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# Impact of left ventricular stroke work index on 30-day mortality in sepsis: a retrospective analysis based on the MIMIC-III database

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## Abstract

**Background** Cardiac dysfunction, commonly observed in sepsis patients, is associated with higher mortality rates. The left ventricular stroke work index (LVSWI), an integrated parameter reflecting overall left ventricular function, may serve as a reliable and practical prognosticator for sepsis.

**Methods** Using the Medical Information Mart for Intensive Care (MIMIC III) database, we carried out a retrospective observational study that included adult patients who met the Sepsis-3 criteria. Kaplan-Meier survival curves and Cox proportional hazard models were applied to examine the association between LVSWI and 30-day all-cause mortality. Restricted cubic spline plots were used to assess the non-linear relationship between LVSWI and mortality, and subgroup analyses were conducted across various variables.

**Results** A total of 1,348 septic patients were included, with 300 (22.3%) fatalities. In multivariate Cox proportional hazard models, a significant negative relationship between LVSWI and mortality was observed, with a 31% reduction in mortality risk associated with an increase of one standard deviation in LVSWI (hazard ratio [HR]: 0.69, 95% confidence interval [CI]: 0.51–0.93, $p = 0.016$), following adjustment for confounders. Restricted cubic spline plots unveiled a non-linear, L-shaped relationship between LVSWI and mortality. Furthermore, a two-piecewise regression model identified the critical inflection point at 27.83 g·m/m$^2$, with HR (95% CI) values of 0.93 (0.90–0.96; $p < 0.001$) on the left and 1.00 (0.99–1.01; $p = 0.913$) on the right.

**Conclusions** The LVSWI exhibited an L-shaped relationship with 30-day mortality in patients with sepsis, underscoring the potential of LVSWI as a dependable prognostic indicator for sepsis. Further studies are needed to

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confirm these findings and to investigate whether early interventions to optimize LVSWI could improve outcomes in this patient population.

**Keywords** MIMIC database, LVSWI, Sepsis-induced cardiomyopathy, Mortality, Sepsis

## Introduction

Sepsis, a severe condition triggered by a host's uncontrolled response to infection, is the primary cause of death in critically ill patients globally [1–3]. It is a multifaceted disease, impacting numerous systems and leading to renal, neurological, immunological, hepatic, circulatory, and respiratory dysfunction and failure [1]. Impairment of the circulatory system, in particular, could contribute to a cascade of interdependent organ failure, thereby playing a central role in the multi-organ dysfunction seen in sepsis [4].

Sepsis-induced cardiomyopathy (SCM), a manifestation of cardiac dysfunction in sepsis, had an estimated occurrence in 10–70% of septic patients and resulted in increased mortality, reportedly [4–7]. SCM is marked by acute left ventricular (LV) systolic dysfunction, LV diastolic dysfunction, and right ventricular (RV) dysfunction, which occur separately or simultaneously [8]. Intriguingly, despite that RV dysfunction resulted in increased mortality in sepsis [9, 10], early studies showed no association between LV dysfunction and mortality in septic patients [8, 11–14]. Paradoxically, recent studies have revealed a U-shaped association between LV ejection fraction (LVEF) and mortality in patients with sepsis [15, 16]. LVEF, traditionally used as a measure of LV systolic function, is influenced by both LV contractility and loading conditions—factors that are frequently abnormal in septic patients [17]. Besides, LVEF demonstrated significant variation among different observers and adjusted over time in line with alterations in physiological processes [18]. Consequently, to better elaborate the correlation between left ventricular function and mortality in sepsis, a reliable and practical parameter reflecting cardiac function is warranted.

The LV stroke work index (LVSWI) provided a comprehensive measure of cardiac performance through a continuous assessment of myocardial systolic and diastolic function. It could potentially provide a more expansive assessment of overall LV function than LVEF, especially for critical care patients whose conditions of preload and afterload were dynamic [19]. Previous studies have demonstrated that LVSWI has superior prognostic value compared to LVEF in patients admitted to cardiac intensive care unit (CICU), highlighting its potential as a valuable predictor of mortality [20]. However, the impact of LVSWI on sepsis is yet to be determined.

Therefore, in the present study, we sought to delineate the role of LVSWI and mortality of septic patients, given the intricate association between LV function and sepsis. By delineating this relationship, we seek to establish LVSWI as a potential prognostic tool for SCM and to provide insights that could guide early therapeutic interventions.

## Methods

### Data source

We conducted a retrospective observational study utilizing data from the Medical Information Mart for Intensive Care (MIMIC III) database. This publicly available database contains de-identified health-related information from over 40,000 patients who were admitted to the critical care units of Beth Israel Deaconess Medical Center between June 2001 and October 2012 [21]. The MIMIC-III database is a repository of extensive information, encompassing demographics, vital signs, test results, and diagnoses categorized using codes from both the International Classification of Diseases, Ninth Revision (ICD-9). The author, Yuewei Li, successfully completed the CITI Data or Specimens Only Research course. Upon receiving the certification (number 10007248), we were granted access to the database and assumed responsibility for data extraction. This study, utilizing an anonymous public database in adherence to the review board's protocol, rendered the necessity for ethical consent unnecessary.

### Study population

The study included adult patients who met the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) criteria [22], which requires the presence of known or suspected infection along with organ dysfunction and a Sequential Organ Failure Assessment (SOFA) score of 2 or higher. For our analysis, only data from the first ICU admission was considered. Patients without available LVSWI measurements were excluded from the study.

### Data extraction

The extraction of data for analyses was accomplished using PostgresSQL software (version 13.7.2) and Navicat Premium software (version 16), facilitated by the execution of a Structured Query Language (SQL). Demographics (gender, age, weight), vital signs, critical illness score, comorbidity organ function support, hemodynamic parameters and laboratory test results were included. Vital signs included heart rate, mean arterial pressure, respiratory rate, temperature, and oxygen saturation. Hemodynamic parameters included cardiac output (CO), cardiac index (CI), left cardiac work index (LCWI), left

ventricular stroke work index (LVSWI), stroke volume index (SVI), systemic vascular resistance index (SVRI) and central venous pressure (CVP). Sequential Organ Failure Assessment (SOFA) score was also extracted. Comorbidities included heart failure (HF), hypertension, atrial fibrillation (AF), acute myocardial infarction (AMI); stroke, diabetes mellitus (DM), hypertension, liver disease, stroke, septic shock and chronic kidney disease (CKD). Acute kidney injury (AKI) was diagnosed according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, which defines AKI based on changes in serum creatinine levels or urine output [23]. Vasopressor use was identified as the administration of dobutamine, dopamine, epinephrine, norepinephrine, or vasopressin during ICU hospitalization. Laboratory tests included white blood cell count (WBC), hemoglobin, platelet count (PLT), hematocrit, international normalized ratio (INR), prothrombin time (PT), activated partial thromboplastin time (APTT), blood urea nitrogen (BUN), creatinine, serum potassium, serum sodium, bicarbonate, lactate and anion gap.

### Outcome

The outcome was 30-day all-cause mortality.

### Statistical analysis

In this study, for continuous variables, the mean ± standard deviation was used to present those that were normally distributed, while the median or intertertile range was used for those that were not. Conversely, categorical variables were conveyed as percentages. In the analysis of baseline characteristics, continuous and categorical variables were compared using one-way analysis of variance (ANOVA) and Chi-square tests, respectively. Random forests were utilized for the imputation of missing data.

The Kaplan-Meier method was employed to explore the relationship between LVSWI and mortality, with comparisons conducted using the log-rank test. Cox proportional models were employed to evaluate the relationship between LVSWI and 30-day mortality, with the results presented as hazard ratios (HR) and 95% confidence interval (CI). Model 1 was crude model. Model 2 adjusted for age, gender, CVP, SVRI, CI and SVI. Model 3 adjusted for model 2 plus SOFA score, BMI, AMI, hypertension, DM, HF, AF, CKD, stroke and AKI.

Restricted cubic spline plots with three knots were employed to assess the non-linear relationship between LVSWI and mortalities. To further investigate the association between the LVSWI and the risk of 30-day mortality, a two-piecewise Cox proportional hazards model was utilized on each side of the inflection point. Additionally, subgroup analyses were conducted in several across various subgroups, namely age, gender, AMI, hypertension, AKI, HF, DM, CKD, AF, stroke, and the use of vasopressors.

## Results

### Patient characteristics

Following the enforcement of the exclusion criteria, our study ultimately included a total of 1348 adult patients with sepsis from the MIMIC-IV database (Fig. 1). The general characteristics of the patients enrolled in the study are summarized in Table 1. The participants had a median age of 70 years, with males comprising 58.23% of the total. In the entire population, the median SOFA scores stood at 6, and the median durations of hospital stays were 7.13. Additionally, the 30-day and 1-year mortalities were 22.3% and 39.3%, respectively.

Based on the tertiles of LVSWI ($g{\cdot}m/m^2$), patients were categorized into three strata: $T1 \le 25.52$, $25.52 < T2 \le 36.92$ and $T3 > 36.92$. Clinical variables varied significantly across these tertiles. Patients in the lowest Tertile displayed elevated SOFA scores and extended lengths of hospital stays in comparison to the other groups. Besides, the T1 group demonstrated a higher propensity for the combination of HF, AF and CKD. The 30-day mortality rates in three groups were 28.3%, 19.6% and 19%, respectively ($p < 0.001$), and the 1-year mortality rates were 45.6%, 34.6% and 37.8%, respectively ($p = 0.002$).

### Association between LVSWI and mortality

The KM survival curve, depicted in Fig. 2, revealed significant differences in 30-day mortality among the three LVSWI tertiles. Patients in the lowest tertile (T1) had the highest mortality rates, with a statistically significant difference observed between groups (Log-rank test, $p = 0.00054$, Fig. 2). Cox proportional hazard models were leveraged to further explore the association between LVSWI and 30-day mortality (Table 2). In model 3, each one standard deviation increase in LVSWI was associated with a 30% decrease in the risk of 30-day mortality (hazard ratio [HR]: 0.7, confidence interval [CI]: 0.52–0.94, $p = 0.019$), after controlling for potential confounding factors. Additionally, in the unadjusted model, patients in the second (T2) and third (T3) tertiles had lower HRs for mortality compared to those in the first tertile (T1), with HRs of 0.65 (95% CI: 0.5–0.86, $p = 0.002$) and 0.63 (95% CI: 0.48–0.82, $p = 0.001$), respectively. These associations persisted even after adjusting for confounders, with the fully adjusted model showing HRs of 0.68 (95% CI: 0.5–0.93, $p = 0.015$) for T2 and 0.680 (95% CI: 0.41–0.99, $p = 0.045$) for T3. These findings indicated that lower LVSWI was significantly associated with higher 30-day mortality, independent of other risk factors.

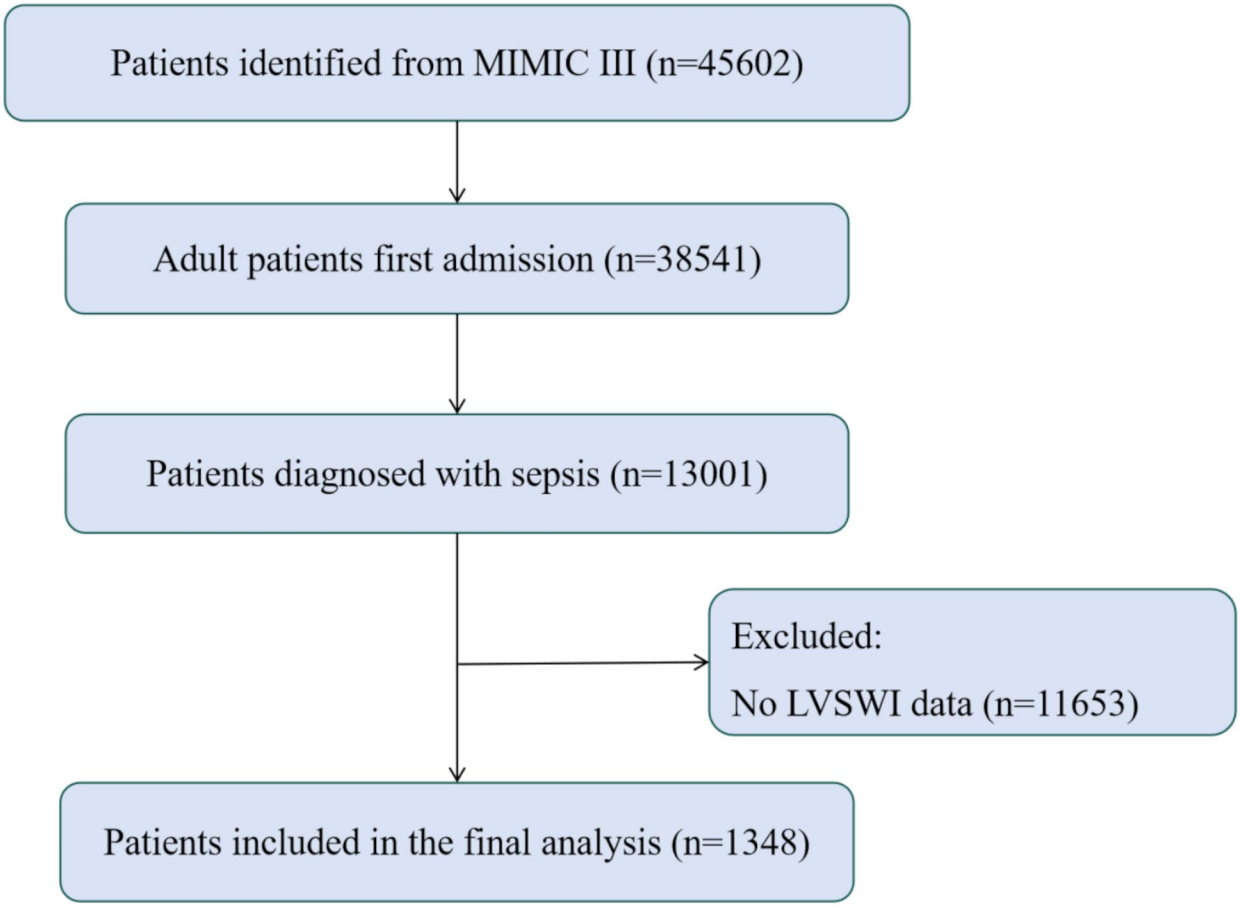


**Fig. 1** Flowchart of the study

#### Non-linear relationship between LVSWI and mortality

Restricted cubic spline plots were employed to evaluate the potential non-linear relationship between LVSWI and mortality (Fig. 3). The results demonstrated a significant L-shaped non-linear relationship between LVSWI and 30-day mortality ($p$ for non-linearity < 0.001), after fully adjusting clinical variables. An inflection point was identified at an LVSWI value of 20.74 using both standard and two-piecewise Cox models (Table 3). Below this threshold, every unit increase in LVSWI was associated with a significantly reduced risk of 30-day mortality (HR: 0.897, 95% CI: 0.843–0.954, $p < 0.001$). However, once LVSWI exceeds the mentioned threshold, further increases in LVSWI lead to an insignificant increase in mortality risk (HR: 0.994, 95% CI: 0.984–1.004, $p = 0.263$). The L-shaped curve thus highlights the nuanced and non-linear relationship between LVSWI and mortality.

#### Subgroup analyses

To explore potential heterogeneity of effects across different subgroups, we conducted stratified analyses based on variables such as age, gender, AMI, hypertension, AKI, HF, DM, CKD, AF, stroke, and the use of vasopressors. The forest plot revealed that association between the LVSWI and mortality predominantly maintained a uniform direction across the majority of subgroups. Besides, none of the $p$-values for interaction were less than 0.05, indicating no significant interactions observed within the stratifications (Fig. 4).

## Discussion

In the retrospective analysis of septic patients, we found that LVSWI, an integrated parameter reflecting global left ventricular function, was substantially relevant to 30-day all-cause mortality. Kaplan-Meier analysis revealed the highest mortality of patients in the tertile with the lowest LVSWI, compared with other tertiles. Additionally, RCS analysis illuminated a non-linear relationship between LVSWI and mortality with the RCS curves exhibiting a L-shaped pattern. Our results notably enhanced the present comprehension of how left ventricular function, evaluated by LVSWI, influences sepsis.

Sepsis-induced cardiomyopathy referred to the intrinsic deterioration in systolic and/or diastolic function of

**Table 1** Clinical characteristics of the study population

| | **Total (*n* = 1348)** | **T1 LVSWI ≤ 25.52 (*n* = 445)** | **T2 25.52 < LVSWI ≤ 36.92 (*n* = 445)** | **T3 LVSWI > 36.92 (*n* = 458)** | ***p*** |
|---|---|---|---|---|---|
| Age, years | 67.4 ± 14.7 | 70.7 ± 13.7 | 68.1 ± 13.9 | 63.6 ± 15.4 | < 0.001 |
| Gender, n (%) | | | | | < 0.001 |
| Female | 563 (41.8) | 229 (51.5) | 163 (36.6) | 171 (37.3) | |
| Male | 785 (58.2) | 216 (48.5) | 282 (63.4) | 287 (62.7) | |
| BMI, ($kg/m^2$) | 28.9 ± 7.5 | 29.2 ± 7.0 | 28.6 ± 7.2 | 28.7 ± 8.3 | 0.472 |
| $SpO_2$, (%) | 97.2 ± 3.0 | 96.7 ± 4.2 | 97.4 ± 2.2 | 97.4 ± 2.1 | < 0.001 |
| Heart rate, (beats/minute) | 90.3 ± 15.6 | 92.9 ± 16.4 | 90.0 ± 14.0 | 88.1 ± 15.9 | < 0.001 |
| MBP, (mmHg) | 75.5 ± 9.5 | 73.9 ± 8.4 | 74.5 ± 7.7 | 78.1 ± 11.2 | < 0.001 |
| CO, (L/min) | 5.7 ± 2.6 | 4.3 ± 1.8 | 5.4 ± 1.7 | 7.4 ± 2.9 | < 0.001 |
| LCWI, ($kg.m/ m^2$) | 3.0 ± 1.4 | 1.9 ± 0.5 | 2.7 ± 0.6 | 4.3 ± 1.5 | < 0.001 |
| LVSWI, ($g·m/ m^2$) | 33.6 ± 15.2 | 19.6 ± 4.2 | 30.7 ± 3.3 | 50.0 ± 13.5 | < 0.001 |
| CI, ($L/min/m^2$) | 2.9 ± 1.2 | 2.2 ± 0.9 | 2.7 ± 0.7 | 3.8 ± 1.3 | < 0.001 |
| SVRI, ($dyne·s/cm^5/m^2$) | 2034.8 ± 907.6 | 2449.5 ± 1047.4 | 2022.7 ± 729.0 | 1643.6 ± 724.6 | < 0.001 |
| SVI, ($mL/m^2$) | 31.8 ± 12.9 | 20.6 ± 5.3 | 30.3 ± 5.6 | 44.3 ± 12.4 | < 0.001 |
| CVP, ($cmH_2O$) | 12.5 ± 6.1 | 13.1 ± 6.3 | 12.0 ± 6.1 | 12.5 ± 6.0 | 0.022 |
| Anion gap, (mEq/L) | 15.1 ± 4.1 | 15.4 ± 4.2 | 14.5 ± 3.8 | 15.3 ± 4.3 | < 0.001 |
| Bicarbonate, (mmol/L) | 20.8 ± 4.8 | 19.9 ± 4.9 | 21.6 ± 4.4 | 21.0 ± 5.0 | < 0.001 |
| Creatinine, (mg/dL) | 1.6 ± 1.3 | 1.6 ± 1.2 | 1.4 ± 1.0 | 1.7 ± 1.5 | < 0.001 |
| BUN, (mg/dL) | 29.9 ± 21.4 | 30.4 ± 21.1 | 27.8 ± 19.5 | 31.6 ± 23.1 | 0.024 |
| Glucose, (mg/dL) | 199.8 ± 86.2 | 210.0 ± 87.4 | 197.7 ± 86.5 | 191.8 ± 83.9 | 0.005 |
| Chloride, (mEq/L) | 106.1 ± 5.5 | 106.4 ± 5.7 | 106.3 ± 4.9 | 105.5 ± 5.7 | 0.025 |
| Sodium, (mEq/L) | 135.2 ± 6.8 | 134.4 ± 10.1 | 135.7 ± 4.1 | 135.5 ± 4.8 | 0.008 |
| Potassium, (mEq/L) | 4.4 ± 0.6 | 4.5 ± 0.6 | 4.4 ± 0.6 | 4.3 ± 0.7 | 0.004 |
| Lactate, (mmol/L) | 3.0 ± 2.1 | 3.4 ± 2.3 | 2.8 ± 1.9 | 2.9 ± 2.1 | < 0.001 |
| WBC, (k/μL) | 14.1 ± 8.4 | 15.3 ± 9.4 | 14.0 ± 8.5 | 12.9 ± 7.0 | < 0.001 |
| Platelet, (k/μL) | 202.5 ± 116.8 | 198.9 ± 114.2 | 206.7 ± 108.7 | 201.9 ± 126.7 | 0.609 |
| APTT | 34.8 ± 12.2 | 36.5 ± 13.8 | 33.8 ± 11.3 | 34.1 ± 11.4 | 0.002 |
| INR | 1.9 ± 1.4 | 2.0 ± 1.7 | 1.7 ± 0.9 | 1.9 ± 1.4 | 0.01 |
| PT | 17.4 ± 6.8 | 18.2 ± 7.2 | 16.7 ± 5.7 | 17.3 ± 7.3 | 0.007 |
| AMI, n (%) | 296 (22.0) | 116 (26.1) | 100 (22.5) | 80 (17.5) | 0.007 |
| Hypertension, n (%) | 484 (35.9) | 169 (38) | 171 (38.4) | 144 (31.4) | 0.049 |
| DM, n (%) | 342 (25.4) | 129 (29) | 107 (24) | 106 (23.1) | 0.096 |
| HF, n (%) | 573 (42.5) | 218 (49) | 179 (40.2) | 176 (38.4) | 0.003 |
| AF, n (%) | 539 (40.0) | 219 (49.2) | 191 (42.9) | 129 (28.2) | < 0.001 |
| CKD, n (%) | 149 (11.1) | 64 (14.4) | 38 (8.5) | 47 (10.3) | 0.017 |
| Stroke, n (%) | 53 (3.9) | 18 (4) | 12 (2.7) | 23 (5) | 0.197 |
| AKI, n (%) | 1195 (88.6) | 412 (92.6) | 384 (86.3) | 399 (87.1) | 0.006 |
| Septic shock, n (%) | 1078 (80.0) | 384(86.3) | 370 (83.1) | 324 (70.7) | < 0.001 |
| Vasopressor, n (%) | 1080 (80.1) | 403 (90.6) | 364 (81.8) | 313 (68.3) | < 0.001 |
| SOFA score | 6.0 (4.0, 9.0) | 7.0 (5.0, 9.0) | 6.0 (4.0, 8.0) | 6.0 (4.0, 9.0) | 0.004 |
| LOS, (days) | 7.1 (3.1, 17.2) | 8.0 (3.4, 18.4) | 5.9 (2.5, 15.2) | 7.7 (3.2, 17.4) | 0.012 |
| 30-day mortality, n (%) | 300 (22.3) | 126 (28.3) | 87 (19.6) | 87 (19) | < 0.001 |
| 1-year mortality, n (%) | 530 (39.3) | 203 (45.6) | 154 (34.6) | 173 (37.8) | 0.002 |

LVSWI: left ventricular stroke work, BMI: Body Mass Index, SOFA: Sequential Organ Failure Assessment, MBP: Mean Blood Pressure, $SpO_2$: Peripheral Oxygen Saturation, CO: Cardiac Output, CI: Cardiac Index, LCWI: Left Cardiac Work Index, SVI: Stroke Volume Index, SVR: Systemic Vascular Resistance, SVRI: Systemic Vascular Resistance Index, CVP: Central Venous Pressure, WBC: White Blood Cell, BUN: Blood Urea Nitrogen, APTT: Activated Partial Thromboplastin Time, INR: International Normalized Ratio, PT: Prothrombin Time, AMI: Acute Myocardial Infarction; DM: Diabetes Mellitus, HF: Heart Failure, AF: Atrial Fibrillation, CKD: Chronic Kidney Disease, AKI: acute kidney injury, LOS: length of stay

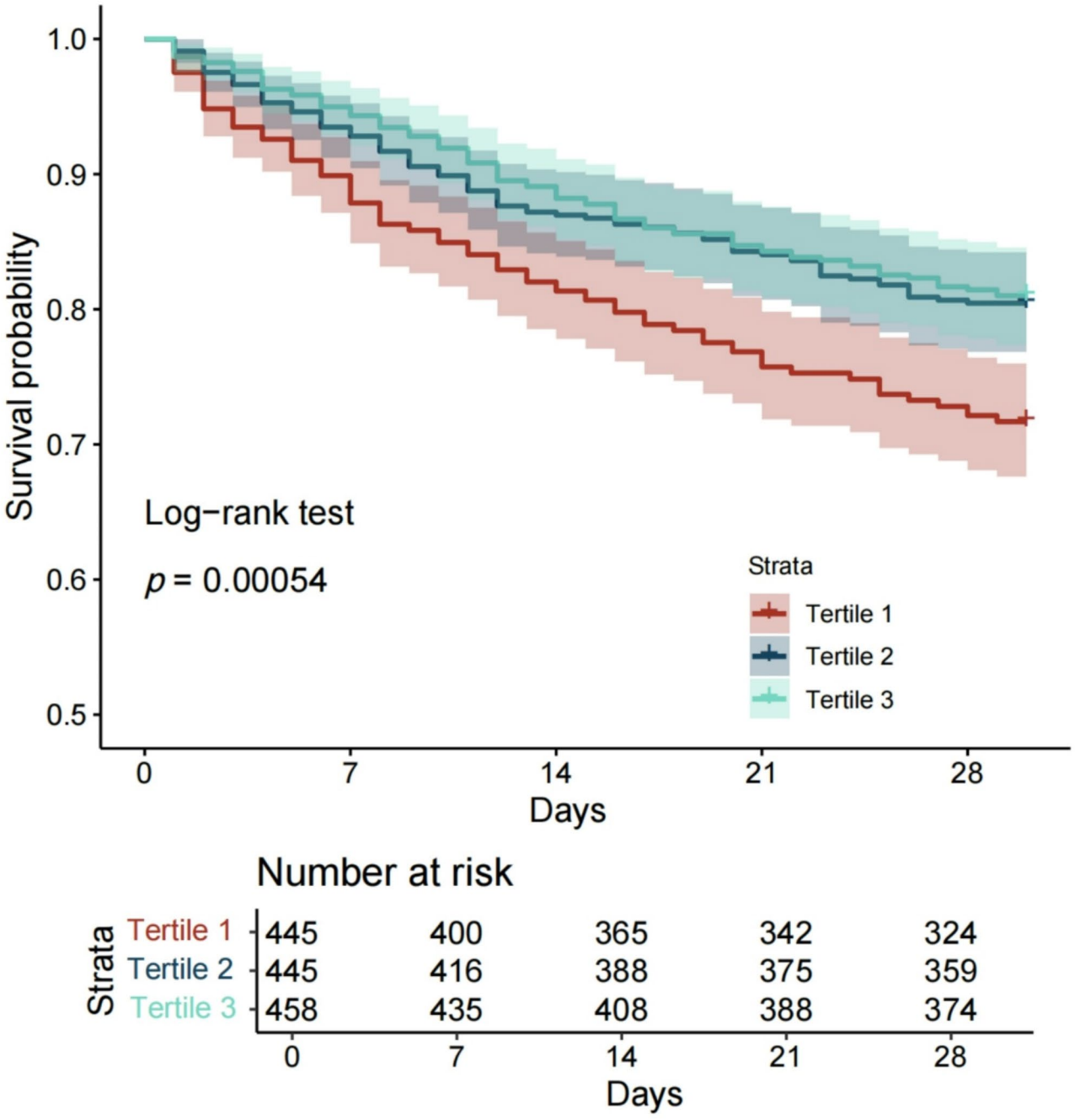


**Fig. 2** Kaplan-Meier survival curve evaluates the association for LVSWI with 30-day mortality. LVSWI: Left Ventricular Stroke Work Index

the left or right ventricles triggered by sepsis, which could occur separately or concurrently [8]. Despite that diagnosis of SCM relies on an evaluation of heart function, the extent to which myocardial dysfunction reflects global organ failure and the extent to which it independently contributes to adverse outcomes has remained ambiguous [24]. LVEF was the primary measure used to evaluate left ventricular systolic function. Two meta-analyses concurrently indicated that LV systolic dysfunction, defined as low LVEF, showed no correlation with mortality in patients with sepsis [12, 25]. Astonishingly, in a study of over a thousand septic patients, Chotalia et al. found that those with a hyperdynamic LVEF (>70%) had a significantly increased 90-day mortality risk compared to those with a normal LVEF (55–70%). This increased risk wasn't observed in the group with a hypodynamic LVEF (<55%) [26]. Paradoxically, in contrast to the previous studies, two subsequent published studies identified a U-shaped relationship between LVEF and sepsis mortality, suggesting that both an excessive increase and decrease in LVEF

**Table 2** Cox regression analysis for 30-day all-cause mortality

| | Model 1 | *p*-value | Model 2 | *p*-value | Model 3 | *p*-value |
|---|---|---|---|---|---|---|
| | HR(95%CI) | | HR(95%CI) | | HR(95%CI) | |
| LVSWI, per SD | 0.79 (0.69–0.9) | 0.001 | 0.85 (0.75–0.97) | 0.014 | 0.69 (0.51–0.93) | 0.016 |
| LVSWI tertiles | | | | | | |
| T1 | 1.0 (Ref) | | 1.0 (Ref) | | 1.0 (Ref) | |
| T2 | 0.65 (0.5–0.86) | 0.002 | 0.67 (0.5–0.92) | 0.012 | 0.77 (0.57–0.95) | 0.016 |
| T3 | 0.63 (0.48–0.82) | 0.001 | 0.65 (0.42–1.01) | 0.013 | 0.76 (0.49–0.98) | 0.038 |
| *p* for trend | | 0.001 | | 0.029 | | 0.027 |

Model 1 was crude model

Model 2 adjusted for age, gender, CVP, SVRI, CI and SVI

Model 3 adjusted for model 2 plus SOFA score, BMI, AMI, hypertension, DM, HF, AF, CKD, stroke, AKI and vasopressor use

could elevate the risk of death [15, 16]. Aside from the small sample sizes, another significant explanation for these paradoxical results could be that LVEF, might not serve as the most accurate indicator of systolic function in sepsis, since its dependency on loading status [24]. As of now, the optimal approach to quantify the severity of septic cardiomyopathy still remains a challenge.

Unlike LVEF, LVSWI integrated both systolic and diastolic functions of the left ventricle. This gives a more comprehensive evaluation of the overall function of the left ventricle, especially in critical care patients where loading conditions were constantly changing [20]. Several studies have highlighted the prognostic value of LVSWI. For instance, in patients with dilated cardiomyopathy and functional mitral regurgitation undergoing mitral valve surgery, LVSWI was identified as the principal predictor for a composite outcome of all-cause mortality, readmission and left ventricular assist device implantation [27]. Similarly, Rico Osteresch al et reported that decreased LVSWI was associated with increased mortality in patients with heart failure subsequent to percutaneous mitral valve repair [28]. Besides, Jentzer and his colleagues identified not only a correlation between LVSWI and prognoses, but also the superiority of LVSWI in discriminating mortality risk compared with LVEF [20, 29]. Furthermore, patients listed for liver transplantation with lower LVSWI had higher mortality risk [30]. In the present study, we assessed 1348 septic patients to elucidate the association between LVSWI levels and mortality and the results showed that compared to other groups, patients in the first tertile notably experienced elevated mortality, after systematically adjusting various potential confounders. Consistent with previous studies, our findings reliably indicated that LVSWI might be a potential prognostic factor.

There's flexibility in calculating the LVSWI, using either systolic blood pressure or mean arterial pressure (MAP), paired with either pulmonary capillary wedge pressure (PCWP) or left ventricular end-diastolic pressure (LVEDP), and factoring in the stroke volume index (SVI) [19, 31]. Existing literatures have affirmed that the parameters were associated with prognosis, thereby substantiating the pronounced correlation observed between LVSWI and outcomes in our analysis. Specifically, episodes of MAP below 60 mmHg can triple the mortality risk of septic patients [32]. PCWP and LVEDP were valuable indicators of left ventricular filling pressure [33], and elevated LV filling pressure was significantly associated with increased mortality in sepsis [34]. Furthermore, SVI could serve as a significant predictor for 30-day mortality in sepsis patients [35].

In our study, we also identified a L-shaped nonlinear relationship between LVSWI and outcomes of septic patients in critical. Alternatively, when LVSWI was the lowest, the risk of sepsis mortality was the highest and as LVSWI levels escalated, the mortality risk dramatically declined. Our results of survival analysis indicated no significant difference in mortality rates among patients within the second to fourth tertiles, which was aligned with the observed L-shaped nonlinear relationship. Based on the LVSWI calculation, a decrease in LVSWI signified either an increase in LVEDP or a decrease in SVI, indicative of diastolic dysfunction or pump failure, both of which were mortality risk factors in sepsis patients [34, 35]. Collectively, effective management of a decrease in LVSWI could markedly lower the risk of death in sepsis patients.

Several limitations in the study must be pointed out. First, due to inherent constraints of this retrospective analysis, causality between LVSWI and mortality cannot be determined. Second, being an observational study, our analysis couldn't completely eliminate the potential for residual, unmeasured, or accidental confounding impacts due to inaccuracies in measurement and variables not considered. Third, most patients enrolled were treated with vasopressors, which possibly augmented LVSWI. Forth, cardiac markers (e.g., myocardial enzymes, troponin and brain natriuretic peptide (BNP)) and cardiac function indicators (e.g., tricuspid annulus systolic plane excursion (TAPSE), global longitudinal strain (GLS), right ventricular stroke work index (RVSWI), LVEF), which

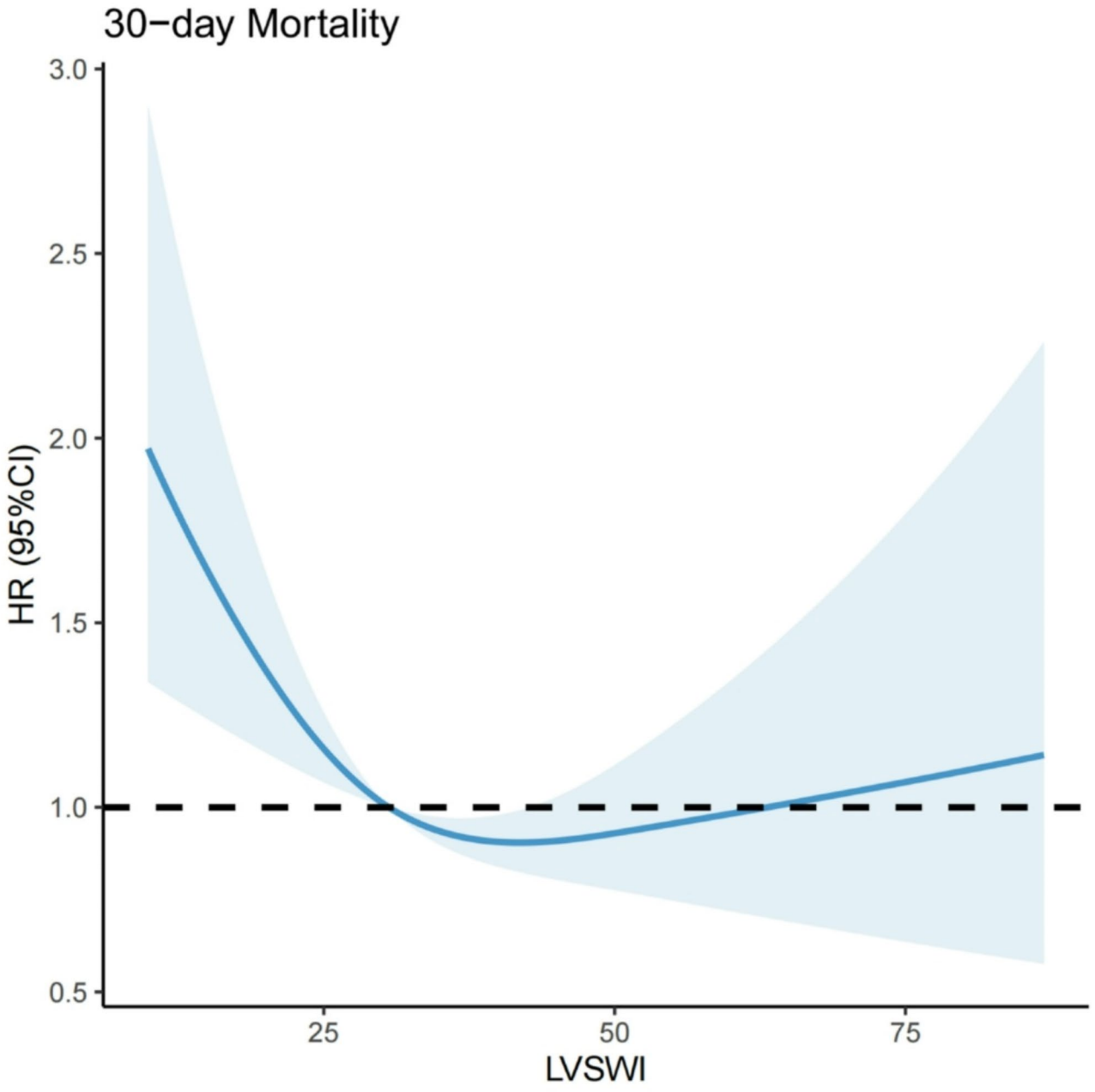


**Fig. 3** Restricted cubic spline analysis. The L-shaped relationship between LVSWI and 30-day mortality. Adjusted factors were age, gender, CVP, SVRI, CI, SVI, SOFA score, BMI, AMI, hypertension, DM, HF, AF, CKD, stroke and AKI. LVSWI: left ventricular stroke work index; CVP, central venous pressure; SVRI, systemic vascular resistance index; CI, cardiac index; SVI, stroke volume index; SOFA, Sequential Organ Failure Assessment; BMI, body mass index; AMI, acute myocardial infarction; DM, diabetes mellitus; HF, heart failure; AF, atrial fibrillation; CKD, chronic kidney disease; AKI, acute kidney injury

**Table 3** Two-piecewise Cox proportional model

| | 30-day mortality | *p* value |
|---|---|---|
| Cutoff value (K) | 27.83 | |
| < K | 0.93 (0.90–0.96) | < 0.001 |
| ≥ K | 1.00 (0.99–1.01) | 0.913 |
| Likelihood Ratio test | | < 0.001 |

had a potential prognostic impact, were not included in our analysis due to unavailability.

## Conclusions

In conclusion, the decreased LVSWI was strongly associated with increased all-cause mortality in patients with sepsis, exhibiting an L-shaped curve as indicated by RCS. The implications of our study hint towards the potential utility of the LVSWI as a prognostic tool for sepsis,

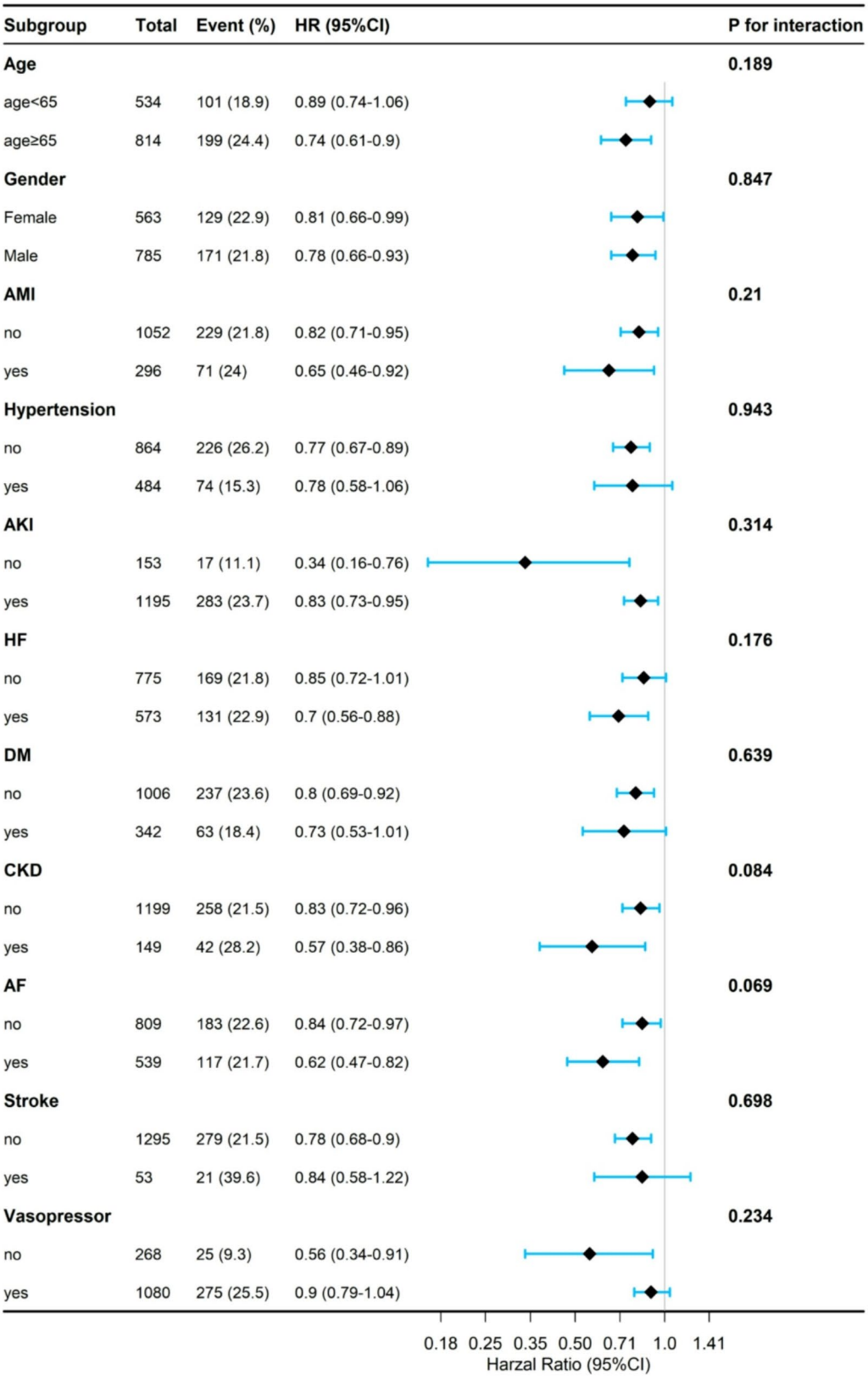


**Fig. 4** Forest plot for subgroup analyses between LVSWI and 30-day mortality. LVSWI: left ventricular stroke work index; SOFA: Sequential Organ Failure Assessment; DM: diabetes mellitus; HF: heart failure; AF: atrial fibrillation

thereby aiding in the early therapeutic intervention for septic patients. Nevertheless, these intriguing findings necessitate further exploration and validation through comprehensive prospective studies.

**Abbreviations**

| | |
|---|---|
| SCM | Sepsis-induced cardiomyopathy |
| LVSWI | Left ventricular stroke work index |
| MIMIC | Medical Information Mart for Intensive Care |
| LVEF | Left ventricular ejection fraction |
| SOFA | Sequential Organ Failure Assessment |

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**Author contributions**
Ming Chen: conceptualization, methodology and editing; Shanping Jiang and Linjie Huang: conceptualization, supervision and editing; Yuewei Li: conceptualization, analysis, visualization and original draft preparation; Zhaolin Li and Shiyi Bu: data curation, analysis, visualization and original draft preparation; Qiujie Wang, Qiaojun Zeng and Weifeng Lin: investigation, software, analysis. All authors reviewed the manuscript."

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**Data availability**
The dataset used in this study is accessible through the MIMIC-III database at https://mimic.physionet.org/. The data referenced in this article can be appropriately requested from the corresponding author.

## Declarations

**Ethics approval and consent to participate**
This study followed Good Clinical Practice (Declaration of Helsinki, 2002). The MIMIC-III database is anonymized and publicly available. Access was granted after one author passed the Protecting Human Research Participants exam (No. 10007248). The project was approved by Massachusetts Institute of Technology (MIT) and Beth Israel Deaconess Medical Center (BIDMC).

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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