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Original Contribution

Point-of-care viscoelastic testing improves the outcome of pregnancies complicated by severe postpartum hemorrhage

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1. Introduction

Postpartum hemorrhage (PPH)—defined as an estimated blood loss >500 mL following vaginal delivery and >1000 mL following cesarean [1,2]—is the leading cause of maternal mortality worldwide accounting for 27% of all maternal deaths, [3,4] and is the foremost cause of direct obstetric death in developed countries [5,6]. It is also a major cause of maternal morbidity and intensive care unit (ICU) admissions [7,8]. The incidence of PPH is increasing [9,10]. This is especially true of severe PPH, defined as an estimated blood loss in excess of 1500 mL [11,12]. Standardized hospital protocols have been developed in an effort to optimize the management of PPH and reduce peripartum morbidity and mortality [13,14]. These protocols generally follow the principles of empiric resuscitation, sometimes referred to as 'damage control resuscitation' [15]. Such protocols, developed initially in trauma medicine, deemphasizes crystalloid infusion in favor of early transfusion of high volumes of fresh frozen plasma (FFP), packed red blood cells (PRBC), and platelets without adjusting blood product transfusions to the results of coagulation tests [16–18]. The objective of these standardized protocols is to minimize dilutional and consumptive coagulopathy and avoid delay in blood product replacement in the setting of ongoing blood loss [19,20]. However, empiric resuscitation is not universally accepted [21].

It has been suggested that blood product resuscitation should be individualized and adjusted according to the results of point-of-care viscoelastic testing (PCVT). This approach has been shown to decrease morbidity and mortality among cardiac, [22,23] liver transplant, [24] and trauma patients [25,26] experiencing severe bleeding. In Europe, PCVT has been used also for the management of obstetric hemorrhage with good success [27,28]. To improve the care of patients with severe PPH, a standardized massive transfusion protocol based on empiric resuscitation principles was implemented on Labor & Delivery at Yale-New Haven Hospital in New Haven, CT in January 2011. Two years later, this was replaced by an individualized PCVT-guided transfusion management approach. The primary objective of this study was to compare clinical outcomes (specifically volume of transfused blood product, rate of volume overload, and rate of ICU admission) and hospital costs

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for patients with severe PPH managed with and without the PCVT-guided transfusion protocol in an historical cohort. We hypothesized that utilization of bedside thromboelastometry can improve clinical outcomes and decrease the cost of care by supporting accurate and clinically effective decisions in transfusion management in patients with severe PPH.

2. Materials and methods

A retrospective cohort study was conducted of consecutive patients with severe PPH managed on Labor & Delivery at Yale-New Haven Hospital in New Haven, CT between January 1, 2011 and July 31, 2015. The first day of the study corresponded with the date on which the massive hemorrhage protocol was introduced. This was replaced by the PCVT-based protocol on May 1, 2014. This study was approved by the Institutional Review Board of the Human Investigation Committee of the Yale University Human Research Protection Program.

The PPH management team included faculty members from obstetric anesthesiology, maternal-fetal medicine, and hematology. Specialists in Gynecologic Oncology were involved in some cases. Severe PPH was diagnosed if the estimated blood loss was 1500 mL or greater [2]. Patients were divided into two cohorts: (i) those where blood product transfusion was guided by PCVT, and (ii) those for whom PCVT was not available, which included all patients prior to May 1, 2014 and those after that date if personnel trained in PCVT were not immediately available. PCVT training included a structured didactic course, a practical hands-on session, skills testing, and subsequent certification. Only personnel who completed the training and received a certificate were allowed to perform PCVT and interpret results. PCVT-certified personnel were subject to Clinical Laboratory Improvement Amendments (CLIA) regulations, [29] which cover quality control rules, proficiency testing, and competency assessment criteria, which all were supervised by representatives of the Department of Laboratory Medicine at Yale-New Haven Hospital. If no PCVT-certified provider was available, the patient received empiric resuscitation according to the conventional protocol.

Viscoelastic testing was performed using a ROTEM *delta* device (Tem Innovations GmbH, Munich, Germany) in accordance with the recommendations of the manufacturer and interpreted by a trained anesthesiologist [30]. This training included didactics and practicum based on the PCVT protocol approved by the U.S. Food and Drug Administration, followed by a mandatory competency test [31,32]. Clinicians performed three separate analyses to assess the status of the patient's hemostatic cascade in the whole blood sample in real time, including: (i) clotting time and clot amplitude at a specific time after activation with tissue factor (EXTEM); (ii) an intrinsically activated test using ellagic acid (INTEM); and (iii) platelet inhibition with cytochalasin D (FIBTEM). Analysis was completed within 5 to 10 min of blood collection in all instances. All tests were performed at the bedside on Labor & Delivery at Yale-New Haven Hospital.

PCVT data are presented on a chart known as a TEMogram (Figs. 1 and 2). The TEMogram provides a graphic and digital representation of the blood clot that is formed after mixing the patient's whole blood with the prescribed reagent solutions and gently rotating the mixture. The clot movement pattern depiction on the TEMogram is generated by special sensors that reflect changes in the viscoelastic properties of the blood during rotation. The following key parameters were routinely analyzed:

(1) Clotting time (CT), which refers to the time elapsed from the beginning of the test until the beginning of clot formation. CT prolongation suggests a deficiency of one or more coagulation factors. CT prolongation only in EXTEM suggests a deficiency in coagulation factors in the extrinsic pathway (due, for example, to the effects of warfarin). CT prolongation only in INTEM is seen most commonly in patients receiving heparin or low-molecular weight heparin; a shortening of the CT in the HEPTEM assay confirms this effect.

(2) Clot formation time (CFT) refers to the time measured from the end of the CT interval until a 20 mm amplitude is reached on the TEMogram. Alpha angle describes the tangent at the 2 mm amplitude point. Both CFT and alpha angle reflect the speed of clot development. Prolonged CFT and/or low alpha angle are most often caused by one or more of the following conditions: thrombocytopenia, platelet dysfunction, hypofibrinogenemia, or dysfunctional fibrin polymerization.

(3) Maximum amplitude of the graph is measured either as an absolute parameter independent of time (maximum clot firmness [MCF]) or at a specific point in time after starting the test (e.g., A5 refers to maximum amplitude at 5 min, A10 refers to maximum amplitude at 10 min, etc.). This measurement reflects the functionality (strength) of the clot. As with CFT and alpha angle, a decrease in the maximum amplitude suggests one or more of the following conditions: thrombocytopenia, platelet dysfunction, hypofibrinogenemia, or dysfunctional fibrin polymerization.

(4) Maximum lysis (ML) refers to the percentage of lost firmness of the clot at a given point in time. It reflects a percentage of remaining clot firmness when compared with MCF at 30 min (LI30), 45 min (LI45), or 60 min (LI60). An abnormally high ML index suggests the presence of hyperfibrinolysis and is an indicator that antifibrinolytic therapy may be required.

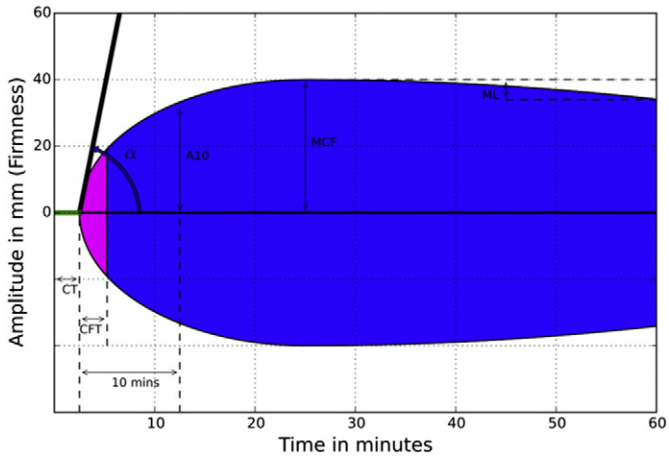

Fig. 1. Diagrammatic Representation of a TEMogram. CT, clotting time; CTF, clot formation time; A10, amplitude at 10 min; MCF, maximum clot firmness; ML, maximum lysis of the clot.

Accurate interpretation of the TEMogram was a critical component of the decision making process, helping to guide blood product transfusion management in patients with severe PPH. Specifically, we used CT, CFT, alpha angle, MCF, and ML to guide blood products transfusion. The following parameters were considered normal for patients in the third trimester of pregnancy: (i) EXTEM: CT 51–63 s, CFT 70–78 s, and MCF 66–71 mm; (ii) INTEM: CT 131–168 s, CFT 58–66 s, and MCF 64–68 mm; and (iii) FIBTEM: CT 50–64 s and MCF 19–22 mm. [33,34] When the amplitude in the FIBTEM assay was <5 mm at 5 min (A5) or <6 mm at 10 min (A10), we administered 5 to 15 units of cryoprecipitate. The goal of the cryoprecipitate administration was to achieve an A10 of 8 mm for patients with surgically-controlled hemorrhage and 10 mm for patients with ongoing hemorrhage. We repeated the test at the end of the cryoprecipitate transfusion and every 20 to 60 min thereafter (depending on the patient's condition) until the bleeding was controlled. If the FIBTEM results were normal, but the CFT and alpha angle demonstrated hypocoagulation accompanied by a

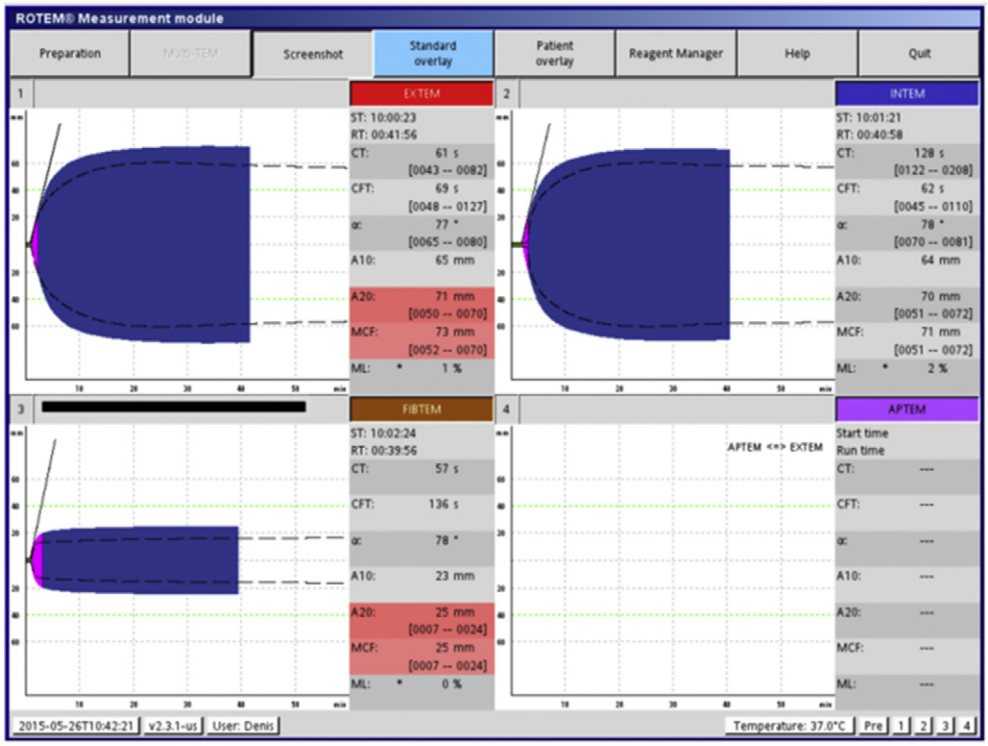

Fig. 2. A representative TEMogram of a healthy primigravida at term. The black dotted line represents normal results. Higher-than-normal amplitude of the EXTEM and FIBTEM graphs (A20 and MCF) are evident. This is a normal finding at term given that pregnancy is a hypercoagulable state.

decrease in EXTEM MCF to <45 mm, we administered one bag (5 units) of platelet concentrate, followed by repeat testing. If isolated CT prolongation was noticed in EXTEM and INTEM assays (EXTEM CT > 80 s), we administered 2 units of FFP, followed by repeat testing. Packed red blood cell transfusions were provided as needed in all the cases to maintain the hematocrit above 21%.

Demographic and clinical outcome data were abstracted from the medical records. This included the types and volume of blood products administered, the types and volume of non-blood product fluids administered (crystalloid, hetastarch, albumin), estimated blood loss, hematocrit on postoperative day 1, whether ICU admission was needed, and total number of days of hospitalization. The actual (not estimated) direct cost, indirect cost, and total cost of hospitalization were calculated for each patient using a database developed by The Joint Data Analytics Team at Yale-New Haven Hospital. Direct cost refers to any expense that was directly attributed to patient care (such as the cost of medications, blood products, bed occupancy, and nursing care); indirect cost refers to any expense that cannot be directly assigned to the patient care (including facility fees and overhead). To avoid the confounding effect of prolonged antepartum hospitalization (due, for example, to preterm premature rupture of membranes) on the cost data, only patients who delivered within 24 h of admission were included in the cost analysis.

Categorical, non-normal continuous, and normally distributed data are presented as number (%), median (interquartile range: 25th–75th percentile), and mean (SD), respectively. Data between PCVT and non-PCVT group were analyzed using Fisher's exact test, nonparametric Wilcoxon rank sum test, or Student *t*-test, as appropriate. Statistical analyses were performed in SAS, version 9.4 (Cary, NC). A two-sided *P*-value of <0.05 was regarded as statistically significant.

3. Results

A total of 20,349 patients delivered on Labor & Delivery at Yale-New Haven Hospital during the study period. This included 13,641 vaginal births and 6708 cesarean deliveries. Of these, 86 patients developed severe PPH, which represented 0.4% of all deliveries. Sixty eight (79.1%) occurred at cesarean and 18 (20.9%) after vaginal delivery, giving an overall prevalence of severe PPH of 1.0% after cesarean and 0.1% after vaginal birth. Among the 86 patients with severe PPH, 28 (32.6%) were managed with PCVT and 58 (67.4%) without PCVT. The cost of hospitalization was calculated for the 54 patients who delivered within 24 h of admission (17 in the PCVT group and 37 in the non-PCVT group).

The baseline characteristics of the two study populations are summarized in Table 1. There were no statistically significant differences between the study groups in terms of maternal age, race/ethnicity, obstetric history (gravidity, parity, gestational age, percentage of singletons), mode of delivery (vaginal or cesarean), incidence of emergent intervention, or antepartum health status (including body mass index, American Society of Anesthesiologists [ASA] functional classification, and preoperative hematocrit). There were no statistically significant differences between the two groups in terms of the underlying etiology of the PPH. Uterine atony and placenta accreta together accounted for >70% of PPH cases. The level of training of the attending anesthesiologists and obstetricians was not different between the groups. Gynecologic Oncologists were more commonly involved in the surgical management of cases managed with non-PCVT compared with PCVT. General anesthesia was provided more frequently in the non-PCVT compared with PCVT group (55.2% [32/58] vs 28.6% [8/28]; $P = 0.04$).

The comparisons of postoperative outcomes are presented in Table 2. There was no statistically significant difference between the PCVT and non-PCVT groups in regards to the amount of crystalloids, colloids, albumin, and cryoprecipitate administered. However, patients in the PCVT group received significantly fewer transfusions of PRBCs ($P < 0.0001$), FFP ($P < 0.0001$), and platelets ($P < 0.0001$). Estimated blood loss was also significantly lower in the PCVT group (median [IQR] 2000 [1600–2500] vs 3000 [2000–4000] mL, $P < 0.001$). Similarly, the incidence of puerperal hysterectomy (25% [7/28] vs 53.5% [31/58], $P = 0.013$) and postoperative ICU admission (3.6% [1/28] vs 43.1% [25/58], $P < 0.001$) were significantly lower in the PCVT group. Indications for ICU admission included mechanical ventilation or congestive heart

Table 1
Demographic and clinical characteristics of the study population[a].

	PCVT ($n = 28$)	Non-PCVT ($n = 58$)	*P*-value
Maternal age (years)	35.0 ± 6.2	33.3 ± 6.6	0.27
Gravidity	3 (2.5–5)	3 (2–4)	0.41
Parity	1 (0.5–2)	1.5 (0–2)	0.63
Race/ethnicity			0.56
- White	12 (42.9%)	32 (55.2%)	
- Hispanic	9 (32.1%)	12 (20.7%)	
- Black	4 (14.3%)	10 (17.2%)	
- Asian	3 (10.7%)	4 (6.9%)	
Gestational age (weeks)	37.0 (35.5–38.9)	36.4 (32.0–37.5)	0.38
Singleton (%)	26 (92.9%)	48 (82.8%)	0.32
Body mass index (kg/m^2)	31.1 ± 5.9	32.4 ± 8.0	0.43
Hematocrit prior to delivery (%)	34.7 (31.5–36.5)	34.3 (31.8–37.3)	0.69
Mode of delivery			
- Vaginal	5 (17.9%)	11 (19.0%)	0.90
- Cesarean	23 (82.1%)	47 (81.0%)	
Emergent delivery, yes	11 (39.3%)	25 (43.1%)	0.74
Primary cause of PPH			0.18
- Uterine atony	10(35.7%)	16 (27.6%)	
- Placenta accreta	10 (35.7%)	24(41.4%)	
- Retained placenta	2 (7.1%)	9(15.5%)	
- Placental abruption	2 (7.1%)	0 (0%)	
- Uterine rupture	0 (0%)	4 (6.9%)	
- Others	4(14.3%)	5(8.6%)	
ASA classification	3 (2–3)	3 (2–3)	0.85
Initial mode of anesthesia			0.04
- Spinal	15 (53.6%)	16 (27.6%)	
- Epidural	5 (17.9%)	10 (17.2%)	
- General endotracheal	8 (28.6%)	32 (55.2%)	
Experience of Attending Anesthesiologist			0.21
- <5 years	1 (3.6%)	7 (12.1%)	
- 5 years or more	27 (96.4%)	51 (87.9%)	
Experience of attending obstetrician			0.15
- <5 years	8 (28.6%)	26 (44.8%)	
- 5 years or more	20 (71.4%)	32 (55.2%)	
Presence of gyn/oncologist	5 (17.9%)	35 (60.3%)	<0.001

[a] Data are expressed as n (%), mean ± SD, or median (interquartile range).

Table 2
Postoperative outcomes of the study population[a].

	PCVT ($n = 28$)	Non-PCVT ($n = 58$)	*P*-value
Hematocrit on postoperative day 1 (%)	24.7 (23.0–26.6)	27.8 (24.5–30.0)	0.004
Hysterectomy, yes	7 (25.0%)	31 (53.5%)	0.013
Estimated blood loss (mL)	2000 (1600–2500)	3000 (2000–4000)	<0.001
Crystalloids (mL)	3500 (3100–4500)	3500 (3000–4100)	0.88
Hextend (mL)	0 (0–250)	0 (0–500)	0.45
Red blood cells (units)			<0.001
- 0	11 (39.3%)	3 (5.2%)	
- 1	7 (25.0%)	3 (5.2%)	
- ≥2	10 (35.7%)	52 (89.6%)	
Fresh frozen plasma (units)			<0.001
- 0	25 (89.3%)	16 (27.6%)	
- ≥1	3 (10.7%)	42 (72.4%)	
Albumin (units)			0.09
- 0	28 (100%)	51 (87.9%)	
- 500 to 1000	0 (0%)	7 (12.1%)	
Cryoprecipitate (units)			0.78
- 0	22 (78.6%)	47 (81.0%)	
- ≥5	6 (21.4%)	11 (19%)	
Platelets (units)			<0.001
- 0	28 (100%)	32 (55.2%)	
- ≥5	0 (0%)	26 (44.8%)	
Length of hospitalization after delivery (days)	4 (3–4)	5 (4–6)	<0.001
ICU admission	1 (3.6%)	25 (43.1%)	<0.001

[a] Data are expressed as n (%), median (interquartile range).

failure. Length of postpartum hospitalization was significantly shorter in the PCVT group (4 [3, 4] vs 5 [4–6] days, $P < 0.001$). Despite having similar preoperative hematocrit measurements (34.7 [31.5–36.5] vs 34.3 [31.8–37.3] %, median [IQR], $P = 0.69$), patients in the PCVT group had significantly lower hematocrit levels on postoperative day 1 (24.7 [23.0–26.6] vs 27.8 [24.5–30.0] %, median [IQR], $P = 0.004$).

The comparisons of the direct, indirect, and total cost of hospitalization between the two groups of patients who gave birth within 24 h of admission are presented in Table 3. Cost of hospitalization was significantly lower for the patients in the PCVT group.

4. Discussion

A retrospective analysis of our first 2 years of experience with the use of PCVT demonstrates that routine bedside thromboelastometry for intraoperative assessment of hemostasis can serve as a foundation for responsible clinically decision making around blood product transfusion management in patients with severe PPH. Point-of-care viscoelastic testing revealed that the expected changes in hemostasis among patients with severe PPH based on the traditional teaching of dilutional and consumptive coagulopathy were often very different from measured changes (for example, see Fig. 3). The ability to demonstrate the absence of clinically significant coagulopathy in real-time during surgery allowed us to avoid unnecessary blood product transfusion. Not only did patients managed with PCVT-based goal-directed therapy require less blood product replacement, but this strategy was also associated with improved patient outcomes and reduced cost of care.

Similar observations have been reported for PCVT-based resuscitation protocols in non-obstetric surgeries in patients at high risk for significant blood loss [22–26]. Initial reports of the effect of replacing standard fixed-ratio transfusion of large-volume FFP with PCVT-guided transfusion in thousands of cardiac patients revealed a significant decrease in the volume of transfusion of pRBCs and FFP [35,36]. Similar to our findings, these reports also documented reduced length of ICU admission and cost of hospitalization. A later randomized controlled prospective clinical trial (RCT) in bleeding adult cardiovascular patients confirmed that the introduction of a PCVT-based algorithm resulted not only in significant reductions in the volume of transfused blood products, but also shortened mechanical ventilation and ICU admission times [22]. This RCT also documented reduced rates of adverse events and 6-month mortality as well as lower hospitalization costs [22]. Such findings have been reported also in a pediatric population. In a subsequent RCT including pediatric cardiac patients, implementation of a FIBTEM/EXTEM-based transfusion protocol resulted in decreased intraoperative blood loss and need for RBC transfusions as well as a shortened ICU stay [23].

Data on the utilization of PCVT for patients with severe hemorrhage have also been subjected to systematic analysis. A recent Cochrane review evaluated 17 RCTs involving 1493 patients [37]. The conclusion of the authors was that implementation of a PCVT-based goal-directed transfusion therapy may result not only in decreased volume of transfused blood products and reduced morbidity, but may also decrease mortality. The authors noted, however, that the level of evidence remains limited. Most of the RCTs involved cardiovascular patients, although PCVT has been shown to be effective in other types of surgeries where massive hemorrhage occurs frequently, such as liver transplantation [24]. A large retrospective analysis of the application of PCVT-guided transfusion therapy during 1105 liver transplant surgeries demonstrated significant reductions in transfusion of RBCs and FFP [38].

The FIBTEM assay of rotational thromboelastography might be especially useful among obstetric patients due to its ability to quickly (within minutes) identify significant fibrinogen deficiency, which can have

Table 3
Cost of hospitalization for patients with severe postpartum hemorrhage managed with or without PCVT[a].

	PCVT ($n = 17$)	Non-PCVT ($n = 37$)	Total ($n = 54$)	*P*-value
Indirect	$5746.65 ($2458.16)	$8585.65 ($4412.28)	$7691.89 ($4101.13)	0.004
Direct	$6056.29 ($2519.45)	$11,833.43 ($7182.55)	$10,014.70 ($6655.29)	<0.001
Total	$11,802.94 ($4936.91)	$20,419.08 ($11,550.47)	$17,706.59 ($10,690.84)	<0.001

[a] Data are expressed as mean (SD).

substantial prognostic value and possible therapeutic value for parturients with PPH. Charbit et al. [39] demonstrated that a fibrinogen value of <2 g/L had a positive predictive value of 100% for severe PPH, whereas a fibrinogen value of >4 g/L had a negative predictive value for severe PPH of 79%. Hypofibrinogenemia in pregnant patients can be rapidly detected by FIBTEM assay. In a large prospective observational study, Huissoud et al. [40] demonstrated that FIBTEM amplitudes of 5 mm or less at 5 min and 6 mm at 15 min had 100% sensitivity and 85% and 88% specificity, respectively, in detecting a circulating fibrinogen concentration of <1.5 g/L among patients with obstetric hemorrhage. The authors concluded that PCVT might be useful in guiding transfusion of blood products, specifically fibrinogen, during PPH. This conclusion was confirmed in a recent RCT [41]. In another report, investigators observed a reduction in volume of transfused blood products, pulmonary edema, and ICU admission among patients with obstetric hemorrhage during the 5 years after a FIBTEM-guided transfusion strategy was implemented; the rate of hysterectomy was also reduced, but the difference did not reach statistical significance [42,43]. An additional prospective observational study showed benefits of PCVT-based management of hemorrhage in bleeding obstetric patients in terms of administration of fibrinogen concentrate, decreased volume of FFP transfusion, decreased platelet transfusions, and reduced rates of transfusion-related volume overload [43]. However, in contrast to our observations, there were no significant differences in the rate of ICU admission or postpartum hysterectomy in this study.

This is the first report on the use of a PCVT-based algorithm among parturients in the United States. We have shown that patients in the PCVT cohort received significantly lower volumes of transfused blood products, underwent fewer hysterectomies, were less frequently admitted to the ICU, and had shorter hospitalizations as compared with those managed using the more traditional empiric protocol. Not surprisingly, direct hospitalization cost was also significantly reduced in these patients.

Compared to other PCVT studies, [33,34] we used a lower amplitude of FIBTEM (more prominent hypofibrinogenemia) as an indication for treatment of fibrinogen deficiency. We were also less aggressive in

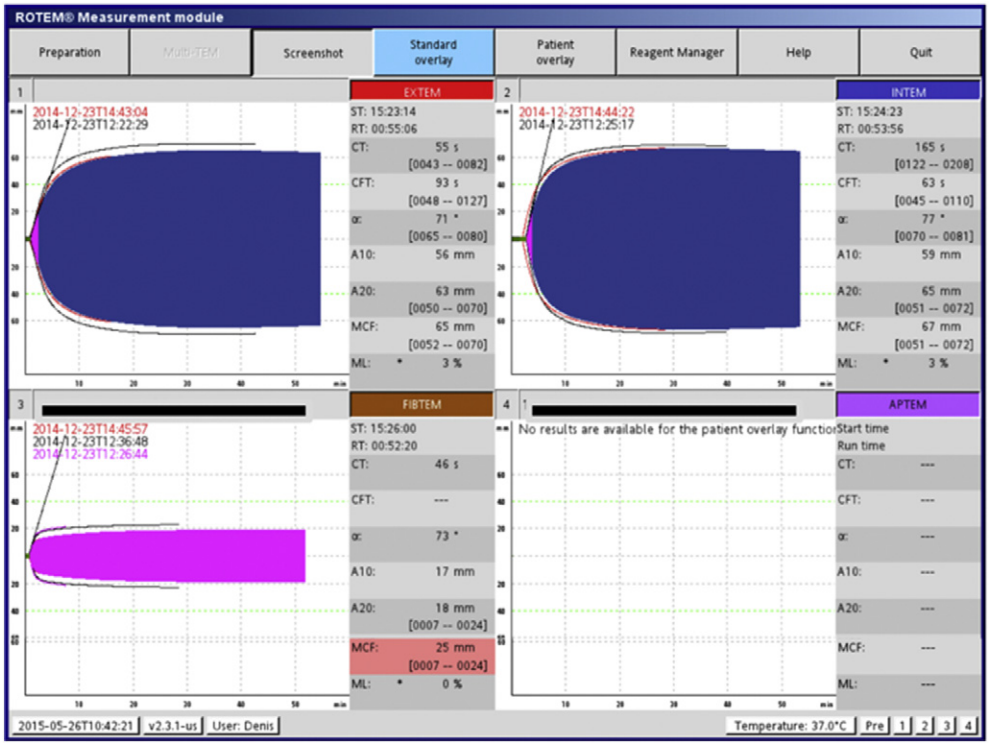

Fig. 3. A TEMogram from a patient experiencing massive intrapartum obstetric hemorrhage. A 32-year-old gravida 3, para 2 was admitted at 37 weeks of gestation for repeat cesarean delivery and puerperal hysterectomy. Her past medical history is remarkable for morbid obesity, two prior cesarean deliveries, and suspected placenta accreta (possible percreta) on imaging. Her preoperative hemoglobin was 9.7 g/dL, hematocrit 28.2%, and platelet count 270,000/μL; prothrombin time/International Normalized Ratio and partial thromboplastin time were normal, and fibrinogen was 499 mg/dL. Placenta percreta was confirmed at the time of surgery. Puerperal hysterectomy was performed with an estimated blood loss of 3.5 L. This patient received 5 L of crystalloids and 1 unit of PRBC (for hematocrit of 19%) during 3-hour-surgery. No FFP, cryoprecipitate or platelets were given. There were no signs of dilutional/consumptive coagulopathy. Her postoperative hematocrit was 22%. The black line represents the preoperative TEMogram (hematocrit 28.2%), red line is the TEMogram after 2 h of surgery (hematocrit 19%), and colored fields are the postoperative TEMogram (hematocrit 22%). Minimal (not clinically significant) changes in the results of rotational thromboelastography allowed the surgical team to proceed without further blood product transfusions.

correcting fibrinogen deficiency compared to European studies [43]. Nonetheless, the clinical outcomes in the PCVT cohort were not inferior to the results of other studies. One of the factors that may contribute to these results was our use of cryoprecipitate rather than fibrinogen concentrate to correct hypofibrinogenemia. Fibrinogen concentrate was not available at our institution for the treatment of patients with hemorrhage-induced hypofibrinogenemia, and cryoprecipitate has been used effectively to correct hypofibrinogenemia by other investigators [44,45]. Based on these findings, we suggest that a more conservative approach to the treatment of hypofibrinogenemia may be acceptable. The cost-effectiveness of fibrinogen concentrate and cryoprecipitate for the treatment of patients with severe obstetric hemorrhage needs further exploration.

Hematocrit threshold for PRBC transfusion has not been systematically studied in patients with severe PPH. In this study, patients in the PCVT group received fewer units of PRBC and had significantly lower hematocrit on the first postpartum day, yet had shorter postpartum hospitalization. Future studies will be needed to investigate the effects of more restrictive PRBC transfusion practice on the clinical outcome among patients with severe PPH.

Limitations of this report include the retrospective nature of the study design as well as the relatively small number of patients. In addition, this was a single-institution study and the care provided was dependent in large part on the availability of PCVT-certified providers. In this study, interpretation of the PCVT and decision making around transfusion was performed by a single anesthesiologist. Involvement of additional providers in this process may have altered the decisions made regarding transfusion. In addition, providers responsible for reporting estimating blood loss were not blinded to the use of PVCT, which may been a source of bias as regards this specific indicator. It is possible that the observed improvements in outcome metrics may be due to confounding factors. For example, while the data on the differences in blood products usage is robust, the study was not sufficiently powered to determine whether the observed reduction in the number of hysterectomies was attributable to chance or represented a major benefit arising from more effective correction of coagulopathy. Another caveat is that patients in the PCVT cohort were less likely to receive general anesthesia. Potential uterine relaxation from inhalational anesthetic agents during general anesthesia might have negatively affected the magnitude of peripartum hemorrhage. Other potential confounders include differences in the qualifications or experience of the anesthesia providers that completed the PCVT training versus those who did not. While the ROTEM device was readily available at all times after its introduction in May 2014 and was used routinely in unplanned/emergency cases, hospital staffing and other resources could have varied at night or on the weekend. An additional source of bias when comparing historical data to more current practice may have been other associated improvements in care or personnel. Despite these limitations, we believe that these data suggest a benefit to the use of PCVT over the more traditional empiric protocols to aid in rapid diagnosis and goal-directed correction of specific components of the hemostatic cascade among patients experiencing severe PPH. Additional large well-designed prospective RCTs are needed to confirm these observations and control for potential confounders before a change in practice can be universally recommended.

5. Conclusions

PCVT-based algorithms facilitate rapid (within minutes) and precise diagnosis of coagulopathy thereby allowing for prompt correction of deficiencies of specific components of the coagulation cascade among patients experiencing severe obstetric hemorrhage. This report suggests that such PCVT-based protocols confer significant benefit over the more traditional empiric protocols in terms of reducing the need for PRBC, FFP, and platelet concentrate transfusions in the setting of severe PPH. This more rapid and individualized approach to the management of coagulopathy may also result in less intraoperative blood loss, lower rates of puerperal hysterectomy and postoperative ICU admissions, as well as a reduction in the length of hospital stay and overall cost of hospitalization.

References

[1] Dahlke JD, Mendez-Figueroa H, Maggio L, et al. Prevention and management of postpartum hemorrhage: a comparison of 4 national guidelines. Am J Obstet Gynecol 2015;213 [76.e1-10].
[2] Rath WH. Postpartum hemorrhage—update on problems of definitions and diagnosis. Acta Obstet Gynecol Scand 2011;90:421–8.
[3] Clark SL, Belfort MA, Dildy GA, Herbst MA, Meyers JA, Hankins GD. Maternal death in the 21st century: causes, prevention, and relationship to cesarean delivery. Am J Obstet Gynecol 2008;199 [36.e1-5].
[4] Abdul-Kadir R, McLintock C, Ducloy AS, et al. Evaluation and management of postpartum hemorrhage: consensus from an international expert panel. Transfusion 2014;54:1756–68.
[5] Say L, Chou D, Gemmill A, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health 2014;2:e323-3.
[6] Cristina Rossi A, Mullin P. The etiology of maternal mortality in developed countries: a systematic review of literature. Arch Gynecol Obstet 2012;285:1499–503.
[7] Callaghan WM, MacKay AP, Berg CJ. Identification of severe maternal morbidity during delivery hospitalizations, United States, 1991–2003. Am J Obstet Gynecol 2008;199:133-e1–8.
[8] Liu S, Joseph KS, Bartholomew S, et al. Temporal trends and regional variations in severe maternal morbidity in Canada, 2003 to 2007. J Obstet Gynaecol Can 2010;32:847–55.
[9] Callaghan WM, Kuklina EV, Berg CJ. Trends in postpartum hemorrhage: United States, 1994–2006. Am J Obstet Gynecol 2010;202 [353.e1-6].
[10] Knight M, Callaghan WM, Berg C, et al. Trends in postpartum hemorrhage in high resource countries: a review and recommendations from the International Postpartum Hemorrhage Collaborative Group. BMC Pregnancy Childbirth 2009;9:55.
[11] McLintock C, James AH. Obstetric hemorrhage. J Thromb Haemost 2011;9:1441–51.
[12] Einerson BD, Miller ES, Grobman WA. Does a postpartum hemorrhage patient safety program result in sustained changes in management and outcomes? Am J Obstet Gynecol 2015;212:e140-.
[13] The Joint Commission. Sentinel Event Alert, Issue 44: Preventing Maternal Death. https://www.jointcommission.org/sentinel_event_alert_issue_44_preventing_maternal_death/; January 26, 2010, Accessed date: 25 January 2017.
[14] Bingham D, Melsop K, Main E. CMQCC Obstetric Hemorrhage Hospital Level Implementation Guide. The California Maternal Quality Care Collaborative (CMQCC). Palo Alto, CA: Stanford University; 2010. https://www.cmqcc.org/resource/1489/, Accessed date: 25 January 2017.
[15] Leduc D, Senikas V, Lalonde AB, et al. Active management of the third stage of labour: prevention and treatment of postpartum hemorrhage. J Obstet Gynaecol Can 2009;31:980–93.
[16] Holcomb JB, Jenkins D, Rhee P, et al. Damage control resuscitation: directly addressing the early coagulopathy of trauma. J Trauma 2007;62:307–10.
[17] American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 76: postpartum hemorrhage. Obstet Gynecol 2006;108:1039–47.
[18] Antony KM, Dildy 3rd GA. Postpartum hemorrhage: the role of the maternal-fetal medicine specialist in enhancing quality and patient safety. Semin Perinatol 2013;37:246–56.
[19] Borgman MA, Spinella PC, Perkins JG, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. J Trauma 2007;63:805–13.
[20] Holcomb JB, Wade CE, Michalek JE, et al. Increased plasma and platelet to red blood cell ratios improves outcome in 466 massively transfused civilian trauma patients. Ann Surg 2008;248:447–58.
[21] Dzik WH, Blajchman MA, Fergusson D, et al. Clinical review: Canadian National Advisory Committee on blood and blood products—massive transfusion consensus conference 2011: report of the panel. Crit Care 2011;15:242.
[22] Weber CF, Görlinger K, Meininger D, et al. Point-of-care testing: a prospective, randomized clinical trial of efficacy in coagulopathic cardiac surgery patients. Anesthesiology 2012;117:531–47.
[23] Nakayama Y, Nakajima Y, Tanaka KA, et al. Thromboelastometry-guided intraoperative haemostatic management reduces bleeding and red cell transfusion after paediatric cardiac surgery. Br J Anaesth 2015;114:91–102.
[24] Song J-G, Jeong SM, Jun IG, Lee HM, Hwang GS. Five-minute parameter of thromboelastometry is sufficient to detect thrombocytopenia and hypofibrinogenaemia in patients undergoing liver transplantation. Br J Anaesth 2014;112:290–7.
[25] Johansson PI, Stensballe J, Ostrowski SR. Current management of massive hemorrhage in trauma. Scand J Trauma Resusc Emerg Med 2012;20:47.
[26] Veigas PV, Callum J, Rizoli S, Nascimento B, da Luz LT. A systematic review on the rotational thromboelastometry (ROTEM®) values for the diagnosis of coagulopathy, prediction and guidance of blood transfusion and prediction of mortality in trauma patients. Scand J Trauma Resusc Emerg Med 2016;24:114.
[27] Solomon C, Collis RE, Collins PW. Haemostatic monitoring during postpartum haemorrhage and implications for management. Br J Anaesth 2012;109:851–63.
[28] de Lange NM, Lancé MD, de Groot R, Beckers EA, Henskens YM, Scheepers HC. Obstetric hemorrhage and coagulation: an update. Thromboelastography,

thromboelastometry, and conventional coagulation tests in the diagnosis and prediction of postpartum hemorrhage. Obstet Gynecol Surv 2012;67:426–35.
[29] Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments (CLIA); 2017 https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/index.html?redirect=/CLIA [accessed 25.01.17].
[30] Haas T, Spielmann N, Mauch J, et al. Comparison of thromboelastometry (ROTEM®) with standard plasmatic coagulation testing in paediatric surgery. Br J Anaesth 2012; 108:36–41.
[31] Schöchl H, Cotton B, Inaba K, et al. FIBTEM provides early prediction of massive transfusion in trauma. Crit Care 2011;15:R265.
[32] David JS, Durand M, Levrat A, et al. Correlation between laboratory coagulation testing and thromboelastometry is modified during management of trauma patients. J Trauma Acute Care Surg 2016;81:319–27.
[33] Huissoud C, Carrabin N, Benchaib M, et al. Coagulation assessment by rotation thromboelastometry in normal pregnancy. Thromb Haemost 2009;101:755–61.
[34] de Lange NM, van Rheenen-Flach LE, Lancé MD, et al. Peripartum reference ranges for ROTEM® thromboelastometry. Br J Anaesth 2014;112:852–9.
[35] Trevisan D, Zavatti L, Gabbieri D, Pedulli M, Giordano G, Meli M. Point-of-care-based protocol with first-line therapy with coagulation factor concentrates is associated with decrease allogenic blood transfusion and costs in cardiovascular surgery: an Italian single-center experience. Minerva Anestesiol 2016;82:1077–88.
[36] Görlinger K, Dirkmann D, Hanke AA. Potential value of transfusion protocols in cardiac surgery. Curr Opin Anaesthesiol 2013;26:230–43.
[37] Wikkelsø A, Wetterslev J, Møller AM, Afshari A. Thromboelastography (TEG) or thromboelastometry (ROTEM) to monitor haemostatic treatment versus usual care in adults or children with bleeding. Cochrane Database Syst Rev 2016; 8:CD007871.
[38] Goerlinger K, Dirkmann D, Müller-Beissenhirtz H, Paul A, Hartmann M, Saner F. Thromboelastometry-based perioperative coagulation management in visceral surgery and liver transplantation: experience of 10 years and 1105 LTX [abstract #O-56]. Liver Transpl 2010;16:S38.
[39] Charbit B, Mandelbrot L, Samain E, et al. The decrease of fibrinogen is an early predictor of the severity of postpartum hemorrhage. J Thromb Haemost 2007;5:266–73.
[40] Huissoud C, Carrabin N, Audibert F, et al. Bedside assessment of fibrinogen level in postpartum haemorrhage by thromboelastometry. BJOG 2009;116:1097–102.
[41] Wikkelsø AJ, Edwards HM, Afshari A, et al, FIB-PPH trial group. Pre-emptive treatment with fibrinogen concentrate for postpartum haemorrhage: randomized controlled trial. Br J Anaesth 2015;114:623–33.
[42] Collis RE, Collins PW. Haemostatic management of obstetric haemorrhage. Anaesthesia 2015;70:S78–86 [e27-8].
[43] Mallaiah S, Barclay P, Harrod I, Chevannes C, Bhalla A. Introduction of an algorithm for ROTEM-guided fibrinogen concentrate administration in major obstetric haemorrhage. Anaesthesia 2015;70:166–75.
[44] Schöchl H, Nienaber U, Hofer G, et al. Research goal-directed coagulation management of major trauma patients using thromboelastometry (ROTEM)-guided administration of fibrinogen concentrate and prothrombin complex concentrate. Crit Care 2010;14:R55.
[45] Ahmed S, Harrity C, Johnson S, et al. The efficacy of fibrinogen concentrate compared with cryoprecipitate in major obstetric haemorrhage—an observational study. Transfus Med 2012;22:344–9.