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2

Risk assessment tools to predict postpartum hemorrhage

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Postpartum hemorrhage (PPH) is a leading cause of maternal morbidity and mortality, and accurate risk assessments may allow providers to anticipate and prevent serious hemorrhage-related adverse events. Multiple category-based tools have been developed by national societies through expert consensus, and these tools assign low, medium, or high risk of hemorrhage based on a review of each patient's risk factors. Validation studies of these tools show varying performance, with a wide range of positive and negative predictive values. Risk prediction models for PPH have been developed and studied, and these models offer the advantage of more nuanced and individualized prediction. However, there are no published studies demonstrating external validation or successful clinical use of such models. Future work should include refinement of these models, study of best practices for implementation, and ultimately linkage of prediction to improved patient outcomes.

Why assess postpartum hemorrhage risk?

Despite advances in the care of patients with postpartum hemorrhage (PPH), this delivery complication continues to contribute significantly to maternal morbidity and mortality [1–3]. Accurately predicting PPH prior to delivery can improve patient outcomes by allowing transfer to higher level of care, advanced preparation (e.g., additional intravenous access and pretransfusion testing), or

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prophylactic therapies (e.g., tranexamic acid). As obstetric hemorrhage is the most common cause of pregnancy-related death on the day of delivery and within 1–6 days postpartum, clinicians who provide inpatient care on labor and delivery units have the potential to significantly alter patient trajectories by proactively identifying patients at risk of this adverse event and standardizing care approaches to minimize patient injury [4].

Most obstetric hemorrhages have also been shown to be preventable, with nearly 90% demonstrating at least one provider-related preventability factor and one-third demonstrating at least one system-related factor [5]. Standardized methods of PPH risk stratification have the potential to address many of these factors, including failure to transfer to higher level of care, delays in diagnosis or treatment, and communication failures within and between care teams. Understanding these benefits, both the American College of Obstetricians and Gynecologists (ACOG) and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) now recommend using an evidence-based PPH risk assessment tool during labor and delivery hospital admissions. Given the potential for meaningful patient benefit in conjunction with these new regulatory requirements, there is a strong incentive for labor and delivery units to implement PPH risk assessment.

Defining postpartum hemorrhage

Before discussing options for and benefits of different risk prediction tools, it is first essential to discuss the importance of defining PPH along a spectrum ranging from estimated blood loss criteria to massive and life-threatening hemorrhage. Historically, PPH has most commonly been defined by estimated blood loss cutoffs of either 1000 ml for any delivery mode or 500 ml and 1000 ml for vaginal and cesarean delivery (CD), respectively. More recent investigations have defined PPH by the need for transfusion of at least 1 unit of packed red blood cells (pRBC), with the understanding that transfusion represents an important marker of PPH severity and potential for morbidity. Finally, PPH can be defined as a severe phenotype, requiring transfusion of $\geq$4 units of pRBC. This definition has been used commonly in research on PPH prediction as this measure is included as a severe maternal morbidity criterion by the United States Centers for Disease Control [6]. In migrating toward a more nuanced definition, Oberhardt et al. recently proposed a comprehensive framework for defining multiple levels of PPH severity (Table 1) [7,8]. In evaluating the performance of any PPH risk prediction tool, it is important to distinguish how PPH is defined in the setting in which the risk prediction tool is used.

Clinical risk factors for predicting postpartum hemorrhage

One major difficulty in predicting PPH stems from a lack of consensus regarding potential risk factors for PPH. A recent meta-analysis attempted to summarize the evidence on risk factors for atonic

Table 1
Proposed framework for phenotyping postpartum hemorrhage.

PPH severity level	Definition	Associated ICD codes
1	Documentation of uterotonic medication administration in the EHR	
2	ICD diagnosis code for postpartum hemorrhage	ICD-9: 66600, 66602, 66604, 66610, 66612, 66614, 66620, 66622, 66624 ICD-10: O720, O721, O722
3	Blood bank documentation of transfusion of 1–3 units of packed red blood cells OR Documentation of Bakri balloon placement in EHR	
4	Blood bank documentation of transfusion of $\geq$4 units of packed red blood cells OR ICD code for hysterectomy during delivery admission	ICD-9: 68.29, 68.39, 68.49, 68.69 ICD-10: 0UT90ZZ, 0UTC0ZZ, 0UTC7ZZ, 0UBC0ZZ, 0U590ZZ

EHR = electronic health record, ICD = International Classification of Diseases, PPH = postpartum hemorrhage.
Data from Oberhardt M, Friedman AM, Perotte R, et al. A principled framework for phenotyping postpartum hemorrhage across multiple levels of severity. AMIA Annu Symp Proc 2019; 2019:691–8.

PPH and identified 47 potential factors, with 15 deemed definite or likely risk factors and the remaining 32 showing contradictory or unclear evidence of association with PPH [9]. The risk factors were categorized into those pertaining to maternal history or demographics, maternal comorbidities, and pregnancy-related, labor-related, and delivery-related factors. Maternal demographic factors that may contribute to the development of PPH include maternal age, race, ethnicity, parity, prior PPH, prior uterine surgery, or family history of PPH. Maternal comorbid medical conditions, such as chronic hypertension, diabetes, anemia, obesity, leiomyoma, thrombocytopenia, and coagulopathy, may also play a role. Multiple pregnancy-related conditions, including polyhydramnios, multiple gestation, macrosomia, placenta previa, placental abruption, and abnormally adherent placenta, are also likely associated with PPH. During labor, additional risk factors may develop, such as induction of labor, chorioamnionitis, prolonged oxytocin exposure, magnesium exposure, and prolonged or precipitous labor. Finally, gestational age at delivery and mode of delivery may affect the risk of PPH. Unfortunately, the evidence supporting or refuting each of these as PPH risk factors varies, and the volume of studies to consider is substantial. Thus, clinical decision support tools have an important role in helping providers aggregate available data into an informed decision regarding PPH risk.

Predicting postpartum hemorrhage: Current state

One of the first organizations to propose standardization of PPH care, including uniform risk assessment, was the California Maternal Quality Care Collaborative (CMQCC), which published a risk tool as part of its “Obstetric Hemorrhage Hospital Level Implementation Guide” in 2010 [10]. Shortly thereafter, other national organizations, including the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN) and the American College of Obstetricians and Gynecologists (ACOG) Safe Motherhood Initiative (SMI), published similar PPH risk prediction tools [11,12]. Each of these three tools was created through expert consensus and assigns low, medium, or high probability of PPH based on the presence or absence of PPH risk factors (Table 2). While these tools have known limitations, their use has been shown to improve patient outcomes, including earlier resolution of bleeding, lower rates of transfusion, and decreased incidence of disseminated intravascular coagulation compared to historic methods of individual clinician risk assessments [13].

In addition to PPH-specific tools, there are currently also early warning systems designed to detect maternal deterioration and alert clinicians to high-risk patients. One such tools is the Modified Early Obstetric Warning Score (MEOWS), which calculates a score based on maternal temperature, systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, oxygen saturation, level of consciousness, and the presence of urine output. While these scoring systems do not replace PPH prediction tools, they can be used in conjunction with such tools to further improve maternal morbidity from PPH {Mackintosh [24] #1280}.

Accuracy of current postpartum hemorrhage risk prediction tools

The accuracy of these risk prediction tools has also been assessed in multiple validation studies. The first such validation study was a retrospective cohort study published in 2013, which evaluated 10,134 vaginal and cesarean deliveries over 1 year at a single institution. International Classification of Diseases (ICD) codes were used to define risk factors, and patients were classified as being at low, medium, or high risk of PPH using the risk tool published by CMQCC [14]. PPH was defined as transfusion of $\geq$1 unit of pRBC, and based on this definition, 139 mothers (1.4%) developed PPH. The rates of PPH were 0.8%, 2.0%, and 7.3% in the low-, medium-, and high-risk groups, respectively. This corresponded to a relative risk of 6.5 for those patients deemed high risk.

A subsequent validation study conducted by Kawakita et al. evaluated the ability of CMQCC, AWHONN, and SMI risk tools to predict transfusion of $\geq$1 unit (PPH) or $\geq$ 4 units (severe PPH) of pRBC following CD [15]. Seventy six out of 6301 patients experienced severe PPH, for a rate of 1.2%. The tools varied significantly in both the proportion of patients classified into each category (Fig. 1), and the positive and negative predictive values of the tool to predict PPH (Table 3). In general, however, negative predictive value was high (96–99%) for both medium- and high-risk classifications for PPH (transfusion $\geq$1 unit pRBC) and was >99% for both medium- and high-risk classifications for severe

Table 2
Comparison of current category-based postpartum hemorrhage risk assessment tools.

	California Maternal Quality Care Collaborative (CMQCC)	Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN)	American College of Obstetricians and Gynecologists Safe Motherhood Initiative (ACOG SMI)
Admission risk factors			
Multiple gestation	Medium	Medium	Medium
Large leiomyomas	Medium	Medium	Medium
Prior postpartum hemorrhage	Medium	Medium (1)/High (>1)	Medium
Prior cesarean delivery or uterine surgery/scar	Medium	Medium	Medium
>4 prior births	Medium (vaginal delivery only)	Medium (vaginal delivery only)	Medium (vaginal or cesarean delivery)
Chorioamnionitis	Medium	Medium	
Induction of labor (with oxytocin) or cervical ripening		Medium	
Family history of PPH in first degree relative		Medium	
Fetal demise		Medium	
Polyhydramnios		Medium	
Macrosomia			Medium (EFW>4000 g)
Obesity			Medium (BMI>40)
Placenta previa, low lying placenta	High	High	High
Suspected or known placenta accreta spectrum disorder	High	High	High
Hematocrit <30 and other risk factors	High	High	Medium
Thrombocytopenia	High (<100,000)	High (<100,000)	High (<70,000)
Active bleeding (greater than show)	High	High	High
Known coagulopathy	High	High	High
Intrapartum risk factors			
Prolonged labor		Medium (>18 h)	
Prolonged second stage	Medium	Medium (>2 h)	Medium
Oxytocin augmentation	Medium ("prolonged" use)	Medium (any use)	Medium (use >24 h)
Chorioamnionitis	Medium	Medium (temperature >100.4 °F)	Medium
Magnesium sulfate treatment	Medium	Medium	Medium
Suspected abruption		High	
New active bleeding	Medium	High	High
Postpartum risk factors			
Vacuum- or forceps-assisted birth	Medium	Medium	
Cesarean delivery	Medium	Medium	
Retained placenta or difficult placental extraction	Medium	High	
Genital tract trauma		Medium (3rd/4th degree perineal laceration, vaginal laceration, cervical laceration, or mediolateral episiotomy)	
Precipitous delivery		Medium	
Shoulder dystocia		Medium	
Concealed abruption		High	
Uterine inversion		High	

BMI = body mass index, EFW = estimated fetal weight, PPH = postpartum hemorrhage.
AWHONN and ACOG SMI tools consider any patient with 2 or more medium risk factors to be high risk.
For each risk assessment tool, low risk patients are those without any listed medium or high-risk factors.

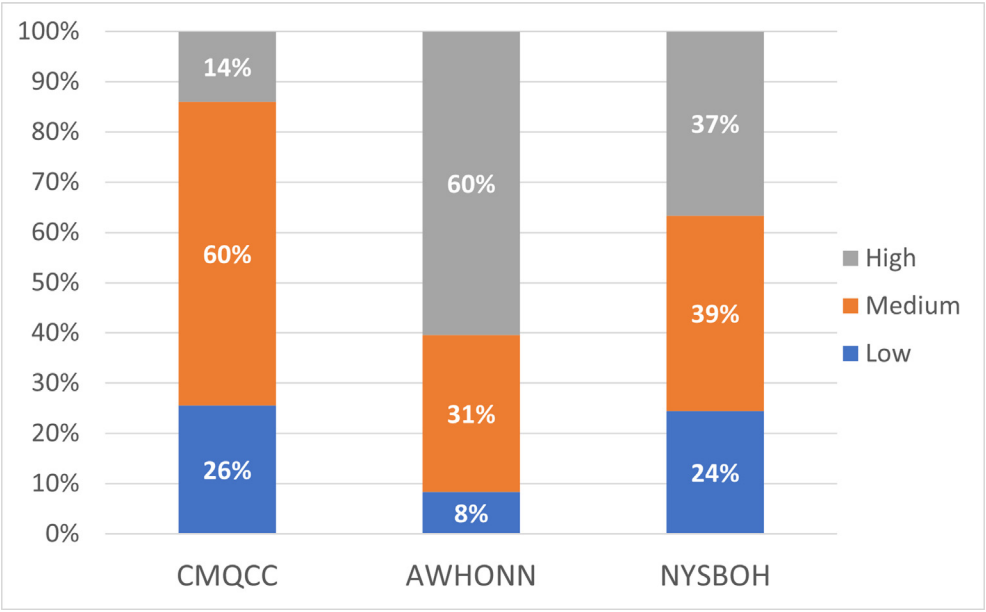

Fig. 1. Distribution of patients assigned to low-, medium-, and high-risk categories for PPH based on assessment tools developed by the California Maternal Quality Care Collaborative (CMQCC), the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN), and the American College of Obstetricians and Gynecologists' Safe Motherhood Initiative (SMI). The three tools were applied to a population of 6301 patients undergoing CD at a single institution [15].

PPH (transfusion ≥4 units pRBC). Positive predictive values were uniformly low, but lowest for medium risk classification for severe PPH (1%). Other validation studies have confirmed similar results (Table 3) [16–18].

Predicting postpartum hemorrhage: Future state

Given the limitations of category-based tools for PPH prediction, future work should shift toward statistical models or machine learning for greater gradation of risk. Instead of low-, medium-, and high-risk predictions, clinicians would be able to see a numeric predicted probability of hemorrhage in their patients. This shift reflects a larger trend in medicine toward reliance on artificial intelligence in settings where the amount of data (in this case risk factors and their combined and weighted contribution to PPH risk) has exceeded the capacity of the human brain to process and apply medical decision-making [19]. Many statistical models for PPH prediction have already been generated and studied; however, none have yet been validated or implemented in clinical practice [20]. Additional research is needed not only to develop and validate accurate models but also to prospectively study their effects on patient outcomes. Machine learning, where models learn and adapt from examples rather than explicit rules or instructions, is another option for future development of PPH risk prediction methods [21].

Genetic contributions to postpartum hemorrhage

Along with the clinical risk factors previously discussed, an additional component of PPH risk may stem from genetic factors that are, so far, unmeasured. A study of nearly 500,000 births from the Swedish birth registry, published in 2014, showed that maternal genetics could account for up to 18% of the variance in occurrence of PPH [22]. While the study of genetic contributions to PPH is still in its infancy, multiple ongoing genome-wide association studies of PPH may help to elucidate genetic loci associated with PPH. This will be the first step in understanding possible genetic mechanisms and

Table 3
Accuracy data for postpartum hemorrhage risk prediction tools.

	In predicting EBL>1000 ml			In predicting transfusion ≥1 unit pRBC			In predicting transfusion ≥4 units pRBC		
	CMQCC [16]	AWHONN	SMI [17]	CMQCC [14, 15, 18]	AWHONN [15]	SMI [15, 17]	CMQCC [15]	AWHONN [15]	SMI [15]
Sensitivity	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium
	0.57	N/A	0.52	0.57–0.83	0.96	0.54–0.88	0.91	0.97	0.91
	High	High	High	High	High	High	High	High	High
	0.10	N/A	0.25	0.22–0.46	0.83	0.35–0.67	0.59	0.88	0.78
Specificity	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium
	0.73	N/A	0.71	0.26–0.72	0.09	0.25–0.70	0.26	0.08	0.25
	High	High	High	High	High	High	High	High	High
	0.95	N/A	0.88	0.88–0.96	0.41	0.66–0.88	0.87	0.40	0.64
Positive Predictive Value	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium
	0.10	N/A	0.09	0.03–0.08	0.07	0.04–0.08	0.01	0.01	0.01
	High	High	High	High	High	High	High	High	High
	0.10	N/A	0.11	0.07–0.23	0.09	0.06–0.12	0.05	0.02	0.03
Negative Predictive Value	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium	Medium
	0.97	N/A	0.96	0.96–0.99	0.97	0.97–0.99	1.00	1.00	1.00
	High	High	High	High	High	High	High	High	High
	0.95	N/A	0.95	0.96–0.99	0.97	0.96–0.99	0.99	1.00	1.00

AWHONN = Association of Women's Health, Obstetric and Neonatal Nurses, CMQCC = California Maternal Quality Care Collaborative, EBL = estimated blood loss, PPH = postpartum hemorrhage, pRBC = packed red blood cells, SMI = Safe Motherhood Initiative.

potentially targeting these areas for predictive testing or therapy. PPH prediction tools may one day be able to incorporate genetic risk in addition to clinical risk factors.

What to do when a patient screens positive for postpartum hemorrhage

Given the recent JCAHO mandates for PPH risk stratification, nearly all institutions have likely enacted some form of PPH risk prediction tool. Unfortunately, however, the simple act of employing a standardized tool is unlikely by itself to change provider behavior or alter patient outcomes. In deciding how and when to perform risk stratification, time and resources must be devoted to planning specific actions that will be tied to each tier of risk. Decisions must be made at a systems level concerning how to respond to varying levels of risk, and provider education must be incorporated into risk tool implementation. Potential actions include pretransfusion testing (e.g., type and screen), ensuring availability of blood products, prophylactic uterotonic administration, prophylactic tranexamic acid administration, or transfer to higher level of care, among others. To maximize the benefit from any predictive tools, these actions should be explicitly stated in an institution's PPH risk prediction plan. In addition, tying recommended or required actions to a patient's predicted risk level via clinical decision support within the electronic medical record could help reduce mental load on clinicians [23].

Summary

Accurately predicting PPH allows clinicians to appropriately prepare for and possibly prevent adverse events and morbidity associated with hemorrhage. There are numerous category-based tools currently available from national societies; however, validation studies have demonstrated very low positive predictive values of these tools. Statistical modeling or machine learning may allow more accurate predictions in the future. Whichever tool is used, institutions should develop specific guidance regarding recommended actions in response to each level of risk.

Practice points

- Every institution should use a standardized risk assessment tool for PPH.
- Current tools assign patients to a low, medium, or high risk of PPH based on the presence or absence of clinical risk factors.
- Standardized and specific recommendations should be implemented for patients predicted to be at increased risk of PPH.
- Clinical decision support is an important tool to assist clinicians in complying with recommended practices and can be incorporated into the electronic medical record.

Research agenda

- Statistical models or machine learning may provide more accurate predictions of PPH, but studies of their accuracy and utility are needed.
- Prospective studies tying risk prediction to improved patient outcomes are needed to determine the importance of PPH risk prediction.

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Declaration of competing interest

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References

[1] Reale SC, Easter SR, Xu X, et al. Trends in postpartum hemorrhage in the United States from 2010 to 2014. Anesth Analg 2020;130:e119–22.
[2] Creanga AA, Syverson C, Seed K, et al. Pregnancy-related mortality in the United States, 2011-2013. Obstet Gynecol 2017;130:366–73.
[3] Joseph KS, Boutin A, Lisonkova S, et al. Maternal mortality in the United States: recent trends, current status, and future considerations. Obstet Gynecol 2021;137:763–71.
[4] Petersen EE, Davis NL, Goodman D, et al. Vital signs: pregnancy-related deaths, United States, 2011-2015, and strategies for prevention, 13 States, 2013-2017. MMWR Morb Mortal Wkly Rep 2019;68:423–9.
[5] Della Torre M, Kilpatrick SJ, JU Hibbard, et al. Assessing preventability for obstetric hemorrhage. Am J Perinatol 2011;28:753–60.
[6] Centers for Disease Control and Prevention. Severe maternal morbidity in the United States (last update: February 2, 2021). Available from: https://www.cdc.gov/reproductivehealth/maternalinfanthealth/severematernalmorbidity.html. Last. [Accessed 27 January 2022]. accessed.
[7] Goffman D, Friedman AM, Sheen JJ, et al. A framework for improving characterization of obstetric hemorrhage using informatics data. Obstet Gynecol 2019;134:1317–25.
[8] Oberhardt M, Friedman AM, Perotte R, et al. A principled framework for phenotyping postpartum hemorrhage across multiple levels of severity. AMIA Annu Symp Proc 2019;2019:691–8.
[9] Ende HB, Lozada MJ, Chestnut DH, et al. Risk factors for atonic postpartum hemorrhage: a systematic review and meta-analysis. Obstet Gynecol 2021;137:305–23.
[10] Bingham D, Melsop K, Main E. CMQCC obstetric hemorrhage hospital level implementation guide. In: The California maternal quality care collaborative. Palo Alto, CA: Stanford University; 2010.
[11] Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN). Postpartum hemorrhage risk assessment table

2017. Available from: https://cdn-links.lww.com/permalink/aog/b/aog_134_6_2019_10_06_kawakita_19-1065_sdc2.pdf. [Accessed 12 April 2021]. Last accessed.
[12] The American College of Obstetricians and Gynecologists (ACOG). Safe motherhood initiative obstetric hemorrhage bundle risk assessment table 2019. Available from: https://www.acog.org/community/districts-and-sections/district-ii/programs-and-resources/safe-motherhood-initiative/obstetric-hemorrhage. [Accessed 12 April 2021]. Last accessed.
[13] Shields LE, Smalarz K, Reffigee L, et al. Comprehensive maternal hemorrhage protocols improve patient safety and reduce utilization of blood products. Am J Obstet Gynecol 2011;205:368.e1–8.
[14] Dilla AJ, Waters JH, Yazer MH. Clinical validation of risk stratification criteria for peripartum hemorrhage. Obstet Gynecol 2013;122:120–6.
[15] Kawakita T, Mokhtari N, Huang JC, et al. Evaluation of risk-assessment tools for severe postpartum hemorrhage in women undergoing cesarean delivery. Obstet Gynecol 2019;134:1308–16.
[16] Ruppel H, Liu VX, Gupta NR, et al. Validation of postpartum hemorrhage admission risk factor stratification in a large obstetrics population. Am J Perinatol 2020;38:1192–200.
[17] Hussain SA, Guarini CB, Blosser C, et al. Obstetric hemorrhage outcomes by intrapartum risk stratification at a single tertiary care center. Cureus 2019;11:e6456.
[18] Wu E, Jolley JA, Hargrove BA, et al. Implementation of an obstetric hemorrhage risk assessment: validation and evaluation of its impact on pretransfusion testing and hemorrhage outcomes. J Matern Fetal Neonatal Med 2015;28:71–6.
[19] Rajkomar A, Dean J, Kohane I. Machine learning in medicine. N Engl J Med 2019;380:1347–58.
[20] Neary C, Naheed S, McLernon DJ, et al. Predicting risk of postpartum haemorrhage: a systematic review. BJOG 2021;128:46–53.
[21] Venkatesh KK, Strauss RA, Grotegut CA, et al. Machine learning and statistical models to predict postpartum hemorrhage. Obstet Gynecol 2020;135:935–44.
[22] Oberg AS, Hernandez-Diaz S, Frisell T, et al. Genetic contribution to postpartum haemorrhage in Swedish population: cohort study of 466,686 births. BMJ 2014;349:g4984.
[23] Miller K, Mosby D, Capan M, et al. Interface, information, interaction: a narrative review of design and functional requirements for clinical decision support. J Am Med Inform Assoc 2018;25:585–92.
[24] Mackintosh N, Watson K, Rance S, et al. Value of a modified early obstetric warning system (MEOWS) in managing maternal complications in the peripartum period: an ethnographic study. BMJ Qual Saf 2014 Jan;23(1):26–34. PMID 23868867.