Published in final edited form as:

J Matern Fetal Neonatal Med. 2020 November ; 33(21): 3614–3618.

doi:10.1080/14767058.2019.1581168.

Utilization and outcomes of massive transfusion protocols in women with and without invasive placentation

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Declaration of Interests:

G.A.D. and M.A.B. are the inventors and patent holders of the dual-balloon catheter tamponade device, the Belfort-Dildy Obstetrical Tamponade System (ebb).

The remaining authors declare no conflict of interests.

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Abstract

Objective: Our objective was to compare women with and without invasive placentation for whom the massive transfusion protocol (MTP) was activated. In addition, we evaluated the differences in clinical management and blood product utilization between the two groups and described the activation of MTP over time.

Study Design: This is a retrospective cohort study of women for whom the MTP was activated from January 2012 through July 2016. Two groups were compared, those with invasive placentation (accreta, increta, percreta) and those without.

Results: We identified 87 women for whom the MTP was activated, the majority (62.1%) did not have invasive placentation. Women with invasive placentation were more likely to have had a prior cesarean delivery and placenta previa (both $p < 0.001$). Women with invasive placentation were more likely to undergo hysterectomy, experience more blood loss, and receive cell salvage (all $p = 0.04$). Blood product utilization was similar between the two groups, with the exception of cell-salvage, which was more commonly used for women with invasive placentation. The proportion of deliveries necessitating MTP activation ranged from 1.4 to 2.6 per 1000 deliveries.

Conclusion: Invasive placentation accounts for less than half of cases complicated by activation of an MTP. Cases with invasive placentation were more likely to result in a vertical uterine and skin incision or a hysterectomy. With the exception of cell-salvage, blood product utilization was similar.

Keywords

postpartum hemorrhage; placenta accreta; morbidly adherent placenta; invasive placentation; blood transfusion

Introduction:

In the United States, maternal hemorrhage and the need for blood transfusion at time of delivery are increasing. Among women who have a postpartum hemorrhage (defined as ≥ 500 mL for a vaginal delivery and ≥ 1000 mL for a cesarean delivery) the incidence of blood transfusion approaches 10%. [1] Certain conditions predispose pregnant women to hemorrhage, including chorioamnionitis, multiple prior cesarean deliveries, cesarean delivery after induction of labor, placenta previa, and invasive placentation (accreta, increta,

percreta).[1,2,3] Preparation for hemorrhage has been shown to improve maternal outcomes; however, the majority of maternal hemorrhages are unpredictable.[3] Approximately 5% of all maternal hemorrhages result in activation of an institutional massive transfusion protocol (MTP) and subsequent large volume transfusion.[4] Between 2000 and 2011, the use of blood transfusion increased by greater than 150% among women undergoing cesarean delivery, and there has been a concomitant 30% increase in the incidence of invasive placentation.[5]

The primary objective of this study was to determine the impact of invasive placentation in women for whom a MTP was activated. Our specific aims were to (1) compare presenting characteristics among women with and without invasive placentation, (2) compare clinical management, in particular blood product utilization, and other outcomes in women with and without invasive placentation, and (3) describe MTP activation over time. We hypothesized that women with invasive placentation would have a different blood product utilization profile from those without invasive placentation.

Methods:

We conducted a multicenter retrospective cohort study of women whose delivery resulted in activation of the MTP at one of two tertiary academic medical centers, both serving as regional referral centers for invasive placentation. This study was approved by the institutional review boards at Beth Israel Deaconess Medical Center and Texas Children's Pavilion for Women.

Using blood bank databases, we identified all women for whom the MTP was activated intrapartum or during the six-week postpartum period and who received at least one transfusion from January 2012 through July 2016. We extracted data from the medical record and reviewed each record to determine comorbidities and accuracy of blood bank data. Invasive placentation was confirmed by pathology report. All women with an antepartum suspicion for invasive placentation were managed in a multidisciplinary approach, including the routine use of maternal-fetal medicine, urology, gynecologic oncology, and obstetric anesthesiology.[2,6] Based on the recent consensus statement from the National Partnership for Maternal Safety, we considered a 1:1 to 2:1 ratio of packed red blood cells to plasma to be optimal.[7] In a prior study, a transfusion ratio of 1:1 packed red blood cells to plasma was deemed achieved if the ratio ranged from 0.8 to 1.2.[8] Thus, we defined an expanded range of 0.8 to 2.2 as the optimal ratio of packed red blood cells to plasma to include both 1:1 and 2:1 management. Intraoperative cell salvage was available and used from January 2012 through December 2015. After December 2015, one of the sites stopped using cell salvage as part of the routine care for women experiencing hemorrhage; thus, we only analyzed cell salvage utilization until December 2015. Both centers followed their own multidisciplinary approach to the management of obstetrical hemorrhage and invasive placentation; however, they each followed the national recommendations at the time.[2]

This was a sample of convenience; thus, we included all women who met the eligibility criteria. Data are presented as proportion or median (interquartile range). We used a Chi-

square or Fisher's exact test for categorical variables and the Wilcoxon rank sum test for continuous variables to compare women with and without invasive placentation. All tests were two sided, and p values <0.05 were considered statistically significant. All analyses were performed with SAS 9.4 (SAS Institute Inc., Cary, NC).

Results:

We identified 90 women for whom the MTP was activated. We excluded three women who did not have any blood products transfused, leaving 87 women included in the analysis —33 (37.9%) from Beth Israel Deaconess Medical Center and 54 (62.1%) from Texas Children's Pavilion for Women. All women received allogeneic donor blood products. The majority of pregnancies (62.1%) were not affected by invasive placentation. The median gestational age at delivery was significantly earlier in the invasive placentation group (33.8 weeks of gestation (31.0-35.7)) compared to those without invasive placentation (38.1 weeks (35.6-39.6); $p<0.001$). The proportion of women with a prior cesarean delivery was 93.9% in the invasive placentation group compared to 27.8% in the group without invasive placentation. In addition, the prevalence of placenta previa was significantly higher in women with invasive placentation compared to those without ($p<0.001$). Baseline characteristics are presented in Table 1.

Vertical skin and uterine incisions, as well as peripartum hysterectomy, were more common in women with invasive placentation compared to those without (all $p<0.001$). Hemorrhage with noninvasive placentation was more likely to be treated with uterine balloon tamponade ($p<0.001$). There were no differences between the two groups in terms of other surgical procedures. Intrapartum characteristics are presented in Table 2.

Estimated blood loss was greater in women with invasive placentation compared to those with normal placentation ($p<0.001$). However, there were no differences in volumes of packed red blood cells, plasma, platelets, or pooled cryoprecipitate between the two groups (all $p \geq 0.10$). The majority of patients in both groups received the recommended ratio of 1:1 to 2:1 packed red blood cells to fresh frozen plasma ($p=0.70$). When compared to women with noninvasive placentation, intraoperative cell salvage was utilized more commonly in cases with invasive placentation ($p<0.001$). Maternal outcomes following MTP activation were similar between those with and without invasive placentation. Blood product utilization and outcomes are presented in Table 3.

The incidence of MTP activation per 1000 deliveries varied with time. The incidence ranged from 1.4 per 1000 in 2016 to a peak of 2.6 per 1000 deliveries in 2015. The proportion of deliveries complicated by invasive placentation ranged from 25.0% to 43.5%.

Comment

Contrary to our hypothesis that those with invasive placentation would have greater blood product needs, these results, other than utilization of cell-salvage, demonstrate that the presence of invasive placentation does not affect blood product utilization in those for whom the MTP was activated. These findings likely represent a universal approach to blood product management in the management of women with and without placental invasion

rather than a disease-specific approach. Not surprisingly, women with invasive placentation were more likely to have had a prior cesarean delivery and placenta previa. In addition, due to the increased antenatal concern for hemorrhage in those with invasive placentation, it is not surprising that women with invasive placentation were more likely to undergo a hysterectomy rather than uterine sparing techniques. To our surprise, we did not observe an increase in the utilization of MTP over time. In addition, despite the national rise in invasive placentation, we did not observe a temporal increase in the prevalence of invasion for those with activation of the MTP. As supported by the literature, this finding could reflect the decrease in hemorrhagic morbidity as experience is gained in managing invasive placentation.[6]

Utilization of cell salvage has long been an area of contentious debate in obstetrics. There are theoretical concerns of amniotic fluid or meconium embolism when utilized at the time of delivery. These concerns have not been validated in the literature and series reporting cell salvage usage have not found an association with any adverse events.[9,10] In our study, the significant difference in the utilization of cell salvage could reflect the preparations made in scheduled deliveries of invasive placentation, as opposed to the deliveries complicated by unexpected severe hemorrhage without invasive placentation. Of note, women with invasive placentation experienced larger estimated blood losses but did not receive significantly more transfusions than those without invasive placentation. Although this was somewhat surprising, this could be explained by the high level of anticipation for bleeding in cases of invasive placentation and perhaps a higher provider tolerance of a lower post-operative blood count. In addition, the use of cell salvage was high in the invasive placentation group, but the transfusion volumes were similar.

Consistent with the recent National Partnership for Maternal Safety consensus statement, our data demonstrates that the majority of patients were managed in a 1:1 to 2:1 ratio of packed red blood cells to fresh frozen plasma during their massive transfusion. Data from the trauma literature suggests a decreased risk of death from exsanguination and improved hemostasis when trauma hemorrhage is managed in a 1:1 fashion; however, the pathophysiology of trauma hemorrhage does not mimic that of obstetrical hemorrhage. [11] As such, results from the trauma literature may not be generalizable to the obstetrical population. While the recommendation from the recent National Partnership for Maternal Safety is a reasonable start, it is based on limited data, and further work is needed to determine the ideal ratio for obstetrical hemorrhage.

One of the limitations of this study is the small sample size, yielding insufficient power to detect potentially meaningful differences for all outcomes of interest. However, the fact that both study sites are regional referral centers for invasive placentation resulted in a relatively large number of women with invasive placentation—all of which were confirmed by pathological examination. Another limitation is that the management protocols at the two institutions differed throughout the study period, though including two centers allowed for greater generalizability.

In conclusion, this study suggests that among pregnancies for which the MTP was activated, maternal outcomes are similar, despite the increased a prior risk of invasive placentation and

differences in baseline characteristics and intrapartum management. While blood product utilization, specifically the ratio of packed red blood cells to fresh frozen plasma, was similar for the two groups with and without invasive placentation, it is still unclear if this ratio is the most appropriate in the management of massive obstetrical hemorrhage, highlighting the need for future work to answer this frequently asked question.

Acknowledgments

This work was conducted with support from The Charles Koch Foundation and Harvard Catalyst | The Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award UL1 TR001102) and financial contributions from Harvard University and its affiliated academic healthcare centers

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Table 1:

Participant characteristics

	Massive transfusion without invasive placentation n=54	Massive transfusion with invasive placentation n=33	p
Maternal age (years)	32.0 (28.0-35.0)	34.0 (28.5-39.5)	0.11
Body mass index (kg/m²)	27.8 (25.4-31.5)	31.0 (28.6-34.7)	0.01
Gestational age at delivery	38.1 (35.6-39.6)	33.8 (30.9-35.7)	<0.001
Gravidity	2.0 (1.0-4.0)	4.0 (3.0-5.0)	<0.001
Race/Ethnicity			0.14
White	18 (33.3)	14 (42.4)	
Asian	9 (16.7)	0 (0.0)	
Hispanic	5 (9.3)	4 (12.1)	
Black	8 (14.8)	5 (15.2)	
Other	1 (1.9)	0 (0.0)	
Unknown	13 (24.1)	10 (30.3)	
Current smoker			1.0
Yes	3 (5.6)	2 (6.1)	
No	51 (94.4)	31 (93.9)	
Number of prior cesarean deliveries			<0.001
0	39 (72.2)	2 (6.1)	
1	10 (18.5)	8 (24.2)	
2	2 (3.7)	14 (42.4)	
3 or more	3 (5.6)	9 (27.3)	
Placenta previa	3 (5.6)	12 (36.7)	<0.001
Chorioamnionitis	3 (5.6)	0 (0.0)	0.29

Data are presented as n (%)

Table 2:

Intrapartum management characteristics

	Massive transfusion without invasive placentation n=54	Massive transfusion with invasive placentation n=33	p
Mode of delivery			<0.001
Vaginal	22 (40.7)	0 (0.0)	
Cesarean	32 (59.3))	33 (100.0)	
Cesarean delivery			<0.001
Low transverse	28 (87.5)	6 (18.2)	
Vertical/transfundal	4 (12.5)	27 (81.8)	
Skin incision *			<0.001
Pfannenstiel	28 (87.5)	7 (21.2)	
Vertical midline	3 (9.4)	25 (75.8)	
Peripartum hysterectomy	17 (31.5)	31 (93.9)	<0.001
Additional procedures			
Dilation and curettage	6 (11.1)	0 (0.0)	0.08
Uterine balloon tamponade	23 (42.6)	1 (3.0)	<0.001
Uterine artery ligation	4 (7.4)	2 (6.1)	1.0
B-Lynch suture	9 (16.7)	1 (3.0)	0.08
Interventional radiology embolization	1 (1.9)	1 (3.0)	1.0
Hypogastric ligation	1 (1.9)	2 (6.1)	0.55
Other	9 (16.7)	10 (30.3)	0.14

Data are presented as n (%)

* Two patients missing data on type of skin incision (one in each group)

Table 3:

Blood bank utilization and outcomes

	Massive transfusion without invasive placentation n=54	Massive transfusion with invasive placentation n=33	p
Intrapartum estimated blood loss (cc)	2000.0 (1000.0-3500.0)	3800.0 (2600.0-6000.0)	<0.001
Packed red blood cells	8.0 (4.0-12.0)	11.0 (7.0-14.0)	0.10
Fresh frozen plasma	4.0 (2.0-6.0)	6.0 (3.0-8.0)	0.20
Packed red blood cells : fresh frozen plasma	2.0 (1.3-2.5)	1.7 (1.4-2.5)	0.68
Proportion with 1:1 to 2:1 packed red blood cells : fresh frozen plasma ¹	31 (57.4)	22 (66.7)	0.70
Platelets	2.0 (0.0-3.0)	1.0 (0.0-3.0)	0.74
Pooled cryoprecipitate	2.0 (0.0-5.5)	4.0 (0.0-12.0)	0.63
Cell salvage ²	1 (1.9)	11 (33.3)	<0.001
Volume infused (cc)	180.0 (180.0-180.0)	250.0 (150.0-1000.0)	0.78
Intensive care unit admission	42 (77.8)	30 (90.9)	0.12
Days in intensive care unit	1.0 (1.0-3.0)	2.0 (1.0-4.0)	0.43
Mechanical ventilation >24hr	10 (18.5)	5 (15.2)	0.69
Length of hospitalization	5.0 (4.0-8.0)	6.0 (5.0-11.0)	0.051
Maternal death	1 (1.9)	1 (3.0)	1.0

¹ 1:1 to 2:1 defined as a ratio of 0.8 to 2.2² Includes data through December 31, 2015

Data are presented as median (interquartile range) or n (%)