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Ailing Song
Shanghai General Hospital
Yuncong Zhou
Shanghai General Hospital
Jinnan Chen
Shanghai General Hospital
Yaping Zhang
Shanghai General Hospital
Ping Zhang
Shanghai General Hospital
Cailing Yang
Shanghai General Hospital
Jinbao Li
Shanghai General Hospital
Yun Zou
72400018109@shsmu.edu.cn

Shanghai General Hospital

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Preoperative EASIX Compared With EuroSCORE II for Mortality Risk Assessment in Cardiac Surgery With Cardiopulmonary Bypass: A Retrospective Cohort Study

Original Research

Ailing Song[a†], Yuncong Zhou[a†], Jinnan Chen[a†], Yaping Zhang[a], Ping Zhang[a], Cailing Yang[a], Jinbao Li[a*], Yun Zou[a*]

[a] Department of Anesthesiology, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, 100 Haining Road, Hongkou District, Shanghai 200080, China

[†] These authors contributed equally.

[*] Corresponding authors: Jinbao Li (lijinbaoshanghai@163.com); Yun Zou (72400018109@shsmu.edu.cn)

Abstract

Background: EuroSCORE II is widely used for mortality risk assessment in cardiac surgery, but it may not fully capture perioperative vulnerability. The Endothelial Activation and Stress Index (EASIX), derived from three routinely available laboratory variables, may provide complementary risk information. We evaluated the prognostic value of preoperative EASIX in relation to EuroSCORE II in patients undergoing cardiac surgery with cardiopulmonary bypass.

Methods: This retrospective single-center study included 1267 adults undergoing cardiac surgery with cardiopulmonary bypass between 2015 and 2025. The primary outcome was in-hospital mortality. EASIX was analyzed as a $\log_2$-transformed continuous variable and using prespecified categories. Associations with mortality were assessed using logistic regression. Predictive performance was evaluated using repeated stratified 10-fold cross-validation. Joint EuroSCORE II–EASIX risk stratification and a fixed-offset EuroSCORE II + EASIX model were used to assess residual and absolute risk. Secondary analyses examined mechanical ventilation duration, intensive care unit (ICU) length of stay, postoperative transfusion, and acute kidney injury (AKI).

Results: In-hospital mortality occurred in 104 patients (8.2%). Each doubling of EASIX was associated with higher mortality after adjustment for the published EuroSCORE II linear predictor (OR, 1.501; 95% CI, 1.269–1.775; $P < 0.001$). The EASIX-only model achieved an AUC of 0.722, compared with 0.767 for EuroSCORE II; the difference was not statistically significant in the primary cross-validated comparison. A refitted EuroSCORE

II + EASIX model achieved an AUC of 0.785 (ΔAUC, 0.018; P = 0.051). Among patients with EuroSCORE II-predicted mortality <4%, observed mortality was 12.17% with EASIX ≥2.32 versus 3.14% with EASIX <2.32 (adjusted OR, 3.30; 95% CI, 1.63–6.68; P < 0.001). EuroSCORE II predicted a mean mortality of 3.25% compared with an observed mortality of 8.21% (O/E ratio, 2.53). In the fixed-offset EuroSCORE II + EASIX model, the O/E ratio decreased to 1.36, although residual miscalibration remained. Higher EASIX was also associated with greater postoperative morbidity.

Conclusions: Preoperative EASIX provides clinically meaningful prognostic information in patients undergoing cardiac surgery with cardiopulmonary bypass. Its simple laboratory-based calculation allows rapid risk assessment and may complement EuroSCORE II by identifying residual risk and reducing absolute-risk underestimation.

Keywords: EASIX; EuroSCORE II; cardiac surgery; cardiopulmonary bypass; in-hospital mortality; risk assessment

1. Background

Patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) frequently have complex cardiovascular disease and substantial perioperative risk [1]. Accurate preoperative risk assessment informs surgical decision-making, anesthetic planning, perioperative monitoring, postoperative intensive care, and resource allocation. The European System for Cardiac Operative Risk Evaluation II (EuroSCORE II), which incorporates patient characteristics, cardiac status, comorbidities, and procedure-related factors, is one of the most widely used models for estimating operative mortality [2, 3].

Although EuroSCORE II has established prognostic value [3-5], some of its clinical and procedural variables may be unavailable or difficult to verify before urgent or emergency surgery. It also does not capture all biological determinants of perioperative vulnerability. These practical and conceptual limitations highlight the potential value of a complementary risk marker that is rapidly available, easy to calculate, and capable of providing biological information which was not explicitly represented in conventional clinical scoring systems.

The Endothelial Activation and Stress Index (EASIX) may represent such a marker. EASIX is calculated from only three routinely measured laboratory variables (including lactate dehydrogenase, serum creatinine and platelet count) with no additional specialized testing [6]. It was originally developed in patients undergoing allogeneic hematopoietic stem-cell transplantation, in whom higher EASIX values were associated with

endothelial complications and mortality [7, 8]. Furthermore, EASIX has subsequently demonstrated prognostic value across diverse clinical settings, with increasing interest in its application to cardiovascular disease, including coronary artery disease, coronary artery bypass grafting, and aortic stenosis [9-11].

The potential relevance of EASIX to cardiac surgery has recently been supported by Rehn et al., who evaluated more than 7000 patients undergoing cardiac surgery with CPB [12]. In that retrospective study, higher preoperative EASIX was independently associated with in-hospital mortality, longer intensive care unit (ICU) stays and mechanical ventilation, and postoperative bleeding, while the addition of EASIX improved the discrimination of conventional clinical models. However, its value alongside EuroSCORE II remains unclear. In particular, it is unknown whether EASIX provides additional information within prespecified EuroSCORE II risk categories or improves absolute risk assessment while preserving the original EuroSCORE II structure.

Therefore, we evaluated preoperative EASIX in an independent study of adults undergoing cardiac surgery with CPB, with particular attention to its prognostic value in relation to EuroSCORE II in this retrospective study. We assessed its association with in-hospital mortality and postoperative morbidity, examined its prognostic information across prespecified EuroSCORE II risk strata, and evaluated its contribution to model discrimination and absolute-risk assessment when considered alongside EuroSCORE II.

2. Methods

2.1 Study design and ethics

This retrospective single-center cohort study included adults undergoing cardiac surgery with cardiopulmonary bypass (CPB) at Shanghai General Hospital between January 2015 and December 2025. Patient selection is summarized in Fig. 1. A total of 1267 patients were included in the final cohort and were categorized as survivors or non-survivors according to in-hospital survival status. The study was approved by the Research Ethics Board of Shanghai General Hospital (approval no. 2026-169), and the requirement for informed consent was waived by the ethics committee. The study was registered with the Chinese Clinical Trial Registry (ChiCTR2600122430).

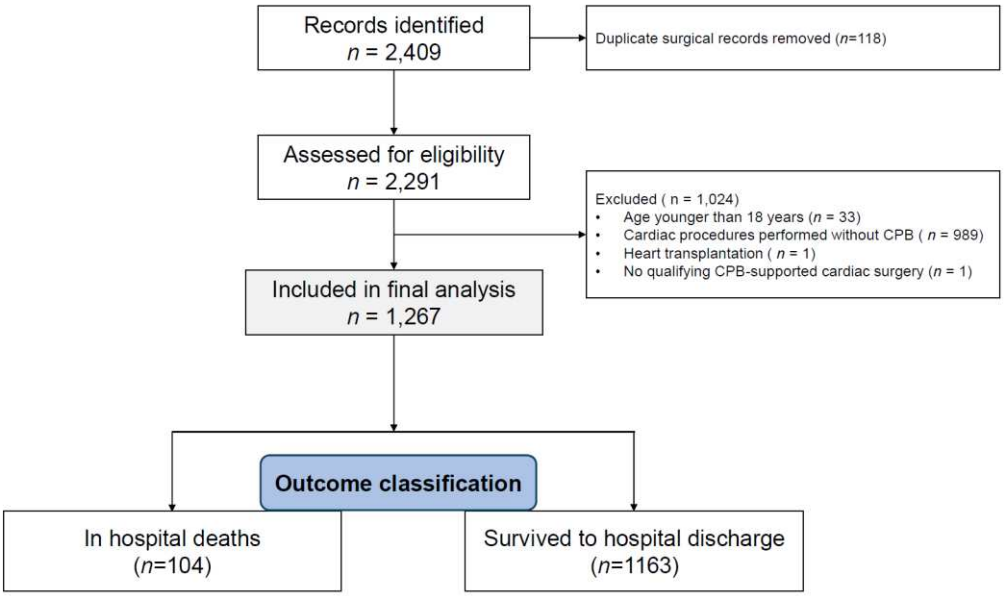


Fig. 1 Study flowchart and cohort selection. A total of 2409 surgical records were identified. After removal of 118 duplicate records, 2291 patients were assessed for eligibility. A further 1024 patients were excluded, including 33 patients younger than 18 years, 989 who underwent cardiac procedures without cardiopulmonary bypass (CPB), 1 heart transplant recipient, and 1 patient without a qualifying CPB-supported cardiac procedure. The final study cohort included 1267 patients, of whom 104 died during hospitalization and 1163 survived to hospital discharge

2.2 Study cohort and data collection

Demographic, clinical, laboratory, operative, and postoperative data were retrospectively extracted from the institutional electronic medical records. Missing preoperative variables required for the analyses were handled using multiple imputation by chained equations, generating 20 completed datasets. EASIX was recalculated within each completed dataset from the corresponding laboratory values. EuroSCORE II was recalculated within each completed dataset using the imputed component variables and the published EuroSCORE II definitions and coefficients. Regression estimates from analyses using multiply imputed data were pooled using Rubin's rules [13, 14]. Further details are provided in Additional file 1.

2.3 EASIX and EuroSCORE II assessment

Preoperative EASIX was calculated using the most recent available laboratory measurements obtained within 7 days before surgery. EASIX was defined as lactate dehydrogenase (LDH, U/L) × serum creatinine (mg/dL) / platelet count (10^9/L) [6, 12]. Serum creatinine values reported in µmol/L were converted to mg/dL by division by 88.4. EASIX was $\log_2$-transformed for continuous analyses; effect estimates represent the association with a

doubling of the original EASIX value. For categorical analyses, EASIX was classified using prespecified cutoffs as low (<0.92), intermediate (0.92 to <2.32), and high (≥2.32). These thresholds were prespecified based on published cutoffs rather than derived from the present study [12]. EuroSCORE II was calculated according to the published definitions and coefficients [2].

2.4 Endpoints

The primary outcome was all-cause in-hospital mortality. Secondary outcomes included duration of mechanical ventilation, ICU length of stay, postoperative transfusion, and postoperative acute kidney injury (AKI). Detailed definitions and assessment procedures for secondary outcomes are provided in Additional file 1, Supplementary Methods.

2.5 Statistical methods

Continuous variables are presented as median (interquartile range, IQR) and categorical variables as number (percentage). Between-group comparisons used the Mann-Whitney U test and Pearson's χ^2 or Fisher's exact test as appropriate. Missing preoperative data were handled using multiple imputation by chained equations with 20 completed datasets, and pooled estimates were obtained using Rubin's rules [13, 14].

The association between EASIX and in-hospital mortality was assessed using logistic regression, with EASIX analyzed after $\log_2$ transformation and by prespecified categories (<0.92, 0.92 to <2.32, and ≥2.32). Models included unadjusted, clinically adjusted, and EuroSCORE II-adjusted analyses. Predictive performance was internally evaluated using repeated stratified 10-fold cross-validation. Discrimination was summarized by the area under the receiver operating characteristic curve (AUC), and overall prediction error by the Brier score. Comparisons included clinical models with and without EASIX, an EASIX-only model, the published EuroSCORE II, and a refitted EuroSCORE II + EASIX model. Apparent-data paired DeLong comparisons were performed as sensitivity analyses [15].

To assess residual risk beyond EuroSCORE II, patients were jointly stratified by EuroSCORE II predicted-risk categories (<4%, 4% to <8%, and ≥8%) and EASIX (<2.32 or ≥2.32). Observed-to-expected (O/E) mortality ratios were calculated, and EASIX-associated mortality risk within EuroSCORE II strata was examined using adjusted logistic regression and interaction testing. To evaluate whether EASIX improved absolute-risk estimation while preserving the published EuroSCORE II structure, a fixed-offset EuroSCORE II + EASIX model was assessed using predicted mortality, O/E ratio, calibration intercept and slope, Brier score, and graphical calibration.

Postoperative mechanical ventilation duration and ICU length of stay were analyzed using negative-binomial regression, whereas postoperative transfusion and AKI were analyzed using logistic regression. Sensitivity and temporal robustness analyses were also performed. Detailed model specifications, cross-validation procedures, calibration methods, and sensitivity analyses are provided in Additional file 1, Supplementary Methods.

3. Results

3.1 Study cohort and baseline characteristics

A total of 2409 surgical records were identified. After removal of 118 duplicate records, 2291 records were assessed for eligibility, of which 1024 were excluded. The final study comprised 1267 adults undergoing cardiac surgery with cardiopulmonary bypass (CPB), including 104 in-hospital deaths and 1163 survivors, corresponding to an in-hospital mortality of 8.2% (Fig. 1). The median age was 62 years, and 564 patients (44.5%) were women. Compared with survivors, non-survivors were older, more frequently had hypertension and New York Heart Association (NYHA) class III–IV symptoms and underwent longer operations with longer CPB times and greater intraoperative blood loss. Both preoperative EASIX and EuroSCORE II were higher among non-survivors. Median EASIX was 2.16 (IQR, 1.13–4.00) in non-survivors when compared with 1.12 (0.72–1.76) in survivors, while median EuroSCORE II was 5.05% (2.33%–9.32%) in contrast to 1.75% (1.07%–3.31%) respectively (Table 1).

Table 1. Clinical characteristics of the overall cohort by in-hospital survival status

Characteristic	Overall (n = 1267)	Survivors (n = 1163)	Non-survivors (n = 104)	*P* value
Demographics and comorbidities				
Age, years	62 (53, 69)	61 (52, 69)	68 (60, 73)	<0.001
Female sex, n (%)	564 (44.5%)	520 (44.7%)	44 (42.3%)	0.636
BMI, kg/m²	23.66 (21.35, 26.18)	23.66 (21.36, 26.22)	23.81 (21.19, 25.96)	0.736
Hypertension, n (%)	528 (41.7%)	461 (39.6%)	67 (64.4%)	<0.001
Diabetes, n (%)	151 (11.9%)	134 (11.5%)	17 (16.3%)	0.146
Preoperative cardiac status				

Characteristic	Overall (n = 1267)	Survivors (n = 1163)	Non-survivors (n = 104)	*P* value
LVEF category				0.349
EF >50%	1071 (84.6%)	987 (84.9%)	84 (81.2%)	
EF ≤50%	196 (15.4%)	176 (15.1%)	20 (18.8%)	
NYHA class				0.006
I–II	266 (21.0%)	255 (21.9%)	11 (10.6%)	
III–IV	1001 (79.0%)	908 (78.1%)	93 (89.4%)	
Operative characteristics				
Surgery time, min	285 (240, 350)	275 (240, 340)	390 (320, 482)	<0.001
Intraoperative blood loss, mL	500 (300, 800)	500 (300, 800)	1000 (575, 1600)	<0.001
CPB time, min	105 (77, 140)	103 (75, 136)	149.5 (117.75, 210.25)	<0.001
Postoperative outcomes				
Ventilation time, h	22.0 (17.0, 38.0)	22.0 (17.0, 30.0)	76.0 (25.8, 209.5)	<0.001
Re-exploration for bleeding, n (%)	53 (4.2%)	41 (3.5%)	12 (11.5%)	<0.001
Postoperative drainage, mL	390 (240, 570)	370 (230, 567.5)	520 (340, 780)	<0.001
ICU stay, days	3 (2, 4)	2 (2, 4)	6 (2, 12)	<0.001
Postoperative transfusion, n (%)	369 (29.1%)	316 (27.2%)	53 (51.0%)	<0.001
Preoperative risk indices				
EuroSCORE II, %	1.85 (1.13, 3.65)	1.75 (1.07, 3.31)	5.05 (2.33, 9.32)	<0.001
EASIX	1.16 (0.74, 1.89)	1.12 (0.72, 1.76)	2.16 (1.13, 4.00)	<0.001

Table note: Data are presented as median (interquartile range) or number (percentage). Continuous variables were compared using the Mann-Whitney U test; categorical variables were compared using Pearson's χ^2 test or Fisher's exact test, as appropriate. Postoperative drainage was defined as the cumulative drainage volume from external surgical drains within the

first 24 hours after surgery. Re-exploration was defined as emergency reoperation for bleeding. Postoperative transfusion was defined as any postoperative transfusion of red blood cells, plasma or platelets. **Abbreviation:** BMI, body mass index; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; CPB, cardiopulmonary bypass; ICU, Intensive care unit; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; EASIX, Endothelial Activation and Stress Index.

3.2 Association of preoperative EASIX with in-hospital mortality and prognostic performance

Higher preoperative EASIX was consistently associated with in-hospital mortality. For each doubling of EASIX, the unadjusted odds ratio (OR) for mortality was 1.868 (95% confidence interval (CI), 1.604–2.175; $P < 0.001$). The association remained significant after adjustment for age, sex, body mass index (BMI), left ventricular ejection fraction (LVEF) category, and surgery type (OR, 1.723; 95% CI, 1.464–2.027; $P < 0.001$), and after adjustment for the published EuroSCORE II linear predictor (OR, 1.501; 95% CI, 1.269–1.775; $P < 0.001$) (Fig. 2A; Additional file 1, Tables S2 and S3). Mortality increased across the prespecified EASIX categories from 3.04% in the low group to 7.38% in the intermediate group and 20.30% in the high group. Compared with the low group, the adjusted ORs were 2.034 (95% CI, 1.076–3.846; $P = 0.029$) and 5.260 (95% CI, 2.744–10.082; $P < 0.001$) for the intermediate and high groups respectively (Additional file 1, Table S4).

EASIX also improved discrimination when added to prespecified clinical models. In repeated cross-validation, addition of EASIX increased the AUC from 0.638 to 0.737 in Model 1 (ΔAUC, 0.098; 95% CI, 0.047–0.149; $P < 0.001$) and from 0.692 to 0.748 in Model 2 (ΔAUC, 0.056; 95% CI, 0.019–0.092; $P = 0.003$) (Fig. 2B; Additional file 1, Table S5). EASIX alone achieved an AUC of 0.722 (95% CI, 0.669–0.774), compared with 0.767 (95% CI, 0.716–0.817) for the published EuroSCORE II. The refitted EuroSCORE II + EASIX model achieved an AUC of 0.785 (95% CI, 0.736–0.835). In the primary cross-validated comparison, the increase over published EuroSCORE II was modest and did not reach statistical significance (ΔAUC, 0.018; 95% CI, −0.000 to 0.037; $P = 0.051$) (Fig. 2C; Additional file 1, Table S6).

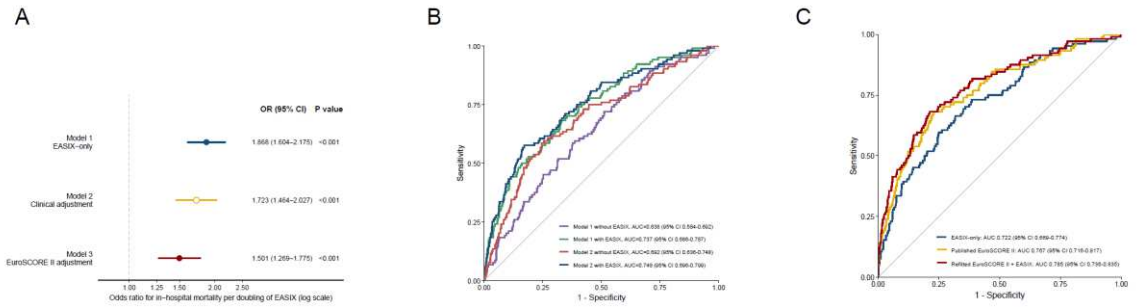
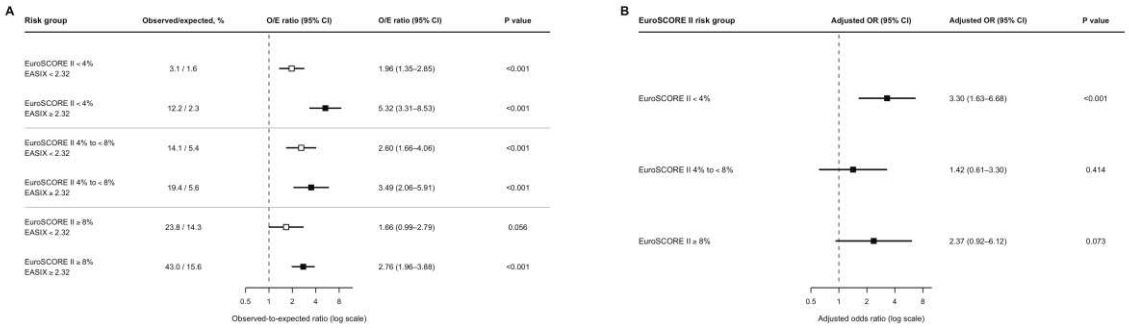


Fig. 2 Association of preoperative EASIX with in-hospital mortality and prognostic performance. (A) Independent association with mortality. Odds ratios are reported per doubling of $\log_2$-transformed EASIX. The clinically adjusted model included age, sex, body mass index, left ventricular ejection fraction category, and surgery type. The EuroSCORE II-adjusted model included the published EuroSCORE II linear predictor and $\log_2$(EASIX). (B) Adding EASIX improves risk prediction beyond basic clinical information. Receiver operating characteristic curves compare two prespecified clinical models with and without EASIX. Model 1 included age, sex, and body mass index; Model 2 additionally included left ventricular ejection fraction category and surgery type. Performance was evaluated using repeated stratified 10-fold cross-validation with fold-specific multiple imputation. (C) EASIX alone provides reasonable discrimination compared with EuroSCORE II. Receiver operating characteristic curves compare the EASIX-only model, the published EuroSCORE II, and the refitted EuroSCORE II + EASIX model within the same internal-validation framework

3.3 EASIX identifies residual mortality risk within prespecified EuroSCORE II risk groups

Observed mortality exceeded published EuroSCORE II predictions across most joint risk strata. Among patients with EuroSCORE II-predicted mortality <4%, observed mortality was 3.14% in those with EASIX <2.32 compared with an expected mortality of 1.60% (O/E ratio, 1.96; 95% CI, 1.35–2.85), whereas patients with EASIX ≥2.32 had an observed mortality of 12.17% compared with an expected mortality of 2.29% (O/E ratio, 5.32; 95% CI, 3.31–8.53) (Fig. 3A; Additional file 1, Table S7). Within the EuroSCORE II <4% category, EASIX ≥2.32 was associated with higher in-hospital mortality after adjustment for the continuous EuroSCORE II linear predictor (OR, 3.30; 95% CI, 1.63–6.68; P < 0.001). The corresponding adjusted ORs were 1.42 (95% CI, 0.61–3.30; P = 0.414) in the 4% to <8% group and 2.37 (95% CI, 0.92–6.12; P = 0.073) in the ≥8% group (Fig. 3B). In the full cohort, EASIX ≥2.32 remained associated with mortality after adjustment for the continuous EuroSCORE II linear predictor (OR, 2.279; 95% CI, 1.433–3.626; P < 0.001). There was no evidence that the association differed across EuroSCORE II risk categories (P for interaction = 0.374).



197

198 **Fig. 3** EASIX identifies residual mortality risk within EuroSCORE II risk groups. (A) High EASIX reveals
199 substantial underestimation of mortality within EuroSCORE II risk groups. Observed-to-expected (O/E)
200 mortality ratios are shown across six groups jointly defined by EuroSCORE II predicted risk (<4%, 4% to <8%,
201 or ≥8%) and EASIX (<2.32 or ≥2.32). Values >1 indicate that observed mortality exceeded that predicted by
202 EuroSCORE II. Confidence intervals were obtained using a multiple-imputation (MI)-aware patient-level
203 bootstrap. (B) Association of high EASIX with mortality within EuroSCORE II risk categories. Adjusted odds
204 ratios compare EASIX ≥2.32 with EASIX <2.32 within each EuroSCORE II risk group, with additional
205 adjustment for the continuous EuroSCORE II linear predictor

206 ### 3.4 Absolute-risk performance after incorporation of EASIX

207 The published EuroSCORE II substantially underestimated absolute mortality risk in the study cohort. Mean
208 predicted mortality was 3.25%, compared with an observed mortality of 8.21%, yielding an O/E ratio of 2.53. In
209 the fixed-offset EuroSCORE II + EASIX model, mean predicted mortality increased to 6.04% and the O/E ratio
210 decreased to 1.36. The Brier score decreased from 0.0715 to 0.0650. The corresponding calibration intercept
211 changed from 1.069 to 0.425 and the calibration slope from 1.084 to 0.773 (Table 2). These findings indicated
212 reduced absolute-risk underestimation after incorporation of EASIX, although residual miscalibration remained.
213 Corresponding discrimination and calibration plots are presented in Additional file 1, Figs. S1 and S3.

Table 2. Predicted and observed mortality with EuroSCORE II and EASIX

Metric	Published EuroSCORE II	Fixed offset EuroSCORE II + EASIX
Mean predicted mortality	3.25%	6.04%
Observed mortality	8.21%	8.21%
O/E ratio	2.53	1.36
Calibration intercept	1.069	0.425
Calibration slope	1.084	0.773
Brier score	0.0715	0.0650

Table note. The published EuroSCORE II predicted mortality was used directly without refitting or recalibration. For the fixed offset EuroSCORE II + EASIX model, the published EuroSCORE II linear predictor was retained with its coefficient fixed at 1 and the model intercept fixed at 0; only the coefficient for $\log_2$(EASIX) was estimated. Performance of the fixed offset model was evaluated using patient-level out-of-fold predictions obtained from 10 repetitions of stratified 10-fold cross-validation. The reported calibration intercept and slope were used only to assess model calibration and did not alter the predicted probabilities. Ideal calibration corresponds to an intercept of 0, a slope of 1, and an observed-to-expected (O/E) mortality ratio of 1. **Abbreviations:** EASIX, Endothelial Activation and Stress Index; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; O/E, observed-to-expected ratio.

3.5 Higher EASIX identifies patients with a more complicated postoperative course

Higher preoperative EASIX was also associated with postoperative morbidity. Compared with the low-EASIX group, the high-EASIX group had longer mechanical ventilation duration (incidence rate ratio (IRR), 1.635; 95% CI, 1.322–2.022; $P < 0.001$) and ICU stay (IRR, 1.269; 95% CI, 1.069–1.506; $P = 0.007$), as well as higher odds of postoperative transfusion (OR, 2.167; 95% CI, 1.466–3.202; $P < 0.001$) and creatinine-defined AKI (OR, 1.977; 95% CI, 1.220–3.202; $P = 0.006$) (Fig. 4; Additional file 1, Table S8). In the intermediate-EASIX group, only postoperative transfusion remained individually significant. Overall between-group tests were significant for all four outcomes.

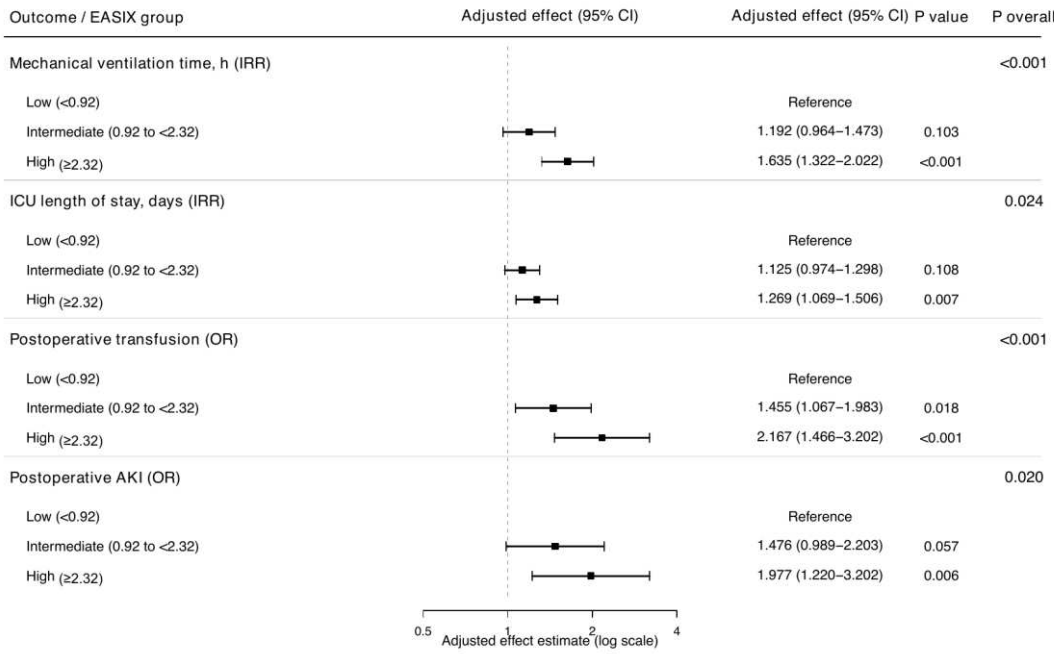


Fig. 4 Higher EASIX identifies patients with a more complicated postoperative course. Adjusted associations of prespecified EASIX categories with postoperative mechanical ventilation duration, ICU length of stay, postoperative transfusion and acute kidney injury. The low-EASIX group (<0.92) was used as the reference. Mechanical ventilation duration and ICU length of stay were analyzed using negative-binomial regression and are reported as incidence rate ratios (IRRs), whereas postoperative transfusion and acute kidney injury were analyzed using logistic regression and are reported as odds ratios (ORs). Models were adjusted for age, sex, body mass index, hypertension, diabetes, NYHA class, LVEF category, chronic lung disease, previous cardiac surgery, preoperative critical state, surgery type, operative urgency, and EuroSCORE II weight of surgery. Estimates were pooled across 20 multiply imputed datasets using Rubin's rules. Overall P values were derived from 2-degree-of-freedom joint Wald tests across the three EASIX groups. Analyses included 1267 patients, except for AKI (n = 1251; 16 patients lacked postoperative serum creatinine results)

3.6 Sensitivity and temporal robustness analyses

The association between continuous EASIX and mortality remained robust after exclusion of values above the 99th percentile (core clinical-adjusted OR per doubling, 1.685; 95% CI, 1.388–2.045; P < 0.001; Additional file 1, Table S2). In the free-intercept offset sensitivity model, EASIX remained independently associated with mortality (OR per doubling, 1.471; 95% CI, 1.250–1.732; P < 0.001), and its incremental contribution was supported by the MI-pooled Wald test (F = 21.576; P < 0.001; Additional file 1, Table S9). In temporal analyses, the EuroSCORE II-adjusted association of EASIX with mortality persisted in both the earlier and contemporary

periods (ORs per doubling, 1.36 and 1.71, respectively), without significant evidence of temporal heterogeneity (P for interaction = 0.090; Additional file 1, Table S10).

4. Discussion

In this retrospective cohort of patients undergoing cardiac surgery with cardiopulmonary bypass, higher preoperative EASIX was consistently associated with in-hospital mortality and remained significant after adjustment for EuroSCORE II. Despite being derived from only three routinely available laboratory variables, EASIX showed reasonable discrimination for mortality and provided additional prognostic information beyond conventional clinical factors and EuroSCORE II. Higher EASIX was also associated with a more complicated postoperative course, including longer mechanical ventilation and ICU stay, greater transfusion requirements, and a higher risk of creatinine-defined AKI.

One of the main advantages of EASIX is its simplicity. EuroSCORE II is a well-established risk model that incorporates multiple patient-, cardiac-, and procedure-related variables [2, 3], whereas EASIX is calculated from only lactate dehydrogenase, serum creatinine, and platelet count [6, 12]. In our study, the EASIX-only model achieved an AUC of 0.722 compared with 0.767 for EuroSCORE II, and the difference was not statistically significant in the primary cross-validated comparison. Although this does not demonstrate equivalence, it indicates that a simple laboratory-based index can provide meaningful prognostic information with substantially fewer variables. EASIX may therefore be useful when a rapid preliminary assessment is needed.

EASIX also appeared to provide information not fully captured by EuroSCORE II. Among patients with EuroSCORE II-predicted mortality below 4%, observed mortality was 12.17% in those with EASIX ≥2.32 compared with 3.14% in those with lower EASIX. High EASIX remained associated with mortality after adjustment for the continuous EuroSCORE II linear predictor, while no significant interaction was observed across EuroSCORE II risk categories. These findings suggest that EASIX may identify residual risk that is not fully represented by conventional clinical risk variables.

This additional information was also reflected in absolute-risk estimation. Discrimination and calibration represent distinct aspects of predictive performance, and good discrimination does not necessarily imply accurate estimation of absolute risk [16-18]. In our cohort, EuroSCORE II predicted a mean mortality of 3.25%, whereas the observed mortality was 8.21%. After EASIX was incorporated into the fixed-offset model, the O/E ratio decreased from 2.53 to 1.36 and the Brier score also improved. Residual miscalibration remained, however,

indicating that EASIX did not fully recalibrate EuroSCORE II. Previous external evaluations have also reported variation in EuroSCORE II calibration across cardiac surgical populations [3, 4, 19]. Similar findings have been reported in additional Asian cohorts [5, 20, 21]. A more appropriate interpretation of our findings is therefore that EASIX provided additional absolute-risk information and reduced the degree of risk underestimation in this study.

The temporal analysis further supported the robustness of these findings. The association between EASIX and mortality was observed in both 2015–2020 and 2021–2025, with no significant interaction by study period. Among patients with EuroSCORE II-predicted mortality below 4%, marked risk underestimation in those with high EASIX was also present in both periods. This suggests that the additional prognostic information carried by EASIX was not confined to a single phase of the study.

The association between EASIX and postoperative outcomes may partly explain its additional prognostic value. Higher EASIX was associated with longer mechanical ventilation and ICU stay, greater transfusion requirements, and higher odds of creatinine-defined AKI. Similar associations between preoperative EASIX and postoperative mortality and morbidity have recently been reported in patients undergoing cardiac surgery with CPB [12]. The three components of EASIX may reflect different aspects of physiological reserve, including tissue stress, renal reserve, and hemostatic disturbance. EASIX has also been linked to endothelial stress and adverse outcomes in several clinical settings [6-8, 22]. CPB itself is associated with inflammatory activation, endothelial and glycocalyx injury, hemostatic disturbance and microcirculatory dysfunction [23-25]. Additional studies have described vascular endothelial dysfunction, inflammatory activation, and microcirculatory impairment during cardiac surgery and CPB [26, 27]. These mechanisms provide a biologically plausible context for the observed associations, although EASIX is not a direct measure of endothelial dysfunction and the underlying mechanisms remain to be confirmed.

From a clinical perspective, the principal value of EASIX lies in its rapid availability. Its three components are routinely measured and require no specialized testing [6, 12]. EASIX should not replace EuroSCORE II, but it may serve as a practical complementary tool, particularly when rapid risk assessment is needed or when complete EuroSCORE II information is not yet available.

Several limitations should be acknowledged. This was a single-center retrospective study, and the number of deaths was limited, particularly in subgroup analyses. The EASIX thresholds, joint EuroSCORE II–EASIX stratification, and fixed-offset model require external validation before clinical implementation [28].

5. Conclusions

In conclusion, preoperative EASIX provides clinically meaningful prognostic information in patients undergoing cardiac surgery with cardiopulmonary bypass. It offers reasonable mortality discrimination using only three routine laboratory variables, provides additional risk information beyond EuroSCORE II, and reduces the degree of absolute-risk underestimation observed with EuroSCORE II. Its simplicity and rapid availability support its potential role as a practical adjunct to conventional perioperative risk assessment.

List of abbreviations

AKI: acute kidney injury

AUC: area under the receiver operating characteristic curve

BMI: body mass index

CI: confidence interval

CPB: cardiopulmonary bypass

EASIX: Endothelial Activation and Stress Index

EuroSCORE II: European System for Cardiac Operative Risk Evaluation II

ICU: intensive care unit

IQR: interquartile range

IRR: incidence rate ratio

LDH: lactate dehydrogenase

LVEF: left ventricular ejection fraction

MI: multiple imputation

NYHA: New York Heart Association

O/E: observed-to-expected

OR: odds ratio

Additional files

Additional file 1

File format: DOCX

Title of data: Supplementary methods, Tables S1-S10, and legends for Figs. S1-S3

Description of data: Supplementary methods, Tables S1-S10, and legends for Figs. S1-S3.

Declarations

Ethics approval and consent to participate: The study was performed in accordance with the Declaration of Helsinki, approved by the Research Ethics Board of Shanghai General Hospital (approval no. 2026-169) and registered with the Chinese Clinical Trial Registry (ChiCTR2600122430, *http://www.chictr.org.cn/)*, registration date: 14 April 2026. The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study.

Human Ethics and Consent to Participate declarations: not applicable

Availability of data and materials: The raw clinical data used in this study were obtained from the electronic medical record system of Shanghai General Hospital. Restrictions apply to the availability of these data due to patient privacy and institutional data protection regulations. Data can be accessed upon reasonable request to the corresponding author and with formal approval from the Research Ethics Board of Shanghai General Hospital.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: AS, YCZ and JC contributed equally to the study conception, data analysis, interpretation, and drafting of the manuscript. YPZ, PZ and CY contributed to data collection and critical revision of the manuscript. YZ and JL supervised the study, interpreted the findings, and critically revised the manuscript. All authors approved the final version of the manuscript.

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