Changes in coagulation status as measured by thromboelastography in patients undergoing revision total hip arthroplasty

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Research article

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Abstract

Background: Venous thromboembolism events (VTEs) continue to be of the most widespread severe complication following total hip arthroplasty (THA) and total knee arthroplasty (TKA). However, there are no optimal accurate monitoring methods to assess the changes in coagulability after anticoagulation and anti-fibrinolysis during the perioperative period. Therefore, the objective of this study is to determine changes in coagulability as measured by thromboelastography (TEG) following revision total hip arthroplasty when the patients received rivaroxaban and tranexamic acid in perioperative period during enhanced recovery after surgery (ERAS).

Methods: We retrospectively reviewed 70 revision TKA patients (mean age 63.69 ± 10.17 years). Perioperative management of each patient was conducted in accordance with ERAS. The patients received tranexamic (TXA) to control perioperative bleeding. TEG was performed pre-operatively and on post-operative days (POD) 1, 3, 5 and 7. TEG-hypercoagulability was classified into three types: enzymatic hypercoagulability, platelet hypercoagulability and mixed hypercoagulability. Screening for coagulation-related complications at three months of follow-up.

Results: The mean duration of surgery was 2.91 ± 0.99 h. the mean intraoperative blood loss of patients was 486.43 ± 346.92 ml. And 55.71% (39) patients received transfusion, the mean blood transfusion volume was 482.86 ± 458.79 ml. There only were 4 (5.71%) patients who suffered postoperative coagulation-related complications. 1 patient with hypercoagulable on preoperative developed intramuscular venous thrombosis at 1 month postoperatively. 1 patient with hypercoagulability at POD5 and POD7 suffered melena at POD5. 2 patients with hypocoagulability developed ecchymosis at POD3. The proportion of postoperative hypercoagulable state is gradually increasing. The distribution of different hypercoagulable states on the postoperative day (POD) 5 and 7 were significantly different from that pre-operation (Pre) and POD1 (POD5 vs Pre: $p=0.011$; POD5 vs POD1: $p=0.001$; POD7 vs Pre: $p=0.001$; POD7 vs POD5: $p<0.001$). We found 32.86%(23) revision THA with hypercoagulable state on POD7. For 78.26%(18) of these patients there was mixed hypercoagulability.

Conclusions: In ERAS, thromboelastography was an effective way to identify hypercoagulable state in patients undergoing revision hip arthroplasty, and mixed hypercoagulability is the predominant hypercoagulable state following revision hip arthroplasty. In addition, it is very important to develop an individualized coagulation management program.

Introduction

ERAS is a concept that is facilitated by the efficient management of multiple processes(e.g. multidisciplinary treatment, blood management, VTE prophylaxias etc.) that all coalesce for the benefit of the patients. Due to the application of ERAS, the incidence of various complications during the perioperative period is greatly reduced, and valuable medical resources are greatly saved.(1–3) Due to the application of ERAS, the incidence of various complications during the perioperative period is greatly

reduced, and valuable medical resources are greatly saved.(4) Hence ERAS has been widely used in major orthopedic surgery. However, venous thromboembolic events (VTEs) continue to be catastrophic complications in major orthopedic surgery.(5, 6) The American Academy of Orthopaedic Surgeons (AAOS) and American College of Chest Physicians (ACCP) recommends that the routine use of anticoagulants is extremely essential for patients following major orthopedic surgery.(7, 8) However, with the routine use of chemoprophylactic agents, a slice of patients may be at the high risk of perioperative bleeding.(9, 10) In addition, perioperative blood loss, the most widespread severe complication following total joint arthroplasty (TJA), lead to significant postoperative anemia and transfusion requirement.(11, 12) Furthermore, revision TJA is considered to have an increased rate of VTE and bleeding complication, compared with conventional primary TJA. Several reasons had been reported as follows: prolonged operative time, more extensive surgical exposure and soft tissue dissection, longer postoperative mobilization et al.(5, 10, 13)

Consequently, it is crucial to consider how to maintain the equilibrium between blood loss and anticoagulant. However, there are no optimal accurately monitoring methods to assess the changes of coagulability after simultaneous using of anticoagulation and anti-fibrinolysis for ERAS during the perioperative period of arthroplasty for ERAS. Routine coagulation tests identify only the first stage of clotting.(14) And they only reflect the changes of performance in plasma (rather than whole blood). (14, 15) Thus they do not give information about overall dynamic clot formation in whole blood.

In contrast, thromboelastography (TEG), a sensitive test for the characterization of the clotting process in whole blood, provides a comprehensive assessment of platelet function, plasma factor activity, fibrin polymerization, and fibrinolysis.(12, 16) Moreover, TEG can offer a comprehensive bedside analysis and immediate results.(17, 18) Besides, TEG is potentially useful in predicting which patients will develop thromboembolic complications and abnormal bleeding.(14, 19, 20) However, to the best of our knowledge, there was no study published about the TEG use following revision THA. Therefore, the objective of this study is to determine changes in coagulability as measured by TEG following revision total hip arthroplasty when the patients received rivaroxaban and tranexamic acid in the perioperative period during ERAS.

Materials And Methods

Patients

This study was approved by the institutional ethical review board of The First Affiliated Hospital of Chongqing Medical University (NO.2018-028). We retrospectively reviewed our institutional database for all patients who underwent revision total hip arthroplasty from April 2014 to December 2017. Patients who underwent revision THA and accepted TEG testing were eligible for inclusion. Exclusion criteria were: 1) the patients had not undergone TEG evaluation, 2) previous history of Deep Vein Thrombosis (DVT) or pulmonary embolism (PE), 3) patients treated with thromboprophylactic agents other than Rivaroxaban (including heparin, enoxaparin, aspirin, warfarin, inferior vena cava filters, or any combination of VTE

prophylactic drugs), 4) patients not treated with tranexamic acid, 5) the patients who had thrombocytopenia, diagnosed with hemophilia or chronic bleeding problems (eg, peptic ulcer), or decreased liver function. 6) pre-operative anemia (hemoglobin < 110 g/L in females and hemoglobin < 120 g/L in males), 7) incomplete medical records. Ultimately, 70 patients undergoing revision THA were analyzed, a flow chart with the number of patients meeting inclusion and exclusion criteria is shown in Fig. 1. Patient consent was waived since there was no intervention related to therapy. All operations were performed by the same surgical team, which was led by a senior surgeon.

Multimodal analgesia protocol

Patients usually took non-steroidal antiinflammatory drugs (NSAIDs) (celecoxib, a selective COX-2 inhibitor) before surgery in order to reduce pain and improve the pain threshold. Perioperative single dose or short duration of highly selective COX-2 inhibitors is safe.⁽²¹⁾ Intraoperative, we used general anesthesia and femoral nerve block combined with "cocktail (1% ropivacaine 10 ml + methylprednisolone 40 mg)" to relieve pain after anesthesia recovery. Patient controlled analgesia (PCA); comprised of 1% ropivacaine 500 mg (50 ml) + normal saline 250 ml, set at a rate of 5 ml/h, and a patient control of 2 ml/time; was used to provide analgesia after surgery. And Celecoxib capsules also used after surgery 3 days, withdrawal depends on the patient's pain.

The program of TXA

In our institution, the patients received intravenously 15 mg/kg TXA before the 30 minutes prior to surgery. Patients received intravenously 1.5 g TXA intraoperatively, and post-operatively the patients received intravenously 15 mg/kg TXA intravenously.

TEG

TEG was performed pre-operatively and on post-operative days 1, 3, 5 and 7. The technical principle of TEG is shown in Fig. 2. All blood samples were run on a computerized thromboelastography coagulation analyzer (Model 5000; Haemonetics Corp, Braintree, MA). All the TEG tests were carried out by experienced personnel. They conducted quality-control checks of TEG according to the manufacturer's standard protocols. We recorded TEG values including R (reaction time), K (coagulation time), α (alpha angle), MA (maximum amplitude), CI (coagulation index). The meaning of each parameter of TEG is shown in Fig. 3. According to the manufacturer's standard, $CI > 3.0$ is identified as hypercoagulable, while $CI < -3.0$ is considered hypocoagulable. And TEG-hypercoagulability was classified into three types: (1) enzymatic hypercoagulability, $CI > 3$, $R \leq 5$ min, $MA \leq 70$ mm; (2) platelet hypercoagulability, $CI > 3$, $R > 5$ min, $MA > 70$ mm; (3) mixed hypercoagulability: $CI > 3$, $R \leq 5$ min, $MA > 70$ mm.

Protocol for Prophylaxis Against Venous Thromboembolism

All patients received daily a combination of mechanical and chemical prophylaxis to prevent VTE. The surgeon determined when to commence anticoagulation after surgery based on intraoperative bleeding and blood transfusion. Patients received daily Rivaroxaban 10 mg and continued for 5 weeks postoperatively if there weren't any coagulation-related complications. Preoperatively, all patients received lower-extremity muscular training. Passive and active physiotherapy was initiated after anesthesia resolution. All patients received intermittent pneumatic stockings on the first day of postoperation.

Screening for Venous Thromboembolism

Post-operation, all patients received daily screenings for clinical symptoms and signs of VTE until discharge. All patients received weekly screenings for venous thromboembolism from discharge until 5 weeks after surgery. All patients received monthly screenings for venous thromboembolism from 5 weeks to 3 months after surgery. In addition, patients received doppler ultrasound immediately, if there was increased pain with leg swelling and a tense, tender calf, pretibial tenderness and a positive Homans' test. Chest computed tomography (CT) angiography was performed immediately when PE was suspected clinically (shortness of breath, chest pain, lightheadedness or chest congestion).

Bleeding complications

Massive hemorrhage events included: fatal bleeding, symptomatic bleeding into a critical area or organ (intracranial, intraspinal, retroperitoneal, intraarticular or pericardial), bleeding causing a fall in Hb level of 2 g/L or more over a 24 hours period, or leading to transfusion, bleeding requiring reoperation and so on. Non-clinical massive hemorrhage events included: ecchymosis, conjunctival hemorrhage, oral mucosa and gum hemorrhage, melena etc. All bleeding events were reviewed by senior surgeons.

Blood Transfusion Protocol

Criteria for transfusion included: (1) the Hb level of the patients was < 70 g/L regardless of accompanying symptoms; (2) any case of symptomatic anemia (such as light-headedness, presyncope and an alteration in mental status or palpitation) as decided by the senior orthopaedic surgeon in the patients with an Hb level of 70 to 100 g/L.

Statistical Analysis

Continuous variables were presented as means $\pm$ standard deviation (SD), and categorical variables were presented as n (%). Paired t test was used to compare the means of continuous variable with a normal distribution. The proportion of categorical data was compared using χ^2 tests or Fisher's exact test where appropriate. In addition, we use the generalized estimating equations (GEE) model to assess the time effect. For all analyses P values less than 0.05 were interpreted as statistically significant. All statistical tests were performed using IBM SPSS Statistics 24.0 and Microsoft Excel 2016.

Results

The basic characteristics

The basic characteristics of patients were shown in Table 1. The mean duration of surgery was 2.91 ± 0.99 h. The mean intraoperative blood loss of patients was 486.43 ± 346.92 ml. And 55.71% (39) patients received transfusion, the mean blood transfusion volume was 482.86 ± 458.79 ml. There were only 4 (5.71%) patients who suffered postoperative coagulation-related complications. 1 patient developed intramuscular venous thrombosis at 1 month postoperatively. The TEG values of this patient indicated a hypercoagulable state on Pre (R = 3.5 min, MA = 66.3 mm, CI = 3.45). 1 patient suffered melena at POD5. The TEG values of this patient showed hypercoagulability at POD5 (R = 4.8 min, MA = 75.1 mm, CI = 3.98) and POD7 (R = 4.3 min, MA = 75 mm, CI = 4.20). And 2 patients developed ecchymosis at POD3 (Case 1) and POD2 (Case 2). The TEG values of these patients showed hypocoagulability at POD3 (Case 1: R = 7.3 min, MA = 47.4 mm, CI = -4.31) and POD 1 (Case 2: R = 2.8 min, MA = 39.7 mm, CI = -3.50).

The perioperative changes of TEG

The average TEG parameters are shown in Table 2. The trends are shown in Fig. 4, Fig. 5, Fig. 6, Fig. 7 and Fig. 8.

R

The differences in mean R were statistically significant before operation and on POD1, 3, 5, 7 (Table 2). And all mean R were less than 5 min on POD1, 3, 5, 7. This result indicated that postoperative coagulation system activation is accelerated, namely, the activity of coagulation factors is increased. This suggests that patients may be more prone to hypercoagulation after surgery. Besides, the average R value increased gradually after surgery, but GEE model analysis showed that R did not change significantly with time (Table 3).

K

The mean K on POD1, 3, 5 are greater than Pre, but the differences in mean K were statistically significant before operation and on days 1 after operation (Table 2). It shows that the patient did not present hyperfibrinogen after surgery. And GEE model analysis results show that the K index decreases with time, with a coefficient of -0.079 and a P value of 0.037 (Table 3, Fig. 5). The decrease of K value indicates that the patient's blood clot is formed quickly and the time required is short, which indicates that the patient's fibrinogen function is hyperactive, so it can be considered that the patient's postoperative coagulation system tends to become hypercoagulable with time.

α

The differences in mean α were statistically significant before operation and on days 7 after operation (Table 2). Except for mean α of POD1, the remaining mean values were greater than the preoperative values. And GEE model analysis results show that α increases with time, $P < 0.001$ (Table 3, Figure). This

indicates that fibrin and platelet functions are active after surgery, and clot formation may be of increased intensity in patients, indicating that the blood may be more prone to hypercoagulation after surgery.

MA

The differences in mean MA were statistically significant before operation and on POD1, 7 (Table 2). But mean MA were greater than pre-operation on POD3, 5, 7. And mean MA was on the rise after surgery, GEE model analysis results show that MA decreases with time and increases with time, $P < 0.001$ (Table 3, Figure). It indicates that the postoperative coagulation status of patients gradually tends to be hypercoagulability.

CI

There was no significant difference of mean CI on Pre and POD1. But the differences in mean CI were statistically significant before operation and on days 3, 5 and 7 after operation (Table 2). The postoperative CI value gradually increased, and the mean CI on POD7 (2.54 ± 2.00) was 2.23 times of CI on Pre (1.17 ± 1.88). CI on POD7 is very close to the maximum value of normal CI. And GEE model analysis results show that CI increases with time, $P < 0.001$ (Table 3, Figure). Therefore, it is reasonable to believe that patients are more prone to hypercoagulability after surgery and more aggressive anticoagulation may be needed.

In summary, the patient received conventional rivaroxaban anticoagulation after hip revision, but the coagulation system of the patient did not return to normal with time, but gradually became hypercoagulable. Therefore, the existing anticoagulation schemes need to be further improved, and individualized anticoagulation may be one of the future research directions.

The status of hypercoagulability

Proportion of different status of hypercoagulability at different time intervals was shown in Fig. 9. In our results, 4 hypertensive and 4 patients with periprosthetic joint infection (PJI) had hypercoagulability state (3 enzymatic, 2 platelet, and 3 mixed hypercoagulability) before surgery. The distribution of different hypercoagulable states on the postoperative day (POD) 5 and 7 were significantly different from that on preoperation (Pre) and POD1 (POD5 vs Pre: $p = 0.011$; POD5 vs POD1: $p = 0.001$; POD7 vs Pre: $p = 0.001$; POD7 vs POD5: $p < 0.001$). We found 32.86% (23) revision THA with hypercoagulable state on postoperative day 7. For 78.26% (18) of these patients, their hypercoagulable state was mixed hypercoagulability ($CI > 3$, $R \leq 5$ min, $MA > 70$ mm). CI value represents overall coagulation status; $CI > 3$ means that the blood sample indicates a hypercoagulable state. Hence, these findings indicated that increased factors were associated with platelet and thrombin, leading to a hypercoagulable state following revision THA. In addition, The GEE model analysis results showed that with the increase of

time, the possibility of patients exhibiting hypercoagulability gradually increased, the OR value was 1.461, and the P value was < 0.001 (Table III). Therefore, existing anticoagulation schemes may have shortcomings in long-term anticoagulation. We need to explore better anticoagulation schemes, such as individualized anticoagulation.

The status of hypocoagulability

There was only 1 patient with hypocoagulability at POD1, 4 patients with hypocoagulability at POD3, 2 patients were hypocoagulable at POD5 and 1 patient was hypocoagulable at POD7.

Discussion

Since ERAS was advocated by University of Copenhagen professor H. Kehlet, ERAS has been widely used in management during the perioperative period. Coagulopathy still is a primary cause of death in general and orthopedic trauma patients.(22) The recent versions of ACCP and AAOS guidelines do not distinguish between revision and primary THA.(7, 8) And there is no optimal coagulation management protocol for revision surgery. In patients undergoing revision surgery, the risk of bleeding complications and VTE is also higher than primary surgery. So, quite a few surgeons have chosen more aggressive chemoprophylaxis due to this characteristic of revision surgery, which could lead to poorer outcomes. Thus, rapid assessment and correction of coagulopathy are vital for the survival of these patients. In 2005, a study by Douglas et al.(15) was the first time evidence was reported that demonstrated the association between hypercoagulability state measured by TEG and postoperative thromboembolic complications in surgical patients. And TEG is a useful adjunctive test for assessment of thrombophilia, even if conventional thrombophilia screen methods were normal.(18) However, to our knowledge, only a handful of studies in the literature have reported coagulation monitoring by TEG following primary arthroplasty (9, 19, 20, 23, 24) but there is no data regarding TEG after revision arthroplasty on ERAS.

We found 32.86% (23) revision THA patients with a hypercoagulable state on postoperative day 7, which was a lot more than the preoperative percentum of hypercoagulable state. For 78.26% (18) of these patients, their hypercoagulable state was mixed hypercoagulability. Therefore, single use of antithrombotic (E.g. Aspirin) or antithrombin (E.g. Low molecular weight heparin) therapy may be inappropriate. How to establish an appropriate personalized anticoagulation program is an important direction for future research. In addition TEG may be an important test to guide individualized anticoagulation.

There are many reasons for hypercoagulability in patients after hip replacement. The concomitant diseases such as hypertension and infection may be the causes of hypercoagulable.(22, 25–27) Furthermore the trauma of subsequent revision surgery, intraoperative blood loss and transfusions may lead to a hypercoagulable state. The main risk factors of thrombosis following trauma of surgery include: physical disruption of the endothelium in trauma or surgery, blood flow is relatively static, stasis and local accumulation of tissue factor, the expression of tissue factors caused by stimulation of inflammatory

mediators.(28) Furthermore, platelet-leukocyte aggregation under inflammatory stimuli following surgery can further promote thrombosis.(28, 29) In a study by Ng et al (30), the development of a hypercoagulable state is related to mild to moderate degree of intraoperative blood loss. In our study, intraoperative blood loss averaged 486.43 ml, which may play a role in inducing a hypercoagulable state. Red blood cell (RBC) transfusions may increase postoperative hypercoagulable state, and in some patients, surgery and perioperative RBC transfusions may have synergistic effects of increased related risk for VTE development.(31) Furthermore, the revision surgery itself may be the cause of postoperative hypercoagulable state, and further studies are needed to explore the correlation between the parameters of revision surgery and postoperative hypercoagulable state.

In our institution, we routinely use rivaroxaban to reduce the risk of thrombosis. Rivaroxaban does not require routine coagulation monitoring, but in certain clinical situations (overdose, impaired renal function, acute bleeding episodes, elderly patients) we should evaluate the anticoagulant effect.(32) The present study found rivaroxaban prolongs R and K (assessment of time to clot formation), while decreasing α angle and MA (assessment of clot strength).(32, 33) Therefore another explanation for hypercoagulable state may be that, the recommended dose of rivaroxaban was insufficient or some patients are not sensitive to rivaroxaban. In addition, we routinely use TXA to reduced postoperative blood loss and the transfusion rate. Previous study reported that they used TEG to monitor coagulation in patients who received TXA, which showed significant reduced R, K and increased MA, α angle, and they found a three-fold increased risk of vascular events in intravenous TXA group compared to placebo.(34) Therefore, in our study the postoperative hypercoagulable state of patients may be attributed to the use of tranexamic acid.

In our study, the proportion of patients with perioperative hypocoagulability is small. Perioperative management of ERAS may be the main reason for these results. Ecchymosis, a local bleeding complication, is mainly caused by vascular wall damage and coagulation dysfunction caused by local bleeding complications.(35) The revision THA inevitably damages the vessel walls and it is more severe than primary THA. Despite there are so many advantages of Rivaroxaban, there was research showing that its application was associated with a higher risk for bleeding complications.(36) In addition, the difference in sensitivity of patients to rivaroxaban may also be an important cause of perioperative hypocoagulability. Therefore, the damage of the blood vessel wall caused by surgery and the use of rivaroxaban may be the main cause of postoperative ecchymosis. On the other hand, according to the relationship between thromboelastography and ecchymosis of case 1 and case 2, Monitoring TEG daily may be a better way to guide individualized anticoagulation.

1 patient suffered melena at POD5. The TEG values of this patient showed hypercoagulable at POD5 and POD7. In a study by Henriksson AE et al. during an acute episode, the coagulation status of a patient with gastrointestinal bleeding was hypercoagulable state.(37) The development of a hypo-fibrinolytic state can promote a hypercoagulable state in patients with upper gastrointestinal bleeding.(38) In addition, hypertension, periprosthetic joint infection, pulmonary infection, intraoperative bleeding 700 ml, postoperative blood transfusion of 600 ml, and surgical trauma may all be the cause of postoperative

hypercoagulability in this patient. The coagulation management of this special patient needs further research.

There are several limitations to this study. This is a retrospective study, which may be more susceptible to selection bias. Furthermore relatively small number of cases, short follow-up and no routine Color Duplex ultrasound might have concealed or diminished the recorded incidence rate of VTE or hypercoagulable state. The heterogeneity of operative procedures may also be limitations of this study. We did not research the potential patient-related risk factors for VTE. Despite these limitations, we believe that our study is worthy of consideration; because it is the first time patients undergoing hip arthroplasty revision, have been examined for changes in perioperative TEG parameters of patient undergoing hip arthroplasty revision; and it provides a reference for the use of TEG to guide individualized anticoagulation.

Conclusion

In conclusion, ERAS might be a useful method to reduce perioperative complications. Mixed hypercoagulability was the main hypercoagulable state following revision hip arthroplasty. TEG was an effective way to identify hypercoagulable state in patients undergoing revision hip arthroplasty. Postoperative abnormal coagulation may be due to individual differences, invariable anticoagulation program, intraoperative blood loss, transfusions and differences in revision and primary arthroplasty. Therefore it is very important to develop an individualized coagulation management program. On ERAS, TEG guiding individualized coagulation management and the relationship between thrombotic/bleeding events and TEG is also worthy of a further study may be a direction of future research.

Abbreviations

VTE

Venous thromboembolism event

THA

Total hip arthroplasty

TKA

Total knee arthroplasty

ERAS

Enhanced recovery after surgery

TEG

Thromboelastography

TXA

Tranexamic

POD

Postoperative day

AAOS

American Academy of Orthopaedic Surgeons

ACCP

American College of Chest Physicians

TJA

Total joint arthroplasty

DVT

Deep Vein Thrombosis

PE

Pulmonary embolism

MDT

Multidisciplinary treatment

NSAIDs

Non-steroidal antiinflammatory drugs

PCA

Patient controlled analgesia

Declarations

Ethics approval and consent to participate

This study was approved by the institutional ethical review board of The First Affiliated Hospital of Chongqing Medical University (NO.2018-028). Patient consent was waived since there was no intervention related to therapy.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Jianye Yang, Sizheng Zhu, Leilei Qin, Jiawei Wang, Steve Sandiford, Feilong Li, Xuan Gong, Xi Liang, Wei Huang, Ning Hu - made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data. Jianye Yang, Sizheng Zhu, Steve Sandiford, Ning Hu - been involved in drafting the manuscript or revising it critically for important intellectual content. Jianye Yang, Sizheng Zhu, Steve Sandiford, Ning Hu - given final approval of the version to be published. Jianye Yang, Sizheng Zhu, Leilei Qin, Jiawei Wang, Steve Sandiford, Feilong Li, Xuan Gong, Xi Liang, Wei Huang, Ning Hu - agreed to be accountable for all aspects of the work. All authors (Jianye Yang, Sizheng Zhu, Leilei Qin, Jiawei Wang, Steve Sandiford, Feilong Li, Xuan Gong, Xi Liang, Wei Huang, Ning Hu) read and approved the final manuscript.

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Tables

Due to technical limitations, the tables are only available as a download in the supplemental files section.

Figures

Figure 1

Flowchart of patient inclusion and exclusion

Figure 2

The technical principle of TEG: Whole blood sample was activated with kaolin. 0.36 mL whole blood specimen is pipetted into an oscillating heated cup. A pin is suspended in the cup by a torsion wire and is connected to a detector system. The cup is oscillated (rotating) relative to the pin through an angle of $4^{\circ}45'$. As clot forms, fibrin form between the cup and pin. So increasing amounts of torque are transmitted to the pin and a trace generated at once with detector system. Later, as the blood begins to undergo fibrinolysis the fibrin bonding of cup and pin is decrease. And decreasing amount of torque are transmitted to detector system. The trace is used to do assesse the entire coagulation process. TEG test was performed at a constant temperature of 37°C .

Figure 3

The R value is the time taken from the beginning of the trace to the amplitude of 2 mm, which reflects the time for the thrombin burst. The k value is measured the time of the amplitude from 2 to 20 mm, which measures the speed of clot strengthening. The MA value is the greatest amplitude of the tracing, which measures the maximum strength of the clot. The α value is the Angle between horizontal line and the tangent to the curve drawn from the amplitude of 2 mm, which is an indication of the rate of clot formation. The CI value a computer calculated linear combination of R, K, MA, and α values. And the manufacturer provides the computational formula: $CI = -0.6516R - 0.3772K + 0.1224MA + 0.0759\alpha - 7.7922$.

Figure 4

Trends of mean R after operation. I bars indicate the 95% confidence intervals of the mean. P value is the comparison between different time points.

Figure 5

Trends of mean K after operation. I bars indicate the 95% confidence intervals of the mean. P value is the comparison between different time points.

Figure 6

Trends of mean R after operation. I bars indicate the 95% confidence intervals of the mean. P value is the comparison between different time points.

Figure 7

Trends of mean MA after operation. I bars indicate the 95% confidence intervals of the mean. P value is the comparisonbetween different time points.

Figure 8

Trends of mean CI after operation. I bars indicate the 95% confidence intervals of the mean. P value is the comparisonbetween different time points.

Figure 9

Proportion of different status of hypercoagulability at different time points

Supplementary Files

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