Introduction of a Novel System for Quantitating Blood Loss After Vaginal Delivery: A Retrospective Interrupted Time Series Analysis (Paper 1); Training for the Surgical Management of Postpartum Hemorrhage: A Four-State Survey of Resident Physicians in Mexico (Paper 2)

Paper 1: Introduction of a Novel System for Quantitating Blood Loss After Vaginal Delivery: A Retrospective Interrupted Time Series Analysis

Paper 2: Training for the Surgical Management of Postpartum Hemorrhage: A Four-State Survey of Resident Physicians in Mexico

by

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Chapter 1

Overview of the thesis papers

Postpartum hemorrhage (PPH) is a leading cause of severe maternal morbidity and preventable maternal mortality worldwide. Moreover, the rate of PPH is increasing in high-income countries including the United States (US). In the present document, we present the results of two patient-oriented research projects related to the measurement of cumulative blood loss and medical education on PPH protocols; both subjects are highlighted by the National Partnership for Maternal Safety (NPMS) obstetric hemorrhage bundle recommendations. The NPMS is a multidisciplinary task force endorsed by all obstetric subspecialty societies in the US.

More timely detection of abnormal bleeding prompts earlier recognition and subsequent treatment of PPH. Therefore, systems that promptly identify PPH after delivery are warranted since there is an underestimation of blood loss (up to 50%) using visual estimation methods. In the *first* paper, we compared the PPH incidence and related outcomes before and after the introduction of a novel device for quantitation of blood loss (after vaginal delivery) that combines volumetric and gravimetric measurements.

Approximately 15% of patients with PPH require surgical intervention; therefore proficiency in surgical techniques among all birth attendants is critically essential. The *second* paper is related to the obstetrics and gynecology (OBGYN) residents overall knowledge and proficiency in performing the most common surgical techniques to manage PPH. In addition to the primary aim mentioned above, we also describe education resources, barriers for training and the decision-making process for the surgical management of PPH. We collected this information via an electronic survey sent to the OBGYN residents of four public hospitals in Mexico.

Chapter 2

Abstract - paper 1

Introduction of a Novel System for Quantitating Blood Loss After Vaginal Delivery: A Retrospective Interrupted Time Series Analysis

Background

Postpartum hemorrhage (PPH) is the most common preventable cause of maternal mortality worldwide. Mechanisms for enhanced detection are needed. While volumetric and gravimetric blood loss measurement techniques have individually been shown to increase the incidence of PPH detection compared to visual estimation of blood loss (vBL), a combination of these quantitative methods has not been evaluated. Therefore, the primary aim of this study was to compare the incidence of immediate PPH detection in vaginal deliveries (VD) before and after implementation of a device for quantitation of blood loss that combines volumetric and gravimetric measurements (tBL).

Methods

After IRB approval, patients who had a vaginal or cesarean delivery (CD) at our institution between October 4 - December 31, 2017 and February 1 - April 30, 2018 were identified. A tBL device was implemented for VD on January 1, 2018. Average weekly incidence of PPH (the primary outcome, defined as immediate post-delivery blood loss $\geq$ 500 mL for VD and $\geq$ 1,000 mL for CD) was compared by delivery type before and after device implementation using segmented quasi-Poisson regression weighted by propensity score odds. Secondary outcomes were blood loss $\geq$ 1,000 mL, overall blood loss, transfusion requirement, secondary uterotonic use, vasopressor administration, surgical procedures, and a composite outcome of interventions related to PPH management. A post-hoc subgroup analysis included comparisons of nadir hematocrit,

hematocrit reduction ≥ 10%, and difference between estimated (vBL or tBL) and calculated blood loss (cBL) between VD before and after introduction of the device.

Results

The weighted relative risk (wRR) of PPH post- vs. pre-implementation of the device was 2.21 (95% confidence interval [CI]: 1.33, 3.66; *p* 0.004) for VD (the treatment series) vs. 0.93 (95% CI: 0.56, 1.54; *p* 0.764) for CD (the control series). There was no evidence of a difference in secondary outcomes post- vs. pre-implementation of the device in VD. In the subgroup of patients who had post-delivery hematocrits measured, the mean difference between delivery blood loss and cBL was smaller in the tBL (mean ± SD: -237 ± 522 mL) vs. vBL group (-600 ± 596 mL; weighted difference in means (95% CI): 358 mL (3, 713); *p* 0.048).

Conclusions

In this interrupted time series analysis, the average weekly incidence of immediate PPH detection increased by over two-fold for VD (the intervention series) but remained constant for CD (the control series) after implementation of a novel device for quantitation of blood loss after VD.

Chapter 3

Abstract - paper 2

Training for the Surgical Management of Postpartum Hemorrhage: A Four-State Survey of Resident Physicians in Mexico

Background

Obstetrics and gynecology (OBGYN) residents in Mexico should be proficient in the surgical management of postpartum hemorrhage (PPH), but the ability of programs to provide this training is unknown.

Objective

The self-reported knowledge, education, and proficiency of common surgical techniques for the management of PPH among OBGYN residents was evaluated. Educational resources, perceived barriers to acquiring skills, and clinical decision-making were explored.

Methods

In July of 2018, an anonymous electronic survey was sent to 86 residents at four hospitals throughout Mexico. Surgical techniques queried included uterine tamponade (UT), uterine compression sutures (UCS), uterine devascularization (UD), hypogastric artery ligation (HAL), and gravid hysterectomy (HT). Participants answered case-based questions about a patient with PPH.

Results

The survey response rate was 59.3% (51/86). Seventy-nine percent of residents reported understanding the rationale and techniques for the surgical intervention of PPH. However, 43.9% reported limited ability to perform these procedures with autonomy. Eighty-six percent of residents reported exposure to these techniques while performing a rescue procedure during PPH, and 49%

reported learning these procedures while performing prophylactic techniques in patients without PPH. Only 25.5% had received simulation training. Lack of a training module for these skills in their curriculum was noted by 74.5%. The majority of the participants chose UCS, UD, HAL and HT as the first, second, third and fourth procedure to perform, respectively.

Conclusion

Most residents reported theoretical knowledge of surgical interventions for PPH, but their self-rated ability to independently perform such skills and a curriculum focused on PPH management was suboptimal.

Chapter 4

Paper 1

Introduction of a Novel System for Quantitating Blood Loss After Vaginal Delivery: A Retrospective Interrupted Time Series Analysis

4.1 Glossary of terms

ACOG = American College of Obstetricians and Gynecologists.

aPTT = Activated partial thromboplastin time.

AR[1] = A first-order autoregressive covariance structure.

BMI = Body mass index.

CBC = Complete blood count.

cBL = Calculated blood loss.

CD = Cesarean delivery.

CI = Confidence interval.

CSE = Combined spinal and epidural anesthesia.

g = Grams.

HCT = Hematocrit.

IQR = Interquartile range.

IRB = Institutional Review Board.

kg = Kilogram.

L&D = Labor and delivery.

m^2 = Square meter.

mL = Milliliters.

NPMS = National Partnership for Maternal Safety.

PPH = Postpartum hemorrhage.

PRBC = Packed red blood cell.

PT = prothrombin time.

SD = Standard deviation.

SE = Standard error.

STROBE = STrengthening the Reporting of OBservational studies in Epidemiology.

tBL = Quantitation of blood loss.

vBL = Visual estimation of blood loss.

VD = Vaginal delivery.

wDM = Weighted difference in means.

wRGM = Weighted ratio of geometric means.

wRR = Weighted relative risk.

4.2 Introduction

Postpartum hemorrhage (PPH) is the most common complication of childbirth and is the most preventable cause of maternal mortality worldwide. (1,2) The incidence of PPH after vaginal delivery (VD) ranges from 0.8% to 7.9% (3–6), and a recognized challenge of resuscitation is that detection of PPH can occur too late. (7,8) Anesthesiologists, the physicians primarily called upon for advanced resuscitation, are not routinely present at the time of VD. More timely detection of abnormal bleeding prompts earlier recognition and subsequent treatment of PPH. Therefore, systems that promptly identify PPH after VD are warranted.

The National Partnership for Maternal Safety (NPMS), a multidisciplinary task force endorsed by all obstetric subspecialty societies, published a Consensus Bundle on Obstetric Hemorrhage in 2015. (9) A key NPMS bundle element for enhanced recognition is to adopt quantitative measurement of cumulative blood loss, based on evidence that blood loss is underestimated by 30-50% using visual estimation and the degree of underestimation increases with the magnitude of hemorrhage. (10,11)

Blood loss at the time of delivery is contained by both conical drapes under the patient and surgical sponges. Gravimetry, or weighing of sponges to calculate blood loss, is recommended by the NPMS. (9) However, the use of gravimetry is a multi-step process requiring calculation and cumulative recording, which can be challenging to perform during an acute bleeding situation. In addition, the use of gravimetry does not incorporate blood loss that is contained in the conical under-buttocks drape. In the present study we have utilized a device for quantitative blood loss (tBL) that tracks cumulative blood loss over time based on gravimetry plus conical drape blood volume, subtracting sponge dry-weight and amniotic fluid volume (Triton™ (labor and delivery) L&D System, Gauss Surgical, Inc., Los Altos, CA).

Prior studies have compared visual estimation of blood loss (vBL) and gravimetry or calibrated drapes and report up to 30% blood loss underestimation by vBL. (10,12,13) In addition, a randomized trial comparing a calibrated drape to gravimetry after VD reported no difference in PPH-related management or interventions. (14) However, the impact of tBL after VD using a system that combines volumetric and gravimetric measurements is unknown. We hypothesized that the transition from vBL to tBL would be associated with an increase in the incidence of PPH ($\geq$ 500 mL blood loss) detection in VDs.

4.3 Methods

4.3.1 Study population

This was a single center, retrospective, interrupted time series analysis. After Institutional Review Board (IRB) approval (number 2016P002891) and waiver of informed consent, all patients who had a singleton VD or cesarean delivery (CD) at our institution between October 4, 2017 - December 31, 2017 (prior to tBL device implementation) and February 1, 2018 - April 30, 2018 (after tBL device implementation) were identified. The tBL device was implemented for VD only, so CDs were included as a control series that would likely also be affected by unofficial concurrent practice changes that could confound any observed association between tBL and immediate PPH detection in VD. (15) Patients were excluded if delivery blood loss data were missing or any measured potential confounders defined in our statistical analysis (mother characteristics, baby characteristics, delivery details, or delivering physician or midwife) was missing. This manuscript adheres to the applicable STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines.

4.3.2 tBL device implementation

On our L&D unit prior to tBL implementation, non-calibrated under buttock drapes were used for all VDs, and obstetricians visually estimated blood loss. For tBL quantitation via the Triton™ L&D System, a calibrated under buttock drape was introduced, and L&D nurses measured the tBL after VD. For CDs that occurred throughout the entire study period, anesthesiologists and obstetricians visually estimated blood loss. The Triton™ L&D System consists of an Apple iPad Pro 32GB Wi-Fi system linked by Bluetooth to a smart wireless scale. The iPad tracks cumulative blood loss over time by gravimetry, calculating sequential sponge weights on the scale and

subtracting pre-entered sponge dry weights. In addition, the iPad has an input feature to enter initial amniotic fluid volume, which is subtracted from the final volume of fluid recorded from a calibrated conical under-buttocks drape. Gravimetric and volumetric data are collected in real time for comprehensive and dynamic blood loss quantitation. An in-service training period from January 1, 2018 - January 31, 2018 ensured that all L&D nurses, obstetricians, and anesthesiologists were oriented to the use of tBL as standard of care.

4.3.3 Predictors

Our main predictor of interest was time period (i.e., post [February 1, 2018 - April 30, 2018] vs. pre tBL device implementation [October 4, 2017 - December 31, 2017]). VD with no evidence of tBL device use in the post-implementation period were excluded from the primary analysis (31.9% [302/947]), but included in a sensitivity analysis as described in the statistical analysis section.

Additional predictors of interest included week of delivery, delivery method, mother characteristics (age, body mass index [BMI], pre-delivery hematocrit [HCT], parity, race), baby characteristics (gestational age, birth weight), and delivering clinician.

4.3.4 Patient care

All patients admitted to L&D for VD or CD received standard of care during labor, delivery and postpartum, and there were no system changes to obstetric care at our institution during the study periods, such as additional care protocols or study-related interventions. Our pre-established protocol for PPH after VD includes the activation of a “Stage 1 Variance” for blood loss exceeding 500 mL. A Stage 1 Variance directs the obstetrician/midwife and anesthesia teams to the bedside.

The following interventions are considered: intravenous fluid resuscitation to maintain hemodynamic stability, additional intravenous access, secondary uterotonic administration, blood product acquisition and transfusion, and discussion of whether to move to the operating room for surgical intervention. All interventions related to PPH were initiated by the providing obstetric and anesthesia care teams in both groups, based on standard clinical criteria of hemodynamics (noninvasive blood pressure or arterial line, heart rate), coagulation tests (prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, complete blood count), and clinical etiology of bleeding in conjunction with vBL or tBL information. In the case of VDs, providers were not blinded to tBL values. Management of all patients was based on the clinical judgment and the decision-making of the medical team. While our L&D unit does not have a formal policy regarding active management of the third stage of labor, all providers are encouraged to use a prophylactic uterotonic, with oxytocin preferred.

4.3.5 Outcomes

The primary study outcome was incidence of immediate PPH detection, defined as $\geq$ 500 mL vBL or tBL immediately after VD or $\geq$ 1,000 mL vBL immediately after CD. While the American College of Obstetricians and Gynecologists (ACOG) defines PPH for VD as cumulative blood loss greater than or equal to 1,000 mL, we defined PPH as immediate blood loss $\geq$ 500 mL for VD because this volume retains utility to alert providers about early variance and remains a valuable clinical trigger for initiating interventions for PPH. (16) Secondary outcomes were blood loss $\geq$ 1,000 mL (regardless of delivery method), overall blood loss, transfusion requirement, secondary uterotonic administration, vasopressor administration, surgical intervention (uterine tamponade with Bakri balloon placement, dilatation and curettage, perineal or vaginal hematoma

evacuation, and/or hysterectomy), and a composite outcome related to PPH management interventions (transfusion, vasopressor administration, and/or surgical procedures). (17) Additional post-hoc secondary outcomes assessed in the subgroup of patients who had both pre- and post-VD HCTs measured during their hospitalization were nadir HCT, postpartum HCT reduction $\geq$ 10%, and the difference between vBL or tBL and calculated blood loss (11) (cBL). Pre-delivery complete blood count (CBC) was obtained from all patients upon admission to the L&D unit; post-delivery HCTs were defined as HCTs collected within the first 24 hours after delivery. Of note, we do not have an established protocol to determine which patients require a postpartum CBC; this was left to each provider's discretion and clinical judgment. Nadir HCT (collected within 24 hours of delivery) was adjusted if the patient received packed red blood cell (PRBC) transfusion by subtracting 3% for every PRBC unit transfused. (18) cBL was calculated utilizing the pregnancy-specific algorithm of Stafford et al. (11) This algorithm derives a cBL in obstetric patients by multiplying calculated pregnancy blood volume (defined as $0.75 \times \{[\text{maternal height (inches)} \times 50] + [\text{maternal weight in pounds} \times 25]\}$) by percent of blood volume lost (defined as {predelivery HCT − postdelivery HCT}/predelivery HCT).

4.3.6 Statistical analysis

4.3.6.1 Mother and baby characteristics

Mother and baby characteristics were compared between VD pre-device implementation vs. VD post-device implementation, CD pre-device implementation, and CD post-device implementation using two-sample *t*-tests for continuous variables and chi-square or Fisher's exact tests for categorical variables, both before and after applying patient-level weights calculated as described in the subsequent sections.

4.3.6.2 Immediate post-delivery blood loss

The mean weekly incidence of immediate PPH detection (defined as immediate post-delivery estimated blood loss ≥ 500 mL for VD and ≥ 1,000 mL for CD) and immediate post-delivery estimated blood loss were compared by delivery method post- vs. pre-introduction of the Triton™ L&D System using segmented quasi-Poisson regression and segmented linear regression, respectively. Segmented regression was used to allow for comparison of both the level (i.e., intercept) and trend (i.e., slope) of outcomes post- vs. pre-device implementation. (15,19) PPH was modeled using quasi-Poisson regression to account for over-dispersion in event count per week. (15) Blood loss was log-transformed for analysis to reduce skewness. Separate regression models for VD (the intervention series) and CD (the control series) were each initially fit for each outcome with a time period (i.e., post- vs. pre-device implementation) term, a week term, and a time period by week interaction term. There was no evidence of an interaction between time period and week (i.e., no evidence of a change in the slope of the weekly incidence of PPH detection or geometric mean blood loss post- vs. pre-device implementation) for either delivery method. Therefore, the final PPH and blood loss models for the combined delivery methods each included a time period term, a week term, a delivery method term, and a time period by delivery method interaction term. A first-order autoregressive (AR[1]) covariance structure was used to account for the correlation between observations from adjacent weeks. To account for variability between time periods and delivery types with respect to mother characteristics, baby characteristics, and distribution of delivering clinicians that could be associated with amount of blood loss or estimates thereof, models were weighted by propensity score odds. Specifically, multilevel multinomial logistic regression was used to estimate the probability (i.e., propensity score) of each patient delivering within each of the four possible period and delivery type combinations (VD pre-device

implementation, VD post-device implementation, CD pre-device implementation, CD-post device implementation) conditional upon mother characteristics (age, BMI, pre-delivery HCT, parity, race), baby characteristics (gestational age, birth weight), and delivering clinician. Mother and baby characteristics were included in the model as fixed effects and delivering clinician was included as a random effect with a compound symmetric covariance structure. Weights were calculated for each patient as the estimated probability of VD pre-device implementation divided by the estimated probability of delivering within the observed period and delivery type combination. Therefore, all VD pre-device implementation were assigned a weight of one, while all other deliveries were assigned weights based on the similarity of their covariate values to VD pre-device implementation. (20) The PPH model was weighted by average patient-level weight within each week and delivery type, while the blood loss model was weighted by individual delivery-level weights.

4.3.6.3 Post-delivery interventions

The incidence of post-delivery interventions including blood transfusion, secondary uterotonic use, vasopressor administration, surgical management, and a composite of PPH interventions (i.e., at least one of the following: blood transfusion, vasopressor administration, surgical management) were compared post- vs. pre-device implementation amongst VD using chi-square tests with patient-level weights (estimated as described in the "Immediate post-delivery blood loss" section). Segmented regression was not used to compare the incidence of post-delivery interventions post- vs. pre-device implementation due to the limited number of events per week that could lead to model instability.

4.3.6.4 Hematocrit-based outcomes (post-hoc subgroup analysis)

Outcomes based on pre and/or post-delivery HCT measurements were compared post- vs. pre-device implementation amongst VDs with at least one post-delivery HCT measurement associated with a calculated percentage blood loss volume between 0-100%. HCT nadir and difference between vBL or tBL and cBL were compared between time periods using segmented linear regression with patient-level weights. A first-order autoregressive (AR[1]) covariance structure was used to account for the correlation between observations from adjacent weeks. The incidence of pre- to post-delivery HCT drop of 10% or more was compared post- vs. pre-device implementation using a chi-square test with patient-level weights. Segmented regression was not used to compare the incidence of this outcome post- vs. pre-device implementation due to the limited number of events per week that could lead to model instability. Weights were calculated for HCT-based outcome analyses in a manner analogous to those calculated for the immediate post-delivery blood loss analyses, with two (instead of four) propensity scores calculated per patient using multilevel binary logistic regression.

4.3.6.5 Sensitivity analyses

The primary analysis excluded patients with vBL despite VD in the post-device implementation period. To account for the possibility that the excluded patients did not represent a random sample of deliveries, a sensitivity analysis repeated all analyses with these patients included in the post-device implementation VD group. While we adjusted post-delivery HCT measurements for blood transfusions in our primary analysis of HCT-based outcomes, a second sensitivity analysis re-examined these outcomes solely amongst patients included in the primary analysis who did not receive a blood transfusion.

4.3.6.6 Hypothesis testing and software

All statistical hypothesis tests were two-sided, with no correction for multiple testing. Statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC).

4.3.6.7 Power analysis

An *a priori* power calculation determined that a minimum of 220 patients per blood loss measurement method would be required to detect an increase in the incidence of immediate PPH (immediate post-delivery blood loss $\geq$ 500 mL) from 1.9% to 8.2% (21) for vBL vs. tBL, respectively, with 80% power at a two-sided α level of 0.05 using a chi-square test.

4.4 Results

A total of 2,433 singleton deliveries were included in the primary analysis: 967 VDs pre tBL device implementation (vBL), 645 VDs post implementation (tBL), 434 CDs pre implementation (vBL), and 387 CDs post implementation (vBL) (Figure 1). The tBL measurement device was employed in 68.1% of singleton VDs in the selected 3-month post-implementation period (Figure 1). Prior to weighting by propensity score odds, there were no differences in mother or baby characteristics between VD groups, but there were differences in most mother and baby characteristics between the CD groups and the VD pre-implementation group (Table 1). After weighting by propensity score odds, the only baseline difference between groups was a slightly higher proportion of patients who had a spontaneous VD (compared to vacuum and forceps) in the post- vs. pre-implementation VD groups (Supplementary Table 1). Oxytocin prophylaxis after VD was administered to 99.7% (964/967) of the patients in the pre-device implementation period and to 99.8% (644/645) of the women in the post-implementation period. A total of 105 clinicians performed VDs and/or CDs during one or more of the study time periods, with 55 clinicians (52.4%) performing both VDs and CD during both study periods. The number of clinicians and median (interquartile range [IQR]) number of deliveries per clinician per delivery type and period was as follows: 89 clinicians performed 10 (4, 17) VDs prior to device implementation, 88 clinicians performed 5 (2, 11) VDs after device implementation, 60 obstetricians performed 7 (4, 10) CDs prior to device implementation, and 61 obstetricians performed 5 (3, 8) CDs after device implementation.

Results of outcome comparisons are shown in Table 2. Immediate PPH after VD (estimated blood loss $\geq$ 500 mL) was identified in 26.8% tBL patients vs. 11.5% of vBL patients (weighted relative risk (wRR) 2.21 (95% confidence interval [CI]: 1.33, 3.66; p 0.004); time period by

delivery method interaction term $p < 0.001$). Immediate PPH after CD (estimated blood loss ≥ 1,000 mL) was identified in 20.2% of patients in the post-implementation period and 20.5% of patients in the pre-implementation period (wRR 0.93 (95% CI: 0.56, 1.54; p 0.764); Figure 2). The wRR of estimated blood loss ≥ 1,000 mL post- vs. pre-implementation of the tBL device was 2.62 (95% CI: 1.28, 5.37; p 0.01; time period by delivery method interaction term $p < 0.001$) for VD vs. 0.80 (95% CI: 0.45, 1.44; p 0.440) for CD. Geometric mean (standard error [SE]) blood loss was 290 (10) mL vs. 307 (4) mL for VD post- vs. pre-implementation (weighted ratio of geometric means [wRGM] 0.97 (95% CI: 0.86, 1.09; p 0.574); time period by delivery method interaction term p 0.062; Table 2; Figure 3). Geometric mean (SE) blood loss was 788 (10) mL vs. 769 (10) mL for CD in the post- vs. pre-implementation periods (wRGM 1.05 (95% CI: 0.93, 1.18; p 0.433); Figure 3). Interestingly, for VDs in the pre-device implementation period, 56.4% of the estimated blood loss was in the range of 300 to <500 mL, while for the post-device implementation period, only 24.7% of the blood loss was in the same range (Figure 3). There was no evidence of a difference in transfusion rate, secondary uterotonic administration, vasopressor administration, surgical procedures, or PPH-related interventions post- vs. pre-device implementation in VDs (Table 2). A sensitivity analysis including VDs both with and without evidence of tBL post device implementation produced similar results to the primary analysis (Supplemental Table 2).

In the subgroup of VD patients for whom pre- and post-delivery HCT values were available (127 patients in the tBL group [19.7%] and 160 patients in the vBL group [16.5%]), there was no difference in mean nadir HCT over the first 24 hours post-delivery in the tBL group (mean ± SD: 29.9% ± 4.3%) vs. vBL group ((28.5% ± 4.8%) (weighted difference in means [wDM] 1.1% (95% CI: -1.6%, 3.7%; $p = 0.431$)). The incidence of HCT drop of 10% or more over the first 24 hours post-delivery was lower in the tBL vs. vBL group (21.3% vs. 31.3%, wRR 0.61 (95% CI: 0.41,

0.92; p = 0.016)). The mean difference between delivery blood loss and cBL was smaller in the tBL (mean ± SD: -237 ± 522 mL) vs. vBL group ((-600 ± 596 mL) (wDM (95% CI): 358 mL (3,713); p 0.048; Figure 4)). A sensitivity analysis of HCT-based outcomes excluding patients who received a blood transfusion showed similar results (Supplementary Table 3).

4.5 Discussion

Better quantitation of blood loss to determine early PPH has become a priority for the purpose of reducing maternal morbidity and mortality. Delayed or imprecise visual estimation of blood loss occurs commonly (22) and is a leading driver of preventable PPH morbidity. (7,8) One of the elements of the NPMS Bundle recommends "measurement of cumulative blood loss (formal, as quantitative as possible)." (9) In our study, tBL was more likely than vBL to identify the clinical trigger of immediate post-delivery blood loss ≥ 500 mL for VD, a finding that is consistent with previous studies. (10–13) While the wRR of immediate PPH for tBL vs. vBL post VD was consistently high for both the primary and sensitivity analyses, weighted geometric mean blood loss remained constant pre and post tBL device implementation for the primary and secondary analyses, respectively. These results suggest that one of the main benefits of tBL may be that it overcomes the clinician's tendency to visually estimate any non-alarming blood loss < 500 mL. This tendency was reflected in preponderance of cases with vBL from 300 to <500 mL. While identification of blood loss ≥ 500 mL may not necessitate immediate intervention, exceeding this threshold may serve as a good indicator of cases that would benefit from close monitoring for blood loss beyond the immediate postpartum period. In fact, our post-hoc comparison of the difference between immediate post-delivery vBL or tBL and 24-hour cBL among the subgroup of patients with one or more post-delivery HCT measurement showed a notably smaller difference between tBL and cBL vs. between vBL and cBL in the primary analysis, first sensitivity analysis, and second sensitivity analysis. While we did not detect a difference in the incidence of post-delivery interventions between the vBL vs. tBL periods, this study was not powered to test whether tBL impacts outcomes. A prior cluster randomized trial of 25,381 vaginal deliveries in 13 European countries reported no improvement or change in PPH outcomes using a calibrated

collector bag after VD compared to vBL. (17) A trial of similar size and design would be required in order to test whether blood loss quantitated by volumetric plus gravimetric methods (as opposed to volumetric assessment alone) vs. vBL impacts patients' outcomes.

Our study demonstrated an increase in the incidence of PPH detection with a quantitative approach compared to vBL after VD. In contrast, a study comparing blood loss measurements after CD by visual estimation, gravimetry, and quantitation utilizing a photographic analysis of blood-soaked sponges and suction canister contents revealed only weak correlation between any measuring modality and the postpartum hemoglobin values. (23) The study was performed under conditions of low blood loss and suggests that vBL during CD is not inferior to gravimetry or more sophisticated measurements under low blood loss conditions. There are several conditions of our study which may explain why PPH incidence was higher using the tBL method. First, the under-buttocks VD drape utilized at our institution has historically been un-calibrated. Implementation of the tBL system required the introduction of drapes that are calibrated. Toledo and colleagues demonstrated that the accuracy of vBL worsens with increased volume (41% underestimation at 2,000 mL) and that the use of calibrated drapes reduces inaccuracy to < 15% error at all volumes measured. (13) Incorporating calibrated VD drapes in the tBL phase may have further enhanced blood loss quantitation compared to the vBL with an unmarked drape. Second, the clinical situation of elective, low-risk CD is relatively standardized compared to VD with varying PPH risk factors including duration of labor, oxytocin exposure, and lacerations. Such a spectrum in clinical presentation may amplify the impact of tBL methodology.

There is an ongoing need for clinicians to evaluate how interventions may impact the incidence of PPH after VD. The rate of blood loss, percentage of blood volume lost, and evaluation of clinical parameters such as the shock index are all outcomes of interest. (24) The use of refined

tBL devices as in our study may have utility to enhance the dynamic comparison of blood loss after any intervention proposed in a research setting.

We acknowledge the limitations of this study. First, the study design was retrospective and we cannot exclude bias, residual confounding, and suboptimal quality of the data. (25) Second, the vBL methodology was not standardized. Third, the time to intervention for PPH management was a variable we could not collect retrospectively, and timing of administration for agents such as secondary uterotonics for uterine atony can play a major role in the final blood loss and associated morbidity. Fourth, although post-delivery HCTs were collected within 24 hours of delivery, the time interval was not controlled, and additional factors such as fluid administration were not considered. Such variables may have impacted our post-delivery HCT and cBL calculation. Fifth, the compliance rate of 68.1% for the tBL device may have introduced selection bias in our study. However, a sensitivity analysis including VDs without evidence of tBL post device implementation produced similar results to the primary analysis. Sixth, given the limited number of events per week for the post-delivery interventions that could lead to model instability using segmented regression, we did not use this statistical approach for these secondary outcomes. Moreover, the conclusion of intervention effectiveness due to the data-driven model specification could threat the validity of the segmented regression analysis. (15) Seventh, the tBL device requires a specific training to obtain accurate blood loss quantitation. Moreover, due to the technology implemented in the device, any technical failure would limit the quantitation of blood loss after vaginal delivery. Eighth, patients who had missing data related to blood loss or any measured potential confounders were excluded, and this could compromise the inferences from our study. However, the missing data rate was low. Single imputation methods, estimating-

equation methods, and methods based on a statistical model (26) are alternatives to the complete-case analysis utilized in the present study.

In conclusion, this is the first study to our knowledge that evaluates a comprehensive tBL device in comparison to a visual estimation for measuring blood loss after VD. Our results support the importance of tBL for timely recognition of PPH, and this practice is in accordance with the NPMS recommendations. No differences were detected in outcomes related to PPH in the setting of a highly resourced and proactive tertiary center. Impact of the device requires further study, with the integration of response protocols and an assessment of effects at lower resource, lower-staffed centers in low- and middle-income countries. Moreover, whether a higher probability of PPH detection using tBL can improve maternal outcomes warrants study in larger samples.

4.6 References

1. Berg C, Harper M, Atkinson S, Bell E, Brown H, Hage M. Preventability of Pregnancy-Related Deaths. Obs Gynecol. 2005;106(6):1228–34.
2. Main EK, McCain CL, Morton CH, Holtby S, Lawton ES. Pregnancy-related mortality in California. Obstet Gynecol. 2015;125(4):938–47.
3. Mehrabadi A, Hutcheon JA, Lee L, Kramer MS, Liston RM, Joseph KS. Epidemiological investigation of a temporal increase in atonic postpartum haemorrhage: A population-based retrospective cohort study. BJOG An Int J Obstet Gynaecol. 2013;120(7):853–62.
4. Kramer MS, Berg C, Abenhaim H, Dahhou M, Rouleau J, Mehrabadi A, et al. Incidence, risk factors, and temporal trends in severe postpartum hemorrhage. Am J Obstet Gynecol. 2013;209(5):449.e1-449.e7.
5. Lutomski JE, Byrne BM, Devane D, Greene RA. Increasing trends in atonic postpartum haemorrhage in Ireland: An 11-year population-based cohort study. BJOG An Int J Obstet Gynaecol. 2012;119(3):306–14.
6. Al-Zirqi I, Vangen S, Forsen L, Stray-Pedersen B. Prevalence and risk factors of severe obstetric haemorrhage. BJOG An Int J Obstet Gynaecol. 2008;115(10):1265–72.
7. Della Torre M, Kilpatrick S, Hibbard J, Simonson L, Scott S, Koch A, et al. Assessing preventability for obstetric hemorrhage. Am J Perinatol. 2011;28(10):753–9.
8. Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. Lancet. 2006;367(9516):1066–74.
9. Main EK, Goffman D, Scavone BM, Low LK, Bingham D, Fontaine PL, et al. National Partnership for Maternal Safety, Consensus Bundle on Obstetric Hemorrhage. Obstet Gynecol. 2015;126(1):155–62.

10. Patel A, Goudar SS, Geller SE, Kodkany BS, Edlavitch SA, Wagh K, et al. Drape estimation vs. visual assessment for estimating postpartum hemorrhage. Int J Gynecol Obstet. 2006;93(3):220–4.

11. Stafford I, Dildy GA, Clark SL, Belfort MA. Visually estimated and calculated blood loss in vaginal and cesarean delivery. Am J Obstet Gynecol. 2008;199(5):1–7.

12. Al Kadri HMF, Al Anazi BK, Tamim HM. Visual estimation versus gravimetric measurement of postpartum blood loss: A prospective cohort study. Arch Gynecol Obstet. 2011;283(6):1207–13.

13. Toledo P, McCarthy RJ, Hewlett BJ, Fitzgerald PC, Wong CA. The accuracy of blood loss estimation after simulated vaginal delivery. Anesth Analg. 2007;105(6):1736–40.

14. Ambardekar S, Shochet T, Bracken H, Coyaji K, Winikoff B. Calibrated delivery drape versus indirect gravimetric technique for the measurement of blood loss after delivery: A randomized trial. BMC Pregnancy Childbirth. 2014;14(1).

15. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: A tutorial. Int J Epidemiol. 2017;46(1):348–55.

16. ACOG. The American College of Obstetricians and Gynecologists. Clinical Management Guidelines for Obstetrician Gynecologists. Postpartum Hemorrhage. J Obstet Gynaecol (Lahore). 2017;130(4):168–86.

17. Zhang WH, Deneux-Tharaux C, Brocklehurst P, Juszczak E, Joslin M, Alexander S. Effect of a collector bag for measurement of postpartum blood loss after vaginal delivery: Cluster randomised trial in 13 European countries. BMJ. 2010;340(7741):301.

18. Walker R. Mathematical calculations in transfusion medicine. Clin Lab Med. 1996;16(4):895–906.

19. Wagner A, Soumerai S, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther. 2002;299–309.

20. Stuart EA, Duckworth K, Simmons J, Barry CL. Using propensity scores in difference-in-differences models to estimate the effects of a policy change. Heal Serv Outcomes Res Methodol. 2014;14(4):166–82.

21. Rubenstein AF, Zamudio S, Al-Khan A, Douglas C, Sledge S, Tully G, et al. Clinical Experience with the Implementation of Accurate Measurement of Blood Loss during Cesarean Delivery: Influences on Hemorrhage Recognition and Allogeneic Transfusion. Am J Perinatol. 2018;35(7):655–9.

22. Frank S, Savage WJ, Rothschild JA, Rivers RJ, Ness PM, Paul SL, et al. Variability in blood and blood component utilization as assessed by an anesthesia information management system. Anesthesiology. 2012;117(1):99–106.

23. Fedoruk K, Seligman KM, Carvalho B, Butwick AJ. Assessing the Association Between Blood Loss and Postoperative Hemoglobin After Cesarean Delivery. Anesth Analg. 2018;Publish Ah(p):1.

24. Borovac-Pinheiro A, Pacagnella RC, Cecatti JG, Miller S, El Ayadi AM, Souza JP, et al. Postpartum hemorrhage: new insights for definition and diagnosis. Am J Obstet Gynecol. 2018;219(2):162–8.

25. Ho AMH, Phelan R, Mizubuti GB, Murdoch JAC, Wickett S, Ho AK, et al. Bias in Before–After Studies: Narrative Overview for Anesthesiologists. Anesth Analg [Internet]. 2018;126(5):1755–62. Available from: http://insights.ovid.com/crossref?an=00000539-201805000-00049

26. Little RJ, D'Agostino R, Cohen ML, Dickersin K, Emerson SS, Farrar JT, et al. The prevention and treatment of missing data in clinical trials. N Engl J Med. 2012 Oct 4;367(14):1355-60.

4.7 Tables.

4.7.1 Table 1. Mother, Baby, and Delivery Characteristics.

	VD		*CD*		*VD tBL post vs. VD vBL pre p-value*[a]	*CD vBL pre vs. VD vBL pre p-value*[a]	*CD vBL post vs. VD vBL pre p-value*[a]
	vBL pre	*tBL post*	*vBL pre*	*vBL post*			
	n = 967	n = 645	n = 434	n = 387			
Age, years (mean (SD))	31.6 (4.9)	32 (4.9)	33.1 (4.9)	32.8 (4.9)	0.104	<0.001	<0.001
Race (n, %)					0.106	0.065	0.107
Asian	108 (11.2)	88 (13.6)	39 (9)	35 (9)			
African American	117 (12.1)	69 (10.7)	64 (14.7)	58 (15)			
Hispanic	62 (6.4)	26 (4)	21 (4.8)	18 (4.7)			
White	573 (59.3)	374 (58)	242 (55.8)	218 (56.3)			
Other	89 (9.2)	71 (11)	59 (13.6)	51 (13.2)			
Unknown	18 (1.9)	17 (2.6)	9 (2.1)	7 (1.8)			
Delivery BMI (kg/m^2) (mean (SD))	26.6 (5.9)	26.3 (5.7)	28.1 (6.7)	28.3 (6.5)	0.361	<0.001	<0.001
Spontaneous vaginal delivery (n, %)	883 (91.3)	602 (93.3)	-	-	0.140	-	-
Manual removal of placenta (n, %)	16 (1.7)	9 (1.4)	-	-	0.680	-	-
Gestational age, weeks (mean (SD))	38.9 (1.6)	38.9 (1.8)	38.4 (1.9)	38.2 (1.9)	0.507	<0.001	<0.001
Birth weight, g (mean (SD))	3292.8 (481.6)	3287.3 (513.5)	3236.3 (593.8)	3222.4 (633.4)	0.826	0.082	0.049

Pre-delivery Hct, % (mean (SD))	35.9 (3.1)	36 (3.1)	35.4 (3.4)	35.8 (3.1)	0.594	0.005	0.560
Pre-delivery Hct < 30% (n, %)	29 (3)	18 (2.8)	21 (4.8)	17 (4.4)	0.808	0.086	0.201
Multiparous (n, %)	495 (51.2)	334 (51.8)	244 (56.2)	204 (52.7)	0.815	0.081	0.612
Anesthesia type (n, %)					0.084	<0.001	<0.001
CSE	16 (1.7)	2 (0.3)	31 (7.1)	24 (6.2)			
Spinal	5 (0.5)	3 (0.5)	254 (58.5)	225 (58.1)			
Epidural	809 (83.7)	563 (87.3)	146 (33.6)	128 (33.1)			
General	-	-	2 (0.5)	6 (1.6)			
Local	53 (5.5)	28 (4.3)	-	-			
Other	3 (0.3)	3 (0.5)	1 (0.2)	4 (1)			
None	81 (8.4)	46 (7.1)	-	-			

VD = Vaginal deliveries (the treatment series); CD = Cesarean deliveries (the control series); vBL = Visual estimation of blood loss; tBL = Gravimetric and volumetric estimation of blood loss; CSE = Combined spinal and epidural anesthesia; SD = Standard deviation; BMI = Body Mass Index; kg = Kilogram; m^2 = Square meter; g = Grams; Hct = Hematocrit.
a = *p*-values corresponding to two-sample *t*-tests for continuous variables and chi-square or Fisher's exact tests for categorical variables.

4.7.2 Table 2. Results of Outcome Comparisons.

	VD				*CD*			
Outcome	*vBL pre*	*tBL post*	*Effect size (95% CI)*	*p-value*	*vBL pre*	*vBL post*	*Effect size (95% CI)*	*p-value*
Immediate post-delivery blood loss	n = 967	n = 645			n = 434	n = 387		
PPH (n, %)	111 (11.5)	173 (26.8)	2.21 (1.33, 3.66)[a]	0.004[a]	89 (20.5)	78 (20.2)	0.93 (0.56, 1.54)[a]	0.764[a]
≥ 1,000 mL blood loss (n, %)	20 (2.1)	43 (6.7)	2.62 (1.28, 5.37)[a]	0.011[a]	89 (20.5)	78 (20.2)	0.8 (0.45, 1.44)[a]	0.440[a]
Blood loss, mL (geometric mean (SE))	307 (4)	290 (10)	0.97 (0.86, 1.09)[b]	0.574[b]	769 (10)	788 (10)	1.05 (0.93, 1.18)[b]	0.433[b]
Post-delivery interventions	n = 967	n = 645						
Blood transfusion (n, %)	13 (1.3)	8 (1.2)	0.89 (0.4, 1.97)[c]	0.782[c]	-	-	-	-
Secondary uterotonic use (n, %)	90 (9.3)	62 (9.6)	1.02 (0.77, 1.35)[c]	0.889[c]	-	-	-	-
Vasopressor administration (n, %)	6 (0.6)	5 (0.8)	1.14 (0.38, 3.43)[c]	0.813[c]	-	-	-	-
Surgical management (n, %)	13 (1.3)	6 (0.90)	0.65 (0.27, 1.56)[c]	0.334[c]	-	-	-	-
PPH management interventions (n, %)[e]	20 (2.1)	13 (2.0)	0.89 (0.47, 1.68)[c]	0.717[c]	-	-	-	-
Hematocrit-based outcomes	n = 160	n = 127						
Hematocrit nadir % (mean (SD))	28.5 (4.8)	29.9 (4.3)	1.1 (-1.6, 3.7)[d]	0.431[d]	-	-	-	-

Hematocrit drop, 10% or more (n, %)	50 (31.3)	27 (21.3)	0.61 (0.41, 0.92)[c]	0.016[c]	-	-	-	-
Difference of vBL or tBL and cBL ((mL) (mean (SD))	-600 (596)	-237 (522)	358 (3, 713)[d]	0.048[d]	-	-	-	-

VD = Vaginal deliveries (the treatment series); CD = Cesarean deliveries (the control series); vBL = Visual estimation of blood loss; tBL = Gravimetric and volumetric estimation of blood loss; cBL = Calculated blood loss; mL = Milliliters; PPH = Postpartum hemorrhage defined as blood loss $\geq$ 500 mL for vaginal deliveries and $\geq$ 1,000 mL for cesarean sections; SE = Standard error; SD = Standard deviation.

a = Relative risks, 95% confidence intervals, and *p*-values calculated using segmented quasi-Poisson regression weighted by propensity score odds.

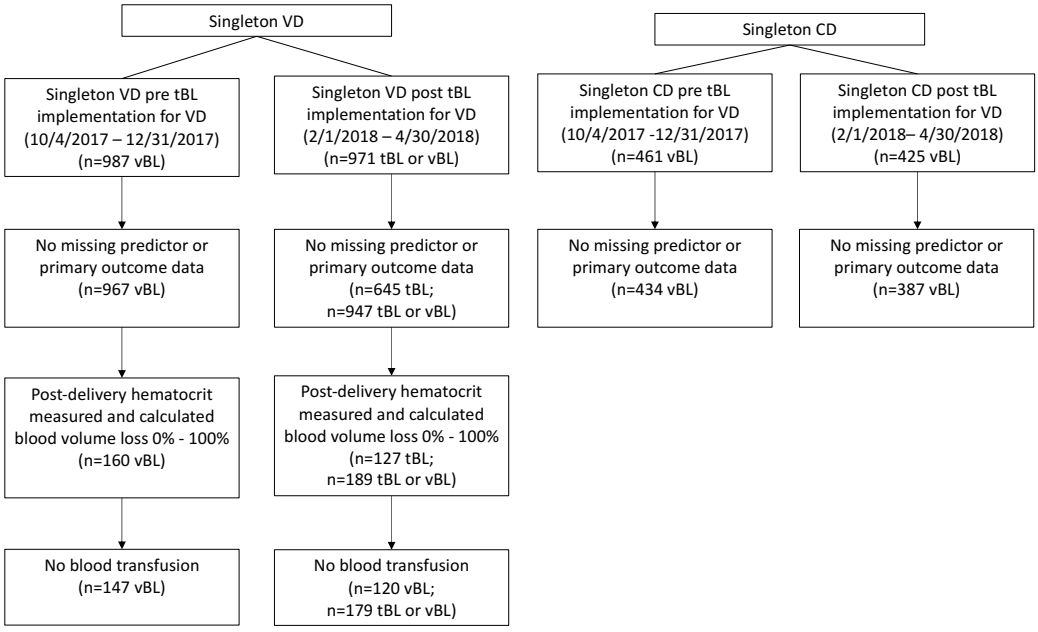
b = Ratios of geometric means, 95% confidence intervals, and *p*-values calculated using segmented linear regression weighted by propensity score odds.

c = Relative risks, 95% confidence intervals, and *p*-values calculated using chi-square tests weighted by propensity score odds.

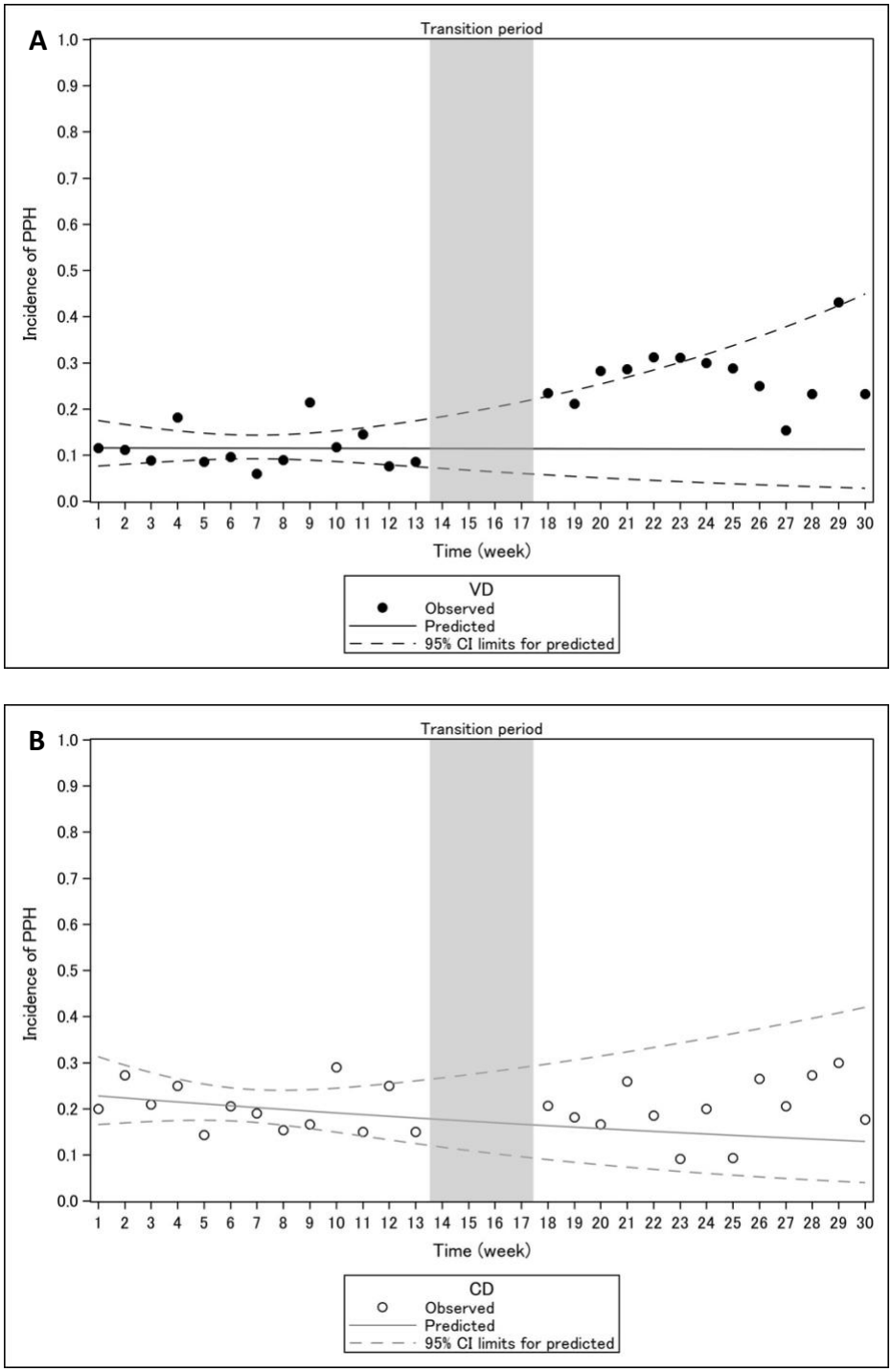
d = Difference in means, 95% confidence intervals, and *p*-values calculated using segmented linear regression weighted by propensity score odds.

e = PPH management interventions: transfusion; vasopressor administration; and/or surgical procedures.

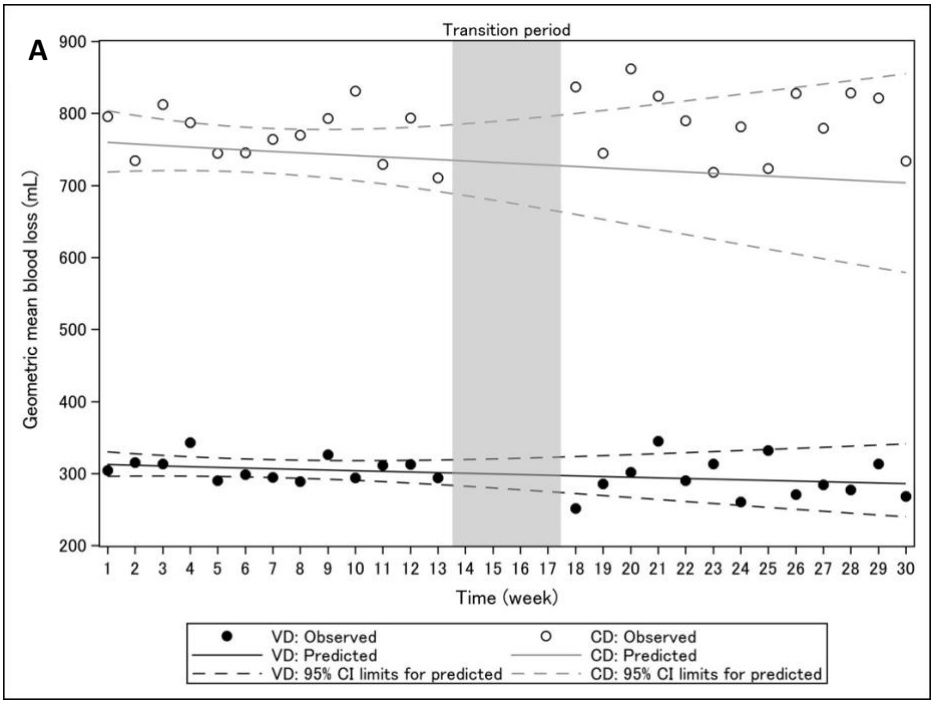
4.8 Figures.

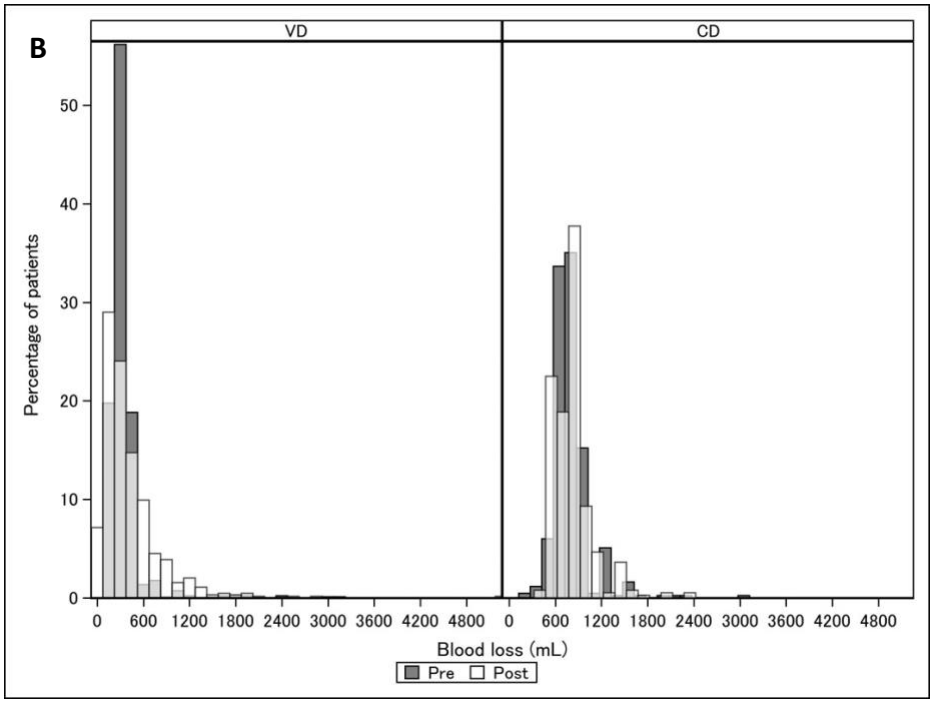


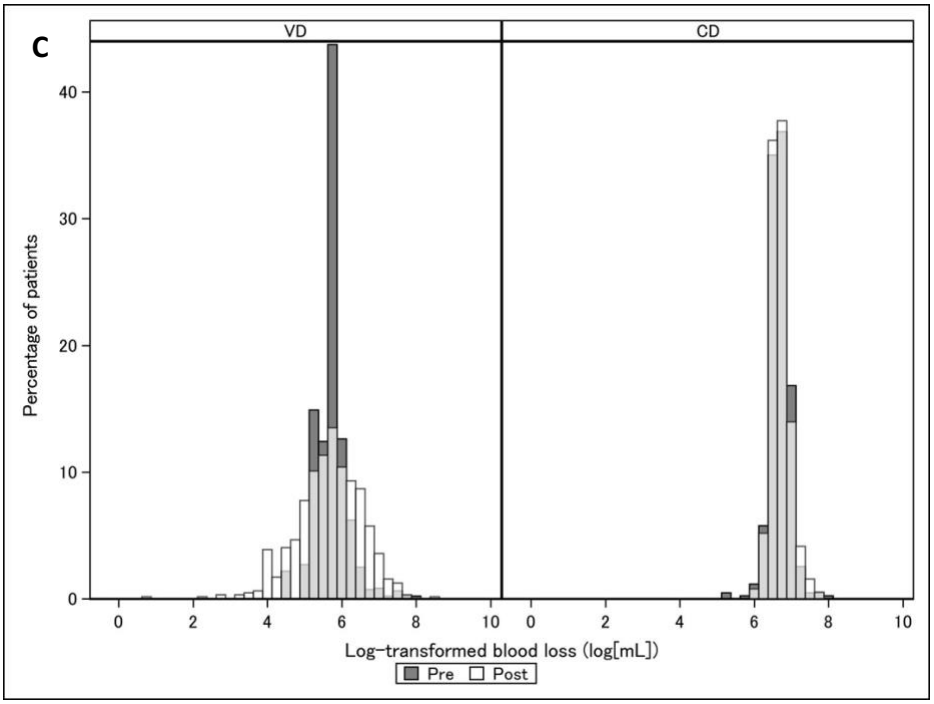
4.8.1 Figure 1. Flow Chart of Patients Recruitment. Singleton VD = Singleton vaginal deliveries (the treatment group); Singleton CD = Singleton cesarean deliveries (the control series); tBL = Quantitative blood loss; vBL = Visual estimation of blood loss; VD = Vaginal delivery; CD = Cesarean delivery.



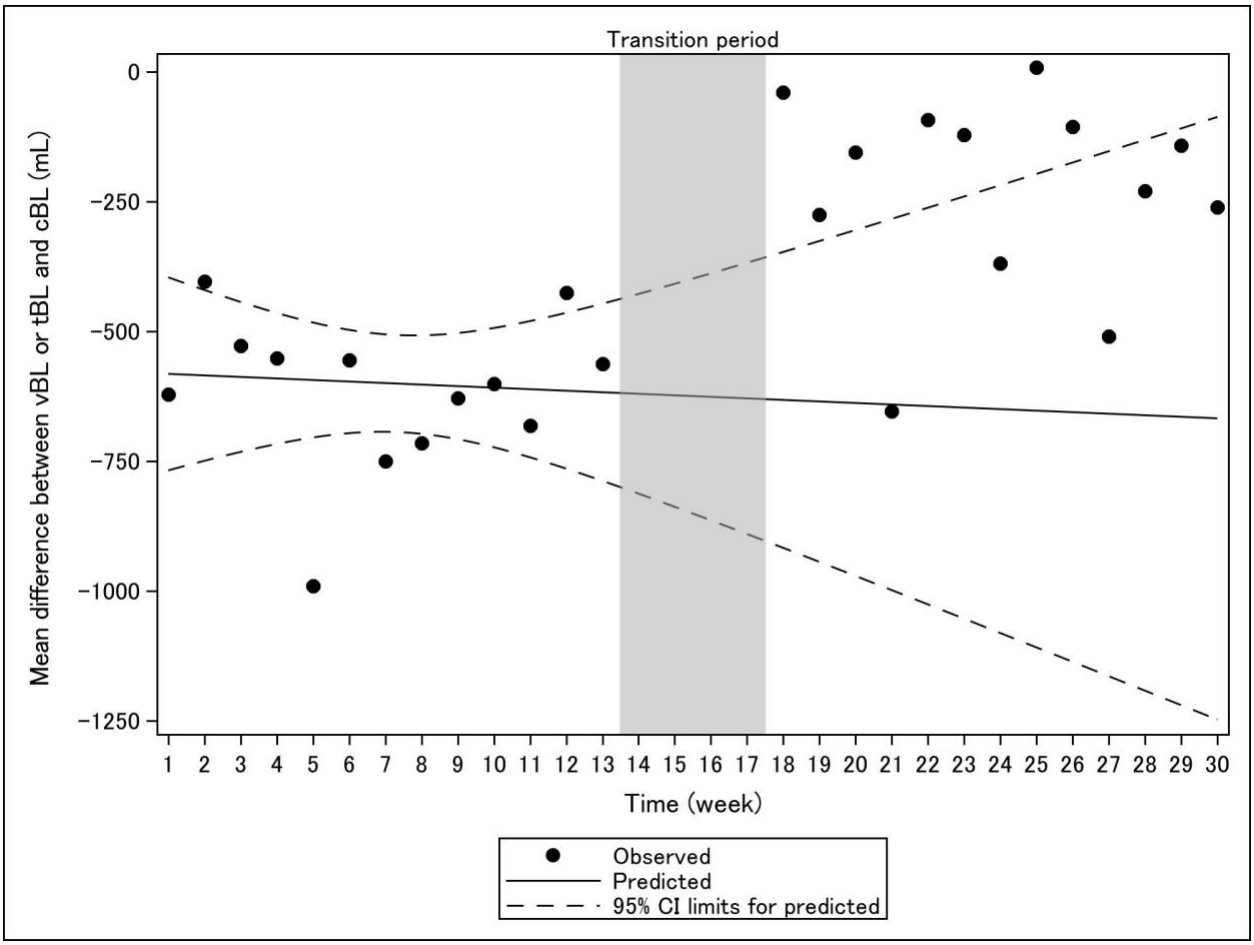
4.8.2 Figure 2. Immediate Postpartum Hemorrhage Before and After the Implementation of a Device for Gravimetric and Volumetric Estimation of Blood Loss after Vaginal Delivery. The device was implemented on January 1, 2018 with a one-month transition period. Predicted weekly incidence of blood loss $\geq$ 500 mL for vaginal deliveries (panel A) and $\geq$ 1,000 mL for cesarean sections (panel B) post device implementation was estimated via a quasi-Poisson regression model developed using only pre-implementation observations. PPH = Postpartum hemorrhage; VD = Vaginal delivery; CD = Cesarean delivery.


A
Transition period
Geometric mean blood loss (mL)
900
800
700
600
500
400
300
200
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
Time (week)
VD: Observed
VD: Predicted
VD: 95% CI limits for predicted
CD: Observed
CD: Predicted
CD: 95% CI limits for predicted


B
VD
CD
Percentage of patients
50
40
30
20
10
0
0 600 1200 1800 2400 3000 3600 4200 4800
0 600 1200 1800 2400 3000 3600 4200 4800
Blood loss (mL)
Pre
Post



4.8.3 Figure 3. Immediate Post-Delivery Blood Loss Before and After the Implementation of a Device for Gravimetric and Volumetric Estimation of Blood Loss after Vaginal Delivery. The device was implemented on January 1, 2018 with a one-month transition period. Predicted weekly geometric mean blood loss (panel A) post device implementation was estimated via a linear regression model developed using only pre-implementation observations. Panel B and C display histograms of blood loss on the original scale and the log-transformed, respectively. Dark gray corresponds to the pre-implementation period, white to the post-implementation period, and light gray to the overlap between periods. VD = Vaginal delivery; CD = Cesarean delivery.



4.8.4 Figure 4. Difference between Immediate Post-Delivery Estimated Blood Loss and 24-hour Calculated Blood Loss Before and After the Implementation of a Device for Gravimetric and Volumetric Estimation of Blood Loss after Vaginal Delivery. The device was implemented on January 1, 2018 with a one-month transition period. Predicted weekly mean difference between estimated blood loss and cBL (calculated blood loss) post device implementation was estimated via a linear regression model developed using only pre-implementation observations. vBL = Visual estimation of blood loss; tBL = Quantitative blood loss.

4.9 Supplementary appendix.

4.9.1 Supplementary Table 1. Mother, Baby, and Delivery Characteristics After Weighting by Propensity Score Odds.

	VD		*CD*		*VD tBL post vs. VD vBL pre p-value*[a]	*CD vBL pre vs. VD vBL pre p-value*[a]	*CD vBL post vs. VD vBL pre p-value*[a]
	vBL pre	*tBL post*	*vBL pre*	*vBL post*			
	n = 967	n = 645	n = 434	n = 387			
Age, years (mean (SD))	31.6 (4.9)	31.7 (6)	31.8 (7.1)	32 (6.9)	0.923	0.649	0.177
Race (n, %)					0.999	0.370	0.837
Asian	108 (11.2)	107 (11.4)	84 (9.4)	101 (12.1)			
African American	117 (12.1)	111 (11.9)	91 (10.2)	101 (12.0)			
Hispanic	62 (6.4)	58 (6.2)	51 (5.7)	47 (5.6)			
White	573 (59.3)	86 (9.2)	82 (9.1)	67 (8.0)			
Other	89 (9.2)	18 (1.9)	13 (1.5)	19 (2.3)			
Unknown	18 (1.9)	558 (59.5)	572 (64.1)	504 (60.0)			
Delivery BMI (kg/m^2) (mean (SD))	26.6 (5.9)	26.5 (7.1)	26.3 (7.9)	26.8 (8.4)	0.979	0.441	0.501
Spontaneous vaginal delivery (n, %)	883 (91.3)	879 (93.7)	-	-	0.048	-	-
Manual removal of placenta (n, %)	16 (1.7)	12 (1.3)	-	-	0.531	-	-
Gestational age, weeks (mean (SD))	38.9 (1.6)	38.9 (2)	38.9 (2.1)	38.8 (2.1)	0.912	0.828	0.267
Birth weight, g (mean (SD))	3292.8 (481.6)	3291.6 (606.6)	3275.6 (737.6)	3254.1 (771.9)	0.961	0.554	0.209

Pre-delivery Hct, % (mean (SD))	35.9 (3.1)	35.9 (3.8)	36.1 (4.6)	36 (4.5)	0.890	0.322	0.545
Pre-delivery Hct < 30% (n, %)	29 (3)	27 (2.8)	24 (2.7)	25 (2.9)	0.843	0.698	0.935
Multiparous (n, %)	495 (51.2)	485 (51.7)	477 (53.5)	407 (48.5)	0.811	0.322	0.259
Anesthesia type (n, %)					N/A	N/A	N/A
CSE	16 (1.7)	2 (0.2)	54 (6.0)	46 (5.4)			
Spinal	5 (0.5)	4 (0.4)	491 (55.1)	444 (52.9)			
Epidural	809 (83.7)	814 (86.7)	345 (38.6)	325 (38.7)			
General	-	-	1 (0.1)	11 (1.3)			
Local	53 (5.5)	41 (4.4)	-	-			
Other	3 (0.3)	5 (0.5)	1 (0.2)	14 (1.6)			
None	81 (8.4)	73 (7.8)	-	-			

VD = Vaginal deliveries (the treatment series); CD = Cesarean deliveries (the control series); vBL = Visual estimation of blood loss; tBL = Gravimetric and volumetric estimation of blood loss; CSE = Combined spinal and epidural anesthesia; SD = Standard deviation; BMI = Body Mass Index; kg = Kilogram; m^2 = Square meter; g = Grams; Hct = Hematocrit;
a = *p*-values corresponding to weighted two-sample *t*-tests for continuous variables and weighted chi-square tests for categorical variables.
N/A = Fisher's exact test cannot be performed with non-integer counts.

4.9.2 Supplementary Table 2. Sensitivity Analysis 1: Outcome Comparisons Incorporating Vaginal Deliveries with Visually Estimated Blood Loss After Device Implementation.

	VD				*CD*			
Outcome	*vBL pre*	*tBL or vBL post*	*Effect size (95% CI)*	*p-value*	*vBL pre*	*vBL post*	*Effect size (95% CI)*	*p-value*
Immediate post-delivery blood loss	n = 967	n = 947			n = 434	n = 387		
PPH (n, %)	111 (11.5)	222 (23.4)	1.85 (1.14, 3.02)[a]	0.015[a]	89 (20.5)	78 (20.2)	0.90 (0.55, 1.46)[a]	0.644[a]
≥ 1,000 mL blood loss (n, %)	20 (2.1)	52 (5.5)	2.26 (1.14, 4.48)[a]	0.022[a]	89 (20.5)	78 (20.2)	0.84 (0.47, 1.49)[a]	0.527[a]
Blood loss, mL (mean (SD))	342 (239)	395 (374)	1.00 (0.91, 1.11)[b]	0.926[b]	801 (259)	821 (266)	1.07 (0.96, 1.19)[b]	0.206[b]
Post-delivery interventions	n = 967	n = 947						
Blood transfusion (n, %)	13 (1.3)	11 (1.2)	0.79 (0.35, 1.78)[c]	0.564[c]	-	-	-	-
Secondary uterotonic use (n, %)	90 (9.3)	88 (9.3)	0.96 (0.72, 1.27)[c]	0.777[c]	-	-	-	-
Vasopressor administration (n, %)	6 (0.6)	7 (0.7)	1.16 (0.39, 3.46)[c]	0.787[c]	-	-	-	-
Surgical management (n, %)	13 (1.3)	10 (1.1)	0.68 (0.29, 1.59)[c]	0.367[c]	-	-	-	-
PPH management interventions (n, %)[e]	20 (2.1)	20 (2.1)	0.88 (0.46, 1.66)[c]	0.689[c]	-	-	-	-
Hematocrit-based outcomes	n = 160	n = 189						
Hematocrit nadir % (mean (SD))	28.5 (4.8)	29.4 (4.3)	0.2 (-2.3, 2.6)[d]	0.893[d]	-	-	-	-

Hematocrit drop, 10% or more (n, %)	50 (31.3)	38 (20.1)	0.62 (0.42, 0.92)[c]	0.017[c]	-	-	-	-
Difference of vBL or tBL and cBL ((mL) (mean (SD))	-600 (596)	-318 (502)	269 (-27, 565)[d]	0.075[d]	-	-	-	-

VD = Vaginal deliveries (the treatment series); CD = Cesarean deliveries (the control series); vBL = Visual estimation of blood loss; tBL = Gravimetric and volumetric estimation of blood loss; cBL = Calculated blood loss; mL = Milliliters; PPH = Postpartum hemorrhage defined as blood loss $\geq$ 500 mL for vaginal deliveries and $\geq$ 1,000 mL for cesarean sections; SD = Standard deviation.
a = Relative risks, 95% confidence intervals, and *p*-values calculated using segmented quasi-Poisson regression weighted by propensity score odds.
b = Ratios of geometric means, 95% confidence intervals, and *p*-values calculated using segmented linear regression weighted by propensity score odds.
c = Relative risks, 95% confidence intervals, and *p*-values calculated using chi-square tests weighted by propensity score odds.
d = Difference in means, 95% confidence intervals, and *p*-values calculated using segmented linear regression weighted by propensity score odds.
e = PPH management interventions: transfusion; vasopressor administration; and/or surgical procedures.

4.9.3 Supplementary Table 3. Sensitivity Analysis 2: Hematocrit-Based Outcomes Excluding Patients who Received a Blood Transfusion.

	VD			
Outcome	*vBL pre* (n=147)	*tBL post* (n=120)	*Effect size (95% CI)*	*p-value*
Hematocrit nadir % (mean (SD))	29 (4.5)	30.4 (3.9)	0.9 (-1.6, 2.6)[a]	0.488[a]
Hematocrit drop, 10% or more (n, %)	38 (25.9)	20 (16.7)	0.52 (0.31, 0.87)[b]	0.009[b]
Difference of vBL or tBL and cBL ((mL) (mean (SD))	-568 (548)	-186 (483)	330 (20, 640)[a]	0.037[a]

VD = Vaginal deliveries; vBL = Visual estimation of blood loss; tBL = Gravimetric and volumetric estimation of blood loss; cBL = Calculated blood loss; mL = Milliliters; SD = Standard deviation.
a = Difference in means, 95% confidence intervals, and *p*-values calculated using segmented linear regression weighted by propensity score odds.
b = Relative risk, 95% confidence interval, and *p*-value calculated using chi-square tests weighted by propensity score odds.

Chapter 5

Paper 2

Training for the Surgical Management of Postpartum Hemorrhage:

A Four-State Survey of Resident Physicians in Mexico

5.1 Glossary of terms

GME = Graduate medical education.

HAL = Hypogastric artery ligation.

HT = Gravid hysterectomy.

L&D = Labor and delivery.

OBGYN = Obstetrics and gynecology.

PGY = Postgraduate year.

PPH = Postpartum hemorrhage.

RPs = Resident physicians.

SBME = Simulation-based medical education.

SRL = Self-regulated learning.

UCS = Uterine compression sutures.

UD = Uterine devascularization.

UT = Uterine tamponade.

5.2 Introduction

Postpartum hemorrhage (PPH) is defined as blood loss of 1,000 mL or more after delivery. (1) PPH is a major cause of maternal mortality and severe morbidity worldwide and is considered largely preventable with timely and appropriate intervention. (2,3) Uterine atony is the most common cause of PPH, and invasive measures should be considered promptly when primary and secondary uterotonic administration fail to achieve hemostasis. (4,5) Approximately 15% of patients with PPH require surgical intervention, (6) therefore proficiency in surgical techniques among all birth attendants is critically important. Previous studies have reported limitations in knowledge of risk factors, diagnosis, causes, and surgical proficiency in the management of PPH among health care providers. (7,8) Evaluating whether education about PPH management is sufficient among obstetrics and gynecology (OBGYN) resident physicians (RPs), particularly in low-resource environments, may identify areas for improvement and mitigate such reported deficiencies over time.

In graduate medical education (GME), the training apprenticeship model complemented by a constructivist approach in which trainees develop skills through experiences and reflections has been well established. (9,10) However, residency training programs in low-income countries have limited resources and infrastructure, and exposure of RPs to a comprehensive curriculum is a challenge. Technical surgical interventions for PPH are ideally learned during OBGYN residency under direct supervision, with gradual autonomy over time as mastery is achieved. (11)

In this study, we collected residents' self-reported knowledge and level of proficiency in performing surgical procedures for the management of PPH. The secondary aims were to determine the educational resources utilized by RPs, and perceived barriers to acquiring advanced skills for the surgical management of PPH. The clinical decision-making process of RPs was also

explored.

5.3 Methods

5.3.1 Population and setting

The four hospitals in four states in Mexico (Guanajuato, San Luis Potosi, Durango, and Zacatecas) were selected using a convenience sampling method. (12) The hospitals in Guanajuato and San Luis Potosi are tertiary academic centers, while the centers in Durango and Zacatecas are secondary academic centers. On average, 9,000 babies are born every year at each of the four hospitals. A neonatal intensive care unit and an intensive care unit is available at each center. After internal research ethics committee review of this quality improvement study at the four public hospitals mentioned above, exemption of review and waiver of consent was granted at each site. A sample including all OBGYN RPs (postgraduate year 1 [PGY-1] through PGY-4) at the four sites was selected to participate in a survey. The primary aim of the survey was to assess residents' self-reported knowledge of and ability to perform the most common surgical techniques to manage PPH including uterine tamponade (UT), uterine compression sutures (UCS), uterine devascularization (UD), hypogastric artery ligation (HAL), and gravid hysterectomy (HT). RPs specified if they had observed or performed the procedures with or without supervision, or had exposure to simulation training for performing the technique.

5.3.2 Survey development and distribution

A panel of five OBGYN physicians (L-M MI; C-Z M; R-A AL; S-G JC; R-C JA) collaborated to create the survey utilized in this study. First, relevant items were identified from a survey created by Bouet et al. (8) to assess French obstetricians' knowledge of PPH surgical management. One additional item was adapted from a survey by Suskin et al. (13) to explore the perceived barriers to training. A cultural translation (English to Spanish) and adaptation of the

selected questions was performed based on the World Health Organization recommendations for translation and adaptation of instruments: forward translation, expert panel back-translation, pre-testing and cognitive interviewing, and final version. (14) To assess the self-perceived proficiency for each technique, a 5-point Likert-type scale based on the Dreyfus framework of expertise was utilized. (15) With the final set of questions, an iterative edition process was performed to provide evidence of validity. (16) Items were adjusted to be clear and understandable, and review by the panel continued until agreement was achieved. Reliability of the questionnaire was assessed by Cronbach's alpha. The survey included 24 closed-ended questions regarding each of the recommended surgical techniques for managing PPH (Supplementary Appendix). In July of 2018, we sent five email requests with an embedded link for completion of the survey via SurveyMonkey (SurveyMonkey Inc, San Mateo, CA).

5.3.3 Statistical analysis

Data are presented as mean (standard deviation), median (interquartile range), or number (%). For subgroup analysis (i.e., PGY-1 vs. PGY-4), nonparametric or parametric test (chi-square or Fisher's exact test) were used to analyze categorical variables, after evaluation for cell size. Moreover, *t*-test or Wilcoxon rank-sum test were used to analyze continuous variables. Reliability of the questionnaire was assessed by Cronbach's alpha. All statistical hypothesis tests were two-sided, with no correction for multiple testing. Statistical analysis were performed using Stata (Stata Corp, TX).

5.4 Results

Fifty-one out of 86 RPs (59.3%) responded to the survey. Internal consistency of the survey was demonstrated with a Cronbach's alpha of 0.92, indicating that the survey was highly reliable for assessment of PPH-related techniques and curriculum. Demographic data of the responders and available resources at their respective training program are shown in Table 1. Eighty-six percent of RPs reported learning these techniques while operating on patients experiencing PPH, and 49% learned the techniques while providing prophylactic measures for patients. Besides clinical training, the most common resources for acquiring surgical skills to control PPH were courses and conferences (64.7%), followed by workshops (52.9%). Only 25.5% reported the use of simulation for this purpose.

Self-reported knowledge about PPH-related surgical techniques are presented in Table 2 and self-reported proficiency (divided by PGY) to perform each of these surgical techniques is shown in Figure 1. Overall, 43.9% rated only basic proficiency to perform the surveyed procedures. RPs reported the greatest knowledge, observation rate, performance, and simulation exposure for UT. For proficiency to perform UT, 33.3% reported themselves as intermediate, 19.6% as advanced and 2% as expert. While 92.2% of RPs reported knowledge of UCS, only 25.5% had ever practiced it on a simulation model. For this procedure, 27.5% reported their proficiency level as novice, 13.7% as advanced, and none as expert. RPs reported lower knowledge of the techniques of UD and HAL. Notably, 82.4% rated their proficiency as only basic for HAL, and only 11.8% had ever practiced on a model. Reported knowledge of the HT, the complex technique and last resort in the setting of persistent PPH, was 72.6%. While 58.8% of RPs reported having performed it under supervision, only 5.9% has ever practiced HT in a simulated setting. Half of the residents (52.9%) self-reported only basic proficiency to perform HT, 17.7% novice,

and only 7.8% advanced.

Residents' perceived barriers in their training to perform the surveyed techniques are shown in Figure 2. A lack of specific training modules for these skills in their curriculum was reported by 74.5%, and 72.6% reported a lack of simulation training at their institution. Other reported barriers were a limited number of trained specialists as educators (43.1%), not enough patients or too many RPs (37.3%) and lack of time due to other clinical obligations (27.5%). None of the RPs reported low exposure to this training as a result of low prioritization.

To explore residents' decision-making, participants answered case-based questions about a patient with PPH from uterine atony despite second line uterotonic administration and UT. RPs ranked the techniques in the order they would have performed them if the patient was hemodynamically stable and desired to have more children. Eighty-four percent answered that the first step they would perform was UCS; 86.3% listed the second step as UD; 82% chose bilateral HAL as third procedure, and finally, 96.1% would perform an HT as the last step.

In an additional analysis, we compared first- and fourth-year RPs to assess differences in knowledge and experience at the beginning versus the end of residency training. The competence to perform procedures was reported higher by most fourth-year RPs (Supplementary Table 1). Notably, despite a majority of the fourth-year RPs reporting knowledge and theory of the surgical techniques, the average self-reported proficiency was below advanced or expert levels (Figure 1). Forty-six percent of fourth-year residents considered their proficiency to perform UCS as intermediate, and only 15.4% and 23.1% reported advanced proficiency to perform UD and HT, respectively. For HAL, 61.5% reported basic knowledge, 15.4% intermediate and none of them advanced or expert. Interestingly, for first-year residents, 80% said that frequently they were the physicians in charge of the Labor and Delivery (L&D) unit, and only 50% had the assistance and

supervision of an attending obstetrician at any time during the shift.

5.5 Discussion

Health systems are constantly evolving, but the dissemination of technology and investment in advanced training for PPH may not be equitable within or between countries. (17) Medical centers in remote locations have limited resources, and often surgery is the only option to control PPH. Hence, all birth attendants should be proficient in the surgical management of PPH. Reinforcing RPs exposure to surgical PPH management is critically important to lower preventable maternal morbidity and mortality. In Mexico, PPH was the leading cause of maternal mortality in 2017, and more than 75% of deaths from PPH occurred in a hospital. (18) OBGYN residency programs in Mexico have no uniform curriculum for PPH management, and our aim in this study was to evaluate OBGYN curricula for adequacy of training to perform PPH-related surgical procedures. To our knowledge, this is the first study to explore the perceptions of Mexican RPs about their exposure to surgical interventions for PPH. Our multicenter survey identified that most of the future OBGYN practitioners had adequate knowledge about available surgical techniques for PPH, but self-rated proficiency to perform such techniques was suboptimal.

The majority of surveyed RPs reported a lack of a specific training module in their curriculum for surgical management of PPH. Prioritizing a standardized OBGYN curriculum to improve PPH-specific surgical skills may be a critical step to decrease preventable maternal mortality from PPH. GME in developing countries is distinctly different compared to higher-resource nations. For instance, we found that 56.9% of the residents had already performed a UCS without supervision of a trained specialist compared to 49% reported in a French survey by Bouet et al. (8) These results illustrate the crucial role that RPs have in PPH management in Mexico, and the importance of early skills acquisition. A large proportion of the first-year RPs were working with autonomy in their L&D unit, with only 50% reporting supervision at any time during a shift.

Simulation-based medical education (SBME) is now a required component in every OBGYN accredited United States residency program. (19) Simulated scenarios promote learning of technical and non-technical skills in a safe environment, but the routine implementation of this valuable educational tool in developing countries has been limited by the scarcity of resources and poor infrastructure. In the present study, only 25.5% of the respondents reported simulation exposure to learn surgical interventions for PPH. Simulation training in low-resource settings has been advocated and deemed feasible by the Alliance for Continuing Education in Health Professions, and more research is needed in this area. (20) In addition to SBME, self-regulated learning (SRL) and active learning techniques have been suggested to promote proficiency during residency training. (21,22)

According to the Dreyfus model, the advanced and expert trainee identifies a situation and decides how to respond in a shorter period than an intermediate trainee. (15) This difference in time may be life-saving for a woman with severe PPH. Despite their level of training, fourth-year RPs surveyed in this study reported a low rate of advanced or expert proficiency in surgical PPH management. Strategies to ensure that OBGYN graduates have maximum proficiency in management of PPH are warranted.

Our study has several limitations. The survey response rate was only 59.3% and we cannot exclude the possibility of response bias. In addition we do not have the data to compare the non-responders. However, the collected surveys were representative of each year of OBGYN residency training, with equal distribution. Second, comparison of the four centers was not possible due to the anonymity of responses, but the objective was to obtain a candid view of trainees' perceptions through anonymous survey, rather than to assess each hospital separately for inter-hospital comparison. Third, these findings cannot be generalized, and external validity of our findings may

be greatest for hospitals with similar resources within Mexico and worldwide. Fourth, we evaluated the reliability of the survey, yet additional sources of evidence validity are needed (16) to confirm the inferences of our study. Fifth, self-reported proficiency could be different from the actual performance as rated by an expert surgeon. Finally, we implemented a nonprobability sampling method (convenience sampling) to select the hospitals included in the study, and this may limit the population represented by the sample. (12)

In conclusion, this study highlights a perception among RPs in Mexico that they gain sufficient knowledge about surgical interventions for PPH in their residency training, but insufficient proficiency to perform these procedures despite early autonomy. Further research is warranted to identify comprehensive and standardized curricula that emphasizes increased supervision, early mastery of surgical techniques, and simulation training for PPH surgical expertise.

5.6 References

1. Shields L, Goffman D, Caughey A. ACOG Practice Bulletin No. 183: Postpartum Hemorrhage. J Obstet Gynaecol (Lahore). 2017;130(4):168–86.
2. Mavrides E, Allard S, Chandraharan E, Collins P, Green L, Hunt B, et al. on behalf of the Royal College of Obstetricians and Gynaecologists. Prevention and management of postpartum haemorrhage. BJOG An Int J Obstet Gynaecol. 2016;124(5):e106–49.
3. Lalonde A. Prevention and treatment of postpartum hemorrhage in low-resource settings. Int J Gynecol Obstet. 2012;117(2):108–18.
4. Mousa HA, Blum J, Abou El Senoun G, Shakur H, Alfirevic Z. Treatment for primary postpartum haemorrhage. Cochrane Database Syst Rev. 2014;(2).
5. Abdul-Kadir R, McLintock C, Ducloy AS, El-Refaey H, England A, Federici AB, et al. Evaluation and management of postpartum hemorrhage: Consensus from an international expert panel. Transfusion. 2014;54(7):1756–68.
6. Sheldon WR, Blum J, Vogel JP, Souza JP, Gülmezoglu AM, Winikoff B, et al. Postpartum haemorrhage management, risks, and maternal outcomes: findings from the World Health Organization Multicountry Survey on Maternal and Newborn Health. BJOG. 2014;121 Suppl:5–13.
7. Carnahan LR, Geller SE, Leshabari S, Sangu W, Hanselman B, Patil CL. Healthcare providers' knowledge and practices associated with postpartum hemorrhage during facility delivery in Dar es Salaam, Tanzania. Int J Gynecol Obstet. 2016;135(3):268–71.
8. Bouet PE, Brun S, Madar H, Schinkel E, Merlot B, Sentilhes L. Surgical management of postpartum haemorrhage: Survey of French obstetricians. Sci Rep. 2016;6:1–6.

9. Teunissen PW, Scheele F, Scherpbier AJJA, Van Der Vleuten CPM, Boor K, Van Luijk SJ, et al. How residents learn: Qualitative evidence for the pivotal role of clinical activities. Med Educ. 2007;41(8):763–70.

10. Reznick RiK, MacRae H. Teaching Surgical Skills — Changes in the Wind. N Engl J Med. 2006;355(25):2664–9.

11. Aggarwal R, Darzi A. Technical-Skills Training in the 21st Century. N Engl J Med. 2006;355(25):2695–6.

12. Battaglia M. Convenience Sampling. In: Lavrakas PJ. Encyclopedia of Survey Research Methods. Thousand Oaks: Sage Publications, Inc; 2011. p 149.

13. Suskin BG, Sciscione AM, Teigen N, Jenkins TC, Wapner RJ, Gregg AR, et al. Revisiting the challenges of training Maternal Fetal Medicine fellows in chorionic villus sampling. Am J Obstet Gynecol. 2016;215(6):777.e1-777.e4.

14. Process of translation and adaptation of instruments. World Health Organization. [Internet]. [cited 2019 Apr 17]. Available from: http://www.who.int/substance_abuse/research_tools/translation/en/

15. Dreyfus SE. The five-stage model of adult skill acquisition. Bull Sci Technol Soc. 2004;24(3):177–81.

16. American Educational Research Association. Standards for educational and psychological testing. 2014.

17. Frenk J, Chen L, Bhutta ZA, Cohen J, Crisp N, Evans T, et al. Health professionals for a new century: transforming education to strengthen health systems in an interdependent world. Lancet. 2010;376(9756):1923–58.

18. General Board of Epidemiology. Weekly Epidemiological Surveillance Report. Information for the epidemiological week 52. Mexico [Internet]. 2017 [cited 2019 Apr 17]. Available from: http://www.omm.org.mx/images/stories/Documentos grandes/BOLETIN_52_2017_COMPLETO.pdf

19. Accreditation Council for Graduate Medical Education. ACGME Program Requirements for Graduate Medical Education in Obstetrics and Gynecology [Internet]. 2017 [cited 2019 Apr 17]. Available from: https://www.acgme.org/Portals/0/PFAssets/ProgramRequirements/220_obstetrics_and_gynecology_2017-07-01.pdf

20. Martinerie L, Rasoaherinomenjanahary F, Ronot M, Fournier P, Dousset B, Tesnière A, et al. Health care simulation in developing countries and low-resource situations. J Contin Educ Health Prof. 2018;38(3):205–12.

21. van Houten-Schat MA, Berkhout JJ, van Dijk N, Endedijk MD, Jaarsma ADC, Diemers AD. Self-regulated learning in the clinical context: a systematic review. Med Educ. 2018;52(10):1008–15.

22. Sawatsky AP, Zickmund SL, Berlacher K, Lesky D, Granieri R. Understanding the challenges to facilitating active learning in the resident conferences: A qualitative study of internal medicine faculty and resident perspectives. Med Educ Online. 2015;20(1).

5.7 Tables.

5.7.1 Table 1. Demographic Data and Educational Resources.

	N = 51
Age, years (median [IQR])	28 [27, 30]
Female gender, n (%)	27 (52.9)
Year of training, n (%)	
1	10 (19.6)
2	13 (25.5)
3	15 (29.4)
4	13 (25.5)
Night shifts per month, n (median [IQR])	10 [8, 11]
Educational resources, n (%)	
Clinical training, patients with PPH [a]	44 (86.3)
Clinical training, patients without PPH [b]	25 (49)
Low/high-fidelity simulation models	13 (25.5)
Workshops	27 (52.9)
Online resources	4 (7.8)
Videos	7 (13.7)
Medical journals	3 (5.9)
Courses and conferences	33 (64.7)
Other	2 (3.9)

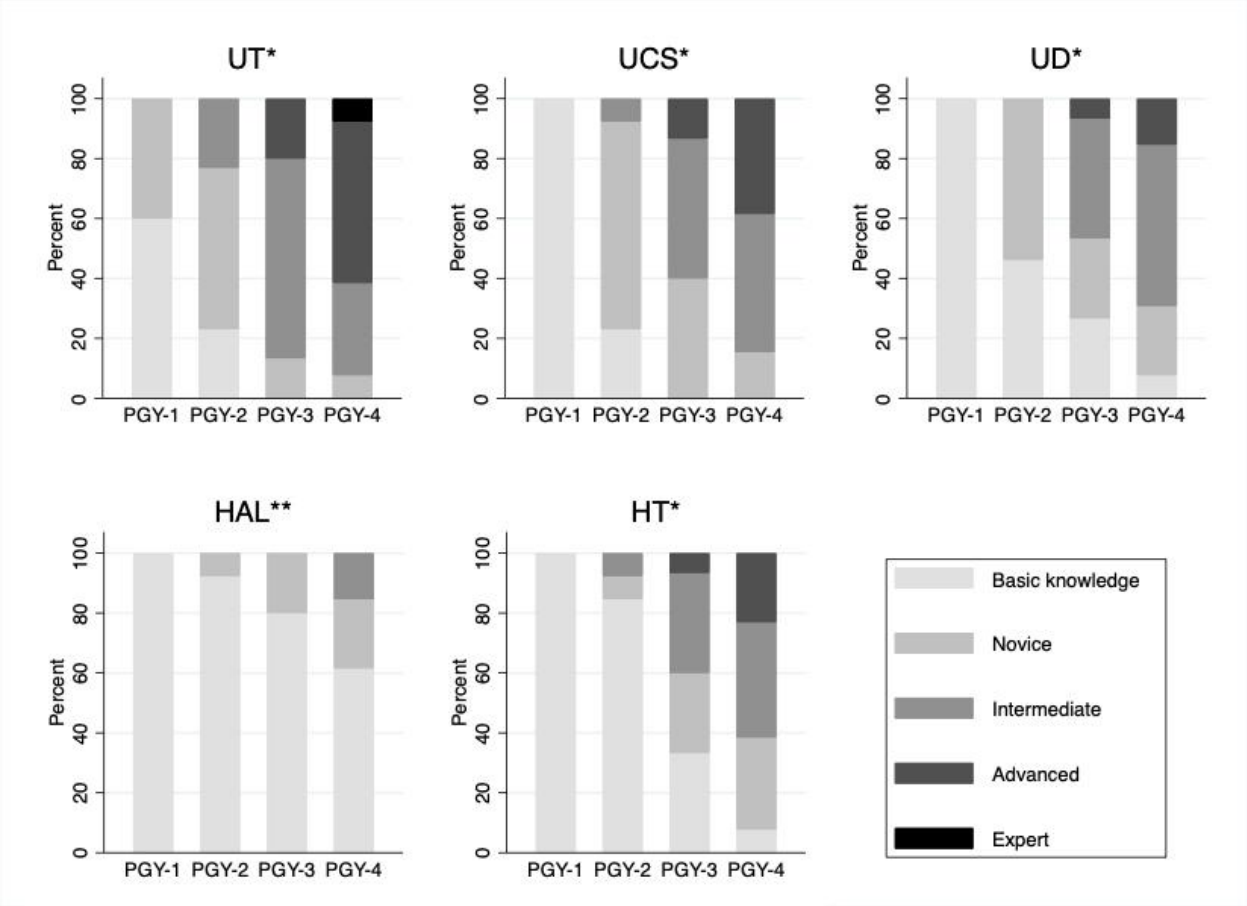
IQR: Interquartile range; PPH: Postpartum hemorrhage.
a = Procedures performed in patients in whom the surgery was required.
b = Procedures performed to prevent PPH.

5.7.2 Table 2. Surgical Techniques to Manage Postpartum Hemorrhage, Overall Knowledge and Experience.

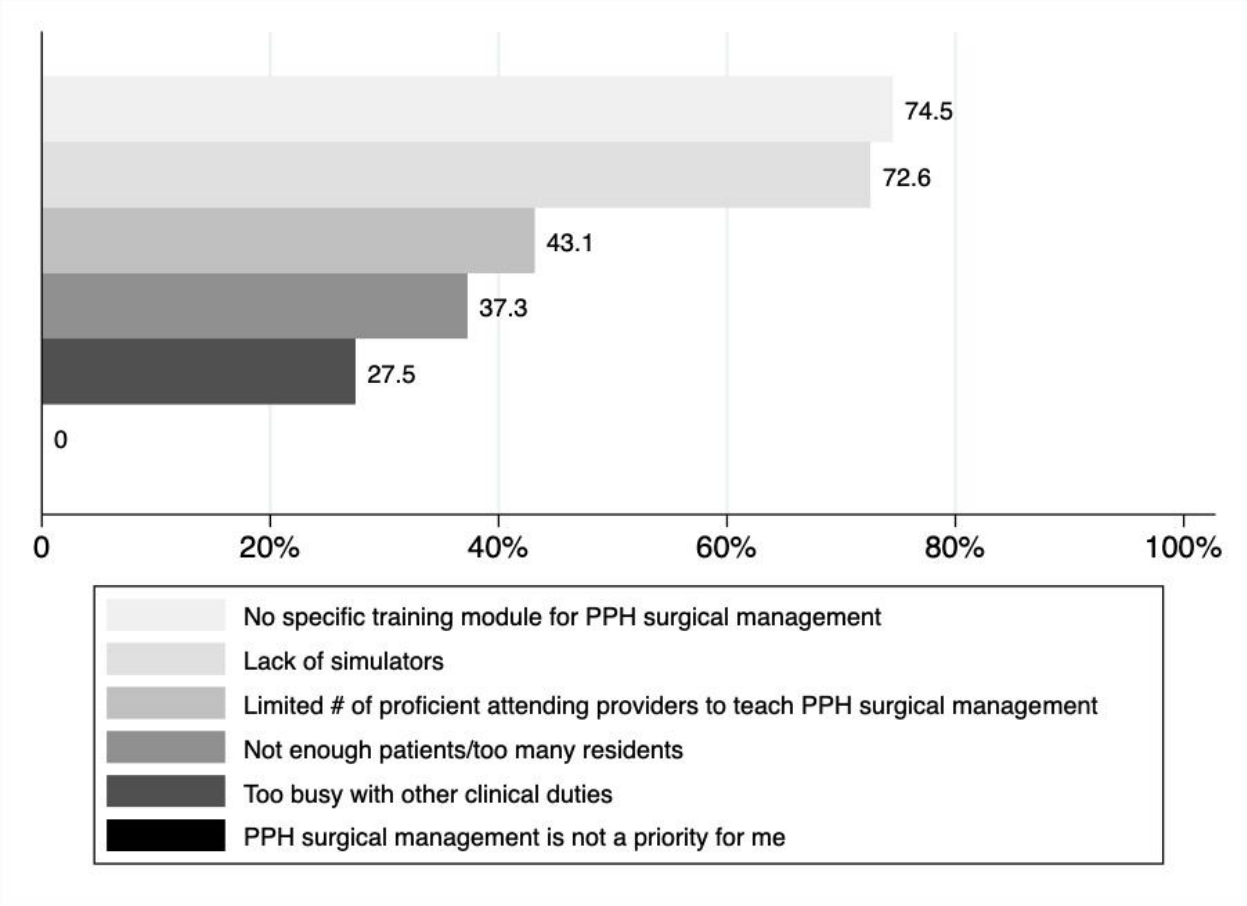
Procedure	*Knowledge of theory and surgical technique N (%)*	*Performance of this technique without supervision N (%)*	*Performance of this technique with a trained specialist N (%)*	*Observation of this procedure N (%)*	*Practice of this technique in a simulated setting N (%)*
Uterine tamponade	48 (94.1)	32 (62.8)	42 (82.4)	48 (94.1)	26 (51.0)
Uterine compression sutures	47 (92.2)	29 (56.9)	40 (78.4)	46 (90.2)	13 (25.5)
Uterine devascularization	39 (78.0)	21 (41.2)	34 (66.7)	39 (76.5)	15 (29.4)
Hypogastric artery ligation	31 (60.8)	4 (7.8)	13 (25.5)	27 (52.9)	6 (11.8)
Gravid hysterectomy	37 (72.6)	12 (23.5)	30 (58.8)	42 (82.4)	3 (5.9)

N = 51.

5.8 Figures.



5.8.1 Figure 1. Self-Reported Competence to Perform Surgical Techniques for Management of Postpartum Hemorrhage. *$p < 0.001$ (comparing 1st, 2nd, 3rd and 4th-year residents), **$p = 0.12$ (comparing 1st, 2nd, 3rd and 4th-year residents). UT = Uterine tamponade; UCS = Uterine compression sutures; UD = Uterine devascularization; HAL = Hypogastric artery ligation; HT = Gravid hysterectomy; PGY-1 = First-year residents; PGY-2 = Second-year residents; PGY-3 = Third-year residents; PGY-4 = Fourth-year residents.



5.8.2 Figure 2. Training Barriers in the Surgical Management of Postpartum Hemorrhage. PPH = Postpartum hemorrhage.

5.9 Supplementary appendix.

5.9.1 Supplementary information, survey.

Training for the Surgical Management of Postpartum Hemorrhage: A Four-State Survey of Resident Physicians in Mexico

1. Age:

2. Gender: Female / Male

3. In what year of the obstetrics and gynecology (OBGYN) residency program are you currently enrolled?
   - 1 / 2 / 3 / 4

4. Are you frequently the physician in charge of the labor and delivery (L&D) unit?
   - Yes / No

5. On average, how many shifts do you have per month?

6. In the L&D unit, do you have the assistance and supervision of an attending OBGYN at any time during the shift?
   - Yes / No

7. In your hospital, what are the resources used to learn the surgical techniques of postpartum hemorrhage (PPH) management?
   Check all that apply:
   - Clinical training, patients with PPH (procedures performed in patients in whom the surgery is required)
   - Clinical training, patients without PPH (procedures performed to prevent PPH)
   - Low/high-fidelity simulation models
   - Workshops
   - Online resources
   - Videos
   - Medical journals
   - Courses and conferences
   - Others

8. Do you know the theory and surgical technique of the *uterine tamponade* (Bakri balloon, Ebb tamponade, Foley catheter)?
   - Yes / No

9. In your clinical practice and/or for educational purposes, have you:

	Yes	No
Performed any of these techniques without supervision		
Performed any of these techniques with the help of a trained specialist		
Seen any of these procedures		

Practiced any of these techniques in a simulated setting		

10. How would you describe your ability to perform these techniques?

- Basic knowledge / Novice / Intermediate / Advanced / Expert

11. Do you know the theory and surgical technique of the *uterine compression sutures* (B-Lynch, Cho, Hayman)?
    - Yes / No

12. In your clinical practice and/or for educational purposes, have you:

	Yes	No
Performed any of these techniques without supervision		
Performed any of these techniques with the help of a trained specialist		
Seen any of these procedures		
Practiced any of these techniques in a simulated setting		

13. How would you describe your ability to perform these techniques?

- Basic knowledge / Novice / Intermediate / Advanced / Expert

14. Do you know the theory and surgical technique of the *uterine devascularization* procedures for PPH (Bilateral uterine artery ligation, Tsirulnikov's triple ligation and/or AbdRabbo's stepwise sequential ligation)?
    - Yes / No

15. In your clinical practice and/or for educational purposes, have you:

	Yes	No
Performed any of these techniques without supervision		
Performed any of these techniques with the help of a trained specialist		
Seen any of these procedures		
Practiced any of these techniques in a simulated setting		

16. How would you describe your ability to perform these techniques?

- Basic knowledge / Novice / Intermediate / Advanced / Expert

17. Do you know the theory and surgical technique of the *hypogastric artery ligation* for severe PPH?
    - Yes / No

18. In your clinical practice and/or for educational purposes, have you:

	Yes	No
Performed this technique without supervision		

Performed this technique with the help of a trained specialist		
Seen this procedure		
Practiced this technique in a simulated setting		

19. How would you describe your ability to perform this technique?

    - Basic knowledge / Novice / Intermediate / Advanced / Expert

20. Do you know the theory and surgical technique of a total or subtotal *gravid hysterectomy*?
    - Yes / No

21. In your clinical practice and/or for educational purposes, have you:

	Yes	No
Performed this technique without supervision		
Performed this technique with the help of a trained specialist		
Seen this procedure		
Practiced this technique in a simulated setting		

22. How would you describe your ability to perform this technique?

    - Basic knowledge / Novice / Intermediate / Advanced / Expert

23. In your hospital, what are the existing barriers for learning surgical techniques of PPH management?
    Check all that apply:
    - Not enough patients/too many residents
    - Limited # of proficient attending providers to teach PPH surgical management
    - There is no specific training module for PPH surgical management
    - Too busy with other clinical duties
    - PPH surgical management is not a priority for me
    - Lack of simulators to practice the surgical techniques

24. Considering the case of a patient with uterine atony after a vaginal delivery, who is hemodynamically stable, and has the desire to have more children.
    What would be the sequence of *surgical procedures* that you would perform after medical treatment and uterine tamponade failed?
    - Uterine devascularization
    - Hypogastric artery ligation
    - Uterine compression sutures
    - Gravid hysterectomy

5.9.2 Supplementary Table 1. Supervision and Self-Assessed Competences for Postpartum Hemorrhage Surgical Management Comparing First- and Fourth-Year Residents.

	First-year n = 10	**Fourth-year** n = 13	**P-value**
Physician in charge of the L&D (n, %)	8 (80)	11 (84.6)	1.00
Assistance and supervision at any time (n, %)	5 (50)	10 (76.9)	0.22
Uterine tamponade, know the theory and surgical technique (n, %)	7 (70)	13 (100)	0.07
Uterine tamponade, self-assessed competence (n, %)			<0.001
Basic knowledge	6 (60)	-	
Novice	4 (40)	1 (7.7)	
Intermediate	-	4 (30.8)	
Advanced	-	7 (53.8)	
Expert	-	1 (7.7)	
Uterine compression sutures, know the theory and surgical technique (n, %)	7 (70)	13 (100)	0.07
Uterine compression sutures, self-assessed competence (n, %)			<0.001
Basic knowledge	10 (100)	-	
Novice	-	2 (15.4)	
Intermediate	-	6 (46.2)	
Advanced	-	5 (38.5)	
Expert	-	-	
Uterine devascularization, know the theory and surgical technique (n, %)	4 (40)	12 (92.3)	0.02
Uterine devascularization, self-assessed competence (n, %)			<0.001
Basic knowledge	10 (100)	1 (7.7)	
Novice	-	3 (23.1)	
Intermediate	-	7 (53.8)	
Advanced	-	2 (15.4)	

Expert	-	-	
Hypogastric artery ligation, know the theory and surgical technique (n, %)	3 (30)	13 (100)	<0.001
Hypogastric artery ligation, self-assessed competence (n, %)			0.14
Basic knowledge	10 (100)	8 (61.5)	
Novice	-	3 (23.1)	
Intermediate	-	2 (15.4)	
Advanced	-	-	
Expert	-	-	
Gravid hysterectomy, know the theory and surgical technique (n, %)	4 (40)	13 (100)	0.02
Gravid hysterectomy, self-assessed competence (n, %)			<0.001
Basic knowledge	10 (100)	1 (7.7)	
Novice	-	4 (30.8)	
Intermediate	-	5 (38.5)	
Advanced	-	3 (23.1)	
Expert	-	-	

L&D = Labor and delivery unit.

Chapter 6

Summary of Paper 1 and Paper 2 conclusions

In the *first* paper we performed a controlled interrupted time series analysis and we found that the average weekly incidence of immediate postpartum hemorrhage detection increased by over two-fold for vaginal deliveries (the intervention series) but remained constant for cesarean deliveries (the control series) after implementation of a novel device for quantitation of blood loss after vaginal delivery. There was no difference in transfusion rate, secondary uterotonic use, vasopressor administration, surgical procedures, or postpartum hemorrhage-related interventions. In the subgroup of patients who had post-delivery hematocrits measured, the mean difference between delivery blood loss and calculated blood loss was smaller in the device group vs. the visual estimation group.

Regarding the *second* paper, most obstetrics and gynecology residents in Mexico reported theoretical knowledge of surgical interventions (i.e. uterine tamponade, uterine devascularization, uterine compression sutures, hypogastric artery ligation, gravid hysterectomy) for postpartum hemorrhage, but their self-rated ability to independently perform such skills and a curriculum focused on postpartum hemorrhage management was suboptimal despite early autonomy.

Chapter 7

Discussion and perspectives

The strengths of the *first* paper include the inclusion of a control series (cesarean deliveries) to control for concurrent events. Moreover, the use of segmented regression permits to assess the trend over time on the primary outcome in each period (i.e. the intercept changed after the introduction of the device). We thoroughly adjusted for confounders using propensity score odds. Nevertheless, residual confounding may limit the validity of our results. Other limitations in our study include the lack of standardization of the visual estimation method. The time to intervention for management was a variable we could not collect retrospectively. The compliance rate of 68.1% for the device may have introduced selection bias in our study. Impact of the device requires further study, with the integration of response protocols and an assessment of effects at lower resource, lower-staffed centers in low- and middle-income countries. Moreover, a larger study is needed to test whether blood loss quantitated by the device impacts patients' outcomes.

For the *second* paper, we performed a multistate survey in Mexico, and we obtained candid responses from the obstetrics and gynecology residents. Moreover, the collected surveys were representative of each year of residency training, with equal distribution. Nevertheless, we acknowledge the limitations of our study, the response rate was not optimal, and we do not have the data to compare the non-responders; this could limit the generalization of our results. Given the anonymity of the survey, we could not perform a subgroup analysis to assess the differences within and between centers. Further research is warranted to identify comprehensive and standardized curricula that emphasize increased supervision, early mastery of surgical techniques, and simulation training for postpartum hemorrhage surgical expertise.