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Predictors of All-Cause Mortality in Patients with Classical Low-Flow Low-Gradient Aortic Stenosis Undergoing Transcatheter Aortic Valve Implantation

ABSTRACT

Background: Classical low-flow low-gradient aortic stenosis (cLFLG AS) is associated with poor prognosis and adverse clinical outcomes despite transcatheter aortic valve implantation (TAVI). Identifying prognostic markers in this high-risk population may improve risk stratification and clinical management. This study aimed to investigate independent predictors of all-cause mortality in patients with cLFLG AS undergoing TAVI.

Methods: In this single-center retrospective study, 151 patients with cLFLG AS undergoing TAVI between January 2018 and December 2024 were included. Multivariable Cox proportional hazards regression analysis was performed to identify predictors of all-cause mortality. Two separate multivariable models incorporating tricuspid annular plane systolic excursion (TAPSE) and TAPSE/systolic pulmonary artery pressure (sPAP) ratio were constructed to evaluate the prognostic impact of right ventricular (RV) systolic function and RV–pulmonary vascular interaction. The prognostic performance of TAPSE was further assessed using receiver operating characteristic (ROC) and restricted cubic spline analyses.

Results: During a median follow-up of 26 (15-42) months, all-cause mortality occurred in 37 (25%) patients. In multivariable analysis, reduced TAPSE remained independently associated with all-cause mortality after adjustment for age and left ventricular ejection fraction (LVEF) (HR: 0.11, 95% CI: 0.04-0.30, $P < .001$). A lower TAPSE/sPAP ratio was also independently associated with mortality (HR: 0.08, 95% CI: 0.01-0.85, $P = .036$). Advanced age and reduced LVEF were independently associated with mortality in both models. Time-dependent ROC analysis demonstrated consistent discriminative performance of TAPSE over time.

Conclusion: Reduced TAPSE, advanced age, and reduced LVEF were independent predictors of all-cause mortality in patients with cLFLG AS undergoing TAVI.

Keywords: Low-flow low-gradient aortic stenosis, right ventricular dysfunction, transcatheter aortic valve implantation, tricuspid annular plane systolic excursion

INTRODUCTION

Classical low-flow low-gradient aortic stenosis (cLFLG AS) is a high-risk subset of patients with severe AS, affecting approximately 5%-10% of this population.[1,2] It is characterized by depressed left ventricular (LV) systolic function, diminished stroke volume, and transvalvular flow, resulting in a low mean gradient despite severe AS. This hemodynamic profile has been associated with poor prognosis and adverse clinical outcomes.[3,4]

Transcatheter aortic valve implantation (TAVI) has been established as an effective and preferred therapeutic option for elderly patients with severe AS.[5] Although TAVI has been demonstrated to improve survival in patients with cLFLG AS, clinical outcomes remain suboptimal compared to other AS phenotypes.[4,6,7] This suggests that factors beyond valvular stenosis, including impaired myocardial function and comorbidities, may play a pivotal role in predicting prognosis.

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In this context, identifying predictors of mortality in patients with cLFLG AS undergoing TAVI is crucial for optimal patient selection and management. Although several predictors of adverse outcomes after TAVI have been identified, patients with cLFLG AS represent a distinct high-risk subgroup with a complex low-flow hemodynamic profile, while data specifically focusing on prognostic markers in this phenotype remain relatively limited. Accordingly, this study sought to investigate independent predictors of all-cause mortality in patients with cLFLG AS undergoing TAVI.

METHODS

Study Design and Population

In this single-center study, 165 consecutive patients with cLFLG AS who underwent TAVI between January 2018 and December 2024 were retrospectively evaluated. Patients with true severe cLFLG AS according to the European Society of Cardiology (ESC) guidelines on valvular heart disease were included. Exclusion criteria were valve-in-valve interventions and insufficient preprocedural data. Specifically, 3 patients who underwent valve-in-valve procedures and 11 patients with incomplete preprocedural echocardiographic or computed tomography (CT) data that precluded confirmation of cLFLG AS were excluded. The final study population consisted of 151 patients. Demographic and clinical characteristics, preprocedural, procedural, and follow-up data were obtained from the hospital database. The local institutional review board approved the study protocol, and the study was conducted in accordance with the Declaration of Helsinki.

Echocardiography

Cardiac chamber dimensions, LV and right ventricular (RV) systolic function and the severity of valvular disease were assessed. In accordance with ESC guidelines for the management of valvular heart disease, cLFLG AS was identified as LV ejection fraction (LVEF) <50%, mean gradient <40 mm Hg, aortic valve area (AVA) ≤1 $cm^2$and stroke volume index (SVi) ≤35 mL/m^2.[5] While AVA was calculated using the continuity equation, SVi was derived from the cross-sectional area of the LV outflow tract (LVOT), LVOT velocity-time integral and body surface area. In patients with atrial fibrillation (AF), pressure gradients were averaged over 5 consecutive beats.[8] Tricuspid annular plane systolic excursion (TAPSE) was measured by placing M-mode cursor along the lateral tricuspid annulus.[9] Although TAPSE values are presented in centimeters, TAPSE was converted to millimeters for calculation of the TAPSE/systolic pulmonary artery pressure (sPAP) ratio; therefore, the ratio is expressed as mm/mmHg.

Dobutamine stress echocardiography (DSE) was performed in 108 patients, whenever feasible, to differentiate true severe from pseudo-severe LFLG AS. Contractile reserve was defined as ≥20% increase in SV during DSE. In patients in whom DSE could not be performed (n=43) or yielded inconclusive results (n=15), CT aortic valve calcium scoring was used to confirm the diagnosis of severe cLFLG AS according to guideline-recommended sex-specific thresholds. Accordingly, the final study cohort consisted exclusively of patients with a confirmed true severe cLFLG AS.

Cardiac Computed Tomography

Contrast-enhanced CT was used for preprocedural evaluation. In patients with LFLG AS, aortic valve calcification has been shown to correlate with stenosis severity and disease progression.[10] The Agatston calcium score thresholds of >2000 AU in men and >1200 AU in women have been proposed as sex-specific cut-offs for severe AS.[11] Therefore, these cut-off values were used to define severe AS in the study.

Transcatheter Aortic Valve Implantation Procedure

All patients were assessed by an interdisciplinary heart team prior to the procedure and the indication for TAVI was determined based on the heart team's decision. Transcatheter aortic valve implantation was performed via transfemoral access. The choice of valve type and the decision of pre- or post-dilatation were left to the discretion of the interventional cardiologists. Unfractionated heparin (50-70 IU/kg) was administered for periprocedural anticoagulation. A suture-mediated closure device was used to achieve hemostasis at the access site.

Study Endpoints

The primary endpoint of the study was all-cause mortality during follow-up. Clinical outcomes were adjudicated according to the standardized definitions of the Valve Academic Research Consortium-3 (VARC-3).[12] Kidney Disease: Improving Global Outcomes definition of acute kidney injury (AKI) was recommended by VARC-3. The AKI was defined as an increase in serum creatinine by ≥0.3 mg/dL within 48 hours or an increase in serum creatinine ≥1.5 times baseline within 7 days; or urine output <0.5 ml/kg/h for 6 hours.[13]

Statistical Analysis

Continuous variables are presented as mean ± standard deviation or median (interquartile range), as appropriate, whereas categorical variables are expressed as frequencies and percentages. The Kolmogorov–Smirnov test was used to assess normality. Survival analyses were performed using

HIGHLIGHTS

- Classical low-flow low-gradient aortic stenosis remains a high-risk condition despite transcatheter aortic valve implantation.
- Right ventricular dysfunction assessed by tricuspid annular plane systolic excursion (TAPSE) predicts adverse outcomes.
- Reduced TAPSE and lower TAPSE/systolic pulmonary artery pressure ratio are associated with all-cause mortality in patients with classical low-flow low-gradient aortic stenosis.
- Reduced left ventricular ejection fraction and advanced age are independently associated with all-cause mortality.
- Right ventricular functional assessment may provide complementary prognostic information beyond LVEF.

the Kaplan–Meier method, and differences between groups were assessed with the log-rank test. Cox proportional hazards regression analysis was performed to identify predictors of all-cause mortality. Variables with a *P* value <.10 in univariate analysis and clinical relevance were considered for multivariable analysis. Given the limited number of mortality events, multivariable models were intentionally simplified to minimize the risk of overfitting. Two separate multivariable models were constructed: model 1 included age, LVEF, and TAPSE, whereas model 2 included age, LVEF, and TAPSE/sPAP ratio as a surrogate marker of RV–arterial coupling.

Hazard ratios (HR) with 95% CI were reported. Internal validation of the primary multivariable model was performed using bootstrap resampling with 1000 iterations to assess model stability and optimism-corrected discrimination.

The prognostic performance of TAPSE was evaluated using time-dependent receiver operating characteristic (ROC) curve analysis, and the optimal threshold was determined by the Youden index. To further assess the relationship between TAPSE and mortality, restricted cubic spline analysis was applied. A nomogram based on the primary multivariable model was constructed for exploratory individualized risk estimation.

A 2-tailed *P* value <.05 was considered statistically significant. All statistical analyses were performed using Jamovi software (The Jamovi Project, Sydney, Australia) and R version 4.0.1 (The R Foundation for Statistical Computing, Vienna, Austria) with the "rms" package.

RESULTS

Baseline clinical, echocardiographic and CT characteristics, procedural aspects and outcomes of the overall study population (n = 151) are shown in Table 1. The median age was 77 (70.5-82) years and 91 (60%) of the patients were male. The prevalence of major comorbidities was as follows: arterial hypertension (81%), coronary artery disease (67%), diabetes mellitus (48%), chronic kidney disease (CKD) (42%), and AF (34%). Baseline echocardiographic evaluation demonstrated a reduced LVEF with a median of 35% (30-45) and a low SVi of 27.9 (18.6-35.9) mL/m^2, consistent with a low-flow hemodynamic profile. The mean AVA was 0.71 ± 0.16 cm^2, and the Agatston score was markedly elevated at 2771 (2094-3500). Median TAPSE was 1.7 (1.4-2.0) cm, and median TAPSE/sPAP ratio was 0.38 (0.28-0.51) mm/mmHg. Over a median follow-up of 26 (15-42) months, 37 (25%) patients died. In-hospital mortality rate was 13%. Acute kidney injury developed in 14% and permanent pacemaker implantation was required in 10%.

In univariable Cox regression analysis, advanced age, reduced LVEF, lower TAPSE, and lower TAPSE/sPAP ratio were associated with increased all-cause mortality. In multivariable Cox regression analysis, reduced TAPSE remained independently associated with all-cause mortality in model 1 after adjustment for age and LVEF (HR: 0.11, 95% CI: 0.04-0.30, *P* < .001). In model 2, a lower TAPSE/sPAP ratio, used as a surrogate marker of RV–arterial coupling, was also independently associated with all-cause mortality after adjustment

Table 1. Baseline Clinical, Echocardiographic, and CT Characteristics, Procedural Aspects, and Outcomes

Variables	Study Population (n = 151)
Demographic and clinical characteristics	
Age, years	77 (70.5-82)
Male sex, n (%)	91 (60)
Arterial hypertension, n (%)	122 (81)
Coronary artery disease, n (%)	101 (67)
Diabetes mellitus, n (%)	72 (48)
COPD, n (%)	27 (18)
Prior stroke, n (%)	12 (8)
Atrial fibrillation, n (%)	51 (34)
Chronic kidney disease, n (%)	64 (42)
Echocardiographic parameters (Preprocedural)	
LVEF, %	35 (30-45)
LVEDD, cm	5.3 (4.7-5.7)
LVESD, cm	4 (3.2-4.4)
Aortic peak velocity, m/s	3.4 (3.1-3.6)
Aortic peak gradient, mm Hg	46.3 ± 10.4
Aortic mean gradient, mm Hg	27.7 ± 6.2
Stroke volume index, mL/m^2	27.9 (18.6-35.9)
AVA, cm^2	0.71 ± 0.16
AR grade, n (%)	
None/trace	23 (15)
Mild	81 (54)
Moderate	33 (22)
Severe	14 (9)
MR grade, n (%)	
None/trace	7 (5)
Mild	39 (26)
Moderate	55 (36)
Severe	50 (33)
TR grade, n (%)	
None/trace	6 (4)
Mild	49 (32)
Moderate	49 (32)
Severe	47 (31)
sPAP, mmHg	45 (35-55)
TAPSE, cm	1.7 (1.4-2)
CT parameter	
Agatston score, AU	2771 (2094-3500)
Procedural characteristics	
Pre-balloon dilatation	37 (25)
Valve size, mm	27.5 (26-29)
Post-balloon dilatation	24 (16)
Echocardiographic parameters (Postprocedural)	
LVEF, %	40 (30-50)
Aortic peak velocity, m/s	1.3 (1.1-1.6)
Aortic peak gradient, mmHg	12 (10-16)

(*Continued*)

Table 1. Baseline Clinical, Echocardiographic, and CT Characteristics, Procedural Aspects, and Outcomes (*Continued*)

Variables	Study Population (n = 151)
Aortic mean gradient, mmHg	7 (5-8)
AR grade, n (%)	
None/trace	67 (44)
Mild	65 (43)
Moderate	15 (10)
Severe	4 (3)
MR grade, n (%)	
None/trace	26 (17)
Mild	50 (33)
Moderate	47 (31)
Severe	28 (19)
TR grade, n (%)	
None/trace	22 (15)
Mild	53 (35)
Moderate	50 (33)
Severe	26 (17)
sPAP, mm Hg	35 (30-50)
TAPSE, cm	1.7 (1.4-2)
TAPSE/sPAP, mm/mm Hg	0.38 (0.28-0.51)
VARC-3 outcomes	
≥Moderate PVL, n (%)	19 (12)
Acute kidney injury, n (%)	21 (14)
Disabling stroke, n (%)	5 (3)
New permanent pacemaker implantation, n (%)	13 (10)
In-hospital mortality, n (%)	19 (13)
Total mortality, n (%)	37 (25)
Follow-up duration, months	26 (15-42)

AR, aortic regurgitation; AVA, aortic valve area; COPD, chronic obstructive pulmonary disease; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; MR, mitral regurgitation; PVL, paravalvular leak; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; VARC-3, Valve Academic Research Consortium-3.

for age and LVEF (HR: 0.08, 95% CI: 0.01-0.85, *P* = .036). Advanced age remained independently associated with mortality in both models (model 1: HR 1.07, 95% CI 1.02-1.11, *P* = .002; model 2: HR 1.07, 95% CI 1.02-1.11, *P* = .004), whereas reduced LVEF also showed an independent but weaker association with mortality in both models.

Bootstrap internal validation of the primary multivariable model (model 1) demonstrated acceptable model stability with an optimism-corrected C-index of 0.77 and a calibration slope of 0.93, suggesting limited model overfitting. Univariable and multivariable Cox regression analyses are presented in Table 2, and a forest plot demonstrating the results of the multivariable analyses is illustrated in Figure 1. In addition, the extended univariable Cox regression analyses are provided in Supplementary Table 1.

Table 2. Univariable and Multivariable Cox Regression Analyses for Predictors of All-cause Mortality

	Univariable Analysis	Multivariable Analysis	
		Model 1	Model 2
Variables	HR (95% CI), *P*	HR (95% CI), *P*	HR (95% CI), *P*
Age, years	1.06 (1.01-1.11, *P* = .010)	1.07 (1.02-1.11, *P* = .002)	1.07 (1.02-1.11, *P* = .004)
LVEF, %	0.94 (0.91-0.98, *P* = .001)	0.95 (0.92-0.99, *P* = .012)	0.95 (0.91-0.99, *P* = .008)
TAPSE, cm	0.11 (0.04-0.28, *P* < .001)	0.11 (0.04-0.30, *P* < .001)	—
TAPSE/sPAP, mm/mm Hg	0.06 (0.01-0.54), *P* = .012	—	0.08 (0.01-0.85, *P* = .036)

HR, hazard ratio; LVEF, left ventricular ejection fraction; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion.

Kaplan–Meier analyses demonstrated significantly reduced survival in patients with advanced age, lower TAPSE, and lower LVEF, with early and sustained separation of survival curves (log-rank *P* < .0001 for age and TAPSE; *P* = .0013 for LVEF) (Figure 2). In the ROC analysis, TAPSE yielded an AUC of 0.728 (95% CI: 0.639-0.817), with an optimal cut-off value of 1.51 cm (sensitivity: 59.5%, specificity: 75.4%) (Figure 3a). Time-dependent ROC analysis revealed consistent discriminative performance of TAPSE at 6, 12, and 24 months (AUC values: 0.73, 0.76, and 0.76; respectively) (Figure 3b). Restricted cubic spline analysis revealed a non-linear relationship between TAPSE and mortality risk, and lower TAPSE values were associated with a markedly increased risk of mortality (Figure 4). Additionally, a Kaplan–Meier analysis based on TAPSE tertiles demonstrated significantly reduced survival in patients with lower TAPSE values (Supplementary Figure 1).

Based on these findings, a nomogram including age, LVEF, and TAPSE was developed for exploratory individualized estimation of 12-month survival probability following TAVI (Supplementary Figure 2). The model demonstrated acceptable discriminative performance and may contribute to integrated prognostic assessment in patients with cLFLG AS undergoing TAVI.

DISCUSSION

In this study, reduced TAPSE, advanced age and reduced LVEF were identified as independent predictors of all-cause mortality in patients with cLFLG AS undergoing TAVI. In addition, the lower TAPSE/sPAP ratio, used as a surrogate marker of RV–arterial coupling, was also independently associated with mortality. These findings suggest that RV systolic dysfunction and impaired RV–pulmonary vascular interaction may provide complementary prognostic information in this high-risk population.

Most previous studies investigating mortality predictors after TAVI have evaluated heterogeneous AS populations. In contrast, cLFLG AS represent a distinct phenotype characterized by impaired LVEF with a complex low-flow

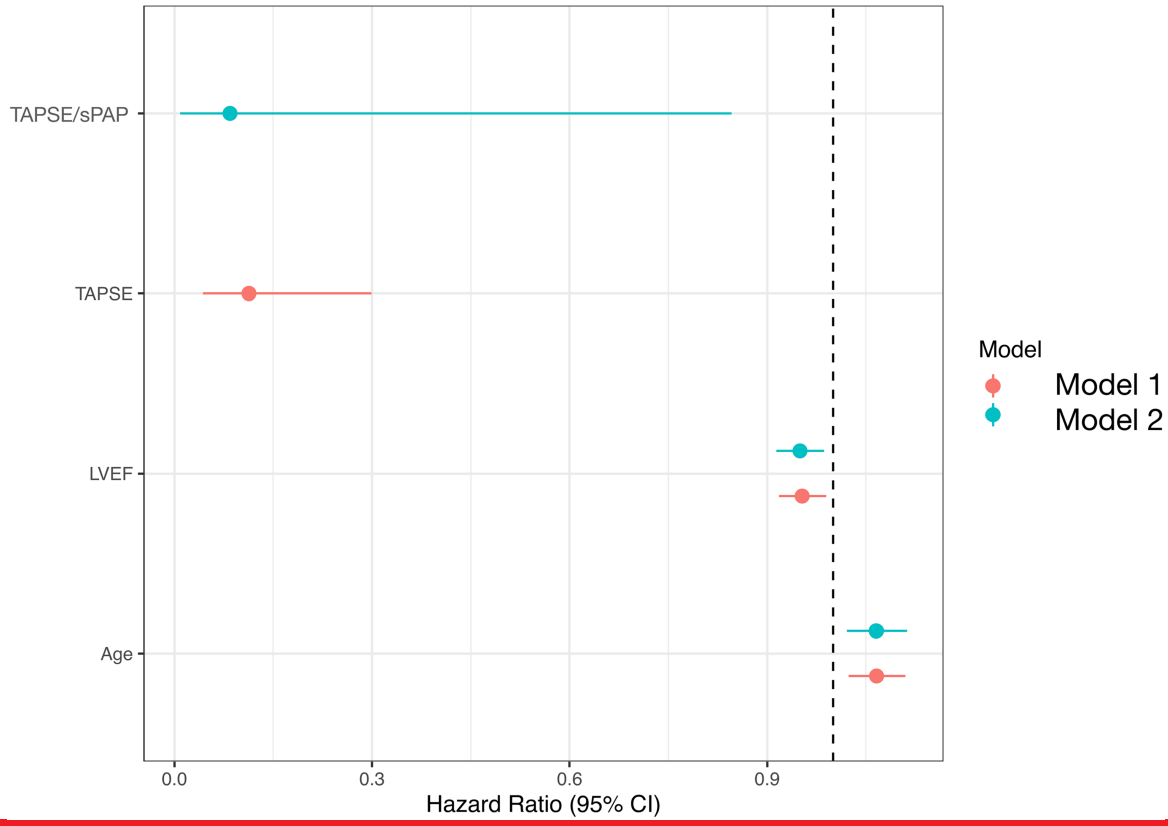

Figure 1. Forest plot of multivariable Cox regression analyses.

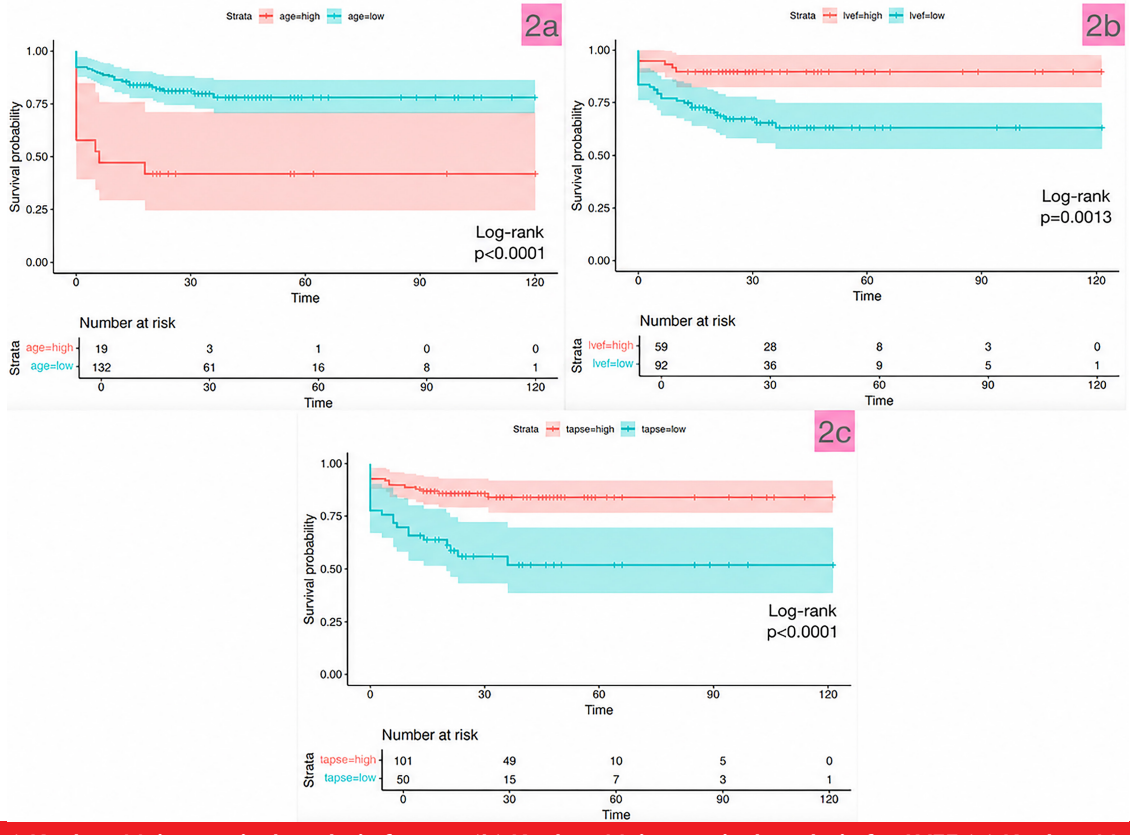

Figure 2. (a) Kaplan–Meier survival analysis for age (b) Kaplan–Meier survival analysis for LVEF (c) Kaplan–Meier survival analysis for tricuspid annular plane systolic excursion.

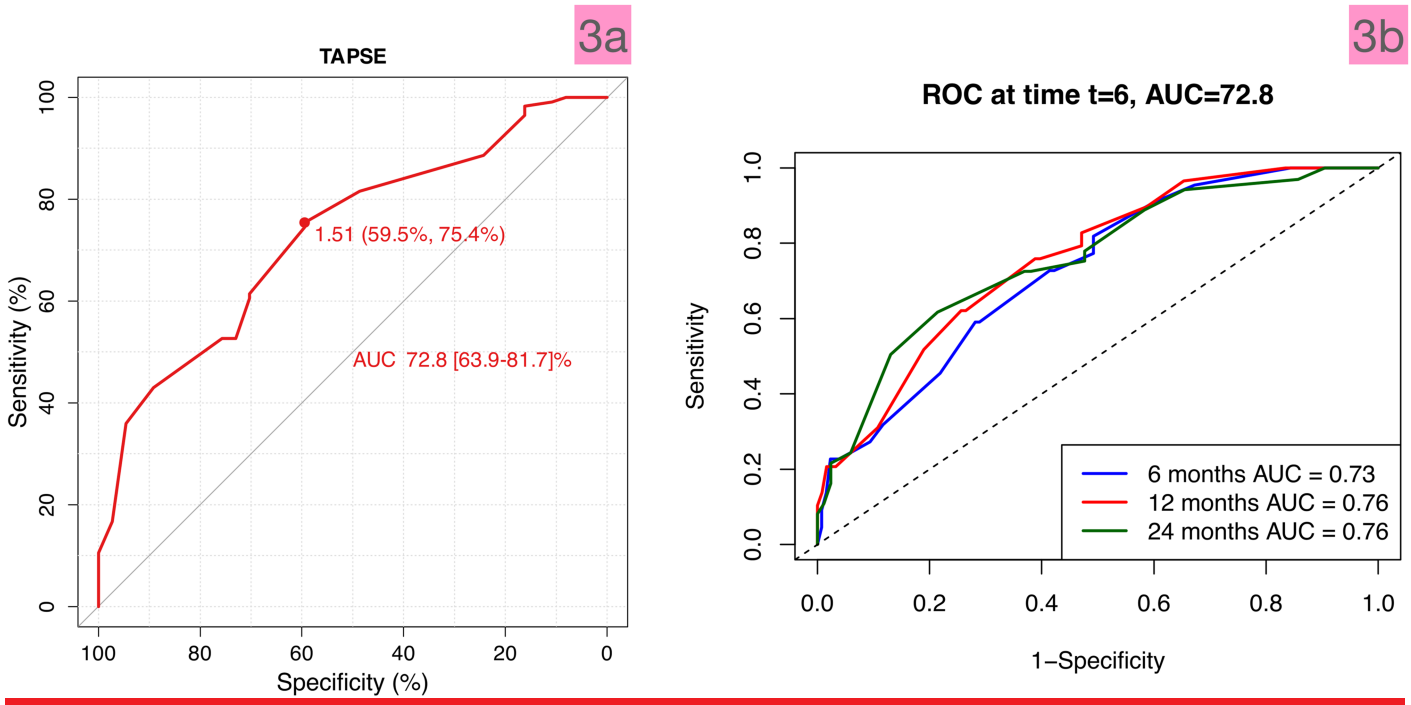

Figure 3. (a). The receiver operating characteristic (ROC) curve of tricuspid annular plane systolic excursion for predicting all-cause mortality (b) Time-dependent ROC analysis of the prediction model.

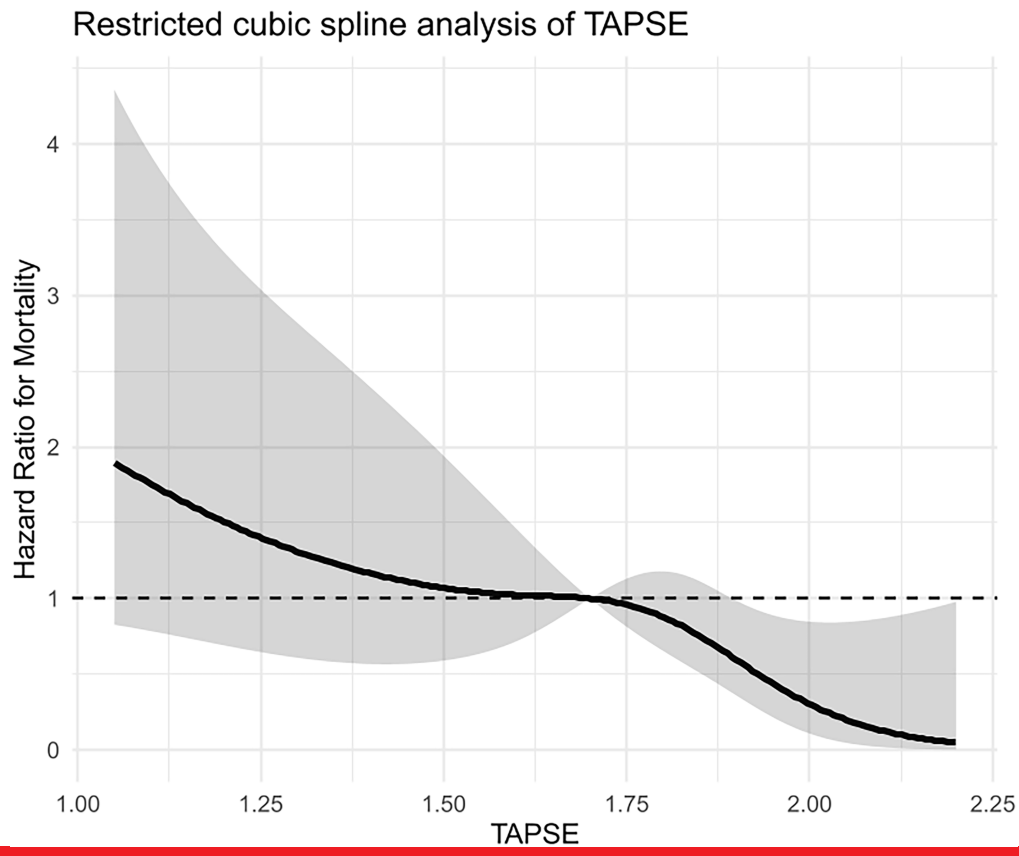

Figure 4. Restricted cubic spline analysis of tricuspid annular plane systolic excursion and all-cause mortality.

hemodynamic profile, which may influence the prognostic significance of clinical and echocardiographic parameters. Therefore, data specifically addressing prognostic markers in this high-risk subgroup remain scarce.

Previous studies have shown that patients with cLFLG AS have the highest mortality rates among different hemodynamic subgroup profiles.[7,14,15] Several factors, including reduced LVEF, advanced age, increased hemodynamic burden, and significant comorbidities, have been implicated in adverse outcomes in this population. These factors underscore the multifactorial nature of mortality risk in low-flow profiles. Ludwig and colleagues investigated 718 patients with cLFLG undergoing TAVI and constructed the RELiEF TAVI score for risk prediction. The RELiEF TAVI score included male sex, underweight, chronic obstructive pulmonary disease (COPD), AF, SVi, non-femoral access, sPAP, and low density of aortic valve calcification.[16] A subgroup analysis from the German Aortic Valve Registry (GARY) revealed that peripheral artery disease, prior myocardial infarction, and pulmonary hypertension were independent predictors of mortality among patients with cLFLG AS.[17] In contrast to these studies, COPD, AF, pulmonary hypertension, SVi, and Agatston score were not found to be associated with mortality in our cohort. This discrepancy may be related to differences in sample size or patient characteristics. Notably, our findings highlight the prognostic relevance of reduced TAPSE, advanced age and reduced LVEF.

Right ventricular systolic dysfunction has been associated with adverse outcomes in patients undergoing TAVI.[18,19] Previous studies have also demonstrated that RV-arterial coupling and reduced RV longitudinal strain are linked to mortality in cLFLG AS.[20,21] In addition to TAPSE, we evaluated the TAPSE/sPAP ratio as a surrogate marker of RV–arterial coupling, reflecting the interaction between RV contractile function and pulmonary vascular load. RV–arterial coupling has emerged as a contemporary parameter providing integrated assessment of RV performance beyond conventional load-dependent measurements. In this study, a lower TAPSE/sPAP ratio was independently associated with increased all-cause mortality after adjustment for age and LVEF. These findings suggest that impaired RV–pulmonary vascular interaction may contribute to adverse outcomes in patients with cLFLG AS undergoing TAVI. Cavalcante and colleagues demonstrated that RV dysfunction, defined as TAPSE <16 mm, has important prognostic value in patients with LFLG AS and may contribute to the decision-making process.[22] In our cohort, reduced TAPSE was significantly associated with all-cause mortality after adjustment for age and LVEF. This relationship was further supported by multiple analyses, including restricted cubic spline analysis, demonstrating a non-linear increase in mortality risk at lower TAPSE values. These findings suggest that the adverse effect of RV dysfunction becomes more evident below certain thresholds. In this setting, reduced TAPSE may reflect the integrated hemodynamic burden of chronic low-flow physiology, pulmonary vascular remodeling, and ventricular interdependence. Although reduced LVEF was also independently associated with all-cause mortality, our findings suggest that RV dysfunction, reflected by TAPSE, may provide complementary prognostic information in patients with cLFLG AS undergoing TAVI. Taken together, these findings support the potential contribution of both LV and RV functional impairment to adverse outcomes in this high-risk population.

Given the particularly vulnerable hemodynamic profile of patients with cLFLG AS, the relatively high in-hospital mortality observed in our cohort is not entirely unexpected. This finding may reflect the advanced disease stage and the substantial burden of comorbidities, including CKD, in this high-risk patient population. In addition, impaired RV function and the relatively high incidence of postoperative AKI may also have contributed to adverse early outcomes. Furthermore, procedural and temporal factors, including differences in operator experience and transcatheter valve technologies, may also have influenced in-hospital outcomes. Recent experience with newer-generation balloon-expandable valves has demonstrated favorable procedural performance and acceptable early clinical outcomes, indicating that ongoing advances in transcatheter valve technology may partly account for differences in outcomes reported across contemporary TAVI studies.[23]

An analysis from the FRANCE 2 registry demonstrated that severe renal failure and moderate to severe periprosthetic regurgitation were associated with cardiovascular mortality in patients with low transvalvular gradient undergoing TAVI.[24] A study including patients with CKD undergoing TAVI revealed that the coexistence of AKI and LFLG AS was associated with poor outcomes.[25] Similarly, CKD, moderate to severe PVL, and AKI were associated with all-cause mortality in univariable analysis in our cohort. However, given the limited number of events and the aim to construct a simplified preprocedural prognostic model, these variables were not included in the final multivariable analyses. Another independent predictor of mortality was advanced age, and this may be explained by the higher burden of comorbidities and increased frailty.

In addition to identifying independent predictors, we developed a nomogram including age, LVEF, and TAPSE to explore individualized estimation of 12-month survival probability following TAVI. While each parameter alone showed moderate predictive performance, their combined use may offer a more comprehensive risk assessment. Therefore, the combined evaluation of these parameters may provide a framework for individualized risk assessment. However, the proposed nomogram should be considered exploratory and requires external validation in independent cohorts before routine clinical application.

Study Limitations

Our study has several limitations due to the retrospective and single center design. These factors may limit the generalizability of our findings and lead to the potential for selection bias. In addition, the exclusion of patients with incomplete preprocedural data may have introduced an additional selection bias. Because the cohort was assembled retrospectively, the complete diagnostic pathway before patient inclusion could not be fully reconstructed. Tricuspid

annular plane systolic excursion shows primarily longitudinal RV function and may not fully reflect global RV function. Additional parameters such as RV strain and fractional area change were not available. Although measurements were performed under standardized conditions, interobserver variability was not evaluated. Although internal validation using bootstrap resampling demonstrated acceptable model stability, the proposed nomogram has not been externally validated in an independent cohort and therefore should be interpreted with caution. External validation in larger multicenter populations is required before broader clinical application.

CONCLUSION

Reduced TAPSE, advanced age, and reduced LVEF were independently associated with all-cause mortality in patients with cLFLG AS undergoing TAVI. In addition, impaired RV–pulmonary vascular interaction, reflected by lower TAPSE/sPAP ratio, was also associated with adverse outcomes. These findings suggest that assessment of RV function may provide complementary prognostic information beyond conventional LV systolic evaluation, particularly in low-flow states. In this context, TAPSE may represent a promising component of a multiparametric risk stratification model.

Ethics Committee Approval: This study was approved by the Ethics Committee of the University of Health Sciences Kartal Koşuyolu Training and Research Hospital (Approval No: 2026/04/1392, Date: 24/02/2026).

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Peer-review: Externally peer-reviewed.

Author Contributions: Concept – B.G.Ş., C.Y., M.F.K., R.Z.; Design – B.G.Ş., C.Y., A.H., İ. B.; Supervision – S.Ç.E, E.A., R.Z.; Resources – B.G.Ş., A.H., E.A., R.Z.; Materials – D. Ş., İ. B., S.T.U., T.U.; Data Collection and/or Processing – M.F.K., D. Ş., A.H.; Analysis and/or Interpretation – B.G.Ş., C.Y., M.F.K., İ. B., S.T.U., T.U.; Literature Search – B.G.Ş., D. Ş., S.Ç.E., S.T.U., T.U.; Writing – B.G.Ş., D. Ş., S.Ç.E., S.T.U., T.U.; Critical Review – S.Ç.E., E.A., R.Z.

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REFERENCES

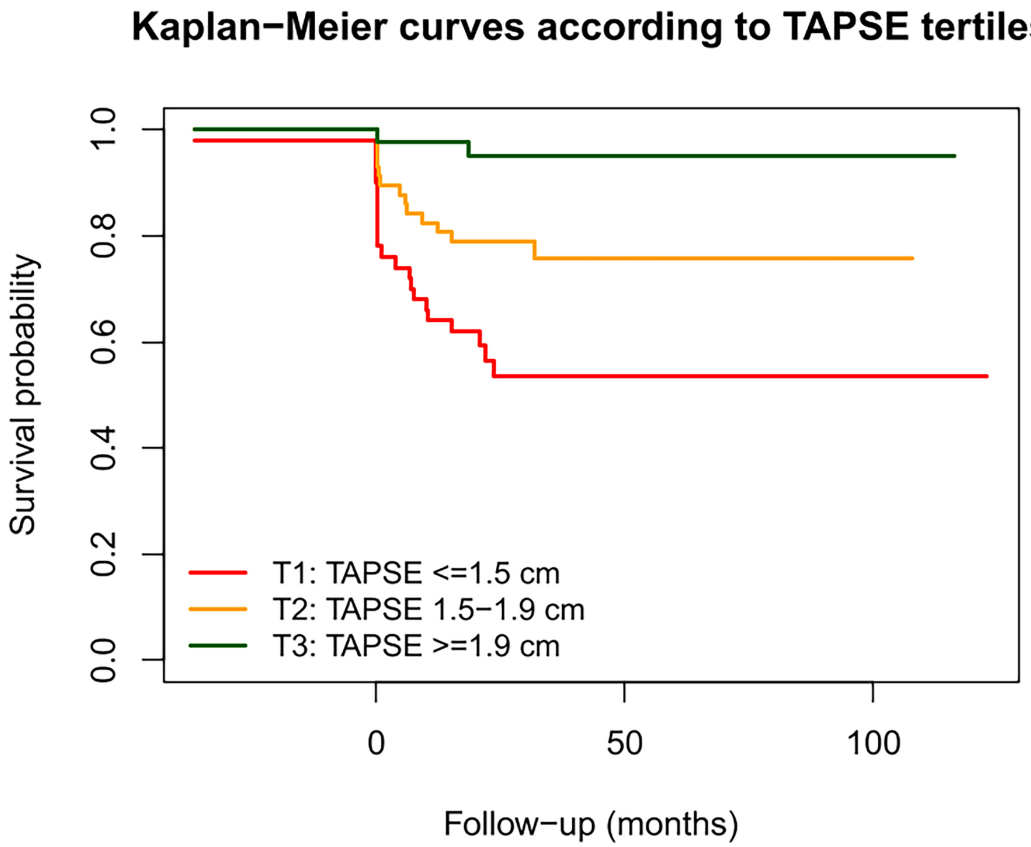
1. Clavel MA, Magne J, Pibarot P. Low-gradient aortic stenosis. *Eur Heart J*. 2016;37(34):2645-2657. [CrossRef]
2. Kulik A, Burwash IG, Kapila V, et al. Long-term outcomes after valve replacement for low-gradient aortic stenosis: impact of prosthesis-patient mismatch. *Circulation*. 2006 ;114(1)(suppl):I553-I558. [CrossRef]
3. Clavel MA, Berthelot-Richer M, Le Ven F, et al. Impact of classic and paradoxical low flow on survival after aortic valve replacement for severe aortic stenosis. *J Am Coll Cardiol*. 2015;65(7):645-653. [CrossRef]
4. Mengi S, Nombela-Franco L, Cepas-Guillén P, et al. Temporal trends in transcatheter aortic valve replacement outcomes in patients with low-flow, low-gradient aortic stenosis: insights from the TOPAS-TAVI registry. *Can J Cardiol*. 2025;41(8):1503-1514. [CrossRef]
5. Praz F, Borger M.A, Lanz J, et al. 2025 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2025;46(44):4635-4736. [CrossRef]
6. Herrmann HC, Pibarot P, Hueter I, et al. Predictors of mortality and outcomes of therapy in low-flow severe aortic stenosis: a Placement of Aortic transcatheter Valves (PARTNER) trial analysis. *Circulation*. 2013;127(23):2316-2326. [CrossRef]
7. Wagener M, Reuthebuch O, Heg D, et al. Clinical outcomes in high-gradient, classical low-flow, low-gradient, and paradoxical low-flow, low-gradient aortic stenosis after transcatheter aortic valve implantation: a report from the SwissTAVI registry. *J Am Heart Assoc*. 2023;12(12):e029489. [CrossRef]
8. Baumgartner H, Hung J, Bermejo J, et al. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2017;30(4):372-392. [CrossRef]
9. Mukherjee M, Rudski L.G, Addetia K, et al. Guidelines for the echocardiographic assessment of the right heart in adults and special considerations in pulmonary hypertension: recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2025;38(3):141-186. [CrossRef]
10. Clavel MA, Pibarot P, Messika-Zeitoun D, et al. Impact of aortic valve calcification, as measured by MDCT, on survival in patients with aortic stenosis: results of an international registry study. *J Am Coll Cardiol*. 2014;64(12):1202-1213. [CrossRef]
11. Pawade T, Clavel M.A, Tribouilloy C, et al. Computed tomography aortic valve calcium scoring in patients with aortic stenosis. *Circ Cardiovasc Imaging*. 2018;11(3):e007146. [CrossRef]
12. Généreux P, Piazza N, Alu M.C, et al. Valve Academic Research Consortium 3: updated endpoint definitions for aortic valve clinical research. *J Eur Heart*. 2021;42(19):1825-1857. [CrossRef]
13. Kidney disease: improving global outcomes (KDIGO) acute kidney injury work group. KDIGo clinical practice guideline for acute kidney injury. *Kidney Int Suppl*. 2012;2:1-138.
14. Gersch S, Lange T, Beuthner B.E, et al. Low-flow in aortic valve stenosis patients with reduced ejection fraction does not depend on left ventricular function. *Clin Res Cardiol*. 2025;114(11):1455-1466. [CrossRef]
15. Yamashita Y, Baudo M, Sicouri S, et al. Clinical outcomes of transcatheter aortic valve replacement in patients with various flow-gradient and ejection fraction profiles. *Anatol J Cardiol*., 2025;29(9):496-502. [CrossRef]
16. Ludwig S, Goßling A, Seiffert M, et al. Risk prediction in patients with low-flow, low-gradient aortic stenosis and reduced ejection fraction undergoing TAVI. *Open Heart*. 2022;9(1):e001912. [CrossRef]
17. Lauten A, Figulla HR, Möllmann H, et al. TAVI for low-flow, low-gradient severe aortic stenosis with preserved or reduced ejection fraction: a subgroup analysis from the German Aortic Valve Registry (GARY). *EuroIntervention*. 2014;10(7):850-859. [CrossRef]
18. Ren B, Spitzer E, Geleijnse M.L, et al. Right ventricular systolic function in patients undergoing transcatheter aortic valve implantation: a systematic review and meta-analysis. *Int J Cardiol*. 2018;257:40-45. [CrossRef]
19. Scheggi V, Bohbot Y, Hasan J, et al. Prognostic impact of right ventricular dysfunction in patients with severe aortic stenosis treated with trans-catheter aortic valve implantation. *Intern Emerg Med*. 2025;20(6):1705-1712. [CrossRef]
20. Vizzardi E, Gavazzoni M, Sciatti E, et al. Right ventricular deformation and right ventricular-arterial coupling in patients with heart failure due to severe aortic stenosis undergoing TAVI: long-term results. *Am J Cardiovasc Dis*. 2020;10(3):150-163.

21. Dahou A, Clavel MA, Capoulade R, et al. Right ventricular longitudinal strain for risk stratification in low-flow, low-gradient aortic stenosis with low ejection fraction. *Heart*. 2016;102(7):548-554. [CrossRef]
22. Cavalcante JL, Rijal S, Althouse A.D, et al. Right ventricular function and prognosis in patients with low-flow, low-gradient severe aortic stenosis. *J Am Soc Echocardiogr*. 2016;29(4):325-333. [CrossRef]
23. Akyüz AR, Konuş AH, Çırakoğlu Ö.F, et al. First experiences with a new balloon-expandable Myval transcatheter aortic valve: a preliminary study *Herz*. 2022;47(5):449-455. [CrossRef]
24. Amabile N, Agostini H, Gilard M, et al. Impact of low preprocedural transvalvular gradient on cardiovascular mortality following TAVI: an analysis from the France 2 registry. *EuroIntervention*. 2014;10(7):842-849. [CrossRef]
25. Nagata H, Miyagi A, Shiohira S, et al. Incidence and prognostic impact of acute kidney injury after transcatheter aortic valve replacement in patients with low-flow and low-gradient aortic stenosis. *Circ Rep*. 2025;7(12):1269-1278. [CrossRef]

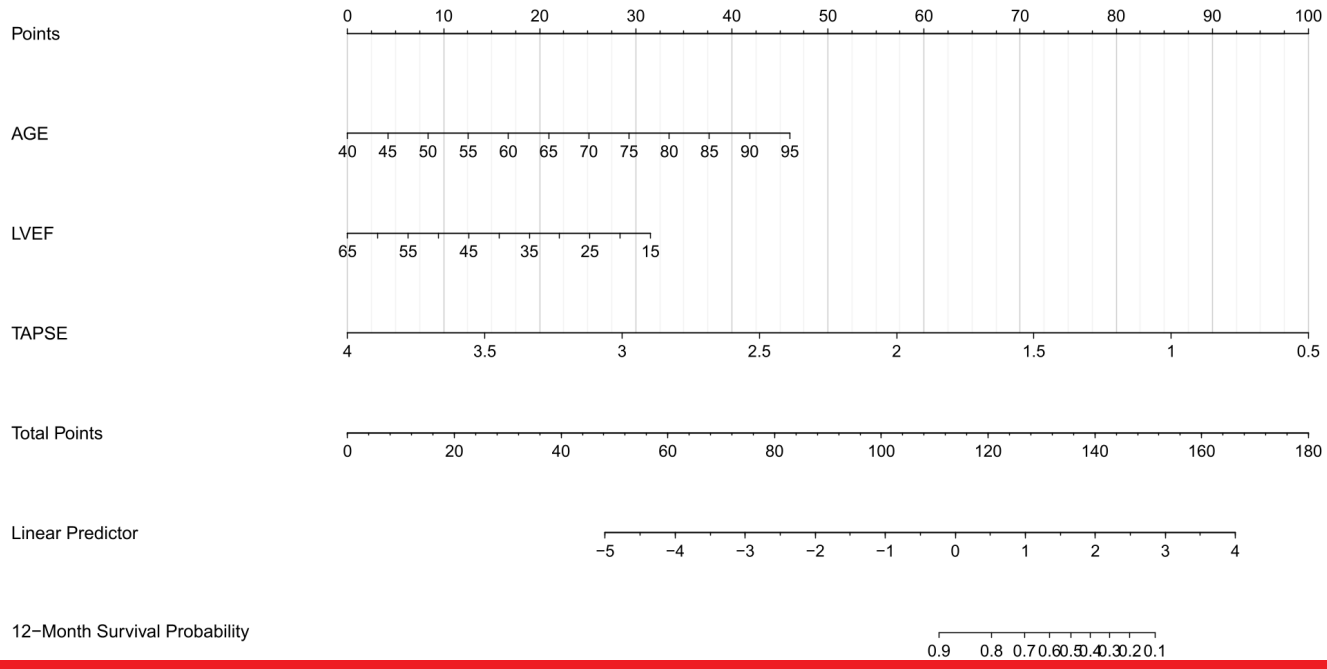
Supplementary Table 1. Expanded univariable Cox Regression Analysis for predictors of all-cause mortality

	Univariable Analysis	
Variables	**HR (95% CI)**	***P***
Age, years	1.06 (1.01-1.11)	0.010
CKD	1.93 (1.01-3.70)	0.048
LVEF, %	0.94 (0.91-0.98)	0.001
Aortic peak velocity, m/s	0.37 (0.18-0.78)	0.008
TAPSE, cm	0.11 (0.04-0.28)	<0.001
TAPSE/sPAP, mm/mm Hg	0.06 (0.01-0.54)	0.012
Preprocedural ≥moderate MR	2.48 (1.03–5.95)	0.042
Postprocedural ≥moderate AR	3.35 (1.45-7.72)	0.005
Postprocedural ≥moderate TR	1.25 (0.65–2.38)	0.504
≥moderate PVL	2.78 (1.17-6.62)	0.021
Postoperative AKI	4.01 (2.01-8.01)	0.001

AKI, acute kidney injury; AR, aortic regurgitation; CKD, chronic kidney disease; CI, confidence interval; HR, hazard ratio; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; PVL, paravalvular leak; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.



Supplementary Figure 1. Kaplan-Meier survival curves according to TAPSE tertiles.



Supplementary Figure 2. Nomogram for predicting all-cause mortality.