Elective Non-Cardiac Surgery in Patients With Severe Aortic Stenosis
— Observations From the CURRENT AS Registry —

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Background: Patients with severe aortic stenosis (AS) might be at high risk for adverse cardiovascular events at the time of non-cardiac surgery.

Methods and Results: The current study population included 348 patients who underwent elective non-cardiac surgery under general or spinal anesthesia during the follow up of 3,815 patients in the CURRENT AS (Contemporary outcomes after surgery and medical tReatmeNT in patients with severe Aortic Stenosis) registry. There were 187 patients with untreated severe AS at time of surgery (untreated severe AS group) and 161 patients who had undergone aortic valve replacement (AVR) before surgery (prior AVR group), including 23 patients with prophylactic AVR. The primary outcome measure was 30-day mortality after non-cardiac surgery. At 30 days after non-cardiac surgery, 8 patients (4.3%) died in the untreated severe AS group, while no patients died in the prior AVR group (P=0.008). The causes of death were cardiovascular in 6 out of 8 patients. Mortality at 30 days was higher in untreated severe AS patients with AS-related symptoms before surgery than in those without AS-related symptoms (7.2% vs. 3.1%). Higher surgical risk estimates of the non-cardiac surgery incrementally increased the risk of 30-day mortality in patients with untreated severe AS, though the difference was not statistically significant (low-risk: 0%, intermediate-risk: 4.3%, and high-risk: 6.6 %, P=0.46).

Conclusions: Symptomatic and asymptomatic severe AS might be associated with higher risk of 30-day mortality if untreated before elective intermediate- and high-risk non-cardiac surgery, while no patient with prior AVR died after elective non-cardiac surgery.

Key Words: Aortic stenosis; Aortic valve replacement; Non-cardiac surgery

Patients with severe aortic stenosis (AS) might be at high risk for adverse cardiovascular events at the time of non-cardiac surgery. Current guidelines recommend that elective non-cardiac surgery should be postponed for symptomatic patients with severe AS until after aortic valve replacement (AVR). In asymptomatic patients with severe AS, the recommendations vary according to the non-cardiac surgery risk categories; AVR is recommended prior to high-risk non-cardiac surgery, whereas no aortic valve intervention is recommended for patients undergoing low- or intermediate-risk surgery.1-3 However, these recommendations were based on previous small, single-center studies comparing the outcomes after...
non-cardiac surgery between those patients with and without severe AS. This has been no previous study exploring the role of prophylactic AVR before non-cardiac surgery.

Therefore, we sought to compare the clinical outcomes after elective non-cardiac surgery between the 2 groups of patients with severe AS with and without prior AVR in a large Japanese multicenter registry of consecutive patients with severe AS.

Methods

Study Population

The CURRENT AS (Contemporary outcomes after surgery and medical treatment in patients with severe Aortic Stenosis) registry is a multicenter, retrospective registry enrolling consecutive patients with severe AS from 27 centers (on-site surgical facility in 20 centers) in Japan between 2003 and 2011 (Supplementary Appendix). The design and patient enrollment of the CURRENT AS registry has been described previously. The institutional review boards in all participating centers approved the protocol (e.g., Kyoto University Graduate School and Faculty of Medicine, Ethics Committee [E1916]), and this study followed the Declaration of Helsinki and the ethical standards of the responsible committee on human experimentation. The present study included 3,815 patients who met the definition of severe AS (peak aortic valve jet velocity \( \text{Vmax} > 4.0 \text{m/s} \), mean aortic pressure gradient \( \text{PG} > 40\text{mmHg} \), or aortic valve area \( \text{AVA} < 1.0 \text{cm}^2 \)) for the first time during the study period. We excluded those patients with previous aortic valve intervention. Written informed consent from each patient was waived because clinical information was obtained from the routine practice, and no patient refused to participate in the study when contacted for follow up. Non-cardiac surgery was captured as a clinical event during follow up. Among 3,815 study patients, there were 393 patients who underwent non-cardiac surgery under general or spinal anesthesia during the follow-up period (Figure 1). We excluded 45 patients who underwent emergent non-cardiac surgery, because the operative mortality in emergent non-cardiac surgery was likely to be more closely related to the pre-operative, non-cardiac conditions rather than the concomitant severe AS. Therefore, the current study population included 348 patients who underwent elective non-cardiac surgery under general or spinal anesthesia during follow up in the CURRENT AS registry. Patients were divided into the 2 groups; 187 patients with untreated severe AS at the time of elective non-cardiac surgery (untreated severe AS group) and 161 patients who had undergone surgical or transcatheter AVR (SAVR or TAVR) before elective non-cardiac surgery (prior AVR group). Prophylactic AVR was defined as AVR that was performed just prior to non-cardiac surgery in patients with no formal indication of AVR to get through non-cardiac surgery and avoid complications from severe AS. This study period (2003–2011) was basically before the introduction of TAVR to the country, and TAVR was conducted in the context of the pivotal clinical trial. Collection of baseline clinical information including symptomatic status was conducted via hospital charts or database review. Symptoms related to AS at the time of elective non-cardiac surgery were classified into angina, syncope, and heart failure symptoms, including both acute heart failure requiring hospitalization and chronic exertional dyspnea. Patients were deemed to be asymptomatic at non-cardiac surgery if they were described as asymptomatic or there were no records regarding the symptoms related to AS defined above. Follow up was commenced on the day of the non-cardiac surgery.

All patients underwent a comprehensive 2-dimensional and Doppler echocardiographic evaluation in each participating center according to the guidelines.
aortic PG were obtained with the use of the simplified Bernoulli equation, and AVA was calculated using the standard continuity equation, and indexed to body surface area.

According to current European Society of Cardiology (ESC)/European Society of Anaesthesiology (ESA) and American College of Cardiology (ACC)/American Heart Association (AHA) guidelines, non-cardiac surgeries, which include open or endovascular procedures, were divided into low-risk (superficial surgery, breast, eye), intermediate-risk (intraperitoneal surgery, carotid endarterectomy, head and neck surgery, orthopedic surgery, urological and gynecological surgery, endovascular aneurysm repair), and high-risk procedures (aortic and major vascular surgery, open lower limb revascularization or amputation, liver resection, repair of perforated bowel) with estimated 30-day cardiac event (cardiac death and myocardial infarction) rates of <1%, 1–5%, and >5%, respectively.2,3

### Outcome Measures
The primary outcome measure in the current analysis was all-cause death at 30 days after the non-cardiac surgery. The causes of death were classified according to the Valve Academic Research Consortium (VARC) definitions, and were adjudicated by a clinical event committee (Supplementary Appendix).11,12 A 3-member adjudication committee composed of 3 cardiologists reviewed the details of deaths. When the members disagreed on the causes of death, a final decision was made by consensus.

### Statistical Analysis
Categorical variables were expressed as numbers and percentages, and continuous variables were reported as the mean and SD or median and interquartile range (IQR).

#### Table 1. Baseline Clinical and Echocardiographic Characteristics of the Study Participants

| Variables                              | Untreated severe AS at non-cardiac surgery (N=187) | Prior AVR at non-cardiac surgery (N=161) | P value |
|----------------------------------------|---------------------------------------------------|-----------------------------------------|---------|
| **Clinical characteristics**           |                                                   |                                         |         |
| Age, years                             | 79.3±8.2                                          | 73.1±7.7                                | <0.001  |
| ≥80                                     | 89 (48%)                                          | 38 (24%)                                | <0.001  |
| Male                                    | 74 (40%)                                          | 73 (45%)                                | 0.28    |
| BMI, kg/m²                              | 21.5±3.6                                          | 22.4±3.9                                | 0.04    |
| <22                                     | 117 (63%)                                         | 86 (53%)                                | 0.08    |
| BSA, m²                                 | 1.46±0.18                                         | 1.52±0.18                               | <0.001  |
| Hypertension                           | 138 (74%)                                         | 106 (66%)                               | 0.11    |
| Current smoking                        | 5 (3%)                                            | 16 (10%)                                | 0.005   |
| History of smoking                     | 39 (21%)                                          | 54 (34%)                                | 0.008   |
| Dyslipidemia                           | 51 (27%)                                          | 67 (42%)                                | 0.005   |
| Diabetes mellitus                      | 50 (27%)                                          | 37 (23%)                                | 0.42    |
| On statin therapy                      | 35 (19%)                                          | 52 (32%)                                | 0.004   |
| On insulin therapy                     | 11 (6%)                                           | 14 (9%)                                 | 0.31    |
| Prior myocardial infarction            | 14 (7%)                                           | 9 (6%)                                  | 0.48    |
| Coronary artery disease                | 47 (25%)                                          | 58 (36%)                                | 0.03    |
| Prior PCI                              | 24 (13%)                                          | 21 (13%)                                | 0.95    |
| Prior CABG                             | 14 (7%)                                           | 6 (4%)                                  | 0.13    |
| Prior open heart surgery               | 17 (9%)                                           | 8 (5%)                                  | 0.14    |
| Prior symptomatic stroke               | 30 (16%)                                          | 18 (11%)                                | 0.19    |
| Atrial fibrillation or flutter          | 43 (23%)                                          | 41 (25%)                                | 0.59    |
| Aortic/peripheral vascular disease      | 34 (18%)                                          | 15 (9%)                                 | 0.02    |
| Creatinine level >2 mg/dL              | 44 (24%)                                          | 22 (14%)                                | 0.02    |
| Hemodialysis                           | 41 (22%)                                          | 20 (12%)                                | 0.02    |
| Anemia*                                | 120 (64%)                                         | 80 (50%)                                | 0.006   |
| Liver cirrhosis (Child-Pugh B/C)       | 3 (2%)                                            | 4 (2%)                                  | 0.56    |
| Malignancy                             | 54 (29%)                                          | 22 (14%)                                | <0.001  |
| Malignancy currently under treatment   | 24 (13%)                                          | 8 (5%)                                  | 0.01    |
| Chest wall irradiation                 | 3 (2%)                                            | 1 (1%)                                  | 0.39    |
| Immunosuppressive therapy              | 10 (5%)                                           | 3 (2%)                                  | 0.09    |
| Chronic lung disease                   | 22 (12%)                                          | 25 (16%)                                | 0.31    |
| Chronic lung disease (moderate or severe) | 4 (2%)                                      | 5 (3%)                                  | 0.57    |
| Logistic EuroSCORE, %                  | 11.4 (6.8–18.9)                                   | 7.0 (4.0–10.6)                          | <0.001  |
| EuroSCORE II, %                        | 3.1 (1.8–4.9)                                     | 1.9 (1.3–3.4)                           | <0.001  |
| STS score (PROM), %                    | 4.5 (2.8–7.7)                                     | 2.9 (1.7–4.2)                           | <0.001  |
| Symptom related to AS at non-cardiac surgery | 56 (30%)                                   | –                                       |         |

(Table 1 continued the next page.)
Cumulative incidence of all-cause death after non-cardiac surgery was estimated by using the Kaplan-Meier method. We assessed the differences between the untreated severe AS and prior AVR groups by using the log-rank test. We did not make any statistical adjustment for the between-group differences in baseline characteristics due to the exploratory nature of the study with low numbers of the endpoint event. In the untreated severe AS group, we compared the cumulative 30-day incidence of all-cause death between the 2 groups of patients with and without AS-related symptoms at the time of non-cardiac surgery. We also estimated the cumulative 30-day incidence of all-cause death according to the surgical risk estimate of the surgical procedures (low-, intermediate-, or high-risk). Statistical analyses were conducted by a physician (T.T.) with the use of JMP 10.0.2 (SAS Institute Inc., Cary, NC, USA). All reported P values were 2-tailed, and P values <0.05 were considered statistically significant.

Results
Baseline Clinical Characteristics
Baseline characteristics were substantially different between the untreated severe AS and prior AVR groups (Table 1). Patients in the untreated severe AS group compared with those in the prior AVR group were much older, and more often had chronic kidney disease as well as anemia. Patients in the untreated severe AS group compared with patients in the prior AVR group less frequently underwent their non-cardiac surgery under general anesthesia (71% vs. 89%, P<0.001). Patients in the untreated severe AS group more often underwent intermediate- or high-risk elective non-cardiac surgery than patients in the prior AVR group (intermediate-risk non-cardiac surgery: 63% vs. 58%; high-risk non-cardiac surgery 25% vs. 16%) (Table 2). Neurological or orthopedic surgery was the most common cause of elective non-cardiac surgery in patients with severe AS (34% [118/348]). Among 187 patients with untreated severe AS, 56 symptomatic patients (30%) preferentially underwent elective non-cardiac surgery despite formal indication of AVR according to physicians’ judgment (low-risk: 9 patients, intermediate-risk: 38 patients [orthopedic: 27 patients, intraperitoneal: 8 patients, and head and neck surgery: 3 patients], and high-risk: 9 patients [open lower limb revascularization: 4 patients, open lower limb amputation: 3 patients, abdominal aortic aneurysm repair: 1 patient, and bile duct surgery: 1 patient]). Among 27 symptomatic patients who underwent elective orthopedic surgery, 22 patients underwent hip fracture surgery despite AS-related symptoms. In contrast, among 161 patients in the prior AVR group, 158 patients had undergone SAVR and only 3 patients had undergone TAVR, because TAVR was not approved in Japan during the study period, and was conducted only in the context of the pivotal clinical trial. Prophylactic SAVR just prior to the elective non-cardiac surgery was performed in 23 patients (14%). No patient underwent prophylactic percutaneous aortic balloon dilation or TAVR before non-cardiac surgery. Regarding anesthetic management, among 187 patients with untreated severe AS who underwent non-cardiac surgery, 54 patients (29%) and 133 patients (71%) received spinal and general anesthesia respectively. Among 54 patients with spinal
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Discussion

The main findings of the present study were as follows; (1) mortality rate at 30 days after elective non-cardiac surgery was substantial in patients with untreated severe AS, while no patient with prior AVR died at 30 days after elective non-cardiac surgery; (2) presence of AS-related symptoms and higher surgical procedure risk numerically and incrementally increased the risk of 30-day mortality after elective non-cardiac surgery in patients with untreated severe AS, though the difference was not statistically significant. Optimal management of patients with severe AS who undergo non-cardiac surgery is clinically important, but still controversial. The adverse hemodynamic effects of anesthesia and surgical procedures are often poorly tolerated in patients with severe AS. Systemic hypotension and tachycardia in patients with small left ventricular cavity or impaired systolic or diastolic function can substantially increase the likelihood of decompensation under stress, thereby leading to complications during or after non-cardiac surgery. Agarwal et al reported that patients with moderate or severe AS undergoing elective non-cardiac surgery had

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There was no intra-operative death under spinal or general anesthesia both in the untreated AS group and in the prior AVR group. At 30 days after non-cardiac surgery, 8 patients (4.3%) died in the untreated severe AS group, while no patients died in the prior AVR group, including those with prophylactic SAVR (P=0.008) (Figure 2). The causes of death were cardiovascular in 6 out of 8 patients (Table 3). Mortality at 30-day was higher in untreated severe AS patients with AS-related symptoms before non-cardiac surgery than in those without AS-related symptoms (7.2% vs. 3.1%, P=0.20) (Figure 3). Higher surgical risk estimates of the non-cardiac surgery incrementally increased the risk of 30-day mortality in patients with untreated severe AS, though the difference was not statistically significant (low-risk: 0%, intermediate-risk: 4.3%, and high-risk: 6.6%, P=0.46) (Figure 4). Even in patients without AS-related symptoms at the time of non-cardiac surgery, the 30-day mortality was 2.5% and 5.4% in the intermediate-risk surgery and high-risk surgery, respectively (Figure 4). No patient died at 30 days after low-risk elective non-cardiac surgery regardless of their symptomatic status at non-cardiac surgery (Figure 4).

Table 2. Surgical Risk Estimate According to Type of Surgery

| Types of Surgery                        | Untreated severe AS at non-cardiac surgery (N=187) | Prior AVR at non-cardiac surgery (N=161) |
|-----------------------------------------|---------------------------------------------------|----------------------------------------|
| Low risk                                |                                                   |                                        |
| Superficial surgery                     | 9 (4.9%)                                          | 25 (15.6%)                             |
| Breast                                  | 7 (3.8%)                                          | 4 (2.5%)                               |
| Dental                                  | 0 (0%)                                            | 3 (1.8%)                               |
| Thyroid                                 | 1 (0.5%)                                          | 0 (0.0%)                               |
| Eye                                     | 1 (0.5%)                                          | 0 (0.0%)                               |
| Orthopedic: minor                       | 0 (0%)                                            | 2 (1.2%)                               |
| Urological: minor (transurethral resection of the prostate) | 5 (2.7%)                                          | 4 (2.5%)                               |
| Intermediate risk                       |                                                   |                                        |
| Intrapertoneal                          | 32 (17.2%)                                        | 34 (21.2%)                             |
| Endovascular aneurysm repair            | 1 (0.5%)                                          | 3 (1.8%)                               |
| Head and neck surgery                   | 8 (4.3%)                                          | 5 (3.1%)                               |
| Neurological or orthopedic: major       | 72 (38.6%)                                        | 46 (28.6%)                             |
| Hip                                     | 61 (32.6%)                                        | 29 (17.9%)                             |
| Spine                                   | 4 (2.1%)                                          | 11 (6.9%)                              |
| Knee                                    | 3 (1.6%)                                          | 4 (2.5%)                               |
| Others                                  | 4 (2.2%)                                          | 2 (1.2%)                               |
| Urological or gynecological: major      | 5 (2.7%)                                          | 5 (3.1%)                               |
| High risk                               |                                                   |                                        |
| Aortic and major vascular               | 4 (2.2%)                                          | 1 (0.6%)                               |
| Open lower limb revascularization or amputation or thromboembolectomy | 27 (14.5%)                                        | 12 (7.5%)                              |
| Liver resection, bile duct              | 6 (3.2%)                                          | 4 (2.5%)                               |
| Oesophagectomy                          | 0 (0.0%)                                          | 1 (0.6%)                               |
| Repair of perforated bowel              | 0 (0.0%)                                          | 0 (0.0%)                               |
| Total cystectomy                        | 0 (0.0%)                                          | 1 (0.6%)                               |
| Pneumonectomy                           | 9 (5.0%)                                          | 7 (4.3%)                               |
| Unknown risk                            | 0 (0.0%)                                          | 4 (2.5%)                               |
| Types of Anesthesia                     |                                                   |                                        |
| General anesthesia                      | 133 (71.1%)                                       | 143 (89.0%)                            |
| Spinal anesthesia                       | 54 (28.9%)                                        | 18 (11.0%)                             |

Data are presented as n or n (%). AS, aortic stenosis; AVR, aortic valve replacement.

anesthesia, 40 patients (74%) had orthopedic surgery.
general anesthesia was substantial in the contemporary study population (30-day mortality overall: 5.9% [n=15/256]; symptomatic patients: 9.4% [n=10/106] vs. asymptomatic patients: 3.3% [n=5/150]). However, there was no previous report evaluating the role of prophylactic AVR prior to non-cardiac surgery.

The strengths of the present study include: (1) assessment of the effects of prior AVR, including prophylactic AVR, on mortality after elective non-cardiac surgery; (2) inclusion of large numbers of consecutive patients with severe AS who underwent elective non-cardiac surgery; and (3) assessment of mortality after non-cardiac surgery according to the non-cardiac surgery risk category in symptomatic and asymptomatic patients with severe AS. It was not possible to ascertain the role of AVR prior to non-cardiac surgery from previous studies because cases were selected on the basis of native AS at the time of index non-cardiac surgery. Another strength of the present study was that consecutive patients with severe AS, including those undergoing non-cardiac surgery during the follow-up period, were followed in the CURRENT AS registry, and that the clinical outcomes of patients undergoing non-cardiac surgery just prior to non-cardiac surgery could be assessed. Considering that there has been no randomized controlled study assessing the risk of untreated severe AS when patients undergo non-cardiac surgery, this observational study sheds new light on optimal management strategies for patients with severe AS who require non-cardiac surgery. This is the first study assessing the effect of prior AVR, including prophylactic AVR, before non-cardiac surgery on clinical outcomes in patients with severe AS. The present study clearly demonstrated that 30-day mortality was substantial in both symptomatic and asymptomatic patients with severe AS undergoing intermediate- and high-risk non-cardiac surgery, while prior AVR, including prophylactic AVR,

a 30-day mortality rate of 2.1%, compared with 1.0% in the propensity score-matched patients without AS (P=0.036), although this study did not evaluate the relationship between perioperative mortality and procedure risks of non-cardiac surgery. Current guidelines recommend that elective non-cardiac surgery should be postponed for symptomatic patients with severe AS until after AVR to avoid hemodynamic instability during and after non-cardiac surgery. This recommendation is reasonable because AVR is recommended in all patients with symptomatic severe AS and with reasonable operative risk, even outside the context of elective non-cardiac surgery. However, non-cardiac surgery might be considered for some patients with untreated severe AS despite formal indication of AVR, but this is reliant on physicians’ judgment; for example, early (within 24 or 48 h) surgical treatment of hip fractures was recommended in patients with hip fracture because increased wait time for surgery was reported to be associated with higher risk of 30-day mortality and other complications. In the current study group, of 50 patients with untreated severe AS who underwent hip surgery due to hip fracture, 22 patients had AS-related symptoms, suggesting that hip surgery was preferentially performed despite formal indication of AVR according to physicians’ judgment. Within 30 days after hip surgery, 2 asymptomatic patients with severe AS and 1 asymptomatic patient died (Table 3).

In contrast, there are only limited data on mortality after elective non-cardiac surgery in asymptomatic patients with severe AS. Calleja et al from the Mayo clinic reported no deaths or myocardial infarction in a series of 30 asymptomatic patients with severe AS undergoing non-cardiac surgery (>75% of patients at intermediate-risk). In contrast, Tashiro et al, also from the Mayo clinic, reported that perioperative mortality in 256 patients with severe AS undergoing intermediate- or high-risk intervention under

| Interval | 0 day | 30 day |
|----------|-------|--------|
| Untreated Severe AS at elective non-cardiac surgery | 187 | 175 |
| N of patients at risk | 187 | 175 |
| Cumulative incidence | 4.3% | 4.3% |
| Prior AVR at elective non-cardiac surgery | 161 | 157 |
| N of patients at risk | 161 | 157 |
| Cumulative incidence | 0% | 0% |

Figure 2. Kaplan-Meier curves for all-cause death after non-cardiac surgery: Untreated severe AS vs. prior AVR at elective non-cardiac surgery. AS, aortic stenosis; AVR, aortic valve replacement.
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Untreated severe AS group might affect worse postoperative outcomes, prophylactic AVR might be a viable option for asymptomatic patients with severe AS undergoing intermediate- and high-risk non-cardiac surgery. It would be essential to balance the procedural risk of non-cardiac before elective non-cardiac surgery was apparently protective for mortality after elective non-cardiac surgery, but the difference was not statistically significant. Given the lower numbers of events, this may be attributable to a lack of power. Although higher-risk baseline profiles in the untreated severe AS group might affect worse postoperative outcomes, prophylactic AVR might be a viable option for asymptomatic patients with severe AS undergoing intermediate- and high-risk non-cardiac surgery. It would be essential to balance the procedural risk of non-cardiac

| Table 3. Characteristics of 8 Patients Who Died Within 30 Days of Elective Non-Cardiac Surgery |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Patient** | **Age (years)** | **Sex** | **Group** | **Vmax (m/s)** | **AVA (mm²)** | **LVEF (%)** | **AS-related symptoms at non-cardiac surgery** | **Types of surgery** | **Anesthesia** | **Surgical risk estimate** |
| 1 | 84 | Male | Untreated severe AS | 4.4 | – | 87 | Asymptomatic | Total hip arthroplasty | General | Intermediate |
| 2 | 71 | Female | Untreated severe AS | 4.97 | 0.88 | 88 | Asymptomatic | Total hip arthroplasty | General | Intermediate |
| 3 | 86 | Female | Untreated severe AS | 4.49 | 0.44 | 69 | Symptomatic | Head | General | Intermediate |
| 4 | 79 | Male | Untreated severe AS | 3.42 | 0.85 | 50.9 | Asymptomatic | Aortic replacement with a Y-shaped vascular prosthesis for abdominal aortic aneurysm | General | High |
| 5 | 78 | Female | Untreated severe AS | 3.1 | 0.70 | 67 | Symptomatic | Femur osteosynthesis | Spinal | Intermediate |
| 6 | 88 | Female | Untreated severe AS | 3.1 | 0.59 | 54 | Symptomatic | Femur osteosynthesis | Spinal | Intermediate |
| 7 | 72 | Female | Untreated severe AS | 3.62 | 0.40 | 38.0 | Symptomatic | Lower limb amputation | General | High |
| 8 | 86 | Female | Untreated severe AS | 4.24 | 0.66 | 62.1 | Asymptomatic | Open lower amputation and thromboembolectomy | General | High |

AS, aortic stenosis; AVA, aortic valve area; LVEF, left ventricular ejection fraction; AVR, aortic valve replacement; Vmax, peak aortic jet velocity.
**Figure 3.** Kaplan-Meier curves for all-cause death after non-cardiac surgery: Patients with untreated severe AS at elective non-cardiac surgery with vs. without AS-related symptoms. AS, aortic stenosis.

**Figure 4.** Cumulative 30-day mortality after elective non-cardiac surgery according to the non-cardiac surgery risk estimate. (A) Untreated severe AS; (B) symptomatic and asymptomatic untreated severe AS; and (C) prior AVR. AS, aortic stenosis; AVR, aortic valve replacement.
surgery with the risk of surgical or transcatheter AVR; low-risk non-cardiac surgery could be safely performed without prophylactic AVR. One of the biggest problems with prophylactic surgical AVR is its heavy physical and psychological burden on a patient who has to receive another invasive procedure to get through non-cardiac surgery, although improved surgical techniques have led to lower operative mortality for SAVR. In this context, TAVR is a very attractive option for prophylactic AVR due to its less invasive nature and early recovery of the patients. In several randomized clinical trials, TAVR was demonstrated to achieve clinical outcomes that are non-inferior or even superior to SAVR in asymptomatic patients with severe AS regardless of the surgical risk. The RECOVERY (The Randomized Comparison of Early Surgery versus Conventional Treatment in Very Severe Aortic Stenosis) trial recently reported that the incidence of the primary outcome measures (death during or within 30 days after surgery or death from cardiovascular causes during the entire follow-up period) in asymptomatic patients with very severe AS was significantly lower among patients who underwent early surgical AVR than among those who were managed conservatively. Considering the favorable clinical outcomes of TAVR, which is less invasive than SAVR, prophylactic TAVR would be a preferred management strategy in asymptomatic patients with severe AS undergoing intermediate- and high-risk non-cardiac surgery.

Study Limitations
This study has several important limitations. First, the number of patients who underwent prophylactic AVR was very limited and, therefore, we compared mortality after non-cardiac surgery between the untreated severe AS and prior AVR patients. The clinical outcomes after non-cardiac surgery might be different between those 2 groups of patients who underwent non-cardiac surgery shortly after and remote from AVR. Second, the number of patients with the endpoint event was very limited and, therefore the current study results were exploratory and only hypothesis-generating. Third, this was a retrospective study, so we could not exclude the possibility of ascertainment bias for symptoms at non-cardiac surgery. However, we thoroughly reviewed all patients’ charts and referred to the hospital database to evaluate symptomatic status. Fourth, we did not make any statistical adjustment for the differences in baseline characteristics due to the low numbers of the endpoint event. However, there have been no previous studies exploring the role of prophylactic AVR before non-cardiac surgery, and this is the first large-scale contemporary multicenter study reporting that mortality rate at 30-days after elective non-cardiac surgery was higher in patients with untreated severe AS than in those with prior AVR. Indeed, the surgical risk score was significantly higher in the untreated severe AS group than in the prior AVR group, which might have affected the current study results. However, the causes of death were cardiovascular in 6 out of 8 patients. Finally, we did not collect data on high-sensitivity cardiac troponin or creatinine kinase to detect acute myocardial injury after non-cardiac surgery. We also did not collect information on the β-blockers use, which was reported to be associated with better clinical outcomes after non-cardiac surgery.

Conclusions
Mortality after elective non-cardiac surgery was substantial in patients with untreated severe AS, while no patient with prior AVR died after elective non-cardiac surgery. Symptomatic and asymptomatic severe AS might be associated with higher risk of perioperative death if untreated before elective intermediate- and high-risk non-cardiac surgery.

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Clinical Trial Registration
URL: http://www.umin.ac.jp/ctr/index.htm. Unique identifier: UMIN00001240.

Disclosures
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**Supplementary Files**

Please find supplementary file(s):

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