The Outcomes of Thoracic Endovascular Aortic Repair in Japan in 2017: A Report from the Japanese Committee for Stentgraft Management

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Introduction

Thoracic endovascular aortic repair (TEVAR) was initially used in treating descending thoracic aortic aneurysms back in 1992.1) It was then approved by the United States Food and Drug Administration in 2005. Since then, TEVAR has been adopted worldwide and has been improved dramatically, both procedurally and in terms of available materials. In Japan, TEVAR is identified as the standard treatment for descending thoracic aneurysms.2) The emergence of fenestrated stent grafts to better fit the angulated morphology of the thoracic arch and of the lower profile and the 2015 approval of TEVAR for aortic dissection have led to an increase in the annual number of TEVAR procedures performed in Japan. However, the outcomes of TEVAR are yet to be evaluated in a large cohort.

Thus, in this study, we aim to report the number of TEVAR procedures conducted in Japan in 2017, including its mortality and complication rates, by using the data from the Japanese Committee for Stentgraft Management (JACSM) nationwide registry; this data covers the outcomes of nearly all of the stent grafts shipped to Japan.3,4)

JACSM and database

The JACSM nationwide registry, including its foundations, structure, and quality control, has already been previously described in detail.3,4) The JACSM, established in December 2006, is composed of 10 societies related to endovascular treatment and determined the practical standards for institutions and for practicing and supervising surgeons. Participating institutions were obligated to report their data on endovascular aneurysm repair (EVAR) and TEVAR, using a web-based case-registry form (http://www.stentgraft.jp/).

The information collected as regards TEVAR included preoperative information, anatomical factors evaluated during operative planning, and data obtained in the immediate postoperative period, at discharge, at 6 months postoperative, and at each year after that. As of 2015, 366 institutes in Japan had been certified for TEVAR by the JACSM.

This registry was conducted in accordance to the principles of the Declaration of Helsinki, the International Conference on Harmonization, and Good Clinical Practice guidelines. The use of registry data was approved by the Institutional Review Board of the University of Tokyo Hospital (approval number: 2019306NI).
Materials and Methods

Groups and categories
Between January 2017 and December 2017, around 6,081 patients who underwent TEVAR were registered. The patients were excluded from this report if they had a history of TEVAR (n=494) or missing data regarding stent graft location (n=10). The final analysis included 5,577 patients (Fig. 1a). The patients were then divided into two groups: dissection (n=2,058) and non-dissection (n=3,519). Patients in the dissection group were further categorized as acute (TEVAR within 2 weeks of onset; n=575), sub-acute (TEVAR between 2 weeks and 2 months of onset; n=363), and chronic (TEVAR more than 2 months after onset; n=1,120). Meanwhile, patients in the non-dissection group were categorized according to the stent graft placement (Ishimaru criteria: Fig. 1b): arch (zone 0 to 2; n=1,492), descending (zone 3 to Th 12; n=1,898), and thoracoabdominal (TAAA) (L1 and distal; n=129) (Fig. 1a).

Type of data collected
Data regarding patient age, sex, rupture, pathogenesis, comorbidities, renal function, condition of the proximal fixation, and preoperative aneurysm diameter were collected from the database for this report. Patient comorbidities included chronic obstructive pulmonary disease, hypertension (with medication), cerebrovascular infarction or hemorrhage, liver dysfunction, hemodialysis, carotid artery disease (≥75% stenosis), coronary heart disease with a history of intervention, history of thoracic surgery, history of abdominal surgery, history of thoracotomy, and Marfan syndrome. Renal function was then determined using serum creatinine level and estimated glomerular filtration rate. The diameter and landing length of the proximal fixation were then categorized in 5-mm increments. The diameters of aortic aneurysms categorized as "saccular" were specifically demonstrated. For the dissection group, data regarding the Stanford classification, complications related to aortic dissection (aortic dilatation, impending rupture, rupture, and malperfusion), and conditions of the dissected lumen (double barrel, thrombosed, or ulcer-like projection) were collected.

Operative procedures
The type of stent grafts and anesthesia, proximal landing condition, occluded aortic branches, bypasses, and additional or emergent procedures (within 24 h after admission) can vary, depending on the discretion of the treating physician.

Outcomes
The intraoperative rates of mortality, vascular injury, rupture, or endoleak and the intraoperative radiation dose were reported. Postoperative mortality or adverse events (e.g., migration, endoleak, thromboembolism, renal insufficiency, hemodialysis, cerebrovascular damage, paraplegia, multiple organ failure, and aneurysm rupture) before discharge from the hospital were also noted.

Categorical variables were presented as numbers and percentages, whereas continuous variables were presented as means ± standard deviations. The duration of hospitalization after the operation is presented as median with interquartile range.
Results

Patient demographics
The mean patient ages were 66.2 ± 13.1 years and 75.7 ± 9.3 years in the dissection and non-dissection groups, respectively. As per our findings, nearly half (41.0%) of the patients in the dissection group were < 65 years old, as were 8.3% of patients in the non-dissection group. Approximately 25% of patients in each group and subgroup were women. The rates of aortic rupture were determined to be 8.4% and 11.1% in the dissection and non-dissection groups, respectively. A degenerative etiology was observed in 74.6% and 90.1% of patients in the dissection and non-dissection groups, respectively. The mean diameters of the aortic aneurysm were 46.4 ± 11.5 mm and 52.1 ± 14.1 mm in the dissection and non-dissection groups, respectively. The mean diameters of saccular type aortic aneurysms were 44.9 ± 12.1 mm and 49.2 ± 14.3 mm in the dissection (n = 377, 18.3%) and non-dissection groups (n = 1,915, 54.4%), respectively (Table 1).

Intraoperative data
Emergent operations were performed for 24.8% and 15.2% of patients in the dissection and non-dissection groups, respectively. The rate of emergent operations was determined to be high in the acute dissection subgroup (77.4%). TEVAR with bypasses was performed for approximately 10% of patients in both groups and was more frequently required in the arch (21.6%) and TAA A (14.0%) subgroups. Bypasses were performed in 20.2% and 24.8% of patients in the dissection and non-dissection groups, respectively. The rate of bypasses was highest in the arch (53.5%) and TAA A (17.1%) subgroups.

The intraoperative mortality rate was 0.3% in both groups. The rates of intraoperative vascular injury were determined to be 1.7% and 3.3% in the dissection and non-dissection groups, respectively. The intraoperative rupture rate was 0.3% in the dissection group, whereas for the non-dissection group, it was 0.5% (Table 2).

Postoperative data
The in-hospital mortality rates (including intraoperative death) were 3.6% and 4.4% in the dissection and non-dissection groups, respectively. The mortality rates of the acute (10.0%) and TAA A subgroups (11.6%) were deemed to be the highest. Renal insufficiency occurred in 8.7% and 13.2% of patients in the acute dissection and TAA A subgroups, respectively. Cerebrovascular damage occurred in 8.5% of patients in the arch subgroup. Multiple organ failure and hemodialysis occurred in 7.0% and 6.2% of patients, respectively, in the TAA A subgroup. The overall rates of paraplegia were 2.2% and 4.8% in the dissection and non-dissection groups, respectively. The rates of paraplegia were 4.5% and 2.3% in the acute dissection and TAA A subgroups, respectively.

Endoleak data were obtained for 5,037 patients for whom contrast-enhanced computed tomography (CT) was performed during their hospital stay. The number of type 1 and 3 endoleaks at hospital discharge was 124 (6.5%) and 157 (4.9%) in the dissection and non-dissection groups, respectively. The rates of type 1 endoleak were found to be 6.9% and 7.2% in the chronic dissection and arch subgroups, respectively. The rates of type 2 endoleak were 5.7% and 5.9% in the sub-acute dissection and TAA A subgroups, respectively (Table 3).

Causes of death
Intraoperative rupture, hemorrhage, or systemic circulatory failure were the most common causes of intraoperative death, accounting for 6 and 10 patients in the dissection and non-dissection groups, respectively. During hospital admission, vascular-related complications (including retrograde type A aortic dissection [RTAD]) were identified to be the most common causes of death in the dissection group. Meanwhile, in the non-dissection group, infection and sepsis were the most common causes of postoperative death (Table 4).

Discussion
The JACSM registry began in July 2006 after the approval of the use of stent graft device in Japan, and the data input and storage have been transferred from the JACSM database to the National Clinical Database (NCD) since January 2016. The 2016 annual data was reported on the JACSM website, and the committee has decided to publish the annual data henceforth. These data can help with preoperative planning for thoracic aortic diseases.

In this study, patients were divided into dissection and non-dissection groups as TEVAR is performed for aortic dissection as well as entry/re-entry closure. The dissection group was categorized according to the timing of the operation: acute (TEVAR within 2 weeks of onset), sub-acute (TEVAR between 2 weeks and 2 months of onset), and chronic (TEVAR more than 2 months after onset). The threshold of 2 months was chosen according to the Japanese Circulation Society (JCS) guidelines published in 2006. However, the sub-acute category was not included in the JCS guideline in 2011, and the threshold was then revised from 2 months to 3 months in the 2020 JCS guideline. To account for the revised guidelines, the JACSM-NCD registry will be adjusted to include an input for day of onset so that the interval between onset and TEVAR can be automatically calculated.

Patients in the acute dissection subgroup were deter-
## Table 1: Patients’ demographics

|                     | Dissection | Non-dissection |
|---------------------|------------|---------------|
| Number of cases     | Total 2058 | 3519          |
| Preoperative data   |            |               |
| Female              | 148/92/275 | 515/25.0%     |
| Age (mean±SD)       | 66±13.1   | 75±9.3       |
| Rupture             | 173/9/26  | 390/11.0%     |
| Rupture (+)         | 1878/75%  | 3113/88.4%    |
| Rupture (-)         | 7/0.3%    | 16/0.4%       |
| Stanford classification |          |              |
| Type A              | 282/13.7% | 1352/90.6%    |
| Type B              | 1776/86.3%| 468/13.7%     |
| Complication of aortic dissection |         |               |
| Aortic dilation     | 520/25.2% | 89/2.5%       |
| Impending rupture   | 93/4.5%   | 28/1.9%       |
| Rupture             | 182/8.8%  | 9/0.3%        |
| Malperfusion        | 249/12.1% | 7/0.3%        |
| Condition of the dissected lumen |        |               |
| Patent (double barrel) | 1307/63.5%| 377/65.6%     |
| Thrombosed          | 261/12.6% | 94/16.3%      |
| U lc er-like projection | 490/23.8%| 104/18.1%     |
| Pathogenesis        |            |               |
| Degenerative        | 1536/74.6%| 232/6.5%      |
| Inflammation        | 2/0.1%    | 12/0.3%       |
| Aortitis            | 1/0.0%    | 5/0.1%        |
| Infection           | 8/0.3%    | 89/2.5%       |
| Connective tissue disorders | 30/1.4% | 9/0.2%        |
| Others              | 481/23.3% | 232/6.5%      |
| Comorbidity          |            |               |
| COPD                | 338/16.4% | 420/28.2%     |
| Hypertension        | 1689/82.0%| 1175/78.8%    |
| Cerebrovascular disease | 182/8.8% | 219/14.7%     |
| Liver dysfunction   | 69/3.3%   | 110/3.1%      |
| Hemodialysis        | 41/1.9%   | 133/3.7%      |
| Carotid artery diseases | 35/1.7% | 48/3.2%       |
| Coronary heart disease | 134/6.5% | 57/3.8%       |
| History of thoracic surgery | 214/10.4% | 62/4.2%      |
| History of abdominal surgery | 75/3.6% | 294/8.3%      |
| History of thoracotomy | 221/10.7%| 393/6.2%      |
| Marfan syndrome     | 29/1.4%   | 10/0.2%       |
| Renal function      |            |               |
| Creatinine (mean±SD) (mg/dL) | 1.12±1.12 | 1.42±1.29 |
| <1.2                | 1566/76.0%| 1089/73.0%    |
| <1.6                | 283/13.7% | 220/14.7%     |
| <2.0                | 83/4.0%   | 74/5.0%       |
| 2.0≤                | 110/5.3%  | 97/6.5%       |
| eGFR (mean±SD)      | 61.1±26.3 | 55.8±22.3     |
| <15                 | 61/2.9%   | 159/4.5%      |
| <30                 | 85/4.1%   | 251/7.1%      |
| <45                 | 322/15.6% | 604/17.1%     |
mined to have a high mortality rate (10.0%), which may be due to the high rate of emergent operations (77.4%) and ruptures (24.0%) in this subgroup. This was in contrast to the mortality rates of the sub-acute (0.8%) and chronic (1.2%) dissection subgroups, which were found to be lower, as were their emergent operation rates (7.4% and 3.5%, respectively). Furthermore, the mean aneurysm diameters of the sub-acute (42.9 mm) and chronic (49.7 mm) dissection groups were below the threshold (55 mm to 60 mm: Class IIa) in the guidelines. These data indicate that a considerable number of TEVAR procedures were performed preemptively for the closure of the entry of the dilating false lumen or to prevent an aortic rupture. These indications for operation cannot be distinguished in the current JACSM registry; therefore, a new input for the indication for TEVAR will be included after 2021.

Vascular-related complications have been identified as the most common cause of postoperative death during admission in the dissection group, including RTAD. The reporting of RTAD will also be added to the registry after 2021.

The non-dissection group was divided into three categories according to the stent graft placement location, as described in the Japan Adult Cardiovascular Surgery Database: arch (zone 0 to 2), descending (zone 3 to Th 12), and TAAA (L1 and distal). Stents were either placed in the arch, descending aorta, and TAAA at a rate of 42.4%, 53.9%, and 3.6%, respectively, which differed from the rates presented in the JACSM database (62.4%, 27.0%, and 10.6%, respectively). This may be due to the fact that TEVAR is not the standard treatment for patients in the arch or TAAA subgroups. Because the mean age and demographics of patients in the arch subgroup were similar to those of patients in the descending subgroup in this study, the indication for TEVAR was likely based on the anatomical suitability and policies of each facility, not on the patients’ comorbidities. In contrast, the mean age and risks of the patients in the TAAA subgroup were deemed higher than those of the patients in the descending subgroup, indicating that TEVAR may be reserved for high risk patients in this subgroup, which may account for the high mortality rate among these patients.

Patients in the arch subgroup had a higher rate of cerebrovascular damage than those in the descending or TAAA subgroup; however, the rate of paraplegia was determined to be similar among the three subgroups. Renal dysfunction was highest in the TAAA category, suggesting that a main cause of paraplegia may be shower embolisms or length of stent graft coverage, not the location of the stent graft.

Type 1 and 3 endoleaks are critical adverse events that can be treated. The high rate of type 1 endoleaks in the arch subgroup may be attributed to a poor fit of the proximal end of the stent graft along the arch (as seen by a beak sign on CT scan). Similarly, the high rate of type 3 endoleaks in the TAAA subgroup may be due to a poor fit of the stent graft at the angulated junction of the aorta and the phrenic arteries.

TEVAR was used effectively to treat patients with thoracic aortic disease in Japan in 2017. Patients with an
acute dissection, or those with stents placed in the arch or TAAA, can have a high risk of mortality and complications. Furthermore, the rate of type 1 and type 3 endoleaks is high. Thus, close and careful follow-up, especially in patients with acute dissections or requiring stents in the arch or TAAA, is necessary to improve the outcomes of TEVAR.

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Table 4 Causes of death

| Causes of death                                      | Dissection | Non-dissection |
|------------------------------------------------------|------------|----------------|
| **[During the operation]**                           |            |                |
| Rupture/haemorrhage/systemic circulatory failure     | 6          | 10             |
| Malperfusion/multiple organ failure (MOF)            | 1          | 0              |
| Retrograde type Aortic dissection (RTAD)             | 0          | 1              |
| Intestinal necrosis                                  | 1          | 1              |
| Antipiracy of contrast agents                        | 0          | 1              |
| **TOTAL**                                            | **8**      | **13**         |
| **[In-hospital (after the operation)]**              |            |                |
| Rupture/haemorrhage                                  | 10         | 19             |
| Malperfusion/multiple organ failure                   | 3          | 0              |
| Cerebrovascular damage                               | 4          | 12             |
| Multiple thromboembolism                             | 0          | 1              |
| Arrhythmia/low output syndrome/heart failure         | 7          | 15             |
| Pneumonia/respiratory failure                        | 8          | 21             |
| Liver failure                                        | 0          | 2              |
| Renal failure                                        | 1          | 7              |
| Intestinal necrosis/enterococitis                    | 2          | 6              |
| Vascular-related complications (including RTAD)      | 17         | 19             |
| Infection/sepsis                                     | 11         | 26             |
| DIC                                                   | 3          | 5              |
| Cancer                                                | 0          | 6              |
| Multiple injury (trauma)                              | 1          | 1              |
| Unknown                                               | 0          | 2              |
| **TOTAL**                                            | **67**     | **142**        |

DIC: disseminated intravascular coagulation
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