Background: The frequency and predictors of thrombocytopenia after transcatheter aortic valve implantation (TAVI) are unclear.

Methods and Results: This study enrolled 342 patients undergoing TAVI (245 with a percutaneous transfemoral approach, 65 with transfemoral surgical cutdown, and 32 with a non-transfemoral approach). Balloon-expandable and self-expanding valves were implanted in 235 and 107 patients, respectively. Platelet counts started to drop immediately, reaching a nadir 2–4 days after TAVI. Clinically significant thrombocytopenia (CSTP) was defined as a platelet count \( \leq 50 \times 10^9/L \) at the time of the nadir or both a platelet count between 80 and \( 51 \times 10^9/L \) and a decrease in platelet count \( \geq 50\% \). CSTP occurred in 16.7% patients. Approach site and TAVI valve selection significantly predicted CSTP. In multivariate analysis, independent predictors of CSTP were liver cirrhosis (odds ratio \( OR \) 7.22; 95% confidence interval \( CI \) 1.05–49.82), baseline platelet count \( \leq \) valve selection significantly predicted CSTP. In multivariate analysis, independent predictors of CSTP were liver cirrhosis (odds ratio \( OR \) 7.22; 95% confidence interval \( CI \) 1.05–49.82), baseline platelet count \( \leq 50 \times 10^9/L \) at the time of the nadir or both a platelet count between 80 and \( 51 \times 10^9/L \) and a decrease in platelet count \( \geq 50\% \). CSTP occurred in 16.7% patients. Approach site and TAVI valve selection significantly predicted CSTP. In multivariate analysis, independent predictors of CSTP were liver cirrhosis (odds ratio \( OR \) 7.22; 95% confidence interval \( CI \) 1.05–49.82), baseline platelet count \( \leq 50 \times 10^9/L \) at the time of the nadir or both a platelet count between 80 and \( 51 \times 10^9/L \) and a decrease in platelet count \( \geq 50\% \). CSTP occurred in 16.7% patients. Approach site and TAVI valve selection significantly predicted CSTP.

Conclusions: TAVI-related CSTP was not rare and was associated with poor mid-term outcomes. CSTP was not only caused by patients' comorbidities and TAVI complications, but also related to TAVI procedural factors.

Key Words: Balloon-expandable valve; Mid-term outcome; Self-expanding valve; Thrombocytopenia; Transcatheter aortic valve implantation (TAVI)
Methods

Patient Population
The study population consisted of 400 consecutive patients who underwent TAVI for symptomatic severe aortic valve stenosis at Teikyo University Hospital from February 2014 through August 2018. Baseline demographics, procedural data, and clinical outcomes were collected retrospectively.

The exclusion criteria based on the TAVI procedure were as follows: (1) patients undergoing TAVI with a clinical trial valve; (2) patients with a second valve implantation because of valve dislodgement; and (4) patients with transcatheter valve-in-valve implantation for degenerated aortic bioprosthetic valves.

This study was approved by the Institutional Review Board of the Teikyo University School of Medicine (Teikyo-14-045, 14-045-2). All patients provided informed consent prior to TAVI.

TAVI
All study patients were treated with TAVI using balloon-
ated at baseline (Term 0) and on Days 1 (Term 1), 2–4 (Term 2), and 5–7 (Term 3) postoperatively to assess changes after TAVI. If more than one measurement per patient in Term 2 was acquired, the lowest measure was recorded, whereas in Term 3 the highest measure was recorded.

The nadir platelet count was determined as the lowest recorded platelet count up to 7 days after TAVI. The severity of thrombocytopenia was subsequently stratified as none (platelet count >120 × 10^9 /L), mild (120–81 × 10^9 /L), moderate (80–51 × 10^9 /L), and severe (≤50 × 10^9 /L) based on the lowest platelet count, consistent with the 2017 new diagnostic criteria for disseminated intravascular coagulation (DIC) from the Japanese Society on Thrombosis and Hemostasis.\textsuperscript{11} Thrombocytopenia was also defined as a percentage decrease in platelet count (DPC) ≥50% determined from the pre- and lowest post-procedural platelet counts. Clinically significant thrombocytopenia (CSTP) was assessed at baseline (Term 0) and on Days 1 (Term 1), 2–4 (Term 2), and 5–7 (Term 3) postoperatively.

### Platelet Counts and Thrombocytopenia

The platelet count was measured before and after TAVI up to Days 5–7 postoperatively. Platelet counts were evaluated at baseline (Term 0) and on Days 1 (Term 1), 2–4 (Term 2), and 5–7 (Term 3) postoperatively to assess changes after TAVI. If more than one measurement per patient in Term 2 was acquired, the lowest measure was recorded, whereas in Term 3 the highest measure was recorded.

The nadir platelet count was determined as the lowest recorded platelet count up to 7 days after TAVI. The severity of thrombocytopenia was subsequently stratified as none (platelet count >120 × 10^9 /L), mild (120–81 × 10^9 /L), moderate (80–51 × 10^9 /L), and severe (≤50 × 10^9 /L) based on the lowest platelet count, consistent with the 2017 new diagnostic criteria for disseminated intravascular coagulation (DIC) from the Japanese Society on Thrombosis and Hemostasis.\textsuperscript{11} Thrombocytopenia was also defined as a percentage decrease in platelet count (DPC) ≥50% determined from the pre- and lowest post-procedural platelet counts. Clinically significant thrombocytopenia (CSTP)

### Table 1. Patient Demographics at Baseline

| Table 1. Patient Demographics at Baseline | All (n=342) | No CSTP (n=285) | CSTP (n=57) | P-value |
|------------------------------------------|------------|----------------|-----------|--------|
| Age (years)                              | 85 [82–88] | 85 [81–88]     | 86 [82–89] | 0.183  |
| Male sex                                 | 83 (24.3)  | 66 (23.2)      | 17 (29.8)  | 0.284  |
| Diabetes                                 | 112 (32.7) | 98 (34.4)      | 14 (24.6)  | 0.149  |
| Hypertension                             | 282 (82.5) | 234 (82.1)     | 48 (84.2)  | 0.703  |
| Dyslipidemia                             | 246 (71.9) | 210 (73.7)     | 36 (63.2)  | 0.106  |
| Chronic kidney disease                   | 196 (57.3) | 161 (56.5)     | 35 (61.4)  | 0.494  |
| Smoking                                  | 76 (22.2)  | 60 (21.1)      | 16 (28.1)  | 0.245  |
| Baseline platelet count (<10/\(\times 10^9\)) | 188 [157–227] | 193 [159–231] | 163 [132–189] | <0.001 |
| Baseline thrombocytopenia (≤120 × 10^9 /L) | 31 (9.1)  | 19 (6.7)       | 12 (21.1)  | 0.001  |
| Active cancer                            | 17 (5.0)   | 13 (4.6)       | 4 (7.0)    | 0.500  |
| Blood diseases                           | 8 (2.3)    | 5 (1.8)        | 3 (5.3)    | 0.133  |
| Liver cirrhosis                          | 5 (1.5)    | 2 (0.7)        | 3 (5.3)    | 0.034  |
| Society of Thoracic Surgeons score (%)   | 7.241 [5.005–10.756] | 7.275 [4.924–10.803] | 7.162 [5.384–10.409] | 0.777  |
| Logistic EuroSCORE (%)                   | 13.010 [9.400–20.070] | 12.810 [9.210–20.450] | 14.370 [10.245–19.730] | 0.405  |
| Procedural access site                    |            |                |           |        |
| Transfemoral (percutaneous)              | 245 (71.6) | 215 (75.4)     | 30 (52.6)  | 0.002  |
| Transfemoral (cutdown)                   | 65 (19.0)  | 48 (16.8)      | 17 (29.8)  |        |
| Non-transfemoral                         | 32 (9.4)   | 22 (7.7)       | 10 (17.5)  |        |
| Transcatheter aortic valve               |            |                |           |        |
| Self-expanding valve                     | 107 (31.3) | 97 (34.0)      | 10 (17.5)  | 0.014  |
| Balloon-expandable valve                 | 235 (68.7) | 188 (66.0)     | 47 (82.5)  |        |

Unless indicated otherwise, data are presented as median [interquartile range] or as n (%). CSTP, clinically significant thrombocytopenia.

### Table 2. Clinical Outcomes

| Table 2. Clinical Outcomes | All (n=342) | No CSTP (n=285) | CSTP (n=57) | P-value |
|----------------------------|------------|----------------|-----------|--------|
| 30-day mortality          | 5 (1.5)    | 1 (0.4)        | 4 (7.0)   | 0.003  |
| Major vascular complications | 17 (5.0)  | 9 (3.2)        | 8 (14.0)  | 0.001  |
| Life-threatening or major bleeding | 42 (12.3) | 22 (7.7)      | 20 (35.1) | <0.001 |
| Periprocedural MI          | 2 (0.6)    | 1 (0.4)        | 1 (1.8)   | 0.306  |
| Stroke                     | 5 (1.5)    | 3 (1.1)        | 2 (3.5)   | 0.195  |
| Multiple blood transfusions | 68 (19.9) | 38 (13.3)      | 30 (52.6) | <0.001 |
| Platelet transfusion       | 5 (1.5)    | 0 (0)          | 5 (8.8)   | <0.001 |
| 1-year mortality           | 43 (12.6)  | 29 (10.2)      | 14 (24.6) | 0.003  |

Unless indicated otherwise, data are presented as n (%). CSTP, clinically significant thrombocytopenia; MI, myocardial infarction.
was defined as severe thrombocytopenia (platelet count ≤120×10^9/L) or both moderate thrombocytopenia (80–120×10^9/L) and a DPC ≥50%.

Clinical Endpoints

Data on vascular complications, bleeding complications, periprocedural myocardial infarction, stroke, and multiple blood transfusions were collected according to the Valve Academic Research Consortium-2 criteria. The incidence of platelet transfusion within 1 week after TAVI was also investigated. Follow-up was performed at 30 days and 1 year after the procedure, and thereafter through clinical outpatient visits or telephone contact. All-cause mortality data at 30 days and 1 year were obtained for all patients.

Statistical Analysis

Categorical data are expressed as frequency counts and percentages. Continuous data are expressed as the median and interquartile range (IQR). Categorical data were compared using the Chi-squared or Fisher’s exact tests. Continuous data were compared between groups using the Mann-Whitney U-test. Univariate and multivariate logistic regression analyses were performed to examine clinical predictors of CSTP-related TAVI. All variables at P≤0.1 in the univariate analysis were included in a multivariate logistic regression analysis. Two-sided P<0.05 was considered statistically significant. All analyses were performed using SPSS statistics version 19.0 (SPSS Inc., Chicago, IL, USA).

Results

In all, 388 patients underwent TAVI. Of these 388 patients, 46 were excluded because of their clinical course after TAVI (Figure 1). Therefore, 342 patients comprised the study population (median age 85 years [IQR 82–88 years]; 24.3% male).

CSTP After TAVI

The median baseline platelet count was 188×10^9/L (IQR 157–227×10^9/L; range 44–612×10^9/L). Thrombocytopenia (platelet count ≤120×10^9/L) at baseline was seen in 31 (9.1%) patients. After TAVI, platelet counts started to drop immediately and reached a nadir (Figure 2). The median nadir platelet count was 108×10^9/L (IQR 82–137×10^9/L; range 15–306×10^9/L). The median DPC was 40.8% (IQR 32.4–50.8%) and 92 patients had a DPC ≥50%. The platelet count recovered by Day 7. Of all 342 patients in the study, 242 (70.8%) had improved platelet counts to >120×10^9/L by Term 3 after TAVI.

Based on the nadir platelet count, 131 (38.3%) patients had no thrombocytopenia, 132 (38.6%) had mild thrombocytopenia, and 65 (19.0%) had moderate thrombocytopenia. The remaining 14 (4.1%) patients had severe thrombocytopenia, which was defined as CSTP. Of 65 patients with moderate thrombocytopenia, 43 had DPC ≥50%. Thus, these 43 patients were reclassified as having

| Table 3. Predictors of TAVI-Related Clinically Significant Thrombocytopenia | Univariate analysis | Multivariate analysis |
| --- | --- | --- |
| | OR (95% CI) | P-value | OR (95% CI) | P-value |
| **Patient background** | | | | |
| Age | 1.04 (0.98–1.10) | 0.166 | | |
| Male sex | 1.41 (0.75–2.65) | 0.285 | | |
| Baseline platelet count ≤120×10^9/L | 3.73 (1.70–8.22) | 0.001 | 2.98 (1.20–7.38) | 0.018 |
| Hypertension | 1.16 (0.54–2.52) | 0.703 | | |
| Diabetes | 0.62 (0.32–1.19) | 0.152 | | |
| Dyslipidemia | 0.61 (0.34–1.12) | 0.109 | | |
| Active cancer | 1.58 (0.50–5.03) | 0.440 | | |
| Blood disease | 3.11 (0.72–13.41) | 0.128 | | |
| Liver cirrhosis | 7.86 (1.28–48.17) | 0.026 | 7.22 (1.05–49.82) | 0.045 |
| Logistic EuroSCORE | 1.00 (0.97–1.02) | 0.858 | | |
| Society of Thoracic Surgeons score | 1.00 (0.96–1.05) | 0.988 | | |
| **TAVI procedure** |  |  |  | |
| Transfemoral (cutdown) | 2.54 (1.30–4.97) | 0.007 | 1.61 (0.74–3.52) | 0.229 |
| Non-transfemoral | 3.26 (1.41–7.54) | 0.006 | 1.30 (0.45–3.76) | 0.825 |
| Balloon-expandable valve | 2.43 (1.17–5.01) | 0.017 | 2.38 (1.04–5.46) | 0.040 |
| **Procedural adverse events** |  |  |  | |
| Major vascular complication | 5.01 (1.84–13.61) | 0.002 | 1.91 (0.52–7.09) | 0.333 |
| Major bleeding complication | 6.46 (3.22–12.97) | <0.001 | 1.98 (0.68–5.73) | 0.209 |
| Multiple blood transfusion | 7.22 (3.88–13.45) | <0.001 | 4.03 (1.72–9.41) | 0.001 |

CI, confidence interval; OR, odds ratio; TAVI, transcatheter aortic valve implantation.
CSTP. Overall, 57 (16.7%) patients were considered as having CSTP in the present study.

Baseline characteristics were dichotomized based on patients with (n=57) and without (n=285) CSTP (Table 1). Clinical outcomes are summarized in Table 2. Patients with CSTP had a significantly higher 30-day mortality rate (7.0% vs. 0.4%; P=0.003) and higher rates of major vascular complications (14.0% vs. 3.2%; P=0.001) and life-threatening or major bleeding (35.1% vs. 7.7%; P <0.001) during the perioperative period. There were no significant differences in myocardial infarction and stroke between the 2 groups. Platelet transfusion was performed for 5 patients after TAVI, all of whom had CSTP. In addition, 1-year mortality was significantly higher in patients with than without CSTP (24.6% vs. 10.2%, respectively; P=0.003).

Predictors of CSTP based on univariate analysis are given in Table 3. Transfemoral TAVI accessed via surgical cutdown, non-transfemoral TAVI, and the use of balloon-expandable valves were significant predictors related to the TAVI procedure. The rate of life-threatening or major bleeding differed significantly among the 3 approach sites (6.1%, 20.0%, and 43.8% for percutaneous transfemoral TAVI, TAVI accessed via surgical cutdown, and non-transfemoral TAVI, respectively; P<0.001). There were no significant differences in the 30-day mortality among the 3 groups (1.2%, 3.1%, and 0% for percutaneous transfemoral TAVI, TAVI accessed via surgical cutdown, and non-transfemoral TAVI, respectively; P=0.417).

Multivariate analysis revealed that liver cirrhosis, baseline platelet count ≤120×10^9/L, multiple blood transfusions, and the use of balloon-expandable valves were independent predictors of CSTP (Table 3).

Table 4 summarizes results of univariate and multivariate logistic regression analyses for 30-day mortality. Multivariate analysis revealed that TAVI-related CSTP (odds ratio [OR] 13.74, 95% confidence interval [CI] 1.06–178.44; P=0.045) was the only independent predictor for 30-day mortality.

At a median follow-up of 2.0 years (IQR 1.1–3.2 years), 58 patients had died. There were significant differences in all-cause mortality between patients with and without CSTP (Figure 3). The 2-year all-cause mortality rate for patients with CSTP was 31.4%, compared with 15.5% for patients without CSTP.

Table 4. Predictors of 30-Day Mortality After TAVI

|                        | Univariate analysis | Multivariate analysis |
|------------------------|---------------------|-----------------------|
|                        | OR (95% CI)         | P-value               | OR (95% CI)         | P-value               |
| **Patient background** |                     |                       |                     |                       |
| Age                    | 1.02 (0.86–1.20)    | 0.858                 |                       |                       |
| Male sex               | 2.11 (0.35–12.83)   | 0.419                 |                       |                       |
| Baseline platelet count ≤120×10^9/L | N/A               | 0.998                 |                       |                       |
| Hypertension           | N/A                 | 0.997                 |                       |                       |
| Diabetes               | 1.38 (0.23–8.35)    | 0.729                 |                       |                       |
| Dyslipidemia           | 1.57 (0.17–14.23)   | 0.688                 |                       |                       |
| Active cancer          | N/A                 | 0.999                 |                       |                       |
| Blood disease          | N/A                 | 0.999                 |                       |                       |
| Liver cirrhosis        | N/A                 | 0.999                 |                       |                       |
| Logistic EuroSCORE     | 1.01 (0.94–1.08)    | 0.788                 |                       |                       |
| Society of Thoracic Surgeons score | 1.01 (0.88–1.15) | 0.905                 |                       |                       |
| **TAVI procedure**     |                     |                       |                       |                       |
| Transfemoral (cutdown) | 2.56 (0.42–15.66)   | 0.309                 |                       |                       |
| Non-transfemoral       | N/A                 | 0.998                 |                       |                       |
| Balloon-expandable valve | 0.68 (0.11–4.12)    | 0.674                 |                       |                       |
| **Procedural adverse events** |               |                       |                       |                       |
| Major vascular complication | 5.02 (0.53–47.50)   | 0.160                 |                       |                       |
| Major bleeding complication | 4.95 (0.80–30.53)   | 0.085                 | N/A                   | 0.998                 |
| Multiple blood transfusion | 6.28 (1.03–38.34)   | 0.047                 | 2.12 (0.16–28.02)     | 0.567                 |
| Platelet transfusion   | 74.22 (8.91–618.18) | <0.001                | N/A                   | 0.997                 |
| TAVI-related CSTP      | 21.43 (2.35–195.55) | 0.007                 | 13.74 (1.06–178.44)   | 0.045                 |
| Stroke                 | N/A                 | 0.999                 |                       |                       |
| Periprocedural MI      | 84.00 (4.43–1,591.94)| 0.003                 | 28.90 (0.16–5,215.25) | 0.204                 |

N/A, not applicable. Other abbreviations as in Tables 2,3.
Discrimination of TAVI-Related CSTP

The definition of thrombocytopenia varies. Based on contemporary expert hematological consensus, a cut-off platelet value of $100 \times 10^9/L$ is used to define thrombocytopenia.13 Clinically, a cut-off value of $150 \times 10^9/L$ is also used.14 Regarding TAVI-related thrombocytopenia, several studies have defined moderate/severe thrombocytopenia as a nadir platelet count <100×10^9/L. Some studies have excluded patients with platelet counts <100×10^9/L at baseline.15 In other studies that have not considered platelet count at baseline, TAVI-related thrombocytopenia was

Table 5. Predictors of Percutaneous TAVI-Related Clinically Significant Thrombocytopenia

| Patient background | Univariate analysis | Multivariate analysis |
|--------------------|---------------------|-----------------------|
|                    | OR (95% CI) | P-value | OR (95% CI) | P-value |
| Age                | 1.03 (0.96–1.10) | 0.486 | 1.13 (1.00–1.27) | 0.050 |
| Male sex           | 1.69 (0.74–3.86) | 0.210 | 1.87 (0.77–4.49) | 0.180 |
| Baseline platelet count ≤120×10^9/L | 5.65 (2.11–15.12) | 0.001 | 4.78 (1.48–15.42) | 0.009 |
| Hypertension       | 0.86 (0.33–2.25) | 0.756 | 0.84 (0.31–2.20) | 0.756 |
| Diabetes           | 0.42 (0.17–1.08) | 0.071 | 0.42 (0.15–1.19) | 0.089 |
| Dyslipidemia       | 0.48 (0.22–1.06) | 0.068 | 0.48 (0.19–1.22) | 0.120 |
| Active cancer      | 2.06 (0.54–7.86) | 0.290 | 2.06 (0.54–7.86) | 0.290 |
| Blood disease      | 11.83 (1.89–74.02) | 0.008 | 5.01 (0.90–27.80) | 0.068 |
| Liver cirrhosis    | N/A                 | 0.999 | N/A                 | 0.999 |
| Logistic EuroSCORE | 0.96 (0.92–1.01) | 0.117 | 0.96 (0.92–1.01) | 0.117 |
| Society of Thoracic Surgeons score | 0.97 (0.90–1.04) | 0.334 | 0.97 (0.90–1.04) | 0.334 |
| TAVI procedure     | Balloon-expandable valve | 2.52 (0.99–6.41) | 0.053 | 2.52 (0.99–6.41) | 0.053 |
| Procedural adverse events | Major vascular complication | 14.13 (3.19–62.72) | <0.001 | 9.01 (1.10–73.74) | 0.040 |
|                    | Major bleeding complication | 5.72 (1.87–17.47) | 0.002 | 1.04 (0.15–7.35) | 0.966 |
|                    | Multiple blood transfusion | 7.06 (3.02–16.55) | <0.001 | 3.63 (1.17–11.30) | 0.026 |

Abbreviations as in Tables 3,4.
defined as a combination of a nadir platelet count $<100 \times 10^9 /L$ and DPC $\geq 50\%$.\textsuperscript{1,2,3}

In the present study, the 2017 new diagnostic criteria for DIC from the Japanese Society on Thrombosis and Hemostasis were used to define thrombocytopenia.\textsuperscript{11} This guideline classifies thrombocytopenia in more detail than the definitions used in other studies. Severe thrombocytopenia was defined as a nadir platelet count of $\leq 50 \times 10^9 /L$. According to the guidelines of the Health, Labor, and Welfare Ministry in Japan for the use of platelet transfusion concentrates, the trigger value for platelet transfusion during surgery is a platelet count of $\leq 50 \times 10^9 /L$. Thus, CSTP defined as a nadir platelet count $\leq 50 \times 10^9 /L$ is acceptable.

In the present study, CSTP was also defined as both moderate thrombocytopenia ($80-51 \times 10^9 /L$) and DPC $\geq 50\%$. The 2017 new diagnostic criteria also proposed defining thrombocytopenia severity according to a combination of the nadir platelet count and DPC. Thus, the definition of CSTP used in the present study was more rigorous than that used in previous studies. In fact, CSTP was an independent predictor of 30-day mortality. In addition, mid-term mortality was greater in patients with than without CSTP. Some previous studies using other definitions may have included cases with insufficient clinical significance. We believe that the definition of CSTP used in the present study is the most appropriate definition for TAVI-related thrombocytopenia.

Cause of TAVI-Related Thrombocytopenia

The mechanisms underlying the development of thrombocytopenia are as follows: (1) decreased platelet production; (2) splenic sequestration; (3) platelet destruction; (4) platelet consumption; and (5) pseudothrombocytopenia.\textsuperscript{18} The causes of TAVI-related thrombocytopenia can be attributed to 3 types of factors, namely those related to patients and the TAVI procedure itself, as well as TAVI complications.\textsuperscript{16,17} Of these 3 types of factors, patient-specific factors and TAVI complications have been reported as independent predictors of TAVI-related thrombocytopenia. As an example of patient-specific factors, patients who underwent TAVI in the present study were elderly and had reduced platelet production. In fact, approximately 9% of the study patients had thrombocytopenia at baseline. This trend was more marked in patients with blood disease and liver cirrhosis. Because platelet counts decrease by approximately 40% after TAVI, patients with lower baseline platelet counts are likely to have clinically relevant thrombocytopenia. Furthermore, it is known that bleeding complications and multiple blood transfusions cause pseudothrombocytopenia.\textsuperscript{16,18} Therefore, complications should be avoided in patients with thrombocytopenia at baseline.

In addition, this study showed that both the approach site for TAVI and transcatheter aortic valve selection are new independent predictors of thrombocytopenia.

ApproachSites for TAVI Procedure

In this study there were differences in the incidence of CSTP depending on the approach site for the TAVI procedure. Previous studies reported no differences in the rates of vascular and bleeding complications between transfemoral and transapical approaches.\textsuperscript{2,19,20} Conversely, bleeding complications are lower for the percutaneous transfemoral TAVI approach than for other approaches, including transfemoral TAVI via surgical cutdown.\textsuperscript{21,22} The approach site selected was strongly associated with the incidence of TAVI complications. Life-threatening or major bleeding complications were less frequent in patients with complete percutaneous transfemoral TAVI (6.1%), whereas transfemoral TAVI accessed via surgical cutdown (20.0%) and non-transfemoral TAVI (43.8%) were associated with more frequent life-threatening or major bleeding complications. However, the access site of the TAVI approach was not found to be an independent predictor of TAVI-related CSTP in multivariate analysis.

Transcatheter Aortic Valve Selection

Implantation of the transcatheter aortic valve has been associated with mechanical platelet destruction, an increase in the coagulation cascade, and platelet consumption due to inflammation. In the present study, the transcatheter aortic valve selected (i.e., the difference between balloon-expandable transcatheter aortic valves and self-expanding valves) was identified as a new predictor of TAVI-related thrombocytopenia. Depending on the shape of the valve and the placement method, intimal injury, shear stress, and inflammation may differ and lead to differences in thrombocytopenia.

This result is consistent with previous studies.\textsuperscript{5,6} These studies revealed that differences in TAVI valves affected DPC severity. However, the nadir platelet count was not considered in those studies. Moreover, these reports defined thrombocytopenia as DPC $>30\%$. Other studies found that the median DPC after TAVI ranged from 34% to 38.6%.\textsuperscript{14,24} Thus, it may not be appropriate to only use DPC $<30\%$ as a definition of CSTP.

Thrombocytopenia as a Marker of Poor Prognosis

In the present study we found that patients with TAVI-related CSTP had a significantly worse perioperative mid-term prognosis. It has been reported that thrombocytopenia after TAVI is also associated with 1-year mortality.\textsuperscript{1} Thrombocytopenia has been established as a useful marker of prognosis for patients in intensive care units.\textsuperscript{25} For patients with TAVI-related CSTP, it is important to carefully monitor and manage these patients.

Study Limitations

The present study was a single-center retrospective observational study and sample size was limited. However, in this study we used a new definition of TAVI-related thrombocytopenia. This new definition is more clinically relevant than the definition used in previous studies. Current research provides more clinically useful information.

The number of patients with transapical, trans-subclavian, and direct aortic access was relatively small. However, the use of the percutaneous transfemoral TAVI approach as the preferred approach will increase in the future. Thus, this limitation may not be resolved. In the present study, almost the same results were confirmed in patients with percutaneous transfemoral TAVI.

It is difficult to differentially diagnose TAVI-related CSTP and heparin-induced thrombocytopenia (HIT) in patients undergoing TAVI. Most patients have undergone coronary angiography with unfractionated heparin within 30 days prior to TAVI. In addition, unfractionated heparin was readministered during TAVI. In the present study, there were 5 patients with an intermediate score for HIT based on the 4Ts scoring system.\textsuperscript{26,27} In these 5 patients, HIT antibodies (anti-platelet factor 4 or heparin antibodies)
had not been investigated. The remaining patients had low scores for HIT, and HIT was excluded in almost all patients except for those 5 patients with an intermediate score.

Conclusions

TAVI-related CSTP was not rare and was associated with poor outcomes. It was not only caused by a patient’s comorbidities and procedural adverse events, but was also related to TAVI procedural factors. TAVI complications should try to be avoided in patients with thrombocytopenia (platelet count ≤120x10^9/L) at baseline. In addition, appropriate selection of the TAVI approach site and transcatheter aortic valve, if possible, may reduce the risk of CSTP.

Acknowledgment

The authors acknowledge the valued contribution of Aki Takahashi.

Sources of Funding

None.

Conflict of Interest

Y.W. is a proctor for Edwards Japan and Medtronic Japan. The other authors report no conflicts of interest.

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