

Preprocedural Laboratory Biomarker Burden and Early Cardiorenal Injury after Transcatheter Aortic Valve Replacement: A Retrospective Cohort Study

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Research Article

Keywords: transcatheter aortic valve replacement, laboratory biomarkers, cardiorenal injury, systemic vulnerability, troponin T, creatinine

Posted Date: August 11th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10345812/v1>

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Additional Declarations: No competing interests reported.

Abstract

Background

Early troponin elevation and creatinine-defined renal injury after transcatheter aortic valve replacement (TAVR) are usually evaluated as separate organ-specific complications. Whether routine preprocedural laboratory abnormalities can identify a shared systemic vulnerability to early postprocedural myocardial or renal biomarker injury remains unclear.

Methods

This retrospective single-center cohort study enrolled patients undergoing TAVR with complete preoperative laboratory measurements and early postoperative troponin T or creatinine data. A four-item biomarker burden score, assigning one point for each abnormal parameter: albumin < 40 g/L, D-dimer > 0.5 mg/L, lymphocyte count < 1.0×10^9 /L, and fibrinogen-to-albumin ratio > 0.10. The primary endpoint was early biomarker-defined cardiorenal injury, defined as either substantial postoperative troponin T elevation or creatinine-defined early renal injury. Multivariable logistic regression assessed composite and organ-specific endpoints, and a stacked model formally compared myocardial and renal effect estimates.

Results

The adjusted analysis included 1,259 patients, of whom 221 (17.6%) developed the primary endpoint. Event rates increased from 10.8% at score 0 to 34.3% at score 4. Each one-point increase was associated with the composite endpoint (adjusted odds ratio [OR] 1.24, 95% confidence interval [CI] 1.09–1.40; $P < 0.001$), troponin elevation (OR 1.17, 95% CI 1.02–1.34; $P = 0.023$), and renal injury (OR 1.42, 95% CI 1.15–1.77; $P = 0.001$). Higher baseline burden remained associated with lower postprocedural albumin and lymphocyte count and higher D-dimer and fibrinogen-to-albumin ratio (all postprocedural score gradients $P \leq 0.002$). The renal association was directionally stronger than the troponin association, although formal heterogeneity was not statistically significant ($P = 0.076$).

Conclusions

Preprocedural inflammatory, nutritional, and coagulation biomarker burden was independently associated with early biomarker-defined cardiorenal injury after TAVR. This multidomain vulnerability framework warrants prospective validation with standardized serial biomarker assessment.

Background

Transcatheter aortic valve replacement (TAVR) has become an established treatment for severe aortic valve disease across contemporary risk profiles [1]. Despite procedural refinement, early myocardial biomarker release and creatinine-defined renal injury remain clinically relevant and are associated with adverse outcomes [2–8]. These complications are typically considered separately, even though both

occur during the same procedural window and arise within a shared hemodynamic, inflammatory, thrombotic, and nephrotoxic environment.

The magnitude of organ injury after a standardized procedural stressor is unlikely to be determined by procedural features alone. Preprocedural hypoalbuminemia, immune-cell abnormalities, and coagulation activation have each been associated with adverse outcomes after TAVR [9–18]. However, isolated biomarkers cannot capture the interaction between nutritional reserve, immune balance, fibrin turnover, and acute-phase activity. A multidomain profile may more closely represent systemic vulnerability: the biological capacity to tolerate rapid pacing, transient hypotension, vascular manipulation, contrast exposure, and the inflammatory-coagulation response induced by TAVR.

An important unresolved question is whether such vulnerability is merely a static preprocedural association or whether it remains biologically evident after the procedure. Paired laboratory measurements provide an opportunity to examine the relation between baseline multidomain burden and the early biological response to TAVR. This state-response framework may also clarify whether myocardial biomarker release and renal injury show comparable susceptibility to the same preprocedural phenotype.

This study therefore evaluated whether a cumulative preprocedural inflammation-nutrition-coagulation biomarker burden: (1) identified a graded risk of early myocardial or renal biomarker injury; (2) remained associated with adverse biomarker profiles after TAVR; and (3) showed differential associations with myocardial and renal endpoint components. Internal validation was retained as a supporting assessment of stability rather than the principal scientific objective.

Methods

Study design and population

This retrospective cohort study used the institutional TAVR registry of West China Hospital, Sichuan University, linked to procedural records, echocardiography, and longitudinal laboratory data. Patients who underwent TAVR between April 2019 and November 2024 were screened. The endpoint-assessable cohort included patients with early postprocedural troponin T or paired creatinine measurements. The adjusted primary analysis required complete score components and prespecified adjustment covariates. Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology statement [19].

Native aortic valve morphology was classified from preprocedural imaging as bicuspid aortic valve (BAV) or tricuspid aortic valve (TAV). Morphology-specific analyses were restricted to patients with an unequivocal classification and were prespecified as supportive analyses to evaluate whether the association between biomarker burden and early organ injury was consistent across anatomically distinct TAVR populations.

The study was approved by the Institutional Review Board of West China Hospital, Sichuan University (No. 2024–2370). The requirement for individual informed consent was waived because of the retrospective design and use of de-identified data.

Biomarker vulnerability score

Preprocedural albumin, D-dimer, fibrinogen, lymphocyte count, platelet count, and related ratios were obtained from routine clinical testing. The fibrinogen-to-albumin ratio (FAR) was calculated as fibrinogen divided by albumin. The multidomain biomarker vulnerability score assigned one point each for albumin < 40 g/L, D-dimer > 0.5 mg/L, lymphocyte count < 1.0×10^9 /L, and FAR > 0.10, producing a score from 0 to 4.

Early biological trajectories

Paired preprocedural and first early postprocedural measurements were evaluated for albumin, D-dimer, lymphocyte count, and FAR. The postprocedural FAR was calculated from contemporaneous fibrinogen and albumin values. To prevent unit-entry artifacts from influencing trajectory analyses, values outside prespecified physiologically plausible ranges were excluded: albumin 15–60 g/L, D-dimer 0.01–50 mg/L, lymphocyte count 0.05 – 10×10^9 /L, fibrinogen 0.5–15 g/L, and FAR 0.01–1.0. These filters were applied without reference to endpoint status.

Study endpoints

The primary endpoint was early biomarker-defined myocardial or renal injury. Marked troponin T elevation was defined as the first postprocedural troponin T value within 24 hours reaching at least 280 ng/L, corresponding to 20 times the institutional upper reference limit of 14 ng/L. This endpoint captured substantial myocardial biomarker release and did not constitute adjudicated periprocedural myocardial infarction [2–4].

Creatinine-defined early renal injury was defined as an increase in serum creatinine of at least 26.5 μ mol/L or at least 1.5 times the preprocedural value [5]. Because urine-output data and fully standardized adjudication windows were unavailable for all patients, this endpoint was treated as a creatinine-defined biomarker injury rather than fully adjudicated acute kidney injury.

Statistical analysis

Continuous variables were summarized as medians with interquartile ranges and compared using the Mann-Whitney U test. Categorical variables were presented as counts with percentages and compared using the chi-square test or Fisher exact test, as appropriate. Multivariable logistic regression estimated associations of the total score and individual binary components with the composite and organ-specific endpoints. Models were adjusted for age, sex, diabetes, baseline estimated glomerular filtration rate (eGFR), and left ventricular ejection fraction (LVEF).

Paired biomarker trajectories were analyzed using generalized estimating equations with an exchangeable working correlation structure. Models included time, score, and a time-by-score interaction, together with the prespecified covariates. D-dimer was log₁₀-transformed and FAR was log-transformed before standardization. The main score coefficient represented the baseline gradient, the linear combination of the score and interaction coefficients represented the postprocedural gradient, and the interaction tested whether the gradient changed after TAVR.

To compare score associations between the myocardial and renal components, participants with both endpoint measurements were arranged in a stacked long format and analyzed using a clustered binomial generalized estimating equation including a score-by-endpoint interaction. Restricted cubic spline analysis was used to assess departure from linearity. Supporting analyses evaluated apparent discrimination, calibration, stratified 10-fold cross-validation, and internal validation with 1,000 bootstrap resamples. All tests were two-sided, and $P < 0.05$ was considered statistically significant. Analyses were performed in Python 3.13.5 using statsmodels 0.14.6 and scikit-learn 1.8.0.

Results

Study population and primary endpoint

The integrated registry contained 1761 records. Early postprocedural troponin T or creatinine data were available in 1401 patients, and 1259 patients with complete score components and adjustment covariates formed the primary analysis cohort (Fig. 1). The troponin and renal endpoint cohorts included 1208 and 1257 patients, respectively. The primary endpoint occurred in 221 patients (17.6%). Baseline characteristics are summarized in Table 1.

Table 1
Baseline characteristics according to the primary endpoint.

Characteristic	Overall N = 1,259	No injury n = 1,038	Cardiorenal injury n = 221	P value
Age, years	73.0 (67.0–78.0)	72.0 (67.0–77.0)	75.0 (69.0–80.0)	< 0.001
Body mass index, kg/m ²	22.7 (20.2–25.0)	22.8 (20.3–25.0)	22.1 (20.0–24.4)	0.052
STS-PROM, %	2.6 (1.8–4.2)	2.5 (1.7–3.8)	3.7 (2.4–6.2)	< 0.001
Baseline eGFR, mL/min/1.73 m ²	71.3 (57.9–85.1)	73.9 (60.7–85.9)	60.8 (39.4–77.4)	< 0.001
LVEF, %	60.0 (44.0–67.0)	60.0 (44.0–67.0)	60.0 (42.0–66.0)	0.227
Male sex	749 (59.5)	631 (60.8)	118 (53.4)	0.050
Hypertension	548 (43.5)	438 (42.2)	110 (49.8)	0.047
Diabetes mellitus	217 (17.2)	175 (16.9)	42 (19.0)	0.504
Coronary artery disease	274 (21.8)	212 (20.4)	62 (28.1)	0.016
Atrial fibrillation	184 (14.6)	156 (15.0)	28 (12.7)	0.426
Values are median (interquartile range) or n (%). eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; STS-PROM, Society of Thoracic Surgeons Predicted Risk of Mortality.				

Table 2
Principal association and trajectory results.

Analysis	N	Events	Adjusted OR / standardized slope	95% CI	P value
Primary composite	1259	221	1.24	1.09– 1.40	< 0.001
Marked troponin T elevation	1208	190	1.17	1.02– 1.34	0.023
Creatinine-defined early renal injury	1257	64	1.42	1.15– 1.77	0.001
Postprocedural Albumin, g/L gradient per score point	1247	-	-0.23 SD	-	< 0.001
Postprocedural D-dimer, mg/L gradient per score point	1159	-	0.21 SD	-	< 0.001
Postprocedural Lymphocyte count, $\times 10^9/L$ gradient per score point	1256	-	-0.06 SD	-	0.002
Postprocedural FAR gradient per score point	1177	-	0.19 SD	-	< 0.001
Endpoint models were adjusted for age, sex, diabetes, baseline eGFR, and LVEF. Trajectory estimates represent the adjusted postprocedural standardized biomarker gradient per one-point score increase.					

Graded association of multidomain burden with early injury

The score distribution was 333 patients with score 0, 353 with score 1, 267 with score 2, 207 with score 3, and 99 with score 4. Primary endpoint rates increased from 10.8% at score 0 to 16.1%, 17.6%, 22.7%, and 34.3% at scores 1 through 4, respectively (Fig. 4A). Each one-point increase was associated with 24% higher adjusted odds of the primary endpoint (OR 1.24, 95% CI 1.09–1.40; $P < 0.001$). Restricted cubic spline analysis supported an approximately linear association (overall $P < 0.001$; P for non-linearity = 0.738; Fig. 4B).

Baseline vulnerability and early postprocedural biological response

Paired measurements were available in 1247 patients for albumin, 1159 for D-dimer, 1256 for lymphocyte count, and 1177 for FAR after data-quality filtering. Higher score categories displayed progressively lower albumin and lymphocyte count and higher D-dimer and FAR before TAVR (Fig. 2). These multidomain gradients remained evident in the early postprocedural measurements: per one-point score increase, the adjusted postprocedural standardized gradient was – 0.23 for albumin, 0.21 for D-dimer, -0.06 for lymphocyte count, and 0.19 for FAR (all $P \leq 0.002$).

Significant time-by-score interactions were present for all four markers (all $P < 0.001$), indicating that the between-score gradients changed after the common procedural perturbation. The adverse gradients

narrowed after TAVR but did not disappear, consistent with partial convergence superimposed on persistent preprocedural multidomain dysregulation. Median values and complete trajectory estimates are provided in Supplementary Tables S1 and S2.

Organ-specific susceptibility and score-component contributions

The score was associated with marked troponin T elevation (adjusted OR 1.17, 95% CI 1.02–1.34; $P = 0.023$) and more strongly, in magnitude, with creatinine-defined renal injury (adjusted OR 1.42, 95% CI 1.15–1.77; $P = 0.001$). In the 1,206 patients with both endpoint components measured, the formal score-by-endpoint interaction was not statistically significant ($P = 0.076$), supporting a directional rather than definitive difference in organ-specific susceptibility (Fig. 3B).

Component-level analyses showed that hypoalbuminemia, lymphopenia, and elevated FAR were independently associated with the composite endpoint. Hypoalbuminemia was associated with both troponin elevation (OR 1.45, 95% CI 1.04–2.03) and renal injury (OR 1.89, 95% CI 1.10–3.26), whereas lymphopenia showed its strongest association with renal injury (OR 2.05, 95% CI 1.20–3.50). Elevated D-dimer showed directionally positive but statistically non-significant associations after adjustment (Fig. 3C and Supplementary Table S3).

Consistency across bicuspid and tricuspid valve morphology

Among 1183 patients with unequivocal native valve morphology, 481 had BAV and 702 had TAV. The primary endpoint occurred in 89 patients with BAV (18.5%) and 122 patients with TAV (17.4%). The biomarker burden score remained associated with the primary endpoint in both subgroups: adjusted OR 1.29 per one-point increase in BAV (95% CI 1.06–1.56; $P = 0.010$) and 1.23 in TAV (95% CI 1.04–1.47; $P = 0.016$). There was no evidence that valve morphology modified this association (P for interaction = 0.739; Supplementary Table S5).

For marked troponin T elevation, the adjusted association was 1.26 (95% CI 1.03–1.54; $P = 0.026$) in BAV and 1.16 (95% CI 0.97–1.39; $P = 0.111$) in TAV, without significant interaction (P for interaction = 0.551). For creatinine-defined early renal injury, the corresponding estimates were 1.29 (95% CI 0.91–1.83; $P = 0.158$) and 1.47 (95% CI 1.10–1.96; $P = 0.009$), respectively, again without evidence of interaction (P for interaction = 0.564). Observed primary endpoint rates increased in parallel across score categories in both morphologies, reaching 35.5% in BAV and 35.6% in TAV at a score of 4 (Supplementary Table S6).

Supporting model performance

The score alone showed modest apparent discrimination (AUC 0.610, 95% CI 0.569–0.649). The apparent AUC was 0.679 for the clinical model and 0.691 for the clinical model plus score. For the combined model, the 10-fold cross-validated AUC was 0.672 and the bootstrap-corrected AUC was 0.681, with a calibration slope of 0.954 and optimism-corrected Brier score of 0.133 (Supplementary Figure S1 and Supplementary Table S4). These analyses supported internal stability but were not interpreted as evidence of stand-alone predictive utility.

Discussion

This study reframed routinely available preprocedural biomarkers as a multidomain biological state rather than a conventional prediction score. Three findings define the revised scientific contribution. First, accumulation of inflammatory, nutritional, and coagulation abnormalities showed a clear graded association with early myocardial or renal biomarker injury. Second, paired measurements demonstrated that the preprocedural vulnerability gradient remained detectable after TAVR despite a substantial shared procedural perturbation. Third, the association was directionally stronger for renal injury, and component-level analyses identified hypoalbuminemia and lymphopenia as particularly relevant to renal susceptibility.

The trajectory analysis distinguishes the present study from prior reports of isolated baseline biomarkers. TAVR induces rapid changes in inflammatory cells, coagulation activity, plasma volume, and tissue perfusion [14–18, 28, 29]. In this cohort, D-dimer and FAR increased and albumin and lymphocyte count decreased across the entire population, reflecting a common procedure-related response. However, patients with greater baseline burden retained a less favorable postprocedural profile. The significant time-by-score interactions indicated partial convergence, rather than simple parallel tracking: the procedural insult compressed some baseline differences but did not erase the underlying multidomain gradient. This pattern supports a state-response phenotype in which preprocedural biology shapes the level from which a patient enters and exits the acute procedural stress period.

The organ-specific findings provide a second layer of biological interpretation. Troponin release after TAVR is influenced by rapid pacing, ventricular hypertrophy, myocardial strain, coronary disease, embolization, and procedural manipulation [2–4]. Renal injury is also sensitive to baseline filtration reserve, hemodynamic instability, contrast exposure, inflammation, microvascular dysfunction, and effective circulating volume [6–8, 27]. Hypoalbuminemia may integrate nutritional reserve, systemic inflammation, antioxidant capacity, and intravascular volume homeostasis [9, 10, 30, 31]. Lymphopenia may reflect neurohormonal stress and impaired immune homeostasis, while FAR combines acute-phase protein elevation with reduced albumin reserve [32–34]. The stronger renal estimates for hypoalbuminemia and lymphopenia are therefore biologically plausible, although the formal heterogeneity test did not cross the conventional threshold and should not be interpreted as proof of differential causality.

The component matrix also clarifies why the total burden may be more informative than any single marker. No component consistently dominated all endpoints. Instead, hypoalbuminemia, lymphopenia, D-dimer elevation, and high FAR contributed complementary signals across nutritional, immune, fibrinolytic, and acute-phase domains. The score therefore functions as a parsimonious phenotype of accumulated biological abnormalities. Its value lies in organizing routinely available data into a coherent vulnerability construct, not in replacing established clinical assessment or serving as a stand-alone decision model.

The morphology analysis provides a complementary test of the proposed systemic-vulnerability framework. BAV and TAV differ substantially in annular geometry, leaflet architecture, calcification pattern, and procedural complexity, yet the score-outcome gradient was nearly identical across the two groups and formal interaction tests were consistently non-significant. This concordance supports the interpretation that the biomarker burden score captures a host-level biological susceptibility rather than a signal confined to a particular valve phenotype. Numerical differences between the myocardial and renal components were not interpreted as morphology-specific effects because the interaction tests were negative and the number of renal events, particularly in BAV, was limited.

The modest AUC is consistent with this interpretation. Biomarker-defined organ injury after TAVR is multifactorial, and no four-item laboratory construct should be expected to capture procedural complexity, valve anatomy, access strategy, pacing burden, bleeding, or contrast exposure. Nevertheless, the graded event rates, approximately linear dose-response, persistent postprocedural biomarker gradients, low bootstrap optimism, and consistent component-level associations support the biological stability of the construct. Prospective studies should test whether integrating procedural stress measures with serial biomarker trajectories improves phenotyping and whether targeted optimization of nutrition, volume status, inflammatory burden, or contrast strategy modifies risk.

This study has limitations. Its retrospective single-center design limits causal inference and external generalizability. Sampling times were determined by clinical practice, and the first postprocedural value may not represent the peak response for every biomarker. Troponin elevation and creatinine-defined renal injury were biomarker endpoints rather than adjudicated myocardial infarction and complete KDIGO acute kidney injury. Finally, external validation and prospective serial sampling are required.

Conclusions

Elevated preprocedural inflammatory, nutritional, and coagulation biomarker burden was independently associated with early biomarker-defined cardiorenal injury after TAVR. The association followed a graded, approximately linear pattern and remained robust after multivariable adjustment. By integrating baseline biological status, early postprocedural biomarker trajectories, and organ-specific susceptibility, this framework provides a more biologically informative interpretation of early cardiorenal injury after TAVR and warrants prospective validation using standardized serial biomarker measurements.

Abbreviations

AUC

area under the receiver operating characteristic curve

CI

confidence interval

CV

cross-validation

eGFR
estimated glomerular filtration rate
FAR
fibrinogen-to-albumin ratio
LVEF
left ventricular ejection fraction
OR
odds ratio
PLR
platelet-to-lymphocyte ratio
ROC
receiver operating characteristic curve
TAVR
transcatheter aortic valve replacement
TnT
troponin T

Declarations

Acknowledgements

None

Conflicts of Interest

The authors declare no conflicts of interest.

Funding

This study was supported by the Sichuan Provincial Youth Science and Technology Fund (Grant No. 2025ZNSFSC1698 and 2025ZNSFSC1554), the Postdoctoral Research Fund of West China Hospital, Sichuan University (Grant No. 2025HXBH163), and the National Natural Science Foundation of China (U23A20395, 82170375). The funding bodies played no role in the design of the study, collection, analysis and interpretation of data, writing of the manuscript, or the decision to submit the article for publication.

Author Contributions

ZZ conceived the research concept, designed analytical methods, drafted the original manuscript, reviewed and revised the article, and applied for research funds. TF participated in methodology design, formal statistical analysis, manuscript revision, and funding application. JW, YP and ZZh conducted data curation, project administration and manuscript review. YF provided overall supervision and revised the

manuscript. MC contributed to conceptualization, study supervision and manuscript review. All authors have read and approved the final manuscript.

Ethical Approval and Informed Consent

This study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of West China Hospital, Sichuan University (Approval No. 2024-2370). Individual informed consent was waived due to the retrospective study design and the use of de-identified clinical data.

Consent for Publication

Not applicable. No personally identifiable information, images or videos are included in this manuscript.

Data Availability

The de-identified minimal dataset will be available from the corresponding author upon reasonable request after institutional approval.

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Figures

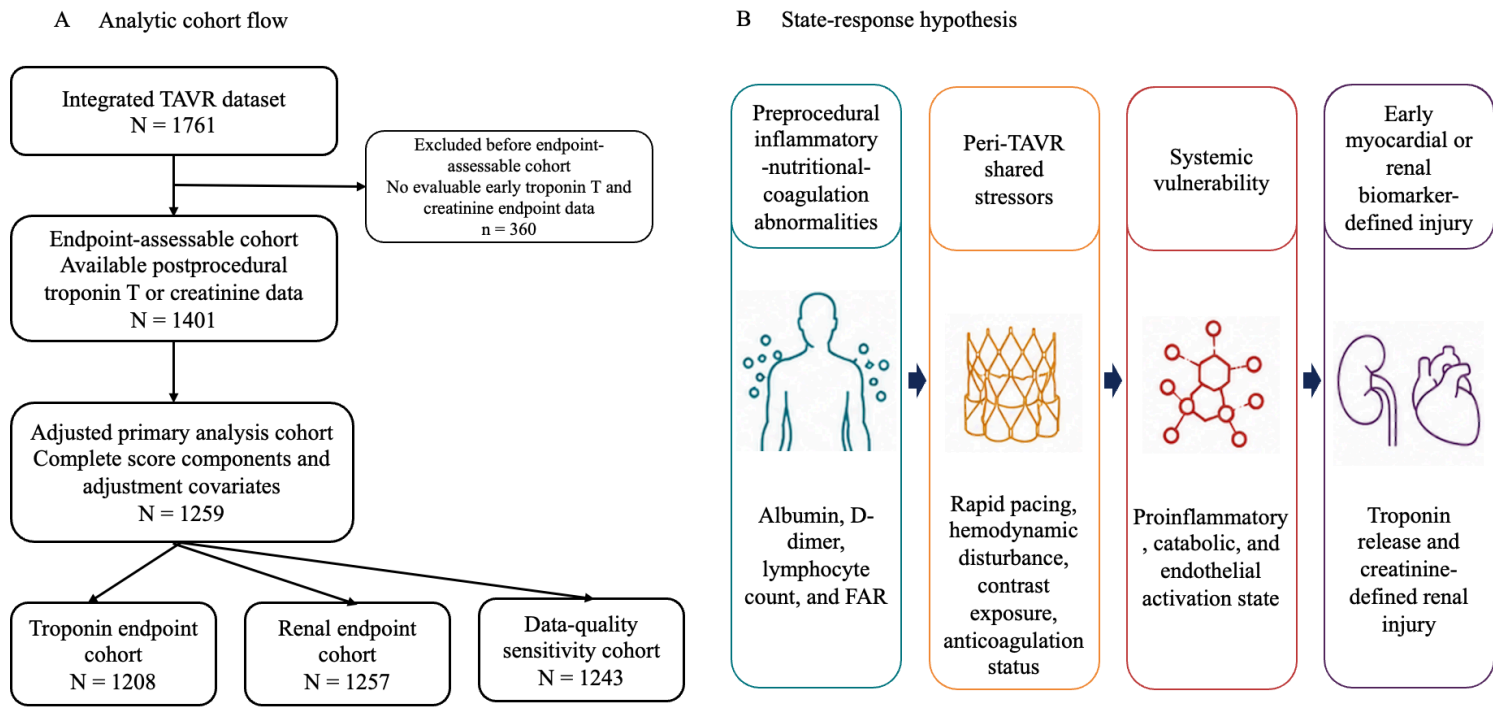


Figure 1

Study design and biological framework. Panel A shows formation of the analytic cohorts. Panel B illustrates the state-response hypothesis linking preprocedural multidomain vulnerability, the shared TAVR-related perturbation, and early organ-specific biomarker injury.

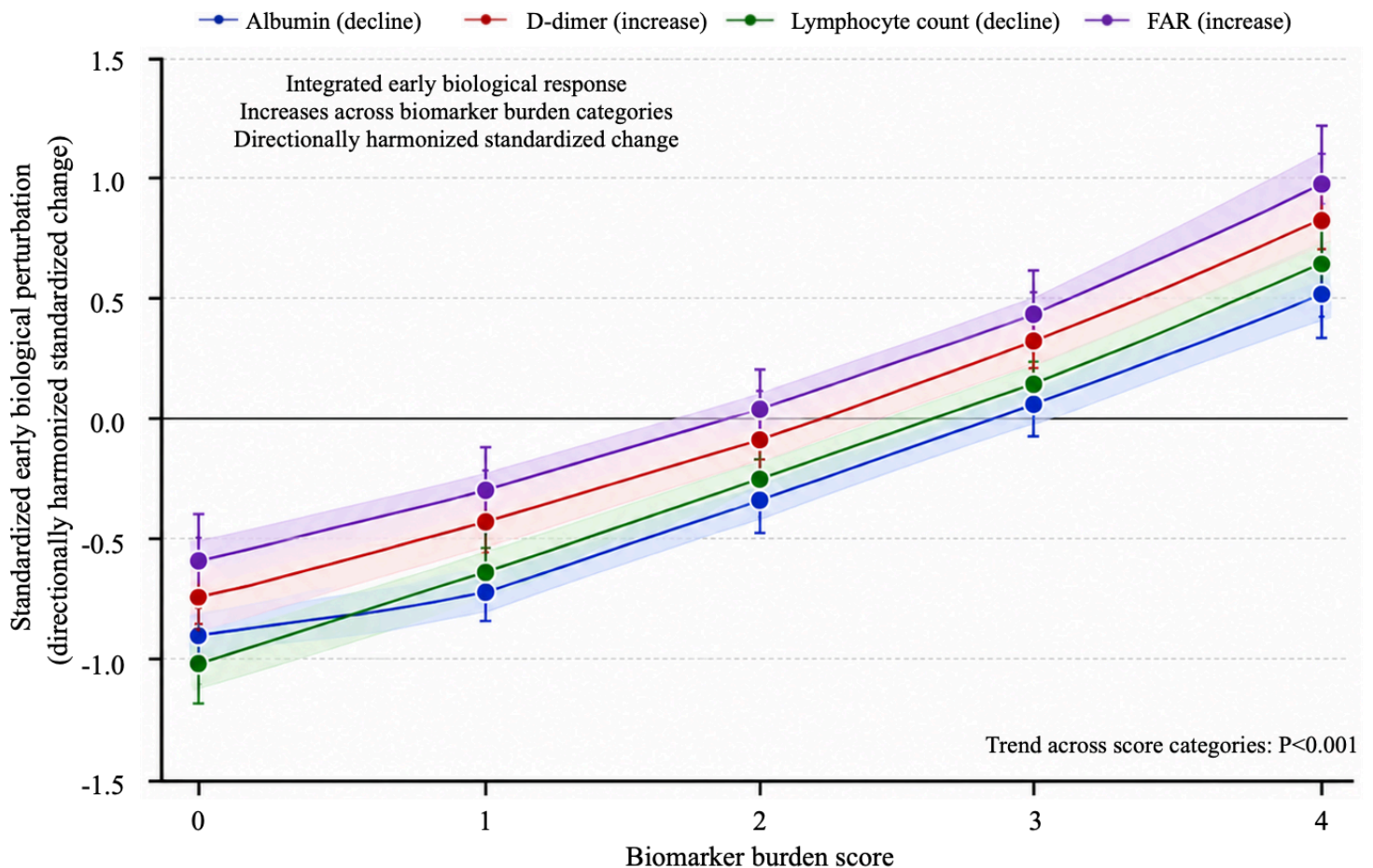


Figure 2

Integrated early biological response across biomarker burden categories. Directionally harmonized standardized changes in albumin, D-dimer, lymphocyte count, and fibrinogen-to-albumin ratio (FAR) are shown across biomarker burden score categories. Changes in albumin and lymphocyte count were directionally reversed so that higher values consistently indicated a greater adverse biological response. Points represent standardized estimates, vertical bars indicate uncertainty, and shaded bands show the corresponding confidence intervals. All four biomarker trajectories increased progressively with higher burden scores, supporting a graded association between baseline multidomain vulnerability and the magnitude of the early postprocedural biological response. Albumin and lymphocyte trajectories are directionally reversed so that higher values indicate greater adverse biological perturbation. Points represent standardized estimates; bands indicate uncertainty.

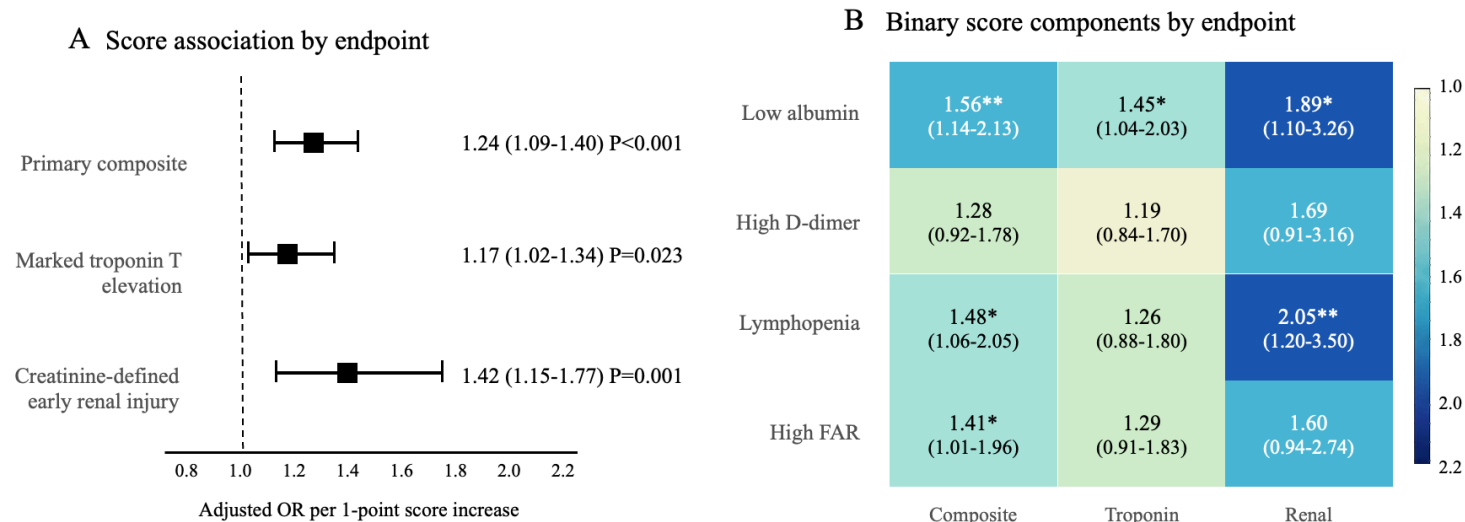


Figure 3

Organ-specific susceptibility and component contributions. Panel A decomposes the primary endpoint. Panel B shows adjusted associations per one-point increase in the total score. Panel C displays adjusted associations of each binary score component with the composite, troponin, and renal endpoints. All models adjusted for age, sex, diabetes, baseline eGFR, and LVEF. *P<0.05; **p<0.01. Formal heterogeneity, renal vs troponin effect: P=0.076

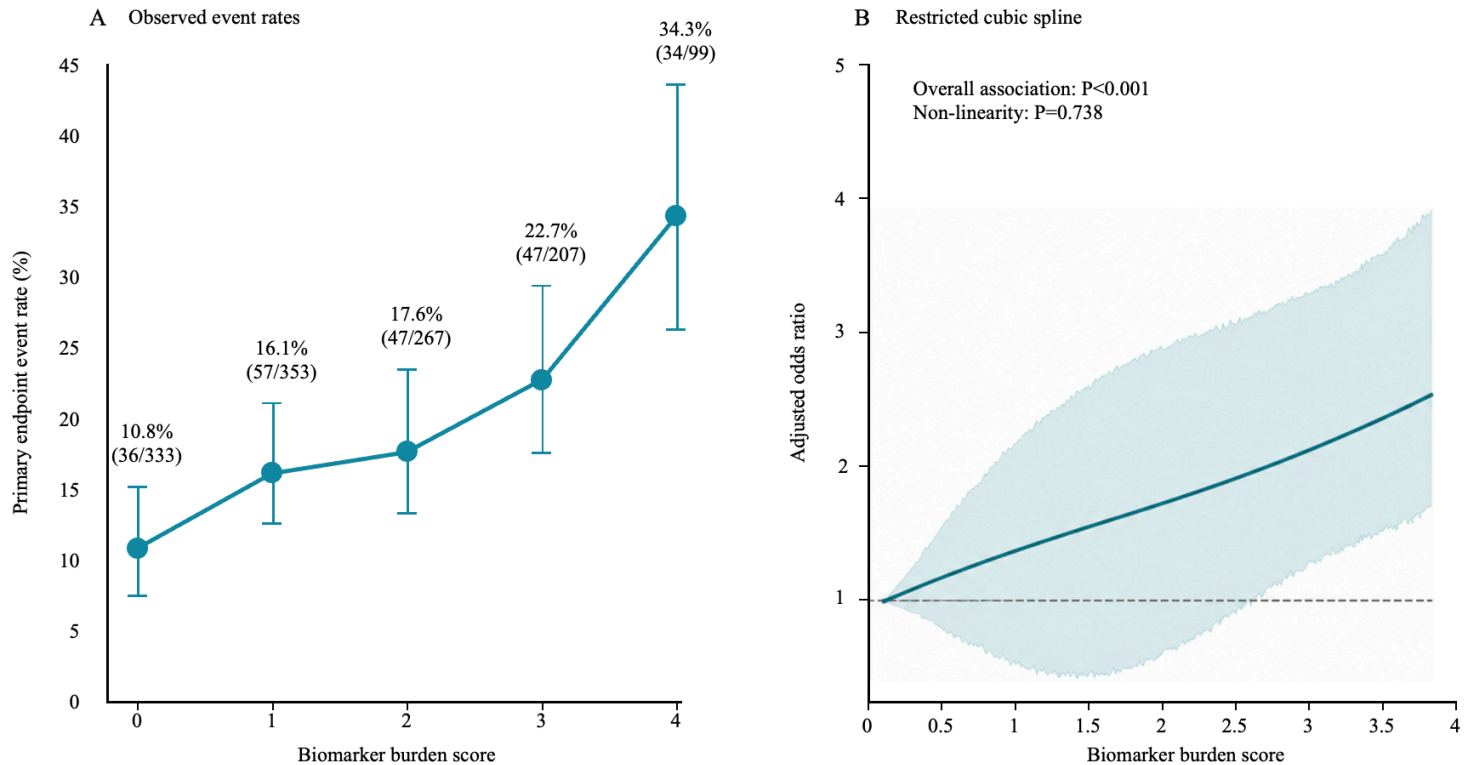


Figure 4

Graded risk and dose-response association. Panel A shows observed event rates with 95% confidence intervals across score categories. Panel B shows the restricted cubic spline association with the primary endpoint.