Journal of Trauma and Acute Care Surgery, Publish Ahead of Print
DOI: 10.1097/TA.0000000000003917

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Aortic balloon occlusion in distal zone 3 reduces blood loss from obstetric hemorrhage in Placenta Accreta Spectrum

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Conflict of Interest Statement:

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

No funding was received for this work.

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No conflicts were declared.

Author Contribution:

SK and RR authored the manuscript. RC, as Director of the Placenta Accreta Program and primary surgeon, along with NA, AF, and BR, developed study protocol and the clinical protocol. All authors assisted with data analysis, interpretation, and critical edits of the manuscript.

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

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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 to 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 through March 2022. Medical records of all patients with PAS were reviewed. Data was extracted from hospital admission through three months postpartum.

Results: Forty-four patients met inclusion criteria. Nine never had the balloon inflated. Eighteen patients had placement in proximal zone 3 while 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% CI: 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 REBOA-related complications in either group.

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Conclusions: 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. REBOA should be considered at other institutions with placenta accreta programs, especially in patients with extensive collateral flow.

Level of Evidence: IV, therapeutic/care management

Key words: Placenta Accreta Spectrum, Postpartum Hemorrhage, REBOA, maternal morbidity and mortality

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Background

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 34-35 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 balloon occlusion of the aorta (REBOA) as an adjunct to hemorrhage control during cesarean hysterectomy for PAS (4-12). A meta-analysis of

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731 PAS patients who underwent cesarean deliveries in which a REBOA catheter was used to occlude the infra-renal 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 to 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 have significant collateralization particularly late in pregnancy (Figure 1).

The uterus and placenta derive their blood supply from the uterine arteries as well as the ovarian, vesical and vaginal arteries (Figure 1A). Additionally, extensive collateral blood flow from the lumbar, median sacral, inferior mesenteric (IMA) and iliolumbar arteries exist (Figure 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 >700ml/minute 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 Riolan and several other collateral pathways that may contribute to persistent pelvic bleeding (Figure 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 (Figure 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

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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 (Figure 2).

In December of 2018 our hospital became an accreta 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 (zone 3B), would reduce blood loss and transfusion volume and may permit a longer duration of occlusion compared to proximal zone 3 occlusion (zone 3A) without increasing ischemic complications.

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 through March 11, 2022. The medical records of all patients identified with PAS during the study period were reviewed and relevant data was extracted from hospital admission through at least three months postpartum. Patients were excluded if they did

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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 10/29/2020 we changed our level of occlusion to distal zone 3, just above the aortic bifurcation. The study compared outcomes of patients enrolled from 2/21/2018 to 9/3/2020 who underwent zone 3A occlusion to those enrolled from 10/29/2020 to 3/11/2022 who underwent zone 3B occlusion (Figure 3). The primary outcomes of interest included estimated surgical blood loss (EBL), red blood cell (RBC) transfusion volume, and total transfusion volume. Secondary outcomes included incidence of massive transfusion (defined as ≥ 10 units RBC transfusion), cumulative aortic occlusion time, REBOA-related complications, and post-operative 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

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indicated for fetal lung development. REBOA is pre-positioned 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 catheter placement. The interventional radiologist places a large bore catheter in the internal jugular vein for transfusion and central monitoring. A 20 gauge x 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-French 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

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aorta. Prior to 10/29/2020, the balloon was positioned just distal to the renal arteries based upon selective injections of the renal arteries (typically at the level of the 2nd lumbar vertebra) (Figure 2A). After 10/29/2020, 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 (Figure 2B). Due to 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 12/21/2018 to 11/18/2021 we used the ER-REBOA catheter (Prytime Medical, Boerne, Tx, USA) for both zone 3A and zone 3B occlusion. We now use the pREBOA-PRO catheter (Prytime Medical, Boerne, Tx, USA), since it became available to us on 11/22/2021. Our center switched catheters because the pREBOA-PRO offers better fidelity for partial REBOA and includes a safety mechanism to prevent vessel injury from over-inflation. After verification of proper positioning via imaging (Figure 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 5-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

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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, USA) 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. Post operatively, patients are admitted to the intensive care unit and undergo lower extremity arterial exams every 30 minutes for the first six hours.

Statistical Analysis

Numeric variables were assessed for normality with the Shapiro-Wilk test. The mean, standard deviation and two-sample t-test p-values are reported for normally distributed variables. The median, inter-quartile range (IQR) and Wilcoxon Rank Sum p-values are reported for non-normally distributed variables. Count, percentage, and Chi-square 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 due to the small sample sizes. Therefore, a multi-variable 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

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previa, urgency of surgery (defined as surgery occurring before the planned procedure date), body mass index (BMI), 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 variance was not satisfied and over dispersion was present in a Poisson generalized linear model (GLM). Therefore, multivariate analysis was based on a negative binomial GLM, 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 that did not have balloon occlusion documented. All patients that had a catheter inserted were included in the analysis and reporting of complications.

The STROBE checklist was used to ensure adequate reporting of our research findings (Supplemental Figure 1, http://links.lww.com/TA/C862).

Results

Forty-nine PAS patients were identified within the study period with forty-four included in the final analysis. Five patients were excluded for having not undergone REBOA placement. Of the forty-four patients that had a REBOA catheter inserted prior to cesarean hysterectomy, eighteen patients had placement in zone 3A while twenty-six patients had placement in zone 3B (Figure 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

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excellence in December 2018. This is reflected in the increase in the percentage of percreta/increta cases in the zone 3B group compared to 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 towards 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 4500 mL (IQR 2750-6000) as compared to 3000 mL (IQR 1875-4125) 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 over-inflation 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

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(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 Riolan, lumbar arteries, and the middle sacral artery we changed the balloon location from infra-renal to mid balloon placement at the third lumbar vertebra. Concurrently, our designation as an accreta center of excellence led to a shift towards 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 Pang 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 (16). They found that patients with prophylactic balloon occlusion of the abdominal aorta had the lowest blood loss as compared to 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

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reduced blood loss, transfusion requirements, hysterectomy rates and intensive care unit admissions. Similarly, the meta-analysis of 731 PAS patients by Chen et al. in China and the Columbian review of 441 patients by Ordoñez et al. 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 (6, 9).

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. 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 units of packed red blood cells), reduction in postoperative ileus, and decreased length of stay in the REBOA group compared to 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 to 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 non-pregnant patients, particularly those with vascular disease. During the endovascular repair of infra-renal aortic

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aneurysms, retrograde blood flow through the inferior mesenteric 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 (18). 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 colleagues 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 (17). They obtained an angiogram with the balloon inflated to visualize the source of hemorrhage, and the extensive collateral circulation can be well seen (Supplemental Figure 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 (18). Zhao and colleagues 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 Figure 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 3rd/4th lumbar vertebra or distance markings on the catheter could be used to accurately position the balloon appropriately within distal zone 3.

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Our study is limited by its retrospective nature and single institution location. Additionally, 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 multi-variable regression model to adjust for relevant covariates. Although the multivariate analysis indicated that distal occlusion may provide superior results compared to 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 utilizes 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. REBOA use 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.

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Figure Legends

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.

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 Riolan 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 inferior mesenteric artery. The utero-ovarian ligament or infundibulopelvic ligament must be ligated surgically to prevent additional flow to the uterus.

Figure 3. Study flow chart and timeline.

Figure 4. REBOA balloon on fluoroscopy. Intraoperative fluoroscopy with REBOA balloon inflated in the distal abdominal aorta at the 3rd lumbar vertebrae.

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Supplemental Figure Legends

Supplemental Figure 1. STROBE Statement checklist.

Supplemental Figure 2. (A) Angiography shows the inflated resuscitative endovascular balloon occlusion of the aorta catheter located in the infra-renal abdominal aorta via left common femoral artery (white arrows), ligated internal iliac artery (black arrow) and many collateral vessels on pelvic cavity. (B) Multifocal extravasation in spite of ligation of left internal iliac artery. Image borrowed with permission, Chang et al, 2019. Please note: the source of this image is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Supplemental Figure 3. An angiogram shows that no blood flow is present in the distal aorta when the occlusion balloon is positioned below the level of the inferior mesenteric artery. Image borrowed with permission, Zhao et al, 2022. Please note: the source of this image is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

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Figure 1

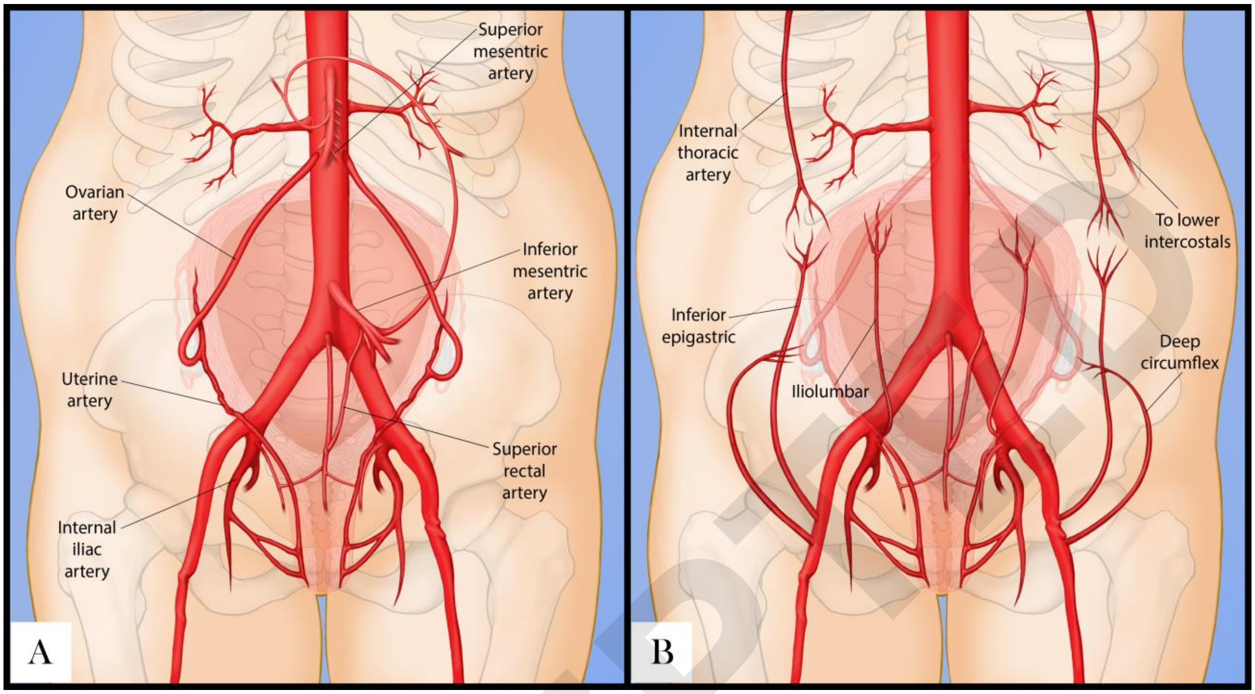

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Figure 2

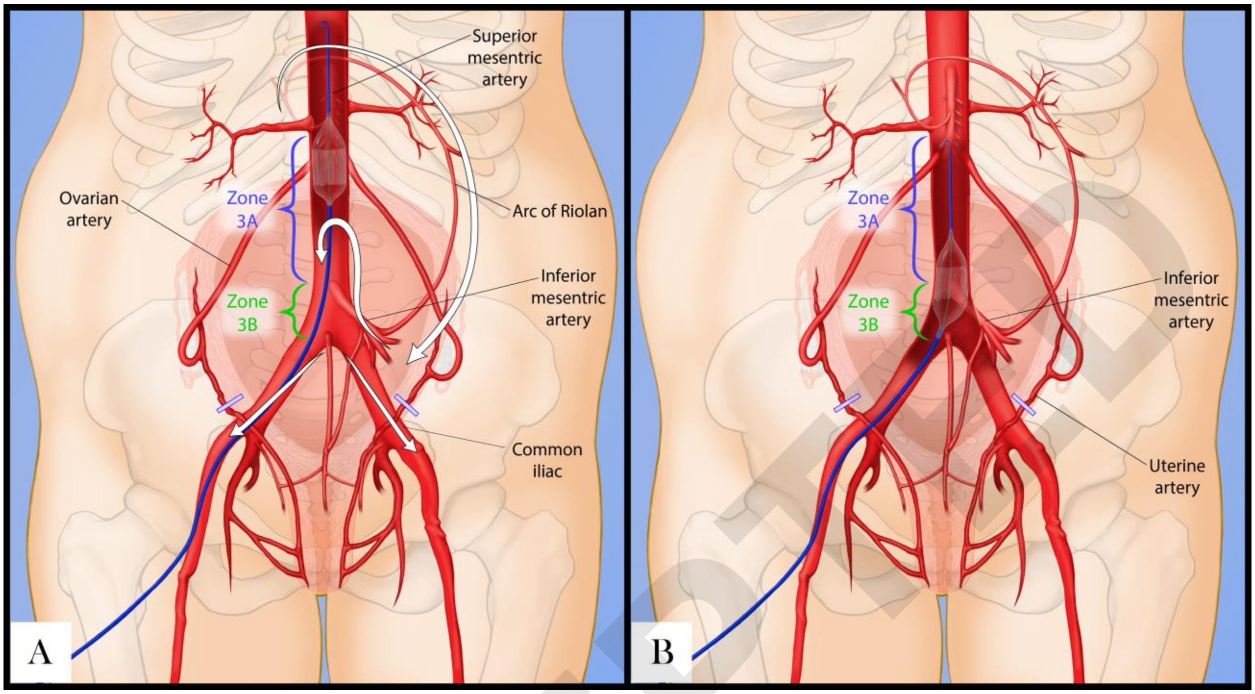

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Figure 3

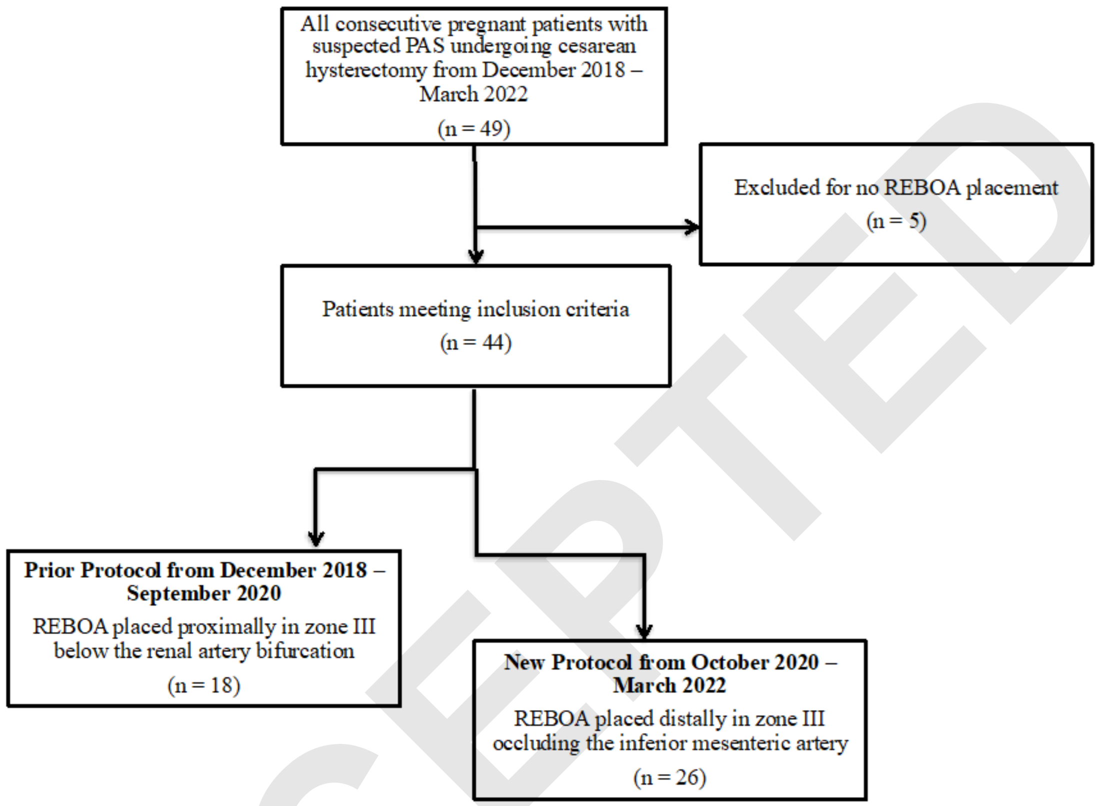

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Figure 4

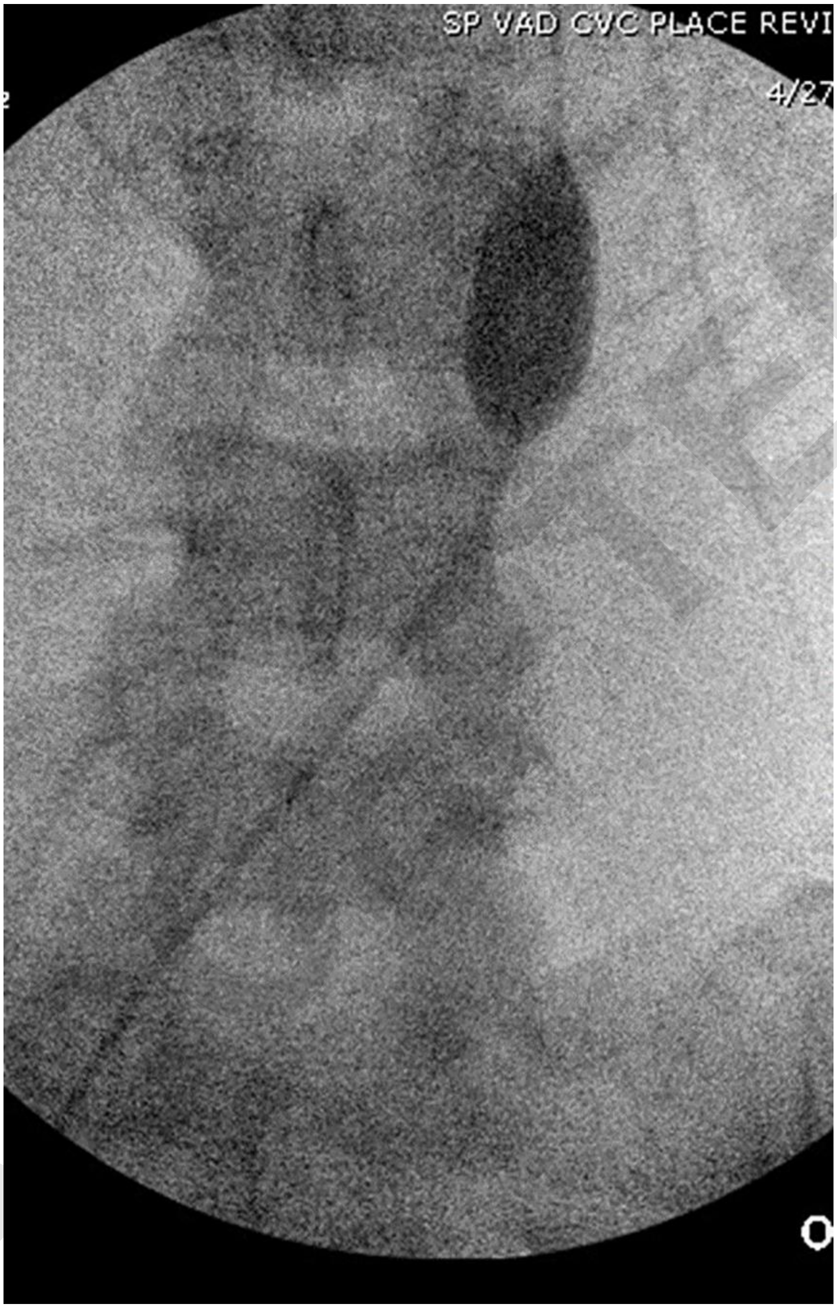

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Table 1 Demographics of patients in both treatment groups

Demographics	**REBOA Zone 3A (n=18)**	**REBOA Zone 3B (n=26)**	**P-value**
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 (weeks)	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 Chi-squared approximation may be incorrect.

The mean, standard deviation and two-sample t-test p-values are reported for normally distributed variables. The median, inter-quartile range and Wilcoxon Rank Sum p-values are reported for non-normally distributed variables. Count, percentage and Chi-square test p-values are reported for categorical and binary variables.

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Table 2 Comparison of perioperative outcomes in the treatment groups using the multi-variable regression model

Surgical outcomes	REBOA Zone 3A (n=18)	REBOA Zone 3B (n=26)	% Change (95% CI) Zone3B: Zone3A *
EBL (mL)			45.9% decrease (23.8%-61.6%)
Mean (sd)	3819 (2695)	2648 (1818)	
Median (IQR)	2750 (2000-4725)	2500 (1200-3750)	
Total RBC (units)			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 (units)			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 units RBC)	4 (22.2%)	4 (15.4%)	-
Duration of aortic occlusion (minutes)			
Zero minutes, number (%)	3 (16.7%)	6 (23.1%)	
Mean (sd) of non-zero 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

** 4 cases had missing data for duration of occlusion

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract page 1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Pages 3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pages 5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Page 6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pages 5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of	Pages 5-6 and Page 8

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		assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	Pages 8-9
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Pages 8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Pages 8-9
		(*b*) Describe any methods used to examine subgroups and interactions	Pages 8-9
		(*c*) Explain how missing data were addressed	Pages 8-9
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 9
		(b) Give reasons for non-participation at each stage	Page 9
		(c) Consider use of a flow diagram	Figure 3
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 2
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Table 2
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	Table 2

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		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Pages 9-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Pages 13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 14
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 2

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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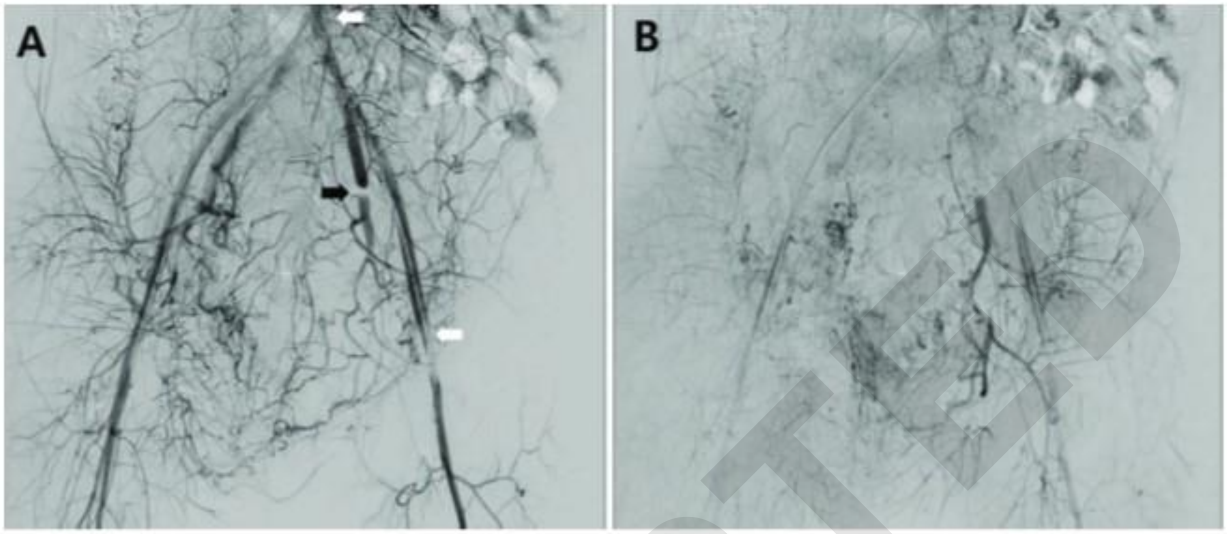
Supplemental Figure 2



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Supplemental Figure 3

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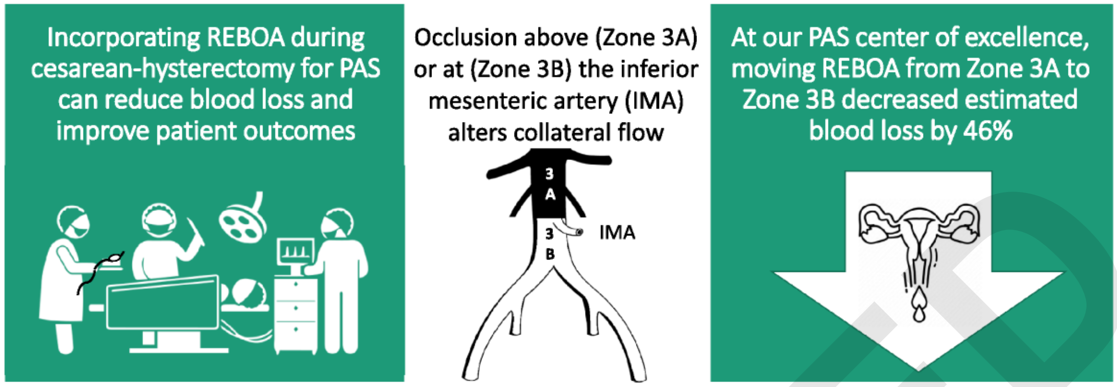
Visual Abstract

Aortic balloon occlusion in distal zone 3 reduces blood loss from obstetric hemorrhage in Placenta Accreta Spectrum (PAS)



Kluck SL et al. *Journal of Trauma and Acute Care Surgery*.
DOI: 10.1097/TA.0000000000003917

@JTraumAcuteSurg

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The Journal of Trauma and Acute Care Surgery®

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