SPECIAL ARTICLE

Placenta Accreta Spectrum Disorders: Knowledge Gaps in Anesthesia Care

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ABSTRACT: Placenta accreta spectrum (PAS) disorder is a potentially life-threatening condition that can occur during pregnancy. PAS puts pregnant individuals at a very high risk of major blood loss, hysterectomy, and intensive care unit admission. These patients should receive care in a center with multidisciplinary experience and expertise in managing PAS disorder. Obstetric anesthesiologists play vital roles in the peripartum care of pregnant patients with suspected PAS. As well as providing high-quality anesthesia care, obstetric anesthesiologists coordinate peridelivery care, drive transfusion-related decision making, and oversee postpartum analgesia. However, there are a number of key knowledge gaps related to the anesthesia care of these patients. For example, limited data are available describing optimal anesthesia staffing models for scheduled and unscheduled delivery. Evidence and consensus are lacking on the ideal surgical location for delivery; primary mode of anesthesia for cesarean delivery; preoperative blood ordering; use of pharmacological adjuncts for hemorrhage management, such as tranexamic acid and fibrinogen concentrate; neuraxial blocks and abdominal wall blocks for postoperative analgesia; and the preferred location for postpartum care. It is also unclear how anesthesia-related decision making and interventions impact physical and mental health outcomes. High-quality international multicenter studies are needed to fill these knowledge gaps and advance the anesthesia care of patients with PAS.

GLOSSARY

FIGO = The International Federation of Gynecology and Obstetrics; **GA** = general anesthesia; **ICU** = intensive care unit; **NA** = neuraxial anesthesia; **PAS** = placenta accreta spectrum; **PAS2** = Pan-American Society for the Placenta Accreta Spectrum; **PPH** = postpartum hemorrhage; **RBC** = red blood cells; **REBOA** = resuscitative endovascular balloon occlusion of the aorta; **TXA** = tranexamic acid

Placenta accreta spectrum (PAS) disorder is a highly morbid condition characterized by abnormal adherence of the placenta to the uterine wall. The incidence of PAS has increased markedly over time, from between 1 in 2510 and 1 in 4017 between the 1970s and 1980s to 1 in 533 between 1982 and 2002.[1] More recent data from the Nationwide Inpatient Sample, a large US hospitalization database, reported that the incidence was 1 in 272 between 1998 and 2011.[2] The escalating incidence of PAS since the 1970s is related to the marked increase in the US cesarean delivery rate from the early to late 2000s.[3]

Patients with a PAS disorder are at substantial risk of major peripartum complications, including massive blood loss, hysterectomy, and intensive care unit admission.[4] Clinical guidelines published by The American College of Obstetricians and Gynecologists, The International Society for Abnormally Invasive Placenta, and The International Federation of Gynecology and Obstetrics (FIGO) highlight the importance of a multidisciplinary team for case management.[5–7]

As a key member of a multidisciplinary team, an anesthesiologist has several important roles. In addition to providing high-quality anesthesia care, anesthesiologists coordinate peridelivery care with the multidisciplinary team (which includes surgeons, transfusion medicine specialists, and critical care physicians), oversee transfusion-related decision making and manage postpartum analgesia. Outcomes in patients with

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PAS may also be optimized through input provided by an anesthesiologist with training and experience in peridelivery and perioperative medical care.[8]

The extent to which anesthetic and analgesic-related practices and interventions influence maternal and neonatal outcomes in patients with PAS is unclear. Most studies of anesthesia practices contain relatively small samples from single obstetric centers.[9–18] The lack of high-quality data from population-based cohorts and randomized trials may explain why there is a lack of consensus statements and guidelines. Consequently, anesthesia and analgesia-related recommendations are predominantly based on expert opinion.[19,20]

In this Special Article, we highlight knowledge gaps related to the anesthetic care of patients with PAS and research needed to fill these gaps. Filling these gaps will provide sufficient evidence to inform future guidelines and consensus statements for anesthesia care.

KNOWLEDGE GAP 1: ANESTHESIA STAFFING

Evidence suggests that, for patients without PAS undergoing cesarean delivery, the presence of an experienced obstetric anesthesiologist is associated with improved anesthetic outcomes. Data from 2 separate observational studies indicate that the presence of a fellowship-trained obstetric anesthesiologist is associated with a lower general anesthesia rate compared with an anesthesiologist without specialist training.[21,22] In contrast, there is sparse information about the level of training and expertise of anesthesia providers who provide care for patients with suspected PAS undergoing cesarean hysterectomy. Moreover, it is unclear whether anesthesia care quality or outcomes differ between specialists trained in managing PAS cases versus nonspecialists. Observational studies examining provider-level factors associated with maternal outcomes may inform future guidelines and recommendations about the level of subspecialist experience required by anesthesia staff.

The logistics of organizing anesthesia staff for suspected PAS cases requiring elective cesarean hysterectomy may vary across institutions. Operating room schedulers or administrators may designate staff from a group of anesthesia providers (physician anesthesiologists or certified nurse anesthetists) who work in the main operating room. Alternatively, large teaching hospitals may assign an anesthesiologist from a dedicated group or division of obstetric anesthesiologists. For nonscheduled cases that require urgent delivery, there may be variability in how hospitals provide an experienced team at short notice.

There is a need for survey data from well-resourced countries to understand anesthesia staffing models for scheduled and unscheduled cases. In addition, studies are needed to evaluate the costs of establishing a dedicated out-of-hours obstetric anesthesia service for PAS cases requiring urgent delivery at high-volume perinatal centers, designated as level IV centers by the American College of Obstetricians and Gynecologists Levels of Maternal Care.[23]

KNOWLEDGE GAP 2: PERIOPERATIVE CARE

There is no consensus on the surgical location for delivery. Location options include an operating room on the labor and delivery unit, the main operating complex, the interventional radiology unit, or a hybrid environment.[20] In a US survey of obstetric anesthesiology division chiefs, 71% of respondents reported that the main operating room was the preferred location for high-risk cases, such as suspected increta or percreta.[24] Descriptive studies of key hospital-level resources (such as turnaround times for ordering and receipt of blood products from a blood bank, availability of rapid transfusion equipment, neonatal resuscitation equipment, specific surgical equipment for cesarean hysterectomy, and proximity to radiology equipment to perform balloon placement or embolization) can inform local decisions about preferred delivery location. Preferences of key clinicians (surgeons, anesthesiologists, radiologists, and neonatologists) about delivery location are also important. For example, gynecological-oncology surgeons may have their preferred equipment and surgical scrub team in surgical location remote from the labor and delivery unit.

Consensus is also lacking on the preferred location and resources for providing postoperative care. Suitable locations include a postpartum unit, a surgical floor unit, a high-dependency unit (ie, "step-down"), or an intensive care unit (surgical or medical). There is a dearth of studies examining the association between key hospital and personnel-level factors (such as the level of experience and training of nursing staff, nursing to bed ratios, and enhanced recovery protocols) and postoperative outcomes. Large-scale observational studies are needed to examine these associations, after accounting for patient-level factors.

KNOWLEDGE GAP 3: ANESTHESIA MODE

Maternal Outcomes

Options for the primary mode of anesthesia for cesarean delivery in patients with suspected PAS include general anesthesia, neuraxial anesthesia (spinal, epidural, or combined spinal-epidural), or both. We summarize the potential advantages and disadvantages of each anesthesia mode in Table 1. Among patients undergoing a cesarean hysterectomy, combined neuraxial plus general anesthesia refers to the use of neuraxial anesthesia for the cesarean delivery followed by elective (planned) conversion to general anesthesia after delivery of the neonate and before hysterectomy.

Table 1. Potential Advantages and Disadvantages of Neuraxial, General, and Combined Neuraxial-General Anesthesia for Cesarean Hysterectomy

Anesthetic modality	Advantages	Disadvantages
Neuraxial anesthesia	Patient is awake	Possible need for emergent conversion to GA
	Bonding possible	Inferior operative conditions
	Lower incidence of Apgar <7	Intraoperative nausea and vomiting
	Minimal effect on uterine tone	Risk of neuraxial block failure
	Possibly lower blood loss	Need for maternal anxiolysis or sedation
	Possibly superior postoperative pain management depending on surgical incision	Concern for epidural hematoma in a high-blood loss surgery
	Reduced ICU admission	Risk of postdural puncture headache
General anesthesia	Airway secured	Failed intubation/airway disasters
	Controlled ventilation	Unwarranted use of general anesthesia if PAS not identified
	Superior operative conditions	Fetal exposure to anesthetic medications
		Volatile anesthetic decreases uterine tone
		Higher magnitude of blood loss
		Higher incidence of Apgar score <7
		Negative effect on neonatal bonding and breastfeeding
		Postoperative nausea and vomiting
		May require high-dose systemic opioid for postoperative pain control
Elective conversion from neuraxial to general anesthesia after delivery	Reduced fetal exposure to anesthetics	Timing of laryngoscopy and intubation may not be ideal
	Patient can see and bond with neonate	Hemodynamic instability after induction of general anesthesia in the presence of a neuraxial sympathectomy and/or possible hemorrhage
	Airway secured for the resuscitation phase of case	

Abbreviations: GA, general anesthesia; ICU, intensive care unit; PAS, placenta accreta spectrum.

Table 2. Study Data of Anesthesia Modes Used for Patients With Placenta Accreta Spectrum Disorders

Reference (first author, year of publication)	Sample size (N)	Country of origin	Patients who underwent cesarean hysterectomy (%)	Primary GA (%)	Primary NA (%)	Conversion from NA to GA (%)[a]
Eller et al (2009)[9]	76	United States (Utah)	97	76	16	8
Lilker et al (2011)[11]	23	Canada (Ontario)	30	26	52	22
Kocaoglu et al (2012)[10]	28	Turkey	61[b]	86	7	7
Grace Tan et al (2013)[25]	27	Australia	100	100	0	0
Shamshirsaz et al (2015) (nonmultidisciplinary group)[16]	33	United States (Texas)	NS	53	25	22
Shamshirsaz et al (2015) (multidisciplinary group)[16]	57	United States (Texas)	NS	46	10	44
Nguyen-Lu et al (2016)[12]	50	Canada (Toronto)	72	12	62	26
Taylor and Russell (2017)[14]	40	United Kingdom	60	5	53	43
Wang et al (2017)[15]	96	China	13	8	72	20
Markley et al (2018)[17]	81	United States (Massachusetts)	93[b]	9	73	19
Riveros-Perez and Wood (2018)[13]	43	United States (Colorado)	91	9	21	70
Binici and Büyükfırat (2019)[18]	43	Turkey	<9	77	19	5

Data presented as n or %. Sum totals in each row may be >100% due to rounding.
Abbreviations: GA, general anesthesia; NA, neuraxial anesthesia.
[a]Includes planned and unplanned conversion from neuraxial to general anesthesia.
[b]All subjects with concurrent placenta previa.

Unplanned conversion from neuraxial to general anesthesia can occur in specific scenarios, such as massive hemorrhage with hemodynamic instability or concern for airway edema, failed neuraxial block with intraoperative breakthrough pain, or relaxation of the muscles in the anterior abdominal wall to optimize surgical access to the intra-abdominal cavity during hysterectomy.

To our knowledge, only 11 studies have reported data on primary modes of anesthesia for cesarean delivery with suspected PAS (Table 2). Among these studies, there was a wide range in the reported frequency of general anesthesia (5%–100%), neuraxial anesthesia (0%–72%), and intraoperative conversion from neuraxial to general anesthesia (7%–70%). Studies using population-wide data can advance our understanding of the mode of anesthesia used for these surgeries, the potential impact on maternal and neonatal morbidity, and the degree to which geographical, clinician and patient-level factors explain variability in practice and outcomes.

For patients undergoing neuraxial blockade as the primary mode of anesthesia, the incidence of intraoperative breakthrough pain and patients' experiences

about the adequacy of breakthrough pain management are unknown. For patients undergoing general anesthesia, we know little about the incidence of failed intubation and secondary airway rescue, anesthetic (inhalational; intravenous) and analgesic drug data, and non-neuraxial analgesia interventions (such as abdominal wall blocks).

Patient, surgical, and physician-level factors may influence the type of anesthetic used by an anesthesiologist. Patient factors may include anticipated difficult airway, morbid obesity, medical comorbidities, and the risk of major blood loss. For example, anesthesiologists may consider general anesthesia to avoid conversion from neuraxial to general anesthesia during major intraoperative hemorrhage. In addition to the potential risk of profound hemodynamic instability due to hemorrhage and a sympathectomy from neuraxial anesthesia, the risk of coagulopathy and need for massive transfusion may also need to be considered.

Surgical factors include the planned surgical incision, timing of hysterectomy (immediately after cesarean delivery or "delayed" to a later date), and the use of vascular interventions. A supraumbilical skin incision or preoperative placement of vascular occlusion devices (such as resuscitative endovascular balloon occlusion of the aorta [REBOA] or internal iliac balloon catheters) may be factors that influence whether or not to perform neuraxial blockade and the type of block (lumbar or thoracic epidural, single-shot spinal, or combined spinal-epidural). The level of provider experience and the availability of more than 1 anesthesia staff member during a case may play a role in anesthetic decision making.

An additional challenge is that anesthetic planning is probably influenced by the suspected degree and extent of placental invasion based on preoperative imaging. However, there are no standardized approaches for classifying PAS subtypes before surgery and no risk-assessment tools or models that accurately quantify each patient's risk of severe hemorrhage and morbidity based on available clinical, radiological, and laboratory data. This information affects anticipatory planning for perioperative hemorrhage. To address inaccuracies in PAS diagnoses in the international literature, an expert panel convened by FIGO has developed a classification system using clinical and histological criteria.[26] Further improvements to the classification of PAS invasiveness would advance multidisciplinary planning for delivery and allow researchers to examine the associations between preoperative PAS staging with peri- and postoperative outcomes.

Data are also lacking on patient-centric outcomes. In an awake patient undergoing neuraxial anesthesia, stimulation from the use of a surgical retractor device, such as a table-fixed Bookwalter retractor, may cause undue discomfort, psychological distress, and ultimately conversion to general anesthesia. It is unclear whether negative patient experiences from inadequate neuraxial anesthesia or psychological distress experienced during high blood-loss surgery are associated with adverse postpartum mental health outcomes such as depression and post-traumatic stress disorder. We also need to determine which anesthesia-related decisions would benefit from patient involvement, such as the use of general versus neuraxial anesthesia.

Neonatal Outcomes

Large-scale, high-quality observational studies examining the association between neonatal outcomes and mode of anesthesia in this setting are lacking. General anesthesia may occur more frequently than neuraxial anesthesia for an unplanned cesarean hysterectomy, especially if there is an urgency to deliver. Other factors related to the timing and indication for delivery could influence neonatal outcome. Prolonged neonatal intensive care unit admission and neonatal morbidity can occur more often after an unplanned versus scheduled cesarean delivery in patients with PAS.[27] Also, patients with suspected PAS commonly undergo planned preterm delivery.[20] To evaluate the potential effect of general anesthesia on the risk of neonatal morbidity, studies will need to disentangle any effect from other important contributors, including preterm delivery and relevant delivery indications such as maternal hemorrhage, preeclampsia, prolonged rupture of membranes, oligohydramnios, and nonreassuring fetal heart rate tracings.

KNOWLEDGE GAP 4: PLANNING AND MANAGING MASSIVE OBSTETRIC HEMORRHAGE

About 47% of patients with suspected PAS experience hemorrhage requiring blood transfusion.[28] Therefore, anticipatory planning for massive intraoperative hemorrhage is critical. Key considerations for hemorrhage management include location and size of intravenous access (peripheral and/or central), blood ordering (number and types of blood components), resources for facilitating massive transfusion (institution-specific massive transfusion protocol, rapid infuser devices, and intraoperative use of cell salvage), and point-of-care devices (including transthoracic echocardiography for assessing intracardiac volume and contractility, and devices for assessing the coagulation profile, such as thromboelastography). However, no outcome-based studies have compared specific approaches for hemorrhage management in patients with PAS. For example, it is unclear whether a formulaic transfusion-based approach is associated with a greater risk of morbidity than a goal-directed approach using point-of-care devices for major hemorrhage from PAS or other causes.

KNOWLEDGE GAP 5: POSTOPERATIVE PAIN MANAGEMENT

Few data exist to inform our understanding of patient-reported postpartum pain outcomes and analgesic use. In a small observational single-center study of 39 patients with suspected PAS who underwent cesarean delivery, Panjeton et al[29] examined whether postoperative opioid consumption varied according to anesthesia mode. Compared to women who received general anesthesia, mean-adjusted postoperative opioid consumption was at least 150 oral morphine mg equivalents lower for women who had neuraxial with conversion to general anesthesia following delivery or neuraxial anesthesia only. To our knowledge, there are no data examining postoperative opioid use in large populations of women with PAS who underwent cesarean hysterectomy. This information gap likely means that anesthesiologists are basing their decisions about postoperative pain management on personal preference, clinical experience, and evidence from studies of uncomplicated cesarean delivery or alternate major abdominal procedures. The risk for chronic or persistent pain or chronic opioid use after cesarean delivery for PAS compared to uncomplicated cesarean delivery is also unknown.

Postoperative analgesia options include long-acting neuraxial opioids, an epidural infusion, patient-controlled epidural analgesia, abdominal wall blocks, intravenous patient-controlled analgesia, and intravenous or oral analgesics. The effectiveness of unimodal versus multimodal analgesic regimens in this patient population is unclear.

Future Directions

To provide a preliminary framework to address these research gaps, we conducted a pilot survey of the authors of this article. Each author provides anesthesia and peridelivery care for patients with suspected PAS at a specialist center. Eight authors practice in the United States, 1 in Canada, and 1 in Israel. The survey response rate was 100%. Table 3 presents key findings of the survey. There was notable variability across the institutions in the case volume, hysterectomies, preferred anesthesia modes for suspected placenta percreta, preoperative blood ordering, and use of prohemostatic agents (tranexamic acid; fibrinogen concentrate). However, all institutions staffed these cases with obstetric anesthesiologists. Although these survey data are based on responses from a small number of respondents, each institution is considered a level 3 or 4 maternal level care center[23] with fellowship-trained obstetric anesthesiologists experienced in the management of patients with PAS. It is unclear whether these responses reflect preferences and practices of each respondent as opposed to those of a group of anesthesiologists based at each institution. Larger surveys will expand knowledge about the variability in anesthesiologists' practices and available resources. Also, there is a lack of studies examining practices and perinatal outcomes in the developing world, especially as advanced antenatal diagnostic information and specialist care are likely not available at many delivery sites.

Table 3. Summary of Survey Data From 10 Specialist Centers

Variables	Median (range) or frequency
Patient volume and cesarean hysterectomies	
Number of suspected PAS patients admitted per month	4 (1–10)
Number of scheduled cesarean hysterectomies per month	2 (0–6)
Number of unscheduled cesarean hysterectomies per month	1 (0–3)
Preferred anesthetic mode and interventions for suspected placenta accreta	
Elective GA for the entire case	40%
Neuraxial with planned conversion to GA	30%
Neuraxial planned for the entire case	30%
Central line	40%
Arterial line	90%
Rapid infuser	100%
Cell salvage	80%
Number of units of blood products ordered before surgery	
RBC	5 (4–10)
Plasma	4 (0–6)
Platelets	0 (0–2)
Cryoprecipitate	0 (0–5)
Pharmacological adjuncts	
TXA used as PPH prophylaxis	40%
TXA used for PPH treatment	30%
Fibrinogen concentrate for PPH treatment	30%
Acetaminophen	90%
Ketorolac	90%
Regional analgesia for postoperative analgesia	
Epidural	40%
Abdominal wall blocks	80%

Abbreviations: GA, general anesthesia; PAS, placenta accreta spectrum; PPH, postpartum hemorrhage; RBC, red blood cells; TXA, tranexamic acid.

International multicenter studies will help advance knowledge and anesthesia care of patients with PAS. A research consortium across multiple tertiary care centers can address this unmet need. For this purpose, in 2019, a working group of obstetric anesthesiologists met at the inaugural Pan-American Society for the Placenta Accreta Spectrum (PAS2) meeting in Boston, MA. PAS2 is a new society comprising multidisciplinary specialists with a primary focus on reducing the morbidity and mortality of PAS through collaborative research, education, and advocacy.[30] A goal of the PAS2 obstetric anesthesia-working group is to bring together investigators with common research interests who can share and leverage resources, ideas, and research expertise. Multicenter studies examining anesthesia interventions and outcomes in patients with PAS will allow

large sample sizes, account for different geographical locations, and allow comparisons of results among centers, all of which increase the generalizability of research findings. We believe that this line of research will enhance the quality of evidence and inform guidelines and consensus statements for the anesthesia care of patients with PAS.

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