

Clinical evaluation of early ICU echocardiographic haemodynamic measures and 28-day mortality in sepsis: a retrospective cohort study

Zheng Yao

yaozheng199@outlook.com

Jiaxiang County People's Hospital

Shijia Zhu

Lvling Town Central Health Center, Heze High-Tech Industrial Development Zone

Zhaotao Fang

Wenshang County Second People's Hospital

Research Article

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Abstract

Purpose

To evaluate whether routinely acquired early intensive care unit (ICU) echocardiographic haemodynamic measures provide prognostic information for 28-day mortality in patients with sepsis who undergo clinically indicated echocardiography.

Methods

This retrospective cohort study used MIMIC-IV version 3.1 linked to MIMIC-IV-ECHO version 1.0. Echocardiographic measurements obtained from 6 h before to 72 h after ICU admission were evaluated. The principal forward-flow measure was left ventricular outflow tract-derived stroke volume index (SVI). Logistic regression assessed associations with 28-day mortality after adjustment for clinical variables, left ventricular ejection fraction (LVEF) and body surface area (BSA).

Results

The SVI-complete cohort included 3,876 patients, with 1,121 deaths (28.9%). Adding SVI to clinical variables, LVEF and BSA increased the area under the receiver operating characteristic curve from 0.742 to 0.745 and reduced Akaike information criterion from 4101.9 to 4091.2. Higher SVI was associated with lower mortality (adjusted OR per 10 mL/m² 0.881, 95% CI 0.821–0.945). In 3,053 patients with additional right-heart data, abnormal right ventricular function (OR 1.300, 95% CI 1.044–1.618) and higher tricuspid regurgitation velocity (OR per 1 m/s 1.281, 95% CI 1.079–1.520) were associated with higher mortality.

Conclusion

Among selected patients with sepsis and clinically available early ICU echocardiography, SVI and right-sided echocardiographic measures were associated with 28-day mortality and provided modest incremental model information. The findings are exploratory and require external validation.

Introduction

Sepsis remains a major cause of ICU mortality despite contemporary guideline-based management, and cardiovascular dysfunction is one of its most clinically important but heterogeneous components [1, 2]. Patients with sepsis may show preserved or impaired left ventricular systolic function, altered preload and afterload, reduced forward flow, right ventricular dysfunction and pulmonary vascular stress. Common severity scores and left ventricular ejection fraction (LVEF) describe important aspects of

illness severity and chamber emptying, but they may not fully characterise haemodynamic reserve [3, 11].

Critical care echocardiography provides bedside measurements that can characterise shock mechanisms, biventricular function and treatment response [4, 16]. Right ventricular dysfunction has prognostic relevance in sepsis, and elevated tricuspid regurgitation (TR) velocity, a Doppler marker related to pulmonary pressure burden, has also been associated with adverse outcomes [12, 13]. More broadly, recent work supports physiologically interpretable approaches that combine complementary cardiovascular measurements in sepsis [14, 15].

A practical question is whether routinely recorded echocardiographic haemodynamic measurements add clinically relevant information beyond clinical variables and LVEF in patients with sepsis who undergo early ICU echocardiography. Stroke volume index (SVI) is a body-size-indexed measure of forward flow and captures a different physiological dimension from LVEF. Because body surface area (BSA) is used in SVI calculation, the role of body size must also be interpreted explicitly [5, 6]. We therefore evaluated LVOT-derived SVI, right ventricular function, TR velocity and BSA in relation to 28-day mortality using linked MIMIC-IV and MIMIC-IV-ECHO data [7, 8]. The study was an exploratory observational evaluation of routinely acquired monitoring data rather than development of a definitive prediction tool.

Methods

Study design and data source

This retrospective cohort study used MIMIC-IV version 3.1 and MIMIC-IV-ECHO version 1.0. MIMIC-IV contains deidentified electronic health record data from Beth Israel Deaconess Medical Center, and MIMIC-IV-ECHO links structured transthoracic echocardiographic measurements to MIMIC-IV records [7, 8]. Database access and initial data extraction were performed by Zheng Yao after completion of the required PhysioNet training and acceptance of the applicable data use agreement. Reporting followed the STROBE statement and the RECORD extension for routinely collected health data [9].

Study population

Adult ICU observations meeting Sepsis-3 criteria were included [1]. The analysis unit in the extracted dataset was the ICU stay. The initial ICU sepsis cohort contained 27,881 observations. Model-specific complete-case cohorts were defined according to availability of BSA, echocardiographic measurements, the outcome and adjustment covariates.

Echocardiographic measurements and derived indices

Echocardiographic measurements were restricted to examinations recorded during the index hospitalisation or ICU stay from 6 h before to 72 h after ICU admission. When multiple values of a given

variable were available, the first available value within this window was used. DuBois BSA was used as the body-size measure [5]. Stroke volume was calculated as $0.785398 \times (\text{LVOT diameter})^2 \times \text{LVOT velocity-time integral}$, and SVI was calculated as stroke volume divided by BSA. Cardiac output and cardiac index were derived from stroke volume, echocardiographic heart rate and BSA. Additional echocardiographic variables included LVEF, right ventricular function, TR velocity, TR pressure gradient, left atrial volume, biplane left ventricular volumes, tricuspid annular plane systolic excursion and inferior vena cava diameter.

Outcome and covariates

The outcome was 28-day mortality. The adjustment set included age, sex, Sequential Organ Failure Assessment (SOFA) score [10], Charlson comorbidity index, septic shock, invasive ventilation, continuous renal replacement therapy, congestive heart failure, renal disease, chronic pulmonary disease and myocardial infarction.

Missing data and selection analysis

Because LVOT-derived haemodynamic variables were not available for all patients, analyses used model-specific complete cases. Baseline characteristics and outcomes were compared between included and excluded patients for the SVI-complete and multi-parameter cohorts. Standardised mean differences (SMDs) quantified imbalance. Logistic regression models using baseline clinical variables were also fitted to assess factors associated with complete-case inclusion. Detailed aggregate data, including variable availability, are provided in Online Resource 1.

Statistical analysis

Continuous variables were summarised as medians with interquartile ranges; categorical variables were summarised as counts and percentages. Logistic regression was used to evaluate associations with 28-day mortality. Sequential models included clinical variables alone, clinical variables plus LVEF, clinical variables plus LVEF and BSA, and clinical variables plus LVEF, BSA and SVI. A multi-parameter model additionally included abnormal right ventricular function and TR velocity. Model performance was summarised using the area under the receiver operating characteristic curve (AUC) and Akaike information criterion (AIC). Associations are reported as adjusted odds ratios (ORs) with 95% confidence intervals (CIs). Comparisons of stroke volume, SVI and cardiac index are provided in Online Resource 1. Because this was a retrospective exploratory analysis, estimates are interpreted as associations rather than causal effects.

Figures were prepared from aggregate results using Python with Matplotlib.

Use of artificial intelligence tools

OpenAI ChatGPT was used to assist with drafting and revising portions of the manuscript, English-language editing, manuscript organisation, journal-format adaptation, reference-format checking and preparation of non-interpretive submission materials. It was not used for data collection, statistical analysis, generation or fabrication of study results, clinical decision-making or independent scientific interpretation. All AI-assisted content was critically reviewed, verified and edited by the authors, who take responsibility for the final manuscript.

Results

Study cohort and echocardiographic data availability

Among 27,881 adult ICU observations with sepsis, 27,881 had complete clinical covariates and 28-day mortality status. Sequential exclusions for the SVI model were missing or invalid DuBois BSA ($n = 9,836$), additional missing LVEF after BSA availability ($n = 11,745$) and additional missing LVOT-derived SVI after BSA and LVEF availability ($n = 2,424$), leaving 3,876 observations in the SVI-complete cohort. An additional 152 observations had missing right ventricular function and 671 had additional missing TR velocity, leaving 3,053 observations in the multi-parameter cohort (Fig. 1).

In the SVI-complete cohort, core clinical variables, BSA, LVEF and SVI were complete by design. Right ventricular function was available in 96.1% and TR velocity in 81.3% of the SVI-complete cohort. In the overall 27,881-observation cohort, LVEF was available in 33.4%, calculated SVI in 14.4%, right ventricular function in 32.6% and TR velocity in 25.9%; detailed availability is reported in Online Resource 1.

Table 1
Baseline characteristics and data completeness in the SVI-complete cohort

Characteristic	Total (n = 3,876)	Survivors (n = 2,755)	Non-survivors (n = 1,121)	Completeness
Age, years	68.35 [56.54, 78.89]	67.42 [55.81, 78.48]	70.30 [58.57, 80.33]	3,876/3,876 (100.0%)
Male sex	2,199 (56.7%)	1,561 (56.7%)	638 (56.9%)	3,876/3,876 (100.0%)
SOFA score	8.00 [5.00, 11.00]	7.00 [4.00, 10.00]	9.00 [6.00, 12.00]	3,876/3,876 (100.0%)
Charlson comorbidity index	6.00 [4.00, 8.00]	6.00 [4.00, 8.00]	7.00 [5.00, 9.00]	3,876/3,876 (100.0%)
Septic shock	1,210 (31.2%)	801 (29.1%)	409 (36.5%)	3,876/3,876 (100.0%)
Invasive ventilation	2,693 (69.5%)	1,850 (67.2%)	843 (75.2%)	3,876/3,876 (100.0%)
Continuous renal replacement therapy	433 (11.2%)	250 (9.1%)	183 (16.3%)	3,876/3,876 (100.0%)
DuBois BSA, m ²	1.91 [1.73, 2.10]	1.93 [1.75, 2.11]	1.86 [1.68, 2.05]	3,876/3,876 (100.0%)
LVEF, %	60.00 [55.00, 65.00]	60.00 [55.00, 65.00]	60.00 [50.00, 65.00]	3,876/3,876 (100.0%)
SVI, mL/m ²	35.07 [27.42, 44.33]	36.21 [28.47, 45.60]	32.86 [25.27, 41.79]	3,876/3,876 (100.0%)
Abnormal RV function	941 (25.3%)	611 (22.2%)	330 (29.4%)	3,724/3,876 (96.1%)
TR velocity, m/s	2.70 [2.36, 3.10]	2.67 [2.34, 3.08]	2.77 [2.42, 3.17]	3,153/3,876 (81.3%)

Continuous variables are median [interquartile range]; categorical variables are n (%). BSA, body surface area; LVEF, left ventricular ejection fraction; RV, right ventricular; SOFA, Sequential Organ Failure Assessment; SVI, stroke volume index; TR, tricuspid regurgitation.

SVI and sequential model performance

The SVI-complete cohort included 3,876 observations, with 1,121 deaths within 28 days (28.9%). The clinical model had an AUC of 0.736 and AIC of 4122.9. Adding LVEF increased AUC to 0.740 and reduced AIC to 4106.0. Adding BSA increased AUC to 0.742 and reduced AIC to 4101.9. After adding SVI, AUC was 0.745 and AIC was 4091.2 (Table 2). Each 10 mL/m² higher SVI was associated with lower odds of 28-day mortality (adjusted OR 0.881, 95% CI 0.821–0.945; $p < 0.001$). The reduction in AIC indicated

additional model information, whereas the small absolute change in AUC supports a cautious interpretation of incremental rather than strong individual-level discrimination.

Table 2
Sequential model performance in the SVI-complete cohort

Model	N	Events	AUC	AIC
Clinical	3,876	1,121	0.736	4122.9
Clinical + LVEF	3,876	1,121	0.740	4106.0
Clinical + LVEF + BSA	3,876	1,121	0.742	4101.9
Clinical + LVEF + BSA + SVI	3,876	1,121	0.745	4091.2

AIC, Akaike information criterion; AUC, area under the receiver operating characteristic curve; BSA, body surface area; LVEF, left ventricular ejection fraction; SVI, stroke volume index.

Comparison of derived LVOT haemodynamic measures

Stroke volume and SVI were both associated with 28-day mortality after adjustment for clinical covariates, LVEF and BSA, with similar AUC values in the SVI-complete cohort. Cardiac index was not significantly associated with mortality in its corresponding complete-case analysis. Full estimates are provided in Online Resource 1. Because cardiac-index analyses used a slightly different sample size, AIC values across these non-identical samples should not be interpreted as direct model comparisons.

Multi-parameter echocardiographic model

The multi-parameter cohort included 3,053 observations, with 924 deaths within 28 days (30.3%). Adding SVI, abnormal right ventricular function and TR velocity to the clinical plus LVEF plus BSA model increased AUC from 0.745 to 0.752 and reduced AIC from 3282.1 to 3261.1. In the full model, higher SVI was associated with lower mortality, abnormal right ventricular function and higher TR velocity were associated with higher mortality, and higher BSA was associated with lower mortality (Table 3 and Fig. 2).

Table 3
Adjusted associations in the multi-parameter echocardiographic model

Variable	Adjusted OR (95% CI)	p value
SVI per 10 mL/m ²	0.891 (0.823–0.966)	0.0050
Abnormal RV function	1.300 (1.044–1.618)	0.0189
TR velocity per 1 m/s	1.281 (1.079–1.520)	0.0047
BSA per 0.2 m ²	0.905 (0.840–0.976)	0.0092

The base adjustment set included clinical variables, LVEF and BSA. BSA, body surface area; CI, confidence interval; OR, odds ratio; RV, right ventricular; SVI, stroke volume index; TR, tricuspid regurgitation.

Complete-case selection analysis

The SVI-complete and multi-parameter cohorts differed from excluded observations, particularly in illness severity and mortality. In the SVI-complete cohort, 28-day mortality was 28.9% versus 18.0% among excluded observations, and median SOFA score was 8 versus 6. In the multi-parameter cohort, mortality was 30.3% versus 18.2% among excluded observations, and median SOFA score was 8 versus 6 (Table 4). Clinical-variable models predicted SVI-complete inclusion with AUC 0.704 and multi-parameter inclusion with AUC 0.705, indicating non-random availability of the required echocardiographic measurements.

Table 4
Complete-case selection analysis

Cohort	Variable	Included	Excluded	SMD
SVI-complete	28-day mortality	1,121 (28.9%)	4,315 (18.0%)	0.261
SVI-complete	SOFA	8.00 [5.00, 11.00]	6.00 [4.00, 8.00]	0.500
SVI-complete	Age	68.35 [56.54, 78.89]	67.90 [56.72, 78.95]	0.002
Multi-parameter	28-day mortality	924 (30.3%)	4,512 (18.2%)	0.285
Multi-parameter	SOFA	8.00 [5.00, 11.00]	6.00 [4.00, 8.00]	0.486
Multi-parameter	Age	69.47 [57.84, 79.98]	67.76 [56.62, 78.82]	0.061

SMD, standardised mean difference; SOFA, Sequential Organ Failure Assessment. Included observations were model-specific complete cases.

Discussion

In this retrospective evaluation of clinically acquired early ICU echocardiographic measurements, LVOT-derived SVI was associated with 28-day mortality after adjustment for clinical severity, comorbidity, LVEF and BSA. Right ventricular dysfunction and higher TR velocity provided complementary right-sided haemodynamic information. Adding these measurements improved model fit and produced only a modest increase in discrimination, which is more consistent with incremental physiological information than with a stand-alone prediction tool.

The findings are physiologically consistent with the limitations of relying on LVEF alone. LVEF describes proportional chamber emptying, whereas SVI quantifies indexed forward flow; similar LVEF values may coexist with substantially different preload, afterload, vascular tone and stroke-volume states in sepsis

[11, 16]. The right-heart findings are also consistent with prior evidence linking right ventricular dysfunction and Doppler-defined pulmonary hypertension with adverse outcomes in sepsis [12, 13].

BSA requires particular caution because it is both the denominator used to derive SVI and an independently entered body-size variable in the reported models [5, 6]. The association of lower BSA with mortality should therefore not be interpreted causally. It may reflect body composition, frailty, nutritional reserve, chronic disease or mathematical coupling with indexed flow, none of which can be fully separated in this dataset. The comparison of unindexed stroke volume and SVI in Online Resource 1 is therefore best viewed as an exploratory assessment of alternative ways to express forward flow.

A key strength is the use of a large deidentified ICU database linked to structured echocardiographic measurements, allowing assessment of routinely acquired monitoring data rather than measurements obtained under an artificial research protocol. At the same time, this is also an important limitation: echocardiography was clinically indicated, and the required measurements were available in only a subset of the overall sepsis cohort. The complete-case analysis showed that included observations were sicker and had higher mortality than excluded observations. The findings therefore apply most directly to patients with sepsis who undergo early echocardiography and have adequate LVOT and right-heart measurements.

Several additional limitations should be considered. First, the study was retrospective and observational, and residual confounding is likely. Second, LVOT-derived stroke volume and SVI depend on image acquisition and measurement quality. Third, the – 6 to + 72 h window was not a protocolised baseline examination; later measurements may partly reflect treatment received after ICU admission and survival to the time of echocardiography. Fourth, variable-specific first available measurements may not always originate from exactly the same examination. Fifth, the extracted analysis unit was the ICU stay; if individual patients contributed more than one eligible stay, within-patient correlation could affect conventional regression standard errors. Finally, no external validation was performed. These limitations preclude causal interpretation and argue against clinical implementation based on the present results alone.

Conclusion

Among selected ICU observations with sepsis and clinically available early echocardiography, lower LVOT-derived SVI, abnormal right ventricular function and higher TR velocity were associated with 28-day mortality. These routinely acquired echocardiographic measurements provided modest incremental information beyond clinical variables and LVEF. The results should be regarded as exploratory and require validation in independent cohorts using more standardised echocardiographic timing and measurement protocols.

Declarations

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval

The MIMIC-IV-ECHO project was approved by the Institutional Review Boards of Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA, and the Massachusetts Institute of Technology, Cambridge, Massachusetts, USA; the requirement for individual patient consent was waived because the project did not affect clinical care and protected health information was deidentified. The present study was a secondary analysis of deidentified, credentialed-access MIMIC-IV and MIMIC-IV-ECHO records and involved no direct participant contact; no additional institutional review board approval was required for this database analysis.

Consent to participate

The requirement for individual informed consent was waived for the source deidentified MIMIC research resources as described above.

Consent for publication

Not applicable. No identifiable individual participant information, images or videos are reported.

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Author Contribution

Z.Y. conceived and designed the study, developed the methodology, performed database access and initial data extraction, contributed to software, validation and data curation, interpreted the results, prepared the original manuscript, and supervised the project. S.Z. and Z.F. contributed to software, validation, formal statistical analysis, data curation, interpretation of the results, and manuscript revision. Z.Y. and S.Z. prepared the visualizations. All authors reviewed and approved the final manuscript. Z.Y. is the guarantor of the work.

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Data Availability

The patient-level data used in this study are available from PhysioNet to credentialed users who complete the required training and accept the applicable data use agreements. MIMIC-IV version 3.1 is available at <https://doi.org/10.13026/kpb9-mt58>, and MIMIC-IV-ECHO version 1.0 is available at <https://doi.org/10.13026/nrjh-5r77>. Aggregate data supporting the tables and figures in this manuscript are provided as Online Resource 1. Raw patient-level MIMIC records and source tables are not redistributed in accordance with the PhysioNet data use agreement.

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Figures

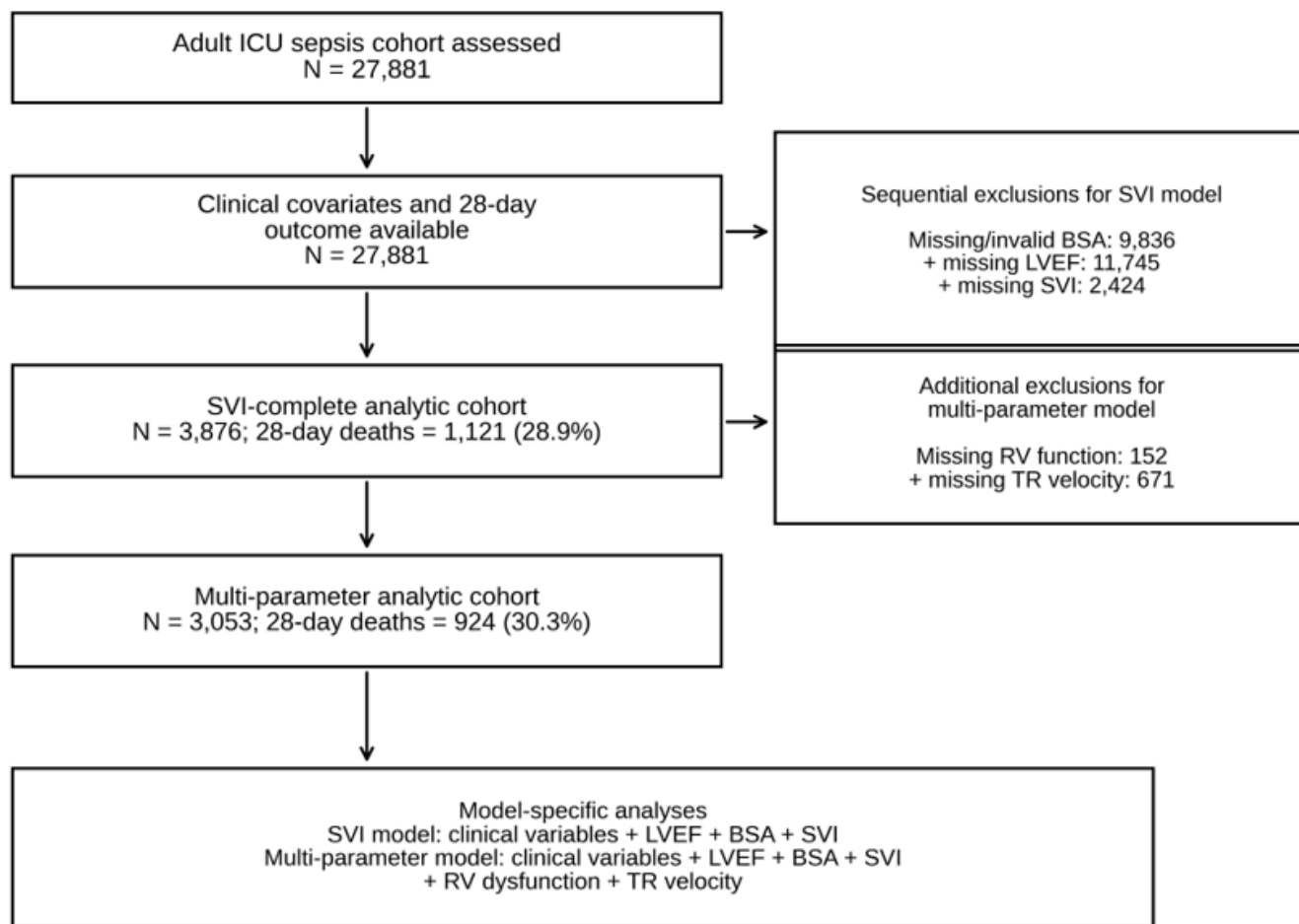


Figure 1

STROBE-style study flow diagram showing sequential exclusions and model-specific analytic cohorts; BSA body surface area, LVEF left ventricular ejection fraction, LVOT left ventricular outflow tract, RV right ventricular, SVI stroke volume index, TR tricuspid regurgitation

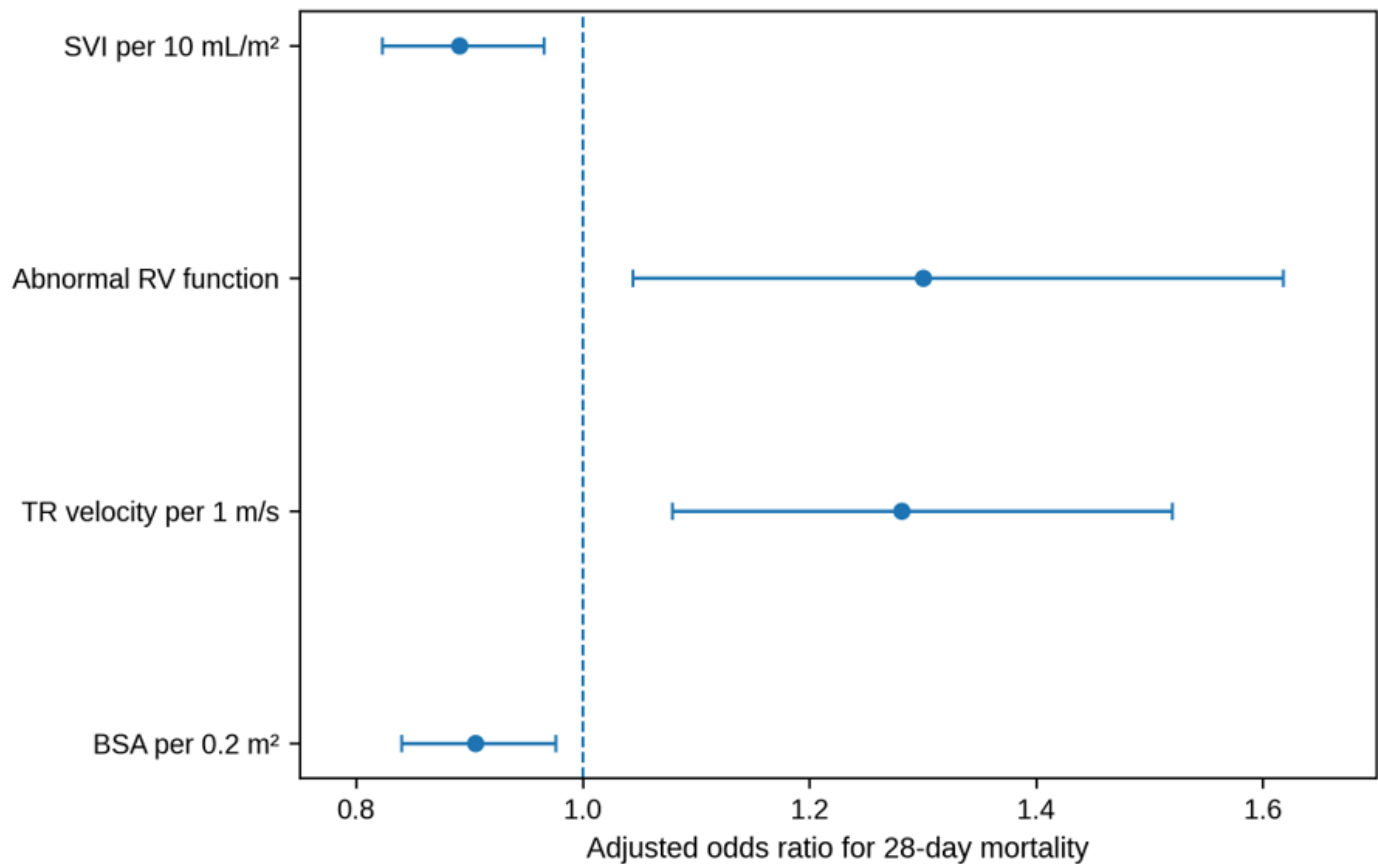


Figure 2

Adjusted odds ratios and 95% confidence intervals from the multi-parameter echocardiographic model; the vertical dashed line denotes an odds ratio of 1.0; BSA body surface area, RV right ventricular, SVI stroke volume index, TR tricuspid regurgitation

Supplementary Files

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