Preoperative Instrumental Activities of Daily Living Predicts Survival After Transcatheter Aortic Valve Implantation

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Background: This aim of this study was to clarify prognosis after transcatheter aortic valve implantation (TAVI) in patients with aortic stenosis (AS) and to identify baseline factors associated with mortality.

Methods and Results: We prospectively enrolled 257 consecutive elderly persons with AS who were referred to Keio University Hospital and who underwent assessment of cardiac, physical (walking speed), cognitive, and renal functions, nutritional status, activities of daily living (ADL), instrumental ADL (IADL) assessed with the Frenchay activities index (FAI), and comorbidities. The primary outcome was postoperative death. Differences in basic characteristics were compared between a group that survived for a median of 661 days (IQR, 0–1,289 days) after TAVI and a group that did not. Multivariate hazard ratios (HR) were calculated for independent factors selected in Cox proportional hazard models. Thirty-one individuals died during follow-up. Walking speed was significantly faster (0.87±0.25 vs. 0.70±0.24 m/s; P<0.001) and FAI was significantly higher (21.2±8.0 vs. 15.7±8.0; P=0.026) in the survival group compared with those who died. Multivariate HR for mortality according to walking speed was 0.05 (95% CI: 0.028–0.091) in model 1 and 0.04 (95% CI: 0.020–0.081) in model 2, and those for FAI were 0.94 (95% CI: 0.92–0.95) and 0.92 (95% CI: 0.90–0.92), respectively.

Conclusions: Preoperative walking speed and IADL are crucial factors associated with prognosis after TAVI even after adjustment.

Key Words: Elderly; Mortality; Transcatheter aortic valve implantation
As an assessment of cardiac status, New York Heart Association class,13 echocardiography findings, and plasma brain natriuretic peptide were analyzed. Echocardiography parameters consisted of left ventricular ejection fraction (LVEF), mean gradient of the aortic valve (mmHg), and aortic valve area (cm²). LVEF was measured on M-mode in accordance with the American Society of Echocardiography guidelines.14 We also obtained background Society of Thoracic Surgeons (STS) risk scores15 for the participants. As an assessment of physical function, grip strength of the left and right hands was measured to determine frailty16 using a Smedley-type hand dynamometer (T.K.K.5401, Takei Scientific Instruments, Tokyo, Japan), in seated patients with the elbow extended to the side of the body.17 The higher value was included in analyses. Walking speed was evaluated on 10-m walking test. The amount of time taken for the patients to walk a distance of 10 m at their own pace with acceleration and deceleration phases of 2 m each was measured using a hand-held stopwatch. The shortest amount of time was included in analyses. As an assessment of nutritional status, we used the Mini Nutritional Assessment-Short Form (MNA-SF) to screen nutritional status during interview,18 and determined nutritional and metabolic status from blood tests. The MNA-SF evaluates dietary intake, weight loss, difficulties with walking, mental stress and/or acute disease, cognitive impairment, and body mass index (BMI). Each item is scored on scales of either 0–2 or 0–3. Total score ranges from 0 (worst) to 14 (best). Scores ≤11 and ≤7 indicate risk for malnutrition, and ≤6 indicates malnutrition. Total protein, serum albumin, hemoglobin, and C-reactive protein (CRP) were also measured. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE),19 which tests orientation, memory, attention, calculation, language, and construction functions. Scores range from 0 to 30, with lower scores indicating worse cognitive function. We evaluated IADL using the Frenchay activities index (FAI),20 which indicates the frequency with which the following tasks are undertaken within specific periods: preparing main meals, washing up after meals, washing clothes, light housework, heavy housework, local shopping, social occasions, walking outside for >15 min, actively pursuing a hobby, driving a car/travelling by bus, travel outings/car rides, gardening, household maintenance, reading books, and gainful work. Each item was scored on a scale of 0–3. Total scores ranged from 0 to 45, with higher scores indicating better IADL. A physical therapist who specializes in ADL assessment assessed these indexes.

As an assessment of background demographics, we collected information on age, sex, family living under one roof, living environment, postoperative hospitalization, medical history and/or comorbidities. Living environment was defined as home, facility or hospital. A history of coronary artery disease was defined as self-reported hospitalization for coronary artery disease. A history of hospitalization for coronary artery disease, A history of hospitalization for heart failure, and/or description of heart failure in the medical records based on the Framingham criteria.21 Cerebrovascular disease was defined as self-reported hospitalization, and/or neurology assessed by physiatrists from medical records. Respiratory disease was defined as spirometric evidence of restrictive and/or obstructive ventilatory impairment or self-reported current respiratory medications. Musculoskeletal disorders were defined as self-reported spine, hip, knee or ankle diseases currently under treatment and/or left with impairment.

We obtained data regarding clinical follow-up at 1 month, 6 months, 1 year, and annually thereafter. Additional follow-up data, including data on death and incidental disease, were collected from the treating hospital or via telephone from the patient’s family or from the patient’s family physician.

**Statistical Analysis**

The primary outcome was postoperative death. Differences in basic characteristics between the group that survived and the group that died after TAVI were analyzed using t-test or chi-squared test. Thereafter, multivariate hazard ratios (HR) were calculated for meaningful independent factors identified from Cox proportion hazards models.
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FAI were 0.94 (95% CI: 0.92–0.95) and 0.92 (95% CI: 0.90–0.92; Table 4), respectively. On ROC analysis the cut-off for walking speed was 0.75 m/s (AUC, 0.663; sensitivity, 63.6%; specificity, 81.3%; P=0.033; 95% CI: 0.500–0.825), and the cut-off for FAI was 20.5 (AUC, 0.702; sensitivity, 61.0%; specificity, 75.0%; P=0.008; 95% CI: 0.578–0.826; Figure 2, Supplementary Figure).

Discussion

The aim of this study was to identify preoperative factors that might be associated with medium–long-term prognosis after TAVI at one of the leading facilities in Japan. The average age was 84.1±5.3 years, and women comprised

Table 2. Causes of Death After TAVI

| Cause                                      | n   |
|--------------------------------------------|-----|
| Pneumonia (aspiration, bacterial)          | 9   |
| Cancer                                     | 4   |
| Sudden death                               | 3   |
| Heart failure                              | 3   |
| Arrhythmia                                 | 2   |
| Novel onset of cerebrovascular disease     | 2   |
| Multiple organ dysfunction                  | 1   |
| Myocardial infarction                      | 1   |
| Esophageal bleeding                        | 1   |
| Multiple organ dysfunction                  | 1   |
| Cause unknown                              | 4   |

TAVI, transcatheter aortic valve implantation.
### Table 3. Univariate Indicators of Death After TAVI

|                | Survival group (n=226) | Death group (n=31) | P-value |
|----------------|------------------------|--------------------|---------|
| Age (years)    | 84.3±4.8               | 83.7±5.5           | 0.595   |
| Sex (F/M)      | 72/154                 | 16/15              | 0.068   |
| BMI (kg/m²)    | 21.9±3.5               | 21.3±4.0           | 0.082   |
| Operation (TF/others) | 203/23 | 26/5              | 0.319   |
| NYHA class (I/II/III/IV) | 12/110/102/2 | 1/12/15/2 | 0.093   |
| LVEF (%)       | 64.4±12.3              | 60.6±16.1          | 0.139   |
| STS score (%)  | 7.0±4.1                | 6.7±4.6            | 0.753   |
| Diabetes mellitus | 54 (23.9)      | 8 (25.8)           | 0.739   |
| Hypertension   | 180 (79.6)             | 21 (67.7)          | 0.227   |
| Chronic kidney failure | 123 (54.4)    | 17 (54.8)          | 0.817   |
| Cerbrovascular disease | 30 (13.3)   | 7 (22.6)           | 0.144   |
| Coronary artery disease | 73 (32.3) | 10 (32.3) | 0.996   |
| Heart failure  | 64 (28.3)              | 13 (41.9)          | 0.121   |
| Respiratory disease | 78 (34.5)  | 13 (41.9)          | 0.418   |
| Musculoskeletal disorder(s) | 63 (27.9) | 6 (19.4) | 0.315   |
| Family living together | 174 (77.0) | 23 (80.6) | 0.464   |
| Living environment (Home/Facility/Hospital) | 210/5/11 | 27/1/3 | 0.433   |
| Hand grip (kg) | 17.8±5.3               | 15.7±5.3           | 0.156   |
| Walking speed (m/s) | 0.87±0.25       | 0.70±0.24          | <0.001  |
| MMSE           | 26.1±3.5               | 26±3.3             | 0.55    |
| FAI            | 21.1±8.0               | 17.1±8             | 0.026   |
| MNA-SF         | 11.2±2.5               | 10.0±2.7           | 0.056   |

Data given as n (%) or mean±SD. Abbreviations as in Tables 1,2.

### Table 4. Factors Associated With Mortality After TAVI

| Factors                        | Univariate model | Multivariate model |
|--------------------------------|------------------|--------------------|
|                                | HR 95% CI P-value| Model 1 HR 95% CI P-value | Model 2 HR 95% CI P-value |
| Walking speed                  | 0.084 0.047–0.152 <0.001 | 0.05 0.028–0.091 <0.001 | 0.041 0.020–0.081 <0.001 |
| FAI                            | 0.935 0.919–0.951 <0.001 | 0.935 0.919–0.952 <0.001 | 0.919 0.900–0.938 <0.001 |

Multiple Cox proportional hazards models: model 1, adjusted for age, sex, BMI, STS score; model 2, model 1 plus operative procedure, comorbidities, family living together, living environment. Abbreviations as in Tables 1,2.

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Figure 2. Receiver operating characteristic curve for (A) Frenchay activities index and (B) walking speed.
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66.2%. The mortality rate was 13.3% during a 661-day follow-up. The reported 1- and 5-year mortality rates were 24.2% and 67.8% in 2011 (PARTNER trial cohort A) and 30.7% and 71.8% in 2010 (PARTNER trial cohort B). The 1-year mortality rate in Japanese patients, however, has recently decreased to 11.3%. A comfortable walking speed was selected as a preoperative indicator of prognosis, consistent with that of a study of mortality in the short term after TAVI. A comfortable walking speed is a representative index of motor function that is included in the diagnostic criteria for sarcopenia and frailty. In addition, a comfortable walking speed is a prognostic factor not only after TAVI but also after cardiovascular disease. Therefore, walking speed should be routinely measured before surgery. Fukui et al reported that candidates for TAVI include those with physical frailty.

The cut-off for walking speed to distinguish all-cause mortality after TAVI was 0.75 m/s in the present study. Walking speed ≤0.8 m/s is generally regarded as a diagnostic criterion for sarcopenia, and this speed affects the prognosis of patients with heart failure aged >65 years. The present result was similar to these and thus is considered valid.

We also found that IADL was a prognostic indicator of post-TAVI outcome. IADL are essential to live independently in a community. The relationship between IADL and prognosis has recently received attention. Factors of mortality including IADL were reported in a representative sample of elderly people. A decline in IADL also affects the prognosis of patients with heart failure aged >65 years. Although a decline in IADL might be difficult to discern during a clinical examination, the IADL of patients with severe AS in the clinical setting should nevertheless be considered.

The cut-off for FAI was 20.5. An FAI cut-off for patients with heart disease has not been defined, but FAI score ≥18 is a useful prognostic cut-off for patients with stroke. The total FAI score is 45 and an IADL score that falls to below half of this value might be associated with various risks for elderly persons. In contrast, STS score or logistic EuroSCORE is often used as a preoperative indicator of prognosis. These include assessments of comorbidity and general status. Walking speed and IADL were notably associated with prognosis after adjustment for STS in the present study. This indicates that a greater emphasis on IADL and physical frailty is required in the risk evaluation when assessing elderly people for surgery.

Study Limitations

The present study has several limitations. It was carried out at a single institution and involved a small patient cohort. Much of the past medical history was obtained by patient self-report and thus may be subject to recall bias. We did not consider types of preoperative risk assessment other than STS. STS score is commonly used, but if other scores were also adjusted, the study might have been more robust. Nevertheless, the present findings suggest that evaluation of comfortable walking speed and of IADL is important to estimate mid- and long-term prognoses after TAVI.

Conclusions

Preoperative walking speed and IADL are important factors associated with mid- and long-term mortality after TAVI.

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Disclosures

The authors declare no conflicts of interest.

The Ethics Review Board at Keio University Hospital approved the study protocol, which was implemented according to the Declaration of Helsinki.

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Supplementary Files

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