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Original Article

Thrombelastogram assesses anticoagulant clinical effect of rivaroxaban versus low molecular weight heparin after total hip arthroplasty

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Abstract: Objective: This study aimed to assess the anticoagulant effect of rivaroxaban and low molecular weight heparin (LMWH) in patients undergoing total hip arthroplasty (THA). Methods: A retrospective study was performed on 110 patients who underwent primary THA in the department of orthopedics and traumatology. These patients were divided into an observation group (treated with rivaroxaban, n=60) and a control group (treated with LMWH, n=50) according to different anticoagulation methods after surgery. Hemoglobin (Hb), platelet count (PLT), thrombelastogram (TEG) parameters, and postoperative complications were monitored before surgery and 1, 3, 5, 7 days after surgery. Results: Hb in the observation group was significantly higher than that in the control group on the 7th postoperative day (P<0.05). PLT in the observation group was significantly higher than that in the control group on the 5th and 7th postoperative day (P<0.05). The number of hypercoagulable patients in the observation group was less than that in the control group on the 3rd, 5th and 7th postoperative day (P<0.05). The coagulation reaction time (R) in the observation group was higher than that in the control group on the 3rd, 5th and 7th postoperative day (P<0.05). The observation group showed lower maximum amplitude (MA) as well as higher coagulation index (CI) than the control group on the 7th postoperative day (P<0.05). However, there was no statistical difference in anticoagulant complications between the two groups (P>0.05). Conclusion: Rivaroxaban has better anticoagulant effect than LMWH, which can reduce the incidence of the hypercoagulable state, and rivaroxaban was effective and safe in clinical use.

Keywords: Total hip arthroplasty, rivaroxaban, low molecular weight heparin, thrombelastogram, anticoagulation

Introduction

Total hip arthroplasty (THA) is a commonly used method for the treatment of femoral neck fracture, femoral head necrosis, and degenerative arthritis of the hip [1, 2]; which has the effect of restoring joint function, relieving pain, as well as improving the quality of life of patients [3, 4]. However, due to the large surgical wounds, excessive perioperative blood loss and high incidence of postoperative thrombosis, preventing and treating thrombosis while stopping bleeding has become key after surgery [5, 6].

Rivaroxaban and low-molecular-weight heparin (LMWH) are often used clinically to prevent deep vein thrombosis in patients undergoing hip joint surgery. The anticoagulant principle of LMWH is to reduce the activity of factor Xa in plasma. While rivaroxaban, an oral anticoagulant, exerts anticoagulant effect by selectively blocking factor Xa in the coagulation cascade [7, 8]. Although both can prevent against postoperative deep vein thrombosis, clinical findings showed that LMWH may lead to thrombocytopenia (0.1%-1%). Rivaroxaban is an oral preparation which pharmacokinetic tests showed that the blood concentration reaches peak value at 4th hour after administration, with a bioavailability of 66%, while the blood concentration of LMWH reaches the peak at 3rd hour after administration, shorter than that of the rivaroxaban, and with a bioavailability of 100%. Therefore, clinical selection of these two drugs remains controversial [9].

The efficacy of anticoagulants has been tested by conventional coagulation tests, which only monitored the stage before fibrin formation but cannot not reflect the whole coagulation process, hence, resulting in an error in predicting the risk of thrombosis [10]. Thrombelastogram (TEG) was initially used to assess the bleeding risk of surgical operation and guide the blood component transfusion as well as evaluate curative effects after infusion [11, 12]. It simulates the whole process from coagulation to fibrinogen dissolution and evaluates the functions of coagulation factors, fibrinogens and platelets [13, 14]. Compared to the conventional coagulation tests, TEG can monitor patients with potential coagulation dysfunction and provide timely intervention, thus reducing the risk of thrombosis [15-17]. A previous study has revealed that TEG is an ideal method for monitoring the postoperative hypercoagulable state, with both sensitivity and specificity to anticoagulants exceeding 90% [18-20]. Therefore, this study applied TEG to monitor the coagulation function of LMWH and rivaroxaban after THA and evaluate their anticoagulant effect.

Data and methods

General data

A retrospective study was conducted on 110 patients aged 40-80 years old with an average age of (62.5±8.2 years old) who underwent primary THA from June 2016 to June 2019. These patients were divided into an observation group (treated with rivaroxaban, n=60) and a control group (treated with LMWH, n=50) according to different anticoagulation methods after surgery. All the above patients signed informed consent forms, and this study was approved by the Ethics Committee of Changyi People's Hospital.

Inclusion and exclusion criteria

Inclusion criteria: (1). Patients undergoing primary unilateral hip arthroplasty. (2). Patients aged over 18 years. (3). Patients with normal preoperative TEG, routine blood work, coagulation function and color Doppler ultrasound of veins of the lower limbs.

Exclusion criteria: Patients who have (1). Congenital coagulation dysfunction. (2). Complicated with severe malnutrition or tumors. (3). Hepatic and renal insufficiency. (4). Receiving anticoagulants or anti-platelet-agglutination agents before surgery. (5). Previous acute cardiovascular and cerebrovascular diseases. (6). Incomplete clinical data. (7). Previous thrombosis. (8). Allergic to LMWH or rivaroxaban.

Methods

Medical records of hospitalized patients in the department of orthopedics and traumatology were collected to analyze the general data, such as age and sex, and clinical testing data. Control group: Subcutaneous injection of 2000 IU of LMWH (Jiuyuan Gene Engineering Co., Ltd., Hangzhou, China, SFDA Approval No. H1990036) was performed 12 h after surgery, once per day, and the dosage was increased to 4000 IU on the 3rd postoperative day, once per day. The anticoagulant therapy was lasted for 14 days. Observation group: 10mg of rivaroxaban (Bayer Healthcare Co., Ltd., Germany, SFDA Approval No. J20180076) was taken orally for anticoagulation, once per day for 35 days [21, 22]. TEG, routine blood tests, coagulation function, and color Doppler ultrasound of veins of the lower limbs were performed before surgery and 1, 3, 5 and 7 days after surgery.

Outcome measures

Monitoring blood: Hemoglobin (Hb) and platelet (PLT) counts.

TEG: (1). Increased blood coagulation: coagulation reaction time (R) no longer than 5 min, coagulation formation time (K) no longer than 1min, maximum amplitude (MA) no less than 70 mm, coagulation index (CI) larger than 3. (2). Decreased blood coagulation: R longer than 10 min, K larger than 3 min, MA less than 50 mm, angle α less than 53°, CI less than -3 [23]. The TEG parameters and incidence of a hypercoagulable state at various time points were recorded.

Recording postoperative hemorrhage and thrombosis: (1). Severe hemorrhage: fatal hemorrhage, major organ bleeding, bleeding at the surgical site, and sharp decrease of Hb. (2). Minor hemorrhage: subcutaneous ecchymosis, incision bleeding, and subcutaneous hematoma. (3). Deep vein thrombosis occurred.

Table 1. Comparison of general data and baseline data

Subjects	Observation group (n=60)	Control group (n=50)	χ^2/t	*P* value
Gender (Male/Female)	37/23	30/20	0.032	0.858
Age (years)	60.3±10.7	58.2±10.2	1.024	0.308
Body mass index (kg/m^2)	22.89±2.18	22.72±2.33	0.403	0.688
Pathogeny			0.021	0.990
Femoral neck fracture	22 (35.0%)	18 (37.5%)		
Osteonecrosis of the femoral head	28 (20.0%)	24 (17.5%)		
Degenerative coxitis	10 (5.0%)	8 (5.0%)		
Course of disease	8.17±3.05	8.97±2.65	0.534	0.128
Co-morbidity				
Hyperlipidemia			1.500	0.221
Yes	13	16		
No	47	34		
Hypertension			0.005	0.941
Yes	20	17		
No	40	33		
Coronary disease			0.009	0.925
Yes	10	8		
No	50	42		
Obesity			0.148	0.700
Yes	10	7		
No	50	43		
Intraoperative bleeding volume (mL)	1385.73±190.29	1345.89±201.56	0.562	0.654

Statistical indicators

SPSS 17.0 statistical software was applied to analyze the data. Continuous variables were expressed as mean ± standard deviation ($\bar{x}$ ± SD). Data in accordance with a normal distribution and homogeneity of variance were compared by t test. The intra-group comparison was conducted by paired t test, and the inter-group comparison was conducted by independent t test (denoted by t). Data not accorded with normal distribution and homogeneity of variance were compared by rank sum test (denoted by Z). Counting data expressed as percentage (%) were analyzed using the Pearson chi-square test and Fisher exact probability (expressed as chi-square). P<0.05 was considered statistically significant.

Results

Comparison of general data and baseline data

The statistical comparison showed that there was no difference between the two groups before testing in general data and baseline data, indicating a comparability (P>0.05), as shown in **Table 1**.

Comparison of Hb and PLT

There was no significant difference in Hb between the two groups before, and 1, 3, 5 days after surgery (P>0.05). The Hb in the observation group was significantly higher than that in the control group on the 7th postoperative day (P<0.05). There was no difference in PLT between the two groups before, and 1, 3 days after surgery (P>0.05). The PLT in the observation group was significantly higher than that in the control group on the 5th and 7th postoperative day (P<0.05). See **Table 2** and **Figure 1**.

Comparison of the number of hypercoagulable patients monitored by TEG

According to the TEG, on the 1st postoperative day, the number of hypercoagulable patients in the two groups accounted for 63.33% and 64.00% respectively. The number of hypercoagulable patients in the observation group

Table 2. Comparison of hemoglobin and platelet count

Subjects	Observation group (n=60)	Control group (n=50)	t	*P* value
Hemoglobin (g/L)				
Preoperative	126.56±13.18	130.84±19.44	1.322	0.190
1 d after surgery	102.17±11.60	106.88±19.00	1.569	0.113
3 d after surgery	98.79±12.60	99.59±13.47	0.320	0.749
5 d after surgery	91.48±13.12	92.67±14.87	0.446	0.657
7 d after surgery	100.56±12.90	93.99±13.82	2.669	0.009
Platelet count ($\times 10^9$/L)				
Preoperative	190.13±81.16	187.83±53.36	0.172	0.854
1 d after surgery	180.46±59.32	175.88±49.03	0.436	0.664
3 d after surgery	165.95±60.40	157.95±45.07	0.774	0.441
5 d after surgery	210.56±70.37	184.44±59.86	2.073	0.041
7 d after surgery	255.78±74.39	222.12±72.05	2.397	0.018

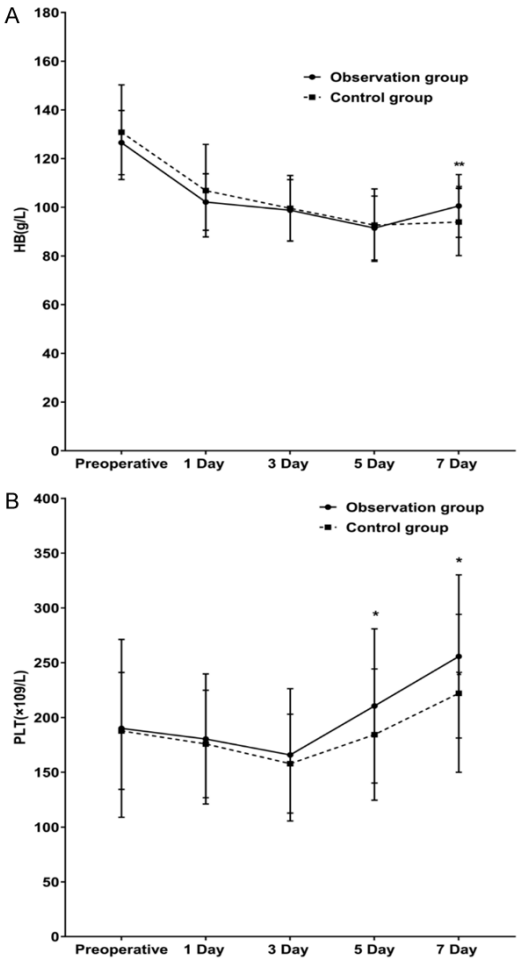

Figure 1. A. Comparison of Hemoglobin before and after surgery. B. Comparison of platelet count before and after surgery. *indicates compared to observation group, P<0.05; **indicates compared to observation group P<0.01. HB: Hemoglobin; PLT: platelet count.

decreased significantly on the 3rd postoperative day and increased on the 5th and 7th postoperative day, and that in the control group gradually increased with time. The number of hypercoagulable patients in the observation group was lower than that in the control group on the 3rd, 5th and 7th postoperative day (P<0.05). See **Table 3** and **Figure 2**.

Comparison of TEG parameters

The comparison of TEG parameters showed that there was no difference in the R value between the two groups before and 1 day after surgery (P>0.05). While the R value in the observation group was higher than that in the control group on the 3rd, 5th and 7th postoperative day (P<0.05). There was no significant difference in the K value and angle α between the two groups before and after surgery (P>0.05). The MA and CI had no difference between the two groups before, and 1, 3 and 5 days after surgery (P>0.05). While the observation group showed lower MA as well as higher CI than the control group on the 7th postoperative day (P>0.05), as shown in **Table 4**.

Comparison of anticoagulant complications

There was no statistical difference in anticoagulant complications between the two groups (P>0.05), as shown in **Table 5**.

Discussion

Due to postoperative immobilization, vascular endothelial cell damage and PLT activation *in vivo*, THA is prone to cause a hypercoagulable state and deep vein thrombosis of patients [24]. Previous studies have found that postoperative bleeding occurred in patients due to the aggravation of fibrinolytic reaction caused by intraoperative trauma, leading to Hb decline after surgery [25, 26]. In our study Hb decline was also found in both groups after surgery, which was correlated with intraoperative and postoperative bleeding. A study revealed that premature destruction of PLT caused by vascular wall injury, intraoperative blood loss, and

Table 3. Comparison of the number of hypercoagulable patients

Subjects	Observation group (n=60)	Control group (n=50)	t	*P* value
Number of hypercoagulable patients				
1 d after surgery	38 (63.33%)	32 (64.00%)	0.005	0.942
3 d after surgery	25 (41.67%)	36 (72.00%)	10.158	0.001
5 d after surgery	36 (60.00%)	42 (84.00%)	7.615	0.006
7 d after surgery	46 (76.67%)	46 (92.00%)	4.685	0.030

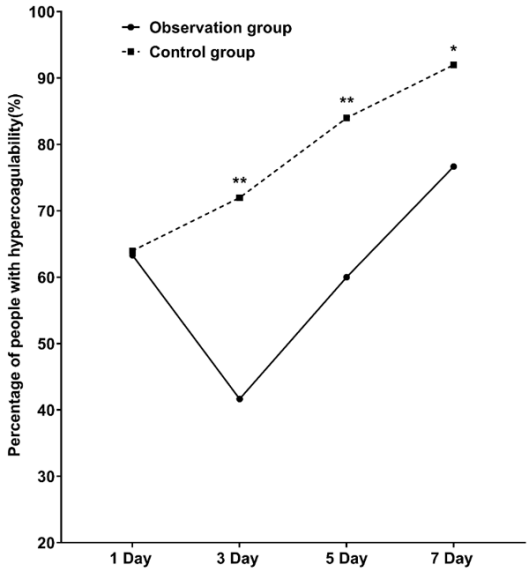

Figure 2. Comparison of the number of hypercoagulable patients. *indicates compared to observation group, P<0.05; **indicates compared to observation group, P<0.01.

changes in PLT surface eventually led to its decrease 1-3 days after surgery and normal increase 3-7 days after surgery, which was also related to the hypercoagulable state of patients after surgery [27].

A study on anticoagulant therapy with LMWH showed that it might induce heparin -induced thrombocytopenia after 5-14 days of administration. The main reason is that the platelet factor 4-heparin complex formed by the combination of heparin and platelet factor 4, which was largely released into the blood after surgery induced the production of IgG antibody, and platelet factor 4-heparin-IgG antibody immune complex was formed by combining with IgG antibody, which could reduce PLT count by promoting its consumption in blood vessels [28]. However, rivaroxaban acts as a factor Xa inhibitor exerts anticoagulant effects [8]. Oral rivaroxaban reaches the peak of blood concentration in 2-4 hours and has the characteristics of stable pharmacokinetics and high bioavailability [29]. In this study, the PLT in both groups showed decreased reactivity on the 1st and 3rd postoperative day, but increased reactivity on the 5th and 7th postoperative day due to the hypercoagulable state of patients. The increase in the observation group was higher than that in the control group because of the thrombocytopenia induced by LMWH, which was consistent with the above research results.

TEG was employed to monitor the hypercoagulable state of patients. The results showed that there was no difference in the number of hypercoagulable patients between the two groups on the 1st postoperative day, while the rivaroxaban group showed fewer hypercoagulable patients than the LMWH group on the 3rd, 5th and 7th postoperative days, which indicated that rivaroxaban had better anticoagulant effect than LMWH. Research abroad found that according to TEG, rivaroxaban has better anticoagulant effect than LMWH [30], which was consistent with the results of our study.

Further study on TEG parameters at different time points found that the R value of rivaroxaban was longer than that of LMWH on the 3rd, 5th and 7th postoperative day, while the MA of rivaroxaban was lower than that of LMWH on the 7th postoperative day. R value refers to the time from the beginning of the testing to fibrin clot formation, reflecting the comprehensive action of coagulation factors [31]. In this study, it was found that the R value of LMWH was shorter than 5 min on the 3rd, 5th and 7th postoperative day, while that of rivaroxaban was above 5 min, suggesting that rivaroxaban had a better anticoagulant effect than LMWH. MA is an index evaluating the hardness of a blood clot, and PLT and fibrinogen stability. In this study, the MA of rivaroxaban was lower than that of LMWH, which also indicates that rivaroxaban was superior to LMWH in anticoagulant effects [32, 33]. K value is an index reflecting the formation rate of blood clots, and our study demonstrated that there was no clear differ-

Table 4. Comparison of thrombelastogram parameters

Subjects	Observation group (n=60)	Control group (n=50)	t	*P* value
R (min)				
Preoperative	5.97±1.30	6.25±1.30	1.726	0.071
1 d after surgery	4.72±1.19	5.14±1.42	1.789	0.055
3 d after surgery	5.15±1.08	4.72±1.09	2.320	0.030
5 d after surgery	5.20±1.27	4.71±1.10	2.422	0.011
7 d after surgery	5.24±1.22	4.63±1.18	2.976	0.001
K (min)				
Preoperative	1.31±0.79	1.32±0.63	0.046	0.934
1 d after surgery	1.54±0.79	1.49±0.59	0.356	0.745
3 d after surgery	1.33±0.49	1.20±0.44	0.987	0.207
5 d after surgery	1.23±0.51	1.28±0.52	0.487	0.667
7 d after surgery	1.19±0.38	1.06±0.31	2.414	0.106
α (°)				
Preoperative	51.21±28.15	59.03±24.43	0.903	0.204
1d after surgery	70.23±6.85	70.21±6.10	0.021	0.988
3d after surgery	72.41±5.31	73.50±5.01	0.798	0.303
5d after surgery	72.75±5.50	72.60±5.37	0.051	0.907
7d after surgery	73.27±4.76	74.26±3.86	1.879	0.058
MA (mm)				
Preoperative	50.10±26.00	55.16±22.76	0.823	0.204
1 d after surgery	62.83±6.81	64.91±7.09	0.994	0.170
3 d after surgery	66.50±6.38	68.83±5.94	1.817	0.093
5 d after surgery	68.71±6.14	68.89±6.34	0.058	0.900
7 d after surgery	68.89±5.61	72.62±5.50	2.523	0.017
CI				
Preoperative	0.49±1.37	0.46±1.75	0.078	0.824
1 d after surgery	1.50±1.87	1.17±1.57	1.923	0.056
3 d after surgery	1.71±1.27	1.96±1.51	0.632	0.433
5 d after surgery	2.23±1.34	2.12±1.53	1.787	0.087
7 d after surgery	2.60±1.81	2.26±1.46	1.723	0.032

Note: R, coagulation reaction time; K, coagulation formation time; MA, maximum amplitude; CI, coagulation index; α, an index reflecting the dynamic state of coagulation.

ence between the two groups, which may be related to the smaller sample size and the large range of normal values of PLT. According to another study, the K value would be lost when the coagulation function was reduced to a certain degree, at which the angle α was taken as an indicator to reflect the coagulation factor [34]. The angle α is an index reflecting the dynamic state of coagulation, and smaller angle α indicates lower the blood coagulation. In our study, there was no difference in angle α between the two groups before and after surgery. However, the angle α in rivaroxaban group showed a downward trend and was lower than that in LMWH group, suggesting that rivaroxaban has a better effect on lowering blood coagulation. CI is a comprehensive evaluation index reflecting the whole coagulation process, which is calculated from the above indexes [35]. In this study, there was no statistical difference in CI between the two groups 1-5 days after surgery, but the CI in the observation group was significantly higher than that in the control group on the 7th postoperative day, indicating that rivaroxaban had better anticoagulant effect than LMWH.

Additional study reported that there was no statistical difference in the incidence of thrombosis after treatment with rivaroxaban and LMWH between the two groups, and the incidence of hemorrhage was 5.9% and 5.8%, respectively [36]. Our study also found that there was also no difference in postoperative thrombosis and hemorrhage, which was consistent with the above results.

Deficiencies and prospects: This is a retrospective study with small sample size. Therefore, a multicenter randomized controlled study with large sample size will be adopted. Moreover, the follow-up time of this study will be increased to better observe the curative effect of rivaroxaban and LMWH.

To sum up, rivaroxaban has little effect on platelets. According to TEG, rivaroxaban has better anticoagulant effect than LMWH, which can reduce the incidence of hypercoagulable state of patients without increasing the risk of bleeding and is safe and effective for clinical use.

Disclosure of conflict of interest

None.

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Table 5. Comparison of postoperative complications

Postoperative complication	Observation group (n=60)	Control group (n=50)	χ^2	*P* value
Lethal hemorrhage	0 (0.00%)	0 (0.00%)		
Important organ hemorrhage	1 (1.67%)	1 (2.00%)		
Obvious bleeding in operative site	1 (1.67%)	1 (2.00%)		
Sharp decline of hemoglobin	1 (1.67%)	1 (2.00%)		
Subcutaneous ecchymosis	13 (21.67%)	12 (24.00%)		
Incision bleeding	2 (3.33%)	1 (2.00%)		
Subcutaneous hematoma	2 (3.33%)	3 (6.00%)		
Deep venous thrombosis	1 (1.67%)	2 (4.00%)		
Total number of cases	21 (35.00%)	20 (40.00%)	0.292	0.589

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References

[1] Watts CD, Houdek MT, Sems SA, Cross WW and Pagnano MW. Tranexamic acid safely reduced blood loss in hemi- and total hip arthroplasty for acute femoral neck fracture: a randomized clinical trial. J Orthop Trauma 2017; 31: 345-351.

[2] Lee GW, Park KS, Kim DY, Lee YM, Eshnazarov KE and Yoon TR. Results of total hip arthroplasty after core decompression with tantalum rod for osteonecrosis of the femoral head. Clin Orthop Surg 2016; 8: 38-44.

[3] De Martino I, De Santis V, D'Apolito R, Sculco PK, Cross MB and Gasparini G. The Synergy cementless femoral stem in primary total hip arthroplasty at a minimum follow-up of 15 years. Bone Joint J 2017; 99-b: 29-36.

[4] Karakoyun O, Erol MF, Aslan A, Kariksiz M and Gunaydin B. Early clinical and radiological results of minimally invasive total hip replacement. J Clin Orthop Trauma 2016; 7: 210-214.

[5] Finnegan MA, Shaffer R, Remington A, Kwong J, Curtin C and Hernandez-Boussard T. Emergency department visits following elective total hip and knee replacement surgery: identifying gaps in continuity of care. J Bone Joint Surg Am 2017; 99: 1005-1012.

[6] Gylvin SH, Jorgensen CC, Fink-Jensen A, Johansson PI and Kehlet H. Psychopharmacologic treatment and blood transfusion in fast-track total hip and knee arthroplasty. Transfusion 2017; 57: 971-976.

[7] Al-Eidan FA. Is the incidence trend of heparin-induced thrombocytopenia decreased by the increased use of low-molecular-weight-heparin? Mediterr J Hematol Infect Dis 2015; 7: e2015029.

[8] Antoniou S. Rivaroxaban for the treatment and prevention of thromboembolic disease. J Pharm Pharmacol 2015; 67: 1119-1132.

[9] Falck-Ytter Y, Francis CW, Johanson NA, Curley C, Dahl OE, Schulman S, Ortel TL, Pauker SG and Colwell CW Jr. Prevention of VTE in orthopedic surgery patients: antithrombotic therapy and prevention of thrombosis, 9th ed: american college of chest physicians evidence-based clinical practice guidelines. Chest 2012; 141: e278S-e325S.

[10] Rizoli S, Min A, Sanchez AP, Shek P, Grodecki R, Veigas P and Peng HT. In trauma, conventional ROTEM and TEG results are not interchangeable but are similar in clinical applicability. Mil Med 2016; 181: 117-126.

[11] Kearon C, Akl EA, Ornelas J, Blaivas A, Jimenez D, Bounameaux H, Huisman M, King CS, Morris TA, Sood N, Stevens SM, Vintch JRE, Wells P, Woller SC and Moores L. Antithrombotic therapy for VTE disease: chest guideline and expert panel report. Chest 2016; 149: 315-352.

[12] Adler M, Ivic S, Bodmer NS, Ten Cate H, Bachmann LM, Wuillemin WA and Nagler M. Thromboelastometry and thrombelastography analysis under normal physiological conditions-systematic review. Transfus Med Hemother 2017; 44: 78-83.

[13] Lau YC, Xiong Q, Ranjit P, Lip GY and Blann AD. Laboratory assessment of anti-thrombotic therapy in heart failure, atrial fibrillation and coronary artery disease: insights using thrombelastography and a micro-titre plate assay of thrombogenesis and fibrinolysis. J Thromb Thrombolysis 2016; 42: 233-244.

[14] Rizoli S, Min A, Sanchez AP, Shek P, Grodecki R, Veigas P, Peng HT. In trauma, conventional Rotem and TEG results are not interchangeable but are similar in clinical applicbility. Mil Med 2016, 181: 117-126.

[15] Sekiya A, Hayashi T, Kadohira Y, Shibayama M, Tsuda T, Jin X, Nomoto H, Asakura H, Wada T, Ohtake S and Morishita E. Thrombosis prediction based on reference ranges of coagulation-related markers in different stages of pregnancy. Clin Appl Thromb Hemost 2017; 23: 844-850.

[16] Wang B, Li XQ, Ma N, Mo D, Gao F, Sun X, Xu X, Liu L, Song L, Li XG, Zhao Z, Zhao X and Miao ZR. Association of thrombelastographic parameters with post-stenting ischemic events. J Neurointerv Surg 2017; 9: 192-195.

[17] Sekiya A, Hayashi T, Kadohira Y, Shibayama M, Tsuda T, Jin X, Nomoto H, Asakura H, Wada T, Ohtake S and Morishita E. Thrombosis prediction based on reference ranges of coagulation-related markers in different stages of pregnancy. Clin Appl Thromb Hemost 2017; 23: 844-850.

[18] Bliden KP, Chaudhary R, Mohammed N, Muresan AA, Lopez-Espina CG, Cohen E, Raviv G, Doubleday M, Zaman F, Mathew B, Tantry US and Gurbel PA. Determination of non-Vitamin K oral anticoagulant (NOAC) effects using a new-generation thrombelastography TEG 6s system. J Thromb Thrombolysis 2017; 43: 437-445.

[19] Samuelson BT and Cuker A. Measurement and reversal of the direct oral anticoagulants. Blood Rev 2017; 31: 77-84.

[20] Samuelson BT, Cuker A, Siegal DM, Crowther M and Garcia DA. Laboratory assessment of the anticoagulant activity of direct oral anticoagulants: a systematic review. Chest 2017; 151: 127-138.

[21] Zou Y, Tian S, Wang Y and Sun K. Administering aspirin, rivaroxaban and low-molecular-weight heparin to prevent deep venous thrombosis after total knee arthroplasty. Blood Coagul Fibrinolysis 2014; 25: 660-664.

[22] Falck-Ytter Y, Francis CW, Johanson NA, Curley C, Dahl OE, Schulman S, Ortel TL, Pauker SG and Colwell CW Jr. Prevention of VTE in orthopedic surgery patients: antithrombotic therapy and prevention of thrombosis, 9th ed: american college of chest physicians evidence-based clinical practice guidelines. Chest 2012; 141: 278-325.

[23] Dias JD, Norem K, Doorneweerd DD, Thurer RL, Popovsky MA and Omert LA. Use of thromboelastography (TEG) for detection of new oral anticoagulants. Arch Pathol Lab Med 2015; 139: 665-673.

[24] Martinelli I, Bucciarelli P and Mannucci PM. Thrombotic risk factors: basic pathophysiology. Crit Care Med 2010; 38: S3-9.

[25] Churchill JL, Toney VA, Truchan S and Anderson MJ. Using aminocaproic acid to reduce blood loss after primary unilateral total knee arthroplasty. Am J Orthop (Belle Mead NJ) 2016; 45: E245-248.

[26] Maempel JF, Wickramasinghe NR, Clement ND, Brenkel IJ and Walmsley PJ. The pre-operative levels of haemoglobin in the blood can be used to predict the risk of allogenic blood transfusion after total knee arthroplasty. Bone Joint J 2016; 98-b: 490-497.

[27] Harr JN, Moore EE, Chin TL, Ghasabyan A, Gonzalez E, Wohlauer MV, Banerjee A, Silliman CC and Sauaia A. Platelets are dominant contributors to hypercoagulability after injury. J Trauma Acute Care Surg 2013; 74: 756-762; discussion 762-755.

[28] Junqueira DR, Zorzela LM and Perini E. Unfractionated heparin versus low molecular weight heparins for avoiding heparin-induced thrombocytopenia in postoperative patients. Cochrane Database Syst Rev 2017; 4: Cd007557.

[29] Alves C, Batel-Marques F and Macedo AF. Apixaban and rivaroxaban safety after hip and knee arthroplasty: a meta-analysis. J Cardiovasc Pharmacol Ther 2012; 17: 266-276.

[30] Kakkar AK, Brenner B, Dahl OE, Eriksson BI, Mouret P, Muntz J, Soglian AG, Pap AF, Misselwitz F and Haas S. Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. Lancet 2008; 372: 31-39.

[31] Reikvam H, Steien E, Hauge B, Liseth K, Hagen KG, Storkson R and Hervig T. Thrombelastography. Transfus Apher Sci 2009; 40: 119-123.

[32] Rafiq S, Johansson PI, Kofoed KF, Lund JT, Olsen PS, Bentsen S and Steinbruchel DA. Thrombelastographic hypercoagulability and antiplatelet therapy after coronary artery bypass surgery (TEG-CABG trial): a randomized controlled trial. Platelets 2017; 28: 786-793.

[33] Sivapalan P, Back AC, Ostrowski SR, Ravn HB and Johansson PI. Transfusion requirements in elective cardiopulmonary bypass surgery patients: predictive value of multiplate and thromboelastography (TEG) platelet mapping assay. Scand J Clin Lab Invest 2017; 77: 345-351.

[34] Nates JL, Cattano D, Costa FS, Chelly JE and Doursout MF. Thromboelastographic assessment of the impact of mexiletine on coagulation abnormalities induced by air or normal saline intravenous injections in conscious rats. Diving Hyperb Med 2017; 47: 228-232.

[35] Orbach-Zinger S, Eidelman LA, Lutsker A, Oron G, Fisch B and Ben-Haroush A. The effect of in vitro fertilization on coagulation parameters as measured by thromboelastogram. Eur J Obstet Gynecol Reprod Biol 2016; 201: 118-120.

[36] Eriksson BI, Kakkar AK, Turpie AG, Gent M, Bandel TJ, Homering M, Misselwitz F and Lassen MR. Oral rivaroxaban for the prevention of symptomatic venous thromboembolism after elective hip and knee replacement. J Bone Joint Surg Br 2009; 91: 636-644.