

OPEN

Aortic balloon occlusion in distal zone 3 reduces blood loss from obstetric hemorrhage in placenta accreta spectrum

Sarah L. Kluck, MD, Rachel M. Russo, MD, MS, Noah B. Appel, MD, Alan I. Frankfurt, MD, Craig Weltge, MD, Tricia Shimer, MD, Brian Feagins, MD, Amin Frotan, MD, Brian Rinehart, MD, and Robert A. Cohen, MD, Dallas, Texas

CONTINUING MEDICAL EDUCATION CREDIT INFORMATION

Accreditation

In support of improving patient care, this activity has been planned and implemented by CineMed and the American Association for the Surgery of Trauma. CineMed is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

AMA PRA Category 1 Credits™

CineMed designates this enduring material for a maximum of 1 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.



JOINTLY ACCREDITED PROVIDER™
INTERPROFESSIONAL CONTINUING EDUCATION

Objectives

After reading the featured articles published in the *Journal of Trauma and Acute Care Surgery*, participants should be able to demonstrate increased understanding of the material specific to the article. Objectives for each article are featured at the beginning of each article and online. Test questions are at the end of the article, with a critique and specific location in the article referencing the question topic.

Disclosure Information

In accordance with the ACCME Accreditation Criteria, CineMed must ensure that anyone in a position to control the content of the educational activity (planners and speakers/authors/discussants/moderators) has disclosed all financial relationships with any commercial interest (termed by the ACCME as “ineligible companies”, defined below) held in the last 24 months (see below for definitions). Please note that first authors were required to collect and submit disclosure information on behalf of all other authors/contributors, if applicable.

Ineligible Company: The ACCME defines an “ineligible company” as any entity producing, marketing, selling, re-selling, or distributing health care goods or services used on or consumed by patients. Providers of clinical services directly to patients are NOT included in this definition.

Financial Relationships: Relationships in which the individual benefits by receiving a salary, royalty, intellectual property rights, consulting fee, honoraria, ownership interest (e.g., stocks, stock options or other ownership interest, excluding diversified mutual funds), or other financial benefit. Financial benefits are usually associated with roles such as employment, management position, independent contractor (including contracted research), consulting, speaking and teaching, membership on advisory committees or review panels, board membership, and other activities from which remuneration is received, or expected.

Conflict of Interest: Circumstances create a conflict of interest when an individual has an opportunity to affect CME content about products or services of a commercial interest with which he/she has a financial relationship.

The ACCME also requires that CineMed manage any reported conflict and eliminate the potential for bias during the session. Any conflicts noted below have been managed to our satisfaction. The disclosure information is intended to identify any commercial relationships and allow learners to form their own judgments. However, if you perceive a bias during the educational activity, please report it on the evaluation. All relevant financial relationships have been mitigated.

AUTHORS/CONTRIBUTORS

Noah B. Appel, Argon Medical, Consulting Fee, Consultant. Sarah L. Kluck, Rachel M. Russo, Alan I. Frankfurt, Craig Weltge, Tricia Shimer, Brian Feagins, Amin Frotan, Brian Rinehart, and Robert A. Cohen have nothing to disclose.

EDITORIAL BOARD MEMBERS

First Name	Last Name	Disclosure?	Name of Commercial Interest	What was Received?	What was the Role?
Michael	Nance	Yes	Endo Pharmaceuticals	Consulting fee	Consultant
Heena	Santry	Yes	NBBJ	Salary	Employee
Jose	Diaz	Yes	Acumed/Acute Innovations	Consulting fee	Consultant
Lena	Napolitano	Yes	Merck Global Negative Advisory Board/Abbvie Critical Care Working Group	Consulting fee	Advisor/Consultant

Roxie Albrecht, Walter Biffl, Karen Brasel, Clay Cothren Burlew, Raul Coimbra, Todd Costantini, Rochelle Dicker, Tabitha Garwe, Kenji Inaba, Rosemary Kozar, David Livingston, Ali Salim, Deborah Stein, Alex Valadka, Robert Winchell, Bishop L. Zakhary, and Ben Zarzau have no disclosures or conflicts of interest to report. The Editorial Office staff has no disclosures to report.

Claiming Credit

To claim credit, please visit the AAST website at <http://www.aast.org/> and click on the “e-Learning/MOC” tab. You must read the article, successfully complete the post-test and evaluation. Your CME certificate will be available immediately upon receiving a passing score of 75% or higher on the post-test. Post-tests receiving a score of below 75% will require a retake of the test to receive credit.

Credits can only be claimed online

Cost

For AAST members and *Journal of Trauma and Acute Care Surgery* subscribers there is no charge to participate in this activity. For those who are not a member or subscriber, the cost for each credit is \$25.

Questions

If you have any questions, please contact AAST at 800-789-4006. Paper test and evaluations will not be accepted.

BACKGROUND:	Peripartum hemorrhage is a significant cause of maternal death. We developed a standardized, multidisciplinary cesarean hysterectomy protocol for placenta accreta spectrum (PAS) using prophylactic resuscitative endovascular balloon occlusion of the aorta (REBOA). We initially placed the balloon in proximal zone 3, below the renal arteries. An internal review revealed more bleeding than expected, and we subsequently changed our protocol to occlude the origin of the inferior mesenteric artery (distal zone 3), to decrease blood flow through collateral circulation. We hypothesized that distal zone 3 occlusion would reduce blood loss and transfusion volume and may permit a longer duration of occlusion compared with proximal zone 3 occlusion without increasing ischemic complications.
METHODS:	We conducted a single-center retrospective cohort study of patients with suspected PAS who underwent REBOA-assisted cesarean hysterectomy from December 2018 to March 2022. Medical records of all patients with PAS were reviewed. Data were extracted from hospital admission through 3 months postpartum.
RESULTS:	Forty-four patients met the inclusion criteria. Nine never had the balloon inflated. Eighteen patients had placement in proximal zone 3, whereas twenty-six patients had placement in distal zone 3. Background and clinical characteristics were similar in both groups. Placental pathology was obtained in every case. After adjusting for relevant risk factors, multivariate analysis revealed that distal occlusion was associated with a 45.9% (95% confidence interval, 23.8–61.6%) decrease in estimated blood loss, 41.5% (13.7–60.4%) decrease in red blood cell transfusion volume, and 44.9% (13.5–64.9%) reduction in total transfusion volume. There were no vascular access or resuscitative endovascular balloon occlusion of the aorta–related complications in either group.
CONCLUSION:	This study highlights the safety of prophylactic REBOA in planned cesarean hysterectomy for PAS and provides a rationale for distal zone 3 positioning to reduce blood loss. Resuscitative endovascular balloon occlusion of the aorta should be considered at other institutions with placenta accreta programs, especially in patients with extensive collateral flow. (<i>J Trauma Acute Care Surg.</i> 2023;94: 710–717. Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc.)
LEVEL OF EVIDENCE:	Therapeutic/Care Management; Level IV.
KEY WORDS:	Placenta accreta spectrum; postpartum hemorrhage; REBOA; maternal morbidity and mortality.

Peripartum hemorrhage from uterine or placental bleeding is a significant cause of maternal death.¹ Potential etiologies of bleeding that may require surgical intervention include uterine atony refractory to medical management, uterine perforation during dilation and evacuation, or hemorrhage secondary to abnormal placentation. In patients with placenta accreta spectrum (PAS), the condition also known as morbidly adherent placenta, the placental trophoblastic tissue invades into or through the myometrium of the uterus. This disease spectrum ranges in severity from placenta accreta (loss of the decidua between the placenta and myometrium), placenta increta (partial thickness myometrial invasion), and placenta percreta (full-thickness ingrowth of the placenta through the myometrium and serosa,

sometimes into neighboring organs). Increasing PAS severity corresponds to higher maternal morbidity and a greater risk of hemorrhage-related mortality.² As such, the American College of Obstetricians and Gynecologists—Society for Maternal Fetal Medicine Obstetric Care Consensus for PAS recommends women with suspected PAS be referred to an accreta center of excellence for multidisciplinary management to reduce the risk of peripartum hemorrhage. The consensus recommends performing a planned cesarean hysterectomy at 34 to 35 weeks gestation to minimize the risk of spontaneous labor that could spawn fatal hemorrhage.

There are several approaches available to decrease surgical blood loss during cesarean hysterectomy, including multivessel surgical ligation, temporary aortic clamping, multivessel embolization, and balloon occlusion of the aorta or iliac arteries.³ Several groups have reported superior outcomes with resuscitative endovascular balloon occlusion of the aorta (REBOA) as an adjunct to hemorrhage control during cesarean hysterectomy for PAS.^{4–12} A meta-analysis of 731 PAS patients who underwent cesarean deliveries in which a REBOA catheter was used to occlude the infrarenal aorta, termed *zone 3*, found that these women experienced significantly less blood loss, received fewer transfusions, and achieved a higher rate of uterine preservation compared with other hemorrhage control strategies.⁹ However, in the 11 studies pooled to generate this meta-analysis, there was no specific standard location of occlusion within zone 3 of the aorta. In other similar accounts of zone 3 REBOA for PAS, there is variation as to whether occlusion is described as below the renal arteries or above the aortic bifurcation.^{6,7,9,12} This distinction may be important, because blood flow to the uterus and placenta has significant collateralization particularly late in pregnancy (Fig. 1).

The uterus and placenta derive their blood supply from the uterine arteries as well as the ovarian, vesical, and vaginal

Submitted: December 2, 2022, Revised: January 23, 2023, Accepted: January 25, 2023, Published online: February 24, 2023.

From the Department of OB/GYN, Texas Health Dallas (S.L.K.), Dallas, Texas; Department of Surgery, Trauma, Acute Care Surgery, and Surgical Critical Care (R.M.R.), UC Davis Medical Center, Sacramento; US Air Force (R.M.R.), Travis, AFB, California; Department of Radiology (N.B.A.), Department of Anesthesia (A.I.F., C.W.), Department of OB/Gyn (T.S.), and Department of Urology (B.F.), Texas Health Dallas; Department of Surgery (A.F.), Trauma Surgery Texas Health Dallas; Department of OB/Gyn Texas Health Dallas (B.R.), Maternal Fetal Medicine Consultants of Dallas; and Placenta Accreta Program (R.A.C.), Medical City Dallas, Dallas, Texas.

This study was presented at the 4th annual meeting of the Pan-American Society for the Placenta Accreta Spectrum, October 8–9, 2022, in Salt Lake City, Utah.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.jtrauma.com).

Address for correspondence: Robert A. Cohen, MD, Placenta Accreta Program, Medical City Dallas, 7777 Forest Ln, Ste C-336, Dallas, TX 75230; email: drbobco26@mac.com.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/TA.0000000000003917

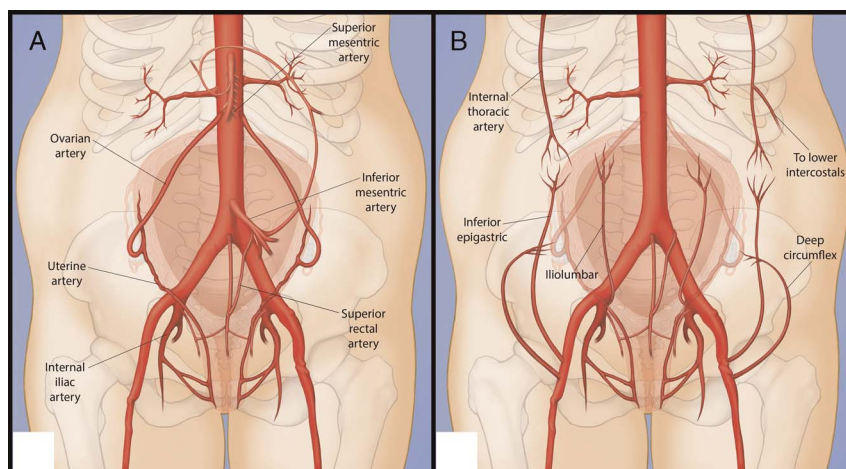


Figure 1. Schematic diagram illustrating the extensive blood supply to the gravid uterus. (A) Typical blood flow to the uterus includes the uterine and ovarian arteries as well as the vesical and vaginal arteries. (B) Numerous arterial collaterals exist in the gravid state helping to support the uterus and placenta.

arteries (Fig. 1A). In addition, extensive collateral blood flow from the lumbar, median sacral, inferior mesenteric artery (IMA), and iliolumbar arteries exist (Fig. 1B). It has also been suggested that external iliac artery anastomoses exist as well.¹³ Proximal zone 3 occlusion, just distal to the renal arteries, facilitates occlusion of the ovarian arteries, which supply >700 mL/min of blood to the uterus and placenta at term.¹⁴ However, occlusion at this location permits collateral flow around the balloon via the arc of Riolo and several other collateral pathways that may contribute to persistent pelvic bleeding (Fig. 2A). More distal occlusion, at L3, which will occlude the origin of the IMA, may reduce collateral circulation but necessitates early surgical control of the ovarian arteries (Fig. 2B). This is typically achieved by ligation of the utero-ovarian ligament (if ovarian conservation is desired) or by ligation of the infundibulopelvic ligament (if oophorectomy is performed). We propose further delineating aortic zone 3 into zone 3A, extending from the lowest

renal artery to above the IMA, and zone 3B, extending from the origin of the IMA to the aortic bifurcation. Hence, proximal occlusion would be in aortic zone 3A, and distal occlusion would be in aortic zone 3B (Fig. 2).

In December of 2018, our hospital became an accretia center of excellence. We developed a standardized multidisciplinary cesarean hysterectomy protocol for PAS that included prophylactic REBOA placement in nearly every case. We initially standardized occlusion in proximal zone 3, just below the renal arteries and above the ovarian arteries. During an internal review in 2020, we noted that surgeons reported more bleeding during occlusion than expected. We subsequently changed our approach, standardizing occlusion in distal zone 3 aligning the mid balloon at the level of the third lumbar vertebra and just above the aortic bifurcation. Herein, we compare outcomes from our program before and after changing our approach to zone 3 occlusion. We hypothesized that distal zone 3 occlusion

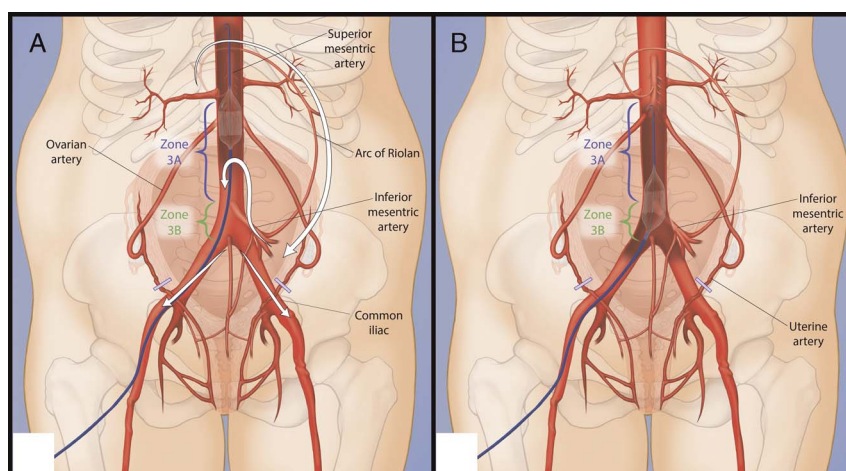


Figure 2. Schematic diagram showing (A) REBOA balloon placement in aortic zone 3A (proximal zone 3) below the renal arteries, demonstrating collateral flow via the Arc of Riolo allowing retrograde flow back down the aorta to the pelvis, and (B) REBOA balloon placement in aortic zone 3B (distal zone 3), immediately above the bifurcation and occluding the IMA. The utero-ovarian ligament or infundibulopelvic ligament must be ligated surgically to prevent additional flow to the uterus.

(zone 3B) would reduce blood loss and transfusion volume and may permit a longer duration of occlusion compared with proximal zone 3 occlusion (zone 3A) without increasing ischemic complications.

PATIENTS AND METHODS

Study Design

We conducted a single-center retrospective cohort study of pregnant patients with suspected PAS who underwent REBOA-assisted cesarean hysterectomy at our accreta center of excellence from December 21, 2018, to March 11, 2022. The medical records of all patients identified with PAS during the study period were reviewed, and relevant data were extracted from hospital admission through at least 3 months postpartum. Patients were excluded if they did not have a REBOA placed.

When our obstetric REBOA program began, we positioned the REBOA in proximal zone 3, just inferior to the lowest renal artery. On October 29, 2020, we changed our level of occlusion to distal zone 3, just above the aortic bifurcation. The study compared outcomes of patients enrolled from February 21, 2018, to September 3, 2020, who underwent zone 3A occlusion to those enrolled from October 29, 2020, to March 11, 2022, who underwent zone 3B occlusion (Fig. 3). The primary outcomes of interest included estimated surgical blood loss, red blood cell (RBC) transfusion volume, and total transfusion volume. Secondary outcomes included incidence of massive transfusion (defined as ≥ 10 U of RBC transfusion), cumulative aortic occlusion time, REBOA-related complications, and postoperative length of stay. Estimated blood loss was calculated based on a combination of suction canister amount, lap sponges, and surgeon's visual estimate. Our institutional review board deemed the study exempt from review.

Patient Selection

Patients were selected for REBOA-assisted cesarean hysterectomy based on our institutional protocol. Patients with ultrasonographic findings suspicious for PAS are referred to the accreta program at our hospital. Magnetic resonance imaging is obtained for further characterization of PAS pathology and for surgical planning. Cesarean hysterectomy is planned for 34 to 35 weeks' gestation. Preoperative multidisciplinary meetings are held to discuss each case and identify any special requirements, such as additional subspecialty consultation or involvement. Patients are admitted preoperatively if needed for antepartum bleeding, contractions, or geographic distance from the hospital and receive corticosteroid injections as indicated for fetal lung development. The REBOA is prepositioned routinely as a part of all planned cesarean hysterectomies when possible.

Surgical Approach

Since 2018, to reduce blood loss from cesarean hysterectomy and avoid vascular access complications from emergent REBOA catheter placement, we preemptively position a deflated REBOA catheter in patients with suspected PAS.¹⁵ We prefer to perform these operations in a standard operating room rather than in a dedicated hybrid operating room to facilitate earlier identification of transvaginal bleeding, as described by Russo et al.⁴ While at many centers REBOA is led by trauma and acute care surgeons, at our center, interventional radiology performs vascular access procedures in the operating room using ultrasonography for vascular access and C-arm fluoroscopy for balloon placement. The REBOA balloon is inflated and deflated by the anesthesiologist at the direction of the operating surgeon.

At the start of the operation, patients received neuraxial anesthesia to allow for parents to meet their newborn then conversion to general anesthesia for the hysterectomy. Patients are positioned supine with legs abducted. They are prepped and draped. The urologist performs cystoscopy and bilateral ureteral

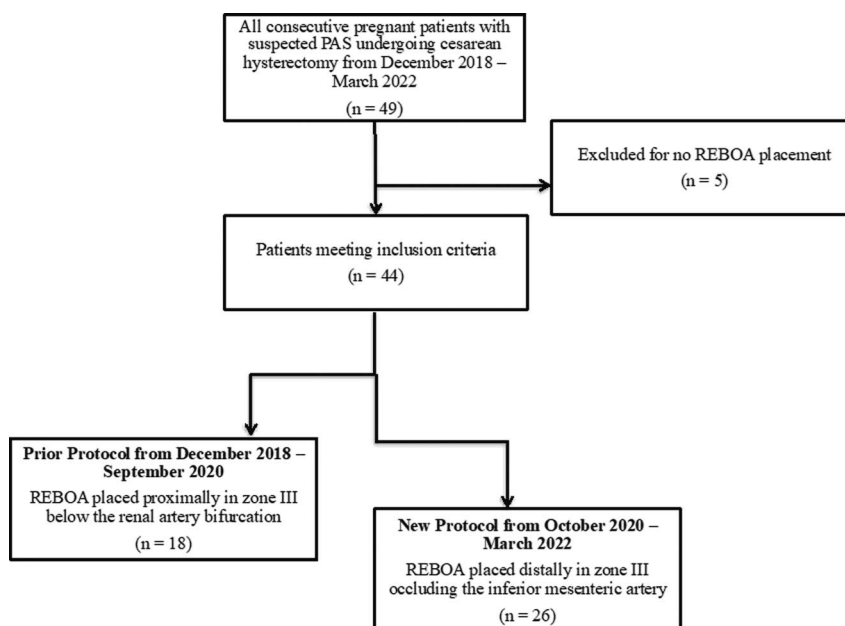


Figure 3. Study flow chart and timeline.

catheter placement. The interventional radiologist places a large bore catheter in the internal jugular vein for transfusion and central monitoring. A 20-gauge \times 6-inch long arterial pressure monitoring catheter is advanced to the left external iliac artery via the left common femoral artery to measure arterial pressure distal to the aortic balloon during occlusion. A 7-Fr sheath is inserted in the right common femoral artery for REBOA access. The selected REBOA catheter is precisely placed under fluoroscopic guidance in zone 3 of the aorta. Before October 29, 2020, the balloon was positioned just distal to the renal arteries based upon selective injections of the renal arteries (typically at the level of the second lumbar vertebra) (Fig. 2A). After October 29, 2020, the balloon position was changed to the distal zone 3 aorta immediately above the bifurcation of the aorta. Position is confirmed based upon selection of the contralateral common iliac artery with a radio-opaque wire, eliminating the need for contrast administration (Fig. 2B). Because of the length of the balloon and the proximity of the IMA to the aortic bifurcation, aligning the mid balloon at the level of the third lumbar vertebra facilitates occlusion of the origin of the IMA and the middle sacral artery at the aortic bifurcation. Test inflation of the balloon is then performed, recording the volume necessary to obliterate the contralateral iliac artery waveform. From December 21, 2018, to November 18, 2021, we used the ER- REBOA PLUS catheter (Prytime Medical, Boerne, TX) for both zone 3A and zone 3B occlusion. We now use the pREBOA-PRO catheter (Prytime Medical, Boerne, TX), since it became available to us on November 22, 2021. Our center switched catheters because the pREBOA-PRO (Prytime Medical, Boerne, TX) offers better fidelity for partial REBOA and includes a safety mechanism to prevent vessel injury from overinflation. After verification of proper positioning via imaging (Fig. 4), the catheter is secured in position, and the balloon left deflated. The sheath is infused with dilute heparinized saline for the duration of the procedure.

The cesarean hysterectomy is then performed according to the five-step approach outlined by Kingdom et al.¹⁵ After the hysterotomy and delivery of the fetus, the uterine myometrium is closed expeditiously and the hysterectomy commences. Importantly, the ovarian arteries are surgically ligated early in the operation. This is accomplished by either ligating the utero-ovarian ligament (if ovarian conservation is desired) or by ligating the infundibulopelvic ligament (if oophorectomy is performed). At the direction of the operating surgeon and if necessary to control hemorrhage, the REBOA balloon is slowly inflated to complete occlusion, as evidenced by loss of the contralateral iliac artery waveform. The operating room nurse tracks the total balloon inflation time, and this is subsequently documented by the surgeon in the operative report. At the conclusion of the case, the REBOA catheter, sheath, and contralateral arterial line are removed in the operating room. Hemostasis at the sheath site is obtained with manual compression alone for 20 minutes or with a closure device such as the ExoSeal vascular closure device (Cordis, Miami Lakes, FL) by the interventional radiologist. Contralateral hemostasis on removal of the arterial line is by manual compression for approximately 10 minutes. The large bore central venous catheter is left in place overnight. Postoperatively, patients are admitted to the intensive care unit and undergo lower extremity arterial examinations every 30 minutes for the first 6 hours.



Figure 4. The REBOA balloon on fluoroscopy. Intraoperative fluoroscopy with REBOA balloon inflated in the distal abdominal aorta at the third lumbar vertebrae.

Statistical Analysis

Numeric variables were assessed for normality with the Shapiro-Wilk test. The mean, SD, and two-sample *t* test *p* values are reported for normally distributed variables. The median, interquartile range (IQR), and Wilcoxon rank sum *p* values are reported for nonnormally distributed variables. Count, percentage, and χ^2 test *p* values are reported for categorical and binary variables. During the statistical analysis of our primary outcomes, it was not possible to create matched groups with acceptable overlap and balance because of the small sample sizes. Therefore, a multivariable regression model was used to adjust for the relevant covariates that influence blood loss, transfusion volume, and morbidity. These covariates include severity of disease (pathology confirmed percreta or increta), presence of placenta previa, urgency of surgery (defined as surgery occurring before the planned procedure date), body mass index, number of prior cesarean sections, and gestational age. The primary outcomes of the multivariate regression were clearly right skewed. Residuals plots of a linear regression model confirmed that homogeneity of

TABLE 1. Demographics of Patients in Both Treatment Groups

Demographics	REBOA Zone 3A (n = 18)	REBOA Zone 3B (n = 26)	<i>p</i>
Maternal age, y	33.1 (3.9)	33.8 (4.1)	0.593
Gravity	4 (3–5.8)	4 (3–5)	0.903*
Parity	2 (2–3)	2 (2–3)	1.000*
Gestational age, wk	33.75 (33.20–34.10)	33.75 (32.29–34.20)	0.990*
Race/ethnicity			0.254**
White	8 (44%)	16 (62%)	
Asian	2 (11%)	1 (4%)	
Black	7 (39%)	4 (15%)	
Other	1 (6%)	4 (15%)	
BMI, kg/m ²	33.4 (6.7)	34.1 (6.5)	0.763
Diabetes	6 (33.3%)	6 (23.1%)	0.684
Placenta previa	16 (88%)	25 (96%)	0.455**
Percreta or increta	10 (55.6%)	22 (84.6%)	0.074**
Previous number of cesarean deliveries	2 (2–3)	2 (1–3)	0.683*
Urgent surgery	3 (16.7%)	8 (30.8%)	0.479

*Normal approximation with continuity correction.

**Expected cell counts <5, so χ^2 approximation may be incorrect.

The mean, SD, and two-sample *t* test *p* values are reported for normally distributed variables. The median, IQR, and Wilcoxon rank sum *p* values are reported for nonnormally distributed variables. Count, percentage, and χ^2 test *p* values are reported for categorical and binary variables.

BMI, body mass index.

variance was not satisfied, and overdispersion was present in a Poisson generalized linear model. Therefore, multivariate analysis was based on a negative binomial generalized linear model, which allows for the conditional mean and variance to differ. The multivariate regression analysis was run twice, once with all patients included, in an intention to treat analysis, and again after excluding patients who did not have balloon occlusion

documented. All patients who had a catheter inserted were included in the analysis and reporting of complications.

The strengthening the reporting of observational studies in epidemiology (STROBE) checklist was used to ensure adequate reporting of our research findings (Supplemental Digital Content, Supplementary Fig. 1, <http://links.lww.com/TA/C862>).

RESULTS

Forty-nine PAS patients were identified within the study period with 44 included in the final analysis. Five patients were excluded for having not undergone REBOA placement. Of the 44 patients who had a REBOA catheter inserted before cesarean hysterectomy, 18 patients had placement in zone 3A, while 26 patients had placement in zone 3B (Fig. 3). A total of nine patients did not require balloon inflation during the case. Background and clinical characteristics are described in Table 1, with groups being similar. Final pathology confirming PAS severity was obtained in every case. The incidence of more severe PAS (percreta or increta) increased over time after the hospital was established as an accreta center of excellence in December 2018. This is reflected in the increase in the percentage of percreta/increta cases in the zone 3B group compared with the earlier zone 3A group (84.6% vs. 55.6%, respectively; *p* = 0.074).

Zone 3B occlusion afforded a longer occlusion time (62 vs. 50 minutes on average) with similar or better outcomes, despite a trend toward more severe PAS in this group. The intention-to-treat multivariate analysis revealed that distal occlusion was associated with a 45.9% (95% confidence interval, 23.8–61.6%) decrease in estimated blood loss, 41.5% (13.7–60.4%) decrease in RBC transfusion volume, and 44.9% (13.5–64.9%) reduction in total transfusion volume (Table 2). When only including patients with specified times of balloon occlusion, the median estimated blood loss in zone 3A occlusion was 4,500 mL (IQR, 2,750–6,000) as

TABLE 2. Comparison of Perioperative Outcomes in the Treatment Groups Using the Multivariable Regression Model

Surgical Outcomes	REBOA Zone 3A (n = 18)	REBOA Zone 3B (n = 26)	% Change (95% CI) Zone 3B: Zone 3A*
EBL, mL			45.9% decrease (23.8–61.6%)
Mean (SD)	3,819 (2,695)	2,648 (1,818)	
Median (IQR)	2,750 (2,000–4,725)	2,500 (1,200–3,750)	
Total RBC, U			41.5% decrease (13.7–60.4%)
Mean (SD)	7.5 (4.6)	6.0 (5.1)	
Median (IQR)	6 (4–10)	5 (2–8.75)	
All blood products, U			44.9% decrease (13.5–64.9%)
Mean (SD)	15.8 (11.0)	12.2 (10.4)	
Median (IQR)	11.5 (6.25–22)	11 (3.25–17.75)	
Massive transfusion (≥ 10 U RBC)	4 (22.2%)	4 (15.4%)	—
Duration of aortic occlusion, min			—
Zero minutes, n (%)	3 (16.7%)	6 (23.1%)	
Mean (SD) of nonzero values**	50.1 (25.3)	62.0 (21.7)	
Death	0	0	—
Postoperative length of stay, d			—
Median (IQR)	5 (4–7.75)	5.5 (4.25–7.75)	

*Intent-to-treat analysis; results reported for significant differences only.

**Four cases had missing data for duration of occlusion.

CI, confidence interval; EBL, estimated surgical blood loss.

compared with 3,000 mL (IQR, 1,875–4,125) in zone 3B occlusion. Multivariate analysis showed a 42.9% (95% confidence interval, 18.8–59.8%) decrease in estimated blood loss, 33.7% (2.9–54.8%) decrease in RBC transfusion volume, and 37% (2.5–59.3%) reduction in total transfusion volume.

There were no vascular access site complications (e.g., bleeding requiring surgical intervention or open repair, hematoma, arterio-venous fistula formation, thrombosis or thromboembolism) in either group. There were no injuries from overinflation with either catheter. There were no ischemic complications, renal, or limb injuries. There were no instances of catheter migration, catheter malposition, or other REBOA-related complications in either group. There were no maternal or fetal injuries related to contrast or radiation exposure from fluoroscopy. There were no perioperative maternal deaths. The median (IQR) postoperative length of stay was similar in both groups: 5 (4–7.75) days in the zone 3A occlusion group and 5.5 (4.25–7.75) days in the zone 3B occlusion group.

DISCUSSION

The gravid uterus and placenta have numerous pelvic collaterals that can contribute to bleeding despite aortic occlusion. To reduce blood flow through the arc of Riouan, lumbar arteries, and the middle sacral artery, we changed the balloon location from infrarenal to mid balloon placement at the third lumbar vertebra. Concurrently, our designation as an accreta center of excellence led to a shift toward higher risk patients with higher PAS severity within our program. After adjusting for the increasing complexity of our patient population over time, the change to distal zone 3 REBOA placement resulted in significantly less blood loss and transfusion requirements during planned cesarean hysterectomies for PAS. We also achieved longer occlusion times, over an hour on average, with no REBOA-related complications.

Our findings support the safety and efficacy of prophylactically positioned REBOA catheters in planned cesarean hysterectomies for PAS, consistent with prior published studies. Shahin and Pang¹⁶ performed a systematic review and meta-analysis to examine the safety and efficacy of different endovascular interventions for hemorrhage control in the management of abnormal placentation. They found that patients with prophylactic balloon occlusion of the abdominal aorta had the lowest blood loss as compared with other endovascular interventions (balloon occlusion of internal iliac arteries, of the uterine artery, of the common iliac arteries; embolization of the uterine artery, of pelvic collateral arteries and of anterior division of internal iliac artery) with no significant endovascular complications. Many studies have reported favorable outcomes with the use of an aortic balloon in the management of PAS, specifically reduced blood loss, transfusion requirements, hysterectomy rates, and intensive care unit admissions. Similarly, the meta-analysis of 731 PAS patients by Chen et al.⁹ in China and the Columbian review of 441 patients by Ordóñez et al.⁶ found reduced blood loss and transfusion volumes with very low REBOA-related complication rates (1.7% and 0.6%, respectively) and no reports of limb loss in the REBOA groups.

Our study is the first to directly compare outcomes of proximal and distal zone 3 occlusion and to define new nomenclature based on anatomic landmarks to standardize the reporting of balloon location within zone 3. Studies have variably reported

on the location of aortic occlusion within zone 3. One study by Ioffe et al.⁷ from Loma Linda University in California describes their experience using distal zone 3 REBOA at the same level we evaluated: above the bifurcation. In their retrospective case-control study including 90 patients undergoing cesarean hysterectomy for PAS, they demonstrated a decrease in blood transfusions (≥ 4 U of packed RBCs), reduction in postoperative ileus, and decreased length of stay in the REBOA group compared with the no REBOA group.⁷ They concluded that more distal zone 3 occlusion preserves the benefits of proximal zone 3 aortic occlusion while (at least theoretically) reducing the risk of ischemia to the colon and potentially allowing for longer occlusion time. Our findings support their conclusions and suggest that more distal occlusion may in fact yield superior temporary hemostasis compared with proximal zone 3 occlusion, by occluding collateral circulation that may otherwise bypass a more proximal balloon placement.

Collateral blood flow to the distal aorta is well described in nonpregnant patients, particularly those with vascular disease. During the endovascular repair of infrarenal aortic aneurysms, retrograde blood flow through the IMA artery and back down the aorta can be observed in the form of a “type II endoleak,” in which retrograde and collateral flow from aortic branches fills the aneurysmal sac around the endograft.¹⁷ Not unlike blood flow in patients with aorto-iliac occlusive disease, flow through collateral pathways is significantly augmented during term pregnancy to meet the demands of the uterus, placenta, and fetus. Chang and colleagues¹⁸ describe the case of a PAS patient with persistent bleeding during a cesarean hysterectomy despite proximal zone 3 aortic occlusion and surgical ligation of the left iliac artery. They obtained an angiogram with the balloon inflated to visualize the source of hemorrhage, and the extensive collateral circulation can be well seen (Supplemental Digital Content, Supplementary Fig. 2, <http://links.lww.com/TA/C863>, borrowed with permission). Other groups using zone 3 REBOA for pelvic surgery have found distal zone 3 positioning to provide favorable hemostasis.¹⁷ Zhao and colleagues¹⁷ describe their experience with pelvic and sacral tumor resection, using fluoroscopy to confirm balloon position below the level of the IMA. Angiography from one of their cases confirms an absence of collateral circulation (Supplemental Digital Content, Supplementary Fig. 3, <http://links.lww.com/TA/C864>, borrowed with permissions). Thus far, most other published protocols in which REBOA is used for PAS involve positioning without the use of fluoroscopy, aided instead by distance markings, anatomic landmarks (external or radiographic), or palpation. We found fluoroscopy to be invaluable in facilitating accurate positioning to occlude the IMA. Positioning above the IMA may increase bleeding, while positioning below the bifurcation can lead to bleeding or iliac artery rupture. More work needs to be done to determine if radiographic anatomic markers such as the third/fourth lumbar vertebra or distance markings on the catheter could be used to accurately position the balloon appropriately within distal zone 3.

Our study is limited by its retrospective nature and single institution location. In addition, the study is limited by its small sample size, which did not make it possible to create matched groups during the statistical analysis of our primary outcomes, prompting the use of the multivariable regression model to adjust for relevant covariates. Although the multivariate analysis

indicated that distal occlusion may provide superior results compared with more proximal occlusion and there is anatomical rationale to support this conclusion, our findings would be stronger if the trends in the univariate analysis could be statistically compared.

It is also possible that, over time, our surgical skills have evolved and likely improved, which could be contributing to the improvement in surgical blood loss. Despite decreasing surgical blood loss with REBOA, even distal occlusion did not eliminate the need for blood transfusion. The average patient still lost a large percentage of their total blood volume. Nonetheless, there were no maternal deaths, vascular access site complications, or REBOA-related complications in either group.

Lastly, we acknowledge that our protocol uses highly specialized expertise including interventional radiologists with access to intraoperative fluoroscopy. This protocol may not be generalizable to all other institutions.

In conclusion, this study highlights the safety of prophylactic placement of REBOA in planned cesarean hysterectomies for PAS and provides a rationale for potentially improved outcomes with distal zone 3 positioning. The use of REBOA should be strongly considered at other institutions with placenta accreta programs, especially in the subset of patients suspected to have extensive vascular collaterals and extrauterine placental invasion.

AUTHORSHIP

S.L.K. and R.M.R. authored the manuscript. R.A.C., as Director of the Placenta Accreta Program and primary surgeon, along with N.B.A., A.I.F., and B.R., developed study protocol and the clinical protocol. All authors assisted with data analysis, interpretation, and critical edits of the manuscript.

ACKNOWLEDGMENTS

We thank Melissa Wong for assistance on the statistical analysis and Todd Krummenacher for developing the images in Figures 1 and 2.

DISCLOSURE

The authors declare no conflicts of interest.

REFERENCES

1. Chichakli LO, Atrash HK, MacKay AP, Musani AS, Berg CJ. Pregnancy-related mortality in the United States due to hemorrhage: 1979–1992. *Obstet Gynecol.* 1999;94(5 Pt 1):721–725.
2. Society of Gynecologic Oncology, American College of Obstetricians and Gynecologists, and the Society for Maternal-Fetal Medicine, Cahill AG, Beigi R, et al. Placenta accreta spectrum. *Am J Obstet Gynecol.* 2018;219(6):B2–B16.
3. Melber DJ, Berman ZT, Jacobs MB, Picel AC, Conturie CL, Zhang-Rutledge K, et al. Placenta accreta spectrum treatment with intraoperative multivessel embolization: the PASTIME protocol. *Am J Obstet Gynecol.* 2021;225(4):442.e1–e10.
4. Russo RM, Girda E, Kennedy V, Humphries MD. Two lives, one REBOA: hemorrhage control for urgent cesarean hysterectomy in a Jehovah's Witness with placenta percreta. *J Trauma Acute Care Surg.* 2017;83(3):551–553.
5. Manzano-Nunez R, Escobar-Vidarte MF, Orlas CP, Herrera-Escobar JP, Galvagno SM, Melendez JJ, et al. Resuscitative endovascular balloon occlusion of the aorta deployed by acute care surgeons in patients with morbidly adherent placenta: a feasible solution for two lives in peril. *World J Emerg Surg.* 2018;13:44.
6. Ordonez CA, Manzano-Nunez R, Parra MW, Rasmussen TE, Nieto AJ, Herrera-Escobar JP, et al. Prophylactic use of resuscitative endovascular balloon occlusion of the aorta in women with abnormal placentation: a systematic review, meta-analysis, and case series. *J Trauma Acute Care Surg.* 2018;84(5):809–818.
7. Ioffe YJM, Burruss S, Yao R, Tse B, Cryer A, Mukherjee K, et al. When the balloon goes up, blood transfusion goes down: a pilot study of REBOA in placenta accreta spectrum disorders. *Trauma Surg Acute Care Open.* 2021;6(1):e000750.
8. Berzon B, Gleenberg M, Offenbacher J, West D. Atypical presentation of hemorrhagic shock in pregnancy: a case highlighting the developing field of emergency medicine in Israel. *BMC Emerg Med.* 2019;19(1):70.
9. Chen L, Wang X, Wang H, Li Q, Shan N, Qi H. Clinical evaluation of prophylactic abdominal aortic balloon occlusion in patients with placenta accreta: a systematic review and meta-analysis. *BMC Pregnancy Childbirth.* 2019;19(1):30.
10. Okada A, Nakamoto O, Komori M, Arimoto H, Rinka H, Nakamura H. Resuscitative endovascular balloon occlusion of the aorta as an adjunct for hemorrhagic shock due to uterine rupture: a case report. *Clin Case Rep.* 2017;5(10):1565–1568.
11. Theodorou CM, Rinderknecht TN, Girda E, Galante JM, Russo RM. Fetal and neonatal outcomes following maternal aortic balloon occlusion for hemorrhage in pregnancy: a review of the literature. *J Trauma Acute Care Surg.* 2022;92(1):e10–e17.
12. Wang X, Yan J, Zhao X, Zheng W, Zhang H, Xin H, et al. Maternal outcomes of abnormally invasive placenta in China and their association with use of abdominal aortic balloon occlusion. *J Matern Fetal Neonatal Med.* 2022;35(25):9376–9382.
13. Palacios Jaraquemada JM, Garcia Monaco R, Barbosa NE, Ferle L, Iriarte H, Conesa HA. Lower uterine blood supply: extrauterine anastomotic system and its application in surgical devascularization techniques. *Acta Obstet Gynecol Scand.* 2007;86(2):228–234.
14. Wang Y, Zhao S. Vascular biology of the placenta. In: *Integrated Systems Physiology: from Molecules to Function to Disease*. San Rafael, CA: Morgan & Claypool Life Sciences; 2010.
15. Kingdom JC, Hobson SR, Murji A, Allen L, Windrim RC, Lockhart E, et al. Minimizing surgical blood loss at cesarean hysterectomy for placenta previa with evidence of placenta increta or placenta percreta: the state of play in 2020. *Am J Obstet Gynecol.* 2020;223(3):322–329.
16. Shahin Y, Pang CL. Endovascular interventional modalities for haemorrhage control in abnormal placental implantation deliveries: a systematic review and meta-analysis. *Eur Radiol.* 2018;28(7):2713–2726.
17. Zhao Z, Wang J, Yan T, Guo W, Yang R, Tang X, et al. A clinical study of the hemodynamic and metabolic effects of zone 3 REBOA for sacral and pelvic tumor resections. *BMC Surg.* 2022;22(1):246.
18. Chang SW, Chang YR, Seon YJ, Park JW, Kim JS. Intraoperative use of resuscitative endovascular balloon occlusion of the aorta for hemorrhage control in woman with placenta percreta involving the bladder. *Perinatology.* 2019;30:175.