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Labor Analgesia: How Can I Improve my Practice?

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We have not quite reached the asymptote of the labor analgesia dose response curve. Childbirth is one of the most painful experiences a patient can undergo. The degree of pain experienced, and the quality of pain relief affect patients' satisfaction with childbirth and may have long-term emotional and psychological effects. The quality of neuraxial analgesia has exceeded parenteral opioids, nitrous oxide, and nonpharmacologic measures, with limited effect on the mode of delivery and maternal and neonatal outcomes. Despite new techniques for labor epidural analgesia (LEA) initiation such as the Dural Puncture Epidural (DPE) or how we deliver epidural medications with Programmed Intermittent Epidural Bolus (PIEB) variance in patient response eludes perfection. In the past decade the evolution of LEA has targeted an enhanced labor experience and successful cesarean anesthesia. This refresher course lecture will provide a detailed review of the evidence to help clinicians provide our patients with a more ideal labor pain experience.

Initiation of Labor Analgesia

Neuraxial analgesia is the gold standard for childbirth pain management. Epidural bolus (EpB) and combined spinal epidural (CSE) technique is the most widely used methods for initiating LEA. In the past the primary form of LEA initiation was a loading EpB. An EpB provides a gradual onset of analgesia with larger volume, low concentrations of local anesthesia with or without opioids. This can be advantageous in cases where large hemodynamic changes may be detrimental. Even with modern low concentrations epidural solutions (e.g. bupivacaine 0.0625%) initiation of analgesia can be slow and motor blockade more dense than is desirable.

In 1989, when LEA was not as widely used Dr. Leighton et al. hypothesized that a combination of intrathecal (IT) morphine and fentanyl might provide a more satisfactory analgesia. The combination of the two did provide a more reasonable analgesia with only a few women then requesting an epidural - this was a jumpstart on the use of IT opioids as part of labor analgesia. In a typical CSE technique, after the epidural space is identified, a spinal needle passed through the epidural needle to puncture the dura-arachnoid membrane and enter the subarachnoid space. Through the spinal needle, a local anesthetic agent, opioid, or both are administered to initiate labor analgesia. A catheter is then inserted through the epidural needle into the epidural space to provide continuous LEA. A CSE exploits the IT space providing fast, reliable lumbosacral analgesia followed by titration of the epidural component. CSE has always represented an elegant, rapid, reliable, and selective childbirth pain management option. Labor progress and obstetric outcomes are similar among patients receiving either CSE or EpB analgesia initiation. The common and most discussed side effects of a CSE are similar to those observed with EpB LEA initiation - hypotension and transient fetal heart rate abnormalities. The administration of IT analgesia has been associated with uterine tachysystole and subsequent fetal bradycardia, but so has EpB – we'll get to the details. The likely determining factor is a decrease in tocolytic-like effects of catecholamine levels with LEA initiation leads to unopposed increase in uterine tone, decreased placental blood flow and eventual fetal bradycardia.

The DPE technique is the latest development in the evolution of LEA initiation. Like a CSE, the DPE passes a spinal needle through the epidural needle to create a dural puncture. However, with a DPE no medications are administered through the spinal needle. After a EpB a small amount of epidural medication flows into the IT space. This "translocation" is thought to be responsible for the possible benefits of the DPE technique. With no medications directly administered into the IT space in contrast to a CSE, the DPE is postulated to reduce the side-effects associated with a CSE. Compared with EpB the DPE technique may have a median time to adequate analgesia less than or equal to EpB. A systematic review showed substantial heterogeneity in results of research comparing DPE to EpB, suggesting inconsistencies in analgesic outcomes, limited differences related to catheter replacement and manipulation, and insufficient evidence to draw conclusions related to headaches and fetal heart rate abnormalities.

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Maintenance of Labor Analgesia

LEA regimens in North America and Europe consist of a local anesthetic in combination with an opioid. These solutions are delivered via continuous epidural infusion (CEI) with or without patient-controlled epidural analgesia (PCEA) boluses. There has been an evolution of labor analgesia, rather than delivering the local anesthetic continuously, small regularly spaced intermittent boluses may lead to a more extensive spread of local anesthetic in the epidural space. The same dose of local anesthetic given via a PIEB may provide improved analgesia. PIEB uses a programmed infusion pump to administer intermittent boluses of epidural solution to maintain analgesia. Systematic reviews have shown that the use of PIEB is associated with several clinically important outcomes such as improved patient satisfaction, reduced local anesthetic consumption and possibly the need for decreased interventions for inadequate analgesia.

Multiple studies compared intermittent epidural boluses to traditional CEI there are no significant differences in mode of delivery between PIEB and CEI. However, there have not been large enough randomized trials between PIEB and CEI to really understand if they equally have little impact on childbirth other than analgesia. The results of RCTs on PIEB are generalizable to parous women and the PIEB regimen has to recognize the more rapid and potentially more painful labor of parous women. PIEB requires many dosing parameters be set which include the interval in which the first bolus is delivered, the bolus interval for the maintenance of labour analgesia and the amount of local anesthetic solution to deliver. There has been limited evidence available to guide the permutations of dose or interval for PIEB for any given local anesthetic solution. The optimal regimen for PIEB eludes us however, one can glean from the series of research what might be an evidence informed set of PIEB variable to safely deliver labor analgesia with modern low-concentration local anesthetic solutions.

Key References

1. George RB, Allen TK, Habib AS: Intermittent epidural bolus compared with continuous epidural infusions for labor analgesia: A systematic review and meta-analysis. Anesth Analg 2013; 116:133–44
2. Carvalho B, George RB, Cobb B, McKenzie C, Riley ET: Implementation of Programmed Intermittent Epidural Bolus for the Maintenance of Labor Analgesia. Anesth Analg 2016 doi:10.1213/ANE.0000000000001407
3. Munro A, George RB: Programmed intermittent epidural boluses (PIEB) for maintenance of labor analgesia: A superior technique and easy to implement. Turk Anesteziyoloji ve Reanimasyon Dern Derg 2017; 45:70–2
4. Munro A, George RB: Programmed intermittent epidural boluses (PIEB): A superior technique for maitenance of labor analgesia. Turk Anesteziyoloji ve Reanimasyon Dern Derg 2017; 45:67–9
5. Sng BL, Sia ATH: Maintenance of epidural labour analgesia: The old, the new and the future. Best Pract Res Clin Anaesthesiol 2017; 31:15–22
6. Lange EMS, Wong CA, Fitzgerald PC, Davila WF, Rao S, McCarthy RJ, Toledo P: Effect of Epidural Infusion Bolus Delivery Rate on the Duration of Labor Analgesia: A Randomized Clinical Trial. Anesthesiology 2018; 128:745–53
7. Bullingham A, Liang S, Edmonds E, Mathur S, Sharma S: Continuous epidural infusion vs programmed intermittent epidural bolus for labour analgesia: a prospective, controlled, before-and-after cohort study of labour outcomes. Br J Anaesth 2018; 121:432–7
8. Kocarev M, Khalid F, Khatoon F, Fernando R: Neuraxial labor analgesia: A focused narrative review of the 2017 literature. Curr Opin Anaesthesiol 2018; 31:251–7
9. Xu J, Zhou J, Xiao H, Pan S, Liu J, Shang Y, Yao S: A Systematic Review and Meta-Analysis Comparing Programmed Intermittent Bolus and Continuous Infusion as the Background Infusion for Parturient-Controlled Epidural Analgesia. Sci Rep 2019; 9:1–12

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10. Wong CA, Mercier FJ: Programmed intermittent epidural bolus technique for maintenance of labour analgesia: does it work for everyone? Br J Anaesth 2019; 123:e190–3
11. Gabriel L, Young J, Hoesli I, Girard T, Dell-Kuster S: Generalisability of randomised trials of the programmed intermittent epidural bolus technique for maintenance of labour analgesia: a prospective single centre cohort study. Br J Anaesth 2019; 123:e434–41
12. Krawczyk P, Piwowar P, Salapa K, Lonc T, Andres J: Do Epidural Catheter Size and Flow Rate Affect Bolus Injection Pressure in Different Programmed Intermittent Epidural Bolus Regimens? An In Vitro Study. Anesth Analg 2019; 129:1587–94
13. Morau E, Jaillet M, Dadure C, Storme B, Bonnin M, Nogue E, Nagot N, Chassard D, Benhamou D: Does programmed intermittent epidural bolus improve childbirth conditions of nulliparous women compared with patient-controlled epidural analgesia?: A multicentre, randomised, controlled, triple-blind study. Eur J Anaesthesiol 2019; 36:755–62
14. Ojo OA, Mehdiratta JE, Gamez BH, Hunting J, Habib AS: Comparison of programmed intermittent epidural boluses with continuous epidural infusion for the maintenance of labor analgesia: A randomized, controlled, double-blind study. Anesth Analg 2020; 130:426–35
15. Roofthooft E, Barbé A, Schildermans J, Cromheecke S, Devroe S, Fieuws S, Rex S, Wong CA, Velde M Van de: Programmed intermittent epidural bolus vs. patient-controlled epidural analgesia for maintenance of labour analgesia: a two-centre, double-blind, randomised study†. Anaesthesia 2020; 75:1635–42
16. Song Y, Du W, Zhou S, Zhou Y, Yu Y, Xu Z, Liu Z: Effect of Dural Puncture Epidural Technique Combined with Programmed Intermittent Epidural Bolus on Labor Analgesia Onset and Maintenance: A Randomized Controlled Trial. Anesth Analg 2021; 132:971–8
17. Heesen M, Hattler J, Klimek M, Rossaint R: In Response: Combined Spinal Epidural Analgesia With or Without Intrathecal Injection. Anesth Analg 2017; 124:1014
18. Richardson MG, Baysinger CL: Dural Puncture Epidural Technique: Not so Fast. Anesth Analg 2017; 125:700
19. Cook TM, Counsell D, Wildsmith JAW: Major complications of central neuraxial block: Report on the Third National Audit Project of the Royal College of Anaesthetists. Br J Anaesth 2009; 102:179–90
20. Leighton BL, DeSimone CA, Norris MC, Ben-David B: Intrathecal narcotics for labor revisited: The combination of fentanyl and morphine intrathecally provides rapid onset of profound, prolonged analgesia. Anesth Analg 1989; 69:122–5
21. Hattler J, Klimek M, Rossaint R, Heesen M: The Effect of Combined Spinal-Epidural Versus Epidural Analgesia in Laboring Women on Nonreassuring Fetal Heart Rate Tracings: Systematic Review and Meta-analysis. Anesth Analg 2016; 123:955–64
22. Gambling D, Berkowitz J, Farrell TR, Pue A, Shay D: A randomized controlled comparison of epidural analgesia and combined spinal-epidural analgesia in a private practice setting: Pain scores during first and second stages of labor and at delivery. Anesth Analg 2013; 116:636–43
23. Contreras F, Morales J, Bravo D, Layera S, Jara Á, Riaño C, Pizarro R, La Fuente N De, Aliste J, Finlayson RJ, Tran DQ: Dural puncture epidural analgesia for labor: A randomized comparison between 25-gauge and 27-gauge pencil point spinal needles. Reg Anesth Pain Med 2019; 44:750–3
24. Goodman SR, Smiley RM, Negron MA, Freedman PA, Landau R: A randomized trial of breakthrough pain during combined spinal-epidural versus epidural labor analgesia in parous women. Anesth Analg 2009; 108:246–51
25. Karen Cristine Abra˜o, MD P, Rossana Pulcineli Vieira Francisco, MD P, Seizo Miyadahira, MD P, Domingos Dias Cicarelli, MD P, Marcelo Zugaib, MD P: Elevation of uterine basal tone and fetal heart rate abnormalities after labor analgesia: A randomized controlled trial. Obstet Gynecol 2009; 113:1374
26. Rupasinghe M, Doyle P: Nonreassuring Fetal Heart Rate Tracings and the Dural Puncture Epidural Technique. Anesth Analg 2017; 124:1014–5
27. Grondin LS, Nelson K, Ross V, Aponte O, Lee S, Pan PH: Success of Spinal and Epidural Labor Analgesia. Anesthesiology 2009; 111:165–72

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28. Wong CA, McCarthy RJ, Sullivan JT, Scavone BM, Gerber SE, Yaghmour EA: Early compared with late neuraxial analgesia in nulliparous labor induction: A randomized controlled trial. Obstet Gynecol 2009; 113:1066–74
29. Shennan AH, MacArthur C, Group C: Effect of low-dose mobile versus traditional epidural techniques on mode of delivery: A randomised controlled trial. Lancet 2001; 358:19–23
30. Ohel G, Gonen R, Vaida S, Barak S, Gaitini L: Early versus late initiation of epidural analgesia in labor: Does it increase the risk of cesarean section? A randomized trial. Am J Obstet Gynecol 2006; 194:600–5
31. Whitty R, Goldszmidt E, Parkes RK, Carvalho JCA: Determination of the ED95 for intrathecal plain bupivacaine combined with fentanyl in active labor. Int J Obstet Anesth 2007; 16:341–5

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Anesthesia for Cesarean Delivery

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Summary:

There are 385,000 births every day around the world, of which 21% will be achieved via cesarean delivery (WHO data), meaning that over 80,000 pregnant people receive anesthesia for cesarean delivery around the world every day. The safe provision of anesthesia for cesarean delivery to the many pregnant people who planned or did not plan to a have a cesarean delivery remains a challenge. Preventing pain during cesarean delivery and the optimal management of pain after cesarean delivery are key to ensure enhanced recovery after cesarean (ERAC) and avoid traumatic experiences. Finally, tackling healthcare disparities is essential to reducing the unacceptably high maternal morbidity and mortality rates in the United States

Objectives:

1. Review the epidemiology of cesarean delivery and associated maternal morbidity and mortality.
2. Describe anesthetic modalities for cesarean delivery and appraise issues related to general anesthesia.
3. Identify select strategies ensuring optimal cesarean delivery neuraxial anesthesia.
4. Assess strategies promoting enhanced recovery and opioid-sparing analgesia after cesarean delivery.
5. Summarize current and future priorities focused on maternal health.

1) Epidemiology of cesarean delivery

Despite global approaches to reduce the cesarean delivery rate worldwide including recommendations to increase the use of elective inductions of labor and promote trials of labor after previous cesarean delivery, the projected cesarean delivery rates by 2030 will continue to increase, with an estimated 28.5% worldwide [1].

Striking the ideal balance between a reduction in the overall cesarean delivery rate without increasing the odds for urgent/emergent cesarean deliveries is complex, with clinical obstetric decisions potentially resulting in unplanned scenarios that could significantly impact anesthetic options. If delivery becomes emergent, the odds for general anesthesia increase, and safe provision of any anesthetic becomes more challenging. For anesthesiologists, predicting and preventing emergent situations is a constant concern driven by the desire to provide anesthesia in the safest manner to facilitate timely delivery of the neonate, while ensuring a positive experience for the patient and family.

Though controversial, the decision-to-delivery interval remains a common auditing tool and has been deemed key to ensure optimal maternal and neonatal outcomes. Obstetric anesthesia practice has significantly evolved, and contemporary approaches for the provision of safe anesthesia in urgent circumstances include (1) neuraxial anesthesia, (2) appropriate communication between obstetricians, perinatologists and anesthesiologists, and (3) ongoing training including drills and simulation. A recent study evaluating the implementation of standardized team communication and processes to improve outcomes during unscheduled cesarean deliveries reported a significant decrease in decision to incision time intervals post-implementation [2].

With the common use of neuraxial anesthesia in obstetrics, and the corresponding decrease in use of general anesthesia, the risks associated with the latter have decreased over time, as has anesthesia-related maternal mortality. The availability of improved anesthesia devices and monitoring as well as the establishment of clinical recommendations for anesthesia management of obstetric patients are believed to explain the decrease in morbidity and mortality associated with general anesthesia. Nonetheless, the role of general anesthesia for cesarean delivery has been revisited [3], because despite recent devices facilitating endotracheal intubation and clinical algorithms guiding anesthesiologists facing challenging scenarios, risks and complications of general anesthesia at the time of delivery for both mother and neonate(s) remain significant.

2) Concerns with general anesthesia

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Circumstances where general anesthesia is 'unavoidable and necessary,' including obstetrical (e.g. postpartum hemorrhage) and maternal indications (e.g, patient refusal to receive neuraxial anesthesia, anticoagulation or coagulopathy) will continue to occur; however unnecessary general anesthesia should be avoided whenever possible, as it is associated with a significantly increased risk of anesthesia complications, severe complications, surgical site infection, and venous thromboembolism, but not of death or cardiac arrest [4]. The Society for Obstetric Anesthesia and Perinatology (SOAP) in its Centers of Excellence (COE) benchmark metrics considers that the overall rate of general anesthesia for cesarean deliveries should be lower than 5% [5], and the Royal College of Anaesthetists recommend a rate lower than 1% for elective cesareans and less than 5% for those classified as emergent [6].

- **Securing maternal airway**

The avoidance of risks inherent to airway manipulation, namely aspiration and 'cannot intubate, cannot ventilate, cannot oxygenate' scenarios, has contributed to the widespread use of neuraxial techniques. Although aspiration remains a serious complication of general anesthesia, because it is so rare, reevaluation of fasting instructions for the pregnant patient undergoing cesarean delivery is occurring in the nascent ERAC protocols [7]. A recent multi-center observational study in the United Kingdom of over 2500 cesarean deliveries reported the incidence of failed intubation to be 1:312. The investigators defined 'difficult airway' as either lack of success to intubate the trachea, more than 2 attempts by a senior anesthetist or written documentation of difficult intubation as entered by the provider in the medical record [8]. In a large, multicenter, contemporary study of more than 14,000 general anesthetics for cesarean delivery from the Multicenter Perioperative Outcomes Group (MPOG) database in the United States, the overall risk of difficult intubation was 1:49 with a risk of failed intubation of 1:808 (failed intubation was defined as any attempt at intubation without successful endotracheal tube placement), demonstrating that difficult intubation in obstetrics remains an ongoing concern [9].

- **Intraoperative awareness**

Intraoperative awareness during general anesthesia for cesarean delivery remains a risk as anesthesiologists aim to limit maternal-fetal drug transmission and uterine atony with judicious administration of hypnotic drugs and volatile anesthetics. Data from England (the DREAMY study) reported an incidence of accidental awareness during cesarean delivery of 1:212 [10]. Though rare, consequences of intraoperative awareness can be catastrophic, including post-traumatic stress disorder, sleep disturbances, and interference with activities of daily living.

- **Post-cesarean pain and maternal health after general anesthesia**

Post-cesarean pain may be more significant (worse) and more difficult to treat in patients who had a cesarean delivery under general compared to neuraxial anesthesia. Neuraxial, compared with systemic opioid analgesia, has been found to be the superior approach to analgesia. Beyond the analgesia itself, neuraxial analgesia is associated with earlier return of bowel function, earlier ambulation and shorter lengths of stay than parenteral analgesia [11].

Long term psychological outcomes may be associated with having general anesthesia for cesarean delivery. Several studies show an association between general anesthesia for cesarean delivery and persistent pain beyond the expected healing time [12]. Although controversial, a recent retrospective study using the New York State inpatient database suggested that general anesthesia for cesarean delivery is associated with severe postpartum depression requiring hospitalization as well as self-harm and suicidal ideation [13].

- **Neonatal outcomes with general anesthesia**

For urgent and emergent cesarean deliveries due to fetal concerns, general anesthesia can be seen as the technique of choice to facilitate an expedited delivery. However, general anesthesia for emergent cesarean delivery is associated with lower neonatal Apgar scores, assisted ventilation and admission to the neonatal intensive care unit [14]. Of importance as well, and less often reported, failed maternal intubation is associated with increased neonatal intensive care unit admissions [15, 16]. Therefore, even though general anesthesia may appear to be saving time, maternal risks and neonatal outcomes may not justify such choice [17]. A retrospective study of over 9000 patients undergoing emergent cesarean delivery evaluated operating room-to-incision intervals for general anesthesia, spinal, labor epidural analgesia conversion to anesthesia and combined spinal-epidural (CSE) anesthesia. Despite general anesthesia being associated with shorter times to delivery (6 versus 13, 11 and 24 minutes, respectively), poor neonatal outcomes, defined as lower Apgar scores at 5-minute were more frequent in the general anesthesia cohort [18]. In a

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2019 meta-analysis of 46 studies which compared neuraxial (spinal, epidural and CSE) with general anesthesia, neonates born to mothers who were under general anesthesia had a lower umbilical vein pH and higher rate of Apgar scores below 6 at 1 minute [19]. In fact, the time needed to initiate the anesthetic technique may not be the principal timing issue in question. One of the major factors associated with prolonged delivery time in emergent situations is transporting the patient to the operating room [20]. In a prospective study of 163 patients undergoing urgent cesarean delivery, decision-to-operating room time was 21.6 (± 19.8) minutes [21].

In emergent scenarios, whether for maternal, obstetric or fetal indications, the perceived lack of time to place a neuraxial block or achieve the required sensory level may be the reason for a general anesthetic to be selected [22]. Despite affording the shortest operating room to incision interval time, general anesthesia, even in urgent cesarean deliveries, is not associated with improved neonatal outcomes [18]. Unequivocally, multiple studies evidence worse neonatal outcomes among babies born to mothers receiving general anesthesia for cesarean delivery, even when deemed urgent [14, 23]. Of relevance, all these publications reported on retrospective data.

When time is of the essence, a standard spinal anesthetic approach can be transformed into a rapid sequence spinal (RSS) for urgent cesarean deliveries. This technique, first described in 2003, simplifies the process aiming to avoid the potential risks of general anesthesia [24]. Steps that are not indispensable for spinal anesthesia placement are omitted, which allows rapid delivery of surgical anesthesia with skin incision allowed as the anesthetic is achieving a T4 dermatomal block. In a retrospective review of 25 cases in which an RSS was utilized, the median time for anesthesia, after excluding cases with an identified delay or a prior epidural block, was 8 (6-8) minutes [25].

Breastfeeding success rates have been noted to be affected by mode of anesthesia. Breastfeeding in neonates born to mothers who received general anesthesia for cesarean delivery is more likely to be unsuccessful (longer time to first feeding, increased number of attempts before success, decreased likelihood of breast feeding at six months) [26].

It should be noted that while maternal exposure to general anesthesia has raised concerns about the possibility of fetal neurotoxicity and short and long-term neurodevelopmental delays [27], there is still no robust evidence that the neonate born to a mother undergoing cesarean delivery under general anesthesia may be negatively impacted [28].

3) Neuraxial Anesthesia

Neuraxial anesthesia for cesarean delivery has been, and continues to be, the gold-standard anesthetic for cesarean delivery [29].

- **Conversion of epidural analgesia to cesarean delivery anesthesia**

The successful and safe conversion of intrapartum epidural analgesia to cesarean delivery anesthesia requires active management of epidural analgesia during the process of labor and the recognition of the possible failing epidural catheter [30]. The SOAP COE designation emphasizes the importance of adequate (and expert) staffing, and neuraxial labor analgesia replacement to avoid the need for conversion to general anesthesia. Reported rates for epidural conversion failure range between 0-21%, and risk factors include maternal characteristics (younger age, high body mass index) as well as anesthetic factors (standard epidural rather than CSE initiating labor analgesia) and multiple epidural top-up administration [31]. If intrapartum neuraxial labor analgesia is suboptimal, a *de novo* single shot spinal anesthetic or the placement of a new epidural catheter is a preferable approach to attempting to dose the *in situ* epidural catheter and hope for a good outcome. Understanding the risk, though low, of a high neuraxial block with a de novo spinal anesthetic provided immediately after dosing an epidural catheter is crucial and was reported in the SOAP serious complication repository (SCORE) project [32].

- **Spinal anesthesia**

The SOAP ERAC Consensus Statement identified 25 components (pre- intra- and post-operatively) [33], of which the most relevant are (1) preventing and managing spinal-induced hypotension, (2) preventing and managing nausea and vomiting, (3) maintaining normothermia, (4) optimizing uterotonics, and (5) initiating opioid-sparing multimodal analgesia. I would add to that, preventing and managing shivering and neuraxial-opioid side effects.

There has been an abundance of clinical trials evaluating the 3 pillars to prevent and manage maternal hypotension following spinal anesthesia for cesarean delivery: (1) fluid administration, (2) maternal positioning and (3) vasopressor administration, with numerous systematic reviews and network meta-analysis [34-36]. Understanding that maternal

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hypotension is primarily driven by a decrease in sympathetic tone in the arterial system secondary to the sympathetic block that occurs with neuraxial anesthesia (not by a reduction in central venous pressure due to increased venous capacitance) and that a marked reduction in systemic vascular resistance, only partially mitigated by an *increase* in maternal cardiac output, heart rate and stroke volume, is key to the prevention and management of hypotension that occurs in over 90% of cases. Identifying the best approach(es) should target not only maternal blood pressure but also maternal cardiac output, fetal perfusion, and neonatal outcomes (umbilical arterial pH and base excess are the usually reported markers of neonatal wellbeing). Certain dogmas, such as the 'maternal tilt' to reduce aorto-caval compression, have been revisited [37, 38]; but it remains that up to 8-10% of pregnant patients will experience supine hypotension and that tilting until delivery of the baby may be necessary, no matter how much coloading and vasopressors occur, and tilting should be considered a therapeutic maneuver.

The most recent recommendations are to (1) provide crystalloid co-loading, (2) start phenylephrine infusion at the time of spinal injection, and (3) provide initial maternal 15° left tilt, until it is established that vasopressor administration is maintaining the maternal blood pressure within 10% of baseline value [39]. Ephedrine, due to its significant transplacental transfer, has repeatedly been shown to increase fetal metabolism and neonatal acidosis and should be abandoned (at least prior to delivery) [40]. Norepinephrine has been proposed (since 2105) as a possible strategy to reduce the likelihood of maternal bradycardia that may occur in the setting of phenylephrine administration [41-43]. However, safe administration of norepinephrine for mothers and in the setting of non-planned cesarean deliveries for fetal compromise remains to be confirmed [44, 45]. In low-resource settings, context-specific management accounting for the availability of experienced staff, medication (vasopressor of choice may not be available or pumps or electrical syringes for continued infusions) and monitoring should be made [46].

- **Pain during cesarean delivery under neuraxial anesthesia**

Inadequate neuraxial anesthesia with intraoperative pain is a serious concern that should ideally prevented, but if not prevented, appropriate measures are needed to avoid persistent pain, postpartum depression, and post-traumatic stress syndrome, and to alleviate the traumatic birth experience [47]. Suboptimal pain management during a cesarean delivery is an important cause for malpractice lawsuits in obstetric anesthesia [48]. Dermatomal level testing to light touch (rather than cold) at T5 appears to provide a more reliable assessment and better reflect the adequacy of the surgical block and careful testing before allowing the surgery to proceed is of course key [49]. Two recent practice guidelines shed light on the need to prevent, recognize and manage the failed block [50-52]. Both emphasize the importance of (1) adequate communication with the obstetricians on the degree of urgency, (2) adequate communication with patients, (3) optimal assessment of the block, (4) recognition and adequate management of discomfort or pain during cesarean delivery, (5) debriefing and documentation, and (6) follow-up of all patients experiencing pain during cesarean delivery.

The use of adjuvants analgesia (intravenous medication, nitrous oxide, unexpected epidural medication) to manage intraoperative pain under neuraxial anesthesia has been reported to occur in up to 15% of cases [53], and may include fentanyl, morphine, ketamine, or dexmedetomidine [54, 55]. Anxiolytics should not be given to manage intra-operative pain, as has been highlighted in the recent clinical recommendations [50, 52].

- **Management of complications associated with neuraxial anesthesia and opioids**

Neuraxial morphine is recommended for opioid-sparing multimodal analgesia at cesarean delivery in the United States and is increasingly used as part of ERAC protocols [33]. Common side effects of neuraxial morphine include nausea and vomiting, pruritus, respiratory depression, and sedation. The 2019 SOAP monitoring recommendations for preventing and detecting respiratory depression associated with neuraxial morphine provide an excellent guide allowing the safe administration of tailored doses [56].

The occurrence of hypothermia and shivering remains an issue and the importance of adequate temperature monitoring in patients receiving neuraxial anesthesia for cesarean delivery has been addressed, and although several modalities to prevent intraoperative hypothermia have been tested, the best strategy remains unclear [57]. Shivering is commonly observed intra and post-operatively can be extremely unpleasant. The prophylactic administration of intravenous dexmedetomidine (10mcg) is effective in reducing shivering [58]. While hypothermia does occur with neuraxial local anesthetic alone due to vasodilation and radiant heat loss, the addition of neuraxial opioids has been reported to

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exacerbate this effect. There have been several reports of a distinct syndrome of intrathecal morphine-induced symptomatic hypothermia with temperatures less than 35^0C, subjective warmth, profuse sweating, nausea, vomiting, and pruritus, and the use of intravenous nalbuphine (5mg) was shown to rapidly reverse these symptoms [59].

4) Opioid-sparing multimodal analgesia and special circumstances

Much has been published about optimal post-cesarean pain management to reduce opioid use during delivery hospitalizations and after discharge. The 2021 PROSPECT guidelines reviewed approaches for scheduled cesarean deliveries [60]; however most cesarean deliveries are not scheduled, and patient-specific approaches are key [61].

Stepwise opioid-sparing multimodal analgesia involves neuraxial opioid use, and standard use of non-opioid analgesics (acetaminophen and non-steroidal anti-inflammatory drugs) [62]. For patients with a history of chronic pain or opioid-tolerance (e.g. opioid use disorder, chronic opioid use), management may require prolonged neuraxial analgesia, the use of clonidine or dexmedetomidine, ketamine or gabapentin, although robust data to guide management is still lacking.[63-65]. The most recent SOAP Consensus statement on the antepartum, peripartum and postpartum management of obstetric patients with OUD (currently in press) will be presented as it relates to cesarean delivery management.

A systematic review and network meta-analysis on the use of truncal block techniques, found that transversus abdominal plane (TAP) and quadratus lumborum (QL) blocks are superior to control in the absence of spinal morphine but provide limited additional benefit when spinal morphine is used [66]. Another systematic review and network meta-analysis compared the postoperative analgesic efficacy of TAP blocks with that of wound infiltration for cesarean delivery without neuraxial opioid administration and found both to be equally effective [67].

5) Maternal health priorities

In the latest CDC statistics, more than 1200 women died last year in the United States from pregnancy-related complications, affecting black women 3-4 times more than white women. Racial and ethnic disparities affect neuraxial labor analgesia rates, general anesthesia rates for cesarean delivery, with poorer intraoperative and post-cesarean pain management, thought to be due to implicit bias, structural racism and lack of workforce diversity [68]. Health equity research is needed to better understand the drivers for such disparities in maternal outcomes and identify effective countermeasures [69]. Maternal and reproductive healthcare is a public health emergency in the changing medical and legal landscape in the United States, and evidence-based, ethical, and equitable healthcare policies are critically needed [70].

References:

[1] Betran AP, Ye J, Moller AB, Souza JP, Zhang J. Trends and projections of caesarean section rates: global and regional estimates. BMJ Glob Health 2021;6(6).
[2] Quant HS, Hamm RF, Schwartz N, Srinivas SK. A multidisciplinary approach to improving process and outcomes in unscheduled cesarean deliveries. Am J Obstet Gynecol MFM 2020;2(1):100070.
[3] Ring L, Landau R, Delgado C. The Current Role of General Anesthesia for Cesarean Delivery. Curr Anesthesiol Rep 2021;11(1):18-27.
[4] Guglielminotti J, Landau R, Li G. Adverse Events and Factors Associated with Potentially Avoidable Use of General Anesthesia in Cesarean Deliveries. Anesthesiology 2019;130(6):912-22.
[5] Society for Obstetric Anesthesia and Perinatology (SOAP) https://www.soap.org/centers-of-excellence_program. Last accessed 07/01/2022.
[6] Purva M, Russell I, Kinsella M. Caesarean section anaesthesia: technique and failure rate. Royal College of Anaesthetists Raising the Standards: A Compendium of Audit Recipes 2012.
[7] Sultan P, Sharawi N, Blake L, Carvalho B. Enhanced recovery after caesarean delivery versus standard care studies: a systematic review of interventions and outcomes. Int J Obstet Anesth 2020;43:72-86.
[8] Odor PM, Bampoe S, Moonesinghe SR, Andrade J, Pandit JJ, Lucas DN, et al. General anaesthetic and airway management practice for obstetric surgery in England: a prospective, multicentre observational study. Anaesthesia 2021;76(4):460-71.

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[9] Reale SC, Bauer ME, Klumpner TT, Aziz MF, Fields KG, Hurwitz R, et al. Frequency and Risk Factors for Difficult Intubation in Women Undergoing General Anesthesia for Cesarean Delivery: A Multicenter Retrospective Cohort Analysis. Anesthesiology 2022;136(5):697-708.
[10] Odor PM, Bampoe S, Lucas DN, Moonesinghe SR, Andrade J, Pandit JJ, et al. Incidence of accidental awareness during general anaesthesia in obstetrics: a multicentre, prospective cohort study. Anaesthesia 2021;76(6):759-76.
[11] Ghaffari S, Dehghanpisheh L, Tavakkoli F, Mahmoudi H. The Effect of Spinal versus General Anesthesia on Quality of Life in Women Undergoing Cesarean Delivery on Maternal Request. Cureus 2018;10(12):e3715.
[12] Komatsu R, Ando K, Flood PD. Factors associated with persistent pain after childbirth: a narrative review. Br J Anaesth 2020;124(3):e117-e30.
[13] Guglielminotti J, Li G. Exposure to General Anesthesia for Cesarean Delivery and Odds of Severe Postpartum Depression Requiring Hospitalization. Anesth Analg 2020.
[14] Beckmann M, Calderbank S. Mode of anaesthetic for category 1 caesarean sections and neonatal outcomes. Aust N Z J Obstet Gynaecol 2012;52(4):316-20.
[15] Quinn AC, Kinsella SM, Gorton HJ, Knight M, Columb MO, Robson SC, et al. Neonatal outcomes after failed tracheal intubation during obstetric general anaesthesia for caesarean section: Secondary analysis of a UKOSS case-control study. Eur J Obstet Gynecol Reprod Biol 2017;217:181-2.
[16] Quinn AC, Milne D, Columb M, Gorton H, Knight M. Failed tracheal intubation in obstetric anaesthesia: 2 yr national case-control study in the UK. Br J Anaesth 2013;110(1):74-80.
[17] McDonnell NJ, Paech MJ. General anaesthesia for emergency caesarean delivery: is the time saved worth the potential risks? Aust N Z J Obstet Gynaecol 2012;52(4):311-2.
[18] Palmer E, Ciechanowicz S, Reeve A, Harris S, Wong DJN, Sultan P. Operating room-to-incision interval and neonatal outcome in emergency caesarean section: a retrospective 5-year cohort study. Anaesthesia 2018;73(7):825-31.
[19] Kim WH, Hur M, Park SK, Yoo S, Lim T, Yoon HK, et al. Comparison between general, spinal, epidural, and combined spinal-epidural anesthesia for cesarean delivery: a network meta-analysis. Int J Obstet Anesth 2019;37:5-15.
[20] Wong TC, Lau CQ, Tan EL, Kanagalingam D. Decision-to-delivery intervals and total duration of surgery for Caesarean sections in a tertiary general hospital. Singapore Med J 2017;58(6):332-7.
[21] Temesgen MM, Gebregzi AH, Kasahun HG, Ahmed SA, Woldegerima YB. Evaluation of decision to delivery time interval and its effect on feto-maternal outcomes and associated factors in category-1 emergency caesarean section deliveries: prospective cohort study. BMC Pregnancy Childbirth 2020;20(1):164.
[22] Palanisamy A, Mitani AA, Tsen LC. General anesthesia for cesarean delivery at a tertiary care hospital from 2000 to 2005: a retrospective analysis and 10-year update. Int J Obstet Anesth 2011;20(1):10-6.
[23] Bidon C, Desgranges FP, Riegel AC, Allaouchiche B, Chassard D, Bouvet L. Retrospective cohort study of decision-to-delivery interval and neonatal outcomes according to the type of anaesthesia for code-red emergency caesarean sections in a tertiary care obstetric unit in France. Anaesth Crit Care Pain Med 2019;38(6):623-30.
[24] Scrutton M, Kinsella SM. The immediate caesarean section: rapid-sequence spinal and risk of infection. Int J Obstet Anesth 2003;12(2):143-4.
[25] Kinsella SM, Girgirah K, Scrutton MJ. Rapid sequence spinal anaesthesia for category-1 urgency caesarean section: a case series. Anaesthesia 2010;65(7):664-9.
[26] Lie B, Juul J. Effect of epidural vs. general anesthesia on breastfeeding. Acta Obstet Gynecol Scand 1988;67(3):207-9.
[27] Sprung J, Flick RP, Wilder RT, Katusic SK, Pike TL, Dingli M, et al. Anesthesia for cesarean delivery and learning disabilities in a population-based birth cohort. Anesthesiology 2009;111(2):302-10.
[28] Robbins LS, Blanchard CT, Biasini FJ, Powell MF, Casey BM, Tita AT, et al. General anesthesia for cesarean delivery and childhood neurodevelopmental and perinatal outcomes: a secondary analysis of a randomized controlled trial. Int J Obstet Anesth 2021;45:34-40.

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[29] Mhyre JM, Sultan P. General Anesthesia for Cesarean Delivery: Occasionally Essential but Best Avoided. Anesthesiology 2019;130(6):864-6.
[30] Bauer ME, Mhyre JM. Active Management of Labor Epidural Analgesia Is the Key to Successful Conversion of Epidural Analgesia to Cesarean Delivery Anesthesia. Anesth Analg 2016;123(5):1074-6.
[31] Mankowitz SK, Gonzalez Fiol A, Smiley R. Failure to Extend Epidural Labor Analgesia for Cesarean Delivery Anesthesia: A Focused Review. Anesth Analg 2016;123(5):1174-80.
[32] D'Angelo R, Smiley RM, Riley ET, Segal S. Serious complications related to obstetric anesthesia: the serious complication repository project of the Society for Obstetric Anesthesia and Perinatology. Anesthesiology 2014;120(6):1505-12.
[33] Bollag L, Lim G, Sultan P, Habib AS, Landau R, Zakowski M, et al. Society for Obstetric Anesthesia and Perinatology: Consensus Statement and Recommendations for Enhanced Recovery After Cesarean. Anesth Analg 2021;132(5):1362-77.
[34] Rijs K, Mercier FJ, Lucas DN, Rossaint R, Klimek M, Heesen M. Fluid loading therapy to prevent spinal hypotension in women undergoing elective caesarean section: Network meta-analysis, trial sequential analysis and meta-regression. Eur J Anaesthesiol 2020;37(12):1126-42.
[35] Heesen M, Hilber N, Rijs K, Rossaint R, Girard T, Mercier FJ, et al. A systematic review of phenylephrine vs. noradrenaline for the management of hypotension associated with neuraxial anaesthesia in women undergoing caesarean section. Anaesthesia 2020;75(6):800-8.
[36] Fitzgerald JP, Fedoruk KA, Jadin SM, Carvalho B, Halpern SH. Prevention of hypotension after spinal anaesthesia for caesarean section: a systematic review and network meta-analysis of randomised controlled trials. Anaesthesia 2020;75(1):109-21.
[37] Lee AJ, Landau R, Mattingly JL, Meenan MM, Corradini B, Wang S, et al. Left Lateral Table Tilt for Elective Cesarean Delivery under Spinal Anesthesia Has No Effect on Neonatal Acid-Base Status: A Randomized Controlled Trial. Anesthesiology 2017;127(2):241-9.
[38] Lee AJ, Landau R. Aortocaval Compression Syndrome: Time to Revisit Certain Dogmas. Anesth Analg 2017;125(6):1975-85.
[39] Kinsella SM, Carvalho B, Dyer RA, Fernando R, McDonnell N, Mercier FJ, et al. International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia. Anaesthesia 2018;73(1):71-92.
[40] Ngan Kee WD, Khaw KS, Tan PE, Ng FF, Karmakar MK. Placental transfer and fetal metabolic effects of phenylephrine and ephedrine during spinal anesthesia for cesarean delivery. Anesthesiology 2009;111(3):506-12.
[41] Mercier FJ, Soued M, Morau E, Ngan Kee WD. Noradrenaline for haemodynamic control in obstetric anaesthesia: Is it now a suitable alternative to phenylephrine? Anaesth Crit Care Pain Med 2019;38(6):591-3.
[42] Ngan Kee WD, Lee SW, Ng FF, Tan PE, Khaw KS. Randomized double-blinded comparison of norepinephrine and phenylephrine for maintenance of blood pressure during spinal anesthesia for cesarean delivery. Anesthesiology 2015;122(4):736-45.
[43] Carvalho B, Dyer RA. Norepinephrine for Spinal Hypotension during Cesarean Delivery: Another Paradigm Shift? Anesthesiology 2015;122(4):728-30.
[44] Vallejo MC, Zakowski MI. Old Ways Do Not Open New Doors: Norepinephrine for First-Line Treatment of Spinal Hypotension. Anesth Analg 2018;126(6):1809-11.
[45] Smiley RM. More perfect? Int J Obstet Anesth 2017;29:1-4.
[46] van Dyk D, Dyer RA, Bishop DG. Spinal hypotension in obstetrics: Context-sensitive prevention and management. Best Pract Res Clin Anaesthesiol 2022;36(1):69-82.
[47] Stanford SE, Bogod DG. Failure of communication: a patient's story. Int J Obstet Anesth 2016;28:70-5.
[48] McCombe K, Bogod DG. Learning from the Law. A review of 21 years of litigation for pain during caesarean section. Anaesthesia 2018;73(2):223-30.
[49] Russell IF. At caesarean section under regional anaesthesia, it is essential to test sensory block with light touch before allowing surgery to start. Int J Obstet Anesth 2006;15(4):294-7.

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[50] Plaat F, Stanford SER, Lucas DN, Andrade J, Careless J, Russell R, et al. Prevention and management of intra-operative pain during caesarean section under neuraxial anaesthesia: a technical and interpersonal approach. Anaesthesia 2022.
[51] Landau R, Janvier AS. Are we finally tackling the issue of pain during cesarean section? Anaesth Crit Care Pain Med 2021;40(5):100938.
[52] Keita H, Deruelle P, Bouvet L, Bonnin M, Chassard D, Bouthors AS, et al. Raising awareness to prevent, recognise and manage acute pain during caesarean delivery: The French Practice Bulletin. Anaesth Crit Care Pain Med 2021;40(5):100934.
[53] Patel R, Kua J, Sharawi N, Bauer ME, Blake L, Moonesinghe SR, et al. Inadequate neuraxial anaesthesia in patients undergoing elective caesarean section: a systematic review. Anaesthesia 2022;77(5):598-604.
[54] Davis PR, Sviggum HP, Delaney DJ, Arendt KW, Jacob AK, Sharpe EE. Intravenous Dexmedetomidine as an Adjunct to Neuraxial Anesthesia in Cesarean Delivery: A Retrospective Chart Review. Anesthesiol Res Pract 2021;2021:9887825.
[55] Clevenger K, Maresh B, Graham H, Hammonds K, Hofkamp MP. The use of adjunct anesthetic medication with regional anesthesia and rates of general anesthesia for 1867 cesarean deliveries from 2014 to 2018 in a community hospital. Proc (Bayl Univ Med Cent) 2020;33(4):536-40.
[56] Bauchat JR, Weiniger CF, Sultan P, Habib AS, Ando K, Kowalczyk JJ, et al. Society for Obstetric Anesthesia and Perinatology Consensus Statement: Monitoring Recommendations for Prevention and Detection of Respiratory Depression Associated With Administration of Neuraxial Morphine for Cesarean Delivery Analgesia. Anesth Analg 2019;129(2):458-74.
[57] Chen WA, Liu CC, Mnisi Z, Chen CY, Kang YN. Warming strategies for preventing hypothermia and shivering during cesarean section: A systematic review with network meta-analysis of randomized clinical trials. Int J Surg 2019;71:21-8.
[58] Sween LK, Xu S, Li C, O'Donoghue MA, Ciampa EJ, Kowalczyk JJ, et al. Low-dose intravenous dexmedetomidine reduces shivering following cesarean delivery: a randomized controlled trial. Int J Obstet Anesth 2021;45:49-55.
[59] Bernstein K, Landau R. Neuraxial Morphine-Induced Hypothermia After Cesarean Delivery Managed With Nalbuphine: A Case Report. A A Pract 2020;14(7):e01220.
[60] Roofthooft E, Joshi GP, Rawal N, Van de Velde M, Anaesthesia PWGotESoR, Pain T, et al. PROSPECT guideline for elective caesarean section: updated systematic review and procedure-specific postoperative pain management recommendations. Anaesthesia 2021;76(5):665-80.
[61] Landau R, Richebe P. Tailoring postoperative pain management with a procedure-specific approach: how to best apply this concept to caesarean deliveries. Anaesthesia 2021;76(5):587-9.
[62] Landau R, Romanelli E, Daoud B, Shatil B, Zheng X, Corradini B, et al. Effect of a stepwise opioid-sparing analgesic protocol on in-hospital oxycodone use and discharge prescription after cesarean delivery. Reg Anesth Pain Med 2021;46(2):151-6.
[63] Ring LE, Landau R. Anesthetic management of the parturient with opioid addiction. Int Anesthesiol Clin 2021;59(3):28-39.
[64] Shatil B, Landau R. Opioid Use and Misuse in Pregnancy. Clin Perinatol 2020;47(4):769-77.
[65] Landau R. Post-cesarean delivery pain. Management of the opioid-dependent patient before, during and after cesarean delivery. Int J Obstet Anesth 2019;39:105-16.
[66] El-Boghdadly K, Desai N, Halpern S, Blake L, Odor PM, Bampoe S, et al. Quadratus lumborum block vs. transversus abdominis plane block for caesarean delivery: a systematic review and network meta-analysis(). Anaesthesia 2021;76(3):393-403.
[67] Sultan P, Patel SD, Jadin S, Carvalho B, Halpern SH. Transversus abdominis plane block compared with wound infiltration for postoperative analgesia following Cesarean delivery: a systematic review and network meta-analysis. Can J Anaesth 2020;67(12):1710-27.
[68] Guglielminotti J, Samari G, Friedman AM, Lee A, Landau R, Li G. Nurse workforce diversity and reduced risk of severe adverse maternal outcomes. Am J Obstet Gynecol MFM 2022;4(5):100689.

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[69] Toyobo O, Guglielminotti J, Andreae DA, Andreae MH. Health equity research in obstetric anesthesia. Curr Opin Anaesthesiol 2022;35(3):306-16.
[70] Landau R, Burgart AM, Sutton CD. Loss of access to legal abortion in America: history, implications, and action items for anesthesiologists. Anaesth Crit Care Pain Med 2022:101125.

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Postpartum Hemorrhage: How to Prepare for It, How to Prevent It, and What to Do When Blood is Pooling on the Floor

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Postpartum hemorrhage: A leading cause of maternal mortality and morbidity.

Postpartum hemorrhage (PPH) is excessive bleeding after delivery and can result in major maternal morbidity and mortality. PPH is responsible for 27% of all maternal deaths worldwide.[1] Compared to developing countries, the proportion of maternal deaths due to PPH is substantially lower in developed countries.[2] In the United States, 777 maternal deaths occurred in 2018, of which 38 (4.6%) were due to hemorrhage.[3] The majority of deaths from PPH are potentially preventable,[4, 5] with a major contributory factor being suboptimal care. Examples of suboptimal care include a delayed response to clinical warning signs, ineffective first-line treatment without care escalation, and inadequate blood product use.[5]

PPH can also cause major complications including organ failure from hypoperfusion, disseminated intravascular coagulation (DIC), intensive care admission, severe anemia, and hysterectomy.[6-9] Transfusion, an indicator of severe PPH, impacts 83% of US women who experience severe maternal morbidity (defined as major complications related to labor and delivery).[10] Other observational data indicate that PPH accounts for nearly half of all cases of severe maternal morbidity.[11]

In the US, the PPH rate has increased significantly over time, from 2.7% in 2000 to 4.3% in 2019 (an average annual percent change of 2.6%).[12] Patient-level risk factors do not fully account for the increase in PPH over time. Given the extent of PPH-related maternal morbidity and the rising rate of PPH, a national maternal health priority is to improve how providers prevent and manage severe PPH.

Standardizing PPH management with bundles and protocols

Standardization of multidisciplinary PPH care has become a national maternal health priority.[13] Accumulating evidence indicates that the use of a comprehensive PPH protocol is associated with reduced rates of hemorrhage-related morbidity.[14-18] Across a healthcare system of 29 delivery units, Shields et al. reported, that over 10 months, a standardized protocol was associated with a 26% reduction in blood product use and a non-significant reduction (15%) in the hysterectomy rate compared with a 2-month pre-implementation period.[15] At a state level, implementation of a quality improvement hemorrhage toolkit [19] across 99 California hospitals was associated with a 20% reduction in the rate of severe maternal morbidity.[14]

Benefits from these initiatives led to the foundation of the National Partnership for Maternal Safety (NPMS) Consensus Bundle for Obstetric Hemorrhage.[20, 21] The bundle comprises 4 action domains: Readiness, Recognition and Prevention, Response, and Reporting, and Systems Learning. More recently, the Joint Commission has mandated that hospitals meet specific standards for reducing 'harm related to maternal hemorrhage'. These standards include PPH risk assessment, stage-based management for PPH treatment, access to a hemorrhage cart, staff education programs, conducting drills, review of hemorrhage cases, and educating postpartum women about PPH warning signs after hospital discharge.[22] However, implementing an institution-specific PPH bundle may not, in itself, result in improved outcomes. For example, in a study evaluating adherence to PPH guidelines in 16 Dutch hospitals, key aspects of care were frequently not performed e.g., HR and BP monitoring during active bleeding and urgent blood product orders.[23] Therefore, lead clinicians should continually assess bundle effectiveness and identify deficiencies in the implementation, acceptability, and sustainability of each bundle element.[24, 25] Further research is awaited to determine whether simulation training leads to sustained improvements in care and maternal outcomes.[26]

PPH risk assessment

Identifying women at risk for PPH is a central aspect of risk management. Patients with abnormal placentation (placenta previa; placenta accreta spectrum disorder) are at very high risk for severe PPH and massive transfusion.[27, 28] Among patients without abnormal placentation, other patient-level risk factors have been identified (Table 1).[29, 30] Variables yet to be conclusively linked to an increased or decreased risk of PPH include maternal age, body mass index, educational level; grand multiparity, and fetal presentation [cephalic vs. breech or other].[29]

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Table 1. Established determinants of severe PPH	
Obstetrical	**Intrapartum**
Previous cesarean or PPH	Instrumental delivery
Multiple pregnancies	Cesarean delivery
Abnormal placentation	Retained placenta
Pre-eclampsia	Uterine exploration
Polyhydramnios	Cervical injury
Diabetes mellitus	Gestational age between 41-42 weeks
Uterine fibroids	Prolonged labor
Uterine rupture	Chorioamnionitis
Macrosomia	Labor augmentation with oxytocin
Placental abruption	Labor induction

Because externally validated PPH prediction tools are not available for clinical use, risk assessment tools developed by the CMQCC, AWHONN (Association of Women's Health, Obstetric and Neonatal Nurses, and NYSBOH (New York Safety Bundle for Obstetric Hemorrhage) are based solely on expert opinion[19, 31, 32]. These tools have suboptimal predictive ability and fail to identify up to 40% of women who experience PPH.[33] Further, PPH risk profiles can vary according to delivery mode.[34, 35] Despite these limitations, risk assessment tools may still have utility as cognitive aids.

How important is blood loss measurement?

Blood loss assessment after delivery is entrenched in obstetric practice, with blood loss volume the most commonly used metric for defining PPH. In 2017, the American College of Obstetricians and Gynecologists (ACOG) revised how PPH is defined: cumulative blood loss ≥1,000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after vaginal or cesarean delivery (includes intrapartum loss).[36]

Blood loss can be assessed in several ways - visual estimation, weighing blood-soaked laps or sponges (gravimetric assessment) or measuring the volume of blood in volumetric drapes after vaginal delivery, or suction canisters during cesarean delivery (volumetric assessment).[37] Clinical and simulation studies have shown that quantitative blood loss (QBL), calculated by adding the gravimetric and the volumetric values, is more accurate than visual estimates, especially as up to 30% of actual blood loss is underestimated with visual estimation.[38-40] A commonly held belief is that performing a QBL can lead to an accurate PPH diagnosis and treatment based on the extent of blood loss. However, this theory has been refuted by a large randomized trial that compared the use of blood collection bags to visual estimation in 25,381 vaginal deliveries; similar rates of severe PPH were observed in each group (1.7% vs. 2.1%, respectively).[41] A possible reason for this finding is that the accurate measurement of blood loss may not change how clinicians manage PPH. Because blood loss quantification may occur after the arrest of postpartum bleeding and not during active bleeding, research is needed to evaluate the timing of initiation of QBL measurement and how this relates to the timing of interventions for PPH management.[42]

New approaches to blood loss measurement have been investigated, such as colorimetric approaches.[43-46] Large prospective trials are needed to determine whether this or other approaches result in more timely PPH detection and clinically meaningful improvements in short- and long-term maternal outcomes.[47] In the meantime, clinicians should not rely solely on QBL or arbitrary blood loss cut-offs to decide if and when to call for help, transfuse blood products, or escalate care.[48] Continuous evaluation of vital signs, estimated *rate* and magnitude of blood loss, and clinical responses to early treatment measures should also be performed. Lastly, patients with occult PPH can develop bleeding in the retroperitoneum or pelvis,[49] thus external bleeding may not occur. Clinicians should have a high index of suspicion for an occult PPH in postpartum patients with evidence of hemodynamic disturbance, lower than expected hemoglobin values, hemostatic derangement, and/or worsening acid-base profiles, especially after cesarean delivery. When occult PPH is suspected, a low threshold for obtaining obstetric input, surgical re-exploration, or urgent abdominal imaging (CT) is advised.

Uterine atony: prophylaxis and treatment

Uterine atony is the most common cause of PPH (>70% of cases in the United States).[7] Other causes include; genital tract lacerations, retained placenta, abnormal placentation, coagulation disturbance, and uterine inversion.[9]

Uterine atony prophylaxis: Active management of the third stage of labor (comprising a uterotonic, early cord clamping, and controlled cord traction) was originally introduced to prevent PPH. Data from multiple studies show that severe blood loss is reduced by nearly 70% with active management; anemia, transfusion, and the need for

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additional uterotonics are also less likely.[50] A uterotonic is the most important component because early cord clamping may be harmful and controlled cord traction is of little benefit.[51]

Oxytocin is the first-line drug for uterine atony prophylaxis for vaginal and cesarean deliveries. Research has shown that a small iv dose of oxytocin (0.35 – 1 u) can initiate adequate uterine tone in healthy women undergoing elective and uncomplicated cesarean delivery. [52,53] Based on data from 2 studies, the ED90 for an oxytocin *infusion* in the same setting was low, ranging between 0.27-0.29 u/min.[54, 55] Due to oxytocin receptor desensitization related to labor and intrapartum oxytocin exposure, higher oxytocin doses are needed to achieve adequate uterine tone in women undergoing intrapartum cesarean delivery (ED90 bolus: 2.99 u (95% CI=2.3-3.7u); ED90 infusion=0.74 u/min (95% CI=0.56-0.93u/min).[55, 56] **Carbetocin,** a synthetic oxytocin analog, is licensed for use outside of the United States. Due to its long half-life (40 min), it is typically administered as a bolus. The recommended dose is 100 mcg. The ED90 doses for healthy women undergoing elective and intrapartum cesarean delivery are 14.8 mcg and 121 mcg, respectively.[57-59] Although the ED90 for elective cesarean delivery is low, a prior study found that 20 mcg was not non-inferior to the recommended 100 mcg dose.[60] An expert consensus group has published recommendations for oxytocin and carbetocin dosing for elective and non-elective cesarean delivery (Table 2).[61] A recent meta-analysis suggested that carbetocin may be the most effective prophylactic uterotonic agent, but the reduction in blood loss compared to oxytocin was not clinically meaningful (-55ml).[62]

Table 2. Oxytocin and carbetocin dosing recommendations [61]

	Elective cesarean section	**Intrapartum cesarean section**
Oxytocin bolus for *initiating* adequate uterine tone	1 unit	3 units
Oxytocin infusion for *maintenance* of adequate uterine tone	2.5 – 7.5 u/hr (0.04 – 0.125 u/min)	7.5 – 15 u/hr (0.125 – 0.25 u/min)
Carbetocin	100 mcg >30 s (smaller doses possible; max dose =100 mcg)	100 mcg >30 s (max dose =100 mcg)

Oxytocin has important cardiovascular dose-dependent side-effects: peripheral vasodilatation, hypotension, increased cardiac output (from compensatory tachycardia and stroke volume), and ST depression.[63] In women with hypovolemia from severe atonic PPH, a high-rate, high-concentration oxytocin infusion may further compromise any hemodynamic instability. Carbetocin has similar cardiovascular side effects. A 25% reduction in mean arterial pressure occurs after 5 u oxytocin and 100 mcg carbetocin.[64]

Uterine atony treatment: **A second-line uterotonic** should be considered when the uterus fails to adequately contract in response to oxytocin. Second-line uterotonic use is not rare; in an observational study of over 2.1 million US women, the hospital-specific frequency of second-line uterotonic use was 7% (95% CI=1.7%-25%).[65] The most common second-line uterotonics are methylergonovine (methergine), 15-methyl prostaglandin F2α, and misoprostol. Dosing, contraindications, and side-effects of each agent are presented in Table 3.

Table 3. Second-line uterotonic dosing, contraindications, and side-effects

Drug	**Dose**	**Contraindications**	**Side-effects**
Methylergonovine	IM: 0.2 mg (IV is not recommended); every 2-4 hr	Hypertension, preeclampsia, cardiovascular disease, drug hypersensitivity	Nausea, vomiting, severe hypertension, especially after IV use
Carboprost	IM: 0.25 mg (IV not recommended); every 15-90 min, eight dose max	Asthma, relative contraindication to hypertension, active hepatic, pulmonary, or cardiac disease	Nausea, vomiting, diarrhea, fever (transient), headache, chills, shivering, hypertension, bronchospasm
Misoprostol	600-1000 mcg oral, sublingual, or rectal; 1 dose	Rare, hypersensitivity to medication or prostaglandins	Nausea, vomiting, diarrhea, shivering, fever, headache.

Because clinical criteria are lacking, the author recommends a second-line uterotonic if there is no or poor uterine tone after a cumulative dose of at least 6 u oxytocin (3 x 2 u boluses) in the presence of an oxytocin infusion. This scenario may occur during an intrapartum cesarean delivery after a prolonged or induced labor, chorioamnionitis, or oxytocin augmentation.[34, 66-68]

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Guidelines are silent regarding preferences or ranking for second-line uterotonics. A prior observational study reported that, among women who underwent cesarean delivery, the risk of major hemorrhage-related morbidity was higher for women who received carboprost than methergine (16% vs 9.2%; RR= 1.7; 95% CI=1.2-2.6) after propensity-score matching.[69]

For PPH treatment, oxytocin is more effective and has fewer side effects than misoprostol. In a 2020 Cochrane network meta-analysis,[70] compared with oxytocin, misoprostol was associated with an increased risk of blood transfusion (RR=1.47; 95% CI=1.02-2.14) and additional blood loss of ≥ 1000 ml (RR=2.57; 95% CI=1.00-6.64). The risk of side effects may be increased with misoprostol, including vomiting (RR=2.47; 95% CI=1.37-1.47) and fever (RR=3.43; 95% CI=0.65-18.18). A combination of oxytocin and misoprostol was not associated with a reduced risk of using an additional uterotonic or a blood transfusion compared with oxytocin monotherapy. Similar trends have been reported in a study of 1,721 women comparing atony prophylaxis with oxytocin alone vs. a misoprostol-oxytocin combination (PPH rate=8.3% vs 8.4%; P=0.98)[71] Severe hyperthermia (core temperature>40°C) and shivering associated with misoprostol is well-reported yet underappreciated,[72, 73] with hyperthermic encephalopathy a potential concern.[74, 75] Furthermore, sublingual, vaginal, and rectal misoprostol has a slow onset of action (11, 20, and 100 mins, respectively), and a longer duration (3, 4, and 11 hrs, respectively).[75] The slow onset time and poor effect relative to oxytocin limits its clinical utility as a treatment for acute severe atonic PPH and likely explains the delayed presentation of hyperthermia. Given the current evidence, the author ranks methylergonovine and carboprost as 1st and 2nd choice second-line uterotonics and does not recommend misoprostol as a second-line uterotonic (except when other agents are contraindicated or not available).

Medical and surgical interventions: Several medical and surgical interventions can be considered for treating major or life-threatening PPH. These include: uterine balloon tamponade, interventional radiology, and surgical approaches (uterine compression sutures, vessel ligation, and hysterectomy).[76]

Transfusion management and hemostatic support

Massive transfusion protocol: When the rate and magnitude of blood loss outpace the time required to prepare and transport crossmatched blood products, activation of a massive transfusion protocol (MTP) ensures timely delivery of sufficient types and volumes of blood products to the primary care team.[77, 78] The Stanford MTP includes 6 units of uncrossmatched, blood group O or type-specific RBCs, 4 units of plasma (thawed or liquid), and 1 apheresis platelet unit.[77, 79] Blood products are transported to the labor and delivery unit or operating room in coolers within 5-10 minutes. After establishing surgical and hemostatic control of bleeding, the care team deactivates the MTP and transitions to cross-matched compatible RBCs. The decision to activate an MTP depends on the rate and magnitude of blood loss, PPH etiology, the response to interventions to control bleeding, and maternal hemodynamics.

Formulaic vs goal-directed approaches to transfusion: Based on evidence from the trauma literature, ACOG guidelines recommend formulaic or fixed ratios of RBCs, FFP, and platelets (PLTs).[76] However, no high-quality trial data exist in obstetrics to substantiate this recommendation. Furthermore, marked differences exist between the obstetric and trauma populations in baseline physiology and pathophysiology of coagulopathy related to hemorrhage.[80] Nonetheless, high FFP use has been reported in a retrospective study of 1495 French patients with severe PPH, in which 69% of transfused patients received FFP.[81]

It is unclear whether early FFP transfusion leads to improved maternal outcomes. In an observational study of 1216 women with persistent PPH (defined as ≥1000 ml blood loss refractory to first-line intervention), FFP transfused within 60 minutes of persistent PPH onset was not associated with reduced severe hemorrhage-related morbidity (defined as death, hysterectomy, or arterial embolization) compared with no or later FFP transfusion.[82] Furthermore, the majority of women with severe atonic PPH (up to 3-4L blood loss) typically have normal coagulation profiles and platelet counts when blood products are administered.[83-86] Given the fibrinogen concentration of FFP (median concentration=2mg/ml; range 0.8-3 mg/ml)[87], FFP may paradoxically lower plasma fibrinogen levels in patients who have moderate PPH and normal coagulation indices.[88] Other potential complications associated with high-volume FFP use include hypervolemia, transfusion-associated circulatory overload, and transfusion-related acute lung injury (the commonest cause of transfusion-related death in the US).[89]

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Any decision to transfuse PLTs warrants careful consideration. A retrospective study of 347 women with moderate-to-severe PPH reported a low overall incidence of PLT transfusion (3.4%), with a PLT count less than 75x 10^9/L recorded in only 2% of women.[90] PLT transfusion was more likely in women with thrombocytopenia before PPH onset or consumptive coagulopathies from amniotic fluid embolism or placental abruption. Women with an overall blood loss <5000ml due to uterine atony or trauma were not associated with having a postpartum PLT count less than 75 x 10^9/L. In other observational studies, the incidence of thrombocytopenia (PLTs<50 - 75 x 10^9/L) among women with massive PPH or receiving massive transfusion was less than 16%.[91, 92] Therefore, a fixed ratio approach may expose women with PLT counts above a threshold level of 75 x 10^9/L to unnecessary PLT transfusion. The author advises that physicians maintain a PLT count greater than 50 x 10^9/L during active PPH.

Superstat laboratory tests (+/ROTEM or TEG assays) should be sent at regular intervals (every 20-30 minutes) during active bleeding. Although 'real-time' results are not possible, laboratory and TEG/ROTEM indices still provide valuable trend data to assess the effectiveness of transfusion decision-making, confirm adequate hemostasis after the surgical arrest of bleeding, and can be used to rule in or out coagulopathy.[93, 94] New cartridge-based point-of-care devices (TEG 6S; ROTEM sigma), overall, have similar accuracy to older generation devices and allow for quicker turnaround times for assessing information about clot formation and lysis.[95, 96]

The presence and extent of coagulation disturbance can vary according to PPH etiology. Compared with other PPH etiologies, women with placental abruption can experience the largest fall in platelet count during massive transfusion,[97] the highest rate of platelet transfusion during severe PPH,[90] and significantly lower ROTEM FIBTEM A5 and prolonged EXTEM CT times.[98] The author recommends close hemostatic monitoring of all women with suspected placental abruption for possible consumptive coagulopathy.

Fibrinogen supplementation and tranexamic acid: During the early phase of postpartum bleeding, a Clauss fibrinogen level <200 mg.dl is an important risk factor for progression to severe hemorrhage and increased blood product requirement.[83, 86, 99, 100] Based on expert opinion and guidelines from the International Society for Thrombosis and Hemostasis, The Royal College of Obstetricians and Gynecologists (United Kingdom), and the Association of Anaesthetists of Great Britain and Ireland, a target fibrinogen level of at least 200 mg/dl has been recommended during active obstetric bleeding, even if the PT and APTT indices are normal.[80, 89, 101-104]

Several studies have evaluated the impact of fibrinogen supplementation with fibrinogen concentrate in women with severe PPH. In a randomized trial of 249 women with early PPH, Wikkelso et al. compared a 2 g fibrinogen concentrate versus saline as a pre-emptive treatment.[105] The frequency of RBC transfusion use did not differ statistically between the fibrinogen concentrate vs. saline groups (20% vs. 22%; P=0.88). The lack of effect may be because a few women (2.2%) had a baseline fibrinogen concentration <200 mg/dl.[105] Using ROTEM, Collins et al. performed a multi-center study to compare the number of RBC units transfused among 55 women with PPH and a FIBTEM A5≤15 mm randomized to fibrinogen concentrate versus placebo.[106] Rates of transfusion did not significantly differ between groups (median [IQR] RBC units=1 (0-2) vs. 1[0-2]; fibrinogen concentrate vs. placebo, respectively). A prespecified subgroup analysis suggested that a FIBTEM A5>12 mm or a fibrinogen level >200 mg/dl may be adequate for hemostasis and not require fibrinogen supplementation. A French trial of 437 patients with persistent PPH after vaginal delivery reported no difference in the rate of hemorrhage-related morbidity (≥4 g/dl Hb decrease and/or ≥ 2 unit RBC transfusion) in women randomized to 3 g fibrinogen concentrate versus placebo.[107] However, several observational studies from single obstetric centers suggest fibrinogen concentrate use is associated with higher plasma fibrinogen levels, lower blood loss values, and reduced FFP usage.[108, 109] If time permits, it is preferable to identify significant hypofibrinogenemia or reduced fibrinogen contribution to clot formation (with TEG or ROTEM) before administering fibrinogen concentrate.

Recent evidence suggests that tranexamic acid (TXA), an antifibrinolytic agent that competitively inhibits plasminogen activation, has clinical utility. The World Maternal Antifibrinolytic (WOMAN) trial was a pragmatic, international, double-blind, placebo-controlled, multicenter study in which 20,060 women with PPH were randomized to receive 1-2 g intravenous TXA vs. placebo in addition to usual care.[110] The main findings indicated a small reduction in the risk of death from exsanguination in women assigned TXA vs placebo (1.5% vs. 1.9%, relative risk=0.81, 95% CI=0.65-1.0; P=0.045). Treatment benefit appeared to be strongest if TXA is administered within 3 hours of birth. Based on these findings, the World Health Organization recommends that all women with PPH receive TXA within 3 hours of birth.[111] Because the majority of study sites were in low-income countries, the

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generalizability of the findings for high-income countries is uncertain. Moreover, the death rate from exsanguination among women with PPH is substantially lower in the United States (approximately 38 per 100,000 PPH events)[112] than in the placebo group in the WOMAN trial, a nearly 40-fold difference. The effect of TXA on mortality reduction was of borderline statistical significance,[113] with a number needed to treat of 250. TXA was not associated with a reduction in hysterectomy, intrauterine tamponade, embolization, or arterial ligation). Further, rates of transfusion (54% in both groups) and the mean number of blood units transfused did not significantly differ between groups. Therefore, the potential impact of TXA in reducing maternal morbidity among in hospitals in the developed world is unclear.[114, 115] High doses (>2g) may increase the risk of renal cortical necrosis in hypoperfused patients.[115]

Three high-quality multicenter RCTs investigated the potential utility of TXA for PPH prophylaxis for vaginal and cesarean delivery. The TRAAP1 study examined whether prophylactic TXA reduces the risk of PPH after vaginal delivery compared with placebo in 3891 patients. PPH was defined as at least 500 ml blood loss. The PPH risk did not differ between groups (TXA=8.1% vs. placebo=9.8%; risk ratio=0.83; 95% CI= 0.68-1.01; P=0.07).[116] The TRAAP2 study examined 4431 women undergoing cesarean delivery. In this study, the risk of PPH (defined as a calculated blood loss > 1000 ml or an RBC transfusion) was lower in the TXA group vs placebo group (26.7% vs. 31.6%; adjusted risk ratio 0.84; 0.75 – 0.94; P=0.003).[117] However, no significant between-group differences were observed in measured blood loss. In a US study of 11,000 patients undergoing cesarean delivery randomized to 1g TXA versus placebo, the risk of PPH-related morbidity (death or blood transfusion) was not different (3.6% vs. 4.3%; RR = 0.91; 95% CI: 0.79 – 1.05).[118] No between-group difference was observed in of thromboembolic even rates in these studies. Based upon this evidence, prophylactic TXA should not be used.

References:

1. Say, L. *Lancet Glob Health* **2014,** *2*, e323-33.
2. Kassebaum, N. J. *Lancet* **2014,** *384*, 980-1004.
3. Hoyert, D. L., Maternal mortality in the United States: Changes in coding, publication, and data release; 2018. In *Nat Vital Stat Rep*, National Center for Health Statistics: Hyattsville, MD, 2020; Vol. 69.
4. Berg, C. J. *Obstet Gynecol* **2005,** *106*, 1228-34.
5. Main, E. K. *Obstet Gynecol* **2015,** *125*, 938-47.
6. Bateman, B. T. *Am J Obstet Gynecol* **2012,** *206*, 63 e1-8.
7. Bateman, B. T. *Anesth Analg* **2010,** *110*, 1368-73.
8. Wanderer, J. P. *Crit Care Med* **2013,** *41*, 1844-52.
9. Al-Zirqi, I. *BJOG* **2008,** *115*, 1265-72.
10. Fingar, K. R. Trends and Disparities in Delivery Hospitalizations Involving Severe Maternal Morbidity, 2006–2015 *Healthcare Cost and Utilization Project (HCUP) Statistical Brief #243*, September 2018.
11. Grobman, W. A. *Obstet Gynecol* **2014,** *123*, 804-10.
12. Corbetta-Rastelli, C. M. *Obstet Gynecol* **2023,** *141*, 152-161.
13. Rosenbaum, T. *Clin Obstet Gynecol* **2017,** *60*, 384-393.
14. Main, E. K. *Am J Obstet Gynecol* **2017,** *216*, 298.e1-298.e11.
15. Shields, L. E. *Am J Obstet Gynecol* **2015,** *212*, 272-80.
16. Einerson, B. D. *Am J Obstet Gynecol* **2015,** *212*, 140-4.e1.
17. Shields, L. E. *Am J Obstet Gynecol* **2011,** *205*, 368 e1-8.
18. Skupski, D. W. *Obstet Gynecol* **2017,** *130*, 770-777.
19. California Maternal Quality Care Collaborative. Obstetric Hemorrhage Toolkit V 3.0. https://www.cmqcc.org/ob_hemorrhage/ob_hemorrhage_compendium_of_best_practices
20. Main, E. K. *Obstet Gynecol* **2015,** *126*, 155-62.
21. Council on Patient Safety in Women's Health Care Obstetric Hemorrhage (+AIM). http://www.safehealthcareforeverywoman.org/default.php. .
22. The Joint Commission, R3 Report Issue 24: PC standards for maternal safety. Oakbrook Terrace, IL, 2019.
23. Woiski, M. *Obstet Gynecol* **2018,** *132*, 656-667.
24. De Tina, A. *Anesth Analg* **2019,** *124*, 1045-1050.
25. Duzyj, C. M. *Am J Perinatol* **2020**.

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26. Baldvinsdottir, T. *PLoS One* **2018,** *13*, e0203806.
27. Silver, R. M. *Obstet Gynecol* **2015,** *126*, 654-68.
28. Mhyre, J. M. *Obstet Gynecol* **2013,** *122*, 1288-94.
29. Stachetti, T. *J Global Health Reports* **2019,** *3*, e2019085.
30. Ende, H. B. *Obstet Gynecol* **2021,** *137*, 305-323.
31. American College of Obstetricians and Gynecologists Safe motherhood initiative. Maternal safety bundle for obstetric hemorrhage. https://www.acog.org/-/media/Districts/District-II/Public/SMI/v2/HEMSlideSetNov2015.pdf?dmc=1&ts=20161030T2140151213.
32. AWHONN Postpartum hemorrhage (PPH) risk assessment table. Version 1.0. http://www.pphproject.org/index.asp (accessed May 8).
33. Ende, H. B. *Obstet Gynecol* **2021,** *138*, 924-930.
34. Butwick, A. J. *Anesth Analg* **2017,** *125*, 523-32.
35. Miller, C. M. *J Perinatol* **2017,** *37*, 243-8.
36. American College of Obstetricians and Gynecologists *Obstet Gynecol* **2017,** *130*, e168-e186.
37. American College of Obstetricians and Gynecologists *Obstet Gynecol* **2019,** *134*, e150-e156.
38. Patel, A. *Int J Gynaecol Obstet* **2006,** *93*, 220-4.
39. Al Kadri, H. M. *Arch Gynecol Obstet* **2011,** *283*, 1207-13.
40. Toledo, P. *Anesth Analg* **2007,** *105*, 1736-40.
41. Zhang, W. H. *BMJ* **2010,** *340*, c293.
42. de Vries, P. L. M. *Bjog* **2023**.
43. Lumbreras-Marquez, M. I. *Anesth Analg* **2020,** *130*, 857-868.
44. Rubenstein, A. F. *Am J Perinatol* **2018,** *35*, 655-9.
45. Konig, G. *J Clin Monit Comput* **2018,** *32*, 303-310.
46. Saoud, F. *Am J Obstet Gynecol* **2019,** *221*, 267.e1-267.e6.
47. Chau, A. *Int J Obstet Anesth* **2020,** *42*, 1-3.
48. Hancock, A. *Best Pract Res Clin Obstet Gynaecol* **2019,** *61*, 28-40.
49. Rafi, J. *JRSM Open* **2018,** *9*, 2054270417746059.
50. Begley, C. M. *Cochrane Database Syst Rev* **2019,** *2*, Cd007412.
51. Weeks, A. D. *Best Pract Res Clin Obstet Gynaecol* **2020**.
52. Carvalho, J. C. *Obstet Gynecol* **2004,** *104*, 1005-10.
53. Butwick, A. J. *Br J Anaesth* **2010,** *105*, 92-93.
54. George, R. B. *Can J Anaesth* **2010,** *57*, 578-82.
55. Lavoie, A. *Anesth Analg* **2015,** *121*, 159-64.
56. Balki, M. *Obstet Gynecol* **2006,** *107*, 45-50.
57. Anandakrishnan, S. *Can J Anaesth* **2013,** *60*, 1054-60.
58. Khan, M. *Can J Anaesth* **2014,** *61*, 242-8.
59. Nguyen-Lu, N. *Can J Anaesth* **2015,** *62*, 866-74.
60. Tabl, S. *Anaesthesia* **2019,** *74*, 190-196.
61. Heesen, M. *Anaesthesia* **2019,** *74*, 1305-1319.
62. Jaffer, D. *Am J Obstet Gynecol* **2022,** *226*, 347-365.
63. Dyer, R. A. *Curr Opin Anaesthesiol* **2011,** *24*, 255-61.
64. Rosseland, L. A. *Anesthesiology* **2013,** *119*, 541-51.
65. Bateman, B. T. *Anesth Analg* **2014,** *119*, 1344-9.
66. Nyflot, L. T. *PLoS One* **2017,** *12*, e0175306.
67. Grotegut, C. A. *Am J Obstet Gynecol* **2011,** *204*, 56 e1-6.
68. Al-Zirqi, I. *Am J Obstet Gynecol* **2009,** *201*, 273 e1-9.
69. Butwick, A. J. *Am J Obstet Gynecol* **2015,** *212*, 642 e1-7.
70. Parry Smith, W. R. *Cochrane Database Syst Rev* **2020,** *11*, Cd012754.
71. Quibel, T. *Obstet Gynecol* **2016,** *128*, 805-11.
72. Elati, A. *Obstet Gynecol* **2012,** *120*, 1140-8.

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73. Durocher, J. *BJOG* **2010,** *117*, 845-52.
74. Kaiser, J. *Obstet Gynecol* **2016,** *127*, 1067-9.
75. Gibbins, K. J. *Am J Obstet Gynecol* **2013,** *208*, 181-3.
76. American College of Obstetricians and Gynecologists *Obstet Gynecol* **2017,** *130*, e168-e186.
77. Goodnough, L. T. *Transfusion* **2011,** *51*, 2540-8.
78. Burtelow, M. *Transfusion* **2007,** *47*, 1564-72.
79. Goodnough, L. T. *Curr Opin Anaesthesiol* **2013,** *26*, 208-14.
80. Collis, R. E. *Anaesthesia* **2015,** *70 Suppl 1*, 78-86, e27-8.
81. Deleu, F. *Int J Obstet Anesth* **2020,** *42*, 11-19.
82. Henriquez, D. *JAMA Netw Open* **2019,** *2*, e1915628.
83. Collins, P. W. *Blood* **2014,** *124*, 1727-36.
84. de Lloyd, L. *Int J Obstet Anesth* **2011,** *20*, 135-41.
85. Gillissen, A. *Blood Adv* **2018,** *2*, 2433-2442.
86. Charbit, B. *J Thromb Haemost* **2007,** *5*, 266-73.
87. Levy, J. H. *Anesth Analg* **2012,** *114*, 261-74.
88. Collins, P. W. *Br J Anaesth* **2014,** *113*, 585-95.
89. Levy, J. H. *Transfusion* **2014,** *54*, 1389-405; quiz 1388.
90. Jones, R. M. *Anaesthesia* **2016,** *71*, 648-56.
91. Bell, S. F. *Int J Obstet Anesth* **2021**, 102983.
92. Lasica, M. *Br J Haematol* **2020,** *190*, 618-628.
93. Butwick, A. *Transfusion* **2020,** *60*, 897-907.
94. Dias, J. D. *Anaesthesia* **2022,** *77*, 700-711.
95. Roberts, T. C. D. *Int J Obstet Anesth* **2021,** *47*, 103192.
96. Bell, S. F. *Int J Obstet Anesth* **2022,** *49*, 103238.
97. Green, L. *Br J Haematol* **2016,** *172*, 616-24.
98. McNamara, H. *Anaesthesia* **2019,** *74*, 984-991.
99. Cortet, M. *Br J Anaesth* **2012,** *108*, 984-9.
100. Gayat, E. *Intensive Care Med* **2011,** *37*, 1816-25.
101. Collins, P. *J Thromb Haemost* **2016,** *14*, 205-210.
102. Levy, J. H. *Blood* **2015,** *125*, 1387-93.
103. Royal College of Obstetricians and Gynecologists *BJOG* **2017,** *124*, e106-e149.
104. Klein, A. A. *Anaesthesia* **2016,** *71*, 829-42.
105. Wikkelso, A. J. *Br J Anaesth* **2015,** *114*, 623-33.
106. Collins, P. W. *Br J Anaesth* **2017,** *119*, 411-421.
107. Ducloy-Bouthors, A. S. *Bjog* **2021**.
108. Matsunaga, S. *Sci Rep* **2017,** *7*, 46749.
109. Seto, S. *Int J Obstet Anesth* **2017,** *32*, 11-16.
110. Woman Trial Collaborators *Lancet* **2017,** *389*, 2105-2116.
111. WHO *WHO recommendation on tranexamic acid for the treatment of postpartum haemorrhage*; World Health Organization: Geneva, 2017.
112. Marshall, A. L. *Am J Obstet Gynecol* **2017,** *217*, 344 e1-344 e6.
113. Dobson, G. P. *J Trauma Acute Care Surg* **2017**.
114. Lier, H. *Anesth Analg* **2019,** *129*, 1574-1584.
115. Sentilhes, L. *Expert Rev Hematol* **2019,** *12*, 753-761.
116. Sentilhes, L. *N Engl J Med* **2018,** *379*, 731-742.
117. Sentilhes, L. *N Engl J Med* **2021,** *384*, 1623-1634.
118. Pacheco, L. D. *N Engl J Med* **2023,** *388*, 1365-1375.

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HELLP! How to keep Mothers with Preeclampsia safe!

Clemens M. Ortner, MD, MS, DESA **Palo Alto / CA**

Epidemiology

Hypertension is the most common medical disorder of pregnancy, affecting 6% to 10% of pregnancies.[1,2] It is a leading cause of maternal mortality and together with hemorrhage it accounts for about one-half of all maternal deaths worldwide.[3] Furthermore hypertensive disorders of pregnancy play a major cause for maternal morbidity and ICU admission with 60% adverse outcome being preventable with early diagnosis and appropriate medical management.[4]

Diagnostic criteria

Hypertensive disorders of pregnancy encompass a range of conditions—chronic hypertension, gestational hypertension, preeclampsia, preeclampsia superimposed on chronic hypertension, and eclampsia.

a) Gestational hypertension presents as elevated blood pressure after 20 weeks' gestation without proteinuria (in the absence of chronic hypertension or systemic manifestations of preeclampsia) that resolves by 12 weeks postpartum.[5,6]
b) Preeclampsia is defined as the new onset of hypertension and proteinuria after 20 weeks' gestation. The diagnosis of preeclampsia should also be considered in the absence of proteinuria when any of the following signs or symptoms of end-organ involvement are present: (1) persistent epigastric or right upper quadrant pain, (2) persistent cerebral symptoms, (3) fetal growth restriction, (4) thrombocytopenia, or (5) elevated serum liver enzymes.[1]
c) The term eclampsia is used when central nervous system (CNS) involvement results in the new onset of seizures in a woman with preeclampsia.
d) HELLP syndrome refers to the development of hemolysis, elevated liver enzymes, and low platelet count in a woman with preeclampsia. This condition may be a variant of severe preeclampsia, but this classification is controversial because the disease may represent a pathophysiologic distinct entity.
e) Chronic hypertension involves either (1) systolic blood pressure of 140 mm Hg or higher and/or diastolic blood pressure of 90 mm Hg or higher presenting before pregnancy or before 20 weeks' gestation or (2) elevated blood pressure that fails to resolve after delivery.
f) Chronic hypertension with superimposed preeclampsia occurs when preeclampsia develops in a woman with chronic hypertension before pregnancy. The diagnosis is made in the presence of new onset of proteinuria or when other manifestations of severe preeclampsia appear.

Pathophysiology

Preeclampsia is a complex multisystem disease currently conceptualized as a two-staged disease (figure 1).[7] It is characterized by diffuse endothelial dysfunction associated with poor placental perfusion, maternal endothelial dysfunction and signs of systemic inflammatory response leading to maternal and neonatal complications. Maternal complications include placental abruption, pulmonary edema, acute renal failure, liver failure, and stroke. Neonatal complications include preterm delivery, fetal growth restriction, hypoxic-ischemic neurologic injury, and perinatal death.[7] Although significant advances have been made in the understanding of the pathophysiology of the disease, the specific proximal cause remains unknown. Management is supportive and delivery of the infant and placenta remains the only definitive cure.

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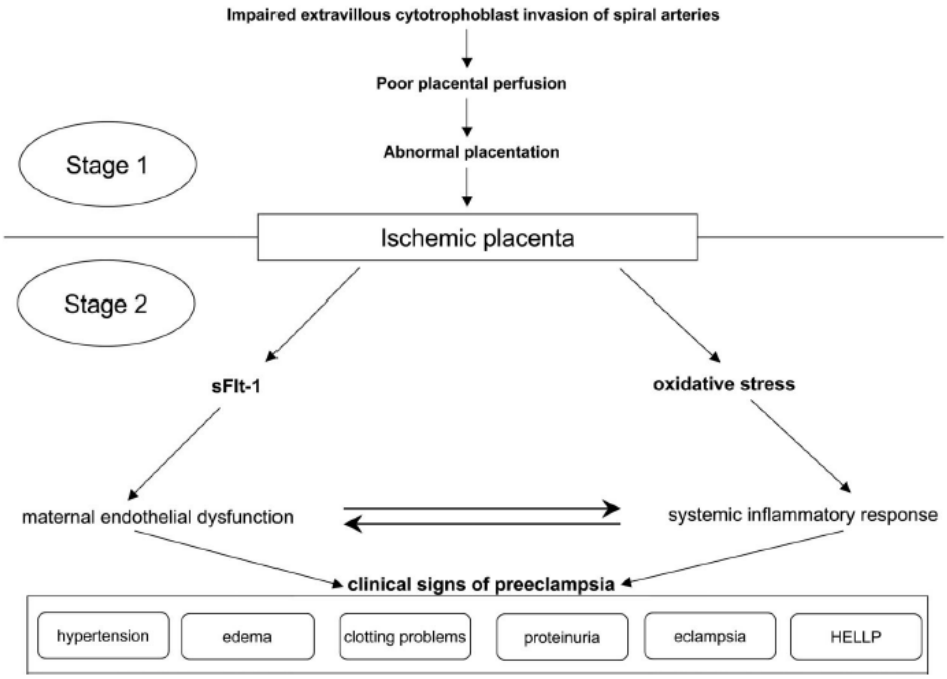
Figure 1:



Cardiopulmonary function

Cardiopulmonary function in women diagnosed with preeclampsia is complex. Patients may present in different hemodynamic states depending on underlying risk factors such as patient age, parity status, history of chronic hypertension, patient BMI, or gestational age.[8] Studies assessing cardiopulmonary status using a pulmonary catheter have shown that most women present in a normo- to hyperdynamic state when untreated. After initiation of antihypertensive treatment and seizure prophylaxis, some women develop decreased cardiopulmonary function. Echocardiographic studies reconfirmed earlier Swan-Ganz studies and describe preeclampsia as an 'ino-vasoconstricted state' with increased systemic vascular resistance, preserved systolic function and increased cardiac output.[9,10] Depending on the study, diastolic dysfunction with raised left ventricular end-diastolic pressures (LVEDP) have been described to be found in 5-20% of preeclamptic women putting them at risk to develop pulmonary edema.[11] Studies using pulmonary ultrasound identified occurrence of symmetric 'comet tail artifacts' indicating interstitial pulmonary syndrome and increased extravascular lung water (EVLW) in up to 25% of women.[12,13] Combining pulmonary ultrasound with transthoracic echocardiography showed an association between interstitial pulmonary ultrasound and increased LVEDPs and suggest using pulmonary ultrasound to predict diastolic dysfunction. Nevertheless, development of clinical pulmonary edema may result as a combination of diastolic dysfunction, low colloid oncotic pressures and endothelial damage at the level of vascular glycocalyx.

Fluid management

Preeclampsia is associated with increased LVEDP, low colloid osmotic pressures and increased capillary permeability rendering the patient at risk to suffer from tissue and pulmonary edema. As a leading cause for ICU admission, 3% of preeclamptic women suffer from pulmonary edema which in 70% of cases occurs in the postpartum period.[14] With excess fluid administration being main risk factor, guidelines suggest restrictive fluid management limiting fluid maintenance to 80ml/hr unless there are other ongoing fluid losses.[15]A fluid pre- or co-load when placing CSE or labor epidural should be avoided, and patients diuresed with furosemide as needed.

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Renal function

Renal manifestations of preeclampsia include persistent proteinuria, changes in the glomerular filtration rate, and hyperuricemia. The presence of proteinuria is a defining element of preeclampsia but is no longer considered essential for diagnosis if other evidence of end-organ injury is present. The characteristic renal histologic lesion of preeclampsia is glomerular capillary endotheliosis, which manifests as glomerular enlargement and endothelial and mesangial cell swelling. [16] During normal pregnancy, the glomerular filtration rate (GFR) increases by 40% to 60% during the first trimester, [17,18] with a resulting decrease in the serum markers of renal clearance, including blood urea nitrogen (BUN), creatinine, and uric acid. In preeclampsia, this increase in GFR is blunted compared with normal pregnancy.[16] Oliguria is a possible late manifestation of severe preeclampsia and parallels the severity of disease. Persistent oliguria requires immediate assessment of intravascular volume status. Progression to renal failure is a rare but serious complication of severe preeclampsia and HELLP syndrome.[19] The true incidence remains unknown. Acute renal failure is divided into three categories: (1) prerenal, which refers to renal hypoperfusion; (2) intrarenal, which suggests intrinsic renal parenchymal damage; and (3) postrenal, which implies obstructive uropathy. The majority of cases (83% to 90%) of acute renal failure in preeclampsia result from prerenal and intrarenal pathologic processes (most commonly acute tubular necrosis) and resolve completely after delivery.[20,21] In contrast, bilateral renal cortical necrosis is a rare and serious condition associated with considerable maternal and perinatal morbidity and mortality. It occurs most commonly in association with known renal parenchymal disease, chronic hypertension with superimposed preeclampsia, placental abruption, DIC, HELLP syndrome, sepsis, or fetal death. [22,23]

Management of hypertensive emergency

Confidential Enquiry into Maternal and Child health 2006-2008 in the United Kingdom described 19 deaths secondary to preeclampsia/eclampsia and stroke with failure to control for blood pressures in all cases. Another review on preeclampsia related strokes identified systolic blood pressures > 155mmHg present in 100% of 28 cases described (with 16 cases occurring in the postpartum period!).[24] Preeclampsia causing a loss in cerebral autoregulation and conferring to a markedly increased risk of intracerebral hemorrhage, guidelines consider occurrence of systolic blood pressures of greater or equal to 155-160 mmHg persisting over 15 minutes as hypertensive emergency requiring prompt treatment within 30 minutes. Though choice of antihypertensive treatment should depend on the physician's individual experience and preference, common guidelines suggest labetalol, hydralazine and nifedipine as first-line agents, and nicardipine, sodium nitroprusside and esmolol as second line agents.[25] Independent of the agent chosen, in order to avoid utero-placental hypoperfusion leading to fetal compromise and need for emergent delivery, blood pressure should be aimed to no more than 15-20% reductions from baseline. Decreasing uterine tone leading to postpartum hemorrhage, nitroglycerine should be avoided around time of delivery, and methylergonovine exaggerating hypertension is considered contraindicated as uterotonic.

Eclampsia

In the untreated disease, eclamptic seizures may occur in 2-10% of preeclamptic women, pathophysiologic as a consequence endothelial disease leading to microemboli causing cerebral vasogenic and cytotoxic edema. Seizure prophylaxis using Magnesium sulfate ($MgSO_4$) is considered standard of care. Eclamptic seizures are a significant cause for maternal mortality with severe and acute headaches, visual disturbances, acute mental status changes or temporary blindness as typical warning symptoms. However, 20-38% of eclamptic seizures have been described without classic signs of preeclampsia occurring before, during or after delivery.

Management of eclamptic seizure includes maintenance of airway, breathing and circulation, and seizure control with a loading bolus of 6 g $MgSO_4$ as first line agent (or 2g if patient on $MgSO_4$ maintenance). Recurrent seizures require additional 2 g $MgSO_4$-bolus, and consideration of alternative treatments (Benzodiazepines), broaden differential diagnosis and neurology consult. In general, eclamptic seizures are not an absolute indication for endotracheal intubation or delivery, which must be decided depending on success of seizure control, maternal and fetal stabilization.

Anesthesia Management

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A) Regional Anesthesia

Epidural analgesia is generally well tolerated decreasing mean arterial pressures and systemic vascular resistance, keeping central venous and pulmonary pressures unchanged.[26] Helping blood pressure control and decreasing uterine artery resistance, studies indicate potential beneficial effects when placing epidural analgesia. Main contraindications for neuraxial analgesia remain coagulopathy and thrombocytopenia, but epidural or spinal anesthesia is considered acceptable, and the risk of epidural hematoma is exceptionally low, if platelet counts are $\geq 70 \times 10^9$ /L, platelet level is stable and function stable, no other coagulopathy is present and patients are on no other antiplatelet or anticoagulant therapy.[27]

For preeclamptic patients undergoing Cesarean delivery (CD), spinal anesthesia (SPA) ist the method of choice provided there is no indwelling epidural catheter present, contraindication to neuraxial anesthesia and left ventricular systolic function is preserved.[28] Compared to the healthy pregnant patient, there is modest afterload reduction leading to less hypotension. Fifty percent of patients will still require some vasopressor for blood pressure control to be chosen following maternal hemodynamic goals independent of fetal heart tracing. [29,30]

B) General Anesthesia

General anesthesia is less desirable than neuraxial anesthesia but may be indicated in the presence of coagulopathy with contraindication for neuraxial anesthesia, pulmonary edema with dyspnea not allowing patient to lie flat, eclampsia leading to decreased mental status, or sustained fetal bradycardia. In patients with preserved systolic function, anesthesia management is similar to none preeclamptic patients, but providers must be prepared for difficult intubation and severe hypertensive response with intubation putting the patient at risk for intracranial hemorrhage.[31]

In order to blunt blood pressure response with intubation general recommendations include intravenous administration of esmolol 1.5mg/kg in patients with normal heart rate, nitroglycerine 2 mcg/kg in patients with lower heart rates, or remifentanil in a dose of 1-1.5mcg/kg.[32]

In patients with pulmonary edema a more careful titration of induction medications is recommended balancing the risks of aspiration and hypoxemia with acute hypotension. Significant diastolic dysfunction causing pulmonary edema may warrant more judicious blood pressure management, whereas systolic dysfunction as underlying cause will necessitate increasing inotropy.[33]

Consideration for monitoring

Invasive monitoring may be considered in preeclamptic women with poorly controlled hypertension, renal failure, pulmonary edema or hemorrhage. Mode of invasive monitoring depend on providers preferences based on individual physicians experience. A possible approach to choose may be placement of arterial line +/- minimal invasive cardiac output monitoring in the spontaneous breathing patient, placement of a central line in the hemorrhaging patient or patient needing vasopressors, and measurement of stroke/pulse pressure variation in the invasively ventilated patient.[33, 34] The use of point-of-care transthoracic cardiopulmonary ultrasound is recommended as long as expertise is available.[34]

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References

1. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000; 183:S1–22
2. Tranquilli AL, Dekker G, Magee L, Roberts J, Sibai BM, Steyn W, Zeeman GG, Brown MA: The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP. Pregnancy Hypertens 2014; 4:97–104
3. GBD 2015 Maternal Mortality Collaborators: Global, regional, and national levels of maternal mortality, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016; 388:1775–812
4. Main EK, McCain CL, Morton CH, Holtby S, Lawton ES: Pregnancy-Related Mortality in California: Causes, Characteristics, and Improvement Opportunities. Obstetrics & Gynecology 2015; 125:938–47
5. Hauth JC, Ewell MG, Levine RJ, Esterlitz JR, Sibai B, Curet LB, Catalano PM, Morris CD: Pregnancy outcomes in healthy nulliparas who developed hypertension. Calcium for Preeclampsia Prevention Study Group. Obstet Gynecol 2000; 95:24–8
6. Barton JR, O'brien JM, Bergauer NK, Jacques DL, Sibai BM: Mild gestational hypertension remote from term: progression and outcome. Am J Obstet Gynecol 2001; 184:979–83
7. Mol BWJ, Roberts CT, Thangaratinam S, Magee LA, Groot CJM de, Hofmeyr GJ: Pre-eclampsia. Lancet 2016; 387:999–1011
8. Melchiorre K, Thilaganathan B: Maternal cardiac function in preeclampsia. Current Opinion in Obstetrics & Gynecology 2011; 23:440–7
9. Dennis AT, Castro J, Carr C, Simmons S, Permezel M, Royse C: Haemodynamics in women with untreated pre-eclampsia*: Haemodynamics in untreated pre-eclampsia. Anaesthesia 2012; 67:1105–18
10. Dennis AT: Management of pre-eclampsia: issues for anaesthetists: Management of pre-eclampsia. Anaesthesia 2012; 67:1009–20
11. Zieleskiewicz L, Bouvet L, Einav S, Duclos G, Leone M: Diagnostic point-of-care ultrasound: applications in obstetric anaesthetic management. Anaesthesia 2018; 73:1265–79
12. Ortner CM, Krishnamoorthy V, Neethling E, Flint M, Swanevelder JL, Lombard C, Fawcus S, Dyer RA: Point-of-Care Ultrasound Abnormalities in Late-Onset Severe Preeclampsia: Prevalence and Association With Serum Albumin and Brain Natriuretic Peptide. Anesthesia & Analgesia 2019; 128:1208–16
13. Zieleskiewicz L, Leone M: Re: Lung and cardiac ultrasound for hemodynamic monitoring of patients with severe pre-eclampsia. J. Ambrozic, G. Brzan Simenc, K. Prokselj, N. Tulz, M. Cvijic and M. Lucovnik. *Ultrasound Obstet Gynecol* 2017; 49: 104-109. Ultrasound Obstet Gynecol 2017; 49:22–22
14. Zieleskiewicz L, Lagier D, Contargyris C, Bourgoin A, Gavage L, Martin C, Leone M: Lung ultrasound-guided management of acute breathlessness during pregnancy: Lung ultrasound in pregnancy. Anaesthesia 2013; 68:97–101
15. NICE guidelines update 2017 1 Guidance Hypertension in pregnancy diagnosis and management Guidance NICE.html
16. Moran P, Baylis PH, Lindheimer MD, Davison JM: Glomerular ultrafiltration in normal and preeclamptic pregnancy. J Am Soc Nephrol 2003; 14:648–52
17. Sims EA, Krantz KE: Serial studies of renal function during pregnancy and the puerperium in normal women. J Clin Invest 1958; 37:1764–74
18. Davison JM, Dunlop W: Renal hemodynamics and tubular function normal human pregnancy. Kidney Int 1980; 18:152–61
19. Abraham KA, Kennelly M, Dorman AM, Walshe JJ: Pathogenesis of acute renal failure associated with the HELLP syndrome: a case report and review of the literature. Eur J Obstet Gynecol Reprod Biol 2003; 108:99–102
20. Sibai BM, Villar MA, Mabie BC: Acute renal failure in hypertensive disorders of pregnancy. Pregnancy outcome and remote prognosis in thirty-one consecutive cases. Am J Obstet Gynecol 1990; 162:777–83
21. Drakeley AJ, Le Roux PA, Anthony J, Penny J: Acute renal failure complicating severe preeclampsia requiring admission to an obstetric intensive care unit. Am J Obstet Gynecol 2002; 186:253–6

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22. Stratta P, Canavese C, Colla L, Dogliani M, Bussolino F, Bianco O, Gagliardi L, Todros T, Iberti M, Veronesi GV: Acute renal failure in preeclampsia-eclampsia. Gynecol Obstet Invest 1987; 24:225–31
23. Ganesan C, Maynard SE: Acute kidney injury in pregnancy: the thrombotic microangiopathies. J Nephrol 2011; 24:554–63
24. MBRRACE-UK Maternal Report 2016 - website.pdf
25. Dyk D van, Dyer RA, Fernandes NL: Preeclampsia in 2021-a Perioperative Medical Challenge for the Anesthesiologist. Anesthesiol Clin 2021; 39:711–25
26. Ankichetty S, Chin K, Chan V, Sahajanandan R, Tan H, Grewal A, Perlas A: Regional anesthesia in patients with pregnancy induced hypertension. J Anaesthesiol Clin Pharmacol 2013; 29:435
27. ACOG practice bulletin.pdf
28. Henke VG, Bateman BT, Leffert LR: Focused review: spinal anesthesia in severe preeclampsia. Anesth Analg 2013; 117:686–93
29. Dyer RA, Emmanuel A, Adams SC, Lombard CJ, Arcache MJ, Vorster A, Wong CA, Higgins N, Reed AR, James MF, Joolay Y, Schulein S, Van Dyk D: A randomised comparison of bolus phenylephrine and ephedrine for the management of spinal hypotension in patients with severe preeclampsia and fetal compromise. International Journal of Obstetric Anesthesia 2018; 33:23–31
30. Higgins N, Fitzgerald PC, Van Dyk D, Dyer RA, Rodriguez N, McCarthy RJ, Wong CA: The Effect of Prophylactic Phenylephrine and Ephedrine Infusions on Umbilical Artery Blood pH in Women With Preeclampsia Undergoing Cesarean Delivery With Spinal Anesthesia: A Randomized, Double-Blind Trial. Anesthesia & Analgesia 2018; 126:1999–2006
31. Pant M, Fong R, Scavone B: Prevention of Peri-Induction Hypertension in Preeclamptic Patients: A Focused Review. Anesthesia & Analgesia 2014; 119:1350–6
32. Park BY, Jeong CW, Jang EA, Kim SJ, Jeong ST, Shin MH, Lee J, Yoo KY: Dose-related attenuation of cardiovascular responses to tracheal intubation by intravenous remifentanil bolus in severe pre-eclamptic patients undergoing Caesarean delivery. British Journal of Anaesthesia 2011; 106:82–7
33. Hofmeyr R, Matjila M, Dyer R: Preeclampsia in 2017: Obstetric and Anaesthesia Management. Best Practice & Research Clinical Anaesthesiology 2017; 31:125–38
34. Dennis AT, Dyer RA: Cardiac output monitoring in obstetric anaesthesia. Int J Obstet Anesth 2014; 23:1–3

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American Society of Anesthesiologists
the ANESTHESIOLOGY annual meeting

Maternal Cardiac Disease: Peripartum Planning

Marie-Louise Meng, MD **Durham, North Carolina**

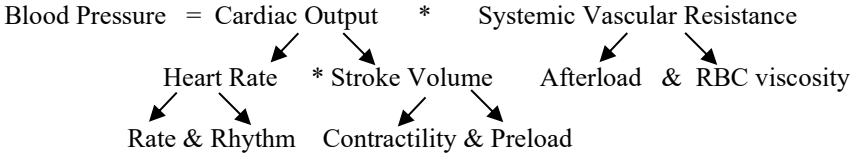
Introduction

Maternal cardiac disease is a leading cause of maternal morbidity and mortality in the United States as the numbers of patients with acquired and repaired congenital heart disease have increased over the last three decades. Obstetricians routinely turn to anesthesiologists to help with the planning and management of the delivery and termination care of these patients. This lecture reviews maternal cardiac lesions, physiologic concerns, anesthetic options, and provides a practical framework for how anesthesiologists should assess these patients and plan delivery care needs.

Hemodynamic changes of pregnancy, peri delivery and postpartum

During pregnancy several changes happen to the cardiovascular system to accommodate the increased blood volume required to grow the fetal placental unit. Beginning in the first trimester, plasma blood volume increases and to accommodate this volume, systemic vascular resistance and pulmonary vascular resistance decrease. The heart rate increases allowing cardiac output to increase. Cardiac output increases 30-50% through pregnancy. During delivery, cardiac output often increases to 15-20% above the pre-labor value. When a woman arrives at labor and delivery, the pain from contractions causes a release of catecholamines. These catecholamines can cause tachycardia and in some patients precipitate arrythmias. Uterine contractions cause a fluctuation or increase of approximately 300ml of preload. This auto-transfusion, as well as the autotransfusion that occurs after delivery with the relief of aortocaval compression, may not be tolerated by all women with cardiac disease. The blood loss at delivery may not be tolerated by all patients, nor the corresponding required resuscitation well tolerated. Through the whole process of labor and delivery, there is an increased maternal oxygen consumption. The diagram below is useful to conceptualize the hemodynamic changes peri-delivery and the issues they may cause, and the plans anesthesiologists can make to mitigate the issues.

Figure 1: Hemodynamic changes peri-delivery



ISSUES:

↑ Catecholamines	→ ↑ Tachycardia & arrhythmias
↓ Systemic vascular resistance	→ ↓ Coronary perfusion = A_oD - LVEDP
↑ Cardiac output (preload changes)	→ ↑ Heart failure
↑ Pulmonary blood flow +↓ Pulmonary vascular resistance	→ ↑ Pulmonary pressure
↓ Oncotic pressure	→ ↑ Pulmonary edema

PLAN:

Avoid sudden alterations in heart rate & rhythm	→ Neuraxial anesthesia for pain control
Control sudden decreases in afterload (SVR)	→ Vasopressors
Support the myocardium	→ Inotropes (and mechanical support)
Maintain preload (control sudden changes in blood volume)	→ Diuresis and pulmonary vasodilators

Heart failure Warning Signs

The most common complication peridelivery in women with heart disease is heart failure. This is due to an inability to augment contractility to accommodate the increases in preload with autotransfusion peri-delivery or postpartum. It is important to remember that pregnant patients are usually volume up, whether the volume is in the forms of

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edema and/or intravascular volume. This fluid needs to leave the maternal body after delivery and patients with decreased contractile function may experience heart failure in the postpartum process of physiologically returning to a pre-pregnancy volume state. Main EK et al. examined pregnancy related deaths in California and determined that those due to cardiovascular causes were largely preventable.(1) Delayed responses to clinical warning signs and ineffective care were the main contributing factors. Anesthesiologists should have a high suspicion for heart failure if there are any change in maternal symptoms such as new or worsening tachycardia, arrhythmia, hypotension, hypoxemia (new O2 requirement in an obstetric patient is never normal and warrants a workup), decreased urine output or decompensation of fetal tracing. Often an augmentation of maternal heart rate is a physiologic response to increase cardiac output in a heart that is struggling to increase contractility.

Framework for planning care of the cardio-obstetric patient

A useful framework for how to approach the anesthesiology care of a pregnant patient with heart disease is presented below and adapted from the references in Circulation and Anesthesiology.(2,3)

WHO: Who is the patient and who is on the Pregnancy Heart Team?

Patient: Cardiovascular disease is a broad term encompassing lesions ranging in type (valvular, shunts, arrythmias, complex congenital, myocardial dysfunction, vascular/aortopathy) and severity. Anesthesiologists should use the specific disease and the patient's current functional condition for risk stratification. The most useful tools for risk stratification currently are the modified WHO risk classification and CARPREG II risk score.(4,5) Additionally, the Registry Of Pregnancy And Cardiac disease (ROPAC) a 'Special' registry within the European Society of Cardiology has multiple publications to guide risk stratification, care and management of cardio-obstetric patients. Below is a revised version on the modified WHO risk stratification table:

Table 1: Modified World Health Organization Classification of Cardiovascular Disease in Pregnancy(2,4)

Risk classification	Cardiac lesions
Class I: No detectable increased risk of maternal mortality and no or minimal increase in maternal morbidity	• Uncomplicated mild pulmonary stenosis • Mitral valve prolapse with no more than trivial mitral regurgitation • Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage) • Isolated ventricular extra-systoles and atrial ectopic beats
Class II: Small increased risk of maternal mortality or moderate increase in morbidity	• Unrepaired atrial or ventricular septal defect • Repaired tetralogy of Fallot • Most arrhythmias
Class II/III: Moderate increased risk of maternal mortality or morbidity	• Hypertrophic cardiomyopathy • Native or tissue valvular heart disease not considered Modified World Health organization I or IV • Repaired coarctation • Marfan syndrome without aortic dilatation • Bicuspid valve with aorta <45 mm • Mild ventricular impairment • Heart transplantation • Coronary artery disease
Class III: Significantly increased risk of maternal mortality or severe morbidity, and expert cardiac and obstetric pre-pregnancy, antenatal, and postnatal care are required	• Mechanical valve • Systemic right ventricle • Fontan circulation • Unrepaired cyanotic heart disease • Other complex congenital heart disease • Marfan syndrome with aorta 40–45 mm • Bicuspid aortic valve with aorta 45–50 mm
Class IV: Pregnancy is highly discouraged, termination of pregnancy is advised	• Pulmonary hypertension • Eisenmenger syndrome • Systemic ventricular ejection fraction <30% • Systemic ventricular dysfunction with New York Heart Association class III–IV • Severe mitral stenosis or symptomatic aortic stenosis • Marfan syndrome with aorta >45 mm • Bicuspid aortic valve with aorta >50 mm • Native severe coarctation • Previous peripartum cardiomyopathy with any residual impairment of ventricular function

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Assessment of pre-pregnancy functional status using the New York Heart Association (NYHA) Functional Classification, changes to NYHA classification through pregnancy and current function status are useful to determine if the patient is compensating well or not and can guide necessary testing and termination or delivery planning. Symptoms of heart failure overlap with common symptoms in pregnancy (dyspnea, orthopnea, fatigue); therefore, when these symptoms are present, it is useful to send an NT-proBNP level to rule out cardiac causes of these symptoms. NT-proBNP has high negative predictive value, that is, if it is normal, the chance of a cardiac cause being the source of the symptoms is low.(6-9) **An elevated NT-proBNP level should prompt further cardiac evaluation with echocardiography and electrocardiography.** Anesthesiologists comfortable with performing cardiac POCUS may utilize this skill to obtain a quick assessment of myocardial function while the team is waiting for an official transthoracic echocardiogram.

Pregnancy Heart Team (PHT): It is useful for centers who care for many patients with cardiovascular disease to form official Pregnancy Heart Teams, a multidisciplinary group of subspecialists that are dedicated to formulating and executing appropriate plans for cardio-obstetric patients during pregnancy, delivery and postpartum. The team may choose to meet monthly to review the list of cardio-obstetric patients and update plans. Often the PHT will require representation from the following medical and nursing subspecialties: Anesthesiologist (Obstetric and Cardiothoracic), Cardiologist, Neonatologist, Hematologist, Cardiothoracic surgeon, ECMO surgeon, Perfusionist, intensivist, Critical Care Obstetric Nurse, Critical Care Nurse). It may be useful to keep an electronic list of high-risk patients and the plans made for them so that providers can easily review the PHT's recommendations when patients arrive to L&D.(10,11)

WHAT: What does the patient need, a termination, vaginal delivery or cesarean delivery?
Vaginal delivery with good neuraxial anesthesia is usually the preferred mode of delivery for patients with cardiovascular disease, unless there is a maternal, obstetric or fetal indication for cesarean delivery. Early analgesia can aid in minimizing tachycardia due to catecholamine release with painful contractions, this may help in avoiding arrhythmias. The anesthesiologist can help with assessing volume status and guiding fluid management through labor. With every uterine contraction the preload to the heart increase by about 300ml, examining the maternal hemodynamic response to this fluid shift with bedside exams and cardiac POCUS may be useful to determine how well the patient's cardiovascular system is tolerating labor.

The second stage of labor defined as the time from full cervical dilation to the delivery of the fetus. It may be useful to allow time in the second stage for **passive descent of the fetus** before initiating the **active, 'pushing' second stage**. The benefit of a prolonged passive second stage is that this passive descent of the fetus may result in the patient spending less time pushing. The mechanic stages of the **Valsalva maneuver** are the following:

- **Stage 1:** Onset of straining- Intrathoracic pressure increases and there is an increase in blood pressure, heart rate does not change
- **Stage 2:** Continued straining- There is a decrease in venous return resulting in a decrease in pulse pressure and stroke volume, blood pressure decreases a bit and heart rate increases
- **Stage 3:** Release of straining- Intrathoracic pressure decreases and venous blood volume returns to the pulmonary vasculature, blood pressure decreases further since there is less preload in the left side of the heart, heart rate remains stably increased
- **Stage 4:** Continued release of Valsalva- venous return increases such that there is now adequate volume in the left heart to improve stroke volume, ejection and blood pressure increases well above previous stage 3 values and heart rate can decrease.

There are two risky changes during the Valsalva maneuver to consider, (1) the acute changes in preload and (2) the large swing in blood pressure from Stage 3 to Stage 4 that can be detrimental to patients with aortic pathology that may not tolerate changes in aortic sheer stress. Therefore, there are some patients for whom an assisted second stage may be recommended (preload dependent lesions, severe aortopathy), yet most patients with cardiac conditions can handle the repeated Valsalva maneuver necessary in the active second stage. The concern with assisted second stage (forceps delivery) is that there is a risk of increased blood loss and 3rd and 4th degree lacerations and consequent

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morbidity with recovery from the forceps delivery; therefore, current recommendations have shifted towards allowing more patients to participate in an active second stage if it is hemodynamically tolerated.(12-15)

The third stage of labor is the time from the delivery of the fetus until delivery of the placenta. The goal after delivery is to ensure placental removal and uterine contraction to prevent postpartum hemorrhage. **If there is no contraindication to oxytocin, it should be dosed as usual at this time.** Some patients may have contraindications to one or several uterotonics. Hemabate (carboprost) should be avoided in patients with pulmonary pathology, asthma, pulmonary edema, pulmonary hypertension. Methergine should be avoided in patients with hypertension or coronary vascular disease.(2)

There are few cardiovascular indications for performing a cesarean delivery rather than allowing a trial of labor. Indications for cesarean delivery include recent Warfarin use (for fetal indication: cannot determine fetal coagulation status), some high degree aortopathies (follow ESC 2018 guidelines based on etiology of aortic disease and vessel size), critical valvular stenosis, decompensated heart failure or severe decompensated pulmonary hypertension.(4,16,17) Maternal or fetal decompensation for any reason may require expedited delivery via cesarean. When cesarean delivery is performed in high risk patients (high pulmonary artery pressure, right heart dysfunction), it may be prudent to avoid uterine exteriorization so as to prevent micro air emboli. (2)

WHEN: When should termination or delivery occur?
The goal is to wait until a pregnancy reaches term to deliver the fetus; however, maternal decompensation may prompt termination or preterm delivery. The urgency of the procedure is usually determined by the obstetric team; however, anesthesiologists can be useful partners in decision making when there is concern for maternal hemodynamic intolerance to pregnancy.

WHERE: Where is the appropriate medical center and location within a hospital for a patient to deliver?
To facilitate providing appropriate care for patient with high-risk maternal or fetal conditions, the American College of Obstetricians and Gynecologists (ACOG) created Maternal Levels of Care designations.(18) This system standardizes integrated systems of perinatal regionalization, provides risk-appropriate maternal care, aids in facilitating transfers of care when necessary and creates a guide for systematic improvement across centers.(18) The classification system establishes four levels of maternal care. Anesthesiologists should be aware of what level of care is available at their center and facilitate transfer of care or acceptance of patients when necessary.

Labor and delivery are usually best done on the labor and delivery suite as the personnel, resources, knowledge ,and response times are available and appropriate to most obstetric patients; however, there may be occasions where delivery is best done in another location in the hospital such as a main operating room or cardiothoracic operating room. In patients with mWHO class III or IV disease where cardiothoracic surgery or ECMO backup are needed, the team may opt to perform a scheduled cesarean delivery in a cardiothoracic or main operating room to be closer to the personnel and resources to employ ECMO quickly. Often, a vaginal delivery in a high-risk patient may benefit from cardiothoracic anesthesiologist or intensivist coming to the labor floor to assist the obstetric anesthesiologist with cardiac POCUS or medication titration. Providing an intensive care nurse on labor and delivery to collaborate with a labor and delivery nurse may also be beneficial in certain cases. It is important to remember that the cardio-obstetric patient is at risk for the usual obstetric issues such as need for intrapartum cesarean delivery or hemorrhage care, which are best managed in the labor and delivery suit as these events and their management are routine for the obstetric care teams. Moving patients to have vaginal deliveries off the labor floor in an intensive care unit may not be advisable as usual maternal care may be compromised (i.e. lack of obstetric anesthesiology presence 24/7, delay in transfer to an operating room for intrapartum cesarean delivery) in these alternative locations.

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HOW: How do we plan our anesthesia and hemodynamic support peri-termination or delivery?

Intrapartum plan

Access and monitoring: Good intravenous access for volume resuscitation should be obtained with central access reserved for patients who may require norepinephrine or prolonged inotropic support. Arterial pressure monitoring can be very useful for patients in whom stable arterial pressure is crucial (left sided stenotic lesions, ventricular dysfunction, pulmonary hypertension). Pulmonary artery catheters should be considered for patients with pulmonary hypertension to monitor response to pulmonary vasodilator medications or for patients with severe ventricular dysfunction to monitor left atrial pressure. Cardiac POCUS is often very useful to determine volume status, myocardial function and response to interventions such as addition of inotropic support.

Hemodynamic support: The anesthesiologist should determine the appropriate hemodynamic goals and greatest peripartum risks to each individual patient and formulate plans accordingly. When multiple conditions are present with competing hemodynamic goals, it may be prudent to use the more severe cardiovascular condition to determine a hemodynamic care plan. The anesthesiologist should ensure that appropriate vasopressor, inotropic and pulmonary vasodilator medications are available.

Anesthetic plan: Usually, neuraxial anesthesia is preferred for both vaginal and cesarean delivery. General anesthesia may be necessary for the usual indications (maternal preference, emergency with no in situ neuraxial nor time for de novo neuraxial anesthesia, or any need for endotracheal intubation).

Postpartum hemorrhage management: There is generally no contraindication to oxytocin infusions so this medication should be employed as usual to facilitate rapid uterine contraction and prevent postpartum hemorrhage. Hemabate (carboprost) should be avoided in patients with pulmonary pathology, asthma, pulmonary edema, pulmonary hypertension. Methergine should be avoided in patients with hypertension or coronary vascular disease.(2) Other options for management of uterine atony include compression sutures during cesarean delivery and Bakri balloon placement for both vaginal and cesarean deliveries.

Postpartum care

Location of recovery: The location of recovery should be determined based on the current patient status, needs of the patient and capacity of the unit. The most common postpartum issue, regardless of cardiac disease, is hemorrhage. Specific to patients with cardiovascular disease are the concerns for fluid shifts and resulting heart failure or arrythmias that can be identified early with frequent examinations and telemetry.(5) Should strict ins and outs monitoring, or telemetry not be possible in the labor and delivery unit, it may be useful to recover patients with cardiovascular disease in an intensive care unit.

Recovery goals: The usual postpartum goals of hemorrhage prevention and pain control are central to the care of all obstetric patients. The nursing team should continue to monitor uterine fundal tone and vaginal bleeding as usual, regardless of whether the patient recovers on the labor and delivery unit or in an intensive care unit. These exams are important not only to improve uterine tone with mechanical force but also to identify early signs of uterine atony or ongoing bleeding. Once hemorrhage is controlled, the next goal is to ensure that the fluid accumulated through pregnancy and delivery can safely leave the maternal third space and vasculature. This is usually accomplished with the natural postpartum maternal auto diuresis but **patients with cardiovascular disease may benefit from medical diuresis and sodium restriction to avoid reaccumulating fluid**. Stool softeners are useful as opioid pain medications, and the manipulation of surgery can lead to constipation. Softening of stool is crucial to prevent repeated Valsalva in the restroom during bowel movements (similar hemodynamic danger as that seen with maternal pushing). Patients with low flow states, pulmonary hypertension, Fontan physiology or other hypercoagulable states may benefit from re-initiation or initiation of anticoagulation.

Conclusion: Anesthesiologists have the potential to assist obstetricians in reducing maternal morbidity due to cardiovascular disease across labor floors in America. Anesthesiologists can identify patients at high risk of heart failure peridelivery and augment care to prevent decompensation. Anesthesiologists may also have a role in assisting in the postpartum recovery care of women at high risk of cardiovascular complications, working with obstetricians to reduce morbidity.

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Maternal Cardiac Disease Delivery Planning Algorithm/Framework

1. WHO: (patient and medical team)

A. Patient:

- Medical, surgical, obstetric, anesthetic history, medications (anticoagulation), allergies
- Modified WHO scale (mWHO II-III, III, IV consider transfer to referral hospital)
- CARPREG II Risk score (CARPREG >1 consider transfer to referral hospital)
- NYHA Class I-IV
- Other data: NT-proBNP, ECG, TTE, CT, MRI

B. Team:

- Obstetrician/Maternal Fetal Medicine
- Anesthesiologist (Obstetric and Cardiothoracic)
- Cardiologist
- Neonatologist
- Hematologist
- Cardiothoracic surgeon/ECMO surgeon/Perfusionist
- Intensivist
- Critical Care Obstetric Nurse/Critical Care Nurse

2. WHAT: Vaginal v. cesarean delivery v. termination

3. WHEN: Target induction/delivery/procedure date (gestational weeks/days):_____

4. WHERE: (Type of medical center and location within medical center)

- Local v. Referral hospital
- L&D suite labor room, L&D operating room, cardiothoracic operating room, intensive care unit

5. HOW:

Peripartum plan

A. Hemodynamic goals:

B. Peripartum risks:

C. Medications:

- Vasopressors: phenylephrine, norepinephrine, vasopressin
- Inotropes: dobutamine, dopamine, milrinone, epinephrine
- Anti-pulmonary HTN: oxygen, calcium channel blockers, prostacyclin agonists, PDE-5 inhibitors, endothelin antagonists, nitric oxide-cyclic guanosine monophosphate enhancers, nitric oxide

D. Anesthesia: spinal, combined spinal epidural, epidural, general

E. Monitoring: non-invasive blood pressure, arterial line, telemetry, central venous pressure, pulmonary artery catheter, cardiac POCUS, transthoracic echocardiogram, transesophageal echocardiogram

F. Venous access: peripheral or central

G. ECMO: VV or VA, back-up, place wires, place sheaths, place cannulas

H. Hemorrhage prevention/management:

- Uterotonics: oxytocin, methergine (avoid in HTN), carboprost (avoid in lung disease), misoprostol (less effective)
- Procedures: compression, suture, Bakri balloon, uterine artery embolization, hysterectomy

Postpartum care

A. Recovery location: (ICU or high-risk maternal unit or post-partum unit)

B. Treatment goals:

- Diuresis for arrhythmia and heart failure prevention with sodium restriction to prevent fluid reaccumulation
- Anticoagulation for thrombosis prevention
- Stool softeners for prevention of Valsalva

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References:

1. Main EK, McCain CL, Morton CH, Holtby S, Lawton ES. Pregnancy-related mortality in California: causes, characteristics, and improvement opportunities. Obstet Gynecol 2015;125:938-47.
2. Meng ML, Arendt KW. Obstetric Anesthesia and Heart Disease: Practical Clinical Considerations. Anesthesiology 2021;135:164-183.
3. Meng ML, Arendt KW, Banayan JM et al. Anesthetic Care of the Pregnant Patient With Cardiovascular Disease: A Scientific Statement From the American Heart Association. Circulation 2023;147:e657-e673.
4. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J 2018;39:3165-3241.
5. Silversides CK, Grewal J, Mason J et al. Pregnancy Outcomes in Women With Heart Disease: The CARPREG II Study. J Am Coll Cardiol 2018;71:2419-2430.
6. Mayama M, Yoshihara M, Uno K et al. Factors influencing brain natriuretic peptide levels in healthy pregnant women. Int J Cardiol 2017;228:749-753.
7. Kampman MA, Balci A, van Veldhuisen DJ et al. N-terminal pro-B-type natriuretic peptide predicts cardiovascular complications in pregnant women with congenital heart disease. Eur Heart J 2014;35:708-15.
8. Tanous D, Siu SC, Mason J et al. B-type natriuretic peptide in pregnant women with heart disease. J Am Coll Cardiol 2010;56:1247-53.
9. Minhas AS, Rooney MR, Fang M et al. Prevalence and Correlates of Elevated NT-proBNP in Pregnant Women in the General U.S. Population. JACC Adv 2023;2.
10. American College of Obstetricians & Gynecologists' Presidential Task Force on Pregnancy Heart Disease Committee on Practice Bulletins Obstetrics. ACOG Practice Bulletin No. 212: Pregnancy and Heart Disease. Obstet Gynecol 2019;133:e320-e356.
11. Magun E, DeFilippis EM, Noble S et al. Cardiovascular Care for Pregnant Women With Cardiovascular Disease. J Am Coll Cardiol 2020;76:2102-2113.
12. Nishimura RA, Tajik AJ. The Valsalva maneuver-3 centuries later. Mayo Clin Proc 2004;79:577-8.
13. Ouyang DW, Khairy P, Fernandes SM, Landzberg MJ, Economy KE. Obstetric outcomes in pregnant women with congenital heart disease. Int J Cardiol 2010;144:195-9.
14. Cauldwell M, Steer PJ, Swan L, Uebing A, Gatzoulis MA, Johnson MR. The management of the third stage of labour in women with heart disease. Heart 2017;103:945-951.
15. Cauldwell M, Von Klemperer K, Uebing A et al. Why is post-partum haemorrhage more common in women with congenital heart disease? Int J Cardiol 2016;218:285-290.
16. Meng ML, Fuller M, Federspiel JJ et al. Maternal Morbidity According to Mode of Delivery Among Pregnant Patients With Pulmonary Hypertension. Anesth Analg 2023.
17. Ruys TP, Roos-Hesselink JW, Pijuan-Domenech A et al. Is a planned caesarean section in women with cardiac disease beneficial? Heart 2015;101:530-6.
18. Obstetric Care Consensus No. 9: Levels of Maternal Care: Correction. Obstet Gynecol 2019;134:883.

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Maternal Morbidity and Mortality – An Anesthesiologist's Role and Perspective

Rachel M. Kacmar, MD **Aurora, Colorado**

Introduction and Definitions

Maternal mortality is defined as a death within 1 year of pregnancy that is caused by a pregnancy complication, the result of a condition initiated by pregnancy or worsening of a chronic condition from physiologic changes of pregnancy.[1] "Maternal death" is a death during pregnancy up to 42 days postpartum while "pregnancy-related death" reflects deaths during pregnancy up to 365 days postpartum.[2] Maternal morbidity definitions vary but in general include unintended outcomes or complications of pregnancy, labor, and/or delivery that have significant short- and/or long-term maternal health consequences.[3, 4] A list of morbidity diagnosis criteria are shown in Table 1.

In the United States (US), approximately 900 women die annually during pregnancy and in the postpartum period. This equates to a maternal mortality ratio (MMR) of approximately 22 per 100,000 live births, which is the highest of any high-resource country.[5] In addition, there is concern that the MMR in the US is up-trending (from 17.5 to 26.4/100,000 live births from 1990-2015 in one study[6] and 18.8- 23.8/100,000 from 2000 - 2014 in another[7]) despite a worldwide reduction. A recent CDC report listed the US MMR at 32.9 deaths/100,000 live births in 2021. The incidence of moderate to severe maternal morbidity (SMM) is orders of magnitude higher than mortality. Almost half the cases of mortality and SMM are preventable and there is intense scrutiny to identify causes and contributing factors, preventative measures that can be employed, and why the US lags behind other high-resource countries.

Etiologies and Contributing Factors for Morbidity and Mortality

Why has MMR in the US continued to rise despite worldwide down-trending, or at least stability? One reason may be evolving and improved reporting and surveillance methods including the implementation of the International Classification of Disease 10th Revision (ICD-10) which includes 4 additional codes for maternal death compared to ICD-9 as well as a "pregnancy check-box" on death certificates (implemented in 2003).[8, 9] The Center for Disease Control (CDC) started tracking maternal deaths in 1986[10] and relies on ICD-10 codes and death certificate information; however, unreliable recording and reporting of maternal deaths was common through the 1990s and the use of a pregnancy status checkbox on death certificates was a voluntary decision by each state until 2015.[11]

Patient-level factors associated with increased risk for SMM and maternal mortality include increased average maternal age (especially ≥ 40 years), maternal co-morbidities (e.g. pulmonary hypertension, PPH, cardiac disease, preeclampsia (preE)), subfertility/ use of in-vitro fertilization and increased cesarean delivery rate. Population- and hospital-level factors include higher prevalence of obesity, diabetes and high school non-completion, proportion of Medicaid/ uninsured and non-white patients, and variable state adoption of the 2003 death certificate.[12, 13] Areas for improvement relate to providers (e.g. inappropriate/ delayed treatment, poor communication, lack of education), patients (e.g. suboptimal control of chronic medical conditions, delay in seeking health care/ adhering to medical advice, significant social conditions) and systems (e.g. policies/ procedures, delay in transfer to higher level of care, communication).[14] Racial and ethnic healthcare disparities also play a significant role and are discussed below. The current leading causes of maternal morbidity and mortality are shown in Tables 1 and 2 below.[15-17]

Table 1. Indicators and *leading causes* of severe maternal morbidity

Acute myocardial infarction^	Eclampsia^	Pulmonary edema^
Acute renal failure^	Heart failure during surgery^	*Sepsis/ severe infection*^
Adult respiratory distress syndrome^	*Hemorrhage*^**	Severe anesthesia complications^
Amniotic fluid embolism	Hysterectomy^	Shock^
Aneurysm	Intensive care unit admission	Sickle cell crisis^
Blood transfusion (>/= 4 U PRBC)^	Internal injuries (thorax, abdomen, pelvis)^	Temporary tracheostomy^
Cardiac arrest/ VFib^	Intracranial injuries	Third/ fourth-degree perineal laceration
Cardiomonitoring^	Operation on heart/ pericardium^	*Thrombotic embolism*^
Cardiomyopathy^	*Preeclampsia*/ HELLP syndrome^	Trauma/ violence^
Conversion of cardiac rhythm^	Psychiatric disorder/ suicide attempt	Uterine rupture
DIC^	Puerperal cerebrovascular disorders^	Ventilation (intubation)^

** *Most common cause of maternal morbidity;* ^*Racial/ ethnic disparities identified within this cause*

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PRBC – packed red blood cells; VFib – ventricular fibrillation; DIC – disseminated intravascular coagulation; HELLP – "hemolysis, elevated liver enzymes, low platelets"

Table 2. Leading causes of maternal mortality in the U.S.

Etiology	% of maternal deaths	Cause-specific MMR^	Trend 1987-2013 (↑ versus ↓)
Cardiovascular disease	26.4*	4.2/100,000	↑
Hemorrhage	11.4 – 14.0	1.8/100,000	←→
Sepsis/ Infection	10.7 - 12.7	2.2/100,000 (UK)	←→
Venous thromboembolism	8.4 - 9.3	1.5/100,000	↓
Preeclampsia & eclampsia	7.4 - 9.4	1.5/100,000	↓
Mental health conditions	7.0		↑
Cerebrovascular accident	2.8 - 6.6		←→
Amniotic Fluid Embolism (AFE)	4.2 – 5.5	1.2-6.6/100,000	?
Anesthesia-related complication	0.2 – 2.3	1/1,000,000	↓

*^per n live births; *includes "cardiovascular conditions" and "cardiomyopathy"*

Etiology and Contributing Factor Details

- *Peripartum hemorrhage (PPH):* There continues to be a significant link between PPH and SMM and mortality. Recent studies indicate the PPH rate is increasing due in large part to increased incidence of uterine atony. An increased incidence of peripartum blood transfusion accompanies the observed increase in PPH, and one study found that massive transfusion was strongly associated with in-hospital maternal death.[18, 19]
- *Preeclampsia/ Hypertensive disorders of pregnancy:* Hypertension-related SMM and maternal mortality is potentially preventable, and early, aggressive blood pressure treatment is paramount. Women with chronic hypertension (HTN) and superimposed preeclampsia have the highest risk for SMM. The leading cause of death in women with preE and eclampsia is intracranial hemorrhage.[16] Use of a HTN management protocol can significantly reduce preE-related SMM and mortality.[18, 20]
- *Cardiovascular Disease:* As the number of women with congenital heart disease and maternal co-morbid conditions that convey risk for cardiac complications increase, authors have suggested a triad of broad cardiovascular screening, patient education (including preconception counseling) and multidisciplinary team planning.[21] Many serious cardiac events (66%) in parturients occur during the antepartum period and almost half are preventable, emphasizing the need for an aggressive approach.[22] A cardio-obstetrics team can provide coordinated care from the antepartum through postpartum periods and women with the most severe cardiac disease should be cared for in centers with both high level obstetrics and cardiac services.[23]
- *Sepsis:* Between 1999 -2006, 15% (22/151) of pregnancy-related deaths in Michigan were directly due to sepsis and sepsis contributed to another 8/151 deaths, leading to an overall MMR of 2.9 per 100,000 live births. Delay(s) in appropriate care were identified in over 70% of maternal deaths due to sepsis and sepsis-contributing deaths.[24] Specifically, delayed antibiotic administration more than doubled the mortality rate.
- *Obesity:* Prepregnancy obesity is associated with increased SMM as well as with other causes of SMM including preeclampsia and infection/ sepsis.[25] High gestational weight gain may increase risk of SMM.
- *Cesarean delivery (CD):* The rate of both SMM and mortality is significantly higher for women undergoing C/D compared to vaginal delivery (VD). Reducing primary CD to decrease repeat CD and its associated risk for SMM (e.g. uterine rupture, invasive placentation, hysterectomy) is a nationwide priority. As a result, there has been a decrease in the primary CD rate, however, this is accompanied by increased instrumental VD, increased incidence of 3rd and 4th degree perineal lacerations and longer labors,[26] which carry potential implications for epidural utilization and even anesthesiology staffing on labor and delivery.
- *SARS-CoV-2 (COVID):* Parturients with COVID are at increased risk for composite morbidity.[27] COVID + parturients were over 5 and 1.5 times more likely to be admitted to the hospital and ICU respectively compared to non-pregnant COVID + women. Pregnant patients had higher risk of receiving mechanical ventilation but there was no difference in risk for death based on pregnancy status.[28] Based on available data it appears severe-critical COVID symptoms carry the highest risk of perinatal complications but all pregnant and recently

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postpartum individuals with COVID have increased risk for composite SMM and mortality. Vaccination has been safe and effecting during pregnancy and breastfeeding and should be encouraged.[29]

- *Anesthesia-related complications*: Thankfully, SMM and maternal mortality related to anesthesia complications remains low and is decreasing. The most significant risk factors for adverse maternal outcomes related to anesthesia are airway management, high neuraxial blockade and dural puncture.[16]

Unconventional and Emerging Causes of Severe Maternal Morbidity and Mortality

Trauma/ Homicide: A review of the Pennsylvania Trauma Outcome Study showed a 1.6-fold higher rate of mortality in pregnant trauma victims compared to nonpregnant women. Pregnant trauma victims were more likely to be dead on arrival and more likely to die during the hospital course. This was true for both violent and non-violent trauma, however violent trauma in pregnancy was associated with a 3.14-fold higher mortality compared to non-violent trauma.[30] Pregnant patients are 5 times more likely to die by homicide than nonpregnant peers who died by violent means. Twelve percent of pregnancy associated deaths in Illinois from 2002-2013 were due to homicide. Gunshot wound was the cause of death in 50% of maternal homicide deaths from 2008-2013.[31]

Self-harm: A significant number of deaths in women of childbearing age are due to suicide/ overdose, however, until recently many analyses of maternal mortality did not include deaths due to self-harm. Thirty percent of maternal deaths in Colorado from 2004-2012 were the result of self-harm; the most common etiology in the study period. The vast majority occurred postpartum and while 54% of women had a prior psychiatric diagnosis documented, nearly half of patients who were on psychopharmacotherapy at conception discontinued medication during pregnancy.[32] In Ontario, Canada from 1990-2015, over 45% of maternal deaths due to injury were further classified as secondary to intentional self-harm or accidental overdose.[33] Risk factors for maternal death due to self-harm include depression, lack of psychopharmacologic medications, prior hospitalization for psychiatric indication, and disengagement from postpartum treatment.[34] Anxiety, depression and other psychiatric symptoms during pregnancy may be more prevalent now due to the COVID pandemic.[35]

- *Suicide:* In both the US and United Kingdom, experts suspect that maternal suicides have been underreported or miscategorized, leading to a suicide-related MMR that far underestimates reality. In Colorado from 2004-2012, suicide was associated with an MMR of 4.6 per 100,000 live births; 10% of patients who ultimately died from self-harm had a prior suicide attempt.[32] In Ohio, firearm (45%) and hanging (31%) were the most common mechanisms of suicide during or within 1 year of pregnancy.[36]
- *Overdose:* Opioid use, misuse, and opioid-related death during pregnancy and the postpartum period is consistently rising in the US.[34] Maternal mortality ratio from overdose was 5 per 100,000 live births in the above review of Colorado maternal deaths. Of the total deaths, 17% had a known substance abuse disorder and in cases when toxicology testing was performed, opioids were the most common substance identified.[32] Drug overdose was the second leading cause of maternal death (11.6%) in Texas from 2011-2012 following cardiovascular disease and again opioids were the most common substance identified.[37]

Disparities in Maternal Morbidity and Mortality

Racial and Ethnic Disparities

Non-Hispanic black women are significantly more likely to die from pregnancy-related causes compared to non-Hispanic white women.[1] In one study the MMR for black women was 2.4 - 3.3 times higher v. white women for preE, eclampsia, placental abruption, placenta previa, and postpartum hemorrhage.[38] Others reported significantly increased MMR related to cardiomyopathy (relative risk (RR) 4.6), hemorrhage (RR 4.9), respiratory conditions (RR 6.1),[39] hypertension (adjusted RR (aRR) 8.5) and hemorrhage (aRR 4.7)[40] in black women compared to white women. The proportion of maternal deaths that are preventable may be higher in black women (46-59% of deaths) v. white women (9-33% of deaths).[41, 42] Preventability is similar between lower and higher level birth facilities.[42]

Maternal mortality rates are also elevated (compared to white women) in women identifying as Native American/ Alaskan, Asian/ Pacific Islander and certain subgroups of Hispanic women.[1] Hispanic women were found to have a 3-fold higher risk of pregnancy-related death due to hypertensive disease compared to white women[43] while another study noted a 6.1 and 3.7 times increased chance to die from a diagnosis of pregnancy-induced HTN and hemorrhage respectively.[40]

Racial and ethnic disparities extend to severe maternal morbidity. Black women have a greater than 2-fold higher risk for SMM compared to white women.[44] Non-Hispanic black women have the highest rates for 22 of 25 of

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the CDC indicators for severe morbidity (Table 1) and are most likely to have severe disease when SMM is secondary to peripartum cardiomyopathy and cerebrovascular events[3, 45]. Black women are also more likely to undergo C/D and experience longer hospital stays versus white women.[46] Compared to white women, Asian/ Pacific Islanders have a higher rate of diabetes (adjusted odds ratio (aOR) of 2.05), postpartum hemorrhage (aOR 1.19 – 1.51), severe postpartum infection (aOR 1.45) and 3rd or 4th degree perineal lacerations (aOR 2.06)[3]

There is widespread emphasis on reducing peripartum racial and ethnic disparities, especially as they relate to SMM and maternal mortality.[44, 47] Factors contributing to the disparities noted above include an increased rate of chronic (i.e. chronic HTN, asthma, diabetes, blood disorders) and pregnancy-related (i.e. preE, gestational diabetes) comorbidities, decreased access to primary and prenatal care due to both insurance status and financial inability to miss work, language/ communication barriers, community factors (i.e. crime, housing, social support, delivery hospital), systemic and institutionalized racism, institutional and clinician implicit bias, lower educational attainment/ health literacy and lower socioeconomic status. [1, 44, 48^]

Facility-based Disparities

Delivery hospital is implicated in maternal health disparities. Several studies demonstrated significantly higher SMM in hospitals that disproportionately care for black women, and black women are more likely to deliver in hospitals with higher SMM rates.[1] Black and Hispanic women are significantly more likely to deliver in hospitals with a poor quality rating compared to white women.[49] The rate of SMM at low-volume centers (<1000 deliveries/ year) is also increasing at a concerning rate. Teaching hospitals with <1000 deliveries/ year had increased risk for SMM compared to non-teaching, low volume centers.[50] Rural residents had a 9% greater probability for SMM and maternal mortality compared to urban residents, have decreased access to care[51] and increased risk for ICU admission.[52]

Recognition Leads to Prevention

Delayed recognition of conditions is significantly associated with SMM and mortality. Data from 2017-2019 from 36 showed 84% of pregnancy-related deaths were preventable.[53] The density of maternal fetal medicine (MFM) physicians is significantly and inversely associated with MMR[54]. Health systems with poor maternal outcomes should prioritize expanding access for not only MFM services but also subspecialty consultation for medically complex parturients. The concept of an obstetric "hospitalist" or "laborist" is promoted to allow immediate availability for bedside assessment to improve early recognition of at-risk women and allow rapid intervention. Because they work frequently in a single setting, these obstetricians understand specific hospital resources and protocols and can initiate diagnostic and therapeutic steps even while the patient's primary provider is being called.[18]

Several maternal mortality risk prediction models have been proposed although no single model has sufficient discrimination for individual patient clinical decision making.[55] Bateman and colleagues created an obstetric comorbidity index (OCI) which includes pregnancy-specific conditions[56] and has been validated as a tool to summarize burden of comorbid illness.[57] Multiple recent studies have correlated increased OCI score with increased SMM.[58, 59] Higher OCI score may also correlate with preventability of SMM.[59] Other authors recently explored OCI scoring with the ICD-10 system which heavily weights comorbidities such as placenta accreta[60] and whether pre-pregnancy health can predict risk for adverse maternal outcomes.[61]

Unfortunately, even when performed, risk stratification is not always effective. A significant number of women who suffered SMM[59] or died during hospital care had no identifiable risk factors for cause of maternal death and a significant percentage of the deaths occurred at a tertiary care center.[62] However, when high risk patients are identified early, multidisciplinary planning can start even before pregnancy. Teams can systematically create detailed ante- and peripartum care plans, anticipate and prepare for complications and communicate regularly with all care team members.[63]

Maternal Early Warning Criteria (MEWC):

The goal of MEWC is early identification of women at risk of a condition associated with SMM and/ or mortality allowing prompt bedside assessment and early diagnostic and therapeutic intervention to prevent progression to SMM or death. The criteria do not depend on existing risk factors and instead are abnormal vital sign parameters which account for physiologic changes of pregnancy and, when met, trigger the above process. Recent studies have shown that a MEWS prioritizes high sensitivity over specificity, demonstrates superb negative predictive value for severe maternal morbidity,[64, 65] may help predict survival in patients admitted to the ICU for reasons related to pregnancy[66] and can significantly decrease the rate of severe maternal morbidity.[67] Automated, EMR-based systems may be used

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to augment nursing-driven MEWS to detect additional at-risk women.[68] Automated pathways for risk assessment for both hemorrhage and hypertensive disorders are not part of a traditional MEWS but should be implemented and incorporated into EMRs to promote earlier diagnosis and treatment.

Addressing Maternal Morbidity and Mortality: Where do we go from here?

Alliance for Innovation on Maternal Health (AIM, saferbirth.org)

Formerly the Council on Patient Safety in Women's Healthcare, since 2015 organizations invested in maternal care, including the ASA and the Society for Obstetric Anesthesia and Perinatology (SOAP) have created 12 safety bundles to aid facilities in promoting Readiness, Recognition and Prevention, Response, and Reporting/ Systems Learning for many factors contributing to SMM and maternal mortality including obstetric hemorrhage, severe hypertension in pregnancy, safe reduction of primary cesarean birth, maternal venous thromboembolism and maternal mental health. There are also resources related to MEWS implementation and review of SMM events. Ideally, each bundle would be fully implemented in every obstetric unit nationwide. However, even partial implementation can significantly decrease risk for severe maternal morbidity.[69, 70] and a diverse group of hospitals in California successfully adopted the majority of the hemorrhage bundle, demonstrating applicability outside large, tertiary centers.[71] Since July 1, 2020 The Joint Commission considers 13 elements of performance (7 for PPH and 6 for hypertensive disorders) during hospital accreditation reviews, most of which are based on bundle components.[72] Anesthesiologists should participate in their facility's efforts to implement the safety bundles and associated tools.

Now run by AOCG, AIM is a collaborative to help states and birthing facilities with evidence-based safety and quality improvement resources based on case reviews of SMM and maternal mortality.[10] Participating hospitals have personal support for safety bundle implementation and the ability to track and benchmark quality performance following implementation through the AIM national data center, providing another opportunity to address state-wide system issues that are barriers for improved maternal outcomes and to coordinate and expand efforts.

Maternal Mortality Review Committees (MMRC) and Perinatal Quality Collaboratives (PQC)

Intra-institutional review of SMM and mortality cases via confidential, standardized, multidisciplinary approach allows identification of contributing provider and system issues to improve quality of care and promote a culture of safety. There is tremendous emphasis on larger scale systematic tracking of SMM and mortality by state and regional perinatal quality care collaboratives.[10] The MMRCs' in-depth analysis of contributing factors and personal/medical circumstances of each death may provide more detailed and accurate data on maternal deaths.[10] Modern data analytic techniques may also improve recognition and review of pregnancy associated deaths.[73]

Forty-four states currently have established MMRC[74], and most others (including the District of Columbia and Puerto Rico) have either legislation pending to create an MMRC or are in the implementation process.[75] Illinois has a second statewide MMRC (MMRC-V) for deaths due to violence, homicide, suicide and substance abuse.[31] A majority of states either have or are developing a PQC which work to identify areas for improvement in maternal and fetal health care processes and quickly implement widespread change to promote quality perinatal care.[75] A national network of PQC now exists[76] and some advocate for a national MMRC, modeled after other high-resource nations, to produce evidence-based plans of action to reduce MMR nationwide.[5]

Introduced in December 2015, "Building U.S. Capacity to Review and Prevent Maternal Deaths" is an initiative working to remove barriers to fully functioning MMRCs and to promote inter-MMRC collaboration. This program created the Maternal Mortality Review Information Application (MMRIA) that allows MMRCs to abstract and analyze data, document committee decisions and share data across MMRCs. Early work has provided insight into maternal mortality that was not possible by individual MMRC working in silos. An example is the identification of system-level (i.e. lack of access to primary care, mental health providers and obstetricians) and community-level factors (lack of access to transportation, affordable groceries and recreation/ fitness public spaces) that contribute to maternal deaths.[2, 77] Resources and ongoing opportunities from the effort can be found at www.ReviewtoAction.org.

The Preventing Maternal Deaths Act of 2018 (H.R.1318) called for all states and Indian tribes/ tribal organizations to establish confidential, multidisciplinary MMRCs that allow for voluntary case reporting of pregnancy-associated and pregnancy-related deaths by family members of the deceased and other appropriate individuals. To accomplish these goals, a yearly budget of $58 million for 2019 – 2023 was established.[78]

Other Pending Legislation Related to Maternal Morbidity and Mortality (Introduced 2018-2020)

The "Maternal CARE Act" would provide grants to health professional training programs to address implicit bias and reduce adverse outcomes and racial disparities in obstetrics. The "MOMMIES Act" would extend postpartum care of

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women who received Medicaid for pregnancy and delivery from 60 to 365 days. The "Rural MOMS Act" includes provisions to improve care for pregnant and postpartum women in rural settings. The "Mothers and Newborns Success Act" focuses on addressing racial, ethnic and geographical inequities in maternal health. The "Black Maternal Health Momnibus" comprehensively addresses Black maternal health issues. Finally, in December 2020 the Surgeon General issued a call to action to improve maternal health that was released concurrently with the Department for Health and Human Services "Action Plan to Improve Maternal Health". Unfortunately, the rise of anti-abortion legislation has been associated with an increase in maternal mortality.[79]

Response by Physicians, Hospitals, Health Systems and Beyond

Moving forward, we must leverage the focus on this topic to improve early recognition and intervention of at-risk women and eliminate preventable SMM and maternal deaths. Regular surveillance of pregnant and postpartum patients is critical. Maternal EWS should be widely implemented, and vital sign parameters should balance high sensitivity with alarm fatigue for bedside providers. Surveillance should also include screening for and treating nonconventional causes of SMM and maternal mortality such as trauma (especially violent) and risk for self-harm including suicide and accidental overdose.[30] This should start with preconception and prenatal care and continue to the "4th trimester" after delivery as this can be an especially vulnerable time.[32, 34] Approximately 1/3 of all pregnancy-related deaths occur outside a medical facility, further demonstrating need for community surveillance.[80] The importance of acting on voiced concerns from patients and family members is emphasized by several campaigns including "Every Mother Counts"[81] and "Hear Her" aimed at safe care and reducing preventable SMM and deaths.

Small volume delivery facilities should focus on awareness of when to seek consultation from and potential transfer to tertiary centers and improve early, standardized, disease-specific treatment.[62, 82]. The Society for MFM and ACOG Levels of Maternal Care outlines recommendations for center capabilities and where patients with specific risk factors should deliver. Level 1 centers are best suited for "Basic Care" and Level IV are "Regional Perinatal Health Care Centers".[83] One goal of this initiative is to pair lower level facilities with Level III/ IV centers to facilitate that consultation and transfer of patients that as needed. The requirements for Level II-IV centers designate "anesthesia services available at all times" and Level III/IV requires an obstetrician onsite at all times and a board-certified anesthesiologist with special training in obstetrics in charge of obstetric anesthesia services.[83]

We must also improve obstetric critical care. Currently there is no ACGME requirement for critical care training during OB-GYN residency, however an ICU rotation is mandatory for MFM fellows.[10] We should encourage intensivist participation in multidisciplinary teams, even potentially a "virtual ICU" where the majority of planning is done ahead of time for potential peripartum complications and/or ICU admission.[63] The Maternal Levels of Care Level III centers require at a minimum an ICU that accepts pregnant patients and Level IV facilities require active ICU collaboration with MFM care team in the management of complex parturients.[83]

By supporting national, state-wide and system-level quality and process improvement efforts directed at maternal health[48] we can build a culture of safety and equity.[1] We need to realize 100% of state participation in multidisciplinary MMRC and encourage those committees to work with underperforming communities and individual hospitals to improve quality of care. Finally, we must set the ideal of access to early, reliable, equitable and high-quality reproductive care for *all* women[44, 48] We need to openly measure, report upon and discuss racial and ethnic maternal health disparity and use this data to make meaningful changes to maternal outcomes.[44]

The Anesthesiologist's Specific Role in Decreasing Maternal Morbidity and Mortality

Be part of the team and embrace the role of peripartum physician! Similar to our identity as perioperative physicians, we should be involved in the care of women throughout pregnancy, during labor and delivery and into the postpartum period. Specifically, we should encourage early antepartum anesthesia consultation for medically complex parturients, participate in multidisciplinary team care planning and coordination, serve on hospital, state and regional MMRC, be part of the effort to implement maternal safety bundles (start with hypertension and hemorrhage, and be aggressive!), use a combination of risk prediction models and MEWC to identify at-risk patients, help with the diagnostic and treatment processes for acute events on labor and delivery and recognize that we likely have the most expertise on the labor and deliver unit when it comes to critical care, transfusion medicine and cardiopulmonary resuscitation. Our involvement and expertise will improve maternal outcomes and it is our responsibility to help lead the many ongoing efforts to reduce severe maternal morbidity and mortality.

1. Howell EA. Reducing Disparities in Severe Maternal Morbidity and Mortality. Clin Obstet Gynecol. 2018;61(2):387-399.

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2. Anonymous. Building U.S. Capacity to Review and Prevent Maternal Deaths. Report from Maternal Mortality Review Committees: A View into Their Critical Role. 2017. Available at: http://reviewtoaction.org/content/report-mmrcs-view-theircritical-role Accessed May 3, 2019.
3. Holdt Somer SJ, Sinkey RG, Bryant AS. Epidemiology of racial/ethnic disparities in severe maternal morbidity and mortality. Semin Perinatol. 2017;41(5):258-265.
4. Callaghan WM, Creanga AA, Kuklina EV. Severe maternal morbidity among delivery and postpartum hospitalizations in the United States. Obstet Gynecol. 2012;120(5):1029-36.
5. Clark SL, Belfort MA. The Case for a National Maternal Mortality Review Committee. Obstet Gynecol. 2017;130(1):198-202.
6. Collaborators GBDMM. Global, regional, and national levels of maternal mortality, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388(10053):1775-1812.
7. MacDorman MF, Declercq E, Cabral H, Morton C. Recent Increases in the U.S. Maternal Mortality Rate: Disentangling Trends From Measurement Issues. Obstet Gynecol. 2016;128(3):447-55.
8. Davis NL, Hoyert DL, Goodman DA, et al. Contribution of maternal age and pregnancy checkbox on maternal mortality ratios in the United States, 1978-2012. Am J Obstet Gynecol. 2017;217(3):352 e1-352 e7.
9. Joseph KS, Lisonkova S, Muraca GM, et al. Factors Underlying the Temporal Increase in Maternal Mortality in the United States. Obstet Gynecol. 2017;129(1):91-100.
10. D'Alton ME, Friedman AM, Bernstein PS, et al. Putting the "M" back in maternal-fetal medicine: A 5-year report card on a collaborative effort to address maternal morbidity and mortality in the United States. Am J Obstet Gynecol. 2019.
11. Slomski A. Why Do Hundreds of US Women Die Annually in Childbirth? JAMA. 2019.
12. Nelson DB, Moniz MH, Davis MM. Population-level factors associated with maternal mortality in the United States, 1997-2012. BMC Public Health. 2018;18(1):1007.
13. Guglielminotti J, Landau R, Wong CA, Li G. Criticality of Maternal Complications During Childbirths. J Patient Saf. 2018.
14. Ozimek JA, Eddins RM, Greene N, et al. Opportunities for improvement in care among women with severe maternal morbidity. Am J Obstet Gynecol. 2016;215(4):509 e1-6.
15. Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-Related Mortality in the United States, 2011-2013. Obstet Gynecol. 2017;130(2):366-373.
16. Abir G, Mhyre J. Maternal mortality and the role of the obstetric anesthesiologist. Best Pract Res Clin Anaesthesiol. 2017;31(1):91-105.
17. Anonymous. Building U.S. Capacity to Review and Prevent Maternal Deaths (2018). Report from nine maternal mortality review committees. Available at: http://reviewtoaction.org/Report_from_Nine_MMRCs. Retrieved April 8, 2019.
18. Stevens TA, Swaim LS, Clark SL. The Role of Obstetrics/Gynecology Hospitalists in Reducing Maternal Mortality. Obstet Gynecol Clin North Am. 2015;42(3):463-75.
19. Mhyre JM, Shilkrut A, Kuklina EV, et al. Massive blood transfusion during hospitalization for delivery in New York State, 1998-2007. Obstet Gynecol. 2013;122(6):1288-94.
20. Gupta M, Greene N, Kilpatrick SJ. Timely treatment of severe maternal hypertension and reduction in severe maternal morbidity. Pregnancy Hypertens. 2018;14:55-58.
21. Wolfe DS, Hameed AB, Taub CC, et al. Addressing maternal mortality: the pregnant cardiac patient. Am J Obstet Gynecol. 2019;220(2):167 e1-167 e8.
22. Pfaller B, Sathananthan G, Grewal J, et al. Preventing Complications in Pregnant Women With Cardiac Disease. J Am Coll Cardiol. 2020;75(12):1443-1452.
23. O'Kelly AC, Scott N, DeFaria Yeh D. Delivering Coordinated Cardio-Obstetric Care from Preconception through Postpartum. Cardiol Clin. 2021;39(1):163-173.
24. Bauer ME, Lorenz RP, Bauer ST, et al. Maternal Deaths Due to Sepsis in the State of Michigan, 1999-2006. Obstet Gynecol. 2015;126(4):747-52.
25. Siddiqui A, Azria E, Howell EA, et al. Associations between maternal obesity and severe maternal morbidity: Findings from the French EPIMOMS population-based study. Paediatr Perinat Epidemiol. 2019;33(1):7-16.
26. Zipori Y, Grunwald O, Ginsberg Y, et al. The impact of extending the second stage of labor to prevent primary cesarean delivery on maternal and neonatal outcomes. Am J Obstet Gynecol. 2019;220(2):191 e1-191 e7.
27. DeBolt CA, Bianco A, Limaye MA, et al. Pregnant women with severe or critical coronavirus disease 2019 have increased composite morbidity compared with nonpregnant matched controls. Am J Obstet Gynecol. 2021;224(5):510 e1-510 e12.
28. Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-June 7, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(25):769-775.
29. Boettcher LB, Metz TD. Maternal and neonatal outcomes following SARS-CoV-2 infection. Semin Fetal Neonatal Med. 2023;28(1):101428.
30. Deshpande NA, Kucirka LM, Smith RN, Oxford CM. Pregnant trauma victims experience nearly 2-fold higher mortality compared to their nonpregnant counterparts. Am J Obstet Gynecol. 2017;217(5):590 e1-590 e9.
31. Koch AR, Geller SE. Addressing maternal deaths due to violence: the Illinois experience. Am J Obstet Gynecol. 2017;217(5):556 e1-556 e6.
32. Metz TD, Rovner P, Hoffman MC, et al. Maternal Deaths From Suicide and Overdose in Colorado, 2004-2012. Obstet Gynecol. 2016;128(6):1233-1240.
33. Ray JG, Zipursky J, Park AL. Injury-related maternal mortality. Am J Obstet Gynecol. 2018;219(3):307-308.
34. Mangla K, Hoffman MC, Trumpff C, et al. Maternal self-harm deaths: an unrecognized and preventable outcome. Am J Obstet Gynecol. 2019.
35. Berthelot N, Lemieux R, Garon-Bissonnette J, et al. Uptrend in distress and psychiatric symptomatology in pregnant women during the coronavirus disease 2019 pandemic. Acta Obstet Gynecol Scand. 2020;99(7):848-855.
36. Hall OT, Hall OE, Rood KM, et al. Pregnancy-Associated Mortality Due to Accidental Drug Overdose and Suicide in Ohio, 2009-2018. Obstet Gynecol. 2020;136(4):654-656.
37. Baeva S, Archer NP, Ruggiero K, et al. Maternal Mortality in Texas. Am J Perinatol. 2017;34(6):614-620.
38. Tucker MJ, Berg CJ, Callaghan WM, Hsia J. The Black-White disparity in pregnancy-related mortality from 5 conditions: differences in prevalence and case-fatality rates. Am J Public Health. 2007;97(2):247-51.
39. Harper MA, Espeland MA, Dugan E, et al. Racial disparity in pregnancy-related mortality following a live birth outcome. Ann Epidemiol. 2004;14(4):274-9.
40. Rosenberg D, Geller SE, Studee L, Cox SM. Disparities in mortality among high risk pregnant women in Illinois: a population based study. Ann Epidemiol. 2006;16(1):26-32.
41. Berg CJ, Harper MA, Atkinson SM, et al. Preventability of pregnancy-related deaths: results of a state-wide review. Obstet Gynecol. 2005;106(6):1228-34.
42. Mehta PK, Kieltyka L, Bachhuber MA, et al. Racial Inequities in Preventable Pregnancy-Related Deaths in Louisiana, 2011-2016. Obstet Gynecol. 2020;135(2):276-283.
43. Hopkins FW, MacKay AP, Koonin LM, et al. Pregnancy-related mortality in Hispanic women in the United States. Obstet Gynecol. 1999;94(5 Pt 1):747-52.
44. Howell EA, Brown H, Brumley J, et al. Reduction of Peripartum Racial and Ethnic Disparities: A Conceptual Framework and Maternal Safety Consensus Bundle. Obstet Gynecol. 2018;131(5):770-782.
45. Creanga AA, Bateman BT, Kuklina EV, Callaghan WM. Racial and ethnic disparities in severe maternal morbidity: a multistate analysis, 2008-2010. Am J Obstet Gynecol. 2014;210(5):435 e1-8.
46. Tangel V, White RS, Nachamie AS, Pick JS. Racial and Ethnic Disparities in Maternal Outcomes and the Disadvantage of Peripartum Black Women: A Multistate Analysis, 2007-2014. Am J Perinatol. 2018.

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47. Jain JA, Temming LA, D'Alton ME, et al. SMFM Special Report: Putting the "M" back in MFM: Reducing racial and ethnic disparities in maternal morbidity and mortality: A call to action. Am J Obstet Gynecol. 2018;218(2):B9-B17.
48. Anonymous. Black women's maternal health: A multifaceted approach to addressing persistent and dire health disparities. National Partnership for Women & Families 2018. http://www.nationalpartnership.org/our-work/resources/health-care/maternity/black-womens-maternal-health-issue-brief.pdf. Accessed May 1, 2019.
49. Howell EA, Janevic T, Blum J, et al. Double Disadvantage in Delivery Hospital for Black and Hispanic Women and High-Risk Infants. Matern Child Health J. 2020;24(6):687-693.
50. Hehir MP, Ananth CV, Wright JD, et al. Severe maternal morbidity and comorbid risk in hospitals performing <1000 deliveries per year. Am J Obstet Gynecol. 2017;216(2):179 e1-179 e12.
51. Kozhimannil KB, Interrante JD, Tofte AN, Admon LK. Severe Maternal Morbidity and Mortality Among Indigenous Women in the United States. Obstet Gynecol. 2020;135(2):294-300.
52. Harrington KA, Cameron NA, Culler K, et al. Rural-Urban Disparities in Adverse Maternal Outcomes in the United States, 2016-2019. Am J Public Health. 2023;113(2):224-227.
53. Anonymous. Trost SL, Beauregard J, Njie F, et al. Pregnancy-Related Deaths: Data from Maternal Mortality Review Committees in 36 US States, 2017–2019. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2022.
54. Sullivan SA, Hill EG, Newman RB, Menard MK. Maternal-fetal medicine specialist density is inversely associated with maternal mortality ratios. Am J Obstet Gynecol. 2005;193(3 Pt 2):1083-8.
55. Aoyama K, D'Souza R, Pinto R, et al. Risk prediction models for maternal mortality: A systematic review and meta-analysis. PLoS One. 2018;13(12):e0208563.
56. Bateman BT, Mhyre JM, Hernandez-Diaz S, et al. Development of a comorbidity index for use in obstetric patients. Obstet Gynecol. 2013;122(5):957-65.
57. Metcalfe A, Lix LM, Johnson JA, et al. Validation of an obstetric comorbidity index in an external population. BJOG. 2015;122(13):1748-55.
58. Somerville NJ, Nielsen TC, Harvey E, et al. Obstetric Comorbidity and Severe Maternal Morbidity Among Massachusetts Delivery Hospitalizations, 1998-2013. Matern Child Health J. 2019;23(9):1152-1158.
59. Easter SR, Bateman BT, Sweeney VH, et al. A comorbidity-based screening tool to predict severe maternal morbidity at the time of delivery. Am J Obstet Gynecol. 2019;221(3):271 e1-271 e10.
60. Leonard SA, Kennedy CJ, Carmichael SL, et al. An Expanded Obstetric Comorbidity Scoring System for Predicting Severe Maternal Morbidity. Obstet Gynecol. 2020;136(3):440-449.
61. Krenitsky NM, Huang Y, Wen T, et al. Longitudinal Risk Adjustment for Maternal End-Organ Injury and Death. J Matern Fetal Neonatal Med. 2021:1-7.
62. Clark SL, Christmas JT, Frye DR, et al. Maternal mortality in the United States: predictability and the impact of protocols on fatal postcesarean pulmonary embolism and hypertension-related intracranial hemorrhage. Am J Obstet Gynecol. 2014;211(1):32 e1-9.
63. Leovic MP, Robbins HN, Starikov RS, Foley MR. Multidisciplinary obstetric critical care delivery: The concept of the "virtual" intensive care unit. Semin Perinatol. 2018;42(1):3-8.
64. Arnolds DE, Smith A, Banayan JM, et al. National Partnership for Maternal Safety Recommended Maternal Early Warning Criteria Are Associated With Maternal Morbidity. Anesth Analg. 2018.
65. Singh A, Guleria K, Vaid NB, Jain S. Evaluation of maternal early obstetric warning system (MEOWS chart) as a predictor of obstetric morbidity: a prospective observational study. Eur J Obstet Gynecol Reprod Biol. 2016;207:11-17.
66. Paternina-Caicedo A, Miranda J, Bourjeily G, et al. Performance of the Obstetric Early Warning Score in critically ill patients for the prediction of maternal death. Am J Obstet Gynecol. 2017;216(1):58 e1-58 e8.
67. Shields LE, Wiesner S, Klein C, et al. Use of Maternal Early Warning Trigger tool reduces maternal morbidity. Am J Obstet Gynecol. 2016;214(4):527 e1-527 e6.
68. Klumpner TT, Kountanis JA, Meyer SR, et al. Use of a Novel Electronic Maternal Surveillance System and the Maternal Early Warning Criteria to Detect Severe Postpartum Hemorrhage. Anesth Analg. 2020.
69. Main EK, Cape V, Abreo A, et al. Reduction of severe maternal morbidity from hemorrhage using a state perinatal quality collaborative. Am J Obstet Gynecol. 2017;216(3):298 e1-298 e11.
70. Bingham D, Scheich B, Bateman BT. Structure, Process, and Outcome Data of AWHONN's Postpartum Hemorrhage Quality Improvement Project. J Obstet Gynecol Neonatal Nurs. 2018;47(5):707-718.
71. Main EK, Dhurjati R, Cape V, et al. Improving Maternal Safety at Scale with the Mentor Model of Collaborative Improvement. Jt Comm J Qual Patient Saf. 2018;44(5):250-259.
72. Anonymous. R3 Report: Provision of Care, Treatment, and Services standards for maternal safety. The Joint Commission: Issue 24, August 21, 2019. https://www.jointcommission.org/standards/r3-report/r3-report-issue-24-pc-standards-for-maternal-safety/. Accessed July 5, 2020.
73. Hollenbach SJ, Drennan K, Pressman EK, Gray L. Improved Recognition of Maternal Deaths Using Modern Data Analytics. Obstet Gynecol. 2021;137(5):772-778.
74. Anonymous. Review to Action MMRC Map. https://reviewtoaction.org/content/mmr-map. Accessed July 1, 2020.
75. Anonymous. State Maternal Mortality Review Committees, PCQs and AIM. American College of Obstetricians and Gynecologists. https://www.acog.org/-/media/Departments/Government-Relations-and-Outreach/MMRC_AIM-State-Fact-Sheet_Mar-2019.pdf?dmc=1&ts=20190518T1430040664. Accessed May 1, 2019. .
76. Henderson ZT, Ernst K, Simpson KR, et al. The National Network of State Perinatal Quality Collaboratives: A Growing Movement to Improve Maternal and Infant Health. J Womens Health (Larchmt). 2018;27(3):221-226.
77. Zaharatos J, St Pierre A, Cornell A, et al. Building U.S. Capacity to Review and Prevent Maternal Deaths. J Womens Health (Larchmt). 2018;27(1):1-5.
78. Anonymous. "Beyond The Preventing Maternal Deaths Act: Implementation And Further Policy Change, " Health Affairs Blog, February 4, 2019. https://www.congress.gov/bill/115th-congress/house-bill/1318/text. Accessed May 1, 2019.
79. Harper LM, Leach JM, Robbins L, et al. All-Cause Mortality in Reproductive-Aged Females by State: An Analysis of the Effects of Abortion Legislation. Obstet Gynecol. 2023;141(2):236-242.
80. Burgess APH, Dongarwar D, Spigel Z, et al. Pregnancy-related mortality in the United States, 2003-2016: age, race, and place of death. Am J Obstet Gynecol. 2020;222(5):489 e1-489 e8.
81. Baumont MS, Dekker CS, Rabinovitch Blecker N, et al. Every Mother Counts: listening to mothers to transform maternity care. Am J Obstet Gynecol. 2023;228(5S):S954-S964.
82. Foley MR. Reestablishing trust in the medical profession: making a significant impact on maternal mortality in the United States. Am J Obstet Gynecol. 2014;211(1):1-2.
83. Anonymous. Obstetric Care Consensus No. 2: Levels of maternal care. Obstet Gynecol. 2015;125(2):502-15.

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Anesthesia for Non-obstetric Surgery During Pregnancy

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Introduction

Surgery during pregnancy is unique because of the need to consider the requirements of two patients. There is difficulty conducting randomized clinical trials in this population, leading to a paucity of data to allow for specific recommendations. Despite the lack of clear evidence, outcomes are generally favorable for both mother and fetus. Coordinated multidisciplinary care allows for safe and effective care of pregnant patients undergoing surgical procedures. It is important to obtain an obstetric consultation before performing non-obstetric surgery because obstetricians are uniquely qualified to determine gestational age of the fetus, discuss the risks, benefits and alternatives of proceeding with surgery during pregnancy, and discuss aspects of maternal anatomy and physiology that may affect intraoperative outcomes of mother and fetus. Ultimately, each case warrants a team approach with input from providers from surgery, anesthesia, obstetrics, and pediatrics to optimize safety for the woman and her fetus.

Timing and Types of Surgery

Approximately 1% of pregnant women will undergo surgery during their pregnancy, which equates to roughly 100,000 women undergoing non-obstetric surgery in the United States each year. Although nearly every type of surgical operation has been performed during pregnancy, the most common conditions that result in non-obstetric surgeries are appendicitis, cholecystitis, trauma, bowel obstruction, and diseases involving the cervix, ovaries, or breasts. A pregnant woman should never be denied medically necessary surgery or have that surgery delayed because this can adversely affect the pregnant woman and her fetus. However, because of the potential for adverse events including spontaneous abortion, preterm labor and/or delivery, and fetal drug exposure, elective surgery should be delayed until after the woman delivers. Surgery is ideally performed in the second trimester when the risk of spontaneous abortion is lower than the first trimester and the incidence of pre-term labor and delivery is lower than the third trimester. Laparoscopic surgery can be performed safely during pregnancy; the specific surgical approach should be based on surgeon preference and potential patient benefits.

Anesthetic Considerations

Physiologic changes of pregnancy

Nearly every organ system is affected by pregnancy. Early changes are hormonally driven, while mechanical effects of the enlarging uterus, increased metabolic demands of the fetus, and the low resistance of placental circulation create further physiologic alterations later in pregnancy. Particularly noteworthy changes occur in the respiratory system, where a 20-30% decrease in functional residual capacity along with an increase in oxygen consumption contributes to rapid desaturation during periods of apnea. Additionally, pregnant patients have mildly increased minute ventilation and lower resting $PaCO_2$. Increased tissue swelling and friability in the oropharynx reduces the size of the glottis opening and decreases the volume of pharyngeal space. Although rates vary widely dependent on circumstance and definition, the incidence of difficult intubation may be as much as ten times higher in a pregnant patient at term compared to a non-pregnant patient. Loss of airway control is the most common cause of anesthesia-related maternal mortality.

Blood volume increases 30-50% during pregnancy, while cardiac output steadily increases throughout pregnancy to reach approximately130-50% of pre-pregnancy values by the late third trimester. The increase in cardiac output is due to both an increase in heart rate and an increase in stroke volume (preload is increased from the rise in blood volume while afterload is decreased due to a decline in vascular resistance). The growing uterus can obstruct venous return, particularly after the 20th week of gestation and when the woman is in a supine position. Approximately 8-10% of pregnant women experience significant hypotension in the supine position. While the precise impact on uteroplacental perfusion is unknown, the supine position is best avoided in patients displaying a drop in blood

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pressure as this may signify reduced cardiac output and uteroplacental perfusion. If possible for the specific surgery being performed, the preponderance of evidence and clinical experience suggests that left uterine displacement reduces the chance for maternal hypotension and reduced cardiac output, and thus should be employed. MRI studies have shown that there is very little caval compression with 30 degrees of left lateral tilt. However, many operations cannot be performed effectively that position. After about 20 weeks' gestation some degree of left lateral tilt (at least 15 degrees) should be applied. If there is maternal or fetal hemodynamic instability, further increase in tilt may be necessary. Left uterine displacement is preferentially performed by placing a wedge under the patient's right hip. Alternatively, the operating room table can be tilted.

Despite gastric emptying and acid secretion being normal during pregnancy, there is reduced lower esophageal sphincter tone due to hormonal changes, mechanical alterations, and increased intraabdominal pressure. These factors increase the risk of gastroesophageal reflux. Although the true risk and rates of aspiration at the time of anesthesia is difficult to ascertain, it seems wise to consider the pregnant patient as having a higher risk for aspiration compared to a non-pregnant patient beginning at about 16-18 weeks gestation. This is true particularly for women with a higher BMI and those with symptomatic reflux disease. Despite this concern, rates of aspiration are very low and are on par with the general population for specific types of surgery.

Type of anesthesia

The anesthetic plan should consider the type of surgery, the mother's underlying medical condition, the effects of anesthesia on both the patient and the fetus, and the relative preferences of the patient, surgeon, and anesthesiologist. There is no data supporting differences in neonatal outcome based on anesthetic type. Regional anesthesia is preferred when it is practical to avoid unnecessary fetal exposure to medications and to reduce the need to instrument the maternal airway. However, because most non-obstetric surgeries in pregnancy are abdominal procedures where muscle relaxation is advantageous, general anesthesia is most often employed. Regardless of anesthetic technique, maintaining normal maternal physiology to optimize uteroplacental blood flow is of paramount importance.

ASA fasting guidelines are applicable. Although no specific method of aspiration prophylaxis has been shown to reduce aspiration risk, many providers provide H2 receptor antagonists, sodium bicitrate, and/or metoclopramide based on personal and institutional preferences.

Antibiotic prophylaxis is administered based on the procedure, with avoidance of aminoglycosides (e.g.intravenous gentamicin, tobramycin, amikacin streptomycin or neomycin) if possible based on a small risk of fetal ototoxicity and nephrotoxicity. There is no proven benefit to routine prophylactic perioperative tocolytic therapy, and these agents should not be used in the absence of uterine contractions and obstetric recommendations.

Pregnant patients can safely undergo sedation as part of "monitored anesthesia care" for indicated procedures. The most used medications are propofol for sedation, fentanyl for analgesia, and midazolam for anxiolysis. All have a long history of safe and effective use. Sedation doses tend to be on the lower end of dosing spectrum to decrease risk for loss of airway reflexes, hypoventilation induced respiratory acidosis, and due to patient request. Although many providers use rapid sequence intubation in all pregnant patients, there is no good evidence that this is beneficial. The incidence of aspiration at induction of anesthesia is low and on par with non-pregnant patients unless they are at higher risk for other reasons such as inadequate fasting times. Preoxygenation is important as apnea leads to a more rapid desaturation in pregnant versus non pregnant patients primarily due to reduced functional residual capacity.

Standard induction and neuromuscular agents should be chosen based on the clinical situation. Pregnancy reduces the minimum alveolar concentration for volatile inhalation agents but appears to have little impact on the dosing of induction agents, which should be titrated to effect. For otherwise healthy patients, propofol is the induction agent of choice. Most providers use succinylcholine to facilitate endotracheal intubation, and there are varying opinions on the use of rapid sequence induction/intubation practices. The choice of maintenance anesthetics should be based on

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usual considerations. Pregnancy is associated with an increased sensitivity to opioids as well as volatile anesthetics. Patients may be more sensitive to neuromuscular blocking agents, accentuating the need to monitor neuromuscular block depth in these patients (e.g. train-of-four). While the safe administration of neostigmine for neuromuscular blockade reversal has been well-established, some providers prefer to co-administer atropine instead of glycopyrrolate because atropine more readily crosses the placenta and can mitigate any effect of neostigmine on fetal heart rate. However, a long history of using glycopyrrolate in combination with neostigmine for fetal surgery has shown no untoward effects on fetal heart rate, thus either anticholinergic is safe. There is not enough data on the use of sugammadex in pregnancy to draw meaningful conclusions at this time, but the Society of Obstetric Anesthesiology and Perinatology currently recommends against its routine use in pregnant women. Levels of pseudocholinesterase are reduced in pregnancy. Though the duration of action of succinylcholine can be prolonged, this is almost never of any clinical significance. Pregnancy is also associated with decreased protein binding, increased volume of distribution, and changes in hepatic/renal elimination that may contribute to minor changes in drug effects and metabolism of some drugs.

The lower limit for acceptable maternal blood pressure is not known and is likely patient dependent. Vasopressor use in pregnancy has generally been studied at the time of cesarean delivery. Phenylephrine is generally preferred due to the tendency of ephedrine to lead to progression of fetal academia. Many anesthesiologists primarily use phenylephrine to support the blood pressure while using ephedrine to keep the heart rate above 60 beats per minute to optimize cardiac output. Norepinephrine is gaining more traction for optimizing cardiac output at cesarean delivery and is a possible alternative to the solely alpha-receptor acting phenylephrine. Controlled hypotension may be hazardous to uteroplacental blood flow and should not be used routinely. Mechanical ventilation should be adjusted to maintain the normal physiologic chronic respiratory alkalosis of pregnancy, usually an $ETCO_2$ of around 30-32 mmHg. The $PaCO_2$ to $EtCO_2$ gradient decreases during pregnancy due to better ventilation-perfusion matching. Carbon dioxide rapidly crosses the placenta, and higher levels may lead to acidosis and myocardial depression in the fetus. On the flip side, severe respiratory alkalosis can compromise uterine blood flow from uterine artery vasoconstriction. Inspired oxygenation of 50 percent or more should be used to optimize maternal PaO_2 and help mitigate against fetal hypoxia. Previous concerns of maternal hyperoxygenation causing free radical production or retinopathy of prematurity in the fetus appear unfounded, as the fetal PaO_2 does not exceed approximately 60 mmHg regardless of maternal PaO_2. Some anesthesiologists send arterial blood samples during mechanical ventilation during pregnancy to be sure that the normal physiologic acid base state of pregnancy is maintained.

As mentioned above, airway management can be more difficult in pregnant patients. Both mask ventilation and intubation have decreased success rates when compared to a non-pregnant population. Appropriate preparation for difficult airway management should be undertaken. The improvements and increased utilization of indirect video laryngoscopy have improved airway management in recent years. Interestingly, a review of maternal mortality in a two-decade period in Michigan showed that while no maternal deaths occurred during induction or maintenance of anesthesia, several deaths occurred from hypoventilation or airway obstruction during extubation or recovery.
To minimize airway management and limit fetal drug exposure, regional anesthesia should be used as the primary anesthetic technique when feasible. Epidural, spinal, and peripheral block techniques are all used successfully. The spread of local anesthetic within the epidural space is greater in pregnancy, and there is also an increased sensitivity to local anesthetics; doses can be slightly reduced for spinal and epidural anesthesia later in pregnancy. Reduced protein binding in pregnancy can increase the risk for local anesthetic toxicity. In addition to surgical anesthesia, these modalities can aid in postoperative pain control, which is important for preventing preterm labor amongst other usual benefits. Many of these women may be on thromboprophylaxis due to elevated risk for thromboembolism so it is important to take a careful history of such prior to proceeding with regional anesthesia. Outside of regional techniques, acetaminophen and opioids provide the bulk of postoperative analgesia. Nonsteroidal anti-inflammatory drugs are best avoided, particularly after 32 weeks because they can cause premature closure of the fetal ductus arteriosus. Isolated doses of ketorolac in mid-pregnancy are likely safe, but there is little evidence on this either way.

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Fetal Considerations

Fetal Monitoring

At a minimum, all patients should have a fetal heart rate (FHR) documented before and after surgery, regardless of gestational age. For fetuses considered viable, a tocodynamometer should be used postoperatively to monitor for uterine contractions (which may signify preterm labor) along with electronic FHR monitoring. Intraoperative FHR monitoring can be done continuously or intermittently using Doppler ultrasound. Sometimes transvaginal ultrasound is used when the surgical procedure does not allow access to the abdomen. Intraoperative fetal heart rate monitoring is only of benefit if it is physically possible to perform based on patient characteristics and the nature of the operation. Continuous FHR monitoring is feasible beginning around 18-22 weeks gestation. If intraoperative FHR is used, there needs to be a qualified person readily available to interpret fetal heart rate patterns. It is not always easy to distinguish whether changes in FHR tracing are due to anesthetic agents or fetal hypoxia. While fetal bradycardia reliably indicates fetal compromise, changes in FHR baseline and variability could have multiple causes. FHR typically displays reduced variability with GA, and baseline FHR may also decrease (but stays in the normal range of 120-160). It is best practice to make sure that an obstetric provider capable of performing cesarean delivery is informed of the case and readily available if needed. If the fetus is viable and intraoperative monitoring is used, there should be a plan in place regarding whether emergency cesarean delivery will be performed in the event of fetal deterioration. This potential scenario should be discussed amongst the surgeon, obstetrician, and patient. The institution should also have neonatal services to care for a potentially compromised pre-term neonate in the event of delivery. Even when there is no plan to deliver the fetus, FHR monitoring can assist in maternal positioning and cardiorespiratory management. In the setting of deterioration in FHR status, intratuterine fetal resuscitation (e.g. repositioning, maternal hemodynamic support, oxygenation optimization, etc.) should be attempted. The ultimate decision on whether to use intraoperative FHR monitoring should be individualized based on gestational age, type of surgery, and available facilities. A 2010 survey of obstetricians reported that 43% routinely used intraoperative FHR monitoring, and there appears to be wide variation in practice across the United States.

Fetal Effects

Possible fetal risks of maternal surgery include: teratogenicity of anesthetic agents or other drugs administered, decreases of uteroplacental perfusion and/or fetal oxygenation, and subsequent preterm delivery or fetal demise. Because fetal hemoglobin has a high affinity for oxygen, mild to moderate decreases in maternal PaO2 are tolerated well. Severe persistent maternal hypoxemia is a threat to fetal life. Although some have speculated that maternal hyperoxia could have potential negative effects such as free radical production and uteroplacental vasoconstriction, this has not been shown to occur clinically. Additionally, because the PaO2 of the fetus never gets above 60 mm Hg there is little concern for causing intrauterine retrolental fibroplasia and/or premature closure of the ductus arteriosis. As mentioned above, maternal PaCO2 should be kept in a normal range for pregnancy because hypoventilation can lead to fetal acidosis while hyperventilation can impair fetal oxygenation and reduce uterine blood flow. There is some evidence in animal models that suggest high-dose volatile anesthetics can lead to fetal acidosis and decreased cardiac function. It is unknown if total intravenous anesthesia may preserve fetal cardiac status more so than volatile anesthesia. If a fetus needs to be delivered during non-obstetric surgery, ventilator support may be needed due to the depressant effects of opioids and other anesthetic agents. These effects are transient until the medications wear off. Potent inhalational anesthetics decrease uterine tone. This is advantageous in inhibiting labor during the operative procedure. In the event of emergent delivery, increased number and/or amounts of utertonic agents may be required to restore uterine tone.

Teratogenicity

No currently used anesthetic agents have been shown to have any teratogenic effects in humans when using standard doses for an isolated surgical procedure at any gestational age. Although data from animal studies is mixed, multiple large retrospective studies have shown no increase in congenital defects in children born to mothers who underwent surgery and anesthesia while pregnant. The use of nitrous oxide and benzodiazepines in the perioperative period has long been controversial. Exposure to high concentrations of nitrous oxide during organogenesis has been shown to

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have deleterious effects in animal studies. Nitrous oxide inhibits methionine synthetase, a key enzyme in DNA production. However, no adverse fetal effects have been noted when administered as part of a pregnant woman's anesthetic. Similarly, preoperative use of benzodiazepines has not been associated with any adverse fetal outcome. Thus, there is no compelling evidence that any specific anesthetic agents should be avoided during pregnancy. Still, it seems prudent to avoid nitrous oxide in the first trimester as there are almost always reasonable alternatives.

Fetal brain development

The effect of anesthetic agents on the developing fetal brain is an area of current research. All general anesthetic drugs readily cross the placenta except for neuromuscular blocking drugs. The potential for commonly used anesthetic agents to modify neuronal apoptosis and other neurodegenerative changes in the developing brain has been evident in animal studies for nearly two decades. The very rapid development of the fetal brain, particularly starting in the 3rd trimester makes this patient group vulnerable. Several studies of fetal anesthetic exposure in rodents, sheep, and non-human primates have shown neuroapoptosis and other neurodegenerative changes with exposure to ketamine, propofol, volatile inhalational agents, and benzodiazepines. Some problems with fetal animal studies include a lack of surgical stimulation in most studies, interspecies differences in brain development, and insufficient data about relative dose, duration, and numbers of exposures. Because of their mechanism of action (at the GABA and NMDA receptors), and interactions with normal neurotransmission, it is plausible to consider that anesthetic agents could have effects on neural development in the rapidly developing immature human brain. Clinical studies in humans have shown mixed results and have typically involved anesthesia in young children. Retrospective studies have shown an association between exposure to general anesthesia as an infant and later neurobehavioral problems in childhood – particularly for prolonged or repeated exposures. However, other studies have reported no association between anesthesia exposure as a child and subsequent neurodevelopmental outcomes. It is virtually impossible to separate the effects of anesthesia from the effects of surgery or the underlying condition requiring intervention itself. Both retrospective and recent prospective studies in infants/children suggest that a single, brief exposure to anesthesia does not increase the risk of neurotoxicity. One retrospective study looking at childhood outcomes after being exposed to anesthesia prenatally during maternal non-obstetric surgery showed an increased association with exposure and worse behavioral scores, but no difference in cognitive, motor, or other outcomes. In December 2016, the Food and Drug Administration communicated a warning that "repeated or lengthy (>3hours) us of general anesthetic and/or sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains". This warning clearly has implications for non-obstetric surgery in pregnant patients. This issue of potential anesthetic neurotoxicity has a greater urgency with the FDA warning. However, the degree of risk remains unclear. One small study found that children exposed to general anesthesia in utero displayed increased behavioral deficits but no difference in learning or intelligence when compared to non-exposed children. More research is needed looking at the effects of prolonged repeated exposure, variability among drug and combinations of drugs, and patient factors that may confer vulnerability. Until such data is available, it seems prudent to minimize exposure to medications during pregnancy if possible.

Dexmedetomidine is a sedative agent that is a highly selective agonist for alpha-2 receptors in the central nervous system and has no interaction with GABA or NMDA. In fetal rat models, dexmedetomidine exposure shows no increase in neuroapoptosis. When dexmedetomidine was added to isoflurane, there was a dose-dependent reduction in neruoapoptotic changes. Similar results were shown when the rats were tested later in life for memory and spatial orientation – namely that dexmedetomidine attenuated with decrement in performance seen in the rats exposed to isoflurane alone. Current literature supports the idea that dexmedetomidine does not cause neurodegenerative changes and has potential to be neuroprotective. Opioids, specifically remifentanil, have not been demonstrated to cause neuroapoptosis, so a combination of these two drugs represents a plausible approach to providing anesthesia/analgesia while limiting potential fetal neurotoxic effects.

Outcomes

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Maternal outcomes after non-obstetric surgery are the same as non-pregnant patients undergoing like procedures. Mortality and morbidity do not appear to be increased based on pregnancy status. Studies analyzing data from the American College of Surgeons National Surgical Quality Improvement Program database for pregnant women undergoing surgery showed that the rate of major complications was approximately 7%, which was not different from the rate in non-pregnant women. It is unclear the exact extent to which pregnancy outcomes are affected by undergoing non-obstetric surgery. The overall miscarriage rate has been shown to be like the general obstetrical population, and there is no increased rate of birth defects in those who underwent non-obstetric surgery while pregnant as previously mentioned. One of the main risks of surgery during pregnancy is preterm labor and delivery, particularly for surgery performed in the third trimester. The rate of fetal delivery related to surgery was about 3.5% in one study. Additionally, the rate of low birthweight infants and early neonatal death were increased in women who had surgery (due to prematurity and growth restriction). recent review looking at over 47,000 surgeries in pregnant patients reported that in every 287 procedures there was one additional stillbirth, every 31 surgeries were associated with one additional preterm birth, every 39 surgeries were associated with one additional low-birth weight infant, and every 25 surgeries were associated with one additional cesarean delivery. Risks are increased with higher risk surgery such as cardiac surgery with cardiopulmonary bypass, where a recent meta-analysis showed maternal death was 11% and pregnancy loss was 33%. Importantly, it is not clear whether this increase resulted from the procedure itself or from an effect of the underlying medical condition necessitating surgery. Because delaying non-elective procedures is dangerous for a woman's health, indicated surgery should proceed efficiently. Surgical delay has been associated with worse outcomes, particularly for infectious indications. Undergoing surgery during pregnancy does not impact subsequent type of delivery, which is based upon standard obstetrical indications. Even patients with recent abdominal incisions can undergo labor and vaginal delivery in most cases.

Conclusion

While elective surgery should be postponed until after delivery, a pregnant patient should not be delayed necessary surgery because delaying such surgery will result in increased morbidity and mortality compared to proceeding with surgery. Anesthetic management of pregnant patients necessitates maternal and fetal considerations. Physiologic and anatomic changes related to pregnancy may require adaptations of surgical and anesthetic technique. No anesthetic agent has been shown to be teratogenic at clinical concentrations and doses; however, it is prudent to minimize fetal drug exposure. Each individual case warrants a team approach with input surgery, anesthesia, and obstetrical teams. Maintenance of maternal oxygenation, acid-base status, and uteroplacental perfusion will assure the best outcome for the fetus.

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