Rotational thromboelastometry-guided perioperative management of coagulation in a patient with Heyde’s syndrome undergoing transcatheter aortic valve implantation

Kumi Fukuhara*, Takashi Kondo, Hirotsugu Miyoshi, Hiroshi Hamada and Masashi Kawamoto

Abstract

Background: Changes in coagulability during the hyperacute phase within 24 h after transcatheter aortic valve implantation (TAVI) for Heyde’s syndrome, or aortic stenosis complicated by gastrointestinal angiodysplasia and acquired coagulation dysfunction, have not been clarified. We evaluated perioperative changes in coagulability using rotational thromboelastometry (ROTEM).

Case presentation: A female patient with Heyde’s syndrome in her 80s underwent TAVI. ROTEM showed coagulation dysfunction before and at 6 h after surgery. Improvements in coagulation function started at 12 h after surgery. Based on ROTEM findings, oral administration of antiplatelet agents was started on the day after surgery. No hemorrhagic complications were observed in the postoperative phase.

Conclusions: Evaluation of coagulation function using ROTEM was useful for monitoring perioperative hemostasis and coagulation in this patient.

Keywords: Heyde’s syndrome, Rotational thromboelastometry, Transcatheter aortic valve implantation

Background

Heyde’s syndrome, or aortic stenosis (AS) complicated by gastrointestinal hemorrhage attributed to gastrointestinal angiodysplasia and acquired coagulation dysfunction, is reported to affect approximately 20% of patients with severe AS [1–3]. In Heyde’s syndrome, blood flow is accelerated and shear stress is generated when passing through the stenotic aortic valve, which leads to destruction and deficiency of high-molecular-weight vWF multimers. This results in a primary hemostatic disorder classified as acquired von Willebrand syndrome type 2A (AVWS-2A) [3]. Normally, vWF binds to coagulation factor VIII and forms a stable inactive complex. In AVWS-2A, clot formation is impaired by dysfunctional interaction between platelets and the blood coagulation system even with normal factor VIII activity and the absence of abnormalities in PT or APTT [4, 5].

Rotational thromboelastometry (ROTEM; TEM international GmbH, Munich, Germany), a coagulation monitoring method using whole blood at the bedside, can easily evaluate blood coagulation abnormalities that cannot be detected by tests of plasma [6, 7]. In the EXTEM assay, activation of the extrinsic blood coagulation pathway by tissue factor is evaluated. In the INTEM assay, activation of the intrinsic blood coagulation pathway by contact coagulation activators is evaluated. Moreover, in the FIBTEM assay, abnormalities in platelet function and decreased capability for fibrin polymerization caused by impairment of coagulation factors can be differentiated by evaluating the capability for fibrin polymerization when platelet aggregation is inhibited by a platelet aggregation inhibitor and the extrinsic coagulation pathway is stimulated by tissue factor [6–8].
Although treatment for AS has been shown to ameliorate Heyde’s syndrome [2], no study has evaluated changes in coagulability over time during the hyperacute phase within 24 h after surgery. We describe the perioperative management of a patient with severe AS diagnosed with Heyde’s syndrome undergoing transcatheter aortic valve implantation (TAVI). We used ROTEM to monitor hemostasis and coagulation in order to assess changes in coagulability over time. The timing of postoperative treatment with antiplatelet agents was determined based on ROTEM results.

Case description
A female patient with AS in her 80s had recurrent gastrointestinal hemorrhage, epistaxis, and submucosal hemorrhage during the course of AS. She was 140 cm tall and weighed 45 kg. Transthoracic echocardiography indicated severe AS with an aortic valve area of 0.55 cm$^2$ (trace) and maximum blood flow rate of 6.8 m/s, and mild aortic valve regurgitation. Left ventricular ejection fraction was 65%. No left ventricular wall motion abnormalities were observed. Coronary angiography did not show any significant stenosis. Blood tests indicated anemia (hemoglobin 11.8 g/dL) and thrombocytopenia (platelet count, 8.0 x 10$^3$/μL). Prothrombin time (PT) and activated partial thromboplastin time (APTT) were within the normal range, while vWF analysis indicated deficiency of high-molecular-weight multimers (Fig. 1a).

Based on these findings, TAVI was scheduled given the patient’s condition. Oral administration of carbazochrome sulfonic acid and tranexamic acid were added prior to surgery, then the bleeding tendency was improved.

General anesthesia was induced with intravenous midazolam (3 mg), fentanyl (100 μg), and rocuronium (50 mg). After tracheal intubation, anesthesia was maintained with propofol (0.5 μg/ml of target control infusion [TCI]) and remifentanil (0.2 μg/kg/min). A prosthetic
valve was placed using the transfemoral approach after 4500 units of heparin were administered. Intraoperative respiration and hemodynamics were stable. After placing the prosthetic valve, 45 mg of protamine were administered and the operation was completed. Intraoperative blood loss was 214 ml without apparent bleeding symptoms, then 900 ml of crystalloid and 500 ml of colloid were infused. After the patient recovered from anesthesia, she was transferred to the intensive care unit.

Tables 1 and 2 shows the results of perioperative laboratory and ROTEM findings. ROTEM clearly indicated coagulation dysfunction preoperatively and at 6 h after surgery, which improved starting at 12 h after surgery. Coagulation testing showed that APTT was slightly increased from immediately to 24 h after surgery and normalized on the third postoperative day. Based on ROTEM findings, oral administration of antiplatelet agents was started on the day after surgery. Subsequently, no bleeding tendency was observed clinically.

On the day after surgery, vWF analysis showed recovery of high-molecular-weight multimers (Fig. 1b). Transthoracic echocardiography indicated decreased AS (mean aortic valve systolic pressure gradient, 14 mmHg). The patient was discharged in good condition.

**Discussion**

Coagulopathy in Heyde’s syndrome is expected to abate when AS is treated and destruction of high-molecular-weight vWF multimers stops. With both surgical aortic valve replacement and TAVI, recovery of high-molecular-weight vWF multimers has been reported on the day after surgery and TAVI, recovery of high-molecular-weight vWF multimers stops. With both surgical aortic valve replacement and TAVI, recovery of high-molecular-weight vWF multimers has been reported on the day after surgery and TAVI, recovery of high-molecular-weight vWF multimers stops.

### Table 1 Blood testing findings

|                        | Before surgery | 6 h after surgery | 24 h after surgery | 3 days after surgery |
|------------------------|----------------|-------------------|--------------------|---------------------|
| **Plt (x 10^3/μL)**    | 80             | 63                | 61                 | 69                  |
| **PT-INR (0.85–1.15)** | 1.02           | 1.1               | 1.07               | 1.05                |
| **APTT (s) [26.9–38.1]** | 32.9           | 38.8              | 39.7               | 35                  |
| **Fib (mg/dL) [200–400]** | 225.6          | 189.5             | 239.9              | 319.2               |

*Plt platelet count, PT-INR prothrombin time-international normalized ratio, APTT activated partial thromboplastin time, Fib fibrinogen*
environment cannot be reproduced; therefore, direct evaluation of abnormal vWF function is speculated to be difficult [13]. Nevertheless, in this patient, abnormal ROTEM findings were observed despite the absence of clear PT or APTT prolongation after surgery, and postoperative improvement in ROTEM findings over time and recovery of high-molecular-weight multimers of vWF were noted. These findings suggest that both coagulation disorders mediated by abnormal vWF function associated with AVWS-2A and impaired interaction between platelets and the blood coagulation system were occurring before surgery, and that ROTEM findings reflected the overall recovery of coagulability achieved by aortic valve replacement and resulting resolution of Heyde’s syndrome.

We used ROTEM to monitor hemostasis and coagulation in the perioperative management of a patient with Heyde’s syndrome undergoing TAVI and assessed changes in coagulability over time. Based on ROTEM findings indicating improvement, oral antiplatelet agents were started and the patient was managed without hemorrhagic complications. In the treatment of Heyde’s syndrome using TAVI, when coagulation dysfunction not detected by common testing methods continues during the acute postoperative phase, the risk of hemorrhagic complications is increased and the use of oral antiplatelet agents is difficult. For this reason, comprehensive evaluation of coagulability by ROTEM might be a useful method to monitor perioperative hemostasis and coagulation.

### Table 2 ROTEM findings

|                  | Before surgery | 6 h after surgery | 12 h after surgery | 24 h after surgery | 3 days after surgery |
|------------------|----------------|-------------------|-------------------|-------------------|---------------------|
| **EXTEM**        |                |                   |                   |                   |                     |
| CT (s) [38–79]   | 59             | 50                | 54                | 57                | 51                  |
| CFT (s) [34–159]| 200            | 130               | 123               | 131               | 103                 |
| A10 (mm) [43–65]| 35             | 44                | 44                | 44                | 49                  |
| MCF (mm) [50–72]| 44             | 52                | 52                | 53                | 56                  |
| **INTEM**        |                |                   |                   |                   |                     |
| CT (s) [100–240]| 308            | 403               | 191               | 240               | 157                 |
| CFT (s) [30–110]| 190            | 182               | 123               | 127               | 102                 |
| A10 (mm) [44–66]| 38             | 37                | 43                | 44                | 47                  |
| MCF (mm) [50–72]| 47             | 46                | 51                | 51                | 52                  |
| **FIBTEM**       |                |                   |                   |                   |                     |
| A10 (mm) [7–23]  | 13             | 14                | –                 | 13                | 16                  |
| MCF (mm) [9–25]  | 14             | 15                | –                 | 14                | 19                  |

Units are given in parentheses and reference ranges are given in square brackets.

ROTEM: rotational thromboelastometry, EXTEM: tissue factor reagent, INTEM: contact coagulation activator reagent, FIBTEM: modified EXTEM test with a platelet aggregation inhibitor, CT: clotting time, CFT: clot formation time, A10: amplitude at 10 min, MCF: maximum clot firmness.

### Acknowledgements
Not applicable.

### Funding
The authors declare that they have no funding.

### Availability of data and materials
The data used in this case report are available from the corresponding author on reasonable request.

### Authors’ contributions
KF and TK performed the anesthesia and wrote the main paper. HM, HH, and MK helped to draft the manuscript. All authors read and approved the final manuscript.

### Ethics approval and consent to participate
Not applicable.

### Consent for publication
Written informed consent was obtained from the patient for the publication of this case report.

### Competing interests
The authors declare that they have no competing interests.

### Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 7 November 2018 Accepted: 3 January 2019
Published online: 11 January 2019

### References
1. Heyde EC. Gastrointestinal bleeding in aortic stenosis. N Engl J Med. 1958; 259:196.
2. Vincentelli A, Susen S, Le Touneau T, Six I, Fabre O, Juthier F, Bauters A, Decoeure C, Goudemand J, Prat A, Jude B. Acquired von Willebrand syndrome in aortic stenosis. N Engl J Med. 2003;349:343–9.
3. Loscabo J. From clinical observation to mechanism—Heyde’s syndrome. N Engl J Med. 2012;367:1954–6.
4. Seyve L, Richarme C, Polack B, Marlu R. Impact of four direct oral anticoagulants on rotational thromboelastometry (ROTEM). Int J Lab Hematol. 2018;40:84–93.

5. Kruse-Jarres R. Acquired bleeding disorders in the elderly. Hematology Am Soc Hematol Educ Program. 2015;2015:231–6.

6. Ganter MT, HOFER OK. Coagulation monitoring: current techniques and clinical use of viscoelastic point-of-care coagulation devices. Anesth Analg. 2008;106:1366–75.

7. Williams B, McNeil J, Crabbe A, Tanaka KA. Practical use of thromboelastometry in the management of perioperative coagulopathy and bleeding. Transfus Med Rev. 2017;31:11–25.

8. Tanaka KA, Key NS, Levy JH. Blood coagulation: hemostasis and thrombin regulation. Anesth Analg. 2009;108:1433–46.

9. Spangenberg T, Budde U, Schewel D, Freker C, Thielsen T, Kuck KH, Schafer U. Treatment of acquired von Willebrand syndrome in aortic stenosis with transcatheter aortic valve replacement. JACC Cardiovasc Interv. 2015;8:692–700.

10. Caspar T, Jesel L, Desprez D, Grunebaum L, Sarnet H, Trinh A, Petit-Eisenmann H, Kindo M, Ohlmann P, Morel O. Effects of transcutaneous aortic valve implantation on aortic valve disease-related hemostatic disorders involving von Willebrand factor. Can J Cardiol. 2015;31:738–43.

11. Tiede A. Diagnosis and treatment of acquired von Willebrand syndrome. Thromb Res. 2012;130(Suppl 2):S2–6.

12. Rodés-Cabau J, Dauerman HL, Cohen MG, Mehta R, Small EM, Smyth SS, Costa MA, Mega JL, O’Donoghue ML, Ohman EM, Becker RC. Antithrombotic treatment in transcatheter aortic valve implantation: insights for cerebrovascular and bleeding events. J Am Coll Cardiol. 2013;62:2349–59.

13. Tanaka KA, Bolliger D, Vadlamudi R, Nimmo A. Rotational thromboelastometry (ROTEM)-based coagulation management in cardiac surgery and major trauma. J Cardiothoracic Vasc Anesth. 2012;26:1083–93.

14. Ziegler B, Solomon C, Cadamuro J, Jones N. Thromboelastometric monitoring of the hemostatic effect of platelet concentrates transfusion in thrombocytopenic children undergoing chemotherapy. Clin Appl Thromb Hemost. 2015;21:558–64.