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Perioperative Management of Patients with Preeclampsia: A Comprehensive Review

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ABSTRACT

Preeclampsia is a common condition of pregnancy characterized by hypertension complicated by cerebral, cardiac, hepatic, renal, hematologic, and placental dysfunction. Patients with preeclampsia frequently undergo cesarean delivery, the most common major surgical procedure in the world. They represent a high-risk perioperative cohort suffering significant preventable morbidity and mortality. This review focuses on the anesthesiologist's role, through a perioperative lens, in reducing maternal complications through management of hypertension and strategies for preserving the function of the brain, heart, liver, kidney, hematologic and coagulation systems, and placenta in patients with preeclampsia undergoing cesarean delivery. Preeclampsia-specific resuscitation, individualized fluid administration, safe neuraxial and general anesthesia, and management of intraoperative bleeding are discussed along with strategies for postoperative analgesia, thromboprophylaxis, and antihypertensive agents in patients who breastfeed. This review discusses recently recognized postoperative deterioration in maternal mental health, the possibility of myocardial injury after cesarean delivery, and the need for long-term cardiometabolic follow-up.

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Preeclampsia is a common progressive hypertensive condition of pregnancy that frequently has severe complications. It is defined as new-onset hypertension occurring after 20 weeks' gestation with evidence of organ dysfunction.[1] It is one of the main causes of death and long-term morbidity in pregnant women and newborn babies.[2–5] Globally, the incidence of preeclampsia is approximately 5%, affecting more than 7 million pregnant people annually.[6,7]

Preeclampsia is responsible for approximately 4.9% of maternal deaths in the United States.[8] Maternal complications from preeclampsia include stroke, heart failure, liver rupture, and hemorrhage.[1,9] Complications are not limited to the short term but extend beyond hospital discharge, with patients who suffer from preeclampsia having increased risk of hypertension, cerebrovascular disease, ischemic heart disease, and renal impairment in later life.[10–12] Preeclampsia can result in fetal growth restriction and prematurity in newborns, who frequently then require neonatal intensive care. The newborn also has a higher life-time risk of death from cardiovascular disease, metabolic syndrome, and type 2 diabetes.[13]

Perioperative Medicine in Patients with Preeclampsia

Anesthesiologists play an essential role in the safe management of patients with preeclampsia who undergo cesarean delivery. Anesthesiologists are actively involved in the preoperative, intraoperative, and postoperative care of these patients. Anesthesiologists may also play a role in multidisciplinary prepregnancy counseling, antenatal care, risk stratification and modification, resuscitation, collaborative decision-making, enhanced recovery and rehabilitation, and assisting with linkages to community support (fig. 1).[14]

Although anesthesiologists also have a major role in providing analgesia for patients with preeclampsia who deliver vaginally, anesthesiologists need to be health advocates for the provision of safe and equitable anesthesia and surgical care for patients with preeclampsia. Particular focus needs to be directed to perioperative care, because cesarean delivery is far more common than in the general obstetric population and is associated with more severe disease and worse outcome.[14–18]

It is estimated that approximately 60% patients with preeclampsia undergoing cesarean delivery experience complications (95% CI, 48.2 to 70.3%).[19] These complications include heart failure, pulmonary edema, hemorrhage, hospital length of stay more than 7 days, anemia, and readmission to hospital.[19] These data are consistent with the work of Coppage and Polzin[20] showing more complications in

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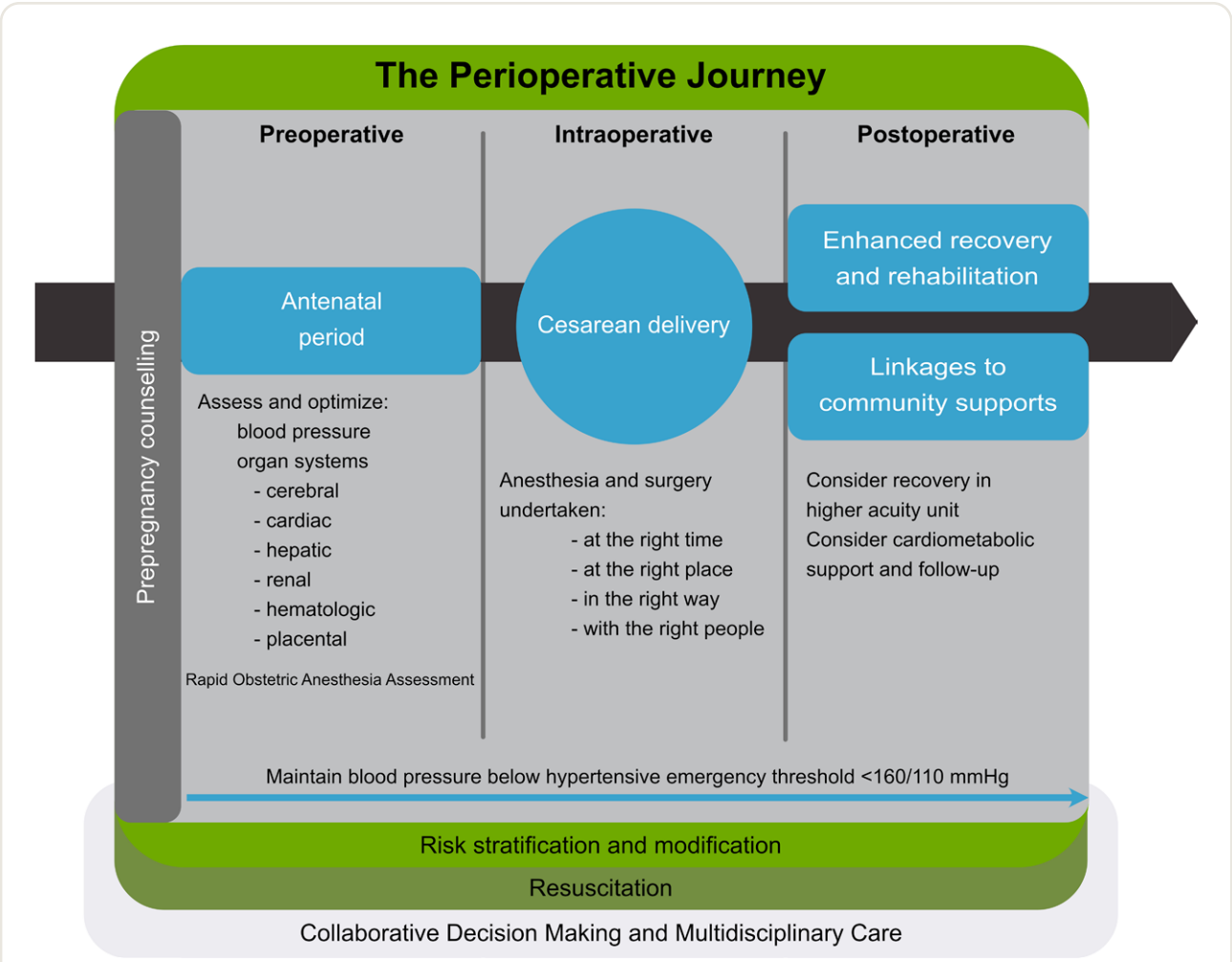

Fig. 1. Perioperative journey for a patient with preeclampsia. The figure shows a framework covering the prepregnancy aspect of counseling, the preoperative period that encompasses the whole of the antenatal period with opportunities for interventions and optimization for surgery, the intraoperative period highlighting the importance of the four rights to reduce morbidity and mortality (right time, right place, right way, and right people), and the postoperative period with consideration of higher acuity monitoring. Enhanced recovery, rehabilitation, and linkages to community support are important at this time. All periods require consideration of risk stratification and modification, resuscitation, and collaborative decision-making. This framework is the PARRCEL (Prepregnancy counseling, Antenatal care, Risk stratification and modification, Resuscitation, Collaborative decision-making, Enhanced recovery and rehabilitation, Linkages to community support) framework of perioperative care of pregnant patients.[14]

patients with preeclampsia undergoing cesarean delivery compared with vaginal birth. Given the additional risks that occur with major surgery, such as hemodynamic and heart rate fluctuations, infection, venous thromboembolism, and the neuroendocrine–metabolic and inflammatory–immune responses associated with recovering from surgery,[21] patients with preeclampsia likely represent a very high-risk surgical group.[22] These risks mean that patients with preeclampsia require a specific focus and an urgent priority to reduce their perioperative morbidity and mortality.

The recognition that preeclampsia is a significant preoperative comorbidity and that cesarean delivery is major surgery means that this surgical population is not forgotten in the perioperative setting and is included in advances and research in the care of surgical patients.[14] The purpose of this comprehensive review is to define patients with preeclampsia as a high-risk perioperative cohort and summarize key perioperative issues and management relevant to anesthesiologists. It is acknowledged that anesthesiologists provide care to patients with preeclampsia in labor who deliver vaginally by way of providing neuraxial analgesia, and important aspects of labor epidural analgesia, including the issue of thrombocytopenia and the conversion of a labor epidural to a cesarean delivery epidural for anesthesia, are covered. Although important, issues of prediction, screening, and pathophysiology of preeclampsia are not specifically covered in this review. We also do not specifically cover the issues of providing anesthesia care to patients with preeclampsia in low-resource settings.

Methods

Electronic search strategies *via* Ovid MEDINE, Ovid EMBASE (from inception until March 31, 2024), and the Cochrane Library were conducted using the search terms *preeclampsia*, *pre-eclampsia*, *hypertension*, *perioperative*, *obstetrics*, *pregnancy*, *caesarean section*, *cesarean delivery*, *management*, *cardiac function*, *hemodynamics*, *anesthesia*, *analgesia*, *neuraxial*, and *complications*. Relevant society, college, and international guidelines were reviewed. These included obstetrics guidelines from the American College of Obstetricians and Gynecologists,[1] the Society of Obstetricians and Gynecologists of Canada,[23] the Royal Australian and New Zealand College of Obstetricians and Gynaecologists,[24] the Royal College of Obstetricians and Gynaecologists United Kingdom,[25] and the International Federation of Gynecologists and Obstetricians[26]; anesthesiology guidelines from the U.S. Society of Obstetric Anesthesiologists and Perinatologists[27] and the Obstetric Anaesthetists Association of the United Kingdom[28]; obstetric medicine guidelines from the Society of Obstetric Medicine Australia and New Zealand[24] and the International Society of Obstetric Medicine[29]; hypertension and cardiology guidelines from the International Society for the Study of Hypertension in Pregnancy,[30] the American Heart Association,[31] and the European Society of Cardiology[32]; and evidence-based guidelines from international bodies, including the National Institute for Health and Clinical Excellence United Kingdom,[25] the Confidential Enquires into Maternal and Child Health in the United Kingdom,[33] MBRRACE-UK: Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the United Kingdom,[34,35] the U.S. Centers for Disease Control and Prevention,[8] and the World Health Organization.[36] Throughout the review, the term *patient(s) with preeclampsia* has been used. This encompasses the singular woman/person and plural women/people.

Definition of Preeclampsia

Preeclampsia is defined as new-onset sustained hypertension (systolic blood pressure greater than or equal to 140 mmHg and/or diastolic blood pressure greater than or equal to 90 mmHg) on two occasions at least 4 h apart, with evidence of organ dysfunction, commencing after 20 weeks' gestation and resolving within 3 months of delivery.[37] A systolic blood pressure greater than or equal to 160 mmHg and/or a diastolic blood pressure greater than or equal to 110 mmHg[38] is classified as a hypertensive emergency.[39]

Preeclampsia falls within the broad category of hypertensive disorders of pregnancy, which also includes chronic hypertension and gestational hypertension. Chronic hypertension is defined as having an onset before 20 weeks' gestation. It may be complicated by superimposed preeclampsia evidenced by worsening blood pressure and organ dysfunction. Gestational hypertension is hypertension (systolic blood pressure greater than or equal to 140 mmHg and/or diastolic blood pressure greater than or equal to 90 mmHg) without any associated organ dysfunction. Up to one in four patients with gestational hypertension progress to developing preeclampsia.[37]

Preeclampsia was previously divided into the categories of mild, moderate, and severe, and also into early (fewer than 34 weeks), preterm (34 to 37 weeks), and late (more than 37 weeks) stages. The contemporary definition now consists of only two categories: preeclampsia without and preeclampsia with severe features.[1] This definition recognizes that severe complications can occur at any gestation beyond 20 weeks, that the severity of preeclampsia is a continuum, that preeclampsia without severe features can become preeclampsia with severe features, and that the timing of when preeclampsia occurs is less relevant than the manifestations of organ dysfunction. Outdated terms for the disorder, including the use of their abbreviations, are pregnancy-induced hypertension (PIH) and preeclamptic toxemia (PET).

Preeclampsia with severe features is the category in which a large majority of complications occur and in which urgent delivery, frequently by cesarean delivery, is required. This is often the time when the anesthesiologist first becomes involved with the patient. The hypertension threshold and organ system dysfunction defining severe features, indications for delivery, and anesthesiology implications are shown in table 1.[1,24,32,37,40–43]

Diagnostic Challenges

Differential diagnoses for the etiology of hypertension in pregnancy, as well as conditions that mimic the organ dysfunction in preeclampsia are shown in table 2.[44–46] Hypertension occurring for the first time in the postpartum period needs to be evaluated with a thorough differential diagnostic process. The presence of postoperative pain, excessive fluid administration, agitation, hypercarbia, hypoxemia, or bladder distension[47] may explain new-onset hypertension. Hypertension presenting for the first time in the postoperative period may also be the first manifestation of chronic hypertension. Only once the known causes of postoperative hypertensive have been excluded should the diagnosis of postpartum preeclampsia be made. Potential misdiagnosis and erroneously labeling a patient with preeclampsia may have a short- or long-term psychologic impact. Because postoperative mental health problems are a leading cause of maternal morbidity and mortality,[34] such diagnostic errors must be carefully avoided.

Organizational Elements of Care

Patients with preeclampsia are high-risk perioperative patients, so a multidisciplinary team approach is beneficial.

Table 1. Definition of Preeclampsia

Definition and Threshold Value, Symptom, or Sign		Indications for Decision to Immediately* Initiate Delivery	Anesthesia Implications†
Hypertension	Systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on two occasions at least 4 h apart after 20 weeks of gestation in a person with previously normal blood pressure‡ *Systolic blood pressure ≥ 160 mmHg and/or diastolic blood pressure ≥ 110 mmHg (severe hypertension can be confirmed within a short interval (min) to facilitate timely antihypertensive therapy*	Repeated episodes of systolic blood pressure ≥ 160 mmHg and/or diastolic blood pressure ≥ 110 mmHg unresponsive to multiple antihypertensive agents (hypertensive emergency)	Additional antihypertensive agents may be required to control blood pressure Arterial blood pressure monitoring may be needed Medications must be available to reduce risk of a hypertensive emergency during tracheal intubation and extubation§
Other organ system involvement			
Cerebral	*New-onset headache unresponsive to medication and not accounted for by alternative diagnoses* *Hyperreflexia with sustained clonus* *Visual symptoms and signs (scotomata, cortical blindness, photopsia, retinal vasospasm, papilledema)* *Posterior reversible encephalopathy (PRES)* *Cerebral edema* *Raised intracranial pressure* *Eclampsia (seizure)* *Stroke (intracranial hemorrhage)*	Neurologic features including severe intractable headache, focal neurologic signs, visual disturbance, motor or sensory changes, stroke, eclampsia	Magnesium sulfate (intravenous or intramuscular) is likely to be required; this will prolong nondepolarizing neuromuscular blocking agents' duration of action if general anesthesia is required Suspect intracranial hemorrhage in patients with severe headache, focal neurologic signs, or eclampsia May require preoperative consultation with neurologist or neurosurgeon Additional brain imaging may be required in the perioperative period Postoperative intensive care/stroke unit care may be required
Cardiac	*Heart failure with preserved ejection fraction*‖ *Heart failure with reduced ejection fraction* *Pulmonary edema* *Myocardial ischemia* *Myocardial edema* *Symptomatic pericardial effusion*	Cardiac features including pulmonary edema, myocardial ischemia/infarction	Heart failure may require inotropic support, central venous access, and more advanced support such as extracorporeal membrane oxygenation if critical Postoperative intensive care or coronary care unit support likely needed
Renal	Proteinuria: 300 mg or more per 24-h urine collection (or extrapolation from a timed collection) or protein/creatinine ratio of ≥0.3 or dipstick reading + 2 (in the absence of other quantifiable methods) *Proteinuria: ≥5 g protein excreted in 24 h* *Urine albumin/creatinine ratio ≥ 8 mg/mmol* *Serum creatinine > 1.1 mg/dl or doubling of serum creatinine concentration in the absence of renal disease*	Rising serum creatinine and >1.1 mg/dl or twice baseline	Increased risk of magnesium toxicity Drug dose adjustments required for renally excreted drugs Renal replacement therapy may be required in the perioperative period
Hepatic	*Severe persistent right upper quadrant or epigastric pain, severe nausea and/or vomiting, unrelated to medications or other causes* *Hepatic subcapsular tearing, stretching, or rupture* *Elevated serum transaminase concentration to at least twice normal concentration*	Abnormal and rising liver enzymes (international normalized ratio > 2 in the absence of disseminated intravascular coagulation or warfarin therapy) Epigastric or right upper quadrant pain unresponsive to analgesia Hepatic hematoma or rupture	Increased risk of bleeding and coagulopathy May require input from hematologist to assist with guiding product replacement Additional surgical teams may be required
Hematologic	Thrombocytopenia: platelet count < 150 × 10^9/l *(<100 × 10^9/l)* *Evidence of hemolysis: lactate dehydrogenase ≥ 600 IU/l, and/or evidence of erythrocyte fragmentation on blood film,* *decreased haptoglobin* *Disseminated intravascular coagulation*	Progressive thrombocytopenia or platelet count < 50 × 10^9/l Hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome	Increased risk of hemorrhage Neuraxial anesthesia may be contraindicated Postoperative deterioration may occur, including with further reduction in platelet count

(*Continued*)

Table 1. (Continued)

Definition and Threshold Value, Symptom, or Sign		Indications for Decision to Immediately* Initiate Delivery	Anesthesia Implications†
Placental and fetal#	*Fetal growth restriction, reduced fetal growth rate associated with abnormal umbilical artery Dopplers or oligohydramnios* *Suspected placental abruption***	Suspected placental abruption with maternal or fetal compromise or vaginal bleeding in the absence of placenta previa Nonreassuring fetal status (including death): clinical, cardiotocography, ultrasound variables including persistent reversed end-diastolic flow in the umbilical artery	General anesthesia may be required due to surgical urgency

The table shows a definition of preeclampsia, including severe features as defined by American College of Obstetricians and Gynecologists and/or the International Society for the Study of Hypertension in italicized font, as well as indications for immediate delivery and anesthetic implications.

*"Immediate" is defined as planned birth within 48 h, regardless of gestation, and precludes expectant management. This usually occurs after stabilization and glucocorticosteroid administration for fetal lung maturation if indicated.[26] Expectant management is in-hospital close monitoring of maternal and fetal status beyond 48 h. In patients with preeclampsia birth should be initiated at 37 weeks' gestation or sooner if indicated. †As well as all routine and additional anesthesia issues for patients with preeclampsia undergoing cesarean delivery. ‡Elevated blood pressure ≥ 160 mmHg (systolic blood pressure) and/or ≥ 110 mmHg (diastolic blood pressure) in the absence of other organ system involvement is defined as severe gestational hypertension. §See table 3. ‖Based on echocardiography heart failure can be subdivided into preserved ejection or reduced ejection fraction. #Placental and fetal abnormalities are no longer considered criteria for preeclampsia according to the American College of Obstetricians and Gynecologists. However, they are recognized in the International Society for the Study of Hypertension 2021 guidelines. **Placental abruption: Retrospective diagnosis at or after birth. Patient may present with vaginal blood loss, abdominal pain, abnormal fetal heart rate trace, hypotension, and/or collapse.

International reports such as MBRRACE-UK[35] highlight the need for maintenance of clinical skills and for earlier identification of these high-risk patients, with transfer to specialist centers for care if available. Every center managing obstetric patients must be appropriately prepared and apply local risk assessment and management protocols at all times and be classified according to the American College of Obstetricians and Gynecologists Levels of Maternal Care.[48] The Joint Commission of the United States defined new requirements for preeclampsia management at all U.S. hospitals to improve the quality and safety of the treatment of pregnant and postpartum patients.[49] Effective from July 1, 2020, six key components for preeclampsia (recognition, prompt management, staff education, simulation drills with team debriefing, site-specific morbidity review, patient education) are required for U.S. hospitals to maintain Joint Commission accreditation.

Risk assessment at the time of hospital admission can assist with patient stratification and care pathways. The obstetric comorbidity index, derived from claims data for maternal morbidity, is a validated scoring system that prospectively identifies women at risk of severe morbidity based on conditions including preeclampsia at hospital admission. Cumulative scores greater than or equal to 9 have been shown to be associated with rates of severe mortality morbidity of nearly 20%.[50] Patients with obstetric comorbidity index scores of this magnitude may benefit from multidisciplinary team care from the time of admission, to enable earlier intervention and treatment as emphasized in United Kingdom maternal mortality reports.[33–35] This scoring system is similar to early warning charts and medical emergency team (rapid response team) responses used to recognize and response to acute physiologic deterioration in patients and to facilitate handover and prompt awareness of clinical deterioration.[51]

Quality assurance and improvement programs in hospitals must emphasize morbidity reduction from preeclampsia to improve practice.[34,35,52] The highest-risk patients with preeclampsia may be those who come from marginalized and vulnerable groups including culturally and linguistically diverse communities, the LGBTQ+ community, people with disabilities, people with mental health conditions,[53] or those who have experienced trauma or who have not engaged with the health system before the late stages of pregnancy. Suboptimal care of such patients can be minimized or eliminated through recognition of unconscious bias and the application of trauma-informed, respectful, equitable, culturally safe, and supportive care—features that ideally should be ubiquitous in pregnancy management.[54]

Preoperative Assessment and Management

Assessment of Preeclampsia Severity

Preoperative assessment of patients with preeclampsia is often conducted in an urgent or emergent context and often after discussion with obstetric and neonatal colleagues to determine timing of delivery. In such cases, the priority is to stabilize the patient, which may involve calling for assistance. Performing a rapid obstetric anesthesia assessment involves obtaining a history, performing a physical examination, and urgently obtaining investigations

Table 2. Differential Diagnosis of Preeclampsia

System Disease	Specific Examples
Cardiovascular disease*	Aortopathy (aortic coarctation, aortic dissection)
	Subclavian stenosis
	Vasculitis
Cerebral disease	Intracranial tumors†
Renal disease	Renal artery stenosis, chronic renal failure
Endocrine disease	Pheochromocytoma*
Autoimmune disease	Such as systemic lupus erythematosus or rheumatoid arthritis
Substance use disorder*	Such as cocaine, cannabis/marijuana, amphetamines, methylenedioxymethamphetamine
Hepatic disease	Acute fatty liver of pregnancy‡
Hematologic disease	Thrombotic microangiopathy including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome§
Placental disease	Gestational trophoblastic disease‖

*Frequently presents with hypertension. †May present with hypertension, headaches, visual disturbance, and seizures. ‡Frequently presents without hypertension can be differentiated from preeclampsia based on the Swansea criteria of clinical, laboratory, ultrasonographic, and histologic features. §Hemolytic uremic syndrome/thrombotic thrombocytopenic purpura is defined as the pentad of thrombocytopenia, microangiopathic hemolytic anemia, neurologic symptoms, renal dysfunction, and fever. Expeditious diagnosis of thrombotic thrombocytopenic purpura/hemolytic uremic syndrome is essential to ensure the commencement of lifesaving treatments, such as plasma exchange. ‖May be associated with endocrine abnormalities such as thyroid dysfunction, which may lead to hypertension.

such as platelet count, hemoglobin value, and blood type and screen (table 3). Distillation of these data enables the anesthesiologist to determine four key factors: surgical urgency, disease severity and stability, required monitoring, and method of anesthesia for cesarean delivery. The severity of the disease informs the extent of stabilization needed before anesthesia and intraoperative monitoring choices.[55] Understanding the reason for cesarean delivery and its urgency and assessment of the patient's conscious and neurologic state, airway, platelet count, and coagulation status inform a risk–benefit analysis of neuraxial *versus* general anesthesia.

Management of Preoperative Hypertension

In patients with preeclampsia, hypertension is divided into nonsevere and severe categories. Nonsevere hypertension is defined as a systolic blood pressure of 140 to 159 mmHg and/or diastolic blood pressure of 90 to 109 mmHg. At these thresholds, treatment of hypertension is recommended[56,57] to reduce the risk of progression to preeclampsia with severe features and associated adverse outcomes, such as hemorrhagic stroke.[24,25,38,58,59]

Oral Antihypertensive Dosages. First-line oral agents for the treatment of nonsevere hypertension include labetalol (100 to 400 mg three or four times daily), nifedipine slow release (20 to 60 mg twice daily), nifedipine immediate release (10 to 30 mg three times daily), or methyldopa (250 to 750 mg three or four times daily), aiming for a target blood pressure less than or equal to 135/85 mmHg.[24,25,37] More than one oral agent may be required to control blood pressure. Therapy should be individualized and take the patient's comorbidities and risk profile into account. Methyldopa should be avoided in patients with a history of anxiety and depression, labetalol should be avoided in patients with asthma, and nifedipine should not be used in patients with aortic stenosis. Other agents such as oral hydralazine, oral clonidine, and oxprenolol may be appropriate where available.[24] In the case of patients with nonsevere hypertension, medication may have been commenced by the obstetric team in the weeks leading up to delivery.

Severe hypertension is defined as a systolic blood pressure greater than or equal to 160 mmHg and/or diastolic blood pressure greater than or equal to 110 mmHg and requires urgent treatment (within 60 min).[1,60] Escalation of hypertension from the nonsevere to severe range usually warrants transition to intravenous (IV) antihypertensive therapy, although oral nifedipine and oral labetalol are recommended if IV access cannot be promptly obtained.[1,60] Persistent systolic blood pressure greater than or equal to 160 mmHg and/or diastolic blood pressure greater than or equal to 110 mmHg constitutes a hypertensive emergency and requires immediate treatment[61,62] to reduce the risks of hemorrhagic stroke, eclampsia, placental abruption, and maternal death.[24,39] Pharmacologic treatment may include IV labetalol, IV hydralazine, or calcium channel blockers.[1,63] Intravenous diazoxide, other β-blockers, clonidine, prazosin, and nitroglycerin may be appropriate where available.[24,64] Drugs that should not be used include high-dose diazoxide, ketanserin, nimodipine, and, as a sole agent, magnesium sulfate. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers should not be used due to fetal concerns.[63] As with nonsevere hypertension, agents should be individualized to the patient.

When treating severe hypertension, close monitoring of the patient is necessary to avoid precipitous reductions in blood pressure, which may impair critical perfusion pressures and result in maternal or fetal complications. Continuous fetal monitoring should occur until blood pressure stablizes.[24,65] A rate of reduction in systolic blood

Table 3. Rapid Obstetric Anesthetic Assessment

Element	Key Data
History	Reason for cesarean delivery and why now (surgical urgency)
	Age
	Parity
	Gestation
	Fetal presentation
	Medications
	Presence of a correctly positioned and effective labor epidural
	Significant past illnesses
	Previous surgery including previous cesarean delivery, and previous back surgery
	Allergies
	Fasting status
Examination	State of consciousness
	Weight and body mass index
	Airway assessment
	Vital signs (blood pressure, heart rate, respiratory rate, temperature)
	Heart sounds
	Chest auscultation
	Oxygen saturation
	Focused neurologic examination*
	Urine output
	Blood loss (quantitative assessment, vaginal blood loss)
	Fetal heart rate
Investigations	Complete blood count (including hemoglobin concentration, platelet count)
	Blood type and screen
	Cross match if appropriate
	Renal function including urine protein
	Liver function

Additional tests such as coagulation tests, fibrinogen concentration, whole-blood viscoelastic testing, glucose concentration, blood gas analysis (pH, lactate, $Paco_2$, and Pao_2), electrocardiograph, transthoracic echocardiography, lung ultrasound, chest x-ray, assessment for fluid responsiveness, and pulse pressure variation may also be indicated. Coagulation is unlikely to be abnormal if aspartate transferase (AST) and alanine transaminase (ALT) are normal and platelet count is normal and there is no eclampsia or suspected placental abruption.

*May be required in the setting of patients with preeclampsia with neurologic features to assess for neurologic deficits suggestive of intracerebral hemorrhage.

pressure of 10 to 20 mmHg every 10 to 20 min is appropriate with a target systolic blood pressure of 135 to 159 mmHg and diastolic blood pressure target of 85 to 109 mmHg.[24,37,62] The commencement of agents, usually initiated by the obstetric team, to treat severe hypertension usually signals the need for urgent delivery, often within 48 h (table 1).

Intravenous Antihypertensive Dosages. Local protocols should be in place to guide the administration of IV antihypertensive agents. In general, hydralazine can be administered as an intermittent IV bolus of 5 to 10 mg over 2 min every 15 to 20 min to a maximum of 25 mg/24 h or as a continuous infusion of 0.5 to 10.0 mg/h.[39] It may be necessary to administer a small IV fluid bolus (250 to 500 ml) if vasodilation and rapid reduction in blood pressure occurs in the presence of hydralazine. Labetalol can be administered as an IV bolus of 10 to 40 mg every 10 to 15 min to a maximum of 80 mg or as a continuous infusion commencing at 20 mg/h and increasing as required by 5 mg every 15 min to a maximum rate of 160 mg/h and a maximum dose of 220 mg/24 h.[39]

There are no randomized controlled trial data to guide blood pressure targets immediately before anesthesia, either with neuraxial techniques or by general anesthesia, in patients with preeclampsia. Dangerous hypertensive responses to laryngoscopy in patients with preeclampsia are well known,[59,66] and severe systolic hypertension (greater than or equal to 160 mmHg) has been associated with stroke and acute pulmonary edema in the perioperative period.[1] The Confidential Enquiries into Maternal Deaths in the United Kingdom support the expeditious preoperative stabilization of patients with preeclampsia with severe features. This includes stabilizing patients with severe hypertension (to levels of less than 160/110 mmHg), even when there are "pressing fetal reasons for urgent caesarean section under general anaesthesia."[33]

The fundamental hemodynamic goals for a patient with preeclampsia should address and optimize intravascular volume, preload, cardiac output (stroke volume and heart rate), blood pressure, organ perfusion, oxygen delivery (flow and oxygen content), and tissue oxygenation (consumption supply balance) to optimize outcomes.[67] In pregnancy, the balance of oxygen supply and demand is complicated by the constant stimulus of the growing fetus and variable flow and resistance of the placental circulation, leading to a constantly adapting maternal cardiovascular system response.[68] In the immediate preoperative setting, stabilizing blood pressure to less than 160/110 mmHg is prudent in anticipation of potential blood pressure fluctuations that may occur with anesthesia for cesarean delivery. Maintaining uterine perfusion by minimizing significant reductions in blood pressure (for example, aiming for blood pressures of 135 to 150/80 to 90 mmHg) is likely to be safe. Fetal monitoring during the urgent treatment of maternal hypertension may be indicated. Extremes of blood pressure are likely to increase the risk of both maternal cerebrovascular and cardiac complications and fetal hypoxemia.

In patients with preeclampsia, neuraxial analgesia does not significantly reduce blood pressure; however, it offers excellent and better analgesia compared with systemic analgesics,[69] reduces pain-mediated hypertensive responses during contractions, and reduces circulating catecholamines.[69] The use of neuraxial labor analgesia in patients with preeclampsia with severe features with planned vaginal delivery should be encouraged. These women are at higher risk for intrapartum cesarean delivery and at higher risk for complications of general anesthesia.

Management and Prevention of Eclampsia

Eclampsia is the word used to describe generalized tonic clonic seizures that occur in patients with preeclampsia

in the absence of any underlying neurologic condition. Eclampsia has long been recognized as a life-threatening complication of preeclampsia.[70] It is one the major causes of intracranial hemorrhage, long-term morbidity, and death in patients with preeclampsia and also leads to significant fetal morbidity and mortality.

Cerebral irritability and cerebral deterioration may precede the seizure, although often there is no warning. Intracranial hemorrhage should be suspected in patients with eclampsia, severe headache, or focal neurologic signs. Although optic nerve sheath diameter assessments in patients with preeclampsia may provide early warning of cerebral complications, more data are needed to assess its usefulness.[71,72]

Posterior reversible encephalopathy syndrome commonly occurs in patients with eclampsia. A study of 110 patients with eclampsia demonstrated 100% prevalence of posterior reversible encephalopathy syndrome on neuroimaging,[73] and another demonstrated a 19.2% incidence in those with preeclampsia and neurologic symptoms.[74] The hallmark findings of posterior reversible encephalopathy syndrome are hypertension with headache, altered mental status, vision loss, seizures, and radiographic vasogenic edema localized to the posterior cerebral white matter.[75] Posterior reversible encephalopathy syndrome does not usually lead to elevated intracranial pressure, and there is minimal risk for brainstem herniation. In patients diagnosed with posterior reversible encephalopathy syndrome, it is a priority to manage and prevent new or recurrent eclampsia with magnesium sulfate and maintain strict blood pressure control to prevent further morbidity. Additional neuroprotective strategies for posterior reversible encephalopathy syndrome are under investigation in pregnant and nonpregnant adults.[76]

Principles of management of eclampsia include recognition of the seizure, activation of alert systems, and immediate initiation of resuscitation with a multidisciplinary team, which includes both prevention of secondary maternal injury and magnesium sulfate administration. Key steps to preventing secondary maternal injury include protecting the airway from aspiration, having immediate access to suction, oxygen administration, prevention of aortocaval compression with left uterine displacement, and administration of magnesium sulfate.

Eclamptic seizures are frequently self-limited; however, eclampsia is a trigger for delivery (table 1). Fetal bradycardia can occur after the maternal seizure, which may have a catecholamine-mediated etiology.[77] Although fetal bradycardia after seizures is also frequently self-limited, placental abruption should be considered, and rapid sonographic assessment of placenta integrity may help guide crisis management, including the need for an emergency cesarean delivery. After the patient has been initially stabilized, the decision regarding the type of delivery involves multidisciplinary collaboration and shared decision-making. Delivery type depends on many factors, including maternal and fetal condition, dilation of the cervix, gestational age, and fetal presentation. The absence of refractory maternal seizures or significantly altered conscious or uncooperative state are reassuring maternal signs if a vaginal delivery is considered. When cesarean delivery is planned, the anesthesiologist may need additional time to assess the history, examination, and investigations of the patient so that anesthesia can be undertaken safely.[33]

Given the complexity of patients with eclampsia, the choice of neuraxial *versus* general anesthesia in this setting must be individualized based on many factors. Moodley *et al.*[78] defined stability in a patient who has a recent seizure (eclampsia) by the following criteria: Glasgow coma score greater than or equal to 14, not requiring rapidly acting antihypertensive medication, platelet count greater than 100×10^9/l, cooperative, normal fetal heart rate pattern on electronic monitoring, and no additional maternal or fetal complications. For patients meeting these criteria, neuraxial anesthesia is considered safe, enables prompt and serial neurologic and mental status evaluations, and avoids the hypertensive risks of general anesthesia and surgery. Patients who are unconscious or uncooperative, have uncontrolled hypertension, or have refractory seizures likely warrant general anesthesia. If a patient with eclampsia requires tracheal intubation, neuroimaging before extubation may be required to evaluate for hemorrhagic stroke or other conditions that may be contraindications to extubation.

First described by Dr. Edmond Lazard in 1925,[79] magnesium sulfate remains the first-line medication for the treatment of seizures and lowers the incidence and recurrence of eclampsia by 50%.[80,81] Magnesium sulfate reduces the likelihood of death compared with diazepam and reduces recurrent seizures compared with diazepam, phenytoin chlorpromazine, promethazine, and pethidine.[82] Associated morbidity with other agents is often driven by an altered consciousness with their administration, which increases the risk of aspiration, pneumonia requiring mechanical ventilation, admission to the intensive care unit, and delayed identification of cerebral hemorrhage or other neurologic complications.[80]

Magnesium Sulfate Dosages. For treatment of a first seizure and for initiation of prophylaxis to prevent seizures, magnesium sulfate is usually administered as an IV bolus of 4 to 6 g over 20 min followed by an IV infusion of 1 to 2 g/h[39] continuing for 24 h after birth or 24 h from the last seizure. If no IV access is available, 10 g of 50% magnesium sulfate solution can be administered intramuscularly 5 g into each buttock.[39] For the treatment of recurrent seizures, the usual dose is a 2-g IV bolus of magnesium sulfate.

When used for seizure prevention, based on the Magnesium Sulphate for Seizure Prophylaxis in Women with Preeclampsia (MAGPIE) trial and the Cochrane systemic review on magnesium sulfate for patients with preeclampsia, the number of

patients with preeclampsia with severe features needed to treat with magnesium sulfate to prevent one seizure is 50.[80] This treatment is recommended[24,37,62] especially for patients with preeclampsia with severe features including persistently severe hypertension (greater than or equal to 160/110 mmHg) and features of cerebral irritability. When magnesium sulfate is contraindicated or ineffective for recurrent seizures benzodiazepines such as lorazepam 2 to 4 mg IV repeated once after 10 to 15 min or diazepam 5 to 10 mg IV every 5 to 10 min to a maximum dose of 30 mg may be used.[39]

Magnesium sulfate is not an antihypertensive agent and does not significantly lower blood pressure, although when combined with opioids, it may produce a synergistic reduction in blood pressure for tracheal intubation. It also does not prevent the ongoing progression of hypertension. Safety strategies are needed in locations where magnesium sulfate is administered to patients, including in emergency transport vehicles. Patients receiving magnesium sulfate therapy are monitored for high plasma levels of magnesium using assessment of clinical signs such as respiratory rate, oxygen saturation, urine output, patellar reflexes, and the presence of clonus.

Magnesium Sulfate Toxicity Ranges, Symptoms, and Signs. Magnesium toxicity occurs when serum magnesium levels exceed 9 mg/dl (greater than 3.5 mM) and is more likely to occur in patients with impaired renal function, which may evolve acutely in the postoperative period. Clinical signs of magnesium toxicity include electrocardiography abnormalities with widened P–Q intervals and QRS complexes, reduction and then loss of deep tendon reflexes (greater than 9 mg/dl [greater than 3.5 mM]), sinoatrial and atrioventricular blockade, respiratory paralysis (greater than 12 mg/dl [greater than 5.0 mM]), and central nervous system depression and then cardiac arrest (greater than 30 mg/dl [greater than 12.5 mM]). pharmacologic treatment for magnesium toxicity is 10 ml of 10% calcium gluconate (1 g calcium gluconate)[83] IV over 10 min; 10% calcium chloride may also be used; however, it contains approximately three times the dose of elemental calcium compared with calcium gluconate. Therefore, the recommendation is to administer 5 ml of 10% calcium chloride (500 mg calcium chloride) IV given over 5 to 10 min.[84]

Cardiac Complications in Patients with Preeclampsia

Cardiac complications include heart failure, pulmonary edema, myocardial ischemia, myocardial edema, and pericardial effusion.[34] Based on echocardiography, heart failure can be subdivided by preserved ejection fraction or reduced ejection fraction.

Echocardiographic Findings in Patients with Preeclampsia. Hemodynamic changes observed in research studies suggest that patients with untreated preeclampsia, before critical decompensation with reduced ejection fraction, have normal to increased cardiac output, normal to increased contractility, diastolic dysfunction putting them at risk of heart failure with preserved ejection fraction, increased pericardial effusions, and increased left ventricular wall dimensions compared to healthy pregnant women.[85,86] A component of the increased left ventricular myocardial dimensions may be from myocardial edema.[87]

Heart Failure as a Complication of Preeclampsia. Heart failure is a known complication of severe hypertension in nonpregnant adults.[42] Therefore, it is not surprising that patients with preeclampsia, which is a cardiovascular condition with the key manifestation of hypertension, are at risk of developing heart failure secondary to hypertension. Care must be taken not to confuse preeclampsia with heart failure with peripartum cardiomyopathy. Peripartum cardiomyopathy is a rare condition presenting with heart failure with reduced ejection fraction (ejection fraction less than 45%, or fractional shortening less than or equal to 30%) in the absence of hypertension where the cause is unknown.[43,88,89]

Patients with preeclampsia complicated by the severe feature of heart failure when misdiagnosed with peripartum cardiomyopathy may have a different risk assessment for future pregnancies, may be advised not to have a further pregnancy, and may receive inaccurate counseling about their prognosis for recovery. Furthermore, coping with a misdiagnosis that has unclear etiology (peripartum cardiomyopathy) may also yield unnecessary negative impact on mental well-being. The distinction between peripartum cardiomyopathy and heart failure in preeclampsia will allow better understanding and prognostication for patients and ensure that clinicians continue to evaluate the other organ systems involved in patients with preeclampsia.

Management of Heart Failure. Transthoracic echocardiography is indicated in any patient with preeclampsia who is suspected of having heart failure to differentiate heart failure with preserved ejection fraction from heart failure with reduced ejection fraction.[42,90–93] Other diagnostic tools include electrocardiography, cardiac troponin, and chest x-ray. N-terminal pro-B-type natriuretic peptide (upper reference limit first and second trimesters, 200 pg/ml; third trimester, 150 pg/ml) and brain natriuretic peptide (B-type natriuretic peptide; upper reference limit, 50 pg/ml)[94] can be useful cardiac markers for detecting deterioration and for monitoring improvement in cardiac function. Cardiac magnetic resonance may be useful in the recovery period and for patient follow-up. Management of patients with heart failure involves a multidisciplinary team, including intensive care physicians and cardiologists.

Patients with heart failure with preserved ejection fraction predominantly present with shortness of breath suggestive of acute pulmonary edema in the setting of hypertension.[43] This is nuanced and may be missed on echocardiography due to a normal ejection fraction if only systolic function is assessed. Heart failure with preserved

ejection fraction may be precipitated by iatrogenic excessive intravenous fluid administration and may occur in up to 9.5% of patients with preeclampsia with severe features. It is one of the leading causes of admission to the intensive care unit and of maternal death in patients with preeclampsia.[19,43,95,96] Treatment of heart failure with preserved ejection fraction in patients with preeclampsia is very similar to its treatment in nonpregnant adults. Activation of emergency protocols and advanced life support procedures may be necessary. Acute reduction in blood pressure may be required with agents such as nitroglycerin (5 μg/min IV, increasing every 3 to 5 min to a maximum dose of 100 μg/min).[32] Furosemide with a bolus dose of 20 to 40 mg IV over 2 min to promote vasodilation and fluid redistribution can be used up to a total dose of 120 mg/h. Morphine 2 to 5 mg IV may be required along with fluid restriction, continuous positive airway pressure, bilevel positive airway pressure, or mechanical ventilation. High-flow nasal oxygen may have a role in management, but further research is needed in this area.

Patients with heart failure with reduced ejection fraction may present with hypotension and tachycardia and may require inotropic agents. The incidence of progression from heart failure with preserved ejection fraction to heart failure with reduced ejection fraction is unclear, and further research is needed in this area.[76] Progression to cardiac arrest may occur. Advanced life support protocols, including the consideration of perimortem cesarean delivery within 5 min of the time of arrest, should be followed.[97]

The Rapid Obstetric Screening Echocardiography (ROSE) scan was developed in 2011 to quickly assess a patient's cardiac function at the bedside and includes assessment of diastolic function an essential component of echocardiography for diagnosing heart failure with preserved ejection fraction. An example of the scanning procedure has been published in appendix A (supplemental data) of Dennis.[98]

Management of Hemolysis, Elevated Liver Enzymes, and Low Platelets (HELLP)

The triad of hemolysis, elevated liver enzymes, and low platelets (HELLP) is a severe feature in patients with preeclampsia and an indication for delivery (table 1). There are no universally agreed upon hematological and biochemical thresholds for defining HELLP syndrome, but by definition, the diagnosis of HELLP requires the presence of hemolysis usually evidenced by a lactate dehydrogenase concentration of greater than or equal to 600 IU/l.[1] Interventions such as glucocorticosteriods,[24] plasma exchange, or plasmapheresis are not recommended for patients with HELLP.[24] Platelet transfusions are generally not recommended[24]; however, there may be situations in which, after weighing up individual risks *versus* benefits, platelet transfusions may be required, such as to facilitate neuraxial placement or in the setting of significant hemorrhage with severe thrombocytopenia. An important aspect of management of patients with HELLP syndrome is the timing of delivery (especially cesarean delivery and neuraxial analgesia/anesthesia) relative to the rapid decrease in platelet count. Ideally, once HELLP is diagnosed, immediate multidisciplinary team planning for delivery should occur. Similar to managing patients with eclampsia, mode and timing of delivery depends on many factors, including maternal and fetal condition, dilation of the cervix, gestational age, and fetal presentation.

Management of Hepatic Complications

Although hepatic rupture is fortunately a rare complication of preeclampsia, it is associated with high mortality. Hepatic rupture should be suspected when a patient with preeclampsia has acute onset of severe epigastric or right upper quadrant pain, often radiating to the back, occasionally with right shoulder tip pain, with abdominal tenderness or peritoneal signs, and hemodynamic features of hypovolemic shock with marked anemia. Hepatic rupture requires rapid recognition, surgical consultation, and often surgical intervention.[99] Intensive resuscitation and administration of blood products are required with surgery under general anesthesia with a large intraoperative team. Given the rarity of hepatic rupture and the high risk of maternal death, team training and simulation of the scenario, along with other antepartum hemorrhage scenarios, would be of value in an obstetric hospital.

Management of Renal Complications

Acute kidney injury (AKI) is defined as an increase in serum creatinine to 1.5 times baseline[100] or an increased serum creatinine of greater than or equal to 0.3 mg/dl or greater than or equal to 50% increase within 48 h or urine output of less than 0.5 ml/kg for more than 6 h.[101] AKI may be prerenal, intrarenal, or postrenal and predisposes patients with preeclampsia to acute pulmonary edema. Renal replacement therapy may be required for the indications of persistent acidemia, hypervolemia, hyperkalemia, or uremia.

Management of Placental Abruption

Placental abruption represents a critical complication in patients with preeclampsia and requires immediate recognition and management due to the life-threatening maternal and fetal risks. In the context of preeclampsia, maternal hypovolemia associated with antepartum hemorrhage may mask underlying maternal hypertension. Therefore, determining whether preeclampsia preceded the abruption is imperative. This is because patients with placental abruption may present for an immediate emergency cesarean delivery under general anesthesia, and if they have the comorbidity of preeclampsia, they require meticulous attention to their hemodynamics at the time of tracheal intubation and extubation. When placental abruption is suspected, assessment of coagulation status is imperative.

Assessing and Managing Coexisting Problems

Patients with preeclampsia may present with other cardiometabolic conditions, such as preexisting or gestational diabetes[102] and increased body mass index (greater than 30 kg/m^2), both of which are risk factors for preeclampsia.[103] Patients with increased body mass may also have obstructive sleep apnea[104] or a potentially difficult airway, further complicating perioperative anesthesia management. Anemia (hemoglobin of less than 110 g/l), a common problem globally in pregnant women, may also be present and is also a risk factor for preeclampsia.[105–107] Correction of anemia and iron deficiency (ferritin of less than 30 μg/l) is especially important in the antenatal period for patients with preeclampsia, given their high risk of surgery and intraoperative hemorrhage.[108,109] Because patients with multiple pregnancies are at risk of preeclampsia, complications related to the births of twins and triplets, such as hemorrhage, may occur in this patient group, necessitating vigilance at all times by the anesthesiologist.

Preoperative Medications

Assessment of patients with preeclampsia before cesarean delivery involves reviewing the medications that they are receiving. In addition to antihypertensive agents administered to manage hypertension, patients with preeclampsia are frequently prescribed aspirin and calcium, both recommended for preeclampsia prevention, and may still be taking them when assessed for surgery and anesthesia if they require delivery, especially if remote from term gestation.

The usual prescription of aspirin is up to 150 mg/day commencing before 16 weeks' gestation, taken at bedtime, until between 34 weeks' gestation to birth, individualized for the patient.[24] Although aspirin is not a contraindication to neuraxial techniques, cumulative risk for patients taking aspirin in the context of low platelets or other anticoagulant therapy should be considered. The American College of Obstetricians and Gynecologists does not recommend calcium supplementation for patients in high-income countries. Other international guidelines, however, recommend that pregnant patients with low dietary calcium intake (less than 1 g/day) receive calcium supplementation typically at a daily dose of 1,000 mg.[24] Patients may also be receiving glucocorticosteroids (betamethasone or dexamethasone) to facilitate fetal lung maturation if preterm birth is anticipated, and for patients with diabetes, insulin may be prescribed.

Omega-3 long-chain polyunsaturated fatty supplementation, oral garlic supplementation, antioxidants (vitamin C and E), oral magnesium, progesterone, statins, low-molecular-weight heparin, nitric oxide, metformin, oral vitamin D supplementation, proton pump inhibitors, and clopidogrel are not recommended to prevent preeclampsia due to lack of evidence of benefit and harm, and therefore these should not be taken or continued in these patients.[24]

Considerations Related to Gestation

Patients with preeclampsia may present with very severe disease at gestations remote from term (*e.g.*, less than 32 weeks' gestation) and present with fetal growth restriction or even at previable gestations. They may also come to surgery later in the disease process, in an attempt to improve fetal maturation, at the cost of more severe maternal disease. In such patients, multidisciplinary team planning is important to determine the safest time, place, and subspecialty teams required for delivery and postoperative care.

Intraoperative Management: Anesthesia for Cesarean Delivery

Human Factors

Cesarean delivery in patients with preeclampsia requires a collaborative approach involving anesthesiologist, obstetrician, midwife, neonatologist, and often intensivist[24,25] Early involvement of the anesthesiologist as part of a multidisciplinary team has been shown to improve outcomes in pregnant patients for both the patient and fetus, and this is now recognized in many professional guidelines.[31,110]

Role definition and introductions, communication, and safety aids are essential for the safe management of patients with preeclampsia in the intraoperative environment. These may include routines such as a preoperative team huddle to ensure that the team is present and that key issues are discussed, the World Health Organization surgical safety checklist, team time out, and team debriefing at the end of surgery. These components address human factors that can lead to poor outcomes in surgical patients.[111]

Positioning

In patients with preeclampsia, like for all obstetric patients, safe positioning on the operating table is essential and includes left lateral tilt to minimize aortocaval compression and positioning for optimal airway management. Patient positioning aids such as the Troop Elevation Pillow System, the Oxford HELP System, or a ramp made from stacked blankets can optimize airway positioning before tracheal intubation for general anesthesia.

Intraoperative Hemodynamic Monitoring

In addition to national anesthesiology monitoring standards, beat-to-beat blood pressure monitoring with an arterial line may be required for patients with preeclampsia. Similar to other unstable patients, indications may include hypertension that is unstable or difficult to control, preeclampsia with severe features especially neurologic symptoms and signs, or the need for frequent blood sampling for hematological (including hemoglobin, platelets, fibrinogen, coagulation status), electrolytes (including calcium, glucose), acid base (including pH, base excess), respiratory (including $Paco_2$, Pao_2), liver, or tissue perfusion (lactate)

assessments, especially in the case of intraoperative hemorrhage. Arterial lines may be necessary for cardiac output monitoring using minimally invasive devices or to monitor blood pressure when vasoactive medications are required to reduce blood pressure. In patients with high body mass, an arterial line may be needed due to the unreliability of noninvasive blood pressure measurements. Arterial lines also have the advantage in that they can remain in place for postoperative monitoring and blood sampling.

Central venous catheters or pulmonary artery catheters, including for measurement of pulmonary capillary wedge pressures, are rarely used. They cannot reliably assess left ventricular filling status in patients on antihypertensive therapy, and they have a high risk of iatrogenic complications precluding their routine use.[112] Indications for their use remain the same as for nonpregnant patients and include infusion of vasoactive medications to diagnose and manage pulmonary hypertension. Transthoracic echocardiography can facilitate assessment and management of volume status, ejection fraction, valvular function, right heart function, and in resuscitation and cardiac arrest.

Choice of Anesthesia

Anesthesia for patients with preeclampsia undergoing cesarean delivery involves a decision between neuraxial and general anesthesia. For cesarean delivery, neuraxial anesthesia is generally preferred to general anesthesia, because it avoids airway instrumentation and its potential complications and provides more stable hemodynamic profiles, superior postoperative analgesia, better early Apgar scores in the neonate, and more rapid maternal baby bonding.[24,113,114] A historical concern for profound sympathectomy-related hypotension from spinal anesthesia among patients with preeclampsia has been disproven.[115] A study comparing rescue phenylephrine dose (in the absence of prophylactic vasopressor infusion) among patients with preeclampsia and healthy normotensive patients undergoing cesarean delivery under spinal anesthesia demonstrated a 33 to 40% reduction in required first phenylephrine dose for spinal hypotension. In this study, hypotension was defined as fall of systolic blood pressure greater than or equal to 20% from baseline or an absolute value of less than 100 mmHg.[116]

Neuraxial Anesthesia

For patients with preeclampsia without a preexisting labor epidural, there is no evidence to suggest superiority of either a spinal or a combined spinal epidural technique for cesarean delivery.[115,117] As with patients without preeclampsia, the decision between spinal or combined spinal epidural anesthesia for cesarean delivery should consider issues such as anticipated duration of surgery, primary or repeat cesarean, concern for adherent placenta, likelihood for intraoperative hemorrhage, high body mass, and predicted or known airway difficulty.

Despite the less common event of hypotension with neuraxial anesthesia in patients with preeclampsia compared with the general obstetric population, preparing for the event of hypotension is important.[118–120] Data are limited regarding colloid preloading or crystalloid coloading in patient with preeclampsia undergoing neuraxial anesthesia.[120] Dyer *et al.*[121] used a 300-ml colloid preload in patients with severe preeclampsia undergoing neuraxial anesthesia in their study comparing phenylephrine with ephedrine and determined that 50 μg phenylephrine was superior to 15 mg ephedrine in returning the hemodynamics of systemic vascular resistance, heart rate, and cardiac output toward baseline.

Management of hypotension in patients with preeclampsia is similar to patients without preeclampsia, with several caveats. As with all obstetric patients, hypotension should be treated. Patients who are symptomatic with nausea, vomiting, and general malaise before delivery, particularly in the context of spinal anesthesia, are likely to have reduced blood pressure or cardiac output in relation to their baseline hemodynamic requirements. Titrated IV doses of phenylephrine (25 to 50 μg) or ephedrine (2.5 to 5 mg) should be introduced at low doses due to the sensitivity of vasopressor medications in this population.[122] Infusion of phenylephrine may not be required in patients with preeclampsia. If required, it should be titrated commencing at a lower rate than for patients without preeclampsia.[120] Bradycardia may occur and may be treated with atropine (0.3 to 0.6 mg) or glycopyrrolate (100 to 200 μg).[119,123–125]

We support conclusions made by Dyer *et al.*[126] that phenylephrine is "the drug of first choice for spinal hypotension in obstetrics in the absence of bradycardia," with norepinephrine being at best noninferior and associated with potential risk to patients. Norepinephrine boluses or infusions for the routine treatment of neuraxial anesthesia hypotension in patients with preeclampsia are potentially dangerous. This is due to dilution errors leading to critical hypertension, unfamiliarity with the drug because it is predominantly only used in the intensive care unit and cardiac anesthesia, and risks of tissue damage due to extravasation when used peripherally. Like Dyer *et al.*, we assert that norepinephrine should be contraindicated for spinal hypotension in patients with hypertensive disorders of pregnancy.[126,127]

Considerations in the Patient with a Labor Epidural Having an Emergency Cesarean Delivery. A benefit of a functional labor epidural is its potential use for anesthesia in the event of an emergency cesarean delivery. A well-functioning epidural labor can typically be converted ("topped-up") to achieve surgical anesthesia for cesarean delivery.

Patients with labor epidurals should be evaluated before dosing for anesthesia for cesarean delivery to confirm catheter location in back, adequacy of providing analgesia for labor, bilateral sensory block and lack of signs

of intrathecal or intravascular catheter migration. A solution of 2% lidocaine with bicarbonate in 5-ml increments up to approximately 20 ml (individualized to patient's weight and preexisting epidural function) may provide the fastest onset of surgical anesthesia for cesarean delivery (13.4 min),[128] However, 3% 2-chloroprocaine may have advantages in this setting because 2-chloroprocaine does not require the mixing of two solutions, making the preadministration time quicker and the risk of drug errors lower compared with lidocaine and bicarbonate. It is safer to administer 2-chloroprocaine as a rapid bolus compared to lidocaine because there is a lower risk of local anesthetic systemic toxicity, less 2-chloroprocaine crosses the placenta, and ion trapping does not occur. 2-Chloroprocaine can be redosed if there is breakthrough pain during surgery. In addition to not being necessary for rapid conversion of labor epidurals to surgical epidural anesthesia, the use of epinephrine-containing local anesthesia solutions such as 2% lidocaine with epinephrine should be avoided in patients with preeclampsia due to the risk of a hypertensive crisis.[129]

Thrombocytopenia and Neuraxial Techniques in Patients with Preeclampsia. The Society for Obstetric Anesthesia and Perinatology consensus statement for neuraxial procedures in obstetric patients with thrombocytopenia provides risk–benefit guidelines for patients with preeclampsia and thrombocytopenia. If the patient does not have bleeding associated with thrombocytopenia, does not have an additional comorbidity of an underlying disorder of hemostasis, has normal coagulation, has no rapid rate of decline in platelet count, and has a platelet count of greater than or equal to 70,000 μ/l measured within 6 h, it may be reasonable to proceed with neuraxial analgesia.[130] In patients with preeclampsia who are also on aspirin therapy, there is a paucity of evidence to guide clinical practice. Neuraxial procedures in the setting of a low but stable platelet count is likely to be safer than the same low but rapidly falling platelet count. In the setting of HELLP, siting an early epidural catheter may be indicated to prevent having to perform a neuraxial procedure once the platelet count has fallen. A thorough risk–benefit analysis should be undertaken and discussed with the patient before performing a neuraxial technique.[130]

Platelet count should be re-evaluated before removal of an epidural catheter when thrombocytopenia is present. The same factors used to assess the safety of placement of an epidural catheter should be considered when determining a safe time to remove the catheter. Although the risk of spinal epidural hematoma is low in healthy patients, the risks in patients with preeclampsia and thrombocytopenia is poorly defined.[130] In all patients who have neuraxial techniques, monitoring for appropriate resolution of sensorimotor blockade and advising patients to report deviations from normal recovery is essential for early detection and management of complications.

General Anesthesia

An adequately planned and well conducted general anesthesia is safe for patients with preeclampsia. General anesthesia may be required for conditions such as fetal compromise, maternal hemodynamic instability, placental abruption, pulmonary edema, coagulopathy, thrombocytopenia, stroke, eclampsia, altered conscious state, or when the patient declines neuraxial anesthesia. General anesthesia requires immediate availability of medication for meticulous control of blood pressure to blunt the response to laryngoscopy, tracheal intubation, skin incision, and extubation to reduce the risk of intracranial hemorrhage, cardiac ischemia, and pulmonary edema.

Preoxygenation aiming for an end-tidal oxygen concentration of greater than or equal to 90% with face mask oxygen is the traditional approach to oxygenation in this setting. However, preoxygenation with high-flow humidified nasal oxygen using systems that enable the application of the face mask over the nasal cannulae, ensuring constant oxygenation (assuming a patent airway), may have a role in the future.[131] Rapid sequence induction with cricoid pressure is the generally accepted method of rapid tracheal intubation and likely reduces the risk of gastric aspiration.

A difficult airway should be anticipated and equipment available; visual and sonographic differences of higher Mallampati classification and more oropharyngeal edema have been noted in patients with preeclampsia compared to nonpregnant patients and pregnant normotensive patients.[132] This is likely to be even more significant if the patient is undergoing an emergency cesarean section having been in labor or pushing in the second stage of labor during which the Mallampati classification may worsen by more than 2 grades.[133] A smaller-than-standard-size tracheal tube should be available and may be required.[134] Video laryngoscopes improve the glottic view and shorten the time to successful tracheal intubation in the general patient population[135]; therefore, it is reasonable to prioritize their use in patients with preeclampsia.

Traditionally, IV anesthetic induction followed by volatile gas maintenance has been used. Randomized comparisons of succinylcholine with rocuronium and total intravenous anesthesia compared with volatile anesthesia maintenance have not been undertaken in this population.

Hemodynamic Control during Tracheal Intubation. A hemodynamic priority in patients with preeclampsia is to ensure that the hypertensive response to tracheal intubation is ablated. An ideal agent would have fast onset and short duration to allow cautious titration to prevent surges in blood pressure while maintaining adequate uterine perfusion. Additionally, it should have minimal off-target side effects and negligible placental transfer to affect neonatal outcomes. Numerous medications have been used successfully to achieve hemodynamic stability

during tracheal intubation including opioids, β-adrenergic antagonists, directly acting vasodilators, α2-agonists, and local anesthetic agents. Specific drugs are detailed in table 4.

The decision to use one agent over another requires individualization based on the side effects and contraindications of each drug or drug combination with regard to the patient's comorbidities, the availability of the medication, and the anesthesiologist's experience and medication preference. Neonatologists should be informed about the use of opioids so that they can anticipate and manage neonatal respiratory depression. If the patient is receiving magnesium sulfate, nondepolarizing neuromuscular blocking agents' duration of action will be prolonged due to potentiation by magnesium. Magnesium sulfate does not affect the duration of action of succinylcholine.

Hemodynamic Control during Tracheal Extubation. When performing tracheal extubation in patients with preeclampsia, hypertensive responses may result from three main sources: the return of sympathetic tone due to arousal and loss of vasodilatory effects from waning plasma levels of anesthetic agents; additional sympathetic stimulation from oropharyngeal suction, tracheal tube–related laryngeal stimulation and surgical pain; and the return of upper airway reflexes that may trigger coughing and bucking on the tracheal tube.

To manage surgical pain, an intraoperative morphine equivalent dose up to 25 to 30 mg may be required.[136] The effectiveness of pain control can be evaluated by assessing the patient's spontaneous respiratory rate under general anesthesia before extubation. If the respiratory rate is fewer than 20 breaths/min, then it is likely that pain is not severe. The use of abdominal wall fascial plane blocks (transversus abdominis plane, quadratus lumborum) are especially helpful in patients who have had general anesthesia for cesarean delivery and no neuraxial morphine.[137] Heightened vigilance and care when undertaking oropharyngeal suctioning is important in this population. Some medications used to control hypertensive tracheal intubation responses can be used for tracheal extubation (table 4).

Specific Intraoperative Issues

Intraoperative Fluid Management. Assessment of fluid status in patient with preeclampsia with severe features can be difficult because of the confounding issues of the presence of hypertension, organ derangement, peripheral edema, intraoperative fluid losses, and lack of readily available assessments of stroke volume and cardiac output. Transthoracic echocardiography provides valuable information about left ventricular volume status but requires a skilled practitioner for reliable measurement and interpretation and is challenging in the intraoperative setting. There are limited generalizable data on fluid management in patients with preeclampsia with no particular fluid strategy favored over another.[138,139]

Preoperatively, NICE guidelines advise not to preload patients with preeclampsia with IV fluid before low-dose epidural analgesia or combined spinal epidural analgesia, to consider a 500-ml crystalloid bolus before or concurrently with the first dose of IV hydralazine, and to limit maintenance fluids to 80 ml/h in labor.[25] For an individual patient, inadequate fluid therapy may result in AKI, whereas excessive fluid administration may result in heart failure with preserved ejection fraction with acute pulmonary edema.[43] Ideally, fluid administration in patients with preeclampsia can be individualized based on pulse pressure variation, fluid responsiveness, changes in stroke volume and cardiac output, lung ultrasound assessment of pulmonary edema, respiratory function, renal function, hemoglobin, serum lactate and pH values, and quantitative assessment of blood loss and urine output. A shift to recording fluid intake and output in patients with preeclampsia, and pregnant patients in general, from simply milliliters to instead milliliters per kilogram may enable earlier recognition of the problem of fluid overload or underresuscitation. Indexing of fluids to body weight may enable fluid losses and gains to be classified according to percentage of blood volume, thereby facilitating accurate more effective resuscitation, multidisciplinary team communication, and better patient outcomes. This area is a gap in knowledge and requires further research. In the event of hypotension, IV fluids and vasopressors can both be safely administered to patients with preeclampsia, with cautious titration to avoid a potentially exaggerated response to vasopressors.

Intraoperative Hemorrhage. Intraoperative hemorrhage is common in patients with preeclampsia. The risk of significant hemorrhage, defined using postpartum hemorrhage terminology (postpartum hemorrhage is defined as greater than 500 ml), for patients with preeclampsia is approximately 25% compared to a rate of 3% in the general obstetric population.[19] The increased hemorrhage risk is likely to be multifactorial due to emergency surgery, maternal anemia, thrombocytopenia or HELLP syndrome, concurrent aspirin therapy, increased body mass increasing surgical complexity and operating time, and the presence of hypertension itself. The management of hemorrhage in patients with preeclampsia undergoing cesarean delivery is a significant clinical challenge because it represents the intersection of two major pathologies (preeclampsia and postpartum hemorrhage) combining to increase the risks of maternal morbidity and mortality. Modifiable factors in the antenatal period, such as correction of anemia and iron deficiency and stabilization of blood pressure should be addressed before cesarean delivery when possible, and resuscitation plans should be discussed in a preoperative team huddle.

Like in other obstetric patients, the most common etiology of hemorrhage during cesarean delivery is uterine atony and/or trauma. First-line uterotonics include oxytocin or carbetocin IV (100 μg). There are many oxytocin protocols

Table 4. Pharmacologic Agents Used to Minimize Hypertension during Tracheal Intubation and Extubation in Patients with Preeclampsia

Drug Class	Drug	Dose	Administration	Suggested Maximal Bolus Dose or Infusion	Advantages	Disadvantages
Opioids	Alfentanil	10 μg/kg	IV bolus	25 μg/kg	Rapid onset, less bradycardia than remifentanil	Fetal respiratory depression
	Remifentanil†	0.5–1 μg/kg	Slow IV bolus; maintenance 0.2 μg · kg^{-1} · min^{-1}	2 μg/kg	Rapid onset, short duration, can be titrated as an infusion. Organ independent clearance	Dose-dependent bradycardia and hypotension. Fetal respiratory depression
	Fentanyl	2.5 μg/kg	IV bolus	3–4 μg/kg	Longer duration of analgesia	Slower onset; dose-dependent respiratory depression in the pregnant patient and neonate
β-Adrenergic antagonists	Labetalol*†	0.25 mg/kg	IV bolus greater than 2 min, repeat every 10 min	1 mg/kg (or 80 mg)	Effective at reducing blood pressure due to both β- and α1-adrenergic antagonism	Asthma exacerbation; temporary myocardial depression; fetal bradycardia
	Esmolol†	1–2 mg/kg	IV bolus, may be followed by infusion	2 mg/kg	Rapid onset, short duration, can be titrated as an infusion; organ independent clearance	Asthma exacerbation; temporary myocardial depression; fetal bradycardia
Directly acting vasodilators	Hydralazine	5–10 mg	Slow IV bolus, repeat every 20 min	10 mg/kg	Direct action on arterioles without myocardial depression	Slower onset; may cause tachycardia, hypotension, headache, flushing, and nausea
	Nitroglycerin†	5 μg/min	IV infusion titrate to effect	100 μg/min	Rapid onset and titratable	Tachycardia, hypotension, flushing and headache, potential for uterine atony
	Magnesium sulfate	30–40 mg/kg	IV bolus	40 mg/kg	Effective when combined with opioids (*e.g.*, alfentanil 7.5 μg/kg)	Only partially effective on its own; high cumulative doses prolong neuromuscular blockade and may lead to hypotonia, respiratory depression and arrhythmias
	Sodium nitroprusside	0.25 μg · kg^{-1} · min^{-1}	IV infusion titrate to effect	5 μg · kg^{-1} · min^{-1}	Extremely potent, rapid onset and titratable	Fetal cyanide toxicity; tachycardia, hypotension, flushing, and headache; does not suppress cough reflex; rarely used
Alpha-2 adrenergic agonists	Dexmedetomidine†	0.5–1 μg/kg	IV bolus greater than 15–20 min; maintenance 0.2–0.7 μg · kg^{-1} · h^{-1}	1 μg/kg	Does not depress myocardial contractility or neonatal well-being; opioid-sparing analgesia; very effective at suppressing cough reflex	Slow onset, long half-life, dose-dependent bradycardia, and hypotension; postoperative sedation may delay parent–infant interaction
Local anesthetic agents	Lidocaine†	1.0–1.5 mg/kg	Slow IV bolus	1.5 mg/kg	Rapid onset; effective at suppressing cough reflexes; more efficacious when combined with other agents; analgesic benefits	Dizziness, blurred vision, headache, tinnitus, perioral numbness, and nausea; toxicity associated with hypotension and arrhythmias

*α- and β-adrenergic antagonists. †Has favorable characteristics for use for tracheal extubation.
IV, intravenous.

that can be used in the setting of obstetric hemorrhage; however, in patients with preeclampsia, special care must be taken to avoid fluid overload from excessive oxytocin dilutant solution. A protocol used at the author's institution for patients with preeclampsia with hemorrhage is oxytocin IV 2 to 5 units every 2 to 3 min (up to 10 IU) followed by a low-volume IV infusion (*via* an infusion pump) such as 40 units in 40 ml saline over 4 h. The secondary uterotonic carboprost can be administered 250 μg intramuscularly every 15 min up to 8 doses. The alternative secondary agent methylergonovine (ergometrine) is contraindicated in patients with preeclampsia due to the association between its use and hypertensive crises and death.[33,61,140] Other anesthesiology interventions for hemorrhage include active warming, calcium administration/replacement to prevent critical physiologic derangement of an ionized calcium less than 1.1 mM (4.4 mg/dl),[141] and early effective resuscitation with crystalloid and blood products. These may include packed red blood cells, platelets, fibrinogen (fibrinogen concentrate or cryoprecipitate), and fresh frozen plasma. Concerns regarding fluid overload and the risk of acute pulmonary edema must be weighed against the significant problem of

hypovolemia (from insufficient crystalloid resuscitation), anemia (from insufficient erythrocyte transfusion), and risk of maternal decompensation and potential cardiac arrest in the event of conversion to general anesthesia. Monitoring all fluid input and output including urine output during cesarean delivery is fundamental, and quantitative measurement of blood loss reduces the risk of inaccurate assessment. All available data need to be assimilated (table 3). An arterial line, *via* blood samples, enables repeat testing of key variables and repeat laboratory tests. Viscoelastic testing such as rotational thromboelastometry can be used to assess whole blood coagulation status. Echocardiography can be of value to diagnose and differentiate hypovolemia from the pathologies of heart failure with reduced ejection fraction and/or right heart failure.

The resuscitation aims are to prevent or correct anemia, hypovolemia, acidemia, coagulopathy, and hypothermia. Values suggestive of critical physiologic derangement include hemoglobin of less than 70 g/l, pH less than 7.2, base excess worse than −6, lactate greater than 4 mM, platelet count less than 50×10^9/l, prothrombin time greater than 1.5 × normal, international normalized ratio greater than 1.5, activated partial thromboplastin clotting time greater than 1.5 × normal, fibrinogen level less than 2.0 g/l, and body temperature less than 35°C (95°F).[141]

Conversion to General Anesthesia. Conversion from neuraxial anesthesia to general anesthesia is a very high-risk situation for maternal morbidity and mortality. Reasons for conversion to general anesthesia include patient discomfort, inadequate neuraxial anesthesia, intraoperative hemorrhage, prolonged surgery, or high neuraxial block with inadequate ventilation.

The 7th National Audit Project of the Royal College of Anaesthetists of the United Kingdom reported a 1 in 8,600 (95% CI, 5,700 to 13,700) risk of perioperative cardiac arrest in obstetric patients undergoing cesarean delivery. The specific context of hypovolemia from intraoperative hemorrhage with required conversion to general anesthesia was identified as a cause of maternal cardiac arrest,[142] highlighting the importance of sufficient crystalloid and erythrocyte transfusion before general anesthesia. In an analysis of complications reported over a 23-yr period to webAIRS, a voluntary reporting database system available to anesthesia clinicians registered with the Australian and New Zealand College of Anaesthetists, the Australian Society of Anaesthetists, and the New Zealand Society of Anaesthetists, difficult tracheal intubation at the time of conversion to general anesthesia was reported as a serious problem in 28 (6%) patients.[143] For patients with preeclampsia, the risks are greater due to increased likelihood of airway edema, the risk of hemodynamic instability (hypertension), and increased risk to the fetus if temporary oxygen desaturation occurs during airway manipulation in the pregnant patient because of a decrease in placental reserve relative to healthy pregnancies.

Conversion from neuraxial to general anesthesia places a high and complex cognitive load onto the anesthesiologist because it includes rapid preparation for and management of a potentially difficult tracheal intubation in conjunction with management of the complication that led to the requirement for conversion to general anesthesia, while preparing and reassuring a usually conscious patient. For these reasons, it is helpful to request a second anesthesiologist, when available. Additional personnel (*e.g.*, a trained nurse or anesthesia assistant) can also be requested if a second anesthesiologist is not available.

Postoperative Management

Location of Care

Postoperative management of patients with preeclampsia, particularly those with complications, should be in a higher acuity area to enable appropriate monitoring by staff with sufficient training. The exact location and monitoring or frequency and duration of blood lab value testing cannot be generalized or universal, because it is hospital dependent and determined by local protocols, staffing models, and local factors that determine the safest management.[144] Locations for recovery may include the labor and delivery unit, maternity ward, or a critical care environment. Wherever the location, patients generally appreciate and prioritize contact with their newborn whether that be in the same room, in the case of healthy term or near-term baby, or *via* a contemporary video or other link with the special care or neonatal intensive care unit.

Postoperative Pain Management

Postoperative pain management in women who undergo cesarean delivery for preeclampsia is an inadequately researched area.[145,146] There are conflicting data regarding the safety of nonsteroidal anti-inflammatory drugs (NSAIDs) for postpartum pain management in patients with preeclampsia, specifically related to a potential risk for worsening hypertension. The International Society for the Study of Hypertension in Pregnancy recommends the use of NSAIDs in situations both in and out of hospital when other analgesia may not be effective, blood pressure is controlled, and there is no AKI or chronic kidney disease, sepsis, or hemorrhage.[37] The Society for Obstetric Medicine in Australia and New Zealand has undertaken a comprehensive review of NSAIDS in patients with preeclampsia. Based on the limited literature of four randomized controlled trials of moderate to very low quality of evidence, and a combined sample size of 170 patients in each arm, Society of Obstetric Medicine Australia and New Zealand recommends against the use of NSAIDs after hospital discharge and limits their recommended use to only the short term during hospitalization.[24] There are no recommendations regarding long-acting NSAIDs in this setting, but it

is reasonable to use short-acting NSAIDs for hospitalized patients with preeclampsia to enable titration or cessation if hypertension is problematic.

Tramadol is an effective analgesic agent; however, it lowers seizure threshold. There is no guidance regarding the use of tramadol in patients with preeclampsia including those with cerebral irritation. In the absence of level 1 evidence, it may be prudent to avoid prescribing tramadol in patients with preeclampsia with severe neurologic features due to the risk of eclampsia. Individualized multimodal analgesia is advocated using agents including neuraxial morphine, regional blocks, acetaminophen, and systemic opioids.

Management of Postoperative Hypertension and Breastfeeding

For patients with preeclampsia, hypertensive agents used in the antepartum period should be continued in the postpartum period to achieve a diastolic blood pressure target less than 85 mmHg. Breastfeeding is recommended and not contraindicated in context of continued antihypertensive therapy.[37] There are no specific recommendations for the subgroup of patients who have undergone cesarean delivery; however, the recommendations to continue antihypertensive agents appear appropriate for this group of patients. The use of angiotensin-converting enzyme inhibitors such as captopril, enalapril, and quinapril is supported and guided by up-to-date information such as is found in LactMed.[147]

Management of Postoperative Fluids and Oliguria

Once blood loss has been replaced, patients with preeclampsia usually have their IV fluids restricted (*e.g.*, 1,000 ml over 24 h and ceased earlier if the patient is drinking) to reduce the risk of pulmonary edema. Spontaneous diuresis usually occurs within the first 12 to 18 h postoperatively.[148] Postoperative oliguria, defined as $0.5\,ml \cdot kg^{-1} \cdot h^{-1}$ for longer than 6 h, may occur and is often multifactorial.[149] In the presence of normal renal function, stable creatinine levels, normal respiratory function, and appropriate resuscitation from any intraoperative hemorrhage, IV fluid boluses are not recommended, and usually no treatment is required.[150] Postoperative oliguria can, however, be associated with worsening postpartum hypertension and pulmonary edema; therefore, to reduce these risks, short-term loop diuretics such as furosemide 20 IV (or orally if no IV access) may be administered.[24]

Pharmacologic Thromboprophylaxis

Patients with preeclampsia are at increased risk of venous thromboembolism after cesarean delivery.[151] Like patients without preeclampsia undergoing cesarean delivery, mechanical thromboprophylaxis is indicated. In addition, most patients with preeclampsia who have undergone cesarean delivery will meet criteria for pharmacologic venous thromboprophylaxis.[152] Appropriate timing after neuraxial anesthesia and weight-based dosing for thromboprophylaxis is necessary. The Society for Obstetric Anesthesia and Perinatology recommend waiting greater than or equal to 12 h after the neuraxial technique and greater than or equal to 4 h after epidural catheter removal before initiating or restarting low-molecular-weight heparin thromboprophylaxis.[153] Thorough risk–benefit analyses need to be performed in postoperative patients with preeclampsia, especially those with additional risk factors for venous thromboembolism, to ensure that earlier pharmacologic thromboprophylaxis is not warranted.

Mental Health and Well-being

Adverse mental health outcomes such as anxiety and depression, posttraumatic stress disorder, and postpartum mood disorders in patients with preeclampsia are increasingly being reported and acknowledged.[154,155] There is little current focus on perioperative preventative measures in this cohort, and this represents a significant knowledge gap. In addition to the care anesthesiologists already provide to patients with preeclampsia, anesthesiologists may be able to engage in other activities that may positively affect the mental health of patients with preeclampsia. These activities include involvement in antenatal classes that specifically include tours of operating suites of hospitals, upskilling in delivering specific trauma-informed care, and advocating for the presence of a support person throughout the entire patient perioperative journey. Consumer engagement and implementation programs are needed in this area.

Long-term Follow-up

In 2011, the American Heart Association drew attention to the fact that patients with preeclampsia are at risk of developing cardiovascular disease in the future by including a history of preeclampsia as a major risk factor for cardiovascular disease in women.[156] After 13 yr, postoperative implementation of risk reduction programs in this population have not transpired.[157] In an attempt to address this, Celi *et al.*[158] created a Cardiometabolic Clinic, a transitional clinic for postpartum women after hypertensive pregnancies. The Cardiometabolic Clinic applies a four-pillar approach: early postpartum management of hypertension, education about cardiovascular disease risk for both patients and providers, transition to primary care, and creation of a sustainable clinical model.[158] In a 5-yr pilot, the Cardiometabolic Clinic was sustainable from a financial standpoint, and patients were receptive to blood pressure and medication management, nutrition consultation, healthy heart lifestyle coaching, and successful transition for follow-up with their primary care physician. Programs such as this are needed on a more widespread basis.

Future Research and Clinical Directions

Alignment with the American Heart Association Definition of Hypertension

In 2017, the American Heart Association and the American College of Cardiology updated the definition of stage 1 hypertension in nonpregnant adults from greater than or equal to 140/90 mmHg to greater than or equal to 130/80 mmHg.[159] These new criteria have not been applied for the diagnosis of preeclampsia. There are suggestions that this is because such a change may not be cost-effective or reduce adverse outcomes[160]; however, evidence suggests that a hypertension threshold of greater than or equal to 130/80 mmHg is associated with better identification of maternal and neonatal risks including evolution to preeclampsia with severe features including eclampsia.[161,162] Seven years have now elapsed since the American Heart Association/American College of Cardiology updated the definition of hypertension in nonpregnant adults in an effort to reduce morbidity and mortality in the general adult population. It is now imperative that the blood pressure threshold for the definition of hypertension in pregnant patients be urgently reviewed and maternal and fetal outcomes assessed within this framework so that the pregnant population may also benefit in the short and long term.[163]

Management of Myocardial Injury after Cesarean Delivery

The issue of myocardial injury after noncardiac surgery, defined as cardiac troponin concentrations exceeding the 99th percentile of the upper reference limit, is a perioperative issue that is being increasingly recognized in contemporary literature.[164] Experienced by approximately 20% of nonpregnant patients after major inpatient surgery, it is strongly associated with short- and long-term mortality. Risk factors include preoperative hypertension, diabetes, emergency surgery, hemorrhage, fluid shifts, platelet and coagulation changes, hypotension, tachycardia, bradycardia, anemia, heart failure, and fluid overload, all of which may occur in patients with preeclampsia undergoing cesarean delivery. In addition, recent data suggest that women who have had preeclampsia are at future risk of myocardial injury after noncardiac surgery in surgery, separate from cesarean delivery.[165] To address the issue of myocardial injury after noncardiac surgery, the American Heart Association recommends that surveillance for myocardial injury by measuring cardiac troponin levels during the first 2 to 3 days after noncardiac surgery in high-risk patients is warranted.[164] Early intervention in patients who develop myocardial injury after noncardiac surgery may include medical therapy such as aspirin.[166]

There are no studies exploring the risk of myocardial injury after cesarean delivery. This represents a significant knowledge gap and major deficiency, given that patients with preeclampsia are at higher risk of short- and long-term cardiovascular complications, morbidity, and mortality. There is an urgent need to examine this issue, including establishing baseline classification of B-type natriuretic peptide, N-terminal pro-B-type natriuretic peptide, cardiac troponin, electrocardiography, and transthoracic echocardiography in patients with and without preeclampsia, and their relationship with short- and long-term cardiovascular outcomes after cesarean delivery. The detection of myocardial injury after cesarean delivery may represent a modifiable factor to reduce long-term cardiovascular complications in patients with preeclampsia.[164]

Summary

Patients with preeclampsia who undergo cesarean delivery are high-risk surgical patients who experience short- and long-term adverse outcomes. Anesthesiologists play a major role in reducing the morbidity and mortality from preeclampsia in the perioperative period by optimizing patients preoperatively, performing resuscitation in critical emergencies, facilitating safe anesthesia for surgery, managing intraoperative emergencies including hemorrhage, and optimizing patient analgesia and fluid in the postoperative period. Anesthesiologists can also apply their knowledge of analgesia, anesthesia, and the intraoperative environment to provide antenatal education and prepare patients with preeclampsia for surgery. With an understanding of perioperative cardiovascular adverse events, anesthesiologists can help identify and reduce cardiovascular risk in patients with preeclampsia. By incorporating the considerations included in this review, obstetric anesthesiologists can advocate for patients with preeclampsia who undergo surgery and provide care for these high-risk cardiovascular patients that is equitable, optimized, and safe.

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