Original Article

Incidence of Vaginal Bleeding Before and After Cardiac Surgery With Cardiopulmonary Bypass

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ABSTRACT

Background: The aim of the present study was to evaluate the incidence of menstrual bleeding in women undergoing cardiac surgery with cardiopulmonary bypass.

Methods: This cross-sectional study recruited 200 women aged 11 years or older (postmenarche) who were scheduled electively for their first cardiac surgery (coronary artery bypass, valve, or congenital). The menstruation status of the patients before and after surgery was assessed. Additionally, the demographic and clinical parameters, as well as postoperative drainage and blood product transfusion, were compared between the patients with and without perioperative menstrual bleeding.

Results: Five (2.5%) women had menstrual bleeding before surgery and 17 (8.5%) experienced vaginal bleeding after the operation. All of these 22 vaginal bleeding cases were self-limited, and there was no need for gynecological intervention. There were no statistically significant differences between the 22 women with vaginal bleeding and the 178 women without vaginal bleeding regarding background clinical variables, blood product transfusion, and postoperative drainage (380 \pm 278 vs 500 \pm 469 mL; P = 0.242).

Conclusions: Perioperative vaginal bleeding in women undergoing cardiac surgery is not uncommon. However, this finding is self-limited and does not increase postoperative drainage or blood product transfusion. (Iranian Heart Journal 2020; 21(2): 71-76)

KEYWORDS: Cardiac surgery, Vaginal bleeding, Menstruation, Postoperative drainage

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Received: May 17, 2019 **Accepted:** July 10, 2019

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nticoagulant and antiplatelet therapy is required in various surgical operations **\Lambda** as well as in intraoperative and postoperative periods of cardiac surgeries with cardiopulmonary bypass (CPB). Therapeutic agents block the function of different coagulation factors and thrombin and finally fibrinogen formation. These therapies can cause various gynecological adverse effects such as menorrhagia. Menorrhagia is a common menstrual disturbance in women taking anticoagulant therapy. 1

Some case reports and investigations in women using antithrombotic drugs have demonstrated a higher incidence rate of menstrual severe bleeding hemorrhagic ovarian cysts ¹⁰ in these patients often requiring medical/surgical interventions. Awareness about the complications of gynecological bleeding among cardiac patients anticoagulant, antiplatelet, taking antithrombotic medications becomes essential rapid diagnosis and appropriate management. ²

Therefore, we aimed to investigate the prevalence of menstrual disturbances in women undergoing elective cardiac surgery. We also sought to find out whether menstrual bleeding in the perioperative influence period would postoperative surgical bleeding.

METHODS

Patient Population

A total of 200 patients, who met the inclusion exclusion and criteria and underwent cardiac surgery in our hospital between October 2018 and April 2018, were retrospectively reviewed. The inclusion criteria were comprised of post- menarcheal age of 11 years or older and undergoing cardiac surgery only. Patients with irregular menstruation and coagulopathies that might affect blood coagulation such as idiopathic

thrombocytopenic purpura and hemophilia were excluded from the study. The study protocol was approved by the institutional review board, and the entire population received assurances as regards the confidentiality of their information.

Data Collection

From the whole study population, data were regarding demographic characteristics (eg, age, height, and weight), preoperative blood laboratory tests (eg, hemoglobin, platelet, partial thromboplastin time, blood type, and the international normalized ratio [INR]), diagnosis, type of surgery, parameters in the intensive care unit and operating room, menstrual cycle, and vaginal bleeding. Apropos of the menstrual cycle, the women were divided into those with their cycle between days 1 and 7, between days 8 and 15, and between days 18 and 28 days, and menopause. A summary of the data collection is illustrated in Tables 1 to 4.

Statistical Analysis

SPSS, version 16.0, for Windows (SPSS, Chicago, IL, USA) was used for the statistical analyses. The definitive statistics were expressed as the mean \pm the standard deviation. The independent samples t-test, the Mann–Whitney U test, and the χ^2 test or the Fisher exact test were employed for the difference of average values between the groups. A P value of 0.05 or less was accepted as statistically significant.

RESULTS

A total of 200 patients were included in this study. The women were divided into 2 groups: a group with perioperative vaginal bleeding (n=22) and a group with no perioperative vaginal bleeding (n=178). The baseline demographic and clinical data were assessed, and there were no statistically significant differences in terms of the variables between the 2 groups (Table 1). Five of the 22 women (2.5%) had menstruation during admission (before surgery). The remaining 17 women (of the 22 women) had disturbances in their menstrual cycle.

The variables of coagulation status, the hemoglobin level, the platelet count, the partial thromboplastin time, blood type, and the INR in conjunction with the postoperative intubation time and the

postoperative drainage amount were compared between the 2 study groups (Table 2).

The inotropes administered to the patients as well as the intraoperative and postoperative complications are presented in Table 3. There were no significant differences in these variables between the 2 groups.

The 2 study groups had similar patterns vis-àvis packed red blood cells, fresh frozen plasma, and platelet transfusion during and after surgery (Table 4).

Table 1: Demographic and clinical characteristics of the study patients

Variable	rograpino ana omnoar	Characteristics of the study particle Vaginal Bleeding Group	Non-Vaginal Bleeding Group	P value
		(n=22)	(n=178)	
Age (y)		36.0±14.3	54.9±14.4	0.0001
Height(cm)		156.0±12.78	157.4±7.57	0.463
Weight(kg)		63.8±10.94	70.09±14.24	0.490
	0+	7(31%)	80(44.9%)	0.297
	A+	10(45%)	43(24%)	
	B+	3(13%)	29(16%)	
Blood group	AB+	2(9%)	6(3.37%)	
Blood group	0-	0	11(6%)	
	A-	0	6(3.37%)	
	B-	0	2(1%)	
	AB-	0	1(0.5%)	
	CAD	3(13%)	75(42%)	0.001
	valvular disease	13(59%)	75(42%)	
Diagnosis	CAD & valvular	0	17(9%)	
	CHD	6(27%)	10(5%)	
	other	0	1(0.5%)	
History of surgery	yes	2(10%)	9(6%)	0.657
	1-7 d	5(22%)	7(3%)	0.001
Menstrual	8-15 d	6(27%)	23(12%)	
cycle	16-28 d	9(40%)	19(10%)	
	menopause	2(9%)	129(72%)	
Drug history	yes	15(69%)	143(81%)	0.231
Operative time	(min)	212±107.7	194.0±53.68	0.079
Aortic cross-c	lamp time (min)	57.90±37.96	57.43±27.79	0.399
Type of operation	CABG	3(13%)	75(42%)	0.001
	cardiac valve replacement	13(59%)	75(42%)	
	CABG&CVR	0	17(9%)	
	CHD surgery	6(27%)	10(5%)	
	other	0	1(0.5%)	
CPB time (min)		96.31±57.34	94.44±38.81	0.437

Table 2: Clinical characteristics of the study patients

Variable	Vaginal Bleeding Group (n=22)	Non-Vaginal Bleeding Group (n=178)	P value
preoperative INR*	1.16±0.137	1.17±0.256	0.811
Preoperative Hg(g/L)*	12.17±1.187	12.42±1.374	0.440
Preoperative PLT(*1000)	219.4±66.33	232.7±55.0	0.306
Preoperative PTT(s)*	37.45±17.88	36.08±13.979	0.642
*ICU INR	1.38±0.25	1.28±0.23	0.064
ICU Hg(g/L)	9.79±1.05	10.04±1.20	0.346
ICU PLT(*1000)	163.9±25.0	175.4±41.0	0.204
ICU PTT(s)	36.45±8.42	35.92±10.89	0.826
*MinHbCPB(g/L)	7.71±0.78	7.72±0.90	0.962
End of surgery Hg(g/L)	9.42±1.19	8.95±1.01	0.045
Hb in ICU discharge (g/L)	9.92±1.39	9.59±1.17	0.227
Postoperative intubation time(hour)	10.09±4.97	11.12±5.54	0.407
Postoperative drainage (mL)	380±278	500±469	0.242

INR, International normalized ratio; Hg, Hemoglobin; PLT, Platelet; PTT, Partial thromboplastic time; ICU, Intensive care unit; MinHbCPB, Minimum hemoglobin in cardiopulmonary bypass

Table 3: Inotrope drug use and intraoperative and postoperative complications

Variable	Vaginal Bleeding Group (n=22)	Non-Vaginal Bleeding Group (n=178)	P value
Epinephrine	1(4.5%)	32(18%)	0.135
Milrinone	1(4.5%)	12(6.7%)	1.000
Total intraoperative complications	0	10(5.6%)	0.386
Total ICU complications	0	2(1.2%)	1.000

ICU, Intensive care unit

Table 4: Packed RBC and blood component transfusion in the 2 study groups

Variable	Vaginal Bleeding Group (n=22)	Non-Vaginal Bleeding Group (n=178)	P value
*Op packed RBCs (unit) (0/1/2/3)	14/5/1/2	75/62/38/3	0.096
*Op FFP (unit) (0/1/2/3)	17/1/3/1	152/4/18/4	0.325
Op platelets (unit) (0/1/2/3)	19/1/2/0	160/3/15/0	0.636
ICU packed RBCs (unit) (0/1/2/3)	12/5/4/1	85/59/19/15	0.695
ICU FFP (unit) (0/1/2/3)	19/1/2/0	172/3/1/2	0.629
ICU platelets (unit) (0/1/2/3)	21/0/1/0	174/1/2/1	0.516

Op, Operation; RBC, Red blood cell; FFP, Fresh frozen plasma; ICU, Intensive care unit

DISCUSSION

In the setting of cardiac surgery, numerous factors can affect menstrual bleeding patterns. The use of heparin, altered platelet function related to the use of CPB, blood dilution, and the use of anesthetic agents are some of the potential mechanisms. 11 In patients with valvular heart disease, these factors, concomitant with the altered hemodynamic status, can clarify the high occurrence of menstrual disorders in the perioperative period.

However, the menstrual bleeding observed in the women in the present study had only a mildly inconvenient character insofar as the volume of the menstrual bleeding was relatively small and it had no influence on surgical bleeding and, consequently, the hematocrit level at discharge from the ICU. There is no difference in the severity of menstrual disturbances between complex and less complex cardiac operations. ¹¹

In conclusion, the menstrual cycle is disturbed by elective open-heart surgery in the majority of fertile women. Nonetheless, the bleeding is neither particularly longlasting nor substantial. Total surgical bleeding is, unaffected moreover. perioperative bleeding. menstrual Cederblad et al ¹² studied 30 normal women whose blood samples were taken on 6 occasions: days 1, 2, and 3 of menstruation; days 5 to 9 (follicular phase); days 12 to 16 (around ovulation); and days 19 to 23 (luteal phase). They found that the concentration of factors II-VII-X was lowermost during menstruation. Their results indicated that the activated partial thromboplastin time might reach its highest levels before menstruation and it might be related to the high intraoperative blood loss in the premenstruation group in that study. Also in their study, Cederblad and colleagues concluded that the menstrual phase was associated with intraoperative blood loss.

A novelty of our study is the fact that we independently assessed cardiac surgery female patients and considered the menstrual phase. Some studies have suggested that platelets play an important role in blood coagulation during the menstrual cycle. ^{14, 15} In a study by Rosin et al, ¹³ platelet–leukocyte interactions by the showing of platelet–leukocyte aggregates and platelet fibrinogen receptor activation by platelet glycoprotein GPIIb/IIIa fibrinogen receptor binding were assessed by

flow cytometry in 20 healthy women throughout their menstrual cycle. They demonstrated that the numbers of plateletgranulocyte aggregates and plateletmonocyte aggregates were high at ovulation in comparison with other time-points of the menstrual cycle. Other blood coagulation factors have been similarly assumed to experience variations throughout a normal menstrual cycle. ¹⁶ The possible reason why patients had more intraoperative bleeding during the pre-menstruation phase might be related to the variation in the estrogen level. Several researchers have found that an abrupt upsurge in the estrogen level leads to a hypercoagulable state. 17, 18 As the estrogen level in serum begins to fall in the premenstrual phase, this may lead to a hypocoagulable condition and intraoperative bleeding. ¹²

CONCLUSIONS

In this study, we found that perioperative vaginal bleeding in women undergoing cardiac surgery is not uncommon. However, this finding is self-limited and does not increase postoperative drainage or blood product transfusion.

REFERENCES

- 1. In this study we found that perioperative vaginal bleeding in women undergoing cardiac surgery is not uncommon. However, this finding is self-limited and does not increase postoperative drainage or blood product transfusion.
- 2. Soni H, Kurkowski J, Guffey D, Dietrich JE, Srivaths LV. Gynecologic Bleeding Complications in Postmenarchal Female Adolescents Receiving Antithrombotic Medications. J Pediatr Adolesc Gynecol. 2018 Jun;31(3):242-246.
- **3.** Sj€alander A, Friberg B, Svensson P, et al. Menorrhagia and minor bleeding symptoms inwomen on oral anticoagulation. J Thromb Thrombolysis 2007; 1:24.

- 4. Huq FY, Tvarkova K, Arafa A, et al: Menstrual problems and contraception in women of reproductive age receiving oral anticoagulation. Contraception 2011; 2:84
- 5. Castellino G, Cuadrado MJ, Godfrey T, et al. Characteristics of patients antiphospholipid syndrome with major bleeding after oral anticoagulant treatment. Ann Rheum Dis 2001; 5:60
- 6. Martinelli I, Lensing AW, Middeldorp S, et al. Recurrent venous thromboembolism and abnormal uterine bleeding anticoagulant and hormone therapy use. Blood 2016: 11:127
- 7. Dietrich JE, Srivaths L: Navigating hormones and gynecologic concerns among female adolescents in the settings of thrombophilia and anticoagulation. J Pediatr Adolesc Gynecol 2015; 6:28
- **8.** Sonmezer M, Atabekoglu C, Cengiz B, et al: Depot-medroxyprogesterone acetate in anticoagulated patients with previous hemorrhagic corpus luteum. Eur Contracept Reprod Health Care 2005; 1:10.
- 9. Peake L, Grover S, Monagle P, et al: Effect of warfarin on menstruation and menstrual management of the adolescent on warfarin. J Paediatr Child Health 2011; 12:47.
- **10.** Wilbur A, Goldstein L, Prywitch B: Hemorrhagic ovarian cysts in patients on anticoagulation therapy: CT findings. J Comput Assist Tomogr 1993; 4:17.
- 11. Hjortdal VE, Larsen SH, Wilkens H, Jakobsen A, Pedersen TA. Menstrual

- bleeding after cardiac surgery. Eur J Cardiothorac Surg. 2014 Jan;45(1):171-3.
- 12. Li C, Yang M, Wang C, Wang C, Fan J, Chen Z, Wei X, Zhang G, Bai Y, Zhu X, Xie Y, Li M. Preoperative Factors Predicting Intraoperative Blood Loss in Female Patients With Adolescent Idiopathic Scoliosis. Medicine (Baltimore). 2015 Jan; 94(1):e359.
- 13. Rosin C, Brunner M, Lehr S, et al. The formation of platelet leukocyte aggregates varies during the menstrual cycle. Platelets 2006;17:61-66.
- 14. Freedman JE, Loscalzo J. Platelet-monocyte bridging thrombosis aggregates: inflammation. Circulation. 2002;105:2130-2132.
- 15. Peters MJ, Dixon G, Kotowicz KT, et al. Circulating platelet neutrophil complexes represent a subpopulation of activated neutrophils primed adhesion, for phagocytosis and intracellular killing. Brit J Haematol. 1999:106:391-399.
- 16. Knol HM, Kemperman RF, Kluin-Nelemans HC, et al. Haemostatic variables during normal menstrual cycle. Thromb Haemost. 2012;107:22-29.
- 17. Ibrahimi E, Koni M. Effects of estrogens and progestagens on the primary variables of haemostasis. Int J Reprod Contracep Obstet Gynecol. 2014;3:31-33.
- 18. Van Rooijen M, Bremme K, Rosing J, et al. 69 rapid activation of haemostasis after hormonal emergency contraception. Thromb Res. 2007;119:S116.