

## Establishing a perinatal red blood cell transfusion risk evaluation model for obstetric patients: a retrospective cohort study

Zhun Xing,<sup>1</sup> Yanjing He,<sup>2</sup> Chao Ji,<sup>3</sup> Chang Xu,<sup>2</sup> Wen Zhang,<sup>2</sup> Yunhui Li,<sup>2</sup> Xiangqian Tan,<sup>2</sup> Ping Zhao,<sup>1</sup> Qiushi Wang,<sup>2</sup> and Liqiang Zheng<sup>3</sup>

**BACKGROUND:** The ability to predict risk factors for blood transfusion after postpartum hemorrhage could enhance the performance of lifesaving procedures in patients who experience postpartum hemorrhage. Therefore, this study aimed to evaluate these risk factors and create a scoring system for blood transfusion evaluations and risk in obstetric patients.

**STUDY DESIGN AND METHODS:** Diagnosis and blood transfusion data of 14,112 women who delivered between January 1, 2015, and December 31, 2015, were analyzed. A binary logistic regression model was used. We conducted univariate analyses of each risk factor as well as multivariable logistic regression analysis. Data of obstetric patients in 2016 validated the receiver operating characteristic curve. A risk prediction score was generated from the transfusion risk factor  $\beta$ -coefficients in the multivariable logistic regression model.

**RESULTS:** In total, 392 (2.94%) of 13,328 patients received transfusions. After multivariable adjustment, polyembryony, anemia, thrombocytopenia, preeclampsia, placenta previa, placental implantation, uterine scarring, uterine rupture, retained placenta, stillbirth, and HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) were significantly associated with perinatal transfusion. Heart disease and hemophilia were not related to transfusion risk. The blood transfusion risk evaluation table was well calibrated.

**CONCLUSIONS:** Our retrospective analysis revealed that diagnoses including polyembryony, anemia, thrombocytopenia, preeclampsia, placenta previa, placenta implantation, uterine scarring, uterine rupture, retained placenta, stillbirth, and HELLP syndrome are significantly associated with perinatal transfusion and are risk factors for blood transfusion. The blood transfusion scoring system could be beneficial for evaluating blood transfusion risk.

The blood volumes of pregnant women are increased during the third trimester of gestation. Compared to those in the nongestational periods, coagulation functions are enhanced and fibrinolysis is suppressed in this period. Thus, women have a greater tolerance for blood loss in the postpartum period.<sup>1</sup> However, pathological events that occur during pregnancy could induce various degrees of postpartum hemorrhage (PPH) and cause loss or consumption of coagulation factors. PPH continues to be the leading cause of maternal mortality. Key lifesaving measures for PPH include accurate evaluation of

**ABBREVIATIONS:** CI = confidence interval; HELLP = hemolysis, elevated liver enzymes, and low platelets; OR = odds ratio; PPH = postpartum hemorrhage; ROC = receiver operating characteristic.

From the <sup>1</sup>Department of Anesthesiology, <sup>2</sup>Department of Blood Transfusion, and the <sup>3</sup>Department of Clinical Epidemiology, Library, Shengjing Hospital of China Medical University, Shenyang, Liaoning Province, China.

*Address reprint requests to:* Qiushi Wang, Department of Blood Transfusion, Shengjing Hospital of China Medical University, No.36, Sanhao Street, Heping District, Shenyang, Liaoning Province, China; e-mail: wangqs18@vip.126.com; or Liqiang Zheng, Department of Clinical Epidemiology, Library, Shengjing Hospital of China Medical University, No.36, Sanhao Street, Heping District, Shenyang, Liaoning Province, China; e-mail: zhenglq@sj-hospital.org.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

This work received support from the Key Clinical Departments Diagnosis and Treatment Capacity Building Projects of Liaoning Province Hospital (LNCCC-D13-2015).

Received for publication April 3, 2018; revision received January 11, 2019, and accepted January 12, 2019.

doi:10.1111/trf.15208

© 2019 The Authors. *Transfusion* published by Wiley Periodicals, Inc. on behalf of AABB.

TRANSFUSION 2019;59;1667-1674

bleeding risk factors, total blood loss, and coagulation status in postpartum women.<sup>2,3</sup>

PPH is defined as a greater than 500 mL blood loss over a 24-hour period for vaginal deliveries and 1000 mL or greater loss for cesarean sections. On the basis of the total blood lost, PPH is divided into four levels: Level 1: blood loss volume, 900 mL (15% of blood volume); Level 2: blood loss volume, 1200–1500 mL (20%–25% of blood volume); Level 3: blood loss volume, 1800–2100 mL (30%–35% of blood volume); and Level 4: blood loss volume, 2400 mL ( $\geq 40\%$  of blood volume).<sup>4</sup> In China, PPH occurs in 2% to 3% of postpartum women, and the incidence rate of Level 4 PPH is approximately 3% to 5%. Up to 25.6% of postpartum women may die because of PPH.<sup>5</sup> Additionally, 4000 postpartum women experience PPH every year in the United Kingdom.<sup>6</sup> Further, 1.1% of postpartum women experience fatal PPH in Japan.<sup>7</sup> According to current data, over 22% of deaths are associated with PPH, with 13% occurring in developed countries and 21% to 31% occurring in developing countries.<sup>8</sup> In the United States, PPH was the third major cause of obstetric-related deaths in 2005.<sup>9</sup>

Known risk factors that induce PPH include the following: age 35 years or older; body mass index greater than 30; previous history of PPH, uterine rupture, placenta previa, polyembryony, and macrosomia; and history of uterine surgery. The bleeding risk for patients with placenta previa has been reported to be increased by 6.7 times.<sup>10,11</sup>

Postpartum women can tolerate mild bleeding,<sup>1</sup> which could mask vital sign changes, thus delaying potentially necessary blood transfusions, aggravating medical conditions, and possibly even leading to death. Patients with severe PPH often require blood transfusions. Some reports have shown that 0.3% to 1% of patients require a blood transfusion.<sup>12,13</sup> It is therefore of great importance to accurately evaluate the risk factors for bleeding in postpartum women. This requires adequate preoperative preparation, appropriate parturition timing, complete blood component preparation, timely administration of blood components, and appropriate intraoperative monitoring of coagulation and hemodynamic factors. Chua et al.<sup>14</sup> reported that placental abruption, placenta previa, preoperative anemia, and cesarean section were factors associated with a high risk of blood transfusion among perinatal and postpartum women. Bao et al.<sup>15</sup> also found that placenta previa was an independent risk factor for blood transfusion among postpartum women and a risk factor for low-to-moderate-volume blood transfusions. However, large-sized studies on the prenatal evaluation of perinatal transfusion risk are lacking. In particular, the role of several underlying diseases in increasing the risk of blood transfusion, or the degree to which they cause the increased risk, has not been reported. Parikh et al.<sup>16</sup> developed a scoring system to predict hypertension risk. In a 3.8-year follow-up of 1717 subjects aged 20 to 69 years, they found that age 35 years or older, female sex, high body mass index, genetic history of hypertension, and smoking were risk factors for hypertension. In that study, a higher risk coefficient indicated a higher risk of hypertension in those patients.

In this study, we screened the patients' data for 13 prenatal complications on the basis of previous reports.<sup>3–5,7,8,11–13</sup>

We analyzed the related morbidities and their correlations with RBC transfusions to identify risk factors associated with blood transfusion and assess patient risk. We developed a similar risk evaluation system for postpartum women to determine the cumulative blood transfusion risk score. This system could help obstetricians and anesthesiologists to predict blood transfusion risk and improve their ability to administer lifesaving procedures to patients with PPH. We evaluated the risk factors for blood transfusion in 14,112 postpartum women who were discharged from our hospital in 2015, from which we developed a scoring system for blood transfusion evaluations in obstetric patients. Herein, we present those results, and the results of internal and external validations for the parturient women in 2015 and 2016 to verify the sensitivity and specificity of the receiver operating characteristic (ROC) curve.

## MATERIALS AND METHODS

### Study population

This was a retrospective cohort study carried out in Shengjing Hospital of China Medical University, which is a Grade III general hospital in Northeastern China, where the annual number of postpartum patient discharges is about 15,000, and over 10,000 neonates are born every year. Obstetric patients often develop complications including placenta previa, uterine scarring, pregnancy-induced hypertension, thrombocytopenia, or other diseases, and many require blood transfusions. For our investigation, the participants were eligible for inclusion if they were hospitalized in Shengjing Hospital of China Medical University between January 2015 and December 2015 and did not meet any of the exclusion criteria. We excluded the following patients: those administered tocolytic treatment while pregnant ( $n = 667$ ); those who had spontaneous abortions at less than 26 gestational weeks ( $n = 219$ ); those who delivered a child at less than 26 gestational weeks ( $n = 148$ ); and those who had missing information on blood transfusions ( $n = 194$ ) or were missing information in their hospital records ( $n = 116$ ). After we applied the exclusion criteria, 13,328 postpartum women remained eligible for the present analysis. The study complies with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Shengjing Hospital of China Medical University. The requirement for informed consent was waived by the Ethics Committee because of the retrospective nature of the study.

To verify the sensitivity and specificity of the stochastic multivariate logistic regression model, we conducted an internal validation of the 2015 parturient women and an external validation of 16,235 selected 2016 parturient women.

### Assessment of risk factors

A standard case report form was developed to assess the participants' characteristics, diagnoses, medical histories,

risk factors, and blood transfusion histories. Data on age, diagnoses, maternal weights, and neonatal weights were collected from the Hospital Information System. Possible transfusion risk factors included:

1. Polyembryony, defined as two or more fetuses in the uterus during one pregnancy
2. Progesterone anemia (hemoglobin of <100 g/L during pregnancy)
3. Thrombocytopenia (platelet count of <100 × 10<sup>9</sup>/L)
4. Preeclampsia, characterized by edema, hypertension, albuminuria, headache, dizziness, vomiting, upper abdominal discomfort, visual disturbances, and/or systolic blood pressure 160 mm Hg or greater (21.3 kPa) at greater than 24 gestational weeks
5. Placenta previa with placentation in the inferior aspect of the uterus, reaching or covering the internal cervical os and positioned lower than the fetal presenting part at greater than 28 gestational weeks
6. Placental implantation, wherein the placental villi penetrate the muscular layer of the uterine wall, representing one of the most severe obstetric complications
7. Scarred uterus which occurs when the gestational sac in a current pregnancy implants into the uterine scar from a previous cesarean delivery, and often leads to massive vaginal bleeding and late uterine rupture
8. Placental abruption, wherein the placenta is implanted in a normal position but becomes partially or entirely separated from the uterine wall at 20 weeks of gestation or during parturition.<sup>17-19</sup>
9. Residual placenta, in which the placenta remains in the uterus for 30 minutes after fetal disengagement, leading to a major cause of PPH
10. Stillbirth, defined as intrauterine fetal death at greater than 20 gestational weeks
11. HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets), a serious complication of pregnancy-induced hypertension in which the primary clinical manifestations include hypertension, proteinuria, and edema, with potential progression to conditions including eclampsia, early placental abruption, disseminated intravascular coagulation, renal failure, acute pulmonary edema, severe ascites, and brain edema
12. Hemophilia (including hemophilia A [factor VIII deficiency] and hemophilia B [factor IX deficiency]), a hereditary coagulation factor deficiency characterized by bleeding from soft tissue, muscle, and joints beginning in childhood
13. Heart disease, caused by congenital or acquired external or internal factors acting on the heart, including coronary atherosclerotic heart disease, rheumatic heart disease, hypertensive heart disease, cor pulmonale, and infectious heart disease

Blood transfusion is defined as the therapeutic infusion of blood components into a patient's veins. Generalized blood transfusions included all blood components including

RBCs, blood plasma, and platelets.<sup>20</sup> However, in this survey, platelet and plasma infusions were not included. The concentration of RBCs was used as a criterion to determine whether a blood transfusion was necessary. The hemoglobin maintenance goal for patients with PPH was 80 g/L or greater. Blood transfusion was performed if the PPH volume was greater than 20% of the total blood volume or if the hemoglobin level was less than 80 g/L.<sup>21</sup> The blood transfusion details of the patients were obtained from the information system in the Department of Blood Transfusion.

### Statistical analysis

Continuous variables are presented as means and standard deviations and were compared using Student's *t* tests. Categorical variables are expressed as frequencies, and Pearson's chi-square tests were used to evaluate independent proportions. A binary logistic regression model was used to fit the predictors to the observed events (perinatal transfusion [yes/no]). Significant predictors of perinatal transfusion were identified by entering candidate risk factors (polyembryony [yes/no], anemia [yes/no], thrombocytopenia [yes/no], preeclampsia [yes/no], placenta previa [yes/no], placental implantation [yes/no], scarred uterus [yes/no], placental abruption [yes/no], residual placenta [yes/no], stillbirth [yes/no], HELLP [yes/no], hemophilia [yes/no], and heart disease [yes/no]) into a stepwise model. These risk factors have been associated with PPH or perinatal transfusion in other studies.<sup>10,11,14,15</sup> We first conducted a series of univariate analyses for each risk factor. Only those variables with a *p* value less than 0.15 were considered for inclusion in the multivariable logistic regression model. We also developed a risk prediction score from  $\beta$ -coefficients for variables associated with perinatal transfusion in multivariable logistic regression models using methods described elsewhere.<sup>22</sup>

We assessed the performance of the risk prediction models by evaluating discrimination using ROC curves, and the corresponding areas under the curves were calculated, as described previously.<sup>23,24</sup> Next, we evaluated the calibration using the modified Hosmer-Lemeshow chi-square statistic.<sup>25</sup> Values exceeding 20 indicated a significant lack of calibration (*p* < 0.01).<sup>26</sup> All analyses were performed using statistical software (SPSS version 13.0, SPSS Inc.; and SAS version 9.2, SAS Institute Inc.). A *p* value less than 0.05 was accepted as significant.

## RESULTS

### Sample

Of 13,328 postpartum women, a total of 392 patients were transfused with RBCs, and the overall transfusion rate was 2.94%. The average age of the patients was 30.52 ± 4.58 years. The average neonatal weight was 2992.04 ± 875.74 g. Other related risk factors are shown in Table 1, which also shows the possible risk factors for patients who underwent or did not undergo RBC transfusions.

**TABLE 1. General information and data on the study patients in 2015**

	With transfusion (n = 392)	Without transfusion (n = 12936)	t/chi-square	p
Age ( $\bar{x} \pm s$ )	31.16 $\pm$ 5.64	30.47 $\pm$ 4.52	2.41	<0.05
Polyembryony, n (%)	31 (7.91)	679 (5.25)	5.33	0.03
Anemia, n (%)	92 (23.47)	423 (3.27)	417.90	<0.01
Thrombocytopenia, n (%)	25 (6.38)	108 (0.83)	112.77	<0.01
Preeclampsia, n (%)	71 (18.11)	1082 (8.36)	45.75	<0.01
Placenta, n (%)	126 (32.14)	378 (2.92)	892.85	<0.01
Placental implantation, n (%)	43 (10.97)	41 (0.32)	672.46	<0.01
Uterine scarring, n (%)	114 (29.08)	1789 (13.83)	72.31	<0.01
Uterine rupture, n (%)*	9 (2.30)	13 (0.10)		<0.01
Retained placenta, n (%)	29 (7.4)	180 (1.39)	88.93	<0.01
Stillbirth, n (%)	11 (2.81)	79 (0.61)	24.16	<0.01
HELLP syndrome, n (%)	9 (2.30)	31 (0.24)	53.76	<0.01
Heart disease, n (%)	2 (0.51)	35 (0.27)	0.16	0.68
Hemophilia, n (%)	2 (0.51)	32 (0.25)	0.26	0.61

HELLP = hemolysis, elevated liver enzymes, low platelets.  
\* P value was calculated by Fisher's exact test.

**TABLE 2. Comparison of general patient information between 2015 and 2016**

	2015 (n = 13328)	2016 (16235)	t/chi-square	p
Age ( $\bar{x} \pm s$ )	30.49 $\pm$ 4.56	30.75 $\pm$ 4.36	5.06	<0.01
Polyembryony, n (%)	710 (5.33)	565 (3.48)	60.53	<0.01
Anemia, n (%)	515 (3.86)	406 (2.5)	45.07	<0.01
Thrombocytopenia, n (%)	133 (1.00)	109 (0.67)	9.61	<0.01
Preeclampsia, n (%)	1153 (8.65)	419 (2.58)	5535.66	<0.01
Placenta, n (%)	504 (3.78)	253 (1.56)	144.99	<0.01
Placental implantation, n (%)	84 (0.63)	85 (0.52)	1.47	0.23
Uterine scarring, n (%)	1903 (14.28)	234 (1.44)	1798.53	<0.01
Uterine rupture, n (%)	22 (0.17)	35 (0.22)	0.97	0.32
Retained placenta, n (%)	209 (1.57)	2 (0.01)	250.01	<0.01
Stillbirth, n (%)	90 (0.68)	119 (0.73)	0.35	0.56
HELLP syndrome, n (%)	40 (0.30)	64 (0.39)	1.85	0.17
Heart disease, n (%)	37 (0.28)	122 (0.75)	30.72	<0.01
Hemophilia, n (%)	34 (0.26)	271 (1.67)	143.35	<0.01

HELLP = hemolysis, elevated liver enzymes, low platelets.

Of the selected 16,235 postpartum women, a total of 447 patients received RBC transfusions, and the overall transfusion rate was 2.75%. The average age of the patients was 30.75  $\pm$  4.36 years. The average neonatal weight was 3042.15  $\pm$  935.68 g. Other related risk factors are shown in Table 2.

### Multivariable models

Table 3 shows the results of the stepwise logistic regression analysis for perinatal transfusion. After a multivariable adjustment, the factors that were significantly associated with perinatal transfusion included polyembryony (odds ratio [OR], 1.59; 95% confidence interval [CI], 1.03–2.36), anemia (OR, 8.48; 95% CI, 6.33–11.28), thrombocytopenia (OR, 7.31; 95% CI, 4.32–11.93), preeclampsia (OR, 2.93; 95% CI, 2.14–3.95), placenta previa (OR, 13.12; 95% CI, 9.89–17.32), placental implantation (OR, 16.02; 95% CI, 9.19–27.85), scarred uterus (OR, 1.95; 95% CI, 1.50–2.53), uterine rupture (OR, 17.24; 95% CI, 5.47–48.44), retained placenta (OR, 3.00; 95%

CI, 1.80–4.83), stillbirth (OR, 3.73; 95% CI, 1.64–7.64), and HELLP (OR, 5.28; 95% CI, 2.09–12.01). Heart disease (OR, 1.73; 95% CI, 0.27–6.23) and hemophilia (OR, 2.35; 95% CI, 0.37–8.09) were unrelated to blood transfusion risk (Hosmer-Lemeshow chi-square statistic, 10.77 [values <20 indicated good calibration];  $p < 0.05$ ).

### Model performance

To verify the sensitivity and specificity of the stochastic multivariate logistic regression model, we conducted an internal validation of 2015 parturient women and an external validation of 16,235 selected 2016 parturient women.

Our model showed good discrimination (c-statistic, 0.835; 95% CI, 0.811–0.858;  $p = 0.0121$ ) (Fig. 1). Verification of the stochastic multivariate logistic regression model sensitivity and specificity using 2015 and 2016 parturient data provided our internal verification result (c-statistic, 0.834; 95% CI, 0.811–0.858;  $p = 0.0121$ ) (Fig. 2) and external verification result (0.692; 95% CI, 0.667–0.717;  $p = 0.0126$ ).

**TABLE 3. Multivariable adjusted OR and 95% CI for perinatal transfusion**

Parameter	Estimate	Standard error	Wald chi-square	Pr > chi-square	Standardized estimate	OR (95% CI)
Polyembryony, n (%)	0.4623	0.2106	4.8181	0.0282	0.0572	1.59 (1.03–2.36)
Anemia, n (%)	2.1371	0.1474	210.2870	<0.0001	0.2269	8.48 (6.33–11.28)
Thrombocytopenia, n (%)	1.9888	0.2587	59.1088	<0.0001	0.1090	7.31 (4.32–11.93)
Preeclampsia, n (%)	1.0737	0.1556	47.5861	<0.0001	0.1664	2.93 (2.14–3.95)
Placenta, n (%)	2.5738	0.1428	324.6928	<0.0001	0.2707	13.12 (9.89–17.32)
Placental implantation, n (%)	2.7736	0.2825	96.3598	<0.0001	0.1210	16.02 (9.19–27.85)
Uterine scarring, n (%)	0.6692	0.1340	24.9460	<0.0001	0.1291	1.95 (1.50–2.53)
Uterine abruption, n (%)	2.8471	0.5499	26.8075	<0.0001	0.0637	17.24 (5.47–48.44)
Retained placenta, n (%)	1.0984	0.2507	19.1924	<0.0001	0.0752	3.00 (1.80–4.83)
Stillbirths, n (%)	1.3166	0.3904	11.3744	0.0007	0.0594	3.73 (1.64–7.64)
HELLP syndrome, n (%)	1.6644	0.4413	14.2218	0.0002	0.0502	5.28 (2.09–12.01)
Heart disease, n (%)	0.5490	0.7646	0.5155	0.4728	0.0159	1.73 (0.27–6.23)
Hemophilia, n (%)	0.8550	0.7448	1.3180	0.2510	0.0238	2.35 (0.37–8.09)

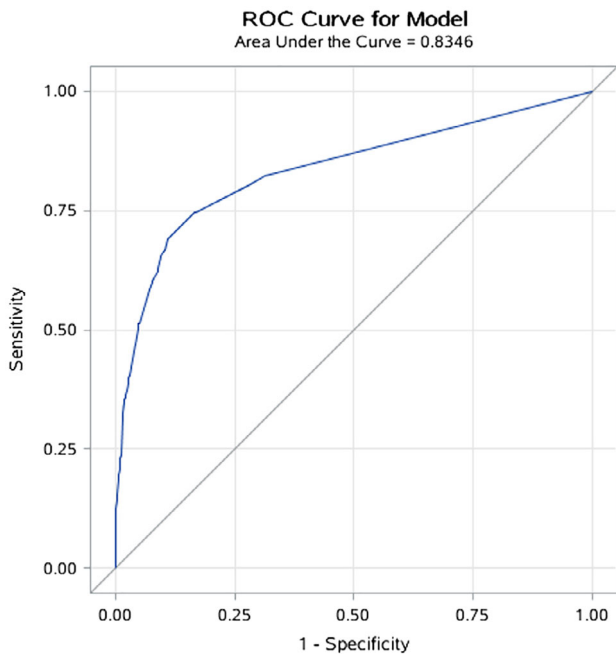
Hosmer and Lemeshow goodness-of-fit test, chi-square 10.77;  $p < 0.01$ .  
 CI = confidence interval; HELLP = hemolysis, elevated liver enzymes, low platelets; OR = odds ratio.

(Fig. 3). To facilitate the prenatal prediction of postpartum blood transfusion risk, we developed a simplified blood transfusion risk evaluation table for postpartum women on the basis of multifactor logistic regression analysis. The table was well calibrated (Fig. 4). In a clinical application, for example, if a patient had a history of uterine scarring, preoperative anemia, and placenta previa, her blood transfusion

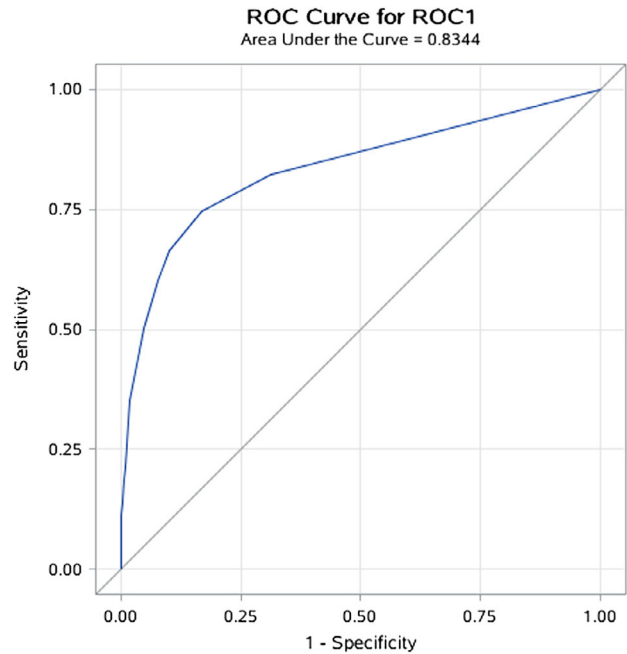
risk score was calculated to be 12, making her final blood transfusion risk approximately 79.4%.

### DISCUSSION

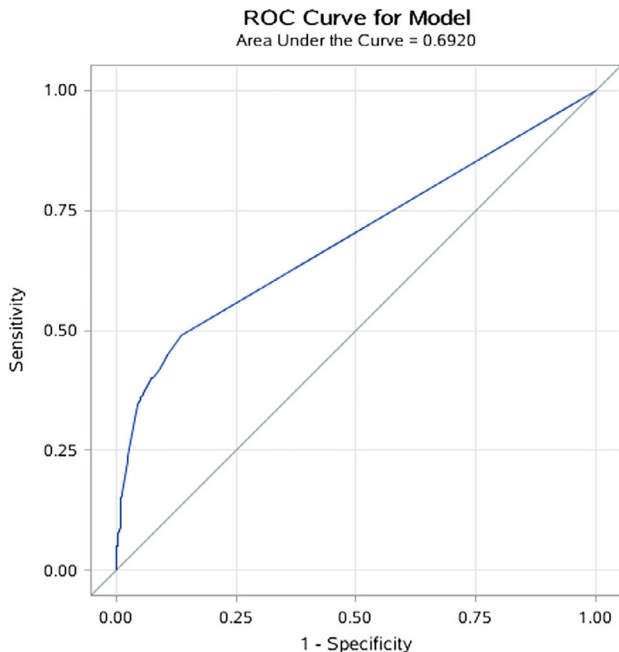
According to different literature reports, the blood transfusion rate for obstetric patients varies in developing countries



**Fig. 1. Receiver operating characteristic curve for perinatal transfusion from the multivariable logistic regression model. The area under the curve (AUC) with a 95% CI is noted under the curve; the p-value refers to evaluation of the prognostic accuracy versus the null hypothesis (area = 0.5). AUC (95% CI), 0.835 (0.811-0.858);  $p < 0.001$ . [Color figure can be viewed at wileyonlinelibrary.com]**



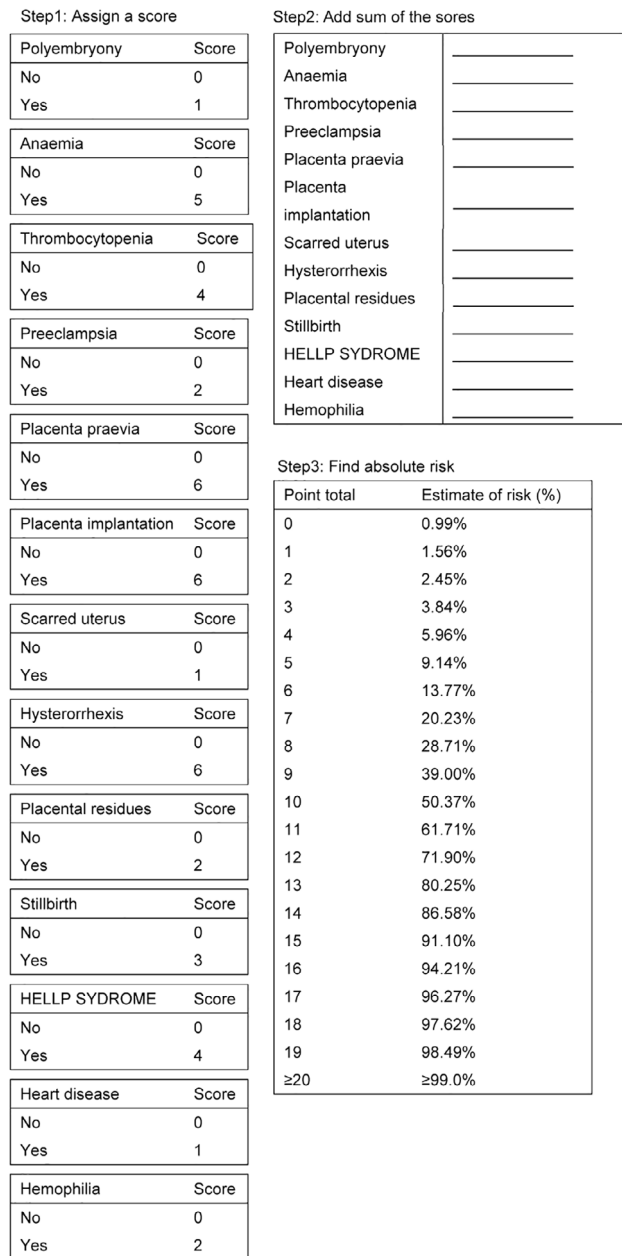
**Fig. 2. Internal validation results for the 2015 data from the multivariable logistic regression model. The area under the curve (AUC) with a 95% CI is noted under the curve; the p-value refers to evaluation of the prognostic accuracy versus the null hypothesis (area = 0.5). AUC (95% CI), 0.834 (0.811-0.858);  $p < 0.001$ . [Color figure can be viewed at wileyonlinelibrary.com]**



**Fig. 3.** External validation results for the 2016 data from the multivariable logistic regression model. The area under the curve (AUC) with a 95% CI is noted under the curve; the p-value refers to evaluation of the prognostic accuracy versus the null hypothesis (area = 0.5). AUC (95% CI), 0.692 (0.667-0.717);  $p < 0.05$ . [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

(up to 25%) versus developed countries (1.1%–7.8%)<sup>16–20</sup>; however, the blood transfusion rate was 0.53% in Shanghai, which is lower than the figures reported in other studies.<sup>15</sup> In our survey, the blood transfusion rate for postpartum women in 2015 was 2.94%, which is similar to that reported in developed countries. This is because of the multidisciplinary patient management for PPH that we initiated in 2013, including prenatal identification of blood transfusion risk and timely initiation of blood management if PPH occurred.<sup>21</sup> In this retrospective analysis, we determined that PPH-inducing factors including polyembryony, anemia, thrombocytopenia, preeclampsia, placenta previa, placental implantation, uterine scarring, uterine abruption, retained placenta, stillbirth, and HELLP syndrome, can increase the perinatal transfusion risk among postpartum women. We developed a simplified blood transfusion scoring system that can evaluate blood transfusion risk coefficients for different complications and determine a cumulative blood transfusion risk, which can identify postpartum blood transfusion risk.

Both prenatal chronic anemia and PPH require blood transfusions. Compared with the former, the latter is often an emergent condition.<sup>10,11,22,27–30</sup> An analysis of the causes of PPH in postpartum women revealed that weak uterine contractions caused by disease is a primary factor. Polyembryony may injure the uterine muscle layer and lead to weakened uterine contractions. Placenta previa and



**Fig. 4.** Risk scores and risk ratio in perinatal transfusion.

placental implantation can result in delayed placental expulsion and thus can cause contraction failure that could lead to severe bleeding. Further, under conditions of gestational hypertension, the use of magnesium sulfate before parturition can cause relaxation of the uterine muscle layer, thus leading to weakened uterine contractions.<sup>22,27–29</sup> As the blood volume is increased and coagulation functions are enhanced during the third trimester,<sup>1–3,27,28</sup> postpartum women develop a greater tolerance to blood loss; therefore, not all postpartum women require a blood transfusion. For patients with severe and acute blood loss, accurately evaluating the blood transfusion risk is beneficial for timely decision making regarding blood transfusions.

Bao et al.<sup>15</sup> reported that placenta previa and placental implantation were risk factors for blood transfusion. To fully and conveniently assess the risk of transfusion in obstetric patients before delivery, we first assessed the risk factors for transfusion on the basis of a large sample of discharged patients. Of the 13 risk factors in our survey, the multifactor logistic analysis showed that a total of 11 factors incorporated in the ROC curve identified a blood transfusion risk predictability of 0.835 (0.811–0.854). The ROC curve is beneficial for use in predicting perinatal transfusions and can also be used as a good predictor of maternal blood transfusion risk. The internal verification using 2015 data revealed a c-statistic value of 0.834 (95% CI, 0.811–0.858;  $p = 0.0121$ ) and the external verification using 2016 data revealed a c-statistic value of 0.692 (95% CI, 0.667–0.717;  $p = 0.0126$ ). Our ROC curve thus effectively predicted transfusion risk. All 11 risk factors for PPH, with the exception of anemia, were also transfusion risk factors.

To facilitate the prediction of blood transfusion risk, we established a simplified scoring system and found a high blood transfusion risk in postpartum women who had polyembryony, anemia, thrombocytopenia, preeclampsia, placenta previa, placental implantation, uterine scarring, uterine rupture, retained placenta, stillbirth, and HELLP syndrome. Some high-risk patients often had several risk factors. Therefore, to more effectively predict blood transfusion risk among postpartum women with multiple high-risk conditions, we first developed a cumulative scoring system to analyze blood transfusion risk. A score of 8 on the transfusion risk scale indicated a transfusion risk of 28.71%. The RBC transfusion risk was 50.37% when the score exceeded 10, and the risk increased to 80.25% when the score reached 13. This indicates that if the blood transfusion risk reaches 8, close attention should be paid to postpartum women with any changes in medical condition, and their condition should be thoroughly evaluated to predict blood transfusion risk.

As for the analysis of prenatal risk factors, we observed that when the OR for patients with gestational anemia was 8.48, their associated risk score was 5, indicating that their anemia constituted a high blood transfusion risk. This increase in risk may be related to a lack of generalized management of antepartum anemia. The results also suggest that prenatal anemia might reduce the risk of blood transfusion and the risk of hemolytic disease of the fetus and newborn. However, most of these patients were diagnosed before parturition, and there was good predictability of their blood transfusion risk. Thus, no emergent blood transfusions were required in most cases.

In addition to anemia, we found that there were several significant blood transfusion risk factors that caused PPH. We found that 10 risk factors increased blood transfusion risk: polyembryony, thrombocytopenia, preeclampsia, placenta previa, placental implantation, scarred uterus, uterine rupture, retained placenta, stillbirth, and HELLP syndrome. This suggests that patients who have these underlying diseases have a high risk of PPH and need additional blood transfusions once

their blood loss causes a state of decompensation. Meanwhile, we found that heart disease and hemophilia did not increase the blood transfusion risk in postpartum women. Placenta previa, placental implantation, and uterine rupture were associated with risk scores of 6, the highest in the assessment of risk factors for maternal blood transfusion, indicating that those factors imparted the highest risks for blood transfusion. Therefore, it is suggested that sufficient prenatal preparation is needed if the above complications occur before delivery. If patients have one or more of the listed medical conditions, adequate blood preparation must be considered before parturition to meet the demands of blood transfusions required during parturition. Overlooking patients' blood transfusion risk could delay the institution of lifesaving measures. When women with a high risk of blood transfusion are in the perinatal stage, multidisciplinary cooperation is needed to initiate stabilization strategies, including circulatory support and maintenance of adequate tissue oxygenation, coagulation function, body temperature, and ionic equilibrium.<sup>29–31</sup> Appropriate preparation and a ready supply of blood components are crucial. Further, it is beneficial to actively promote a large number of blood transfusion regimens for rapid salvage. A survey on the administration of blood transfusions to postpartum women will be reported in another article.

This study had several limitations. First, this was a retrospective analysis conducted at a single hospital with regional and unit limitations. In the future, a multicenter survey may help better evaluate the blood transfusion risks in these patients. In previous literature reports, uterine massage, intrauterine balloon tamponade, and uterine artery ligation were helpful for reducing the volume of blood loss and the blood transfusion volume.<sup>32,33</sup> In this report, we analyzed only the diagnoses related to transfusion risk. We will examine this issue in our future report on reducing blood transfusion volumes.

By retrospectively analyzing the data of 13,328 postpartum women, we identified PPH-inducing factors discussed in previous reports that could increase the perinatal transfusion risk in the postpartum period. These factors included polyembryony, anemia, thrombocytopenia, preeclampsia, placenta previa, placental implantation, uterine scarring, uterine rupture, retained placenta, stillbirth, and HELLP syndrome. Our multifactor logistic analysis facilitated the prediction of blood transfusion risk in patients with these conditions. Further, our simplified blood transfusion scoring system allowed us to evaluate the blood transfusion risk coefficients for the different complications leading to the development of a cumulative blood transfusion risk, which will be beneficial for identifying postdiagnosis blood transfusion risk.

#### ACKNOWLEDGMENTS

The study was designed by ZX and QSW. The first draft was written by ZX and QSW. PZ, LQZ, YJH, CX, WZ, YHL, and XQT performed

data collection and survey, CJ contributed to draft statistical analysis, and LQZ contributed the final statistical analysis. All authors approved the final version of the manuscript.

### CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

### REFERENCES

- Zhou L, Fan L. Characteristics of coagulation function during pregnancy. *Zhonghua Chenke Jijiu Dianzi Zazhi* 2014;3:81-5.
- Bose P, Regan F, Paterson-Brown S. Improving the accuracy of estimated blood loss at obstetric haemorrhage using clinical reconstructions. *BJOG* 2006;113:919-24.
- Abdul-Kadir R, McLintock C, Ducloy AS, et al. Evaluation and management of postpartum hemorrhage: consensus from an international expert panel. *Transfusion* 2014;54:1756-68.
- Obstetrics group of the Chinese medical association society branch of Obstetrics and gynecology. Obstetric hemorrhage prevention and treatment guidelines (draft). *Zhonghua Fuchanke Zazhi* 2009;44:554-7.
- Liu XH, Chen M. Past, present and future of postpartum hemorrhage. *Shiyong Fuchanke Zazhi* 2013;29:561-3.
- Royal College of Obstetricians and Gynaecologists (RCOG). Prevention and management of postpartum haemorrhage. London: Royal College of Obstetricians and Gynaecologists; 2009.
- Kamei Y, Kubo T, Yano T. Hypovolemic shock in obstetrics: the present state and the management. *Obstet Gynecol Ther* 2009;99:279-83.
- Hogan MC, Foreman KJ, Naghavi M, et al. Maternal mortality for 181 countries, 1980-2008: a systematic analysis of progress towards Millennium Development Goal 5. *Lancet* 2010;375:1609-23.
- Kung HC, Hoyert DL, Xu J, et al. Deaths: final data for 2005. *Natl Vital Stat Rep* 2008;56:1-120.
- Liu CX, Zhuang YY, Liu SS. How to set up and standardize training system of the treatment of postpartum hemorrhage in China. *Zhongguo Shiyong Fuke yu Chanke Zazhi* 2014;30:249-51.
- Yu L, Chen DJ. Prediction and prevention of postpartum hemorrhage in women with high-risk pregnancies. *Zhongguo Shiyong Fuke yu Chanke Zazhi* 2014;30:251-4.
- Balki M, Dhumne S, Kasodekar S, et al. Blood transfusion for primary postpartum hemorrhage: a tertiary care hospital review. *J Obstet Gynaecol Can* 2008;30:1002-7.
- James AH, Paglia MJ, Gernsheimer T, et al. Blood component therapy in postpartum hemorrhage. *Transfusion* 2009;49:2430-3.
- Chua SC, Joung SJ, Aziz R. Incidence and risk factors predicting blood transfusion in caesarean section. *Aust N Z J Obstet Gynaecol* 2009;49:490-3.
- Bao Y, Xu C, Qu X, et al. Risk factors for transfusion in cesarean section deliveries at a tertiary hospital. *Transfusion* 2016;56:2062-8.
- Parikh NI, Pencina MJ, Wang TJ, et al. A risk score for predicting near-term incidence of hypertension: the Framingham Heart Study. *Ann Intern Med* 2008;148:102-10.
- Rouse DJ, MacPherson C, Landon M, et al. Blood transfusion and cesarean delivery. *Obstet Gynecol* 2006;108:891-7.
- Ozumba BC, Ezegwui HU. Blood transfusion and caesarean section in a developing country. *J Obstet Gynaecol* 2006;26:746-8.
- Fawcus S, Moodley J. Postpartum haemorrhage associated with caesarean section and caesarean hysterectomy. *Best Pract Res Clin Obstet Gynaecol* 2013;27:233-49.
- Imarengiaye CO, Ande AB. Risk factors for blood transfusion during c-section in a tertiary hospital in Nigeria. *Med Sci Monit* 2006;12:CR269-72.
- Xing Z, Wang QS, Yang QN, et al. Massive transfusion protocol application in postpartum hemorrhage. *Zhongguo Shuxie Zazhi* 2015;28:1381-5.
- Sheiner E, Sarid L, Levy A, et al. Obstetric risk factors and outcome of pregnancies complicated with early postpartum hemorrhage: a population-based study. *J Matern Fetal Neonatal Med* 2005;18:149-54.
- Harrell FE Jr, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med* 1996;15:361-87.
- Pencina MJ, D'Agostino RB. Overall C as a measure of discrimination in survival analysis: model specific population value and confidence interval estimation. *Stat Med* 2004;23:2109-23.
- Hosmer DW, Hosmer T, Le Cessie S, et al. A comparison of goodness-of-fit tests for the logistic regression model. *Stat Med* 1997;16:965-80.
- D'Agostino RB Sr, Grundy S, Sullivan LM, et al. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. *JAMA* 2001;286:180-7.
- Magann EF, Evans S, Hutchinson M, et al. Postpartum hemorrhage after vaginal birth: an analysis of risk factors. *South Med J* 2005;98:419-22.
- Magann EF, Evans S, Hutchinson M, et al. Postpartum hemorrhage after cesarean delivery: an analysis of risk factors. *South Med J* 2005;98:681-5.
- Rouse DJ, Leindecker S, Landon M, et al. The MFMU Cesarean Registry: uterine atony after primary cesarean delivery. *Am J Obstet Gynecol* 2005;193:1056-60.
- Al-Zirqi I, Vangen S, Forsen L, et al. Prevalence and risk factors of severe obstetric haemorrhage. *BJOG* 2008;115:1265-72.
- Pavord S, Maybury H. How I treat postpartum hemorrhage. *Blood* 2015;125:2759-70.
- Hill JS, Devenie G, Powell M. Point-of-care testing of coagulation and fibrinolytic status during postpartum haemorrhage: developing a thrombelastography<sup>®</sup>-guided transfusion algorithm. *Anaesth Intensive Care* 2012;40:1007-15.
- de Lange NM, Lancé MD, de Groot R, et al. Obstetric hemorrhage and coagulation: an update. *Thromboelastography, thromboelastometry, and conventional coagulation tests in the diagnosis and prediction of postpartum hemorrhage. Obstet Gynecol Surv* 2012;67:426-35. ■