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Risk factors and prediction of perioperative obstetric bleeding and advisability of terlipressin for correction

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ABSTRACT

Postpartum hemorrhage (PPH) is the main cause of maternal morbidity and mortality. In most cases, PPH is a result of ineffective uterine contraction. Terlipressin contributing to uterine vessel constriction is injected in high-risk patients to reduce the incidence of hypotonic bleeding during cesarean section. However, there are no studies devoted to preventive injection of terlipressin in high-risk patients.

Objective. To study the risk factors of obstetric hemorrhage and effect of terlipressin on the incidence and severity of perioperative obstetric hemorrhage.

Material and methods. A prospective randomized study included 105 women after caesarean section. In the first group (70 women), 0.4 mg of terlipressin was intraoperatively injected into the uterine incision. In the control group (35 patients), terlipressin was not administered.

Results. Three out of 70 (4.3%) patients had blood loss ≥1000 ml after terlipressin injection. In the control group, pathological blood loss occurred in 14 out of 35 (40%) women. Baseline heart rate (HR) and stroke volume (SV) were significant risk factors for obstetric hemorrhage ≥1000 ml. HR increase per a unit of measurement is associated with increase of odds ratio (OR) of bleeding by 21% (p=0.026), SV increase per a unit of measurement — with decrease of OR by 7% (p=0.031). Prognostic formula for bleeding risk assessment in patients not receiving terlipressin includes HR, SV and serum bilirubin measured one hour before surgery. Sensitivity of this model is 85.7%, specificity is 90.6%. AUC=0.915 indicates favorable predictive efficiency of this formula.

Conclusion. Terlipressin is effective for preventing pathological perioperative blood loss ≥1000 ml, herewith its intramuscular administration does not affect systemic hemodynamics.

Keywords: *caesarean section, postpartum hemorrhage, terlipressin, heart rate, stroke volume.*

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Introduction

Postpartum hemorrhage occurs in approximately 1—6% of all births. According to the World Health Organization (WHO), postpartum hemorrhage is the main cause of maternal and fetal morbidity requiring intensive care. Postpartum hemorrhage leads to 25% maternal mortality [1, 2].

In Russia, postpartum hemorrhage is the most significant cause of maternal mortality and morbidity along with extragenital diseases and hypertensive disorders during pregnancy [3].

Postpartum hemorrhage was traditionally defined as blood loss >500 mL for vaginal delivery and >1000 mL for cesarean section. The American College of Obstetrics and Gynecology revised this definition in 2017. To date, postpartum hemorrhage is cumulative blood loss >500 mL with signs and symptoms of hypovolemia within 24 hours of delivery regardless of delivery route [4].

The main causes of postpartum hemorrhage are uterine atony, genital tract ruptures, retained placenta, uterine inversion, abnormal placentation and blood clotting disorders. Uterine atony or lack of effective uterine contraction accounts for 70—80% of all postpartum hemorrhages [4—6]. It is known that cesarean section is an independent risk factor for postpartum hemorrhage [7—9].

Uterotonics (oxytocin, carbetocin) are routinely used to prevent hypotonic bleeding to influence uterine contractility and reduce the risk of blood loss during delivery [6].

A new direction in prevention of blood loss during cesarean section in high-risk patients (multiple pregnancies, uterine fibroids, two or more scars on the uterus, placenta previa) is a local

pharmacological effect on uterine vessels promoting their contraction. Terlipressin is increasingly being used for this purpose. It is a pro-drug of endogenous vasopressin [10—14].

High effectiveness of terlipressin for prevention of blood loss during cesarean section has been described [15, 16]. However, there are still no data on effects of terlipressin on the incidence and severity of perioperative obstetric bleeding depending on risk factors.

The objective of the study was to study the risk factors of obstetric hemorrhage and effect of terlipressin on the incidence and severity of perioperative obstetric hemorrhage.

Material and methods

A prospective randomized study was performed at the Perinatal Center of the Voronezh Regional Clinical Hospital No. 1. The local ethical committee approved the study design (protocol No. 04/10dated November 11, 2021). There were 105 pregnant women who signed an informed consent. We randomized patients into 2 groups using a table of random numbers (Statistica 12 software). The first group (group T) included 70 women (standard prevention of obstetric hemorrhage with injection of oxytocin and local administration of 0.4 mg of terlipressin into uterine incision). The second group (group K) included 35 patients (the same preventive measures without terlipressin).

Inclusion criteria: pregnant women aged 20—46 years, gestational age 35—41 weeks, risk of obstetric hemorrhage. The risk of obstetric hemorrhage was assessed according to the clinical guidelines of the Ministry of Health of the Russian Federation (3 risk groups) [17].

In both groups, spinal anesthesia was performed under aseptic conditions with a 0.5% solution of ropivacaine hydrochloride (L2—L3, lateral decubitus position). Clinical and laboratory monitoring included assessment of objective status, blood count (XP-300, Japan), biochemical and electrolyte blood test (HumaStar 600 Human, Germany), homeostasis (TS-4000 High Technology Inc, USA), acid basic balance and gas composition (ABL-800, Denmark), hemodynamic assessment using a NICCOMO impedance cardiography monitor (Germany), 12-lead ECG (MAK 600, USA).

Data distribution normality was analyzed using the Shapiro-Wilk test. We compared distributions and medians, as well as tested between-group differences using nonparametric Mann—Whitney, Kruskal—Wallis, Wilcoxon and Friedman tests depending on the number of groups and their relationship with each other. Predictive value of final models was determined using ROC curve for each model and appropriate AUC values. Differences were significant at p-value <0.05.

Analysis was performed using statistical package Statistica version 12.0, as well as R software environment.

Results and discussion

Age of women, parity of pregnancy and childbirth, as well as risk of anesthesia were similar **(table 1)**.

Risk factors of intraoperative bleeding (myoma, multiple pregnancies, ⩾2 uterine scars, anomalies of placenta previa) were similar **(fig. 1)**.

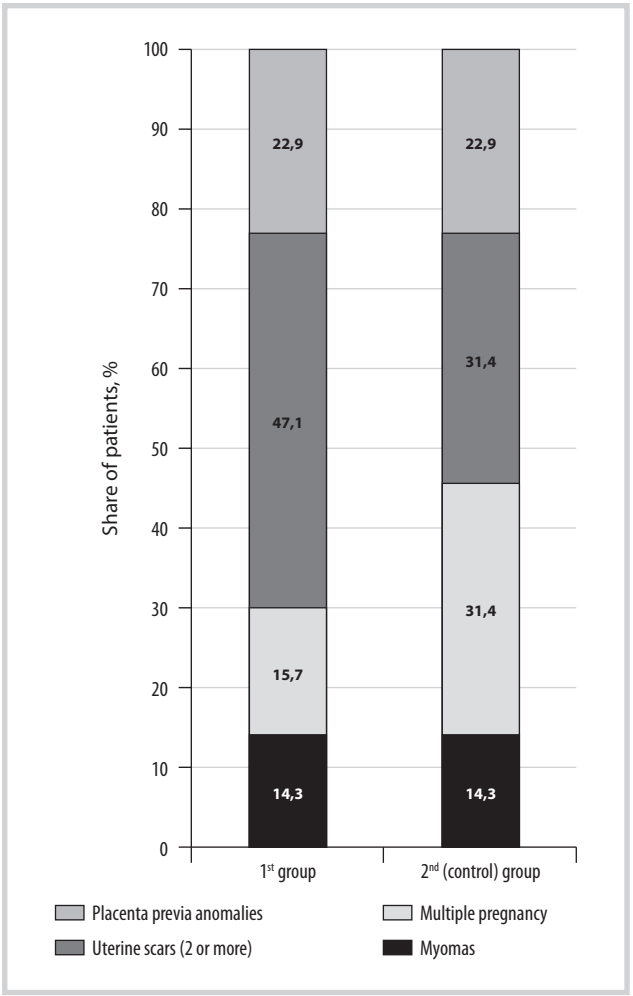

Fig. 1. **Frequency of detection of risk factors for perioperative obstetric bleeding.**

Table 1. **Characteristics of patients in study groups**

Variable	1 group (n=70)	2 group (n=35)	p (Mann—Whitney U-test)
Age, years	32.4 (31—35)	32 (29—36)	0.86
Body weight, kg	71 (68—78)	77 (69—86.5)	0.07
Body weight gain, kg	13.7 (9.5—17)	12.75 (8—16.5)	0.67
Body height, cm	164.3 (160—168)	150.9 (158—168)	0.63
Gestational age, weeks	38 (38—39)	38 (38—39)	0.59
Pregnancy parity	2.7 (1—4)	2.9 (1—4)	0.63
Birth parity	2.1 (1—30)	2.2 (1—3)	0.75
ASA grade	2.97 (2—3)	2.97 (2—3)	0.97

Table 2. **Perioperative hemodynamic parameters**

Variable	Time point	1 group (n=70)	2 group (n=35)
HR	At baseline	84 (80-92)	84 (80-92)
	After spinal anesthesia	69 (56-87)	78 (58-84)
	After terlipressin	84 (80-92)	84 (80-94)
	End of surgery	84 (80-86)	84 (80-93)
	Friedman test	<0.001	<0.002
	Mann—Whitney *U*-test	p_{1-4}>0.05	p_{1-4}>0.05
Cardiac output, l/min	At baseline	3.1 (2.5—3.7)	2.8 (1.8—3.7)
	After spinal anesthesia	3.4 (2.6—4.1)	3.2 (2.3—4.2)
	After terlipressin	4 (3.1—4.9)	3.8 (2.6—4.8)
	End of surgery	3.6 (2.6—4.3)	3.8 (2.5—4.7)
	Friedman test	<0.0001	< 0.0001
	Mann—Whitney *U*-test	p_{1-4}>0.05	p_{1-4}>0.05
Indexed stroke volume, ml/m^2	At baseline	35 (28—41)	34 (21—41)
	After spinal anesthesia	34 (26—38)	34 (25—41)
	After terlipressin	42 (31—52)	42 (28—56)
	End of surgery	40 (30—48)	39 (31—46)
	Friedman test	<0.0001	0.001
	Mann—Whitney *U*-test	p_{1-4}>0.05	p_{1-4}>0.05
SVR	At baseline	1308 (1007—1600)	1551 (1173—2075)
	After spinal anesthesia	1070 (792—1409)	1117 (872—1530)
	After terlipressin	878 (660—1196)	1020 (791—1255)
	End of surgery	915 (710—1137)	975 (631—1127)
	Friedman test	<0.0001	<0.0001
	Mann—Whitney *U*-test	p_{1-4}>0.05	p_{1-4}>0.05

Note. HR — heart rate, SVR — systemic vascular resistance.

Perioperative hemodynamic parameters are presented in **table 2**.

Between-group differences of HR and SVR in various surgical stages were significant throughout the entire follow-up period. However, between-group differences of HR and SVR were significant at all stages. These indicators decreased after spinal anesthesia due to sympathetic blockade. During the next stage, heart rate increased and SVR slightly decreased in both groups. Similar dynamics of heart rate throughout the follow-up period in both groups confirmed no significant between-group differences in this value. Dynamics of SVR was also similar in both groups and had no significant difference at any time point.

Cardiac output and stroke volume were low at baseline. Cardiac output increased slightly after spinal anesthesia and significantly increased after administration of terlipressin. In the control group, these values significantly increased. At the end of surgery, cardiac output and stroke volume were approximately at the same level with slight decrease.

The main compensatory mechanisms for prevention of major blood loss during delivery are hemostatic changes and cardiovascular restructuring. These processes begin around the sixth week of pregnancy with blood volume increase by 45% (1200—1600 ml) reaching a maximum volume of 4700—5200 ml at approximately 32 weeks [18]. Uterine blood flow increases from 100 ml/min at the beginning of pregnancy and reaches 700 ml/min by term (approximately 10% of cardiac output). Uterine contraction, local decidual hemostatic and systemic clotting factors control blood loss during labor, and their imbalance can lead to postpartum hemorrhage [19].

Women in labor can lose more than 1000 ml of blood without clinical signs of shock due to blood volume increase during pregnancy. Tachycardia is often the only sign, even in 25—35% blood loss. This masks severity of bleeding as one of the reasons complicating clinical assessment of obstetric hemorrhage [2].

Thus, baseline diagnosis should include fast assessment of general status and risk factors. Signs or symptoms of blood loss (tachycardia and hypotension) may be masked in postpartum women. Therefore, significant blood volume loss (>25%) should be feared if these signs are present. Continuous assessment of vital signs and total blood loss are important for favorable outcomes.

Perhaps, aortocaval compression preventing venous return and reducing cardiac output together with sympathetic blockade following spinal anesthesia can contribute to dynamic changes of parameters. Intraoperative blood loss >1 L cannot be ignored. Aortocaval compression can also influence baseline low cardiac output and stroke volume, which are accompanied by compensatory reactions (increased heart rate).

Blood loss decreases blood volume, cardiac output and stroke volume. Reduced total blood volume is accompanied by decrease of end-diastolic volume and stroke volume, as well as tachycardia. These are hemodynamic mechanisms for compensation of hypovolemia. However, hypercatecholaminemia and tachycardia are not accompanied by significant increase of SVR. These changes may be explained by spinal anesthesia. These influences of sympatholysis following central blocks on hemodynamic parameters are described in the literature [20].

Cardiac output and stroke volume significantly increase at the end of surgery that is likely due to elimination of aortocaval compression after delivery. This finding confirms the role of this mechanism in dynamics of parameters. To eliminate aortocaval compression syndrome, it is advisable to tilt (ro-

Table 3. **Comparison of blood loss during delivery**

Parameter	Blood loss, ml	
	1 group (n=70)	2 group (n=35)
Min	240	550
Median [25%; 75%]	530 [450; 615]	950 [765; 1200]
Max	2570	2000

Table 4. **Univariate and multivariate analysis of preoperative parameters associated with blood loss ≥1000 ml**

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
HR	1.17	[1.04; 1.32]	0.010	1.36	[1.02; 1.83]	0.046
SVR (100 units)	1.14	[0.99; 131]	0.058	1.05	[0.75; 1.47]	0.777
Stroke volume	0.94	[0.89; 1.00]	0.017	0.93	[0.80; 1.08]	0.374
Shock index (0.1 units)	4.32	[1.30; 14.39]	0.017	0.43	[0.03; 5.27]	0.507
Bilirubin	0.79	[0.58; 1.09]	0.139	0.61	[0.32; 1.17]	0.130
Total serum protein	0.99	[0.85; 1.16]	0.183	0.97	[0.78; 1.20]	0.790
Potassium	2.66	[0.72; 9.91]	0.141	0.12	[0.01; 2.79]	0.189

Table 5. **Coefficients of prognostic formula for assessing the risk of blood loss ≥1000 ml**

Variable	Coefficient (SD)	OR	95% CI	p
Shift	–8,87 (6.58)	0.00014	[0.00; 56.08]	0.178
HR	0.19 (0.08)	1.21	[1.03; 1.41]	0.026
Stroke volume	–0.077 (0.036)	0.93	[0.86; 0.99]	0.031
Bilirubin	–0.49 (0.27)	0.61	[0.36; 1.04]	0.070

tate) the table to the left by ⩾ 30° rather 15° as previously recommended [21].

Between-group comparison of blood loss is presented in **table 3**.

In the control group, abnormal blood loss (⩾1000 ml) was observed in 14 out of 35 cases (40%). We analyzed risk factors of bleeding in this group of pregnant women and developed appropriate predictive model. In the main group, 3 out of 70 (4.3%) patients had bleeding >1000 ml.

Similar to our data, Yu.S. Raspopin et al. [16] reported significantly lower incidence of abnormal blood loss after injection of terlipressin. In the world literature, we found no reports devoted to injections of terlipressin for prevention of abnormal blood loss in high-risk patients.

We studied the risk factors of obstetric hemorrhage using logistic regression («bleeding >1000 ml» as a binary variable, yes/no). Independent variables included all preoperative indicators, namely parameters of central hemodynamics and cardiac function, leukocyte count and biochemical blood test, as well as some indicators of clotting.

To assess the overall value of each indicator regarding blood loss >1000 ml, we first performed univariate analysis. Finally, we obtained only 3 indicators significantly associated with blood loss >1000 ml (heart rate, stroke volume and shock index). Thus, heart rate increase per a unit was associated with 17% higher odds ratio of bleeding >1000 ml (p=0.010). Stroke volume increase was followed by 6% decrease of appropriate OR (p=0.017). Shock index increase by 0.1 unit was associated with 4.3-fold increase of OR for bleeding >1000 ml (p=0.017).

Results of multivariate and univariate analysis are presented in **table 4**.

To remove uninformative indicators, we finally performed logistic regression with step-by-step exclusion of uninformative variables **(table 5)**.

Thus, only HR and stroke volume were significant risk factors of bleeding >1000 ml. HR increase by a unit was associated with 21% higher OR of bleeding >1000 ml (p=0.026). Stroke volume increase by a unit was associated with 7% lower OR of bleeding >1000 ml (p=0.031).

Classic markers of hemodynamic stability are not only heart rate and blood pressure, but also skin color and temperature, diuresis [22]. These parameters can change not only due to blood loss, but also due to other factors such as pain, hypothermia, intake of analgesics or beta blockers, etc. [23].

HR >100—120 bpm occurs after blood loss 750—1500 ml, while blood pressure decreases after loss of 1500—2000 ml [24]. In our patients, median heart rates did not reach these critical values.

In our study, only preoperative HR and stroke volume were significant predictors among all possible factors of obstetric hemorrhage. Similarly, R.C. Pacagnella et al. [25] reported a significant correlation between heart rate and blood loss. Heart rate >105 bpm within 21—40 postpartum minutes detected blood loss ⩾1000 ml with 90% specificity. Unlike these authors, we found no prognostic significance of shock index.

Pregnancy is accompanied by changes in all organs and systems. Increased HR and stroke volume indicating high probability of severe blood loss are apparently associated with a greater number of vascular collaterals requiring higher cardiovascular function, especially in patients with complications of pregnancy (myoma, multiple pregnancies, two or more uterine scars, placenta previa).

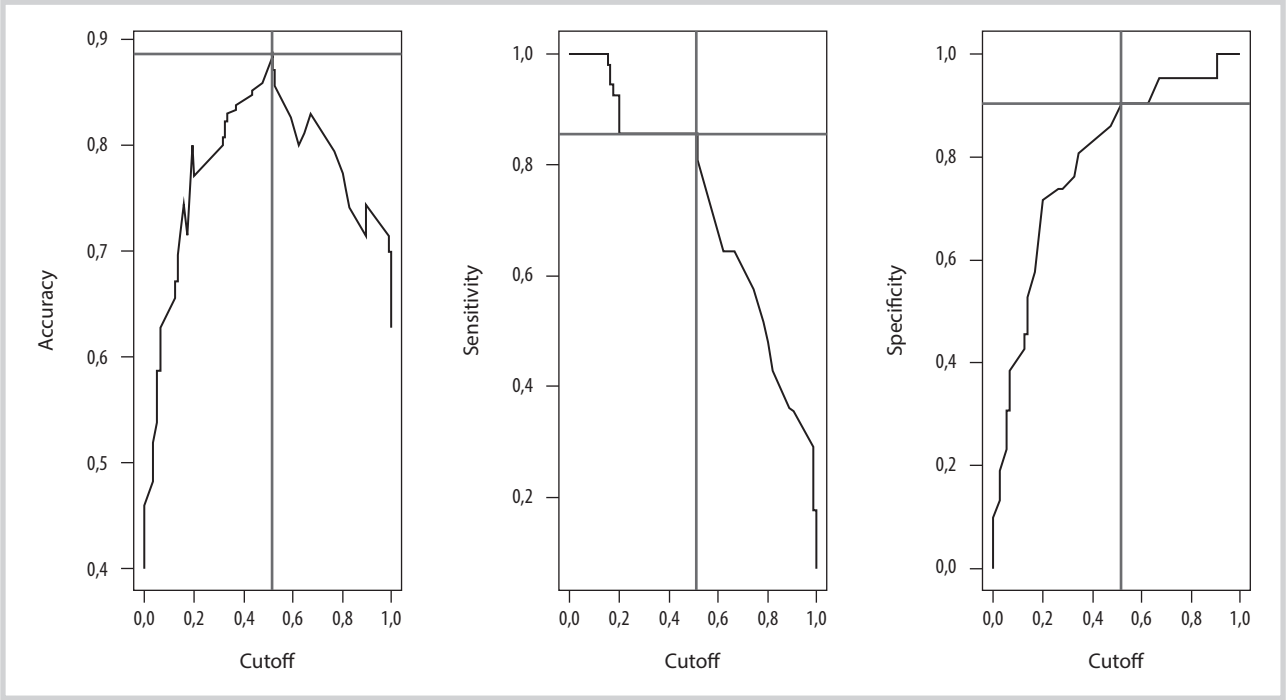

Fig. 2. **Accuracy, sensitivity and specificity of the predictive formula at the selected classification threshold of 0.513.**

Predictive formula for assessing the risk of bleeding >1000 ml in patients not receiving intraoperative terlipressin includes 3 preoperative indicators (heart rate, stroke volume and bilirubin:

$$OR=exp(-8.87+0.19\cdot HR - 0.077\cdot SV-0.49\cdot Bilirubin)$$

$$Probability=OR/(1+OR)$$

The threshold value is 0.513 with maximum accuracy of 88.6%. For this threshold, sensitivity of the model is 85.7%, specificity — 90.6% **(fig. 2)**. AUC indicates good predictive effectiveness of this formula. ROC curve of predictive formula for assessing the risk of blood loss >1000 ml with threshold value of 0.513 is presented in **fig. 3**.

Importantly, this model for predicting bleeding >1000 ml was developed exclusively for pregnant women with high risk of bleeding due to complicated obstetric-gynecological anamnesis and/or complications of pregnancy (myoma, multiple pregnancies, two or more uterine scars placenta previa). In this regard, this model cannot be extended to all pregnant women. Other studies are needed to develop predictive models for bleeding >1000 ml in other obstetric pathological states.

Conclusion

1. Baseline heart rate and stroke volume are significant risk factors of obstetric hemorrhage >1000 ml. HR increase by a unit was associated with 21% higher OR of bleeding >1000 ml (p=0.026). Stroke volume increase by a unit was associated with 7% lower OR of bleeding >1000 ml (p=0.031).
2. Predictive formula for assessing the risk of bleeding >1000 ml in patients not receiving intraoperative terlipressin includes heart rate, stroke volume and bilirubin measured one hour before surgery. Sensitivity of the model is 85.7%, specificity — 90.6%. AUC 0.915 indicates good predictive effectiveness of this formula.
3. Terlipressin is effective for prevention of abnormal perioperative blood loss > 1000 ml, while its administration into the uterine muscle does not affect systemic hemodynamics.

Author participation
All authors participated equally in developing the concept of the article, collecting, processing and statistical analysis of data, writing and editing.

No conflict of interests to declare.

REFERENCES

1. Kumari U, Naniwal A, Rani V, Chandat R, Yadav S, Pipal DK. A Study of Clinical Characteristics, Demographic Characteristics, and Fetomaternal Outcomes in Cases of Placenta Previa: An Experience of a Tertiary Care Center. *Cureus.* 2022;14(12):32125. https://doi.org/10.7759/cureus.32125
2. Hofer S, Blaha J, Collins PW, Ducloy-Bouthors AS, Guasch E, Labate F, Lança F, Nyfløt LT, Steiner K, Van de Velde M. Haemostatic support in postpartum haemorrhage: A review of the literature and expert opinion. *European Journal of Anesthesiology*. 2023;40(1):29-38. https://doi.org/10.1097/EJA.0000000000001744
3. Sidorova IS, Nikitina NA, Guseva EV. Results of a confidential audit of maternal mortality from preeclampsia and eclampsia in Russia 2017—2018. *Akusherstvo i ginekologiya*. 2020;1:119-127. (In Russ.). https://doi.org/10.18565/aig.2020.1.119-127
4. Wormer KC, Jamil RT, Bryant SB. *Acute Postpartum Hemorrhage*. 2023 May 08. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
5. Jones AJ, Federspiel JJ, Eke AC. Preventing postpartum hemorrhage with combined therapy rather than oxytocin alone. *American Journal of Obstetrics and Gynecology*. 2023;5(2):100731. https://doi.org/10.1016/j.ajogmf.2022.100731

6. Hofer S, Blaha J, Collins PW, Ducloy-Bouthors AS, Guasch E, Labate F, Lança F, Nyfløt LT, Steiner K, Van de Velde M. Haemostatic support in postpartum haemorrhage: A review of the literature and expert opinion. *European Journal of Anesthesiology*. 2023;40(1):29-38. https://doi.org/10.1097/EJA.0000000000001744
7. Konoplyannikov AG, Mikhaleva LM, Olenev AS, Kudryavtseva YaYu, Songolova EN, Gracheva NA, Biryukov AE, Mikhalev SA, Kryuchkova DI. Analysis of the structure of maternal mortality. *Voprosy ginekologii, akusherstva i perinatologii*. 2020;19(3):133-138. (In Russ.). https://doi.org/10.20953/1726-1678-2020-3-133-138
8. Zwart JJ, Richters JM, Ory F, de Vries JI, Bloemenkamp KW, van Roosmalen J. Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: A nationwide population-based study of 371,000 pregnancies. *BJOG*. 2008 June;115(7):842-50. PMID: 18485162. https://doi.org/10.1111/j.1471-0528.2008.01713.x
9. Perotto L, Zimmermann R, Quack Lötscher KC. Maternal mortality in Switzerland 2005—2014. *Swiss Medical Weekly*. 2020;150:w20345. https://doi.org/10.4414/smw.2020.20345
10. Sharman A, Low J. Vasopressin and its role in critical care. *Continuing Education in Anaesthesia. Critical Care and Pain*. 2008;8(4):134-137.
11. Favory R, Salgado DR, Vincent JL. Investigational vasopressin receptor modulators in the pipeline. *Expert Opinion on Investigational Drugs*. 2009;18(8):1119-1131. https://doi.org/10.1517/13543780903066764
12. Jamil K, Pappas SC, Devarakonda KR. *In vitro* binding and receptor-mediated activity of terlipressin at vasopressin receptors V1 and V2. *Journal of Experimental Pharmacology*. 2018;10:1-7. https://doi.org/10.2147/JEP.S146034
13. Glavaš M, Gitlin-Domagalska A, Dębowski D, Ptaszyńska N, Łęgowska A, Rolka K. Vasopressin and Its Analogues: From Natural Hormones to Multitasking Peptides. *International Journal of Molecular Sciences*. 2022;23(6):3068. https://doi.org/10.3390/ijms23063068
14. Papaluca T, Gow P. Terlipressin: Current and emerging indications in chronic liver disease. *European Journal of Gastroenterology and Hepatology*. 2018;33(3):591-598. https://doi.org/10.1111/jgh.14009
15. Rostovtsev AV, Aleksandrovich YuS, Ryazanova OV, Akimenko TI, Pshenisnov KV. Pharmacological management of postpartum haemorrhage messenger of anesthesiology and resuscitation. *Messenger of Anesthesiology and Resuscitation*. 2022;19(6):97-105. (In Russ.). https://doi.org/10.21292/2078-5658-2022-19-6-97-105
16. Raspopin YuS, Pylaeva NYu, Shifman EM, Belyanina AA, Molchanova IV. Safety of terlipressin in prevention of postpartum hemorrhage in pregnant women with hypertensive disorders during pregnancy: A multiple-center cohort study. *Russian Journal of Anesthesiology and Reanimatology*. 2022;3:46-54. (In Russ.). https://doi.org/10.17116/anaesthesiology202203146
17. *Poslerodovoe krovotechenie. Klinicheskie rekomendatsii*. 2021. Odobreno Nauchno-prakticheskim Sovetom Ministerstva zdravookhraneniya Rossijskoj Federatsii. (In Russ.). Accessed June 23, 2023. https://cr.minzdrav.gov.ru/recomend/119_2
18. Tan EK, Tan EL. Alterations in physiology and anatomy during pregnancy. *Best Practice and Research. Clinical Obstetrics and Gynaecology*. 2013;27(6):791-802. https://doi.org/10.1016/j.bpobgyn.2013.08.001
19. Gill P, Patel A, Van Hook J. *Uterine atony*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021. Accessed March 29, 2024. https://www.ncbi.nlm.nih.gov/books/NBK493238
20. *Krovoobrashhenie i anesteziya. Otsenka i korrektsiya sistemnoj gemodinamiki vo vremya operatsii i anestezii*. Lebedinskii KM, ed. Vtoroe izdanie, ispravlennoe. SPb: Chelovek; 2015. (In Russ.).
21. Lee AJ, Landau R. Aortocaval Compression Syndrome: Time to Revisit Certain Dogmas. *Anesthesia and Analgesia*. 2017;125(6):1975-1985. https://doi.org/10.1213/ANE.0000000000002313
22. Bruijns SR, Guly HR, Bouamra O, Lecky F, Lee W. The value of traditional vital signs, shock index, and age-based markers in predicting trauma mortality. *Journal of Trauma and Acute Care Surgery*. 2013;74:1432-1437. https://doi.org/10.1097/TA.0b013e31829246c7
23. Kuster M, Exadaktylos A, Schnüriger B. Non-invasive hemodynamic monitoring in trauma patients. *World Journal of Emergency Surgery*. 2015;10:1116. https://doi.org/10.1186/s13017-015-0002-0
24. Kortbeek JB, Turki S, Ali J, Antoine JA, Bouillon B, Brasel K, Brenneman F, Brink PR, Brohi K, Burris D, Burton RA, Chapleau W, Cioffi W, de Sales Collet e Silva F, Cooper A, Cortes JA, Eskesen V, Fildes J, Gautam S, Gruen RL, Gross R, Hansen KS, Henny W, Hollands MJ, Hunt RC, Jover Navalon JM, Kaufmann CR, Knudson P, Koestner A, Kosir R, Larsen CF, Livaudais W, Luchette F, Mao P, McVicker JH, Meredith JW, Mock C, Mori ND, Morrow C, Parks SN, Pereira PM, Pogetti RS, Ravn J, Rhee P, Salomone JP, Schipper IB, Schoettker P, Schreiber MA, Smith RS, Svendsen LB, Taha W, van Wijngaarden-Stephens M, Varga E, Voiglio EJ, Williams D, Winchell RJ, Winter R. Advanced trauma life support, 8th edition, the evidence for change. *Journal of Trauma*. 2008;64(6):1638-1650. PMID: 18545134. https://doi.org/10.1097/TA.0b013e3181744b03
25. Pacagnella RC, Borovac-Pinheiro A, Silveira C, Siani Morais S, Argenton JLP, Souza JP, Weeks AD, Cecatti JG. The golden hour for postpartum hemorrhage: Results from a prospective cohort study. *International Journal of Gynecology and Obstetrics*. 2022;156(3):450-458. Epub 2021 July 22. PMID: 34254311. https://doi.org/10.1002/ijgo.13823

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