH, Chappell LC, Bahl R, Bambridge G, Barnfield S, Ficquet J, Gill C, Girling J, Harding K, Khalil A, Sharp A, Simpson N, Tuffnell D; PARROT trial group. Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial. *Lancet* 2019;**393**:1807–1818.
29. Shields LE, Wiesner S, Klein C, Pelletreau B, Hedriana HL. Early standardized treatment of critical blood pressure elevations is associated with a reduction in eclampsia and severe maternal morbidity. *Am J Obstet Gynecol* 2017;**216**:415.e1–415.e5.
30. ElFarra J, Bean C, Martin JN Jr. Management of hypertensive crisis for the obstetrician/gynecologist. *Obstet Gynecol Clin North Am* 2016;**43**:623–637.
31. Magee LA, Cham C, Waterman EJ, Ohlsson A, von Dadelszen P. Hydralazine for treatment of severe hypertension in pregnancy: meta-analysis. *BMJ* 2003;**327**:955–960.
32. Shekhar S, Gupta N, Kirubakaran R, Pareek P. Oral nifedipine versus intravenous labetalol for severe hypertension during pregnancy: a systematic review and meta-analysis. *BJOG* 2016;**123**:40–47.
33. Ruys TP, Roos-Hesselink JW, Hall R, Subirana-Domènech MT, Grando-Ting J, Estensen M, Crepaz R, Fesslova V, Gurvitz M, De Backer J, Johnson MR, Pieper PG. Heart failure in pregnant women with cardiac disease: data from the ROPAC. *Heart* 2014;**100**:231–238.
34. Anthony J, Sliwa K. Decompensated heart failure in pregnancy. *Card Fail Rev* 2016;**2**:20–26.
35. Bakacak M, Serin S, Ercan O, Köstü B, Bakacak Z, Kiran H. Association of serum N-terminal pro-brain natriuretic peptide levels with the severity of preeclampsia. *J Matern Fetal Neonatal Med* 2016;**29**:2802–2806.
36. Giannubilo SR, Cecchi S, Tidu E, Ciavattini A. Maternal NT-proBNP in chronic hypertensive pregnancies and superimposed preeclampsia. *Int J Cardiol* 2014;**176**:1227–1229.
37. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P; ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016;**37**:2129–2200.
38. van Hagen IM, Cornette J, Johnson MR, Roos-Hesselink JW. Managing cardiac emergencies in pregnancy. *Heart* 2017;**103**:159–173.
39. Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, Smith D; Magpie Trial Collaboration Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. *Lancet* 2002;**359**:1877–1890.
40. Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P; Canadian Hypertensive Disorders of Pregnancy (HDP) Working Group. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. *Pregnancy Hypertens* 2014;**4**:105–145.
41. Rolnik DL, Wright D, Poon LC, O’Gorman N, Syngelaki A, de Paco Matallana C, Akolekar R, Cicero S, Janga D, Singh M, Molina FS, Persico N, Jani JC, Plasencia W, Papaioannou G, Tenenbaum-Gavish K, Meiri H, Gizurason S, Maclagan K, Nicolaides KH. Aspirin versus placebo in pregnancies at high-risk for preterm preeclampsia. *N Engl J Med* 2017;**377**:613–622.
42. Hofmeyr G, Lawrie TA, Atallah AN, Tortonzi M. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev* 2018;**10**:CD001059.
43. Committee on Obstetric Practice. Committee Opinion No.713: antenatal corticosteroid therapy for fetal maturation. *Obstet Gynecol* 2017;**130**:e102–e109.
44. Lenders JW. Pheochromocytoma and pregnancy: a deceptive connection. *Eur J Endocrinol* 2012;**166**:143–150.
45. Lenders JWM, Langton K, Langenhuijsen JF, Eisenhofer G. Pheochromocytoma and pregnancy. *Endocrinol Metab Clin North Am* 2019;**48**:605–617.
46. Robson SC, Boys RJ, Hunter S, Dunlop W. Maternal hemodynamics after normal delivery and delivery complicated by postpartum hemorrhage. *Obstet Gynecol* 1989;**74**:234–239.
47. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol* 2000;**183**:S1–S22.
48. Benschop L, Duvekot JJ, Versmissen J, van Broekhoven V, Steegers EAP, Roeters van Lennep JE. Blood pressure profile 1 year after severe preeclampsia. *Hypertension* 2018;**71**:491–498.
49. Podymow T, August P. Antihypertensive drugs in pregnancy. *Semin Nephrol* 2011;**31**:70–85.
50. Redman CW, Kelly JG, Cooper WD. The excretion of enalapril and enalaprilat in human breast milk. *Eur J Clin Pharmacol* 1990;**38**:99–99.
51. Walters BN, Thompson ME, Lee A, de Swiet M. Blood pressure in the puerperium. *Clin Sci (Lond)* 1986;**71**:589–594.
52. McDonald SD1, Malinowski A, Zhou Q, Yusuf S, Devereaux PJ. Cardiovascular sequelae of preeclampsia/eclampsia: a systematic review and meta-analyses. *Am Heart J* 2008;**156**:918–930.
53. Cirillo PM, Cohn BA. Pregnancy complications and cardiovascular disease death: 50-year follow-up of the Child Health and Development Studies pregnancy cohort. *Circulation* 2015;**132**:1234–1242.
54. Behrens I, Basit S, Lykke JA, Ranthe MF, Wohlfahrt J, Bundgaard H, Melbye M, Boyd HA. Association between hypertensive disorders of pregnancy and later risk of cardiomyopathy. *JAMA* 2016;**315**:1026–1033.
55. Behrens I, Basit S, Lykke JA, Ranthe MF, Wohlfahrt J, Bundgaard H, Melbye M, Boyd HA. Hypertensive disorders of pregnancy and peripartum cardiomyopathy: a nationwide cohort study. *PLoS One* 2019;**14**:e0211857.
56. Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA. Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study. *Lancet* 2005;**366**:1797–1803.
57. Black MH, Zhou H, Sacks DA, Dublin S, Lawrence JM, Harrison TN, Reynolds K. Hypertensive disorders first identified in pregnancy increase risk for incident prehypertension and hypertension in the year after delivery. *J Hypertens* 2016;**34**:728–735.