Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) in the Multidisciplinary Management of Morbidly Adherent Placenta

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ABSTRACT **Background:** Morbidly adherent placentation (MAP) increases the risk for obstetric hemorrhage. Cesarean hysterectomy is the prevalent perioperative approach. Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a minimally invasive and relatively simple endovascular procedure to temporarily occlude the aorta and control below diaphragm bleeding in trauma. It has been effectively used to reduce obstetric hemorrhage.

Objectives: To evaluate whether REBOA during cesarean delivery (CD) in women with morbidly adherent placentation is a safe and effective treatment modality.

Methods: We introduced REBOA for CD with antepartum diagnosis of MAP in 2019 and compared these patients (RG) to a standard approach group (SAG) treated in our center over the preceding year, as a control. All relevant data were collected from patient electronic files.

Results: Estimated blood loss and transfusion rates were significantly higher in SAG; 54.5% of SAG patients received four RBC units or more vs. one administered in RG. No fresh frozen plasma, cryoprecipitate, or platelets were administered in RG vs. mean 3.63, 6, and 3.62 units, respectively in SAG. Ten SAG patients (90.9%) underwent hysterectomy vs. 3 RG patients (30%). Five SAG patients (45%) required post-surgical intensive care unit (ICU) admission vs. no RG patients. Bladder injury occurred in five SAG cases (45%) vs. 2 RG (20%). One RG patient had a thromboembolic event. Perioperative lactate levels were significantly higher in SAG patients.

Conclusions: Use of REBOA during CD in women with MAP is safe and effective in preventing massive bleeding, reducing the rate of hysterectomy, and improving patient outcome.

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Obstetric hemorrhage is a leading cause of maternal morbidity and mortality worldwide [1]; women with morbidly adherent placentation (MAP) are at especially high risk. MAP results from placental implantation at an area of defective decidualization, typically caused by pre-existing damage to the endometrial-myometrial interface, such as scarring after previous uterine surgery, which allows the anchoring villi of the placenta to attach directly to or invade the myometrium [2]. The rising incidence of MAP due to the increasing rates of cesarean deliveries (CD) constitutes a major concern.

Blood loss at delivery with invasive placentation may exceed 5 liters, and maternal mortality has been reported to be as high as 7%. Peripartum hysterectomy, either at the time of delivery or after is considered the standard approach [3]. A multidisciplinary approach was shown to decrease the morbidity related to the surgical approach for MAP, still leaving the blood loss and massive transfusion as a major complication leading to prolonged hospitalization and intensive care admissions.

Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a minimally invasive and relatively simple endovascular procedure. It involves placement of an endovascular balloon in the aorta to achieve temporary occlusion, which results in control of bleeding originating below the diaphragm [4,5]. REBOA was initially used to treat traumatic hemorrhagic shock. Recently, there has been a growing interest in this method to control obstetric hemorrhage [6,7]. REBOA may provide an alternative to more complicated methods, such as embolization, in an invasive radiology suite when these services are not available. Deployment of REBOA is rapid and relatively simple, thus making it possible to use in almost any setting [8].

We describe the experience of a large maternity center that implemented a multidisciplinary team approach for focal or complete MAP using REBOA and compared it with a similar approach without the use of REBOA.

PATIENTS AND METHODS

This study includes all women who had a CD with an antepartum diagnosis of MAP between January 2018 and July 2021 at Shaare Zedek Medical Center, which is a tertiary teaching hospital. The labor and delivery department consists of 20 delivery rooms with 3 operating rooms. Approximately 16,000 deliveries

are attended annually with a CD rate of 11%. All patient care is covered by the national health insurance plan.

A multidisciplinary institutional protocol for management of placenta accreta spectrum was implemented in 2014 [9]. The pre-delivery stage includes a MAP outpatient risk assessment for all suspected cases based on clinical history and sonographic imaging at the mid-trimester routine fetal anatomy scan. Patients defined as being at risk of MAP undergo antenatal surgical, obstetric anesthesia, and urological consultations that include cystoscopy and neonatology evaluations. A repeat ultrasound assessment is performed at admission and defined for the high- or low-risk magnitude for MAP [10,11]. Sonographic evaluations are performed in our feto-maternal ultrasound institute. Patients with an uncertain sonographic diagnosis of MAP are further evaluated using magnetic resonance imaging scan (e.g., posterior placenta). Planned CD is performed between 34- and 35-weeks gestation, except in cases of emergency delivery due to antenatal bleeding or other complications. The surgical team includes a board-certified obstetrician, a gynecologic oncology trained surgeon, and the obstetrician on call. The ICU and the blood bank are informed of the upcoming surgery. A cell saver device with technical support is present in the operating room. The surgery protocol includes massive transfusion protocol activation, cystoscopic insertion of ureteral catheters, visual assessment of abnormal vascular pattern on the uterine wall and bladder, vertical or fundal/posterior wall uterine incision, delivery of the neonate, prophylactic placement of vessel loops on the iliac vessels, avoidance of active placenta delivery, and observation for spontaneous placenta detachment for 5–10 minutes during an inspection of the adjacent organs and vessels followed by either hysterectomy with the placenta left in situ, or closure of the uterine incision, or uterine repair in cases where the placenta detached spontaneously and placental bed bleeding is under control.

In March 2019, we introduced REBOA as a new treatment modality for all cases of CD with an antenatal assessment of high-risk MAP (REBOA group [RG]). We compared this group with the standard approach group (SAG), which consisted of all women who underwent MAP and CD and who were treated with the multidisciplinary approach without the use of REBOA.

Women in both groups had a preoperative high suspicion of placental invasion according to known parameters of invasion (e.g., presence of lacunae, absence of sonolucent zone, abnormal vasculature) [2,12]. Women diagnosed with low-risk suspicion of MAP, in either group, were excluded from the study. Pathology reports of uterine tissue, either hysterectomy specimen or segmental uterine wall resection, were submitted to pathology assessment. MAP diagnosis was reviewed to confirm placental invasion.

In the REBOA protocol we implemented an endovascular catheter (RESCUE BALLOON® Occlusion Catheter, Tokai Medical Products, Aichi, Japan) that was inserted by a vascular surgeon under ultrasound guidance using a femoral artery access through a 8F introducer sheath and placed in immediate location above the aortic bifurcation, Zone III (which extends distally from the most caudal renal artery to the aortic bifurcation) [4]. The use of the 8F introducer enables simpler extraction of the catheter in cases of repeated inflation and deflation maneuvers. The balloon was inflated immediately after delivery of the neonate and clamping of the umbilical cord. After deciding on local uterine wall excision and metroplasty or hysterectomy guided by the antenatal MAP assessment and surgical findings, the balloon was repetitively deflated and inflated according to the surgical homeostasis requirements. The device was removed at the end of the surgery and the arterial puncture site was closed with an ANGIO-SEAL® VIP vascular closure device (Terumo Medical Corporation, USA). The duration of aortic occlusion was recorded and strictly limited to 15 minutes after first inflation. If more time was needed; the balloon was deflated for one minute and then re-inflated for up to 15 minutes. The REBOA insertion and inflation procedure was performed without intraoperative anticoagulation.

All demographic, obstetric, and anesthetic data were retrieved from patient medical electronic records. Specifically, the variables included estimated blood loss (EBL) as primary outcome, and use of blood products, rate of hysterectomy, and total time of aortic occlusion as secondary outcome. Other parameters included hemodynamic instability events (systolic blood pressure < 80 mmHg or heart rate > 130/min), anesthesia and surgery time, the maximum perioperative serum lactate level (defined as the highest measurement of lactate using a standard blood gas analyzer during the surgery and within the first postoperative hour), ICU admission rate, postoperative ischemic lower limb complications, and prolonged hospitalization (more than 7 days).

Descriptive statistics and comparison were performed accordingly. Continuous variables were expressed as median and categorical variables as frequencies and percentages. Mann-Whitney U test was used for pairwise comparison. A *P*-value ≤ 0.05 was considered significant (two-tailed).

The study was approved by the institutional review board for clinical studies at Shaare Zedek Medical Center, Approval ID: 0287-17-SZMC.

RESULTS

Demographic and obstetric characteristics of women in the study as well as collected data parameters are presented in Table 1. There were 11 women in the standard approach group (n=11) and 10 women in the REBOA group (n=10). There was no significant difference in patient demographics. Or obstetrical history; maternal age, parity, and number of previous CDs were similar. There were no significant differences in neonatal characteristics. The gestational age at delivery and the neonatal

Table 1. Description of the study groups demographic and operative characteristics

	Standard approach group, n=11	REBOA group, n=10	*P*-value
Maternal characteristics			
Maternal age (years), mean ± SD	33.8 ± 4.5	35 ± 5.019	0.498
Number of previous CD, mean ± SD	2.54 ± 0.93	3.2 ± 2.41	0.395
Parity, mean ± SD	3.82 ± 2.38	7 ± 2.4	0.234
Neonatal characteristics			
Birth weight in grams, mean ± SD	2315.45 ± 605.48	2405.7 ± 678.48	1.0
Apgar 1	6.27 ± 2.57	5.9 ± 3.13	0.72
Apgar 5	7.63 ± 1.8	7.4 ± 1.64	0.53
Surgery (CD) characteristic			
Massive transfusion (› 4 PRBC units), n (%)	6 (54.5)	0 (0)	
PRBC units, median	4 (0-9)	1	
FFP units, mean ± SD	3.63 ± 3.17	0	
Cryoprecipitate units, mean ± SD	6 ± 6.99	0	
Platelets units, mean ± SD	3.62 ± 3.17	0	
Estimated intraoperative blood loss (ml), mean ± SD	4400 ± 2787.0	1060 ± 296.64	0.01
Intraoperative crystalloids (ml), mean ± SD	5154.5 ± 2765.25	2000 ± 917.6	0.024
Hysterectomy, n (%)	10 (90.9)	3(30)	
Emergency CD (%)	36%	20%	
Mode of anesthesia, general / neuraxial (%)	100 / 0	60 / 40	
Total anesthesia time (in minutes), mean ± SD	191.36 ± 48.07	179 ± 21.12	0.34
Total surgery time (in minutes), mean ± SD	149.81 ± 47.69	119 ± 29.41	0.11
Intraoperative hemodynamic instability (BP < 80, HR > 130), n (%)	4 (36)	0 (0)	
Balloon inflation time (in minutes), mean ± SD	–	19.12 ± 6.05	
Bladder injury, n (%)	5 (45)	2 (20)	
Postoperative characteristics			
ICU Admission, n (%)	5 (45)	0	
ICU Days, mean ± SD	1.9 ± 2.54	0	
Re-laparotomy within 48 hours (cases)	0	0	
Postsurgical hospitalization (days) > 7 days, n (%)	5 (45)	5 (50)	
Maximum perioperative serum lactate level (mmol/L), mean ± SD	3.02 ± 2.63	1.345 ± 0.694	0.0433
Lactate > 2.5 mmol/L, n (%)	4 (36.3)	1 (10)	
Placenta pathology report confirmed MAP n (%)	11 (100%)	10 (100%)	

CD = cesarean delivery,
FFP = fresh frozen plasma,
MAP = morbidly adherent placenta,
PRBC = packed red blood cells units,
SD = standard deviation

birth weight were comparable and inherent to the protocol determinants.

The study groups differed significantly in their operative and perioperative characteristics. The REBOA group was characterized by a significantly lower rate of hysterectomy. Only three were performed in RG (30%) vs. ten (90.9%) in SAG. Mean volumes of estimated blood loss (EBL) were significantly lower in the RG: 1060 ± 694.55 ml vs. 4400 ± 2787.0 ml in the SAG (P = 0.02). Notably, in the REBOA group, only one PRBC unit was transfused in one case, while in the SAG, a median of four PRBC units were administered, with six patients (54.5%) receiving more than four units. The same pattern was observed for other blood products as well: none with the REBOA whereas in SAG mean values for units of fresh frozen plasma, cryoprecipitate, and platelet administered were 3.63, 6, and 3.62, respectively. Inherently, no woman in the RG had any events of hemodynamic instability, whereas 36% of the patients in SAG had at least one such event. Women in the RG had a lower rate of urinary bladder injury: two incident (20%) vs. five cases (45%) in SAG. There was no significant difference in surgery and anesthesia times between SAG and RG (P = 0.11 and P = 0.34, respectively).

The mean REBOA balloon inflation time was 19.2 ± 6.05 min. There was one thromboembolic event, without significant lower limb ischemia, in the RG which was successfully treated in an angiography suite. No other associated complications were noted, despite undergoing occlusion of the aorta without receiving intraoperative anticoagulation. To assess the grade of tissue ischemia and further evaluate the hemodynamic instability and possible other organ ischemia due to balloon inflation, we calculated the maximum perioperative serum lactate level, which was defined as the highest measurement of lactate using a standard blood gas analyzer, during the surgery and within the first postoperative hour. The mean increase in lactate was significantly lower in the RG 1.14 ± 0.694 vs. 3.02 ± 2.63 in the SAG (P = 0.0433).

None of the patients in the RG required a stay in the ICU in the immediate postoperative period while five (45%) in the SAG were admitted to ICU for at least 24 hours. None of the patients had bleeding control re-laparotomy or infectious morbidity, and the rate of prolonged hospital stay was similar in both groups.

DISCUSSION

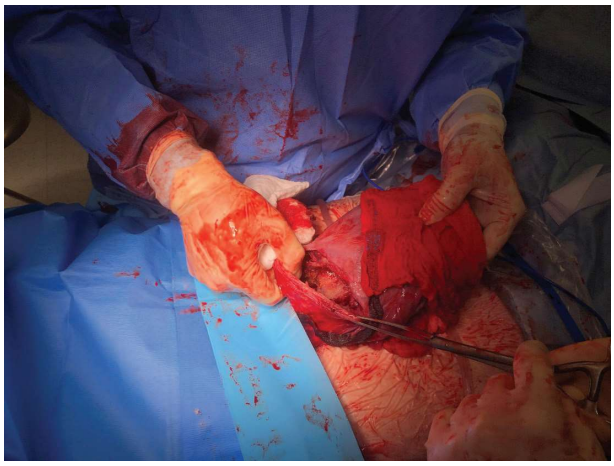
The use of REBOA in the obstetric unit has become more prevalent in recent years [13]. Our study presents a single center comparison of peripartum outcome of women with MAP using two multidisciplinary approaches: use of a resuscitative endovascular balloon vs. a group in which the perioperative management did not include use of REBOA.

Compared to other invasive endovascular methods, REBOA deployment requires very little additional infrastructure and thus can be used virtually in any center of any size [8]. Specifically, we showed a significant reduction in hemodynamic instability and hemorrhagic complications of MAP surgery and blood products transfusion. The use of REBOA in MAP CD in our study was associated with a significantly reduced rate of bleeding and blood products transfusion with minimal complications. This significant improvement is compared to other reported measures for MAP surgery bleeding control and their complications, including interventional radiology methods [12,14]. What is noticeable is the marked reduction in hysterectomies. According to previous reports, in centers that do not use any invasive methods to control bleeding, approximately 71% of total accreta cases require hysterectomy [15]. Moreover, up to 90% of patients with placenta accreta require blood transfusion. Even when a bilateral internal iliac balloon is inserted, the rate of hysterectomy is reduced, but not significantly [16].

A large cohort study of women with suspected placenta accreta who underwent prophylactic pelvic artery catheterization performed at Sheba Medical Center, Israel [16], showed a median estimated blood loss of 2000 ml. In addition, prophylactic pelvic artery catheterization, balloon occlusion, and embolization (PACBOE) in an emergency setting involves a high incidence of complications such as thrombosis requiring bypass, internal iliac dissection, ischemia of the sciatic nerve, and necrosis of the proximal vagina and cervix [17]. Notably, reports have described rates of hysterectomy up to 45% [17,18]. Sivan et al. [16] concluded that PACBOE should be offered electively in a tertiary hospital with an experienced interventional radiologist and/or collaborative team of experts. In an emergency setting they lean toward performing a standard CS and hysterectomy if needed. Ojala and colleagues [17] concluded that arterial occlusion should be implemented as part of a protocol only when experienced interventional radiology support is readily available [14].

In our study, the two groups did not differ significantly in mean length of hospitalization, with five patients in the SAG (45%) and five (50%) in the RG requiring more than 7 days of postsurgical hospitalization. None of the patients in the REBOA group required ICU admission, while 45% of the patients in the standard approach group were admitted to ICU. This rate is similar to previous reports of series from other centers [13] where of 12 patients, none required ICU admission and no REBOA-related complications were reported. Another retrospective study [19] also showed that patients who underwent prophylactic temporary balloon occlusion of infrarenal abdominal aorta prior to caesarean section, had a very low rate of ICU admissions (1.3%). The hospital stay in this series was 5.1 ± 0.8 days, comparable to patients without aortic balloon insertion (6.7 ± 1.0). Matsuoka et al. [20] shared their experience where out of eight cases of placenta previa accrete, four underwent cesarean hysterectomy with a blood loss ranging from 2400 ml to 5200 ml, and one case with use of REBOA without hysterectomy and a significantly lower blood loss (840 ml).

Figure 1. Intraoperative images of uterus with an inflated REBOA balloon, showing marked reduction in bleeding



None of our patients in either group presented with postoperative infection. A thromboembolic event occurred in only one case of the RG, despite all women undergoing occlusion of the aorta without receiving intraoperative anticoagulation.

As seen from our data set, occlusion of the aorta was performed for relatively short periods, significantly shorter than with perioperative internal iliac artery balloon occlusion [19]. Based on our experience and literature, occlusion of the aorta for short periods of 15 to 20 minutes is probably uneventful [13]. In some more challenging cases, with longer operating times, it is feasible to either perform a partial occlusion or repeated short periods of aortic occlusion, depending on the situation [21].

When reviewing changes in serum lactate levels, as a marker for tissue hypoxia and hypoperfusion [22,23], the increase was significantly higher in the SAG. A possible explanation may be that the reduction in effective blood volume caused by hemorrhage outweighs the temporary reduction in perfusion caused by the inflation of REBOA. Most studies use cutoffs between 2.0 and 2.5 mmol/L for elevated lactate while significantly high levels usually defined as a lactate > 4 mmol/L [23]. None of the patients in the RG had a lactate measurement > 2.5 mmol/L, while 36.3% in SAG had significantly elevated lactate levels.

Nonoptimal surgical conditions make it difficult to preserve the uterus. Conservative management of placenta percreta involves high maternal morbidity [24]. Using an effective method to reduce the amount of bleeding and enable a controlled dissection of the placenta is thus desirable. An intraoperative image of uterus with an inflated REBOA balloon can be seen in Figure 1. With regards to neonatal outcome, the results are consistent with values in literature for outcome in CD under general anesthesia [25].

One of the limitations of our study is its retrospective nature. With data retrieved from hospital records, we cannot rule out minor inaccuracies. Another limitation is the rather limited sample size, although the number of cases is comparable to the largest case series that were published on this subject before.

CONCLUSIONS

The use of REBOA during CD in cases of MAP contributes to significant reduction in perioperative blood loss as well as reducing the rate of cesarean hysterectomy. This method ensures better operating conditions, improves patient outcome, and may be successfully used as a safe and easy alternative to other invasive radiology methods.

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Science is built with facts as a house is with stones,
but a collection of facts is no more a science than a heap of stones is a house.
Jules Henri Poincaré (1854–1912), mathematician, physicist, and philosopher

Don't get so tolerant that you tolerate intolerance.
Bill Maher (born 1956), comedian, actor, and writer

Capsule

Immunology T cells develop survival skills

Mouse thymocyte survival depends on the suppression of cell death by the inhibitor of κB kinase (IKK) complex, which phosphorylates and inactivates the cell death-promoting kinase receptor-interacting protein kinase 1 (RIPK1). Using lineage-specific, conditional knockout mice, **Carty** and colleagues investigated the role of IKK in the survival of mature naïve T cells after they left the thymus. In addition to inhibiting RIPK1-dependent cell death, IKK also activated prosurvival signaling, which depended on the transcription factor nuclear factor-κB and one of its targets, the cytokine receptor interleukin-7R.

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Capsule

Through the cochlear aqueduct

Although gene therapy can treat genetic hearing loss in neonatal mice, treating adult animals is more difficult because of the location of the cochleae and the risk of damage to inner ear structures. **Mathiesen** and co-authors showed that the cochlear aqueduct connects the cerebrospinal fluid (CSF) and cochlear fluid in adult mice. Tracers injected into the CSF reached the mouse inner ear, and intracisternal injection of an adeno-associated virus carrying the solute carrier family 17 member 8 gene (*Slc17A8*) restored vesicular glutamate transporter-3 protein in the inner hair cells of the cochlea and rescued hearing in mice that lacked *Slc17A8*. These findings suggest that CSF administration of gene therapy through the cochlear aqueducts could eventually be a treatment for genetic deafness in adult patients.

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