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A Predictive Model for Critical Hemorrhage in Retained Products of Conception: A Multicenter Cohort Study

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Abstract

Women with retained products of conception (RPOC) may experience critical hemorrhage requiring emergent surgical intervention. We aimed to develop a prediction model for critical hemorrhage in RPOC to guide decisions regarding the need for surgical intervention. A mixed-method multicenter cohort study including women diagnosed with RPOC between April 2014 and May 2024 was conducted. Conservative management was initially provided, with surgical intervention performed when critical hemorrhage occurred. The primary outcome was critical hemorrhage during conservative management. A multivariable logistic regression model was developed to identify risk factors and construct an individualized prediction model. Model performance was assessed using the area under the receiver operating characteristic curve (AUC) with 5-fold stratified cross-validation. Among 224 women managed conservatively, 187 (83%) completed treatment without critical hemorrhage, whereas 37 (17%) required intervention. No critical hemorrhage occurred in women without detectable blood flow. In women with blood flow, assisted reproductive technology (ART) use, low serum hemoglobin (Hb) at initial visit and large RPOC diameter were key predictors. The model achieved a cross-validated AUC of 0.872 (95% confidence interval: 0.826–0.917). We also developed an integer-based WATCH score to quantify individualized hemorrhage risk. This model may support timely intervention and reduce unnecessary procedures while preserving fertility.

Introduction

Retained products of conception (RPOC) represent a pathological condition that can arise following any pregnancy termination, affecting up to 6% of all pregnancies [1]. It is characterized by the retention of pregnancy-related tissues, most commonly placental villi, within the uterine cavity [2]. This retained tissue may display abnormal blood flow as well as abnormally dilated blood vessels within the consecutive uterine myometrium. Most women with RPOC experience relatively small amounts of abnormal uterine bleeding, which eventually resolve naturally accompanied with the disappearance of the retained tissue [3]. However, the abnormal blood flow can also lead to life-threatening critical hemorrhage, making RPOC a critical condition to evaluate and manage sufficiently.

Despite its clinical significance, there are no standardized guidelines or protocols for managing RPOC. Treatment options vary widely between institutions from dilatation and uterine curettage, hysteroscopic resection (HR), uterine artery embolization (UAE) with or without HR, hysterectomy, medical therapy, to conservative management [1, 3–5]. Surgical interventions, while effective in resolving the condition, carry risks such as impaired endometrial function, intrauterine adhesions, and reduced ovarian function [6–8]. These potential complications underscore the need for selective intervention, prioritizing women who are at risk of critical hemorrhage, and at the same time avoiding overtreatment which may compromise future fertility.

What remains uncertain in the management of RPOC is how to accurately identify women who will eventually encounter critical hemorrhage. Blood flow has been reported as a key predictive factor [9–12].

Our studies for critical hemorrhage prediction have consistently focused on blood flow, utilizing power Doppler color scoring (PDCS), a four-level grading system, to classify the degree of blood flow [11, 12]. In our prospective study, PDCS was identified as the most potent predictive factor. However, classifications based on imaging, including PDCS, are prone to subjective interpretation limiting its generalizability. Additionally, while we identified other predictive factors such as assisted reproductive technology (ART) usage and serum hemoglobin (Hb) at the initial visit, these findings lacked universality due to being derived from single-center studies [12]. Other reported risk factors include RPOC diameters, trimesters at the current pregnancy termination, previous cesarean section (CS), and manual removal of the placenta (MRP) [13–15]. However, evaluating only the presence or absence of each predictive factor is insufficient for comprehensive assessment. Consequently, there is a need for an objective and universal predictive model for critical hemorrhage which can guide optimal surgical intervention, ensuring neither overtreatment nor undertreatment for women with RPOC. In this study, we aimed to develop a multivariable prediction model to identify women with RPOC who are at risk of developing critical hemorrhage during conservative management.

Results

Patient Characteristics

A total of 250 RPOC women were enrolled in this study. Of these, 5 were lost to follow-up, 21 received active management such as UAE, and the remaining 224 women were followed up with conservative management. Among them, 187 women (83%) completed conservative management without critical hemorrhage (no hemorrhage group), while 37 women (17%) developed critical hemorrhage and were primarily treated with UAE (hemorrhage group) (Fig. 1).

The clinical characteristics of the hemorrhage and non-hemorrhage groups of RPOC women receiving conservative management are shown in Table 1. In the hemorrhage group, serum Hb at the initial visit tended to be lower, and the maximum RPOC diameter tended to be larger. There were no substantial differences between the two groups in terms of age, history of endometriosis or uterine surgery (such as uterine curettage, hysteroscopic surgery, CS, or myomectomy), mode of delivery, or the presence of post-delivery intrauterine interventions (such as uterine curettage or MRP). Notably, there were no cases of critical hemorrhage in the group without blood flow at the initial visit.

Multivariable Logistic Analysis

First, cases without blood flow at the initial visit were considered to have a low hemorrhage risk, and a scoring system was created for cases with blood flow. Based on our previous research and clinical perspective, we listed potential risk factors for critical hemorrhage, including serum Hb at the initial visit, ART usage, maximum RPOC diameter, and trimester. To minimize the AIC, three variables—serum Hb at

the initial visit, ART usage, and maximum RPOC diameter—were selected for the prediction model of critical hemorrhage risk in RPOC (Table 2).

In the predictive logistic model, the factor most strongly associated with critical hemorrhage was serum Hb at the initial visit (odds ratio [OR] = 0.70; 95% CI = 0.57–0.86; p < 0.001). Other factors included ART usage (OR = 1.89; 95% CI = 0.87–4.13; p = 0.11) and maximum RPOC diameter (OR = 1.32; 95% CI = 1.03–1.69; p = 0.026). The ROC AUC of the selected model for estimating the risk of massive hemorrhage in RPOC was 0.872 (95% CI = 0.826–0.917) (Supplementary Fig. S1).

Integer-Based Scoring System

To create an integer-based scoring system for clinical use, the coefficients of each variable were calculated as simple integer ratios based on the change in the coefficient when the maximum RPOC diameter changes by 1 mm, using the logistic model selected above. The relationship between each variable's coefficient, the integer-based score, and diagnostic predictive power is shown in Fig. 2. We named this scoring system the WATCH (Warning and Assessment Tool for Critical Hemorrhage) score.

Observed Hemorrhage Rate by Predicted Probability Group

The predicted hemorrhage rate based on the WATCH score was divided into two risk groups (danger zone and less dangerous zone) at a threshold of 20%, which was set based on the Youden index (18%) (Supplementary Fig. S2). In our dataset, in the less dangerous zone, the actual observed hemorrhage rate was 9% (12 cases out of 133), while in the danger zone, 41.7% (25 cases out of 60) experienced hemorrhage (Supplementary Fig. S2).

Discussion

The most clinically meaningful contribution of this multicenter cohort study is the establishment of a practical and objective tool that enables individualized prediction of critical hemorrhage in women with retained products of conception (RPOC). Although most women with RPOC experience only mild uterine bleeding and ultimately achieve spontaneous resolution with conservative management, critical hemorrhage occurs in only a subset of cases but can develop abruptly and unexpectedly. Critical hemorrhage in RPOC is a sudden and unpredictable event that often occurs outside the hospital setting, making it difficult for clinicians to determine which women can safely continue conservative management and which require earlier intervention. In routine outpatient practice—where most women with RPOC are initially evaluated and the majority ultimately achieve resolution with conservative management—the subset who develop critical hemorrhage face two opposing but equally problematic clinical scenarios. One is delayed intervention, allowing bleeding to progress to emergency procedures; the other is unnecessary surgical intervention performed out of caution, potentially compromising future fertility. By integrating simple and universally obtainable clinical parameters, our predictive model

provides a framework for early identification of women at high risk for massive bleeding *before* catastrophic events occur, thereby supporting safer and more fertility-preserving management strategies.

Blood flow has long been recognized as a key indicator of hemorrhage risk [9, 10, 13, 16], and our findings reaffirm its central role. Previous retrospective and prospective studies, including our own, have demonstrated the strong association between vascularity and hemorrhage severity. Mori et al. [11] highlighted the strength of blood flow intensity as an indicator, while Sonehara et al. [12] confirmed its predictive potential through a prospective study. Other studies, such as those by Akiba et al. [16] and Kamaya et al. [9], have also emphasized the importance of vascularity in predicting severe postpartum hemorrhage or the need for surgical intervention. However, existing vascularity classifications—including PDCS, Kamaya's four-level grading, and the Gutenberg system [17] —are limited by subjectivity and variability in ultrasound settings, reducing their reproducibility across facilities (Supplementary Fig. S3). These systems require consistent machine settings and operator expertise, which are difficult to standardize in real-world clinical environments.

To overcome these limitations, we simplified vascularity assessment into a binary "present" or "absent" classification. This approach markedly enhances objectivity and applicability in diverse clinical settings. Importantly, no woman with absent blood flow experienced critical hemorrhage, underscoring the reliability of this simplified method as an initial triage step. This finding is particularly valuable in outpatient practice, where rapid and reproducible assessment is essential. By reducing the complexity of vascularity evaluation, clinicians can more confidently identify women at negligible risk of hemorrhage and safely continue conservative management without unnecessary anxiety or intervention.

Among women with detectable blood flow, assisted reproductive technology (ART) usage, lower serum hemoglobin (Hb) at the initial visit, and larger RPOC diameter emerged as significant predictors of critical hemorrhage. These findings are consistent with prior studies and highlight the multifactorial nature of hemorrhage risk [11, 12]. ART usage is known to increase the risk of postpartum hemorrhage (PPH) [18–20] and placenta accreta spectrum (PAS) [21–23], both of which are closely related to RPOC [24–26]. However, evidence directly linking ART to RPOC-related PAS remains limited. Jwa et al. evaluated 132 women with RPOC using the Japanese ART registry and reported that women with RPOC were significantly more likely to have PAS than those without RPOC (24.2% vs 0.45%, $p < 0.001$) [27]. Although focal PAS is believed to be included within the spectrum of RPOC, definitive diagnosis requires uterine specimens, and hysterectomy is rarely performed in reproductive-aged women with RPOC, making confirmation difficult. Takahashi et al. retrospectively reviewed 323 women with RPOC and found that hypervascularity and ART usage were associated with an increased need for hemostatic procedures for subsequent bleeding [10]. Furthermore, recent evidence indicates that among ART procedures, frozen embryo transfer (FET) carries a higher risk of PAS than fresh embryo transfer, and that within FET, hormone replacement cycles confer a greater risk than natural ovulatory cycles [10]. These findings suggest that ART-related abnormalities in placentation or impaired decidualization may contribute not only to PAS but also to the hemorrhagic complications observed in RPOC. Although detailed ART

protocol information was unavailable for many emergency referrals in our study, the consistent association between ART and severe bleeding across multiple studies underscores the importance of ART as a clinically meaningful predictor in our model.

Serum Hb, although an indirect marker of cumulative blood loss, demonstrated a strong inverse association with hemorrhage risk. This finding aligns with previous reports and suggests that lower Hb levels at the initial visit may serve as an indirect indicator of substantial blood loss during delivery or the postpartum period. Such cumulative blood loss may characterize the subgroup of women who are predisposed to developing critical hemorrhage when RPOC is present. The predictors identified in our multivariable analysis offer additional insights into this relationship. In theory, cumulative blood loss during delivery and postpartum should correlate more directly with the risk of critical hemorrhage; however, these metrics are notoriously difficult to quantify. Accurate estimation of intrapartum blood loss is hindered by the inability to distinguish amniotic fluid from blood, and postpartum bleeding is challenging to track once women are discharged from the hospital. In this context, serum Hb at the initial visit—despite being only an indirect reflection of prior blood loss—served as a practical and clinically meaningful surrogate. It showed a significant odds ratio of 0.71 (95% CI 0.57–0.87, p = 0.001), indicating that each 1.0 g/dL increase in Hb was associated with a 29% reduction in the likelihood of critical hemorrhage. This result is consistent with the findings of Kamaya et al., who reported a similar odds ratio of 0.69 (95% CI 0.55–0.86, p < 0.0009) [9]. Together, these observations underscore the importance of serum Hb at the initial visit as an accessible and objective predictor of hemorrhage risk in women with RPOC.

RPOC diameter has been consistently recognized as a potential predictor of critical hemorrhage in prior studies [9–13, 16, 28, 29]. A retrospective study of 56 women with RPOC compared those with severe postpartum hemorrhage (n = 14) to those without (n = 42) and evaluated clinical factors including maximum diameter, hypervascularity, and the interval from pregnancy to RPOC suspicion. The median RPOC diameter (mm) was significantly larger in women with severe PPH than in those without [44.0 (15–72) vs 23.5 (3–58), p = 0.0103], and the authors proposed 44 mm as the optimal cutoff value [13]. Notably, RPOC diameter remained an independent predictor of severe PPH even after accounting for hypervascularity, underscoring its clinical relevance. In our study, RPOC diameter also demonstrated a significant association with hemorrhage risk, with each 1.0-mm increase corresponding to a 2% increase in the likelihood of critical hemorrhage. Because RPOC diameter is a basic and routinely obtained measurement during gynecologic ultrasound examinations, it represents a practical and easily applicable parameter for risk prediction in everyday clinical practice.

While these individual predictors provide valuable insights, their greatest clinical value emerges when they are integrated into a unified scoring system. The WATCH score translates complex risk information into a simple numerical and visual format that can be readily used in outpatient settings. This enables clinicians to stratify women into high- and low-risk groups with confidence, facilitating timely and appropriately targeted intervention. High-risk women can be monitored more closely or undergo planned intervention before massive bleeding occurs, while low-risk women can safely continue conservative

management, avoiding unnecessary surgical procedures. This risk-stratified approach directly contributes to fertility preservation by minimizing avoidable uterine interventions.

The WATCH score also addresses a major gap in existing literature. Previous studies have identified individual predictors of hemorrhage or the need for surgical intervention, but few have translated these findings into a clinically applicable tool that supports real-time decision-making. Our scoring system is derived from objective, routinely available clinical parameters—history taking, basic blood tests, and standard ultrasound imaging—making it feasible for use in a wide range of clinical environments, including community hospitals and outpatient clinics. The multicenter design of this study further enhances the real-world relevance of the WATCH score, as it reflects a diverse patient population and varying clinical practices.

Another strength of this study is the simplification of blood flow interpretation. By reducing vascularity assessment to a binary classification, we improved reproducibility and minimized operator-dependent variability. This is particularly important in settings where ultrasound expertise varies or where standardized machine settings cannot be guaranteed. The WATCH score's reliance on simple, objective parameters enhances its potential for widespread adoption and integration into routine clinical workflows.

Despite these strengths, several limitations should be acknowledged. The sample size and number of participating institutions were modest, which may limit the generalizability of our findings. Additionally, detailed ART protocol information was unavailable for many emergency referrals, preventing further analysis of embryo transfer types. Future studies with larger cohorts and external validation are warranted to confirm the robustness and generalizability of the WATCH score. Prospective validation studies, particularly those incorporating standardized ultrasound protocols and detailed ART data, will further strengthen the evidence supporting the WATCH score's clinical utility.

In conclusion, we developed a simple and objective scoring system that enables individualized prediction of critical hemorrhage in women with RPOC. By facilitating early identification of high-risk cases and supporting timely, appropriately targeted intervention, the WATCH score has the potential to reduce unnecessary surgical procedures and promote safer, fertility-preserving management strategies. Further validation in larger and more diverse populations will help establish its role in routine clinical practice.

Methods

This study was conducted and reported in accordance with the STROBE and TRIPOD statement.

Study Design

This mixed-method multicenter cohort study included 250 women diagnosed with RPOC between April 2014 and May 2024 at two university hospitals (Nagoya and Gunma University Hospital) and one general hospital (Okazaki City Hospital) in Japan. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Nagoya University Hospital (#2016-04488938, 27/01/2017). Written informed consent was obtained from all women who were prospectively enrolled in the study. For retrospective cases, information was made available on the hospital website, and an opt-out option was provided.

Participants

RPOC was diagnosed based on retained tissue detected by transvaginal ultrasound after spontaneous abortion, artificial abortion, or delivery. Additional imaging techniques, such as 3D computed tomography, were used as supplementary diagnostic tools. Critical hemorrhage was defined by the presence of active genital hemorrhage and at least one of the following: loss of consciousness, a shock index of 1 or more, or a serum Hb level of less than 10 g/dL. Women with RPOC were initially managed conservatively unless they experienced critical hemorrhage. In cases of critical hemorrhage, uterine artery embolization (UAE) was performed as the primary treatment. The observation period was defined as the time from the initial visit for RPOC to when the retained tissue was reduced to less than 10 mm on transvaginal ultrasound and serum human chorionic gonadotropin (hCG) levels became negative.

Variables

Candidate variables for predicting the need for surgical intervention were prespecified based on clinical relevance and previous studies. Variables such as multiple birth, trimester at pregnancy termination, postpartum obstetric interventions, and mode of delivery of the present pregnancy were selected based on their potential clinical relevance to increased hemorrhage. In addition, variables including the presence of blood flow within the RPOC, serum hemoglobin levels, and maximum diameter at initial visit, and the mode of conception were selected according to previous studies [11, 12]. Continuous variables included maternal age, gravidity, parity, serum hemoglobin at the initial visit, and maximum RPOC diameter. Binary or categorical variables included ART usage, presence or absence of multiple pregnancy, postpartum intrauterine interventions during the preceding pregnancy, method of conception, and the presence or absence of blood flow on transvaginal ultrasound. This classification facilitated a clear identification of each predictor's type for model development and statistical analysis. No specific blinding procedures were applied because all predictors were obtained from routinely recorded clinical data or objective ultrasound measurements, minimizing the risk of assessment bias.

Missing Data

Missing values for predictors, except for hCG, were handled using multiple imputation to reduce bias and maintain statistical power. hCG measurements were excluded from the analysis due to differences in assay methods across participating institutions.

Statistical Analysis and Model Development

Patient background characteristics were compared between the hemorrhage and no-hemorrhage groups using Fisher's exact test for categorical variables and the Mann–Whitney U test for continuous variables. Categorical variables are presented as counts and percentages, whereas continuous variables are shown as medians and ranges. In line with the variable selection framework recommended by Chowdhury and Turin [30], we first identified clinically important and previously reported candidate variables (Hb at the initial visit, ART, maximum RPOC diameter, and trimester). We noted that no hemorrhages occurred in women with absent blood flow (e.g., PDCS = 1), and based on our prior findings, these cases were assumed to be at very low risk and excluded from the model-building process. For women with detectable blood flow (PDCS ≥ 2), we performed an all-possible subset selection to minimize the Akaike Information Criterion (AIC). Variable selection was performed once on the full dataset. Internal validation was subsequently performed on the selected model. The final predictive model was thus obtained via logistic regression with the selected explanatory variables. Model performance was assessed using receiver operating characteristic (ROC) analysis with 5-fold stratified cross-validation for internal validation, stratified on the outcome (critical hemorrhage). The area under the ROC curve (AUC) and the corresponding 95% confidence interval (CI) were calculated, with the latter derived by the DeLong method. Optimal cutoffs were determined using the Youden index (computed from the ROC of the apparent fit), which maximizes the sum of sensitivity and specificity. Data from women who presented with critical hemorrhage on their initial visit were excluded from the final analysis, because their initial Hb levels might already have been influenced by blood loss. Missing values for other participants were imputed using an appropriate algorithm.

To facilitate clinical application, we converted the final logistic regression coefficients into an integer-based scoring system, which we named the WATCH (Warning and Assessment Tool for Critical Hemorrhage) score. A higher WATCH score corresponds to a lower predicted risk of hemorrhage. We then visualized the relationship between each woman's WATCH score and her predicted hemorrhage probability, proposing a threshold near the Youden index to classify women into two distinct risk groups. All tests were two-sided, and statistical significance was defined as $p < 0.05$. Analyses were performed using IBM SPSS Statistics (version 26; IBM Corp., Armonk, NY, USA) and R software (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria), by the statisticians, B.C. and K.N.

Declarations

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authorship Contributions Statement:

TN, RS and SK conceived and designed the experiments. YK, MS, TS, and SI collected data. KN and BC performed statistical analysis. NM and AM contributed to project administration. SK and TN drafted while SO, MG and AI reviewed and edited. HK supervised the entire study. All authors reviewed the manuscript.

Additional Information

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

Not applicable because data includes patient data.

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Trial registration: #2016-04488938

date of registration: Jan 27, 2017

enrollment of first subject: Feb 13, 2017

Attestation statements:

- The subjects in this trial have not concomitantly been involved in other randomized trials.
- Data regarding any of the subjects in the study has not been previously published unless specified.
- Data will be made available to the editors of the journal for review or query upon request.

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Tables

Table 1 and 2 are available in the Supplementary Files section.

Figures

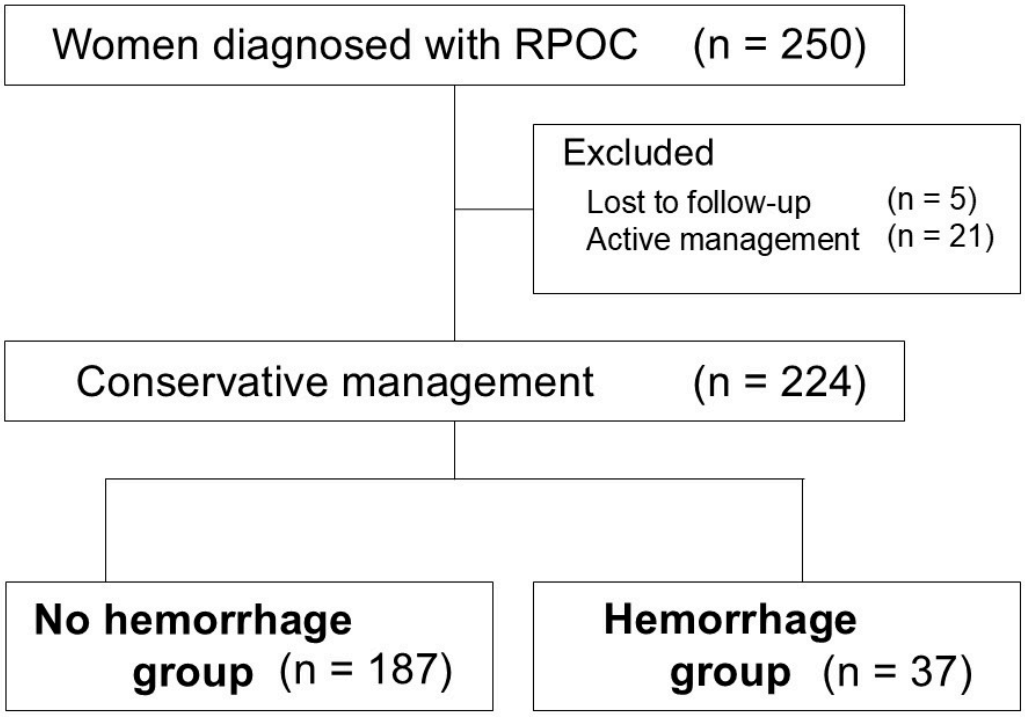

Figure 1

Study Flowchart.
A total of 250 women were diagnosed with RPOC. Among the 224 women enrolled, 83.5% (187/224) completed treatment with conservative management without experiencing critical hemorrhage (no hemorrhage group), while 16.5% (37/224) required intervention due to critical hemorrhage (hemorrhage group).
RPOC, retained products of conception.

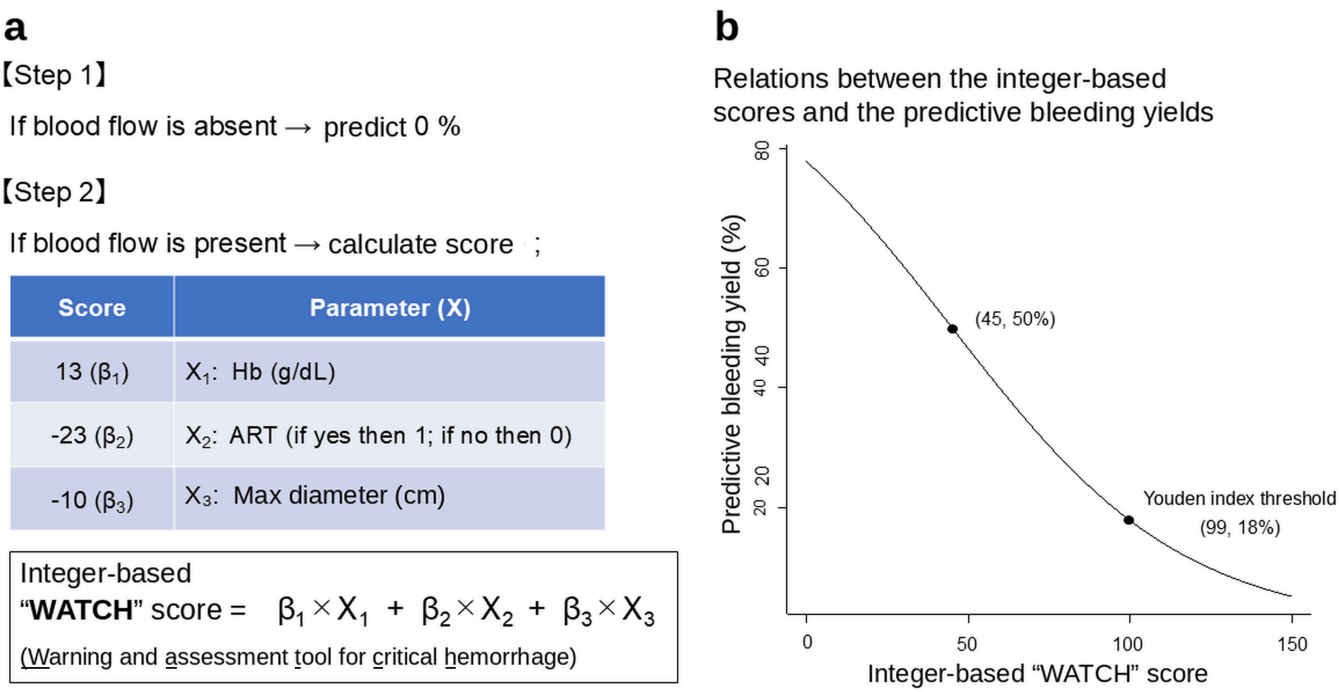

Figure 2

Scoring System estimating the risk for critical hemorrhage.

a If blood flow is absent, the risk for critical hemorrhage is predicted as 0%. If blood flow is present, the score for each factor was multiplied by the unit of each parameter, and the total score was calculated as the sum of these scores. A higher score indicates a lower hemorrhage risk.

b The relationship between the integer-based score and the diagnostic predictive yield is shown. The score at which the predictive yield reaches 50% is 45, and the Youden Index threshold, which corresponds to a predictive yield of 18%, is at a score of 99.

Hb, serum hemoglobin; ART, assisted reproductive technology.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

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