OBSTETRICS

Outcomes following a clinical algorithm allowing for delayed hysterectomy in the management of severe placenta accreta spectrum

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BACKGROUND: The incidence of placenta accreta spectrum is rising. Management is most commonly with cesarean hysterectomy. These deliveries often are complicated by massive hemorrhage, urinary tract injury, and admission to the intensive care unit. Up to 60% of patients require transfusion of ≥4 units of packed red blood cells. There is also a significant risk of death of up to 7%.

OBJECTIVE: The purpose of this study was to assess the outcomes of patients with antenatal diagnosis of placenta percreta that was managed with delayed hysterectomy as compared with those patients who underwent immediate cesarean hysterectomy.

STUDY DESIGN: We performed a retrospective study of all patients with an antepartum diagnosis of placenta percreta at our large academic institution from January 1, 2012, to May 30, 2018. Patients were treated according to standard clinical practice that included scheduled cesarean delivery at 34–35 weeks gestation and intraoperative multidisciplinary decision-making regarding immediate vs delayed hysterectomy. In cases of delayed hysterectomy, the hysterotomy for cesarean birth used a fetal surgery technique to minimize blood loss, with a plan for hysterectomy 4–6 weeks after delivery. We collected data regarding demographics, maternal comorbidities, time to interval hysterectomy, blood loss, need for transfusion, occurrence of urinary tract injury and other maternal complications, and maternal and fetal mortality rates. Descriptive statistics were performed, and Wilcoxon rank-sum and chi-square tests were used as appropriate.

RESULTS: We identified 49 patients with an antepartum diagnosis of placenta percreta who were treated at Vanderbilt University Medical Center during the specified period. Of these patients, 34 were confirmed to have severe placenta accreta spectrum, defined as increta or percreta at the time of delivery. Delayed hysterectomy was performed in 14 patients: 9 as scheduled and 5 before the scheduled date. Immediate cesarean hysterectomy was completed in 20 patients: 16 because of intraoperative assessment of resectability and 4 because of preoperative or intraoperative bleeding. The median (interquartile range) estimated blood loss at delayed hysterectomy of 750 mL (650–1450 mL) and the sum total for delivery and delayed hysterectomy of 1300 mL (70 –2150 mL) were significantly lower than the estimated blood loss at immediate hysterectomy of 3000 mL (2375–4250 mL; $P<.01$ and $P=.037$, respectively). The median (interquartile range) units of packed red blood cells that were transfused at delayed hysterectomy was 0 (0–2 units), which was significantly lower than units transfused at immediate cesarean hysterectomy (4 units [2–8.25 units]; $P<.01$). Nine of 20 patients (45%) required transfusion of ≥4 units of red blood cells at immediate cesarean hysterectomy, whereas only 2 of 14 patients (14.2%) required transfusion of ≥4 units of red blood cells at the time of delayed hysterectomy ($P=.016$). There was 1 maternal death in each group, which were incidences of 7% and 5% in the delayed and immediate hysterectomy patients, respectively.

CONCLUSION: Delayed hysterectomy may represent a strategy for minimizing the degree of hemorrhage and need for massive blood transfusion in patients with an antenatal diagnosis of placenta percreta by allowing time for uterine blood flow to decrease and for the placenta to regress from surrounding structures.

Key words: delayed hysterectomy, placenta accreta spectrum, placenta increta, placenta percreta

Placenta accreta spectrum (PAS) is a disease of the 20th and 21st centuries. It was first described in 1937 by Irving and Hertig[1] as, "the abnormal adherence, either in whole in or in part, of the afterbirth to the underlying uterine wall." In this condition, failure of the placenta to separate normally after delivery may lead to massive hemorrhage. PAS is classified by the depth of placental invasion. The most aggressive form of PAS is placenta percreta, which occurs in approximately 6% of these patients.[2] In this process, the placenta penetrates the full thickness of the myometrium and uterine serosa with possible involvement of adjacent organs, including the bladder, parametria, and bowel.

The incidence of PAS has increased strikingly from 1 in 30,000 deliveries in the 1930s to 1 in 533 deliveries in 2005. It has been estimated that, if the cesarean delivery rate continues to rise at its current pace, by 2020 there will be 4504 additional patients (or nearly 9000 cases) with PAS and 130 additional maternal deaths annually.[3]

Maternal morbidity from PAS is significant and includes massive hemorrhage with the need for large volume blood transfusion, coagulopathy, visceral injury, infection, thromboembolism, and need for reoperation. Postpartum hemorrhage is common in these patients, with average estimated blood loss (EBL) ranging from 2000–4000 mL.[4–6] Overall morbidity rates have been reported to range from 24–67%.[4–6] Furthermore, the maternal mortality rate has been estimated to be as high as 7%.[7] Patient

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AJOG at a Glance

Why was this study conducted?

The study was conducted to assess the surgical outcomes (which include operative time, blood loss, transfusion requirements, and complications) of patients with an antenatal diagnosis of placenta percreta that was managed with delayed hysterectomy compared with those patients who underwent immediate cesarean hysterectomy after the addition of a clinical algorithm that encourages intraoperative multidisciplinary assessment for consideration of cesarean delivery with delayed hysterectomy.

Key findings

Patients with an antenatal diagnosis of placenta percreta who underwent delayed hysterectomy experienced significantly lower blood loss and lower likelihood of blood product transfusion and were significantly less likely to require transfusion of $\geq$4 units of red blood cells compared with patients who underwent immediate cesarean hysterectomy.

What does this add to what is known?

Surgical outcomes in our cohort of patients with placenta percreta support the consideration and continued study of delayed hysterectomy as a strategy to reduce operative blood loss and blood transfusion requirement significantly in the most severe cases of placenta percreta.

outcomes have been shown to be improved significantly by planned, as opposed to emergent, delivery[4,6,8] and by care at an experienced center of excellence with multidisciplinary care.[4,5,8]

Cesarean hysterectomy remains the most widely accepted and preferred approach to PAS according to an Obstetric Care Consensus document developed jointly by the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine and endorsed by The Society of Gynecologic Oncology.[9] More conservative surgical approaches have been reported but are generally considered investigational and include cesarean delivery with placenta left in situ until delayed hysterectomy.[9] Fertility-sparing strategies such as the Triple-P procedure, with resection of the placenta with the involved uterine wall and uterine reconstruction, or leaving the placenta in situ after cesarean delivery and allowing it to regress spontaneously have been reported.[10,11] Evidence-based recommendations and considerations related to alternative strategies to immediate cesarean hysterectomy have been presented by the International Federation of Obstetricians and Gynecologists in a consensus guideline that focuses on conservative management of PAS and in evidence-based guidelines by the International Society for Abnormally Invasive Placenta that specifically address the paucity of published studies on delayed hysterectomy.[12,13] Women with the most severe adherent placentation, such as placenta percreta, have been described as optimal candidates for these alternative surgical approaches because of the increased risk of blood loss and potential bladder and tissue damage with immediate cesarean hysterectomy.[12,14]

Given the morbidity of this entity, novel treatment strategies that may decrease maternal complications are needed. We describe our experience with an alternative approach for the treatment of placenta percreta, which is akin to the evidence-based concept of "damage control resuscitation" in trauma patients, in which surgical times are reduced, and definitive treatment is deferred, until physiologic condition normalizes.[15] Our staged procedure includes multidisciplinary planning and consideration of a staged procedure, with cesarean delivery followed by delayed hysterectomy, for the most severe cases of PAS.

Materials and Methods

We identified all patients who underwent scheduled cesarean delivery with an antenatal diagnosis of placenta percreta who were treated at our institution between January 1, 2012, and May 30, 2018. A retrospective chart review was performed. We collected data regarding demographics, maternal comorbidities, operative findings, pathologic findings, time to interval hysterectomy, blood loss, need for transfusion, occurrence of urinary tract injury and other maternal complications, and maternal and fetal deaths. Patients were identified from a prospective database of all patients with an antenatal diagnosis of placenta accreta that was created during the study period. Study data were collected and managed with REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Vanderbilt University Medical Center.[16] REDCap is a secure, web-based application designed to support data capture for research studies by providing (1) an intuitive interface for validated data entry, (2) audit trails for tracking data manipulation and export procedures, (3) automated export procedures for seamless data downloads to common statistical packages, and (4) procedures for importing data from external sources. The Vanderbilt Institutional Review Board approved the study on March 29, 2013 (Institutional Review Board #130373) and again on December 21, 2018. Statistical assessment of our data was performed with descriptive statistics and Wilcoxon rank-sum and chi-square tests, as appropriate, for continuous and categorical variables, respectively. Statistical analysis was completed using R software 3.5.2 (http://www.r-project.org).

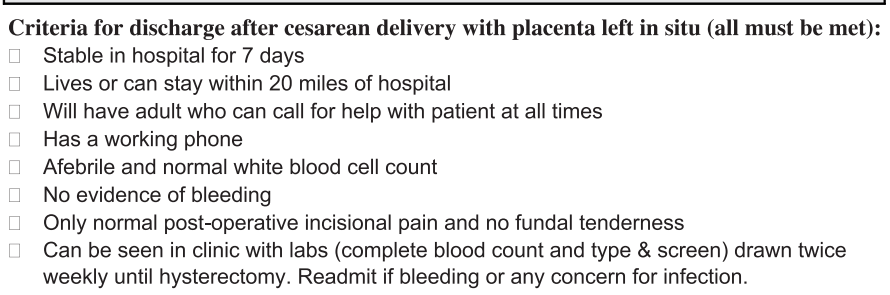
Because of the increasing incidence of invasive placentation, in 2012, we established a multidisciplinary team to determine best practice guidelines for the management of severe PAS. This team has remained largely stable through the course of data collection for this cohort. Based on these best practices, at our institution, all patients

who receive an antenatal diagnosis of placenta percreta are treated by a multidisciplinary care team that comprises representatives from maternal-fetal medicine, gynecologic oncology, urology, emergency general surgery, and anesthesiology. Antenatal consultation with neonatology is performed routinely. Consultation from transfusion medicine, vascular surgery, and interventional radiology is readily available. Patients may be identified by referral or by routine screening ultrasound imaging. All patients have a routine ultrasound evaluation to assess for fetal anomalies and placentation at 18−22 weeks gestation. Patients who are identified with risk factors for PAS, such as placenta previa, have a repeat obstetric ultrasound evaluation 4−6 weeks later to reassess the placenta. Concern for placenta percreta triggers reassessment by pelvic ultrasound imaging that is performed by maternal-fetal medicine specialists in our Fetal Center with or without subsequent magnetic resonance imaging. Patients with a high suspicion for placenta percreta are referred to a gynecologic oncologist for antenatal consultation. Throughout the time of data collection, we had 2 gynecologic oncologists at our institution who were involved in developing clinical protocols for and clinical management of each case of suspected PAS. Women with suspected placenta percreta were counseled preoperatively by 1 of these gynecologic oncologists (M.A.C.) and were informed of the evidence-based estimates of severe morbidity and death with both immediate and delayed hysterectomy. Over the course of this study (2012−2018), these patients were followed in our Fetal Center, where they were counseled by at least 1 of 3 maternal-fetal medicine specialists who were also involved in determining clinical protocols for and clinical management of each case of suspected PAS. At least 1 of these gynecologic oncologists and/or maternal-fetal medicine specialists (M.A.C., L.C.Z., J.M.N., and K.A.B.) were present for each of the deliveries.

Cesarean delivery is planned before the onset of labor, usually at 34−35 weeks estimated gestational age, depending on concurrent maternal and fetal indications. Anesthesia is generally combined thoracic epidural and general endotracheal anesthesia. Before start of the surgery, a member of the urology physician team performs cystoscopy to evaluate for bladder invasion and places bilateral ureteral catheters. Ureteral catheter placement is deferred in cases in which urgent delivery is undertaken for maternal hemorrhage or fetal distress. Both the maternal-fetal medicine and gynecologic oncology teams are present to observe the bladder appearance by cystoscopy. As of 2017, before abdominal entry, our emergency general surgery team places a femoral artery catheter that would be used for rapid access for resuscitative endovascular balloon occlusion of the aorta. The addition of resuscitative endovascular balloon occlusion of the aorta to our Best Practice Guidelines for severe PAS was at the recommendation of our emergency general surgery colleagues and concordant with their use in the trauma patient population, as part of our continuous quality improvement process for evaluating and updating our management strategy for severe PAS. The cesarean delivery is performed by the maternal-fetal medicine team. After entry via midline vertical incision, we use intraoperative, multidisciplinary decision-making regarding immediate vs delayed hysterectomy. In cases in which members of our maternal-fetal medicine and gynecologic oncology team think that immediate hysterectomy poses excessive maternal risk, we proceed with a plan to leave the placenta in situ. This decision is based primarily on the extent of parametrial invasion, as assessed by intraoperative observation. In cases in which immediate hysterectomy is deemed possible and safe or where there is an obstetric contraindication to placental retention, we proceed with immediate cesarean hysterectomy. For cases with a decision for placental retention, the hysterotomy is created with the use of a fetal surgery entry technique to minimize blood loss, as previously described.[17] Briefly, the placenta is mapped intraoperatively with transuterine ultrasound images. Stay sutures are placed through the uterine wall, and a small hysterotomy is made with the use of electrocautery. As the incision is carried through the myometrium, Allis-Adair clamps are used along the edge of the incision to control bleeding and expose the amniotic membrane. The membranes are entered, and a full-thickness, running, locking chromic suture is used to secure the membrane to the uterine wall. A surgical stapler is used to extend the incision. The fetus is delivered; the umbilical cord is ligated, and the placenta is left in situ. The hysterotomy is closed with a full-thickness, running, locked delayed absorbable suture, with care to include the membranes, and is supplemented with figure of 8 sutures, as necessary. If there is no bleeding, the uterus is left in situ with plans for scheduled, delayed hysterectomy. A gynecologic oncologist is present and scrubbed for the delivery in case immediate cesarean hysterectomy should be necessary.

Our initial approach for patients in whom we left the placenta in situ was to perform serial imaging to confirm placental regression from the involved pelvic structures before proceeding with hysterectomy. We subsequently have modified this approach, based on early experiences, to now plan the hysterectomy for 4−6 weeks after cesarean delivery with preoperative magnetic resonance imaging to confirm adequate placental regression. All hysterectomies are performed by a gynecologic oncologist via laparotomy. The patient is hospitalized for approximately 7 days after the cesarean delivery and treated with broad-spectrum intravenous antibiotics for 72 hours. We encourage those interested in breastfeeding to start pumping breastmilk within the first 24 hours of delivery if they are stable medically and without active vaginal bleeding. If there is no evidence of

FIGURE 1
Discharge criteria



Discharge criteria after cesarean delivery with plan for delayed hysterectomy in cases of placenta percreta. All criteria must be fulfilled before discharge.

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bleeding or infection after 7 days and the patient meets our criteria for discharge (Figure), then she is discharged to local housing with weekly outpatient visits. Hysterectomy may be performed before the scheduled date for bleeding, infection, or other complications that indicate contraindication to ongoing expectant management.

Results

We identified 49 patients with an antepartum diagnosis of suspected placenta percreta who had been treated at Vanderbilt University Medical Center between January 1, 2012 and May 30, 2018. Of these, 34 patients had confirmed severe PAS, which included increta and percreta, during cesarean delivery and on postoperative pathologic results. Of the 15 patients without confirmed severe PAS, 2 had normal placentation with spontaneous separation of the placenta during delivery, and 13 had PAS without invasion beyond the endometrium, and they underwent immediate cesarean hysterectomy. Of the 34 patients with intraoperative confirmation of severe PAS, delayed hysterectomy was performed in 14 patients (41.2%): 9 as scheduled and 5 before the scheduled date. Intraoperative and pathologic specimen examination confirmed placenta percreta in all cases of delayed hysterectomy. Immediate cesarean hysterectomy was completed in 20 patients (58.8%): 16 after intraoperative assessment of resectability and 4 because of preoperative or intraoperative bleeding. Intraoperative and pathologic specimen examination confirmed placenta percreta in 9 patients who underwent immediate hysterectomy (45%), whereas final pathologic results reported placenta increta in 11 of these patients (55%). In cases of immediate hysterectomy, ureteral catheters were placed preoperatively in 15 of 20 patients (75%). Of the 5 patients who did not receive ureteral catheters, 2 were deferred because of the urgent nature of the surgery, and 3 resulted from deviation from our management guidelines because of surgeon preference. All patients in the delayed hysterectomy group received preoperative ureteral catheters by urology. The median (interquartile range [IQR]) age of the patients included was 31 years (IQR, 29−34.75 years). Demographic data of our population by type of delivery are given in Table 1. Overall, race was non-Hispanic white in 19 cases (56%), African American in 5 cases (14%), Hispanic in 4 cases (12%), and Asian (including middle eastern and Hawaiian) in 6 cases (18%). The median gravidity was 5 (IQR, 3−5), with the number of previous cesarean deliveries in our patient population being 1−2 in 65%, 3−4 in 31%, and >4 in 3.1%. The median gestational age at delivery was 34.7 weeks (IQR, 33.1−34.7 weeks). Antenatal complications included vaginal bleeding in 7 patients, gestational diabetes mellitus in 3 patients, and type 1 diabetes mellitus, preeclampsia with severe features, gestational hypertension, and HIV/AIDS in 1 patient each.

Table 2 presents a comparison of surgical outcomes at the time of hysterectomy by type of procedure (delayed vs immediate). The median EBL at delayed hysterectomy of 750 mL (IQR, 650−1450 mL) was significantly lower than the EBL at immediate hysterectomy of 3000 mL (IQR, 2375−4250; $P<.01$). Accordingly, the resultant need for blood transfusion was significantly lower for delayed hysterectomy, with a median 0 (IQR, 0−2) units of red blood cells (RBC) transfused vs 4 units (IQR, 2−8.25) at immediate cesarean hysterectomy ($P<.01$). Nine of 20 patients (45%) required transfusion of ≥4 units of RBC at immediate cesarean hysterectomy; only 2 of 14 patients (14.2%) required transfusion of ≥4 units of packed red blood cells at the time of delayed hysterectomy ($P=.016$). The 4 patients who underwent immediate hysterectomy because of preoperative or intraoperative bleeding rather than perceived resectability had similar EBL to the rest of the immediate hysterectomy group, with EBL ranging from 2750−5000 mL. Only 1 of the 4 patients (25%) required ≥4 units of RBC, and the other 3 patients (75%) in this group received 2−3 units of RBC. Median surgical time (skin-to-skin) for delayed hysterectomy was 127 minutes (IQR, 105−145 minutes), which was significantly lower than surgical time for immediate cesarean hysterectomy of 254 minutes (IQR, 202.5−321.5 minutes; $P<.001$). One patient in each group experienced a urinary tract injury (cystotomy) during hysterectomy that was recognized and repaired. There was 1 maternal death in each group, which accounted for incidences of 7% and 5% in the patients with delayed and immediate hysterectomy, respectively.

Because the delayed hysterectomy is a staged procedure, we also compared surgical outcomes between our study groups by using composite results from both the cesarean delivery and hysterectomy procedures in the delayed hysterectomy group (Table 3). Compared

with immediate cesarean hysterectomy, we found that the total surgical time (skin-to-skin) for the delayed hysterectomy group was higher at 392 minutes (IQR, 345−436 minutes; $P<.001$). Despite the increased surgical time, we found that the total EBL ($P=.037$), number of RBC units transfused ($P<.001$), and need for ≥4 units of RBC transfusion ($P=.016$) remained significantly lower for the delayed hysterectomy group. As expected, although the length of admission after hysterectomy was not significantly different between the groups, the delayed hysterectomy group incurred longer overall median hospital admission length of 13.5 days (IQR, 10.75−15 days) vs 5 days (IQR, 4−5.5 days; $P<.001$), driven by the planned postoperative observation period after cesarean delivery with placenta left in situ.

In the patients who underwent cesarean delivery with delayed hysterectomy, the median EBL at cesarean delivery was 350 mL (IQR, 162.5−500 mL). No patient required transfusion at the time of cesarean delivery. Postpartum complications in the time between cesarean delivery and delayed hysterectomy included ileus or small bowel obstruction that resolved with nonoperative treatment in 3 patients and deep venous thrombosis, pyelonephritis, and systemic inflammatory response syndrome in 1 patient each. One patient in this group declined hysterectomy and was lost to follow up until she represented 2 years later with a cesarean scar pregnancy with placental invasion into maternal bladder, for which she refused treatment. She was ultimately delivered at 31 weeks gestation by cesarean delivery with bilateral salpingectomy and recommendation for delayed hysterectomy; however, to date, this patient remains lost to follow up. There was 1 neonatal death in an infant with multiple fetal anomalies that included bilateral renal agenesis, which had been diagnosed antepartum and for which the patient declined termination of pregnancy.

Postoperative complications after delayed hysterectomy included ileus or small bowel obstruction that responded to nonoperative treatment and pneumonia in 2 patients each and pulmonary embolism, pyelonephritis, and postoperative hemorrhage that required return to operating room in 1 patient each. There was 1 maternal death at the time of delayed hysterectomy because of severe hemorrhage, shock, and cardiac arrest.

Among the women who underwent immediate cesarean hysterectomy, 1 woman had massive antepartum hemorrhage and cardiac arrest. She was found to have a ruptured bladder and required partial cystectomy. Her postoperative course was complicated by the need for return to the operating room for closure of an open abdomen. Other postoperative complications in this group included ileus in 1 patient and prolonged urinary retention in 1 patient with cerebral palsy. There was 1 intraoperative maternal death because of sudden cardiac collapse that occurred after completion of an uncomplicated cesarean hysterectomy after multidisciplinary agreement that the patient's PAS was amenable to immediate hysterectomy.

TABLE 1
Demographic data of our study population

Variable	Hysterectomy	
	Delayed (n=14)	Immediate (n=20)
Age, y[a]	29 (29−30.75)	33 (30.75−36.25)
Parity[a]	3 (2.25−4)	2 (1.75−2.25)
Race, n (%)		
White	8 (57)	11 (55)
African American	2 (14)	3 (15)
Hispanic	2 (14)	2 (10)
Other	2 (14)	4 (20)
Body mass index, kg/m^2[a]	27.34 (25.05−32.27)	29.07 (23.72−33.90)
Previous cesarean deliveries, n (%)		
1−2	7 (54)	14 (74)
3−4	5 (38)	5 (26)
>4	1 (8)	0
Gestational age at diagnosis, wk[a]	30 (27.3−31.4)	24.9 (21.4−31.5)
Year of delivery, n (%)		
2012	2 (14.3)	0
2013	1 (7.1)	0
2014	8 (57.1)	2 (10)
2015	2 (14.3)	3 (15)
2016	0	6 (30)
2017	0	7 (30)
2018	1 (7.1)	3 (15)

[a] Data are given as median (interquartile range).

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Comment

Principal findings

The results of this retrospective cohort of all patients who were diagnosed with placenta percreta over a 6-year period at our large academic institution indicate that cesarean delivery with delayed hysterectomy had several benefits (which included decreased blood loss at hysterectomy, lower need for blood product transfusion, and

TABLE 2
Comparison of surgical outcomes between delayed hysterectomy and immediate hysterectomy

Variable	Hysterectomy		*P* value
	Delayed (n=14)	Immediate (n=20)	
Gestational age at delivery, wk[a]	33.7 (32.9–34.4)	33.8 (32.2–34.8)	.76
Surgical time, min[a]	127 (105–145)	254 (202.5–321.5)	<.001
Type of delivery, n (%)			<.001
Modified uterine entry	13 (93)	4 (20)	
Standard hysterotomy	1 (7)	16 (80)	
Estimated blood loss at delivery, mL[a]	350 (162–500)	N/A	N/A
Estimated blood loss at hysterectomy, mL[a]	750 (650–1450)	3000 (2375–4250)	.007
Red blood cell units transfused at hysterectomy[a]	0 (0–2)	4 (2–8.25)	<.001
Transfusion ≥4 units red blood cells, n (%)	2 (14)	11 (55)	.016
Posthysterectomy length of stay, d[a]	4.5 (3.8–6.3)	5 (4–5.5)	.85
Maternal death, n (%)	1 (7)	1 (5)	.79

N/A, not available.

[a] Data are given as median (interquartile range).

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decreased portion of the patients who required transfusion of ≥ 4 units of RBCs) over immediate hysterectomy in our population,. These benefits were significant when we compared surgical outcomes for immediate vs delayed hysterectomy and when we compared cesarean hysterectomy with composite surgical outcomes for both components of the staged procedure, cesarean delivery and delayed hysterectomy. Although we also found a significantly decreased operative time for delayed, compared with immediate, hysterectomy, the 2-part surgical procedure did have an overall higher composite operative time and a significantly longer overall hospital admission because of our required postoperative observation period and stringent criteria for discharge of the patients with placenta in situ. Finally, we found similar rates of urinary tract injury, other surgical complications, and maternal death between the immediate and delayed hysterectomy groups, but these were overall rare occurrences within our population.

Results in the context of what is known

Several case series have been published on women with PAS, but there is less data on the specific outcomes for women with the most severe form, placenta percreta. Across these series, maternal hemorrhage is the most common complication, which requires large volume blood product transfusions in approximately 42% of cases.[18] These series report median EBLs of 2600–4061 mL (range, 150–30,000 mL) and urinary tract injuries in 7–37% of cases.[4,6]

TABLE 3
Comparison of surgical outcomes between composite of cesarean delivery + delayed hysterectomy and immediate cesarean hysterectomy

Variable	Hysterectomy		*P* value
	Delayed (n=14)	Immediate (n=20)	
Total surgical time, min[a]	392 (345–436)	254 (202.5–321.5)	<.001
Estimated blood loss, mL[a]	1300 (700–2150)	3000 (2375–4250)	.037
Red blood cell units transfused[a]	0 (0–2)	4 (2–8.25)	<.001
Transfusion ≥4 units red blood cells, n (%)	2 (14)	11 (55)	.016
Postoperative length of stay, d[a]	13.5 (10.8–15)	5 (4–5.5)	<.001

[a] Data are given as median (interquartile range).

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Authors who have looked specifically at different types of PASs have reported even worse outcomes for more severe forms that include increta and percreta. For example, a study of 156 women that compared placenta accreta with placenta percreta found a significantly higher composite morbidity rate in cases of placenta percreta when compared with placenta accreta (86.3% [44/51] vs 26.7% [28/105]; $P<.001$).[19] In 2015, Shamshirsaz et al[5] described the outcomes of 90 women with PAS who were cared for with a standard multidisciplinary approach that included cesarean hysterectomy; they specifically described the outcomes of the subgroup of 57 women with placenta increta and percreta. Among those women with the most severe PAS, the median EBL was 2100 mL (range, 900−18,000 mL), with 25 women (60%) requiring transfusion of ≥4 units of RBC. Cystotomy occurred in 15 patients (36%), either incidental or planned for resection of the involved bladder. Our outcomes as compared with these series are summarized in Table 4. The EBL of the patients who underwent delayed hysterectomy in our population was overall lower than that of the patients who underwent cesarean hysterectomy in previous studies. Consistently, fewer patients in our series of delayed hysterectomies required transfusion of ≥4 units of RBC. The risk of urinary tract injury was equal to or less than that reported in previous series of PAS that was treated by immediate cesarean hysterectomy.

Data on cesarean delivery with delayed hysterectomy is even more scarce. In a cohort of patients with placenta percreta who were treated at Duke University, Lee et al[20] showed that, in 13 of 21 patients with suspected placenta percreta who underwent delayed hysterectomy, there were no cases of emergent hysterectomy, delayed hemorrhage, or sepsis. They also found, similar to our experience, that delayed hysterectomy was associated with a lower EBL that included 900 mL for cesarean delivery and 700 mL for delayed hysterectomy. Furthermore, only 46% of these patients (6/13) required transfusion, and none of the patients required ≥4 units of RBC. They had no ureteral injuries at the time of delayed hysterectomy, and 23% of these patients (3/13) ultimately underwent robotic hysterectomies.

TABLE 4
Outcomes of 34 patients in our study and comparison with other study populations

Variable	Estimated blood loss, mL	Patients who required transfusion ≥4 units packed red blood cells, %	Patients with urinary tract injury, %
Delayed hysterectomy (n=14)[a]	750 (650−1450)	14	7
Immediate cesarean hysterectomy (n=20)[a]	3000 (2375−4250)	45	5
Shamshirsaz et al[5] (increta/percreta; n=58)[b]	2100 (900−18,000)	60	38
Hoffman et al[6] (accreta; n=29)[b]	4061 (500−30,000)	41	7
Eller et al[4] (accreta; n=60)[b]	2600 (150−9000)	42	44

[a] Data are given as median (interquartile range); [b] Data are given as mean (range).
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We performed delayed hysterectomy in 41.2% of our patients with severe PAS that was diagnosed during this study period. Although 5 patients had their interval hysterectomies performed before the scheduled date, we were able to gain significant time between cesarean delivery and hysterectomy, with a mean interval between the procedures of 39 days. This interval is similar to data from Duke University where delayed hysterectomies were performed at a median time from cesarean delivery of 41 days (range, 26−68 days).[20] Significant differences between our protocol and the data from Duke University are that we reserve uterine artery embolization for select cases of immediate postoperative bleeding in which allowing time for placental regression is deemed paramount, and our hysterectomies are performed via laparotomy.

Clinical implications

In our study, we demonstrate the potential to reduce severe maternal morbidity, such as hemorrhage and need for massive transfusion, by performing delayed hysterectomy for the most severe cases of PAS. By allowing time for uterine blood flow to decrease and for the placenta to regress from surrounding structures, delayed hysterectomy has the potential to decrease the transfusion requirement and potentially the risk of urinary tract injury that is associated with surgery for placenta percreta. Despite these benefits, patients who are treated with this algorithm continue to have significant morbidity and risk of death, which may not be avoidable.

Research implications

Given the significant risk for adverse outcomes, improvements in the management of placenta percreta are needed. Several studies and reports in recent years have addressed advances in the care of these high-risk cases. Improved imaging, operative technique, transfusion protocols, and multidisciplinary care are just some examples of these advances. The potential for safer treatment in select patients with delayed hysterectomy remains controversial. A randomized trial that would compare primary cesarean hysterectomy with delayed hysterectomy would be necessary to answer definitively the question of which approach is superior. Additional research is needed to

investigate the components of intraoperative decision-making factors that account for the decision to delay hysterectomy. It must be stated that these features are not agreed on universally. Given the rarity of this condition, such a study would be difficult to conduct, even with a multicenter protocol. However, additional studies that would compare the outcomes and costs that are associated with the 2 approaches might provide important insight regarding the relative merits of each approach.

Strengths and limitations

The main strength of this study is that it was conducted in a single center of excellence with a dedicated multidisciplinary team, where we treat a high number of patients with PAS. Our expertise in fetal surgery provides the opportunity for the performance of cesarean delivery with minimal blood loss that allows for delayed hysterectomy in cases in which this was determined to be the safest surgical approach. Because intraoperative hemorrhage would be a contraindication to placental retention and delayed hysterectomy, it is possible that excessive intraoperative bleeding in the immediate hysterectomy group would skew our results; however, the EBL and RBC units transfused for the 4 patients who underwent immediate hysterectomy because of preoperative or intraoperative bleeding rather than perceived resectability were similar to the remainder of the immediate hysterectomy group. A weakness of the study is its retrospective nature and the inherent limitations of retrospective data collection. Although we made all efforts to compare surgical outcomes objectively between our 2 groups at the time of delivery and hysterectomy, it must be acknowledged that the groups likely differed in a priori surgical risks. For example, the delayed hysterectomy group likely represents cases with the most significant placental invasion, thus explaining the decision to leave the placenta in situ. The fact that the outcomes for the patients who underwent delayed hysterectomy were equivalent to the outcomes for a group of patients who may actually be at less risk for complications emphasizes the safety of this approach. Additionally, the use of fetal surgery entry rather than standard hysterotomy for delivery may have contributed to a lower EBL at the time of delivery in these women. Through this report, we are not attempting to demonstrate superiority of delayed hysterectomy, rather feasibility of this approach in the most severe, surgically challenging cases of PAS, for which any surgical option poses a high risk of severe morbidity and death to the affected patient. Finally, the infrequent nature of placenta percreta and therefore relatively low numbers of cases limited our ability to find statistically significant results with respect to more rare surgical complications, such as urinary tract injury and maternal death.

Conclusions

This study presents a paradigm for the management of the most severe cases of PAS that differs from the generally accepted management guidelines, but it is consistent with current International Federation of Obstetricians and Gynecologists guidelines and with data presented by other authors. We would not recommend that this protocol be extended to the treatment of all patients with PAS; however, our study adds to the limited existing literature that supports delayed hysterectomy as a reasonable, conservative surgical approach in the most severe, potentially life-threatening cases of placenta percreta or in situations in which immediate hysterectomy is deemed too dangerous because of the extent of placental invasion or lack of appropriate resources. ■

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