ORIGINAL RESEARCH

Prevalence and Prognostic Significance of Malnutrition in Older Japanese Adults at High Surgical Risk Undergoing Transcatheter Aortic Valve Implantation

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BACKGROUND: The usefulness of preprocedural nutritional status to stratify prognosis after transcatheter aortic valve implantation has been evaluated; however, the studies conducted so far have been relatively small and/or focused on a single nutritional index. This study sought to assess the prevalence and prognostic impact of malnutrition in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation.

METHODS AND RESULTS: We applied the Controlling Nutritional Status score, Geriatric Nutritional Risk Index, and Prognostic Nutritional Index to 1040 consecutive older Japanese patients at high surgical risk who underwent transcatheter aortic valve implantation. According to the Controlling Nutritional Status score, Geriatric Nutritional Risk Index, and Prognostic Nutritional Index, 16.6%, 60.5%, and 13.8% patients had moderate or severe malnutrition, respectively; 89.3% were at least mildly malnourished by at least 1 score. Worse nutritional status was associated with older age, lower body mass index, higher degree of frailty, worse symptoms and renal function, atrial fibrillation, and anemia. During a median follow-up of 986 days (interquartile range, 556–1402 days), 273 (26.3%) patients died. Compared with normal nutrition, malnutrition was associated with an increased risk for all-cause death (adjusted hazard ratio for moderate and severe malnutrition, respectively: 2.19 (95% CI, 1.45–3.31; \(P<0.001\)) and 6.13 (95% CI, 2.75–13.70; \(P<0.001\)) for the Controlling Nutritional Status score, 2.02 (95% CI, 1.36–3.02; \(P=0.001\)) and 3.24 (95% CI, 1.86–5.65; \(P<0.001\)) for the Geriatric Nutritional Risk Index, and 1.60 (95% CI, 1.06–2.39; \(P=0.024\)) and 2.32 (95% CI, 1.50–3.60; \(P<0.001\)) for the Prognostic Nutritional Index).

CONCLUSIONS: Malnutrition is common in patients undergoing transcatheter aortic valve implantation and is associated with increased mortality.

Keywords: body mass index ■ frailty ■ nutrition assessment ■ nutritional status ■ prognosis ■ transcatheter aortic valve replacement

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Transcatheter aortic valve implantation (TAVI) was established as a therapeutic alternative to surgical aortic valve replacement for inoperable or high-risk patients with severe aortic stenosis.1–3 Although indications for TAVI have been expanded to include patients who are at a lower surgical risk,4–6 long-term prognosis after TAVI remains poor. Thus, optimal patient risk stratification based on modifiable clinical characteristics is essential to improve prognosis after TAVI.
Malnutrition, a risk factor that is modifiable by providing intervention in terms of dietary patterns, is known as a driver of disease progression by causing cytokine activation and is associated with poor prognosis irrespective of body mass index, Society of Thoracic Surgeons Predicted Risk of Mortality score, Clinical Frailty Scale, left ventricular ejection fraction, or renal function.

What Are the Clinical Implications?
• These data support the importance of evaluating nutritional status of all candidates for transcatheter aortic valve implantation.
• Prospective multicenter studies are warranted to assess the impact of nutritional interventions on outcomes of patients undergoing transcatheter aortic valve implantation.

Computed Tomographic Data Analysis
All computed tomographic examinations were performed as previously described. Images were reconstructed and assessed by using 3mensio Valves software version 7.0 or 8.0 (Pie Medical Imaging, Maastricht, The Netherlands). The aortic annulus and left ventricular outflow tract (LVOT) area were measured in the mid-systole. The LVOT calcification was classified in a semiquantitative fashion as previously described: mild calcification was recorded in the presence of 1 nodule of calcification extending <5 mm in any dimension and covering <10% of the perimeter of the LVOT, moderate calcification was documented in the presence of 2 nodules of calcification or 1 extending >5 mm in any direction or covering >10% of the perimeter of the LVOT, and severe calcification was considered in cases of multiple nodules of calcification of a single focus extending >10 mm in length or covering >20% of the perimeter of the LVOT.
Malnutrition Screening Tools
All patients were screened for malnutrition using 3 scoring systems (Figure 2A). The CONUT score was developed by Ulíbarri et al in 2005 as a screening tool for malnutrition among patients admitted in a hospital.16 It takes into account serum albumin level, total cholesterol level, and lymphocyte count. A score of 0 to 1 is considered normal; scores of 2 to 4, 5 to 8, and 9 to 12 reflect mild, moderate, and severe malnutrition, respectively.

The GNRI, which is also a widely used index for assessing nutritional status, is calculated using the following formula: 1.489×serum albumin (g/L) + 41.7×(current body weight [kg]/ideal body weight [kg]).17 The ideal body weight is calculated as follows: body height (cm)−100−[(body height [cm]−150)/4] for male patients, and body height (cm)−100−[(body height [cm]−150)/2.5] for female patients.18 As defined in previous studies, a score of ≥100 was considered normal; scores of 97.50 to 99.99, 83.50 to 97.49, and <83.50 reflected mild, moderate, and severe malnutrition, respectively.

The PNI was calculated using the following formula: 10×serum albumin (g/dL) + 0.005×total lymphocyte count (/μL).19 A score of >38 is considered normal; scores of 35 to 38 and <35 reflect moderate and severe malnutrition, respectively. Note that there is no “mild” category for the PNI.

Outcome Measures and Follow-Up
The primary outcome measure of this study was all-cause mortality after TAVI. The causes of death were categorized as cardiovascular and noncardiovascular deaths. The definition of cardiovascular mortality was also applied to the Valve Academic Research Consortium–2 criteria and included death attributed to cardiac causes and noncoronary vascular conditions, such as stroke associated with neurological events, procedure-related aortic dissection, rupture, or other vascular diseases. All procedure- and valve-associated deaths and sudden, unwitnessed, and unknown deaths were also classified as cardiovascular mortality. The secondary end point was heart failure hospitalization after TAVI. For patients with multiple hospitalizations, only the first episode was included in the analysis. Information on the occurrence of adverse events after discharge was obtained from follow-up outpatient visits or telephone interviews conducted on the 30th day, the sixth month, and annually thereafter. The study conformed to the principles outlined in the Declaration of Helsinki and was approved by the local ethics committee. Written informed consent was obtained from all patients before the TAVI procedure.

Statistical Analysis
Categorical variables were described as numbers and percentages and compared using the χ2 test. Continuous variables were described as mean±SD or median (interquartile range [IQR]) and were compared using the independent Student t test or Kruskal–Wallis test depending on their distributions. Venn diagrams were used to illustrate the relationship between the 3 nutritional scoring systems.

The cumulative event rates were analyzed using the Kaplan–Meier estimation. Poisson models were used to estimate the incidence rates. A Cox proportional hazards regression analysis was performed to identify predictors of mortality. To test the predictive ability of the nutritional status, multivariable Cox proportional hazard models were constructed, which comprised variables known to be associated with poor prognosis based on clinical plausibility20,21 or P values <0.05 in the univariate analysis. Model 1 was adjusted for...
preprocedural variables, and model 2 was additionally adjusted for postprocedural variables including echocardiographic data and in-hospital outcomes. For post hoc analyses, we dichotomized patients based on (1) age (at the median of 85 years), (2) sex, (3) BMI level (at the median of 22 kg/m²), (4) Clinical Frailty Scale (CFS) (at the median score of 3), (5) chronic renal failure status, and (6) left ventricular ejection fraction (LVEF) (“preserved [≥50%]” or not) to assess the interaction of nutritional status with these factors.

Receiver operating characteristic curves were used to illustrate and assess the predictive performance of the 3 nutritional indexes for mortality, and the best discriminatory thresholds were calculated by determining the Youden index. Moreover, the areas under the curve between the indexes were compared using the method of DeLong et al.²²

All statistical analyses were performed using JMP 14.2.0 (SAS Institute Inc., Cary, NC) and R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

Figure 2. Prevalence of malnutrition according to the 3 scoring indexes. A, Formula and prevalence of malnutrition for each nutritional index. B, Venn diagrams demonstrating the frequency of malnutrition according to each nutritional index with the percentages of the total 1040 patients. The overlapping area shows the frequency with which the identification of malnutrition by an index overlaps with the others. CONUT indicates Controlling Nutritional Status; GNRI, Geriatric Nutritional Risk Index; and PNI, Prognostic Nutritional Index.
Austria). All reported P values were 2-tailed, and P values <0.05 were considered statistically significant.

RESULTS
Baseline Patient Characteristics
A total of 1040 patients (median age, 85 years; 32.9% men; and median Society of Thoracic Surgeons Predicted Risk of Mortality score of 6.0%) were included in the analysis. Of the patients, 142 (13.7%) patients were underweight (BMI<18.5 kg/m²), 679 (65.3%) patients had normal weight (18.5≤BMI≤24.9 kg/m²), 190 (18.3%) patients were overweight (25.0≤BMI≤29.9 kg/m²), and 29 (2.8%) patients were obese (BMI≥30.0 kg/m²). Common comorbidities were hypertension (85.4%), dyslipidemia (54.9%), coronary artery disease (33.7%), diabetes (22.0%), and atrial fibrillation (22.0%). Additional data on the baseline clinical characteristics are outlined in Table 1.

Prevalence and Clinical Associations of Malnutrition
The prevalence of malnutrition differed according to the 3 nutritional indexes as follows: 72.2% with the CONUT score, 75.3% with the GNRI, and 13.8% with the PNI. Among them, the CONUT score, GNRI, and PNI, 172 (16.6%), 629 (60.5%), and 144 (13.8%) patients had moderate to severe malnutrition, respectively (Figure 2A). Although the 3 nutritional indexes were correlated with each other (CONUT score versus GNRI, r=-0.63, P<0.001; CONUT score versus PNI, r=-0.81, P<0.001; GNRI versus PNI, r=0.83, P<0.001), only 144 (13.8%) patients were categorized as undernourished (any degree of malnutrition) in all 3 indexes, and only 111 (10.7%) patients were categorized as normally nourished in any of the indexes (Figure 2B). The prevalence of malnutrition was higher in men than in women based on the CONUT score (79.0% versus 68.9%; P<0.001); whereas the prevalence of malnutrition did not differ significantly according to sex based on the GNRI (72.2% versus 76.8%; P=0.126) and NRI (14.6% versus 13.5%; P=0.633). The prevalence of malnutrition was higher in patients with a BMI<22 kg/m² than in those with a BMI≥22 kg/m² (78.8% versus 65.5% for the CONUT score, 89.1% versus 61.2% for the GNRI, 18.5% versus 9.1% for the PNI; P<0.001 for all comparisons) and was also higher in patients with a CFS>4 than in those with a CFS≤3 (78.5% versus 66.0% for the CONUT score, 84.1% versus 66.5% for the GNRI, 19.7% versus 8.0% for the PNI; P<0.001 for all comparisons) (Table 2).

Compared with patients with normal nutrition, those with malnutrition according to any of the 3 nutritional indexes were older, leaner, and fatter and had worse New York Heart Association functional class and higher Society of Thoracic Surgeons scores. They also had a higher prevalence of atrial fibrillation, anemia, and kidney dysfunction. Moreover, echocardiographic data showed that lower LVEF and mean aortic gradient and higher degrees of mitral and tricuspid regurgitation were observed in patients with worse nutritional status (Tables S1A through S1C).

Procedural Characteristics and In-Hospital Outcomes
The procedural characteristics and in-hospital outcomes are listed in Table 3. Most patients (86.6%) underwent TAVI via the transfemoral approach. TAVI was performed using balloon-expandable and self-expandable valves in 801 (77.0%) and 239 (23.0%) patients, respectively. Emergent and urgent procedures were performed in 45 (3.3%) patients and were more frequently performed in patients with worse nutritional status according to any of the 3 nutritional indexes. In-hospital death was identified in 15 (1.4%) patients, including cardiovascular death in 7 patients and noncardiovascular death in 8 patients. Compared with patients with normal nutrition, those with malnutrition had a higher in-hospital mortality rate and a longer hospital stay after TAVI (Tables S2A through S2C).

Postprocedural Echocardiographic Data
All patients underwent the postprocedural echocardiographic follow-up (Table 4). On the whole, acceptable THV function was obtained (indexed effective orifice area of 1.17 cm² [IQR, 1.00–1.36 cm²]; mean pressure gradient of 10.5 mm Hg [IQR 8.0–13.5 mm Hg]), whereas moderate and severe prosthesis–patient mismatches were identified in 76 (7.3%) and 8 (0.8%) patients, respectively. Moderate to severe paravalvular leakage was observed in only 2 (0.2%) patients. Compared with patients with normal nutrition, those with malnutrition had a lower mean pressure gradient for any of the 3 nutritional indexes, whereas larger indexed effective orifice area was observed in those with worse nutritional status according to the GNRI only. The incidence of prosthesis–patient mismatch was comparable between patients with each nutritional status based on any of the 3 indexes (Tables S3A through S3C).

Nutritional Scores and Long-Term Clinical Outcomes
At a median follow-up of 985.9 days (IQR, 556.0–1402.3 days), a total of 274 patients with all-cause death were identified: 59 (21.5%) patients died for cardiac reasons, and the remaining 215 (78.5%) patients died for noncardiac reasons (Figure 3). Rehospitalization attributed to heart failure was required in 91 patients. The results of the univariate analysis for the association
Table 1. Baseline Characteristics of Patients

|                     | Total (N=1040) | CONUT score |                      |                      |                      |                      |                      |                      |                      |                      |
|---------------------|----------------|-------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
|                     |                | Normal/mild, 0–4 (N=868) | Moderate/severe, 5–12 (N=172) | P value | Normal/mild, ≥97.5 (N=411) | Moderate/severe, <97.5 (N=629) | P value | Normal, >38 (N=896) | Moderate/severe, ≤38 (N=144) | P value |
| **Demographics**    |                |              |                      |                      |                      |                      |                      |                      |                      |                      |
| Age, y              | 85 (82–88)     | 85 (82–88)  | 87 (83–90)           | 0.004               | 84 (80–87)           | 86 (83–89)           | <0.001              | 85 (82–88)           | 87 (83–90)           | 0.002               |
| Male sex            | 342 (32.9)     | 269 (31.0)  | 73 (42.4)            | 0.004               | 137 (33.3)           | 205 (32.6)           | 0.803               | 292 (32.6)           | 50 (34.7)            | 0.614               |
| Height, cm          | 146.7 (142.9–156.2) | 148.5 (142.9–155.9) | 150.0 (142.9–159.0) | 0.142               | 149.0 (143.0–158.5)  | 148.5 (142.5–155.5)  | 0.066               | 148.6 (143.0–156.4)  | 149.4 (142.1–155.7)  | 0.810               |
| Weight, kg          | 49.2 (42.2–56.8) | 49.8 (42.5–57.3) | 46.8 (40.6–55.1)     | 0.032               | 53.8 (47.0–60.7)     | 45.9 (40.0–53.8)     | <0.001              | 49.9 (42.6–57.5)     | 45.8 (40.0–54.0)     | <0.001              |
| Body mass index, kg/m² | 22.0 (19.7–24.4) | 22.3 (19.9–24.6) | 21.2 (18.8–23.6)     | <0.001              | 23.6 (21.8–25.7)     | 20.7 (18.7–23.2)     | <0.001              | 22.3 (19.9–24.6)     | 20.6 (18.6–23.2)     | <0.001              |
| Clinical Frailty Scale | 3 (3–4)       | 3 (3–4)     | 4 (3–5)              | <0.001              | 3 (3–4)              | 4 (3–4)              | <0.001              | 3 (3–4)              | 4 (3–6)             | <0.001              |
| NYHA functional class III/IV | 465 (44.7)   | 358 (41.2)  | 107 (62.2)           | <0.001              | 148 (36.0)           | 317 (50.4)           | <0.001              | 375 (41.9)           | 90 (62.5)            | <0.001              |
| STS-PROM score, %   | 6.0 (4.1–8.9) | 5.6 (3.9–8.3) | 8.2 (5.4–12.9)       | <0.001              | 5.0 (3.6–7.5)        | 6.7 (4.5–9.9)        | <0.001              | 5.6 (3.9–8.3)        | 8.3 (5.8–13.8)       | <0.001              |
| **Comorbidities**   |                |              |                      |                      |                      |                      |                      |                      |                      |                      |
| Hypertension        | 888 (85.4)     | 744 (85.7)  | 144 (83.7)           | 0.504               | 370 (90.0)           | 518 (82.4)           | 0.001               | 771 (86.1)           | 117 (81.3)           | 0.142               |
| Dyslipidemia        | 571 (54.9)     | 495 (57.0)  | 76 (44.2)            | 0.002               | 275 (65.9)           | 296 (47.1)           | <0.001              | 508 (56.7)           | 63 (43.8)            | 0.004               |
| Diabetes            | 229 (22.0)     | 194 (22.4)  | 35 (20.4)            | 0.560               | 109 (26.5)           | 120 (19.1)           | 0.005               | 198 (22.1)           | 31 (21.5)            | 0.878               |
| Atrial fibrillation | 229 (22.0)     | 164 (18.9)  | 65 (37.8)            | <0.001              | 70 (17.0)            | 159 (25.3)           | 0.002               | 173 (19.3)           | 56 (38.9)            | <0.001              |
| Coronary artery disease | 350 (33.7)   | 279 (32.1)  | 71 (41.3)            | 0.022               | 150 (36.5)           | 200 (31.8)           | 0.118               | 290 (32.4)           | 60 (41.7)            | 0.031               |
| Previous coronary bypass | 53 (5.1)     | 44 (5.1)    | 9 (5.2)              | 0.929               | 27 (6.6)             | 26 (4.1)             | 0.084               | 47 (5.3)             | 6 (4.2)              | 0.575               |
| Previous valve surgery | 26 (2.5)     | 22 (2.5)    | 4 (2.3)              | 0.871               | 12 (2.9)             | 14 (2.2)             | 0.487               | 23 (2.6)             | 3 (2.1)              | 0.724               |
| Peripheral artery disease | 90 (8.7)     | 70 (8.1)    | 20 (11.6)            | 0.143               | 30 (7.3)             | 60 (9.5)             | 0.205               | 75 (8.4)             | 15 (10.4)            | 0.429               |
| Chronic obstructive pulmonary disease | 107 (10.3) | 87 (10.0)  | 20 (11.6)            | 0.533               | 45 (11.0)            | 62 (9.9)             | 0.572               | 88 (9.8)             | 19 (13.2)            | 0.231               |
| Cerebrovascular disease | 120 (11.5)  | 98 (11.3)   | 22 (12.8)            | 0.578               | 40 (9.7)             | 80 (12.7)            | 0.137               | 101 (11.3)           | 19 (13.2)            | 0.510               |
| Active cancer       | 53 (5.1)       | 43 (5.0)    | 10 (5.8)             | 0.645               | 15 (3.7)             | 38 (6.0)             | 0.080               | 48 (5.4)             | 5 (3.5)              | 0.316               |
| **Blood tests**     |                |              |                      |                      |                      |                      |                      |                      |                      |                      |
| Hemoglobin, g/dL    | 11.2 (10.1–12.3) | 11.4 (10.3–12.5) | 10.2 (9.2–11.2)     | <0.001              | 11.8 (10.8–12.8)     | 10.8 (9.7–11.9)     | <0.001              | 11.4 (10.3–12.5)     | 10.1 (9.1–11.1)      | <0.001              |

(Continued)
### Table 1. (Continued)

| Echocardiographic data | Total (N=1040) | CONUT score | GNRI | PNI |
|------------------------|----------------|-------------|------|-----|
|                        | Normal/mild, 0–4 (N=868) | Moderate/severe, 5–12 (N=172) | P value | Normal/mild, ≥97.5 (N=411) | Moderate/severe, <97.5 (N=629) | P value | Normal, >38 (N=896) | Moderate/severe, ≤38 (N=144) | P value |
| eGFR, mL/min per 1.73 m² | 51.2 (38.4–64.4) | 52.0 (39.2–65.6) | 47.6 (31.4–57.9) | <0.001 | 52.7 (39.3–65.0) | 49.5 (37.7–64.0) | 0.043 | 51.9 (39.2–65.0) | 43.3 (30.7–57.7) | <0.001 |
| Albumin, g/dL | 3.8 (3.4–4.1) | 3.9 (3.6–4.1) | 3.1 (2.9–3.4) | <0.001 | 4.1 (3.9–4.3) | 3.5 (3.3–3.7) | <0.001 | 3.8 (3.6–4.1) | 3.0 (2.8–3.2) | <0.001 |
| Total cholesterol, mg/dL | 168 (146–193) | 173 (153–197) | 142 (122–164) | <0.001 | 177 (155–199) | 164 (143–188) | <0.001 | 171 (150–195) | 152 (131–177) | <0.001 |
| eGFR, mL/min per 1.73 m² | 51.2 (38.4–64.4) | 52.0 (39.2–65.6) | 47.6 (31.4–57.9) | <0.001 | 52.7 (39.3–65.0) | 49.5 (37.7–64.0) | 0.043 | 51.9 (39.2–65.0) | 43.3 (30.7–57.7) | <0.001 |
| Albumin, g/dL | 3.8 (3.4–4.1) | 3.9 (3.6–4.1) | 3.1 (2.9–3.4) | <0.001 | 4.1 (3.9–4.3) | 3.5 (3.3–3.7) | <0.001 | 3.8 (3.6–4.1) | 3.0 (2.8–3.2) | <0.001 |
| Total cholesterol, mg/dL | 168 (146–193) | 173 (153–197) | 142 (122–164) | <0.001 | 177 (155–199) | 164 (143–188) | <0.001 | 171 (150–195) | 152 (131–177) | <0.001 |

### Echocardiographic data

| Echocardiographic data | Total (N=1040) | CONUT score | GNRI | PNI |
|------------------------|----------------|-------------|------|-----|
|                        | Normal/mild, 0–4 (N=868) | Moderate/severe, 5–12 (N=172) | P value | Normal/mild, ≥97.5 (N=411) | Moderate/severe, <97.5 (N=629) | P value | Normal, >38 (N=896) | Moderate/severe, ≤38 (N=144) | P value |
| Aortic valve area, cm² | 0.66 (0.55–0.76) | 0.66 (0.56–0.77) | 0.64 (0.52–0.72) | 0.002 | 0.69 (0.60–0.78) | 0.64 (0.53–0.75) | <0.001 | 0.66 (0.56–0.77) | 0.64 (0.53–0.75) | 0.071 |
| Indexed aortic valve area, cm²/m² | 0.50 (0.42–0.57) | 0.50 (0.40–0.51) | 0.40 (0.30–0.50) | 0.006 | 0.50 (0.40–0.50) | 0.50 (0.40–0.50) | 0.005 | 0.50 (0.40–0.50) | 0.50 (0.40–0.50) | 0.005 |
| Mean aortic gradient, mm Hg | 46.0 (35.6–60.2) | 46.1 (36.3–60.2) | 44.5 (32.1–59.7) | 0.006 | 47.0 (37.7–60.2) | 45.3 (34.2–60.1) | 0.250 | 46.7 (36.5–60.5) | 43.0 (30.4–57.3) | 0.006 |
| Left ventricular ejection fraction, % | 62.3 (55.1–66.5) | 62.6 (56.5–65.9) | 58.1 (46.7–64.1) | <0.001 | 63.3 (56.0–66.3) | 61.5 (52.7–65.2) | <0.001 | 62.7 (56.4–65.9) | 58.0 (46.8–63.9) | <0.001 |
| Systolic pulmonary arterial pressure, mm Hg | 31.8 (26.0–38.0) | 31.0 (26.0–37.0) | 35.0 (28.0–44.0) | <0.001 | 30.0 (26.0–36.0) | 32.6 (27.0–40.0) | <0.001 | 31.0 (26.0–37.0) | 35.0 (29.0–45.0) | <0.001 |

### MDCT data

| MDCT data | Total (N=1040) | CONUT score | GNRI | PNI |
|-----------|----------------|-------------|------|-----|
|           | Normal/mild, 0–4 (N=868) | Moderate/severe, 5–12 (N=172) | P value | Normal/mild, ≥97.5 (N=411) | Moderate/severe, <97.5 (N=629) | P value | Normal, >38 (N=896) | Moderate/severe, ≤38 (N=144) | P value |
| Annulus area, mm² | 396.1 (351.4–453.5) | 392.7 (349.7–446.4) | 419.4 (366.4–493.0) | <0.001 | 394.0 (352.8–484.6) | 398.0 (350.9–455.7) | 0.497 | 393.1 (350.4–449.1) | 408.6 (369.2–466.8) | 0.007 |
| Annulus perimeter, mm | 71.4 (67.6–76.3) | 71.2 (67.4–75.8) | 73.0 (68.7–79.5) | <0.001 | 71.3 (67.8–75.9) | 71.5 (67.5–76.5) | 0.524 | 71.3 (67.4–76.2) | 72.2 (68.7–77.2) | 0.036 |
| LVOT area, mm² | 390.4 (329.8–477.6) | 384.9 (325.6–467.3) | 422.9 (357.9–529.5) | <0.001 | 386.5 (324.0–468.4) | 392.1 (334.5–483.7) | 0.227 | 388.6 (326.7–475.2) | 407.2 (353.7–503.2) | 0.033 |
### Table 1. (Continued)

| Constrast | Total (N=1040) | CONUT score | GNRI | PNI |
|-----------|----------------|-------------|------|-----|
|           | Normal/mild, 0–4 (N=868) | Moderate/severe, 5–12 (N=172) | P value | Normal/mild, ≥97.5 (N=411) | Moderate/severe, <97.5 (N=629) | P value | Normal, >38 (N=896) | Moderate/severe, ≤38 (N=144) | P value |
| STJ height, mm | 18.6 (16.8–20.6) | 16.8 (16.8–20.5) | 19.1 (16.8–21.3) | 0.102 | 18.7 (16.8–20.7) | 18.6 (16.8–20.6) | 0.723 | 18.6 (16.8–20.6) | 18.8 (16.7–21.2) | 0.731 |
| STJ diameter, mm | 24.6 (22.8–27.0) | 24.5 (22.6–26.8) | 25.7 (23.3–27.4) | 0.001 | 24.6 (22.6–26.9) | 24.8 (22.8–27.1) | 0.304 | 24.6 (22.7–26.9) | 25.2 (23.3–27.3) | 0.022 |
| Mean SOV diameter, mm | 29.5 (27.7–31.8) | 29.3 (27.7–31.5) | 30.4 (28.2–32.6) | 0.001 | 29.3 (27.7–31.8) | 29.6 (27.7–31.8) | 0.539 | 29.4 (27.7–31.7) | 29.8 (28.2–32.3) | 0.054 |
| Left coronary artery height, mm | 13.4 (11.9–14.8) | 13.4 (11.8–14.8) | 13.4 (12.1–14.6) | 0.928 | 13.4 (11.9–14.8) | 13.4 (11.9–14.8) | 0.997 | 13.4 (11.8–14.8) | 13.1 (12.3–14.3) | 0.389 |
| Right coronary artery height, mm | 15.0 (13.1–17.0) | 14.9 (13.0–16.9) | 15.3 (13.5–17.3) | 0.053 | 14.9 (13.0–17.0) | 15.0 (13.2–17.0) | 0.620 | 15.0 (13.1–17.1) | 15.0 (13.3–17.0) | 0.705 |
| LVOT calcification ≥moderate | 68 (6.5) | 47 (5.4) | 21 (12.2) | 0.002 | 18 (4.4) | 50 (8.0) | 0.020 | 50 (5.6) | 18 (12.5) | 0.004 |

Values are number (percentage) or median (interquartile range). CONUT indicates Controlling Nutritional Status; eGFR, estimated glomerular filtration rate; GNRI, Geriatric Nutritional Risk Index; LVOT, left ventricular outflow tract; MDCT, multidetector computed tomography; NYHA, New York Heart Association; PNI, Prognostic Nutritional Index; SOV, sinus of Valsalva; STJ, sinotubular junction; and STS-PROM, Society of Thoracic Surgeons Predicted Risk of Mortality.

### Table 2. Prevalence of Malnutrition by Sex, Body Mass Index, and Clinical Frailty Scale

| CONUT score | Male sex (N=342) | Female sex (N=698) | P value | BMI<22 kg/m² (N=524) | BM≥22 kg/m² (N=516) | P value | CFS<3 (N=523) | CFS≥4 (N=517) | P value |
|-------------|----------------|----------------|---------|----------------------|----------------------|---------|----------------|----------------|---------|
| Normal      | 72 (21.1) | 217 (31.1) | 0.001 | 111 (21.2) | 178 (34.5) | <0.001 | 178 (34.0) | 111 (21.5) | <0.001 |
| Mild        | 197 (57.6) | 382 (54.7) | 0.214 | 305 (57.8) | 276 (53.5) | 0.001 | 284 (54.3) | 295 (57.1) |
| Moderate    | 68 (19.9) | 91 (13.0) | 101 (19.3) | 58 (11.2) | 58 (11.1) | 101 (19.5) |
| Severe      | 5 (1.5) | 8 (1.2) | 9 (1.7) | 4 (0.8) | 3 (0.6) | 10 (1.8) |

| GNRI | Male sex (N=342) | Female sex (N=698) | P value | BMI<22 kg/m² (N=524) | BM≥22 kg/m² (N=516) | P value | CFS<3 (N=523) | CFS≥4 (N=517) | P value |
|------|----------------|----------------|---------|----------------------|----------------------|---------|----------------|----------------|---------|
| Normal      | 95 (27.8) | 162 (23.2) | 0.214 | 57 (10.9) | 200 (38.8) | <0.001 | 175 (33.5) | 82 (15.9) | <0.001 |
| Mild        | 42 (12.3) | 112 (16.1) | 52 (9.9) | 102 (19.8) | 84 (16.1) | 30 (13.5) |
| Moderate    | 175 (52.2) | 355 (50.9) | 327 (62.4) | 203 (39.3) | 236 (45.1) | 294 (56.9) |
| Severe      | 30 (8.8) | 69 (9.9) | 88 (16.8) | 11 (2.1) | 25 (5.4) | 71 (13.7) |

| PNI | Male sex (N=342) | Female sex (N=698) | P value | BMI<22 kg/m² (N=524) | BM≥22 kg/m² (N=516) | P value | CFS<3 (N=523) | CFS≥4 (N=517) | P value |
|-----|----------------|----------------|---------|----------------------|----------------------|---------|----------------|----------------|---------|
| Normal      | 292 (85.4) | 604 (86.5) | 0.877 | 427 (81.5) | 469 (90.9) | <0.001 | 481 (92.0) | 415 (80.3) | <0.001 |
| Mild        | ... | ... | ... | ... | ... | ... |
| Moderate    | 27 (7.9) | 50 (7.2) | 49 (9.4) | 28 (5.4) | 25 (4.8) | 52 (10.1) |
| Severe      | 23 (6.7) | 44 (6.3) | 48 (9.2) | 19 (3.7) | 17 (3.3) | 50 (9.7) |

Values are number (percentage). BMI indicates body mass index; CFS, Clinical Frailty Scale; CONUT, Controlling Nutritional Status; GNRI, Geriatric Nutritional Risk Index; and PNI, Prognostic Nutritional Index.
Table 3. Procedure Characteristics and In-Hospital Outcomes

| Total (N=1040) | CONUT score | GNRI | PNI | CONUT score | GNRI | PNI |
|----------------|-------------|------|-----|-------------|------|-----|
|                | Normal/ mild, 0–4 (N=868) | Moderate/severe, 5–12 (N=172) | P value | Normal/ mild, ≤97.5 (N=411) | Moderate/severe, >97.5 (N=629) | P value | Normal, >38 (N=896) | Moderate/severe, ≤38 (N=144) | P value |
| Local anesthesia | 636 (61.1) | 537 (61.9) | 98 (57.0) | 0.232 | 253 (61.6) | 382 (60.7) | 0.789 | 541 (60.4) | 94 (65.3) | 0.260 |
| Emergent and urgent procedure | 45 (3.3) | 21 (2.4) | 24 (14.0) | <0.001 | 4 (1.0) | 41 (6.5) | <0.001 | 20 (2.2) | 25 (17.4) | <0.001 |
| Access site | | | | | | | | | | |
| Transfemoral | 901 (86.6) | 753 (86.8) | 148 (86.1) | 0.805 | 362 (88.1) | 539 (85.7) | 0.266 | 768 (85.7) | 133 (92.4) | 0.021 |
| Alternative | 139 (13.4) | 115 (13.3) | 24 (14.0) | 0.948 | 49 (11.9) | 90 (14.3) | 0.232 | 128 (14.3) | 11 (7.6) | 0.058 |
| Prosthesis type | | | | | | | | | | |
| SAPIEN XT | 214 (20.6) | 184 (21.2) | 30 (17.4) | 0.563 | 95 (23.1) | 119 (18.9) | 0.179 | 197 (22.0) | 17 (11.8) | 0.016 |
| SAPIEN 3 | 587 (56.4) | 482 (55.5) | 105 (61.1) | 0.805 | 234 (56.9) | 353 (56.1) | 0.266 | 344 (40.0) | 96 (66.7) | 0.001 |
| Evolut R/PRO | 222 (21.3) | 188 (21.7) | 34 (19.8) | 0.887 | 76 (18.5) | 146 (23.2) | 0.266 | 193 (21.5) | 29 (20.1) | 0.016 |
| Prosthesis size | | | | | | | | | | |
| 20mm | 15 (1.4) | 11 (1.3) | 4 (2.3) | 0.004 | 5 (1.2) | 10 (1.6) | 0.799 | 11 (1.2) | 4 (2.8) | 0.061 |
| 23mm | 437 (42.1) | 379 (43.7) | 58 (33.9) | 0.001 | 180 (43.8) | 257 (40.9) | 0.385 | 387 (43.2) | 50 (35.0) | 0.001 |
| 26mm | 437 (42.1) | 367 (42.3) | 70 (40.9) | 0.001 | 168 (40.9) | 269 (42.8) | 0.385 | 377 (42.1) | 60 (42.0) | 0.001 |
| 29mm | 150 (14.4) | 111 (12.8) | 39 (22.8) | 0.001 | 58 (14.1) | 92 (14.7) | 0.001 | 121 (13.5) | 29 (20.3) | 0.001 |
| Length of hospital stay after TAVI, days | 9 (6–14) | 9 (6–13) | 13 (7–21) | <0.001 | 8 (6–12) | 10 (7–15) | <0.001 | 9 (6–13) | 14 (8–25) | <0.001 |
| All-cause mortality | 15 (1.4) | 9 (1.0) | 6 (3.5) | 0.396 | 4 (1.0) | 11 (1.8) | 0.291 | 9 (1.0) | 6 (4.2) | 0.012 |
| Acute kidney injury | 57 (5.5) | 36 (4.2) | 21 (12.2) | <0.001 | 20 (4.9) | 37 (5.9) | 0.479 | 40 (4.5) | 17 (11.8) | 0.001 |
| Disabling stroke | 14 (1.3) | 11 (1.3) | 3 (1.7) | 0.632 | 3 (0.7) | 11 (1.8) | 0.146 | 10 (1.1) | 4 (2.8) | 0.149 |
| PVL≥moderate | 2 (0.2) | 1 (0.1) | 1 (0.6) | 0.275 | 2 (0.5) | 0 | 0.054 | 2 (0.2) | 0 | 0.440 |
| Life-threatening/disabling bleeding | 41 (3.9) | 32 (3.7) | 9 (5.2) | 0.361 | 10 (2.4) | 31 (4.9) | 0.037 | 30 (3.4) | 11 (7.6) | 0.027 |
| Coronary obstruction | 7 (0.7) | 5 (0.6) | 2 (1.2) | 0.432 | 3 (0.7) | 4 (0.6) | 0.857 | 6 (0.7) | 1 (0.7) | 0.973 |
| Major vascular complications | 44 (4.2) | 37 (4.3) | 7 (4.1) | 0.908 | 17 (4.1) | 27 (4.3) | 0.903 | 36 (4.0) | 8 (5.6) | 0.413 |
| Conversion to open surgery | 11 (1.1) | 8 (0.9) | 3 (1.7) | 0.369 | 2 (0.5) | 9 (1.4) | 0.125 | 7 (0.8) | 4 (2.8) | 0.060 |
| New pacemaker implantation | 80 (7.7) | 65 (7.5) | 15 (8.7) | 0.588 | 26 (6.3) | 54 (8.6) | 0.174 | 72 (8.0) | 8 (5.6) | 0.279 |

Values are number (percentage) or median (interquartile range). CONUT indicates Controlling Nutritional Status; GNRI, Geriatric Nutritional Risk Index; PNI, Prognostic Nutritional Index; PVL, paravalvular leakage; and TAVI, transcatheter aortic valve implantation.
between all-cause mortality and clinical findings are presented in Table S4. Worsening malnutrition status as a continuous variable was associated with a higher incidence of all-cause mortality for any malnutrition indexes (Figure 4). The Kaplan–Meier analysis also showed that moderate to severe malnutrition was related to a higher incidence of all-cause mortality than the other nutritional groups regardless of the malnutrition index used. Patients with mild malnutrition had a higher mortality rate than those with normal nutritional status by the CONUT score, whereas comparable mortality rates between the 2 groups were observed by the GNRI. Similarly for cardiovascular mortality and heart failure hospitalization, worsening malnutrition status was associated with worse prognoses by the CONUT score and the PNI, whereas there was a trend for a higher event rate in the worse malnutrition groups, albeit with no significant group difference by the GNRI (Figure 5).

In the multivariable analyses, compared with normal nutritional status, moderate or severe malnutrition was independently associated with the risk of all-cause death during the follow-up period, irrespective of the malnutrition indexes used (Table 5). In addition, we dichotomized patients according to the median age of 85 years, the median BMI of 22 kg/m², the median CFS of 3, the LVEF of 50%, chronic renal failure status, and sex. Regardless of the stratification based on these factors, worsening malnutrition status was independently
associated with a higher incidence of mortality without significant interactions (Figure S1A through S1C).

The c-statistics did not differ among the 3 nutritional indexes for all-cause mortality, cardiovascular mortality, and heart failure hospitalization. However, the CONUT score and the PNI have higher sensitivity than the GNRI for all of these outcomes (Figure 6).

Nutritional Status at 1-Year Follow-Up

We also retrospectively collected data on the nutritional status at 1 year after TAVI of 934 patients who survived at 1-year follow-up and assessed temporal changes of nutritional status according to each nutritional index (Figures S2A to S2C). Of a total of 934 patients, 98 (10.5%) patients had no follow-up data on nutritional status, who also tended to be in worse preprocedural nutritional status. Improved, stable, and worsened nutritional categories were, respectively, observed in 212 (22.7%), 483 (51.7%), and 141 (15.1%) patients for the CONUT score; in 212 (22.7%), 452 (48.4%), and 172 (18.4%) patients for the GNRI; and in 64 (6.9%), 707 (75.7%), and 65 (7.0%) patients for the PNI.

DISCUSSION

In this study, we evaluated the prevalence and prognostic impact of malnutrition, which was assessed by 3 existing indexes, in patients undergoing TAVI. Malnutrition was common but was associated with a poor prognosis after TAVI, regardless of the nutrition index used and irrespective of age, sex, BMI, frailty, kidney function, and LVEF.

Few previous studies have assessed the prevalence of malnutrition in patients undergoing TAVI. Honda et al reported that two-thirds of 150 patients undergoing TAVI were malnourished using the CONUT score, and Doi et al also reported that 65% of 288 patients undergoing TAVI were malnourished or at risk of malnutrition using the Mini Nutritional Assessment–Short Form. Aortic stenosis is a chronic, progressive disease with a prolonged inflammatory process that may cause reduced mobility, loss of muscle mass, decreased appetite, and poor nutritional status. Moreover, most of the patients undergoing TAVI are elderly, although indications for TAVI have recently been expanded to include younger patients. Aging also decreases one’s metabolic reserve of albumin, and therefore, the nutritional status of the elderly can be easily affected by relatively small stresses. Nevertheless, malnutrition in candidates for TAVI is often unrecognized and, thus, untreated in clinical practice. In our study, comparing the clinical significance of 3 nutritional indexes in a large cohort of 1040 patients, the prevalence of malnutrition depended on the nutritional index used, ranging from 13.8% with the PNI, to 72.2% with the CONUT score, and to 75.3% with the GNRI. In particular, the PNI identified far fewer patients as malnourished compared with the other indexes. Because the PNI only identifies patients as moderately or severely malnourished, it may therefore underestimate the overall prevalence of malnutrition. Indeed, a higher concordance for the prevalence of moderate to severe malnutrition was observed between the PNI (13.8%) and the CONUT score (16.6%), perhaps reflecting the similarity of the variables on which these 2 indexes are based; on the other hand, a higher prevalence of moderate to severe malnutrition was found with the GNRI (60.5%), which considers anthropometric factors and serum markers. Therefore, clinical cardiologists should understand that...
Malnutrition is prevalent in candidates for TAVI and that the nutritional indexes are often not interchangeable. Lower BMI, which is believed to reflect undernourishment, is associated with worse prognosis in patients with heart failure, a phenomenon that is often termed the obesity paradox. In our study, patients with a lower BMI had higher degrees of malnutrition; however, it should be noted that malnutrition was highly prevalent also in those with a BMI >22 kg/m² using the CONUT and GNRI criteria (65.5% and 61.2%, respectively). A high prevalence of malnutrition in patients who were overweight or obese has also been reported in previous investigations on acute coronary syndrome and heart failure, highlighting that malnutrition does not simply manifest as being underweight. In addition, it is important to note that malnutrition is not only common in patients who are frail with CFS≥4 but also is relatively prevalent in patients with CFS≤3. Indeed, as shown in Figure 5, malnutrition degrees and clinical outcomes.

Figure 5. Malnutrition degrees and clinical outcomes. Kaplan–Meier curves for (left) all-cause mortality, (middle) cardiovascular mortality, and (right) heart failure hospitalization by the CONUT score, GNRI, and PNI. CONUT indicates Controlling Nutritional Status; GNRI, Geriatric Nutritional Risk Index; and PNI, Prognostic Nutritional Index.
Figures S1A to S1C, multivariable analyses revealed no significant interaction between the malnutrition groups and BMI groups and between the malnutrition groups and CFS groups regarding overall survival. Therefore, we should be quantitatively screening nutritional status using objective indexes without being bound by anthropometric and visual factors.

This study demonstrated that worsening malnutrition status was associated with increased long-term mortality in patients undergoing TAVI, irrespective of age, sex, BMI, frailty, kidney function, and LVEF. The predictive role of malnutrition indexes in mortality was also confirmed after adjusting by clinical variables with known poor prognosis, including CFS, Society of Thoracic Surgeons Predicted Risk of Mortality score, dyslipidemia, atrial fibrillation, peripheral artery disease, active cancer, hemoglobin, estimated glomerular filtration rate, brain natriuretic peptide, left ventricular ejection fraction, moderate to severe mitral regurgitation, transfemoral approach, and moderate to severe left ventricular outflow tract calcification. Model 2 was additionally adjusted for the following postprocedural variables: conversion to open surgery, new pacemaker implantation, prostheses–patient mismatch, and moderate to severe paravalvular leakage. CONUT indicates Controlling Nutritional Status; GNRI, Geriatric Nutritional Risk Index; HR, hazard ratio; and PNI, Prognostic Nutritional Index.

### Table 5. Multivariable Cox Regression Analyses of Malnutrition for All-Cause Mortality

| Multivariable analysis | CONUT score | GNRI | PNI |
|------------------------|-------------|------|-----|
|                        | HR  | 95% CI |  P value | HR  | 95% CI |  P value | HR  | 95% CI |  P value |
| Normal nutrition       | ... | ...     | Reference | ... | ...     | Reference | ... | ...     | Reference |
| Mild malnutrition      | 1.22 | 0.87–1.72 | 0.26 | 1.06 | 0.63–1.79 | 0.82 | ... | ... | ...
| Moderate malnutrition  | 2.22 | 1.46–3.35 | <0.001 | 2.02 | 1.36–3.01 | 0.001 | 1.64 | 1.09–2.46 | 0.018 |
| Severe malnutrition    | 6.20 | 2.76–13.91 | <0.001 | 3.26 | 1.87–5.69 | <0.001 | 2.32 | 1.50–3.60 | <0.001 |

Model 1 was adjusted for the following preprocedural variables: age, sex, body mass index, Clinical Frailty Scale, New York Heart Association class III/IV, Society of Thoracic Surgeons Predicted Risk of Mortality score, dyslipidemia, atrial fibrillation, peripheral artery disease, active cancer, hemoglobin, estimated glomerular filtration rate, brain natriuretic peptide, left ventricular ejection fraction, moderate to severe mitral regurgitation, transfemoral approach, and moderate to severe left ventricular outflow tract calcification. Model 2 was additionally adjusted for the following postprocedural variables: conversion to open surgery, new pacemaker implantation, prostheses–patient mismatch, and moderate to severe paravalvular leakage. CONUT indicates Controlling Nutritional Status; GNRI, Geriatric Nutritional Risk Index; HR, hazard ratio; and PNI, Prognostic Nutritional Index.
option to consider palliative care instead of a futile invasive procedure for these patients is increasingly recognized. Futility risk models after TAVI, consisting of many comorbidities such as atrial fibrillation, chronic renal failure, liver disease, pulmonary disease, anemia, and cancer, were previously reported; however, these models did not include a detailed evaluation of nutritional status. Our study showed a prohibitive risk of mortality (80%) at 5 years in patients with preprocedural moderate or severe malnutrition, which was observed in 20% of the study population. We ought to acknowledge that worse nutritional status as a potential surrogate marker for diminished physiological reserve is associated with early mortality after TAVI. Objective nutritional indexes such as the CONUT score, GNRI, and PNI would be useful for the preprocedural risk stratification.

Limitations
This study has several limitations that warrant discussion. First, this is a single-center observational study including a retrospective analysis with all inherent limitations. Data are limited to Asian patients, without information regarding educational background, family structure, or socioeconomic status, which may improve understanding of the causes of malnutrition. Therefore, confirmation of our findings by other investigators and in other countries with different health care and social systems is important. Second, the nutritional status assessed by the 3 simple objective scoring systems was not validated by more complex comprehensive nutritional assessments, such as subjective evaluation (eg, the Subjective Global Assessment and Mini Nutritional Assessment). In addition, we did not compare the prognostic value of these 3 scoring tools with comprehensive nutritional assessments. However, some subjective nutritional evaluations may be inaccurate for older patients with cognitive impairments, most of whom have indication for TAVI rather than surgical aortic valve replacement. From this perspective, the objective nutritional indexes assessed in this study will be useful for the nutritional screening of candidates for TAVI. Third, although nutritional status was assessed not only at the TAVI procedure but also at the 1-year follow-up, the clinical effect of nutritional interventions for patients who were undernourished was not determined. Fourth, we did not routinely perform the follow-up computed tomography. Therefore, the presence of leaflet thrombosis on THV, which might have affected outcomes after TAVI, was not assessed in this study.

CONCLUSIONS
Malnutrition is common in patients undergoing TAVI and is associated with a poor prognosis after TAVI. Adequate nutritional assessment before TAVI may
allow clinicians to identify patients at elevated risk for all-cause mortality and cardiovascular events and who may benefit from nutritional support. These findings warrant further investigation into the clinical effect of nutritional interventions for patients who are undernourished.

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Supplemental Material
Table S1–S4.

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SUPPLEMENTAL MATERIAL
Table S1A. Baseline Characteristics According to CONUT Score

| Demographics | CONUT score | 0-1 Normal (N = 289) | 2-4 Mild (N = 579) | 5-8 Moderate (N = 159) | 9-12 Severe (N = 13) | P value |
|--------------|-------------|----------------------|--------------------|------------------------|----------------------|---------|
| Age, years   | 84.0 (80.5-87.0) | 85.0 (82.0-89.0) | 87.0 (84.0-90.0) | 84.0 (79.5-89.5) | <0.001 |
| Male         | 72 (24.9) | 197 (34.0) | 68 (42.8) | 5 (38.5) | 0.001 |
| Height, cm   | 148.6 (143.3-155.1) | 148.3 (142.5-157.0) | 150.0 (142.0-159.0) | 151.0 (146.6-157.0) | 0.421 |
| Weight, kg   | 51.0 (44.5-58.7) | 49.0 (42.0-56.4) | 46.8 (40.7-55.1) | 45.9 (39.4-56.4) | 0.010 |
| Body mass index, kg/m² | 23.1 (20.3-25.4) | 21.8 (19.8-24.1) | 21.3 (18.9-23.6) | 19.9 (17.0-24.2) | <0.001 |
| Clinical Frailty Scale | 3 (3-4) | 4 (3-4) | 4 (3-5) | 5 (4-7) | <0.001 |
| NYHA functional class III/IV | 106 (36.7) | 252 (43.5) | 96 (60.4) | 11 (84.6) | <0.001 |
| STS-PROM score, % | 5.1 (3.6-7.5) | 5.9 (4.1-8.6) | 8.0 (5.3-12.5) | 11.7 (6.2-23.4) | <0.001 |

| Comorbidities | CONUT score | 0-1 Normal (N = 289) | 2-4 Mild (N = 579) | 5-8 Moderate (N = 159) | 9-12 Severe (N = 13) | P value |
|---------------|-------------|----------------------|--------------------|------------------------|----------------------|---------|
| Hypertension  | 249 (86.2) | 495 (85.5) | 136 (85.5) | 8 (61.5) | 0.205 |
| Dyslipidemia  | 159 (55.0) | 336 (58.0) | 71 (44.7) | 5 (38.5) | 0.015 |
| Diabetes mellitus | 55 (19.0) | 139 (24.0) | 32 (20.1) | 3 (23.1) | 0.361 |
| Atrial fibrillation | 42 (14.5) | 122 (21.1) | 55 (34.6) | 10 (76.9) | <0.001 |
| Coronary artery disease | 80 (27.7) | 199 (34.4) | 68 (42.8) | 3 (23.1) | 0.010 |
| Previous coronary bypass | 16 (5.5) | 28 (4.8) | 8 (5.0) | 1 (7.7) | 0.950 |
| Previous valve surgery | 4 (1.4) | 18 (3.1) | 4 (2.5) | 0 (0) | 0.357 |
| Peripheral artery disease | 18 (6.2) | 52 (9.0) | 19 (12.0) | 1 (7.7) | 0.219 |
| Chronic obstructive pulmonary disease | 34 (11.8) | 53 (9.2) | 19 (12.0) | 1 (7.7) | 0.562 |
|                                | Cerebrovascular disease | Active cancer | | | |
|--------------------------------|-------------------------|--------------|---|---|---|
|                               | 35 (12.1)               | 63 (10.9)    | 19 (12.0) | 3 (23.1) | 0.630 |
| Blood tests                   |                         |              |           |           |     |
| Hemoglobin, g/dl              | 11.8 (10.9-12.8)        | 11.3 (10.0-12.3) | 10.2 (9.3-11.2) | 9.6 (8.7-11.4) | <0.001 |
| eGFR, ml/min/1.73 m²          | 55.1 (44.0-66.9)        | 50.6 (38.1-65.0) | 46.2 (31.0-56.8) | 54.5 (41.2-72.7) | <0.001 |
| Albumin, g/dl                 | 4.0 (3.7-4.2)           | 3.8 (3.5-4.1) | 3.2 (2.9-3.4) | 2.4 (2.3-2.8) | <0.001 |
| Total cholesterol, mg/dl      | 193.0 (178.5-213.5)     | 163.0 (146.0-183.0) | 143.0 (127.0-165.0) | 120.0 (97.5-141.0) | <0.001 |
| Lymphocyte count, μl          | 1693 (1434-2006)        | 1154 (979-1402) | 1043 (763-1180) | 806 (738-1035) | <0.001 |
| Brain natriuretic peptide, pg/ml | 108.9 (61.3-254.9) | 191.9 (76.9-440.3) | 346.9 (164.8-647.7) | 701.8 (371.8-1515.9) | <0.001 |
| Echocardiographic data        |                         |              |           |           |     |
| Aortic valve area, cm²        | 0.67 (0.57-0.77)        | 0.66 (0.56-0.77) | 0.64 (0.52-0.73) | 0.58 (0.51-0.70) | 0.011 |
| Indexed aortic valve area, cm²/m² | 0.50 (0.40-0.51) | 0.50 (0.40-0.51) | 0.41 (0.40-0.50) | 0.40 (0.30-0.50) | 0.018 |
| Mean aortic gradient, mmHg    | 46.0 (35.8-58.7)        | 46.7 (36.6-61.0) | 45.5 (23.7-60.5) | 36.5 (23.6-42.5) | 0.039 |
| Left ventricular ejection fraction, % | 64.0 (59.2-66.2) | 62.1 (55.1-65.5) | 59.0 (47.0-64.1) | 53.3 (37.6-59.2) | <0.001 |
| Left ventricular end-diastolic diameter, mm | 42.9 (39.9-46.4) | 44.4 (40.4-48.1) | 45.3 (40.7-50.8) | 45.4 (38.0-48.4) | 0.002 |
| Aortic regurgitation ≥ moderate | 10 (3.5)               | 35 (6.0)     | 15 (9.4)   | 1 (7.7)   | 0.080 |
| Mitral regurgitation ≥ moderate | 7 (2.4)                | 22 (3.8)     | 14 (8.8)   | 5 (38.5)   | <0.001 |
| Tricuspid regurgitation ≥ moderate | 6 (2.1)               | 16 (2.8)     | 10 (6.3)   | 4 (30.8)   | 0.001 |
| Systolic pulmonary arterial pressure, mmHg | 31.0 (26.0-36.1) | 31.0 (26.0-37.0) | 35.0 (27.3-43.3) | 45.0 (36.2-52.0) | <0.001 |
| MDCT data                     |                         |              |           |           |     |
| Annulus area, mm²             | 389.7 (344.8-433.9)     | 393.7 (353.8-456.5) | 416.1 (365.8-493.5) | 422.9 (371.2-463.7) | <0.001 |
| Annulus perimeter, mm         | 70.9 (66.8-74.8)        | 71.4 (67.8-76.6) | 72.9 (68.6-79.6) | 73.1 (68.8-77.4) | 0.001 |
| LVOT area, mm²                | 368.3 (314.0-442.4)     | 391.1 (333.3-482.0) | 422.6 (354.7-536.7) | 442.8 (388.7-501.7) | <0.001 |
| STJ height, mm                | 18.4 (16.8-20.0)        | 18.6 (16.8-20.6) | 19.1 (16.8-21.4) | 18.8 (17.0-20.7) | 0.190 |
|                        | Group 1     | Group 2     | Group 3     | Group 4     | P-value |
|------------------------|-------------|-------------|-------------|-------------|---------|
| STJ diameter, mm       | 24.2 (22.4-26.3) | 24.7 (22.7-27.1) | 25.7 (23.3-27.4) | 25.0 (23.3-28.1) | 0.001   |
| Mean SOV diameter, mm  | 28.8 (27.4-30.9) | 29.7 (27.7-31.9) | 30.5 (28.3-32.7) | 30.0 (27.9-31.8) | <0.001  |
| Left coronary artery height, mm | 13.1 (11.5-14.5) | 13.5 (11.9-15.0) | 13.3 (12.0-14.6) | 13.9 (12.8-14.4) | 0.068   |
| Right coronary artery height, mm | 14.8 (12.9-16.7) | 14.9 (13.1-17.0) | 15.4 (13.5-17.3) | 14.9 (13.4-17.9) | 0.179   |
| LVOT calcification ≥ moderate | 15 (5.2) | 32 (5.5) | 20 (12.6) | 1 (7.7) | 0.023   |

Values are n (%) or median (interquartile range).

CONUT = Controlling Nutritional Status; eGFR = estimated glomerular filtration rate; LVOT = left ventricular outflow tract; MDCT = multidetector computed tomography; NYHA = New York Heart Association; SOV = sinus of Valsalva; STJ = sinotubular junction; STS-PROM = Society of Thoracic Surgeons predicted risk of mortality
**Table S1B. Baseline Characteristics According to GNRI**

| GNRI          | ≥100 Normal (N = 257) | 97.50-99.99 Mild (N = 154) | 83.50-97.49 Moderate (N = 530) | <83.50 Severe (N = 99) | P value |
|---------------|-----------------------|-----------------------------|-------------------------------|------------------------|---------|
| **Demographics** |                       |                             |                               |                        |         |
| Age, years    | 84.0 (80.0-86.5)       | 85.0 (81.0-88.0)            | 86.0 (83.0-89.0)              | 88.0 (84.0-90.0)       | <0.001  |
| Male          | 95 (40.0)              | 42 (27.3)                   | 175 (33.0)                    | 30 (30.3)              | 0.214   |
| Height, cm    | 150.1 (144.4-159.0)    | 146.8 (142.0-155.8)         | 148.5 (142.0-155.7)           | 149.0 (143.4-154.7)    | 0.007   |
| Weight, kg    | 54.6 (49.1-62.1)       | 51.9 (45.3-58.8)            | 46.7 (40.8-54.5)              | 40.6 (35.9-46.3)       | <0.001  |
| Body mass index, kg/m² | 23.8 (22.3-25.8) | 23.1 (21.0-25.3)            | 21.1 (19.1-23.5)              | 18.4 (16.9-20.2)       | <0.001  |
| Clinical Frailty Scale | 3 (3-4)               | 3 (3-4)                     | 4 (3-4)                       | 4 (3-6)                | <0.001  |
| NYHA functional class III/IV | 87 (33.9)            | 61 (39.6)                   | 261 (49.3)                    | 56 (56.6)              | <0.001  |
| STS-PROM score, % | 4.6 (3.2-7.3)           | 5.6 (4.1-8.1)               | 6.4 (4.3-9.0)                 | 8.9 (6.2-13.5)         | <0.001  |
| **Comorbidities** |                   |                             |                               |                        |         |
| Hypertension  | 229 (89.1)             | 141 (91.6)                  | 438 (82.6)                    | 80 (80.8)              | 0.005   |
| Dyslipidemia  | 176 (68.5)             | 99 (64.3)                   | 256 (48.3)                    | 40 (40.4)              | <0.001  |
| Diabetes mellitus | 71 (27.6)          | 38 (24.7)                   | 102 (19.3)                    | 18 (18.2)              | 0.038   |
| Atrial fibrillation | 49 (19.1)            | 21 (13.6)                   | 117 (22.1)                    | 42 (42.4)              | <0.001  |
| Coronary artery disease | 91 (35.4)           | 59 (38.1)                   | 165 (31.1)                    | 35 (35.4)              | 0.324   |
| Previous coronary bypass | 20 (7.8)            | 7 (4.6)                     | 24 (4.5)                      | 2 (2.0)                | 0.099   |
| Previous valve surgery | 8 (3.1)              | 4 (2.6)                     | 11 (2.1)                      | 3 (3.0)                | 0.826   |
| Peripheral artery disease | 20 (7.8)            | 10 (6.5)                    | 47 (8.9)                      | 13 (13.1)              | 0.325   |
| Chronic obstructive pulmonary disease | 30 (11.7)          | 15 (9.7)                    | 50 (9.4)                      | 12 (12.1)              | 0.720   |
|                                | 27 (10.5) | 13 (8.4) | 67 (12.6) | 13 (13.1) | 0.439 |
|--------------------------------|-----------|----------|-----------|-----------|-------|
| Cerebrovascular disease        |           |          |           |           |       |
| Active cancer                  | 13 (5.1)  | 2 (1.3)  | 32 (6.0)  | 6 (6.1)   | 0.056 |

**Blood tests**

| Test                          | Mean (95% CI) |
|-------------------------------|--------------|
| Hemoglobin, g/dl              | 12.0 (11.0-13.2) |
| eGFR, ml/min/1.73 m²          | 53.2 (40.2-67.4) |
| Albumin, g/dl                 | 4.2 (4.1-4.4)  |
| Total cholesterol, mg/dl      | 180.0 (158.0-202.5) |
| Lymphocyte count, μl          | 1304 (1077-1592) |
| Brain natriuretic peptide, pg/ml | 95.4 (56.1-211.5) |

**Echocardiographic data**

| Test                          | Mean (95% CI) |
|-------------------------------|--------------|
| Aortic valve area, cm²        | 0.69 (0.61-0.79) |
| Indexed aortic valve area, cm²/m² | 0.50 (0.40-0.50) |
| Mean aortic gradient, mmHg    | 46.0 (36.7-58.4) |
| Left ventricular ejection fraction, % | 62.9 (58.7-66.2) |
| Left ventricular end-diastolic diameter, mm | 44.9 (41.6-47.4) |
| Aortic regurgitation ≥ moderate | 18 (7.0) |
| Mitral regurgitation ≥ moderate | 0 (0)     |
| Tricuspid regurgitation ≥ moderate | 4 (1.6) |
| Systolic pulmonary arterial pressure, mmHg | 30.0 (26.0-35.0) |

**MDCT data**

| Test                          | Mean (95% CI) |
|-------------------------------|--------------|
| Annulus area, mm²             | 398.7 (351.8-452.8) |
| Annulus perimeter, mm         | 72.1 (67.8-76.4)  |
| LVOT area, mm²                | 398.3 (328.2-469.0) |
| STJ height, mm                | 19.0 (17.1-20.7)  |
|                          |                |                |                |                |          |
|--------------------------|----------------|----------------|----------------|----------------|----------|
| STJ diameter, mm         | 24.6 (22.8-26.8)| 24.5 (22.5-27.0)| 25.0 (22.8-27.3)| 24.3 (22.9-26.1)| 0.262    |
| Mean SOV diameter, mm    | 29.3 (27.8-31.7)| 29.0 (27.7-31.9)| 29.7 (27.7-31.8)| 29.1 (27.8-31.0)| 0.581    |
| Left coronary artery height, mm | 13.4 (12.2-14.8) | 13.4 (11.5-14.7) | 13.4 (11.8-14.8) | 13.0 (12.3-14.3) | 0.800    |
| Right coronary artery height, mm | 14.8 (12.9-17.2) | 14.9 (13.0-16.7) | 15.0 (12.9-17.1) | 14.9 (13.3-16.5) | 0.947    |
| LVOT calcification ≥ moderate | 14 (5.5)       | 4 (2.6)        | 36 (6.8)       | 14 (14.1)      | 0.005    |

Values are n (%) or median (interquartile range).
eGFR = estimated glomerular filtration rate; GNRI = Geriatric Nutrition Risk Index; LVOT = left ventricular outflow tract; MDCT = multidetector computed tomography; NYHA = New York Heart Association; SOV = sinus of Valsalva; STJ = sinotubular junction; STS-PROM = Society of Thoracic Surgeons predicted risk of mortality.
| Demographics                                      | >38 Normal (N = 896) | 35-38 Moderate (N = 77) | <35 Severe (N = 67) | P value |
|--------------------------------------------------|----------------------|-------------------------|---------------------|---------|
| Age, years                                       | 85.0 (82.0-88.0)     | 87.0 (84.0-90.0)        | 87.0 (82.0-91.0)    | 0.004   |
| Male                                             | 292 (32.6)           | 27 (35.1)               | 23 (34.3)           | 0.877   |
| Height, cm                                       | 148.6 (143.0-156.4)  | 150.0 (142.0-157.7)     | 149.0 (142.3-155.0) | 0.966   |
| Weight, kg                                       | 49.9 (42.6-57.5)     | 45.8 (40.1-54.2)        | 45.2 (39.8-52.7)    | 0.001   |
| Body mass index, kg/m²                           | 22.3 (19.9-24.6)     | 21.1 (18.6-24.1)        | 20.4 (18.4-22.5)    | <0.001  |
| Clinical Frailty Scale                           | 3 (3-4)              | 4 (3-5)                 | 5 (3-7)             | <0.001  |
| NYHA functional class III/IV                     | 375 (41.9)           | 49 (63.6)               | 41 (61.2)           | <0.001  |
| STS-PROM score, %                               | 5.6 (3.9-8.3)        | 7.9 (5.4-13.7)          | 8.5 (6.1-14.5)      | <0.001  |
| Hypertension                                     | 771 (86.1)           | 63 (81.8)               | 54 (80.6)           | 0.334   |
| Dyslipidemia                                     | 508 (56.7)           | 35 (45.5)               | 28 (41.8)           | 0.014   |
| Diabetes mellitus                                | 198 (22.1)           | 19 (24.7)               | 12 (17.9)           | 0.606   |
| Atrial fibrillation                              | 173 (19.3)           | 28 (36.4)               | 28 (41.8)           | <0.001  |
| Coronary artery disease                          | 290 (32.4)           | 31 (40.3)               | 29 (43.3)           | 0.090   |
| Previous coronary bypass                         | 47 (5.3)             | 2 (2.6)                 | 4 (6.0)             | 0.511   |
| Previous valve surgery                           | 23 (2.6)             | 1 (1.3)                 | 2 (3.0)             | 0.730   |
| Peripheral artery disease                        | 75 (8.4)             | 9 (11.7)                | 6 (9.0)             | 0.633   |
| Chronic obstructive pulmonary disease            | 88 (9.8)             | 9 (11.7)                | 10 (14.9)           | 0.414   |
|                          | Count | Mean  | 95% CI  | p-value |
|--------------------------|-------|-------|---------|---------|
| Cerebrovascular disease  | 101 (11.3) | 10 (13.0) | 9 (13.4) | 0.802 |
| Active cancer            | 48 (5.4) | 3 (3.9) | 2 (3.0) | 0.579 |

**Blood tests**

| Test                               | Count | Mean  | 95% CI  | p-value |
|------------------------------------|-------|-------|---------|---------|
| Hemoglobin, g/dl                   | 11.4 (10.3-12.5) | 10.2 (9.3-11.3) | 9.7 (8.8-10.8) | <0.001 |
| eGFR, ml/min/1.73 m²               | 51.9 (39.2-65.0) | 44.4 (31.6-55.0) | 42.0 (27.8-61.1) | <0.001 |
| Albumin, g/dl                      | 3.8 (3.6-4.1) | 3.2 (3.0-3.3) | 2.8 (2.6-3.0) | <0.001 |
| Total cholesterol, mg/dl           | 171.0 (150.0-195.0) | 158.0 (139.5-178.0) | 146.0 (122.0-175.0) | <0.001 |
| Lymphocyte count, μl               | 1305 (1056-1637) | 1054 (785-1196) | 945 (699-1161) | <0.001 |
| Brain natriuretic peptide, pg/ml  | 162.7 (72.7-353.0) | 316.0 (180.0-581.2) | 530.6 (230.9-954.4) | <0.001 |

**Echocardiographic data**

| Test                               | Count | Mean  | 95% CI  | p-value |
|------------------------------------|-------|-------|---------|---------|
| Aortic valve area, cm²             | 0.66 (0.56-0.77) | 0.64 (0.54-0.72) | 0.62 (0.50-0.76) | 0.189 |
| Indexed aortic valve area, cm²/m²  | 0.50 (0.40-0.50) | 0.50 (0.40-0.52) | 0.49 (0.37-0.60) | 0.876 |
| Mean aortic gradient, mmHg         | 46.7 (36.5-60.5) | 45.5 (34.4-56.8) | 39.0 (29.1-57.9) | 0.011 |
| Left ventricular ejection fraction, % | 62.7 (56.4-65.9) | 58.3 (47.2-63.8) | 56.4 (44.7-64.4) | <0.001 |
| Left ventricular end-diastolic diameter, mm | 44.0 (40.2-47.6) | 46.0 (41.0-50.9) | 44.0 (40.6-48.1) | 0.093 |
| Aortic regurgitation ≥ moderate    | 45 (5.0) | 9 (11.7) | 7 (10.5) | 0.030 |
| Mitral regurgitation ≥ moderate    | 29 (3.2) | 6 (7.8) | 13 (19.4) | <0.001 |
| Tricuspid regurgitation ≥ moderate | 25 (2.8) | 3 (3.9) | 8 (11.9) | 0.006 |
| Systolic pulmonary arterial pressure, mmHg | 31.0 (26.0-37.0) | 35.0 (29.0-45.8) | 36.0 (29.0-45.0) | <0.001 |

**MDCT data**

| Test                               | Count | Mean  | 95% CI  | p-value |
|------------------------------------|-------|-------|---------|---------|
| Annulus area, mm²                  | 393.1 (350.4-449.1) | 419.2 (387.2-479.7) | 398.0 (360.0-455.7) | 0.009 |
| Annulus perimeter, mm              | 71.3 (67.4-76.2) | 72.9 (70.1-78.2) | 71.2 (67.5-76.2) | 0.024 |
| LVOT area, mm²                     | 388.6 (326.7-475.2) | 410.0 (363.9-528.9) | 392.5 (334.7-488.2) | 0.068 |
| STJ height, mm                     | 18.6 (16.8-20.6) | 19.0 (16.4-21.7) | 18.6 (16.8-20.7) | 0.915 |
| Metric                                      | Group 1          | Group 2          | Group 3          | p-value |
|--------------------------------------------|------------------|------------------|------------------|---------|
| STJ diameter, mm                           | 24.6 (22.7-26.9) | 25.9 (23.3-27.8) | 24.6 (23.3-26.8) | 0.041   |
| Mean SOV diameter, mm                      | 29.4 (27.7-31.7) | 30.1 (28.5-32.8) | 29.6 (28.0-32.1) | 0.097   |
| Left coronary artery height, mm            | 13.4 (11.8-14.9) | 13.2 (12.0-14.4) | 13.0 (12.3-14.3) | 0.690   |
| Right coronary artery height, mm           | 15.0 (13.1-17.1) | 15.3 (13.3-17.3) | 14.8 (13.2-16.5) | 0.346   |
| LVOT calcification ≥ moderate               | 50 (5.6)         | 10 (13.0)        | 8 (11.9)         | 0.017   |

Values are n (%) or median (interquartile range).
eGFR = estimated glomerular filtration rate; LVOT = left ventricular outflow tract; MDCT = multidetector computed tomography; NYHA = New York Heart Association; PNI = Prognostic Nutritional Index; SOV = sinus of Valsalva; STJ = sinotubular junction; STS-PROM = Society of Thoracic Surgeons predicted risk of mortality.
| CONUT score | 0-1 Normal (N = 289) | 2-4 Mild (N = 579) | 5-8 Moderate (N = 159) | 9-12 Severe (N = 13) | P value |
|-------------|---------------------|--------------------|------------------------|----------------------|---------|
| Local anesthesia | 194 (67.1) | 343 (59.2) | 92 (57.9) | 6 (46.2) | 0.065 |
| Emergent and urgent procedure | 1 (0.4) | 20 (3.5) | 18 (11.3) | 6 (46.2) | <0.001 |
| Access site | | | | | |
| Transfemoral | 250 (86.5) | 503 (86.9) | 136 (85.5) | 12 (92.3) | 0.894 |
| Alternative | 39 (13.5) | 76 (13.1) | 23 (14.5) | 1 (7.7) |
| Prosthesis type | | | | | |
| SAPIEN XT | 59 (20.4) | 125 (21.6) | 29 (18.2) | 1 (7.7) | 0.205 |
| SAPIEN 3 | 161 (55.7) | 321 (55.4) | 93 (58.5) | 12 (92.3) |
| CoreValve | 3 (1.0) | 11 (1.9) | 3 (1.9) | 0 |
| Evolut R/PRO | 66 (22.8) | 122 (21.1) | 34 (21.4) | 0 |
| Prosthesis size | | | | | |
| 20 mm | 4 (1.4) | 7 (1.2) | 3 (1.9) | 1 (7.7) | 0.031 |
| 23 mm | 129 (44.6) | 250 (43.2) | 54 (34.2) | 4 (30.8) |
| 26 mm | 127 (43.9) | 240 (41.5) | 62 (39.2) | 8 (61.5) |
| 29 mm | 29 (10.0) | 82 (14.2) | 39 (24.7) | 0 |
| Length of hospital stay after TAVI, days | 11 (8-16) | 13 (9-19) | 23 (13-37) | 43 (17-52) | <0.001 |
| All-cause mortality | 3 (1.0) | 6 (1.0) | 5 (3.1) | 1 (7.7) | 0.151 |
| Acute kidney injury | 10 (3.5) | 26 (4.5) | 19 (12.0) | 2 (15.4) | 0.002 |
| Disabling stroke | 4 (1.4) | 7 (1.2) | 3 (1.9) | 0 | 0.861 |
| Event                                      | Control Group | DirectAoV Treatment | Placebo Group | DirectAoV Treatment | p-value |
|--------------------------------------------|---------------|---------------------|---------------|---------------------|---------|
| PVL ≥ moderate                             | 1 (0.4)       | 0                   | 1 (0.6)       | 0                   | 0.314   |
| Life-threatening/disabling bleeding        | 8 (2.8)       | 24 (4.2)            | 9 (5.7)       | 0                   | 0.341   |
| Coronary obstruction                       | 1 (0.4)       | 4 (0.7)             | 2 (1.3)       | 0                   | 0.708   |
| Major vascular complication                | 9 (3.1)       | 28 (4.8)            | 7 (4.4)       | 0                   | 0.455   |
| Conversion to open surgery                 | 0             | 8 (1.4)             | 3 (1.9)       | 0                   | 0.050   |
| New pacemaker implantation                 | 16 (5.6)      | 49 (8.5)            | 15 (9.4)      | 0                   | 0.156   |

Values are n (%) or median (interquartile range).

CONUT = Controlling Nutritional Status; PVL = paravalvular leakage; TAVI = transcatheter aortic valve implantation.
| GNRI | Normal (N = 257) | Mild (N = 154) | Moderate (N = 530) | Severe (N = 99) | P value |
|------|-----------------|---------------|------------------|----------------|---------|
| <100 |                 |               |                  |                |         |
| ≥100 |                 |               |                  |                |         |
| Normal | 108 (42.0) | 50 (32.5) | 207 (39.1) | 40 (40.4) | 0.274 |
| Mild | 2 (0.9) | 2 (1.3) | 24 (4.5) | 17 (17.2) | <0.001 |
| Access site | | | | | |
| Transfemoral | 223 (86.8) | 139 (90.3) | 452 (85.3) | 87 (87.9) | 0.414 |
| Alternative | 33 (13.2) | 15 (9.7) | 78 (14.7) | 12 (12.1) |         |
| Prosthesis type | | | | | |
| SAPIEN XT | 64 (24.9) | 31 (20.1) | 108 (20.4) | 11 (11.1) | 0.088 |
| SAPIEN 3 | 138 (53.7) | 96 (62.3) | 288 (54.3) | 65 (65.7) |         |
| CoreValve | 5 (2.0) | 1 (0.7) | 9 (1.7) | 2 (2.0) |         |
| Evolut R/PRO | 50 (19.5) | 26 (16.9) | 125 (23.6) | 21 (21.2) |         |
| Prosthesis size | | | | | |
| 20 mm | 5 (2.0) | 0 | 6 (1.1) | 4 (4.1) | 0.059 |
| 23 mm | 101 (39.3) | 79 (51.3) | 217 (40.9) | 40 (40.8) |         |
| 26 mm | 110 (42.8) | 58 (37.7) | 255 (42.5) | 44 (44.9) |         |
| 29 mm | 41 (16.0) | 17 (11.0) | 82 (15.5) | 10 (10.2) |         |
| Length of hospital stay after TAVI, days | 10 (8-14) | 11 (8-17) | 14 (10-22) | 31 (18-50) | <0.001 |
| All-cause mortality | 1 (0.4) | 3 (2.0) | 6 (1.1) | 5 (5.1) | 0.030 |
| Acute kidney injury | 11 (4.3) | 9 (5.8) | 29 (5.5) | 8 (8.1) | 0.584 |
| Disabling stroke | 2 (0.8) | 1 (0.7) | 0 | 3 (3.0) | 0.377 |
| Event                                    | Group 1 | Group 2 | Group 3 | Group 4 | p-value |
|------------------------------------------|---------|---------|---------|---------|---------|
| PVL ≥ moderate                           | 1 (0.4) | 1 (0.7) | 0       | 0       | 0.278   |
| Life-threatening/disabling bleeding      | 5 (2.0) | 5 (3.3) | 27 (5.1)| 4 (4.0) | 0.155   |
| Coronary obstruction                     | 3 (1.2) | 0       | 3 (1.2) | 1 (1.0) | 0.378   |
| Major vascular complication             | 10 (3.9)| 7 (4.6)| 21 (4.0)| 6 (6.1) | 0.817   |
| Conversion to open surgery              | 1 (0.4) | 1 (0.7) | 5 (0.9) | 4 (4.0) | 0.082   |
| New pacemaker implantation              | 16 (6.2)| 10 (6.5)| 51 (9.6)| 3 (3.0) | 0.054   |

Values are n (%) or median (interquartile range).

GNRI = Geriatric Nutrition Risk Index; PVL = paravalvular leakage; TAVI = transcatheter aortic valve implantation.
|                         | PNI                        | >38 Normal (N = 896) | 35-38 Moderate (N = 77) | <35 Severe (N = 67) | P value  |
|-------------------------|----------------------------|----------------------|-------------------------|---------------------|----------|
| Local anesthesia        |                            | 542 (60.4)           | 52 (67.5)               | 42 (62.7)           | 0.441    |
| Emergent and urgent procedure |                      | 20 (2.2)             | 10 (13.0)              | 15 (22.4)           | <0.001   |
| Access site             |                            |                      |                         |                     |          |
| Transfemoral            |                            | 768 (85.7)           | 72 (93.5)               | 61 (91.0)           | 0.059    |
| Alternative             |                            | 128 (14.3)           | 5 (6.5)                 | 6 (9.0)             |          |
| Prosthesis type         |                            |                      |                         |                     |          |
| SAPIEN XT               |                            | 197 (22.0)           | 9 (11.7)                | 8 (11.9)            | 0.097    |
| SAPIEN 3                |                            | 491 (54.8)           | 50 (64.9)               | 46 (68.7)           |          |
| CoreValve               |                            | 15 (1.7)             | 1 (1.3)                 | 1 (1.5)             |          |
| Evolut R/PRO            |                            | 193 (21.5)           | 17 (22.1)               | 12 (17.9)           |          |
| Prosthesis size         |                            |                      |                         |                     |          |
| 20 mm                   |                            | 11 (1.2)             | 1 (1.3)                 | 3 (4.6)             | 0.103    |
| 23 mm                   |                            | 387 (43.2)           | 26 (33.8)               | 24 (36.4)           |          |
| 26 mm                   |                            | 377 (42.1)           | 31 (40.3)               | 29 (43.9)           |          |
| 29 mm                   |                            | 121 (13.5)           | 19 (24.7)               | 10 (15.2)           |          |
| Length of hospital stay after TAVI, days |        | 12 (9-18)            | 25 (13-39)              | 28 (16-51)          | <0.001   |
| All-cause mortality     |                            | 9 (1.0)              | 3 (3.9)                 | 3 (4.5)             | 0.042    |
| Acute kidney injury     |                            | 40 (4.5)             | 11 (14.3)               | 6 (9.0)             | 0.003    |
| Disabling stroke        |                            | 10 (1.1)             | 3 (3.9)                 | 1 (1.5)             | 0.236    |
| Event                                | n (%)          | n (%)          | n (%)          | p-value |
|--------------------------------------|----------------|----------------|----------------|---------|
| PVL ≥ moderate                       | 2 (0.2)        | 0              | 0              | 0.742   |
| Life-threatening/disabling bleeding  | 30 (3.4)       | 9 (11.7)       | 2 (3.0)        | 0.010   |
| Coronary obstruction                 | 6 (0.7)        | 1 (1.3)        | 0              | 0.533   |
| Major vascular complication          | 36 (4.0)       | 4 (5.2)        | 4 (6.0)        | 0.700   |
| Conversion to open surgery           | 7 (0.8)        | 3 (3.9)        | 1 (1.5)        | 0.114   |
| New pacemaker implantation           | 72 (8.0)       | 5 (6.5)        | 3 (4.5)        | 0.484   |

Values are n (%) or median (interquartile range).

PNI = Prognostic Nutritional Index; PVL = paravalvular leakage; TAVI = transcatheter aortic valve implantation.
| CONUT score | 0-1 | 2-4 | 5-8 | 9-12 | P value |
|-------------|-----|-----|-----|------|---------|
| Normal (N = 289) | 1.63 (1.45-1.95) | 1.65 (1.40-1.94) | 1.66 (1.43-2.01) | 1.60 (1.53-1.79) | 0.902 |
| Mild (N = 579) | 1.15 (1.00-1.32) | 1.17 (0.99-1.37) | 1.19 (1.01-1.39) | 1.18 (1.05-1.26) | 0.508 |
| Moderate (N = 159) | 10.9 (8.4-13.9) | 10.7 (8.0-13.6) | 9.7 (7.8-12.3) | 9.3 (5.3-13.7) | 0.009 |
| Severe (N = 13) | 63.1 (59.1-66.3) | 61.6 (55.3-65.5) | 60.8 (48.8-64.5) | 53.8 (40.1-61.6) | <0.001 |
| Effective orifice area, cm² | 1.63 (1.45-1.95) | 1.65 (1.40-1.94) | 1.66 (1.43-2.01) | 1.60 (1.53-1.79) | 0.902 |
| Indexed effective orifice area, cm²/m² | 1.15 (1.00-1.32) | 1.17 (0.99-1.37) | 1.19 (1.01-1.39) | 1.18 (1.05-1.26) | 0.508 |
| Mean pressure gradient, mmHg | 10.9 (8.4-13.9) | 10.7 (8.0-13.6) | 9.7 (7.8-12.3) | 9.3 (5.3-13.7) | 0.009 |
| Left ventricular ejection fraction, % | 63.1 (59.1-66.3) | 61.6 (55.3-65.5) | 60.8 (48.8-64.5) | 53.8 (40.1-61.6) | <0.001 |
| PPM | 24 (8.3) | 51 (8.8) | 8 (5.0) | 1 (7.7) | 0.440 |
| Moderate PPM | 24 (8.3) | 45 (7.8) | 7 (4.4) | 0 | 0.183 |
| Severe PPM | 0 | 6 (1.0) | 1 (0.6) | 1 (7.7) | 0.049 |
| PVL ≥ moderate | 1 (0.4) | 0 | 1 (0.6) | 0 | 0.314 |

Values are n (%) or median (interquartile range).

CONUT = Controlling Nutritional Status; PPM = prosthesis-patient mismatch; PVL = paravalvular leakage.
| GNRI        | ≥100 (N = 257) | 97.50-99.99 (N = 154) | 83.50-97.49 (N = 530) | <83.50 (N = 99) | \( P \) value |
|-------------|----------------|-----------------------|-----------------------|-----------------|----------------|
| Effective orifice area, cm² | 1.68 (1.49-1.98) | 1.64 (1.38-1.93) | 1.63 (1.42-1.95) | 1.63 (1.35-1.87) | 0.194          |
| Indexed effective orifice area, cm²/m² | 1.13 (0.99-1.30) | 1.12 (0.98-1.32) | 1.19 (1.01-1.38) | 1.24 (1.02-1.48) | 0.003          |
| Mean pressure gradient, mmHg | 10.9 (8.4-14.2) | 11.5 (9.1-14.7) | 10.1 (7.8-13.0) | 9.2 (7.7-11.9) | <0.001         |
| Left ventricular ejection fraction, % | 63.0 (58.5-66.3) | 63.0 (58.0-66.0) | 61.7 (55.1-65.1) | 58.2 (45.6-63.7) | <0.001         |
| PPM         |                |                       |                       |                 |                |
| Moderate PPM| 25 (9.7)       | 11 (7.1)              | 40 (7.6)              | 8 (8.1)         | 0.733          |
| Severe PPM  | 0              | 1 (0.7)               | 5 (0.9)               | 2 (2.0)         | 0.133          |
| PVL ≥ moderate | 1 (0.4)   | 1 (0.7)               | 0                     | 0               | 0.278          |

Values are n (%) or median (interquartile range).

GNRI = Geriatric Nutrition Risk Index; PPM = prosthesis-patient mismatch; PVL = paravalvular leakage.
Table S3C. Post-Procedural Echocardiographic Data According to PNI

|                  | PNI          |   |   |   |   |   |
|------------------|--------------|---|---|---|---|---|
|                  | >38          |   | 35-38 |   | <35 |   |
|                  | Normal (N = 896) |   | Moderate (N = 77) |   | Severe (N = 67) |   |
|                  |              |   |          |   |          |   |
| Effective orifice area, cm² | 1.65 (1.42-1.95) | 1.72 (1.49-2.03) | 1.63 (1.43-1.85) |   | 0.383 |
| Indexed effective orifice area, cm²/m² | 1.16 (1.00-1.35) | 1.24 (1.04-1.46) | 1.20 (1.04-1.37) |   | 0.051 |
| Mean pressure gradient, mmHg | 10.7 (8.2-13.7) | 9.8 (7.4-12.2) | 9.4 (7.7-12.4) |   | 0.005 |
| Left ventricular ejection fraction, % | 62.1 (56.9-65.8) | 60 (46.3-64.2) | 59.6 (44.9-64.5) |   | <0.001 |
| PPM              | 77 (8.6)     | 2 (2.6) | 5 (7.5) |   | 0.106 |
| Moderate PPM     | 70 (7.8)     | 2 (2.6) | 4 (6.0) |   | 0.148 |
| Severe PPM       | 7 (0.8)      | 0      | 1 (1.5) |   | 0.461 |
| PVL ≥ moderate   | 2 (0.2)      | 0      | 0      |   | 0.742 |

Values are n (%) or median (interquartile range).

PNI = Prognostic Nutritional Index; PPM = prosthesis-patient mismatch; PVL = paravalvular leakage.
Table S4. Univariate Cox Regression Analyses for Predictors of All-Cause Mortality

| Pre-procedural Variables | Univariate Analysis |   |   |
|--------------------------|---------------------|---|---|
|                          | HR                  | 95% CI | P value |
| Age (per 1 year increase)| 1.03                | 1.01-1.05 | 0.011 |
| Men                      | 1.63                | 1.28-2.07 | <0.001 |
| Height (per 1 cm decrease)| 0.99                | 0.98-1.01 | 0.28  |
| Weight (per 1 kg decrease)| 1.02                | 1.01-1.03 | 0.001 |
| Body mass index (per 1 kg/m² decrease) | 1.10 | 1.07-1.15 | <0.001 |
| Clinical Frailty Scale (per 1 group increment) | 1.33 | 1.24-1.42 | <0.001 |
| NYHA class III/IV        | 1.49                | 1.17-1.90 | 0.001 |
| STS-PROM score (per 1.0% increase) | 1.05 | 1.03-1.06 | <0.001 |
| Hypertension             | 0.79                | 0.57-1.10 | 0.17  |
| Dyslipidemia             | 0.70                | 0.55-0.89 | 0.004 |
| Diabetes mellitus        | 0.97                | 0.72-1.30 | 0.83  |
| Atrial fibrillation      | 1.75                | 1.34-2.28 | <0.001 |
| Coronary artery disease  | 1.12                | 0.88-1.43 | 0.36  |
| Previous coronary bypass | 0.82                | 0.49-1.37 | 0.45  |
| Previous valve surgery   | 1.90                | 0.90-4.06 | 0.09  |
| Peripheral artery disease| 1.56                | 1.08-2.24 | 0.018 |
| Chronic obstructive pulmonary disease | 1.21 | 0.85-1.21 | 0.29  |
| Cerebrovascular disease  | 1.02                | 0.71-1.45 | 0.92  |
| Active cancer            | 1.95                | 1.27-2.99 | 0.002 |
| Hemoglobin (per 1.0 g/dl decrease) | 1.19 | 1.10-1.28 | <0.001 |
| eGFR (per 15 ml/min/1.73 m² decrease) | 1.22 | 1.11-1.35 | <0.001 |
| Albumin (per 0.5 g/dl decrease) | 1.83 | 1.62-2.07 | <0.001 |
| Total cholesterol (per 40 mg/dl decrease) | 1.37 | 1.19-1.58 | <0.001 |
| Lymphocyte count (per 400 /μl decrease) | 1.44 | 1.29-1.63 | <0.001 |
| Brain natriuretic peptide (per 100 pg/ml increase) | 1.04 | 1.02-1.06 | <0.001 |
| Aortic valve area (per 0.1 cm² decrease) | 1.05 | 0.98-1.13 | 0.24  |
| Mean aortic gradient (per 10 mmHg decrease) | 1.08 | 1.01-1.15 | 0.036 |
| Left ventricular ejection fraction (per 10% decrease) | 1.27 | 1.13-1.41 | <0.001 |
| Aortic regurgitation ≥ moderate | 1.48 | 0.96-2.26 | 0.074 |
| Mitral regurgitation ≥ moderate | 2.17 | 1.34-3.51 | 0.002 |
Tricuspid regurgitation \( \geq \) moderate 1.30 0.69-2.45 0.41
Systolic pulmonary arterial pressure (per 10 mmHg increase) 1.07 0.99-1.19 0.078
Transfemoral approach 0.71 0.53-0.95 0.021
LVOT calcification \( \geq \) moderate 1.06 0.65-1.73 0.814
Malnutrition degree according to nutrition scores

| CONUT score | Normal nutrition | Mild malnutrition | Moderate malnutrition | Severe malnutrition | Reference |
|-------------|------------------|-------------------|-----------------------|---------------------|-----------|
| Normal nutrition | - | - | - | - | Reference |
| Mild malnutrition | 1.57 | 1.13-2.18 | 0.008 |
| Moderate malnutrition | 4.13 | 2.86-5.97 | <0.001 |
| Severe malnutrition | 10.3 | 5.34-19.95 | <0.001 |

| GNRI | Normal nutrition | Mild malnutrition | Moderate malnutrition | Severe malnutrition | Reference |
|------|------------------|-------------------|-----------------------|---------------------|-----------|
| Normal nutrition | - | - | - | - | Reference |
| Mild malnutrition | 1.11 | 0.67-1.86 | 0.68 |
| Moderate malnutrition | 2.74 | 1.92-3.90 | <0.001 |
| Severe malnutrition | 6.24 | 4.04-9.63 | <0.001 |

| PNI | Normal nutrition | Moderate malnutrition | Severe malnutrition | Reference |
|-----|------------------|-----------------------|---------------------|-----------|
| Normal nutrition | - | - | - | - | Reference |
| Moderate malnutrition | 2.48 | 1.71-3.59 | <0.001 |
| Severe malnutrition | 3.88 | 2.69-5.61 | <0.001 |

| Post-procedural Variables | Conversion to open surgery | New pacemaker implantation | PPM | PVL \( \geq \) moderate | Reference |
|---------------------------|-----------------------------|----------------------------|------|-----------------------------|-----------|
| Conversion to open surgery | 3.28 | 1.54-6.96 | 0.002 |
| New pacemaker implantation | 1.16 | 0.75-1.79 | 0.509 |
| PPM | 0.68 | 0.43-1.09 | 0.112 |
| PVL \( \geq \) moderate | 1.04 | 0.15-7.42 | 0.968 |

CI = confidence interval; CONUT = Controlling Nutritional Status; eGFR = estimated glomerular filtration rate; GNRI = Geriatric Nutrition Risk Index; HR = hazard ratio; LVOT = left ventricular outflow tract; NYHA = New York Heart Association; PNI = Prognostic Nutritional Index; PPM = prosthesis-patient mismatch; PVL = paravalvular leakage; STS-PROM = Society of Thoracic Surgeons predicted risk of mortality.
Figure S1A. Forest Plot for the Adjusted Hazard Ratios of All-Cause Mortality According to the CONUT Score.

| Multinutrition degree according to CONUT score | All-cause mortality | Adjusted HR (95% CI) | P value |
|-----------------------------------------------|---------------------|----------------------|---------|
| Overall (N = 1,040)                           |                     |                      |         |
| Normal (N = 289)                              |                     | 1.00 (reference)     |         |
| Mild (N = 579)                                |                     | 1.22 (0.87-1.72)     | 0.25    |
| Moderate (N = 159)                            |                     | 2.18 (1.45-3.31)     | <0.001  |
| Severe (N = 13)                               |                     | 6.13 (2.75-13.7)     | <0.001  |
| Age                                           | P for interaction   | 0.01                 |         |
| ≤ 85 years (N = 526)                          |                     |                      |         |
| Normal (N = 168)                              |                     | 1.00 (reference)     |         |
| Mild (N = 299)                                |                     | 1.15 (0.70-1.91)     | 0.56    |
| Moderate (N = 63)                             |                     | 1.54 (0.99-2.36)     | 0.052   |
| Severe (N = 7)                                |                     | 5.16 (1.49-17.88)    | 0.010   |
| > 85 years (N = 512)                          |                     |                      |         |
| Normal (N = 121)                              |                     | 1.00 (reference)     |         |
| Mild (N = 269)                                |                     | 1.28 (0.80-2.07)     | 0.31    |
| Moderate (N = 96)                             |                     | 2.34 (1.35-4.07)     | 0.002   |
| Severe (N = 6)                                |                     | 8.50 (2.73-25.38)    | <0.001  |
| Sex                                           | P for interaction   | 0.37                 |         |
| Male (N = 342)                                |                     |                      |         |
| Normal (N = 72)                               |                     | 1.00 (reference)     |         |
| Mild (N = 187)                                |                     | 0.92 (0.53-1.60)     | 0.75    |
| Moderate (N = 88)                             |                     | 1.51 (0.79-3.02)     | 0.22    |
| Severe (N = 5)                                |                     | 6.52 (1.83-23.21)    | 0.004   |
| Female (N = 698)                              |                     |                      |         |
| Normal (N = 217)                              |                     | 1.00 (reference)     |         |
| Mild (N = 380)                                |                     | 1.33 (0.85-2.07)     | 0.21    |
| Moderate (N = 91)                             |                     | 2.64 (1.54-4.58)     | 0.001   |
| Severe (N = 8)                                |                     | 8.42 (2.80-25.38)    | <0.001  |
| Body mass index                               | P for interaction   | 0.77                 |         |
| BMI > 22 kg/m² (N = 516)                      |                     |                      |         |
| Normal (N = 178)                              |                     | 1.00 (reference)     |         |
| Mild (N = 276)                                |                     | 1.13 (0.73-1.75)     | 0.49    |
| Moderate (N = 58)                             |                     | 1.93 (1.03-3.63)     | 0.041   |
| Severe (N = 4)                                |                     | 6.45 (1.47-28.30)    | 0.014   |
| BMI ≤ 22 kg/m² (N = 524)                      |                     |                      |         |
| Normal (N = 111)                              |                     | 1.00 (reference)     |         |
| Mild (N = 303)                                |                     | 1.32 (0.81-2.16)     | 0.26    |
| Moderate (N = 101)                            |                     | 2.56 (1.44-4.54)     | 0.001   |
| Severe (N = 9)                                |                     | 7.54 (2.04-28.37)    | <0.001  |
| Clinical Frailty Scale                        | P for interaction   | 0.52                 |         |
| CFS ≤ 3 (N = 523)                             |                     |                      |         |
| Normal (N = 178)                              |                     | 1.00 (reference)     |         |
| Mild (N = 264)                                |                     | 1.10 (0.64-1.87)     | 0.74    |
| Moderate (N = 58)                             |                     | 1.98 (1.02-3.85)     | 0.045   |
| Severe (N = 3)                                |                     | 6.60 (1.35-30.14)    | 0.019   |
| CFS ≥ 4 (N = 517)                             |                     |                      |         |
| Normal (N = 111)                              |                     | 1.00 (reference)     |         |
| Mild (N = 295)                                |                     | 1.30 (0.82-2.04)     | 0.26    |
| Moderate (N = 101)                            |                     | 2.33 (1.37-3.97)     | 0.002   |
| Severe (N = 16)                               |                     | 8.38 (3.01-25.33)    | <0.001  |
| Chronic renal failure                         | P for interaction   | 0.44                 |         |
| No CRF (N = 533)                              |                     |                      |         |
| Normal (N = 100)                              |                     | 1.00 (reference)     |         |
| Mild (N = 191)                                |                     | 1.34 (0.65-2.69)     | 0.51    |
| Moderate (N = 30)                             |                     | 2.40 (1.02-5.68)     | 0.046   |
| Severe (N = 5)                                |                     | 6.84 (1.59-29.43)    | 0.010   |
| CRF (N = 707)                                 |                     |                      |         |
| Normal (N = 164)                              |                     | 1.00 (reference)     |         |
| Mild (N = 288)                                |                     | 1.30 (0.79-2.18)     | 0.40    |
| Moderate (N = 127)                            |                     | 2.33 (1.49-3.78)     | 0.001   |
| Severe (N = 8)                                |                     | 7.98 (2.71-23.49)    | <0.001  |
| Left ventricular ejection fraction            | P for interaction   | 0.06                 |         |
| LVEF ≥ 50% (N = 865)                          |                     |                      |         |
| Normal (N = 260)                              |                     | 1.00 (reference)     |         |
| Mild (N = 400)                                |                     | 1.20 (0.83-1.75)     | 0.34    |
| Moderate (N = 100)                            |                     | 2.13 (1.34-3.38)     | 0.001   |
| Severe (N = 7)                                |                     | 3.67 (1.30-10.43)    | 0.015   |
| LVEF < 50% (N = 174)                          |                     |                      |         |
| Normal (N = 29)                               |                     | 1.00 (reference)     |         |
| Mild (N = 86)                                 |                     | 0.99 (0.38-2.57)     | 0.98    |
| Moderate (N = 53)                             |                     | 1.95 (0.69-5.73)     | 0.22    |
| Severe (N = 6)                                |                     | 7.51 (1.63-34.68)    | 0.010   |

BMI = body mass index; CFS = Clinical Frailty Scale; CI = confidence interval; CONUT = Controlling Nutritional Status; CRF = chronic Renal Failure; HR = hazard ratio; LVEF = left ventricular ejection fraction
Figure S1B. Forest Plot for the Adjusted Hazard Ratios of All-Cause Mortality According to the GNRI.

| Malnutrition degree according to GNRI | All-cause mortality | Adjusted HR (95% CI) | P value |
|---------------------------------------|---------------------|----------------------|---------|
| Overall (N = 1040)                    |                     |                      |         |
| Normal (N = 267)                      | ■                   | 1.00 (reference)     |         |
| Mild (N = 154)                        | ■                   | 1.08 (0.84–1.32)     | 0.77    |
| Moderate (N = 530)                    | ■                   | 2.02 (1.36–3.02)     | 0.001   |
| Severe (N = 99)                       | ■                   | 3.24 (1.86–5.65)     | <0.001  |
| Age                                   |                     |                      |         |
| ≤ 85 years (N = 539)                  |                     |                      |         |
| Normal (N = 170)                      | ■                   | 1.00 (reference)     |         |
| Mild (N = 87)                         | ■                   | 0.89 (0.64–1.23)     | 0.76    |
| Moderate (N = 294)                    | ■                   | 1.61 (1.09–2.39)     | 0.030   |
| Severe (N = 37)                       | ■                   | 3.76 (1.71–8.27)     | <0.001  |
| > 85 years (N = 512)                  |                     |                      |         |
| Normal (N = 87)                       | ■                   | 1.00 (reference)     |         |
| Mild (N = 67)                         | ■                   | 1.45 (0.66–3.25)     | 0.35    |
| Moderate (N = 296)                    | ■                   | 2.14 (1.18–3.97)     | 0.016   |
| Severe (N = 62)                       | ■                   | 3.08 (1.45–6.43)     | 0.005   |
| Sex                                   |                     |                      |         |
| Male (N = 542)                        |                     |                      |         |
| Normal (N = 95)                       | ■                   | 1.00 (reference)     |         |
| Mild (N = 42)                         | ■                   | 1.66 (0.79–3.54)     | 0.18    |
| Moderate (N = 175)                    | ■                   | 2.19 (1.19–4.06)     | 0.010   |
| Severe (N = 30)                       | ■                   | 3.33 (1.35–8.21)     | 0.009   |
| Female (N = 698)                      |                     |                      |         |
| Normal (N = 162)                      | ■                   | 1.00 (reference)     |         |
| Mild (N = 112)                        | ■                   | 0.78 (0.36–1.66)     | 0.52    |
| Moderate (N = 355)                    | ■                   | 1.79 (1.05–3.08)     | 0.034   |
| Severe (N = 69)                       | ■                   | 3.07 (1.51–6.24)     | 0.002   |
| Body mass index                       |                     |                      |         |
| BMI > 22 kg/m² (N = 518)              |                     |                      |         |
| Normal (N = 209)                      | ■                   | 1.00 (reference)     |         |
| Mild (N = 102)                        | ■                   | 1.55 (0.80–3.00)     | 0.20    |
| Moderate (N = 203)                    | ■                   | 2.65 (1.54–4.54)     | <0.001  |
| Severe (N = 11)                       | ■                   | 4.92 (2.72–8.87)     | <0.001  |
| BMI ≤ 22 kg/m² (N = 524)              |                     |                      |         |
| Normal (N = 257)                      | ■                   | 1.00 (reference)     |         |
| Mild (N = 53)                         | ■                   | 0.48 (0.19–1.23)     | 0.13    |
| Moderate (N = 527)                    | ■                   | 1.33 (0.73–2.43)     | 0.35    |
| Severe (N = 88)                       | ■                   | 2.27 (1.12–4.65)     | 0.023   |
| Clinical Frailty Scale                |                     |                      |         |
| ≤ 3 (N = 523)                         |                     |                      |         |
| Normal (N = 175)                      | ■                   | 1.00 (reference)     |         |
| Mild (N = 84)                         | ■                   | 1.53 (0.74–3.18)     | 0.25    |
| Moderate (N = 236)                    | ■                   | 2.22 (1.21–4.08)     | 0.01    |
| Severe (N = 28)                       | ■                   | 3.33 (1.51–7.20)     | 0.004   |
| > 3 (N = 517)                         |                     |                      |         |
| Normal (N = 82)                       | ■                   | 1.00 (reference)     |         |
| Mild (N = 70)                         | ■                   | 0.80 (0.37–1.72)     | 0.56    |
| Moderate (N = 254)                    | ■                   | 1.76 (1.03–3.00)     | 0.040   |
| Severe (N = 71)                       | ■                   | 3.11 (1.53–6.35)     | 0.002   |
| Chronic renal failure                 |                     |                      |         |
| No CRF (N = 333)                      |                     |                      |         |
| Normal (N = 94)                       | ■                   | 1.00 (reference)     |         |
| Mild (N = 43)                         | ■                   | 1.40 (0.51–3.84)     | 0.51    |
| Moderate (N = 173)                    | ■                   | 1.65 (0.71–3.81)     | 0.24    |
| Severe (N = 23)                       | ■                   | 1.96 (0.57–7.11)     | 0.29    |
| CRF (N = 707)                         |                     |                      |         |
| Normal (N = 163)                      | ■                   | 1.00 (reference)     |         |
| Mild (N = 111)                        | ■                   | 0.91 (0.49–1.70)     | 0.77    |
| Moderate (N = 357)                    | ■                   | 1.94 (1.20–3.19)     | 0.005   |
| Severe (N = 70)                       | ■                   | 3.55 (1.87–6.79)     | <0.001  |
| Left ventricular ejection fraction    |                     |                      |         |
| ≥ 50% (N = 865)                       |                     |                      |         |
| Normal (N = 230)                      | ■                   | 1.00 (reference)     |         |
| Mild (N = 138)                        | ■                   | 0.88 (0.49–1.58)     | 0.66    |
| Moderate (N = 431)                    | ■                   | 1.68 (1.22–2.29)     | 0.004   |
| Severe (N = 83)                       | ■                   | 2.74 (1.45–5.18)     | 0.002   |
| ≤ 50% (N = 174)                       |                     |                      |         |
| Normal (N = 24)                       | ■                   | 1.00 (reference)     |         |
| Mild (N = 16)                         | ■                   | 2.44 (0.65–9.21)     | 0.19    |
| Moderate (N = 98)                     | ■                   | 1.74 (0.59–5.16)     | 0.31    |
| Severe (N = 36)                       | ■                   | 4.27 (1.15–15.81)    | 0.030   |

BMI = body mass index; CFS = Clinical Frailty Scale; CI = confidence interval; CRF = chronic Renal Failure; GNRI = Geriatric Nutrition Risk Index; HR = hazard ratio; LVEF = left ventricular ejection fraction.
Figure S1C. Forest Plot for the Adjusted Hazard Ratios of All-Cause Mortality According to the PNI.

| Mainnutrition degree according to PNI | All-cause mortality | Adjusted HR (95%CI) | P value |
|-------------------------------|---------------------|---------------------|---------|
| **Overall**                   |                     |                     |         |
| (N = 1040)                    |Overall              | 1.00 (reference)    |         |
|                               |Moderate (N = 77)    | 1.60 (1.06-2.39)    | 0.024   |
|                               |Severe (N = 67)      | 2.32 (1.50-3.60)    | <0.001  |
| **Age**                       |                     |                     |         |
| ≤ 85 years (N = 525)          |                     |                     |         |
| Normal (N = 471)              | 1.00 (reference)    |                     |         |
| Moderate (N = 29)             | 2.16 (1.14-4.1)     | 0.024               |
| Severe (N = 28)               | 3.76 (1.71-8.27)    | 0.001               |
| > 85 years (N = 512)          |                     |                     |         |
| Normal (N = 425)              | 1.00 (reference)    |                     |         |
| Moderate (N = 46)             | 1.30 (0.76-2.23)    | 0.33                |
| Severe (N = 33)               | 2.07 (1.14-3.70)    | 0.018               |
| **Sex**                       |                     |                     |         |
| Male (N = 342)                |                     |                     |         |
| Normal (N = 292)              | 1.00 (reference)    |                     |         |
| Moderate (N = 27)             | 1.90 (0.94-3.82)    | 0.073               |
| Severe (N = 23)               | 4.12 (1.89-8.99)    | <0.001              |
| Female (N = 668)              |                     |                     |         |
| Normal (N = 604)              | 1.00 (reference)    |                     |         |
| Moderate (N = 50)             | 1.38 (0.62-2.93)    | 0.22                |
| Severe (N = 44)               | 1.87 (1.06-3.29)    | 0.032               |
| **Body mass index**           |                     |                     |         |
| BMI > 22 kg/m² (N = 516)      |                     |                     |         |
| Normal (N = 469)              | 1.00 (reference)    |                     |         |
| Moderate (N = 26)             | 2.23 (1.09-4.68)    | 0.028               |
| Severe (N = 19)               | 3.09 (1.42-6.72)    | 0.005               |
| BMI ≤ 22 kg/m² (N = 524)      |                     |                     |         |
| Normal (N = 427)              | 1.00 (reference)    |                     |         |
| Moderate (N = 49)             | 1.50 (0.90-2.51)    | 0.12                |
| Severe (N = 48)               | 2.17 (1.26-3.72)    | 0.005               |
| **Clinical Frailty Scale**    |                     |                     |         |
| CFS ≤ 3 (N = 523)             |                     |                     |         |
| Normal (N = 461)              | 1.00 (reference)    |                     |         |
| Moderate (N = 25)             | 0.94 (0.36-2.42)    | 0.90                |
| Severe (N = 17)               | 3.70 (1.75-7.83)    | 0.001               |
| CFS ≥ 4 (N = 517)             |                     |                     |         |
| Normal (N = 413)              | 1.00 (reference)    |                     |         |
| Moderate (N = 52)             | 1.82 (1.14-2.90)    | 0.012               |
| Severe (N = 50)               | 2.39 (1.43-4.00)    | 0.001               |
| **Chronic renal failure**     |                     |                     |         |
| No CRF (N = 333)              |                     |                     |         |
| Normal (N = 307)              | 1.00 (reference)    |                     |         |
| Moderate (N = 14)             | 3.34 (1.16-9.48)    | 0.023               |
| Severe (N = 17)               | 4.69 (1.81-10.41)   | 0.003               |
| CRF (N = 707)                 |                     |                     |         |
| Normal (N = 594)              | 1.00 (reference)    |                     |         |
| Moderate (N = 63)             | 1.45 (0.92-2.29)    | 0.11                |
| Severe (N = 50)               | 2.50 (1.26-5.00)    | 0.002               |
| **Left ventricular ejection fraction** |                 |                     |         |
| LVEF ≥ 50% (N = 965)          |                     |                     |         |
| Normal (N = 773)              | 1.00 (reference)    |                     |         |
| Moderate (N = 55)             | 1.43 (0.87-2.36)    | 0.16                |
| Severe (N = 42)               | 2.34 (1.39-3.93)    | 0.001               |
| LVEF < 50% (N = 174)          |                     |                     |         |
| Normal (N = 123)              | 1.00 (reference)    |                     |         |
| Moderate (N = 26)             | 2.44 (1.18-5.12)    | 0.019               |
| Severe (N = 25)               | 3.02 (1.34-6.65)    | 0.008               |

BMI = body mass index; CFS = Clinical Frailty Scale; CI = confidence interval; CRF = chronic Renal Failure; HR = hazard ratio; LVEF = left ventricular ejection fraction; PNI = Prognostic Nutritional Index.
Figure S2A. Temporal Changes of Nutritional Status According to the CONUT Score

CONUT = Controlling Nutritional Status.
Figure S2B. Temporal Changes of Nutritional Status According to the GNRI

GNRI = Geriatric Nutrition Risk Index.

[Diagram showing changes in nutritional status with numbers and colors indicating different stages of GNRI.]
Figure S2C. Temporal Changes of Nutritional Status According to the PNI

PNI = Prognostic Nutritional Index.