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ORIGINAL ARTICLE

Retrospective Study

Incidence, prognosis, and risk factors of sepsis-induced cardiomyopathy

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Abstract

BACKGROUND

At present, large-scale studies on the clinical characteristics of sepsis-induced cardiomyopathy (SIC) are lacking.

AIM

To investigate the clinical characteristics of SIC.

METHODS

Based on the analysis of the MIMIC-III public database, we performed a large-scale retrospective study involving sepsis patients who were admitted to the intensive care unit (ICU) and had no concomitant cardiac disease. We used propensity score matching analysis and multivariate logistic regression to ensure the robustness of the results. The primary outcome was hospital mortality, and the secondary outcomes included the number of patients who received mechanical ventilation or renal replacement therapy during their hospital stay, the number of patients administered with vasopressors, the length of ICU stay, and the length of hospital stay.

RESULTS

In the present study, after screening 38605 patients, 3530 patients with sepsis were included. A total of 997 patients met the SIC diagnostic criteria, and the incidence of SIC was 28.20% (95% confidence interval [CI]: 26.80%-29.70%). Compared to patients in the non-SIC group, patients in the SIC group were of older age and had a higher Simplified Acute Physiology Score (SAPS)-I score, SAPS-II score, and

Elixhauser comorbidity index (ECI). A total of 367 (36.8%) of 997 patients in the SIC group and 818 (32.3%) of 2533 patients in the non-SIC group died in the hospital, which resulted in a significant between-group difference (odds ratios = 1.22, 95%CI: 1.05-1.42; P = 0.011). For the secondary outcomes, more patients in the SIC group received mechanical ventilation and vasopressors. Multivariate logistic regression analysis showed that age, male sex, ECI, hemoglobin level, diabetes, and mechanical ventilation use on the first day of ICU admission were risk factors for SIC.

CONCLUSION

Compared with non-SIC patients, hospital mortality is higher in SIC patients.

Key Words: Sepsis-induced cardiomyopathy; Sepsis; Septic shock; Incidence; Hospital mortality; MIMIC-III

Core Tip: We performed a large-scale, retrospective study to investigate the clinical characteristics of sepsis-induced cardiomyopathy (SIC). Our study showed that the incidence of SIC was 28.20% (95% confidence interval: 26.80%-29.70%). Hospital mortality was higher in SIC patients than in non-SIC patients.

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INTRODUCTION

Sepsis-induced cardiomyopathy (SIC) is a complication of sepsis and septic shock that was first described by Parker *et al*[1,2] in 1984. SIC is characterized by reduced left ventricular ejection fraction (LVEF) and the reduced LVEF could be reversed within 7-10 d in survivors; however, these reversions were less significant in those who died[1,3,4]. The pathologic mechanism of SIC is still unclear, although it is speculated to be related to myocardial inhibitors released by the pathogens and the host, as well as global ischemia after septic distributive shock[5-12].

At present, large-scale studies on the clinical characteristics, such as the incidence, prognosis, and risk factors of SIC, are lacking. A few small studies have been performed to investigate the incidence, risk factors, and mortality of SIC, although these studies demonstrated conflicting results, with the incidence of SIC varying from 13.8%-64%[13-20]. One retrospective cohort study involving 210 adult patients with sepsis or septic shock reported that SIC developed in 13.8% of sepsis patients[14]. Another study screened 67 sepsis patients who had no previous cardiac disease and survived more than 48 h after admission to the intensive care unit (ICU); the results showed that the incidence of SIC within 60 h of ICU admission was 60%[17]. Furthermore, the mortality of patients with SIC varied greatly among the studies, ranging from 24.1%-90%[13-20]. To further investigate the clinical characteristics of SIC, we performed a large-scale, retrospective study.

MATERIALS AND METHODS

This study was performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement[21]. This was a single-center, retrospective study based on the third edition of the MIMIC-III database, which was developed and maintained by the Laboratory for Computational Physiology at MIT [22,23]. The MIMIC-III database is a single-center database including longitudinal data on 38605 patients who were admitted to the ICU of Beth Israel Deaconess Medical Center from 2002 to 2011 for a total of 53423 distinct admissions. This study was

was waived.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest to disclose.

Data sharing statement: The Datasets are available from the corresponding author on reasonable request. The details of the data screening codes for our analyses, which were provided by the authors of the MIMIC-III database, can be found at GitHub (https://github.com/MIT-LCP/mimic-code).

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approved by the ethics committee of Guangzhou Red Cross Hospital (Approval No. AF/SC-107/02.0). As the present study was based on the analysis of MIMIC-III public database, informed consent form was waived.

Patients

We screened the discharge diagnosis of patients in MIMIC-III database by ICD-9 and ICD-10 codes. Adult patients (age ≥ 18 years) who had a discharge diagnosis of sepsis, severe sepsis, or septic shock and were admitted to the ICU of Beth Israel Deaconess Medical Center from 2002 to 2011 in the MIMIC-III database were screened for inclusion.

To exclude the effects of concomitant cardiac disease on cardiac function, in the present study, patients who had a discharge diagnosis of any other cardiac disease, such as acute coronary syndrome, chronic heart dysfunction, severe valvular heart disease, severe cardiac arrhythmia, ischemic heart disease, hypertensive heart disease, congenital heart disease, rheumatic heart disease, myocarditis, infective endocarditis, any other cardiomyopathy (such as hypertrophic cardiomyopathy, dilated cardiomyopathy, restrictive cardiomyopathy, ischemic cardiomyopathy, and stress-induced cardiomyopathy), echocardiographic manifestation of intracardiac thrombus, mass, vegetation, pulmonary hypertension, or echocardiographic evidence of severe basal septal hypertrophy with an outflow gradient, were under age 18, had severe hypoxemia, were pregnant, or had no echocardiography examination were excluded.

SIC diagnosis

The definitions and diagnostic criteria for sepsis, severe sepsis, and septic shock were unchanged between 2002 and 2011, according to the Surviving Sepsis Campaign Guidelines[24-26].

Due to the lack of a gold standard and unified consensus for the diagnosis of SIC at present, referring to the inclusion standard of previous studies[13-20] and international cardiac failure guidelines[27-29], the diagnostic criteria for SIC used in the present study were as follows: (1) The admission and discharge diagnoses including sepsis, severe sepsis or septic shock[24-26]; (2) Existing left ventricular systolic dysfunction with a LVEF < 50% or patients with no LVEF value reported but were reported in the echocardiography data as having global left ventricular hypokinesis or global left ventricular systolic dysfunction, considered to be due to sepsis; and (3) No concomitant cardiac disease by screening the discharge diagnosis of patients in the MIMIC-III database by ICD-9 and ICD-10 codes.

Data collection

The following demographic data and admission information were collected: Age, gender, weight, height, body surface area (BSA), body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate, respiratory rate, temperature, Simplified Acute Physiology Score-I (SAPS-I), SAPS-II, Sequential Organ Failure Assessment (SOFA), Elixhauser comorbidity index (ECI), admission type (emergency or elective), and sepsis type (sepsis, severe sepsis, or septic shock).

Additionally, data regarding the use of mechanical ventilation (MV) or renal replacement therapy (RRT) within the first day of ICU admission were collected.

Microbiology events were recorded and the following laboratory results were also collected: White blood cell (WBC) count, hemoglobin, blood platelet count (PLT), serum potassium, serum sodium, serum chloride, serum bicarbonate, pH, partial pressure of carbon dioxide, partial pressure of oxygen, and lactate value. The maximum levels of blood creatinine, blood urea nitrogen (BUN), cardiac troponin T, creatinine kinase (CK), and creatine kinase-MB (CK-MB) during hospital stay were also collected.

Comorbidities

We recorded the chronic comorbidities of our study cohort. The MIMIC-III database contains over 15693 different diagnoses classified by ICD 9 and ICD 10 codes. For describing chronic diseases more concisely, we used Elixhauser's comorbidity classification[30] according to an algorithm provided by the authors of the MIMIC-III database[31]. Chronic diseases can effectively be reflected by the Elixhauser comorbidity classification, and they have been validated for both ICD-9 and ICD-10 codes[32].

Primary and secondary outcomes

The primary outcomes were SIC incidence rate and hospital mortality rate, and the secondary outcomes included the number of patients who received MV or RRT during their hospital stay, the number of patients administered vasopressors (including norepinephrine, dopamine, epinephrine, and vasopressin), the length of ICU stay, and the length of hospital stay.

Statistical analysis

The details of the data screening strategies used are shown in the Supplementary File. Other source codes for our analyses, which were provided by the authors of the MIMIC-III database, can be found at GitHub[31,33]. Categorical variables including demographic data, admission information, and interventions are shown as frequencies, and continuous variables including vital signs and laboratory parameters are presented as the mean ± SD or median with interquartile range (25%, 75%). We used the analysis of variance or non-parametric tests to analyze continuous variables as appropriate. Categorical variables were analyzed using Pearson's χ^2 test or Fisher's exact test.

We used binary multivariate logistic regression analysis (method: forward, LR) to analyze the risk factors for SIC. Variables with P values < 0.10 between groups, or if the variables could complicate the relationships of outcomes in biology, or if the variables were previously considered to be potential confounders were included in the logistic regression analysis model. The risk factors selected by multivariate logistic regression analysis are expressed as odds ratios (ORs) and 95% confidence intervals [CIs].

As some variables are missing a moderate amount of data, a complete case analysis in multivariable logistic regression analysis will exclude any patient with a single missing datapoint which will lead to a significant selection bias. Hence, multiple imputation strategies are used to overcome this deficit in the multivariate logistic regression analysis.

Sensitivity analysis

For the primary outcome of hospital mortality, in order to ensure the robustness of our results, we used the propensity score matching (PSM) method to adjust and balance the influence of confounding factors between groups. Variables that may be related to the incidence of SIC were included. Each SIC patient was matched with a non-SIC patient at a proportion of 1:1 with the closest propensity score. The matching tolerance was 0.02.

Subgroup analysis

We also performed subgroup analyses to further investigate whether the primary outcome with regards to hospital mortality differed among the subgroups. The subgroups included age (< 60 years; ≥ 60 years), BMI (≥ 28 kg/m^2; < 28 kg/m^2), gender, SOFA score (≥ 2 points; < 2 points), SBP (≥ 90 mmHg; < 90 mmHg), MAP (< 65 mmHg; ≥ 65 mmHg), and use of MV or RRT in the first day of ICU admission.

We used PostgreSQL 10.0 software (University of California, Berkeley, California, USA) and Navicat premium 12.0 software (premiumSoft Cybertech Ltd, Kowloon, Hong Kong, China) for database management and data retrieval and screening; SPSS 23.0 software (IBM Corp., Armonk, NY, United States) was used for statistical analyses. P < 0.05 was considered to indicate statistical significance.

RESULTS

Initially, 38605 patients in the MIMIC-III database were screened for eligibility, and 6011 records were included. After removing duplicate records or readmissions to the ICU, 3622 sepsis patients were left. We further screened the echocardiography reports, and 92 patients were removed due to too much missing data, being difficult to assess left ventricle systolic function, severe valvular disease, severe cardiac arrhythmia, or pulmonary hypertension. Ultimately, 3530 patients were included in the present study (Figure 1). According to the presence or absence of SIC, the patients were divided into an SIC group or a non-SIC group. In total, there were 997 patients in the SIC group and 2533 patients in the non-SIC group. The SIC incidence rate was 28.20% (95%CI: 26.80%-29.70%). Of the included patients, 3044 were reported with the explicit LVEF value, 484 in the SIC group with no explicit LVEF value were reported with global left

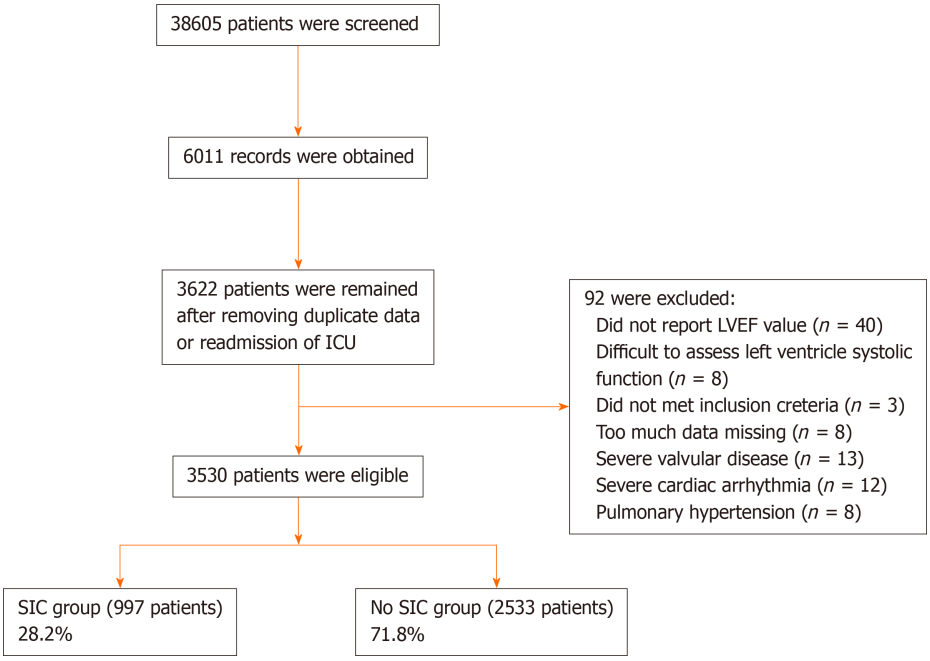

Figure 1 Study screening and selection process. ICU: Intensive care unit; LVEF: Left ventricular ejection fraction; SIC: Sepsis-induced cardiomyopathy.

ventricular hypokinesis, or global left ventricular systolic dysfunction, and 2 in the non-SIC group were reported with normal cardiac index.

The clinical characteristics and laboratory results of the included patients are shown in Table 1. There were more male patients in the SIC group compared with those in the non-SIC group (634/997 patients, 63.6% *vs* 1383/2533 patients, 54.6%, $P < 0.001$). Compared to patients in the non-SIC group, patients in the SIC group had a significant older age (68.42 ± 15.21 years *vs* 64.46 ± 15.39 years, $P < 0.001$), higher SAPS-I score (21.40 ± 5.36 *vs* 20.90 ± 5.47, $P = 0.013$), SAPS-II score (46.57 ± 14.86 *vs* 44.09 ± 15.43, $P < 0.001$), and ECI score (15.30 ± 8.73 *vs* 13.76 ± 8.97, $P < 0.001$), and lower SBP (108.20 ± 14.05 mmHg *vs* 111.42 ± 14.89 mmHg, $P < 0.001$). Patients in both groups had similar BSA (1.86 ± 0.45 m^2 *vs* 1.88 ± 0.45 m^2, $P = 0.224$) and BMI (28.85 ± 13.46 kg/m^2 *vs* 29.24 ± 8.77 kg/m^2, $P = 0.345$), temperature (36.84 ± 0.79°C *vs* 36.88 ± 0.77°C, $P = 0.267$), MAP (72.61 ± 10.15 mmHg *vs* 73.20 ± 10.22 mmHg, $P = 0.130$), and SOFA score (7.02 ± 3.71 *vs* 6.89 ± 3.88, $P = 0.342$) (Table 1).

There were no significant differences between two groups with regard to RRT use (249/2533 patients *vs* 120/997 patients, $P = 0.054$) and MV use (1232/2533 patients *vs* 516/997 patients, $P = 0.095$) in the first day of ICU admission. The culture positive rates of microbiology samples were similar between the two groups (1387/2533 patients *vs* 560/997 patients, $P = 0.448$) (Table 1).

Compared with the non-SIC group, there were more severe sepsis patients (567/997 patients *vs* 1315/2533 patients, $P = 0.003$), and more emergency admission to ICU patients in the SIC group (960/997 patients *vs* 2396/2533 patients, $P = 0.036$) (Table 1). In terms of comorbidities, patients in the SIC group had more renal failure (324/997 patients *vs* 614/2533 patients, $P < 0.001$), diabetes (424/997 patients *vs* 809/2533 patients, $P < 0.001$), and less liver failure (960/997 patients *vs* 2396/2533 patients, $P < 0.001$) compared with non-SIC patients.

Laboratory tests results

Patients in the SIC group had similar WBC count (15.93 ± 9.65 × 10^9/L *vs* 16.50 ± 12.92 × 10^9/L, $P = 0.206$) and PLT count (199.63 ± 124.20 × 10^9/L *vs* 195.01 ± 137.10 × 10^9/L, $P = 0.356$), but a higher hemoglobin level (9.57 ± 1.81 g/dL *vs* 9.37 ± 1.88 g/dL, $P = 0.004$) compared with those in the non-SIC group. There were no significant differences with regard to the serum sodium level, potassium level, and chloride level (Table 1).

Compared with patients in the non-SIC group, patients in the SIC group had a higher creatine level (2.38 ± 2.02 mg/dL *vs* 2.21 ± 2.08 mg/dL, $P = 0.023$), BUN level (43.79 ± 27.74 mg/dL *vs* 39.02 ± 27.97 mg/dL, $P < 0.001$), lactate level (3.59 ± 3.16 mmol/L *vs* 3.30 ± 2.77 mmol/L, $P < 0.001$), and blood glucose level (146.09 ± 51.54 mg/dL *vs* 140.88 ± 46.90 mg/dL, $P = 0.023$) (Table 1).

Table 1 Baseline demographic data and clinical characteristics of patients included in the study

Covariate	Original patients (before matching)			PSM adjusted patients (after matching)			Missing data (%)
	Non-SIC (*n* = 2533)	SIC (*n* = 997)	*P* value	Non-SIC (*n* = 809)	SIC (*n* = 809)	*P* value	
Age (yr)	64.46 ± 15.39	68.42 ± 15.21	0.000	68.06 ± 14.34	67.86 ± 15.37	0.791	0.0
Gender (Male), *n* (%)	1383 (54.6)	634 (63.6)	0.000	513 (63.4)	510 (63.0)	0.877	0.0
Height (cm)	169.22 ± 10.52	169.74 ± 12.16	0.236	169.34 ± 10.74	169.74 ± 11.28	0.466	12.1
Weight (kg)	84.19 ± 27.24	81.91 ± 25.49	0.027	80.74 ± 23.35	82.21 ± 26.16	0.233	6.2
BSA (m^2)	1.88 ± 0.45	1.86 ± 0.45	0.224	1.91 ± 0.33	1.93 ± 0.36	0.218	12.6
BMI (kg/m^2)	29.24 ± 8.77	28.85 ± 13.46	0.345	28.14 ± 7.69	28.59 ± 9.58	0.295	12.6
Temperature (°C)	36.88 ± 0.77	36.84 ± 0.79	0.267	37.02 ± 0.79	36.85 ± 0.76	0.000	2.1
SBP (mmHg)	111.42 ± 14.89	108.20 ± 14.05	0.000	110.55 ± 15.17	108.69 ± 14.21	0.011	1.6
DBP (mmHg)	57.60 ± 10.08	57.69 ± 10.09	0.821	59.18 ± 10.22	57.90 ± 9.99	0.011	1.6
MAP (mmHg)	73.20 ± 10.22	72.61 ± 10.15	0.130	75.09 ± 10.52	72.68 ± 9.96	0.000	1.5
HR (beats min^{-1})	91.97 ± 17.38	92.32 ± 17.10	0.594	91.50 ± 17.23	92.41 ± 17.27	0.289	1.5
RR (min^{-1})	21.20 ± 4.73	21.15 ± 4.45	0.789	21.32 ± 4.64	21.20 ± 4.46	0.572	1.5
SpO_2 (%)	96.84 ± 2.70	96.91 ± 2.92	0.458	96.75 ± 3.02	96.91 ± 2.75	0.269	1.6
SOFA score	6.89 ± 3.88	7.02 ± 3.71	0.342	6.86 ± 3.72	6.99 ± 3.72	0.496	0.0
SAPS-I score	20.90 ± 5.47	21.40 ± 5.36	0.013	22.03 ± 5.32	21.29 ± 5.27	0.005	0.0
SAPS-II score	44.09 ± 15.43	46.57 ± 14.86	0.000	46.15 ± 15.18	46.32 ± 15.00	0.825	0.0
ECI	13.76 ± 8.97	15.30 ± 8.73	0.000	14.56 ± 8.63	15.20 ± 8.83	0.142	0.0
Microbiology, *n* (%)							
Positive	1387 (54.8)	560 (56.2)	0.448	463 (57.2)	453 (56.0)	0.616	0.0
Negative	1146 (45.2)	437 (43.8)		346 (42.8)	356 (44.0)		
Interventions, *n* (%)							
Renal replacement use (1^{st} d)	249 (9.8)	120 (12.0)	0.054	81 (10.0)	98 (12.1)	0.178	0.0
Mechanical ventilation use (1^{st} d)	1232 (48.6)	516 (51.8)	0.095	341 (42.2)	414 (51.2)	0.000	0.0
Comorbidities, *n* (%)							
Renal failure	614 (24.2)	324 (32.5)	0.000	282 (34.9)	249 (30.8)	0.081	0.0
Liver failure	418 (16.5)	74 (7.4)	0.000	17 (2.1)	71 (8.8)	0.000	0.0
Diabetes	809 (31.9)	424 (42.5)	0.000	337 (41.7)	333 (41.2)	0.840	0.0
COPD	552 (21.8)	195 (19.6)	0.144	186 (23.0)	162 (20.0)	0.146	0.0
Coagulopathy	869 (34.3)	317 (31.8)	0.155	283 (35.0)	255 (31.5)	0.140	0.0
Admission type, *n* (%)							
Emergency	2396 (94.6)	960 (96.3)	0.036	780 (96.4)	785 (97.0)	0.485	0.0
Elective	137 (5.4)	37 (3.7)		29 (3.6)	24 (3.0)		0.0
Sepsis type, *n* (%)							
Sepsis	548 (21.6)	168 (16.9)	0.003	174 (21.5)	143 (17.7)	0.064	0.0
Severe sepsis	1315 (51.9)	567 (56.9)		411 (50.8)	454 (56.1)		0.0
Septic shock	670 (26.5)	262 (26.3)		224 (27.7)	212 (26.2)		0.0
Laboratory tests							
WBC (10^9/L)	16.50 ± 12.92	15.93 ± 9.65	0.206	17.15 ± 12.94	15.61 ± 9.17	0.006	0.3

Hemoglobin (g/dL)	9.37 ± 1.88	9.57 ± 1.81	0.004	9.42 ± 1.91	9.57 ± 1.79	0.099	0.3
Platelet (10^9/L)	195.01 ± 137.10	199.63 ± 124.20	0.356	202.55 ± 139.20	200.23 ± 125.24	0.725	0.2
Sodium (mmol/L)	139.96 ± 5.62	140.04 ± 5.17	0.705	139.92 ± 5.59	140.02 ± 5.20	0.695	0.1
Potassium (mmol/L)	3.78 ± 0.62	3.82 ± 0.60	0.064	3.76 ± 0.63	3.81 ± 0.61	0.094	0.1
Chloride (mmol/L)	102.19 ± 7.57	102.09 ± 6.80	0.716	101.71 ± 7.25	102.25 ± 6.78	0.117	0.1
BUN (mg/dL)	39.02 ± 27.97	43.79 ± 27.74	0.000	40.22 ± 27.95	42.90 ± 27.39	0.052	0.2
Creatine (mg/dL)	2.21 ± 2.08	2.38 ± 2.02	0.023	2.43 ± 2.26	2.33 ± 2.04	0.389	0.1
Lactate (mmol/L)	3.30 ± 2.77	3.59 ± 3.16	0.012	3.20 ± 2.55	3.46 ± 3.01	0.074	14.5
Albumin (g/dL)	2.68 ± 0.67	2.78 ± 0.60	0.001	2.71 ± 0.66	2.76 ± 0.60	0.196	39.3
Bilirubin (mg/dL)	3.69 ± 7.35	1.82 ± 3.58	0.000	2.70 ± 5.50	1.78 ± 3.57	0.001	25.6
PH	7.34 ± 0.11	7.34 ± 0.11	0.358	7.34 ± 0.10	7.34 ± 0.11	0.592	27.3
PO_2 (mmHg)	132.70 ± 86.45	140.77 ± 92.91	0.037	128.11 ± 81.34	136.85 ± 90.36	0.081	27.2
PCO_2 (mmHg)	41.20 ± 14.08	39.92 ± 11.76	0.030	40.70 ± 14.25	39.81 ± 11.62	0.239	27.3
Bicarbonate (mmol/L)	20.74 ± 5.61	20.32 ± 5.34	0.042	20.35 ± 5.49	20.32 ± 5.18	0.916	0.1
Glucose (mg/dl)	140.88 ± 46.90	146.09 ± 51.54	0.004	145.48 ± 48.58	144.89 ± 48.96	0.808	1.6
CK-MB (%)	6.83 ± 6.87	5.82 ± 6.00	0.063	6.87 ± 7.11	5.40 ± 5.64	0.037	80.7
CK (U/L)	68.00 (31.00-194.00)	74.50 (32.00-229.00)	0.374	66.50 (30.00-212.25)	76.00 (32.00-269.00)	0.382	24.9
Troponin T (ng/mL)	0.33 ± 1.06	0.38 ± 1.24	0.319	0.41 ± 1.41	0.39 ± 1.25	0.814	34.0

Data shown are the mean ± SD, median (interquartile), or *n* (%). The definitions and diagnostic criteria for sepsis, severe sepsis, and septic shock were made according to the Surviving Sepsis Campaign Guidelines[24,25]. SIC: Sepsis-induced cardiomyopathy; PSM: Propensity score matching; BSA: Body surface area; BMI: Body mass index; SOFA: Sequential organ failure assessment, ranging from 0 to 24, with higher scores indicating a greater degree of organ failure; ECI: Elixhauser comorbidity index, and we used the modified van Walraven Elixhauser comorbidity score in our study, which consists of 30 comorbidity diseases, ranges from -19 to 89 points, with higher scores indicating a greater risk of hospital mortality; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; HR: Heart rate; RR: Respiratory rate; SAPS-I: Simplified acute physiologic score-I; SAPS-II: Simplified acute physiologic score-II; ICU: Intensive care unit; COPD: Chronic obstructive pulmonary disease; WBC: White blood cell; PCO_2: Partial pressure of carbon dioxide; PO_2: Partial pressure of oxygen; BUN: Blood urea nitrogen.

There were no significant differences with regard to CK, CK-MB, and troponin T levels between the two groups. However, there were a large number of missing values for CK, CK-MB, and troponin T (Table 1). The results should be interpreted with great caution.

Primary outcome and PSM analysis

For the primary outcome of hospital mortality, 367 (36.8%) of 997 patients in the SIC group and 818 (32.3%) of 2533 patients in the non-SIC group died in the hospital, which resulted in a significant between-group difference (OR = 1.22, 95%CI: 1.05-1.42; P = 0.011) (Table 2).

In order to test the robustness of the primary outcomes, PSM analysis was performed. The variables included in PSM are as follows: Age, gender, height, weight, BSA, BMI, SBP, MAP, SOFA score, SAPS-I score, SAPS-II score, ECI, sepsis type, admission type, diabetes, renal failure, liver failure, hemoglobin, BUN, creatine, and lactate. When the baseline demographic data and clinical characteristics were adjusted, results were consistent with the overall findings. The propensity score matched hospital mortality rates for the SIC group and non-SIC group were 35.4% (286/809 patients) *vs* 30.0% (243/809 patients). The adjusted OR was 1.27 (95%CI: 1.03-1.57, P = 0.023) (Table 2).

Subgroup analyses for primary outcomes

Subgroup analyses with regard to hospital mortality according to gender, age (≥ 60 years, < 60 years), BMI (≥ 28 kg/m^2, < 28 kg/m^2), SOFA score (≥ 2 points, < 2 points), SBP (≥ 90 mmHg, < 90 mmHg), MAP (≥ 65 mmHg, < 65 mmHg), and MV and RRT use in the first day of ICU admission revealed that the patients in the SIC group with a BMI ≥ 28 kg/m^2, or SOFA score ≥ 2 points, SBP ≥ 90 mmHg, MAP ≥ 65 mmHg, no RRT use in the first day of ICU admission, or female gender had a higher risk of hospital

Table 2 Comparison of primary and secondary outcomes, *n* (%)

Outcome	Original patients (before matching)				PSM adjusted patients (after matching)			
	Non-SIC (*n* = 2533)	SIC (*n* = 997)	OR (95%CI)	*P* value	Non-SIC (*n* = 809)	SIC (*n* = 809)	OR (95%CI)	*P* value
Hospital mortality	818 (32.3)	367 (36.8)	1.22 (1.05-1.42)	0.011	243 (30.0)	286 (35.4)	1.27 (1.03-1.57)	0.023
Mechanical ventilation use	1478 (58.3)	619 (62.1)	1.17 (1.01-1.36)	0.042	431 (53.3)	500 (61.8)	1.42 (1.16-1.73)	0.001
RRT use	290 (11.4)	116 (11.6)	1.02 (0.81-1.28)	0.876	91 (11.2)	94 (11.6)	1.04 (0.76-1.41)	0.815
Norepinephrine use	1276 (50.4)	589 (59.1)	1.42 (1.23-1.65)	0.000	433 (53.5)	474 (58.6)	1.23 (1.01-1.50)	0.040
Epinephrine use	63 (2.5)	62 (6.2)	2.59 (1.81-3.70)	0.000	25 (3.1)	46 (5.7)	1.88 (1.14-3.09)	0.012
Dopamine use	279 (11.0)	188 (18.9)	1.88 (1.54-2.30)	0.000	105 (13.0)	141 (17.4)	2.08 (1.08-1.86)	0.013
Vasopressin use	508 (20.1)	258 (25.9)	1.39 (1.17-1.65)	0.000	178 (22.0)	206 (25.5)	1.21 (0.96-1.52)	0.102
Length of ICU stay (d)								
Overall	9.25 ± 11.66	9.11 ± 11.33	NA	0.749	9.35 ± 12.00	8.69 ± 9.74	NA	0.222
Survivors	8.82 ± 12.00	8.70 ± 11.77		0.827	8.71 ± 11.85	8.25 ± 9.55		0.479
Non-Survivors	10.15 ± 10.85	9.81 ± 10.51		0.616	10.82 ± 12.24	9.49 ± 10.03		0.167
Length of hospital stay (d)								
Overall	24.83 ± 26.05	21.45 ± 20.84	NA	0.000	23.38 ± 23.01	21.22 ± 19.46	NA	0.042
Survivors	23.71 ± 23.69	21.92 ± 20.28		0.093	21.62 ± 19.17	21.40 ± 17.13		0.844
Non-Survivors	27.19 ± 30.29	20.61 ± 21.75		0.000	27.44 ± 29.69	20.84 ± 23.13		0.004

Vasopressor use including the use of norepinephrine, epinephrine, dopamine, or vasopressin. SIC: Sepsis-induced cardiomyopathy; PSM: Propensity score matching; RRT: Renal replacement therapy; ICU: Intensive care unit; NA: Not available.

death. However, there are no significant interactions between subgroups, and further studies are needed with respect to these aspects (Figure 2).

Secondary outcomes

Before PSM, more patients in the SIC group received MV (619/997patients *vs* 1478/2533 patients; OR = 1.17, 95%CI: 1.01-1.36; $P = 0.042$) compared with patients in the non-SIC group. Furthermore, the proportion of each commonly used vasoactive medication in the SIC group was significantly higher than that in the non-SIC group, including norepinephrine (589/997 patients *vs* 1276/2533 patients, OR = 1.42, 95%CI: 1.23-1.65; $P < 0.001$), dopamine (188/997 patients *vs* 279/2533 patients, OR = 1.88, 95%CI: 1.54-2.30; $P < 0.001$), epinephrine (62/997 patients *vs* 63/2533 patients, OR = 2.59, 95%CI: 1.81-3.70; $P < 0.001$), and vasopressin (258/997 patients *vs* 508/2533 patients, OR = 1.39, 95%CI: 1.17-1.65; $P < 0.001$). No significant differences were observed between the two groups for the use of RRT and length of ICU stay (Table 2).

It is interesting that the length of hospital stay was shorter in SIC group patients compared with those in the non-SIC group (21.45 ± 20.84 d *vs* 24.83 ± 26.05 d, $P < 0.001$). This may be due to the fact that non-survivors died earlier in the SIC group compared to the non-SIC group (20.61 ± 21.75 d *vs* 27.19 ± 30.29 d, $P < 0.001$) (Table 2).

These results were consistent after PSM analysis except for vasopressin use.

Survivors and non-survivors in SIC group

We also analyzed the clinical characteristics between survivors and non-survivors in the SIC group. The results showed that both groups differed in many aspects (Table 3). Compared with the surviving group, the non-surviving group of SIC patients were older (70.42 ± 13.97 years *vs* 67.26 ± 15.80 years, $P = 0.002$), had a lower temperature (36.74 ± 0.88°C *vs* 36.90 ± 0.73°C, $P = 0.002$), SpO_2 (96.43 ± 3.60% *vs* 97.19 ± 2.40%, $P < 0.001$), SBP (105.59 ± 14.34 mmHg *vs* 109.72 ± 13.65 mmHg, $P < 0.001$), DBP (56.53 ± 10.70 mmHg *vs* 58.36 ± 9.67 mmHg, $P = 0.006$), and MAP (71.41 ± 10.91 mmHg *vs* 73.32 ± 9.62 mmHg, $P = 0.005$), had a higher SOFA score (8.29 ± 3.91 *vs* 6.28 ± 3.38, $P < 0.001$), SAPS-I score (23.19 ± 5.66 *vs* 20.37 ± 4.89, $P < 0.001$), SAPS-II score (52.87 ± 14.94 *vs* 42.90 ± 13.54, $P < 0.001$), and ECI score (16.92 ± 8.93 *vs* 14.36 ± 8.47, $P < 0.001$).

Table 3 Baseline demographic data and clinical characteristics of patients with sepsis-induced cardiomyopathy

Covariate	Survivors (*n* = 630)	Non-survivors (*n* = 367)	*P* value	Missing data (%)
Age (yr)	67.26 ± 15.80	70.42 ± 13.97	0.002	0
Gender (Male), *n* (%)	402 (63.8)	232 (63.2)	0.851	0
Height (cm)	169.92 ± 12.52	169.44 ± 11.51	0.575	12.4
Weight (kg)	83.44 ± 26.22	79.15 ± 23.91	0.014	6.7
BSA (m^2)	1.88 ± 0.46	1.83 ± 0.43	0.128	12.8
BMI (kg/m^2)	29.38 ± 15.02	27.92 ± 10.06	0.124	12.8
Temperature (°C)	36.90 ± 0.73	36.74 ± 0.88	0.002	2.9
SBP (mmHg)	109.72 ± 13.65	105.59 ± 14.34	0	1.9
DBP (mmHg)	58.36 ± 9.67	56.53 ± 10.70	0.006	1.9
MAP (mmHg)	73.32 ± 9.62	71.41 ± 10.91	0.005	1.8
HR (beats/min)	91.36 ± 16.88	93.95 ± 17.38	0.022	1.8
RR (/min)	20.98 ± 4.33	21.44 ± 4.65	0.119	1.8
SpO_2 (%)	97.19 ± 2.40	96.43 ± 3.60	0	2
SOFA score	6.28 ± 3.38	8.29 ± 3.91	0	0
SAPS-I score	20.37 ± 4.89	23.19 ± 5.66	0	0
SAPS-II score	42.90 ± 13.54	52.87 ± 14.94	0	0
ECI	14.36 ± 8.47	16.92 ± 8.93	0	0
Microbiology, *n* (%)				
Positive	354 (56.2)	206 (56.1)	0.985	0
Negative	276 (43.8)	161 (43.9)		
Interventions, *n* (%)				
Renal replacement use (1^{st} 24 h)	69 (11.0)	51 (13.9)	0.168	0
Mechanical ventilation use (1^{st} 24 h)	296 (47.0)	220 (59.9)	0	0
Comorbidities, *n* (%)				
Renal failure	189 (30.0)	135 (36.8)	0.027	0
Liver failure	46 (7.3)	28 (7.6)	0.849	0
Diabetes	272 (43.2)	152 (41.4)	0.588	0
COPD	117 (18.6)	78 (21.3)	0.303	0
Coagulopathy	172 (27.3)	145 (39.5)	0	0
Admission type, *n* (%)				
Emergency	608 (96.5)	352 (95.9)	0.632	0
Elective	22 (3.5)	15 (4.1)		0
Sepsis type, *n* (%)				
Sepsis	143 (22.7)	25 (6.8)	0	0
Severe sepsis	336 (53.3)	231 (62.9)		0
Septic shock	151 (24.0)	111 (30.2)		0
Laboratory tests				
WBC ($10^9/L$)	15.88 ± 9.23	16.03 ± 10.36	0.809	0.1
Hemoglobin (g/dL)	9.56 ± 1.84	9.59 ± 1.76	0.812	0.2
Platelet ($10^9/L$)	214.36 ± 127.73	174.26 ± 113.66	0	0.1

Sodium (mmol/L)	140.05 ± 4.93	140.03 ± 5.58	0.965	0
Potassium (mmol/L)	3.78 ± 0.61	3.88 ± 0.59	0.018	0
Chloride (mmol/L)	102.26 ± 6.58	101.78 ± 7.18	0.287	0.1
BUN (mg/dL)	39.46 ± 24.07	51.24 ± 31.80	0	0.2
Creatine (mg/dL)	2.23 ± 1.94	2.63 ± 2.13	0.003	0.2
Lactate (mmol/L)	2.98 ± 2.12	4.62 ± 4.19	0	14.1
Albumin (g/dL)	2.83 ± 0.58	2.69 ± 0.61	0.004	39.8
Bilirubin (mg/dL)	1.49 ± 3.16	2.34 ± 4.10	0.002	26.8
PH	7.35 ± 0.11	7.32 ± 0.12	0.001	26.3
PO_2 (mmHg)	142.73 ± 93.83	137.98 ± 91.67	0.495	26.3
PCO_2 (mmHg)	40.36 ± 10.79	39.30 ± 13.01	0.23	26.3
Bicarbonate (mmol/L)	21.01 ± 5.00	19.13 ± 5.69	0	0.1
Glucose (mg/dL)	144.45 ± 47.67	148.89 ± 57.53	0.193	1.8
CK-MB (%)	5.73 ± 5.64	6.00 ± 6.73	0.767	78.5
CK (U/L)	413.37 ± 1425.54	313.84 ± 842.98	0.284	22.4
Troponin (ng/mL)	0.42 ± 1.41	0.31 ± 0.87	0.264	33.4
Outcomes, *n* (%)				
Mechanical ventilation use	343 (54.4)	276 (75.2)	0	0
RRT use	44 (7.0)	72 (19.6)	0	0
Norepinephrine use	322 (51.1)	267 (72.8)	0	0
Epinephrine use	27 (4.3)	35 (9.6)	0.001	0
Dopamine use	94 (14.9)	94 (25.6)	0	0
Vasopressin use	95 (15.1)	163 (44.4)	0	0
Length of ICU stay (d)	8.71 ± 11.77	9.81 ± 10.51	0.138	0
Length of hospital stay (d)	21.94 ± 20.29	20.61 ± 21.75	0.332	0

Data shown are the mean ± SD or *n* (%). The definitions and diagnostic criteria for sepsis, severe sepsis, and septic shock were made according to the Surviving Sepsis Campaign Guidelines[24,25]. BSA: Body surface area; BMI: Body mass index; SOFA: Sequential organ failure assessment, ranging from 0 to 24, with higher scores indicating a greater degree of organ failure ; ECI: Elixhauser comorbidity index, and we used the modified van Walraven Elixhauser comorbidity score in our study, which consists of 30 comorbidity diseases and ranges from -19 to 89 points, with higher scores indicating a greater risk of hospital mortality; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; HR: Heart rate; RR: Respiratory rate; SAPS-I: Simplified acute physiologic score-I; SAPS-II: Simplified acute physiologic score-II; ICU: Intensive care unit; COPD: Chronic obstructive pulmonary disease; WBC: White blood cell; PCO_2: Partial pressure of carbon dioxide; PO_2: Partial pressure of oxygen; BUN: Blood urea nitrogen.

Additionally, compared to survivors in the SIC group, a higher proportion of non-surviving SIC patients received MV in the first day of ICU admission (220/367 patients *vs* 296/630 patients, $P < 0.001$). And the non-surviving group of SIC patients had more comorbidities of renal failure (135/367 patients *vs* 189/630 patients, $P < 0.001$) and coagulopathy (145/367 patients *vs* 172/630 patients, $P < 0.001$), a lower platelet count (174.26 ± 113.66×10^9/L *vs* 214.36 ± 127.73×10^9/L, $P = 0.000$) and albumin level (2.69 ± 0.61 g/dL *vs* 2.83 ± 0.58 g/dL, $P = 0.004$), and a higher creatine level (2.63 ± 2.13 mg/dL *vs* 2.23 ± 1.94 mg/dL, $P = 0.003$), BUN level (51.24 ± 31.80 mg/dL *vs* 39.46 ± 24.07 mg/dL, $P < 0.001$), lactate level (4.62 ± 4.19 mmol/L *vs* 2.98 ± 2.12 mmol/L, $P < 0.001$), and bilirubin level (2.34 ± 4.10 mg/dL *vs* 1.49 ± 3.16 mg/dL, $P = 0.002$) (Table 3).

With regard to outcomes, compared with the survivor group, a higher proportion of patients in the non-survivor group received MV (276/367 patients *vs* 343/630 patients, $P < 0.001$) and RRT (72/367 patients *vs* 44/630 patients, $P < 0.001$) during hospital stay. Furthermore, the proportion of each commonly used vasoactive medication in the non-survivor group was significantly higher than that in the survivor group, including

Subgroup	No. of patients	No SIC group No./total No. (%)	SIC group No./total No. (%)	Unadjusted odds ratio (95%CI)	*P* value	Interaction of subgroup (*P* value)
Overall	3530	818/2533 (32.3)	367/997 (36.8)	1.22 (1.05-1.42)	0.011	
Gender						0.22
Male	2017	470/1383 (34.0)	232/634 (36.6)	1.12 (0.92-1.36)	0.253	
Female	1513	348/1150 (30.3)	135/363 (37.2)	1.37 (1.07-1.75)	0.014	
BMI (kg/m^2)						0.14
< 28	1431	331/1082 (30.6)	112/349 (32.1)	1.07 (0.83-1.39)	0.598	
≥ 28	1655	356/1135 (31.4)	201/520 (38.7)	1.38 (1.11-1.71)	0.004	
Age (years)						0.83
< 60.00	1230	281/975 (28.8)	81/255 (31.8)	1.15 (0.85-1.55)	0.358	
≥ 60.00	2299	536/1557 (34.4)	286/742 (38.5)	1.20 (1.00-1.43)	0.054	
SOFA						0.54
< 2	217	30/165 (18.2)	9/52 (17.3)	0.94 (0.42-2.14)	0.89	
≥ 2	3313	788/2368 (33.3)	358/945 (37.9)	1.22 (1.05-1.43)	0.01	
SBP (mmHg)						0.85
< 90	136	42/79 (53.2)	32/57 (56.1)	1.13 (0.57-2.24)	0.73	
≥ 90	3338	760/2417 (31.4)	328/921 (35.6)	1.21 (1.03-1.42)	0.02	
MAP (mmHg)						0.25
< 65	690	220/489 (45.0)	92/201 (45.8)	1.03 (0.74-1.44)	0.85	
≥ 65	2786	583/2008 (29.0)	268/778 (34.4)	1.28 (1.08-1.53)	0.01	
Vasopressor use						0.32
< 2	218	123/151 (81.5)	56/67 (83.6)	0.79 (0.37-1.69)	0.706	
≥ 2	3345	1529/2299 (66.5)	658/1046 (62.9)	1.17 (1.01-1.36)	0.042	
RRT use						0.99
Yes	369	94/249 (37.8)	51/120 (42.5)	1.22 (0.78-1.90)	0.38	
No	3161	724/2284 (31.7)	316/877 (36.0)	1.21 (1.03-1.43)	0.02	
Mechanical ventilation use						0.89
Yes	1748	473/1232 (38.4)	220/516 (42.6)	1.19 (0.97-1.47)	0.1	
No	1782	345/1301 (26.5)	147/481 (30.6)	1.22 (0.97-1.54)	0.09	

Figure 2 Subgroup analyses with regard to hospital mortality. BMI: Body mass index; SOFA: Sequential organ failure assessment, ranging from 0 to 24, with higher scores indicating a greater degree of organ failure; SBP: Systolic blood pressure; MAP: Mean arterial pressure; RRT: Renal replacement therapy.

norepinephrine (267/367 patients *vs* 322/630 patients, $P < 0.001$), dopamine (94/367 patients *vs* 94/630 patients, $P < 0.001$), epinephrine (35/367 patients *vs* 27/630 patients, $P = 0.001$), and vasopressin (163/367 patients *vs* 95/630 patients, $P < 0.001$). No significant differences were observed between the two groups for the length of ICU stay and hospital stay (Table 3).

Multivariate logistic regression analysis

The multivariate logistic regression analysis showed that age (OR = 1.012, 95%CI: 1.006-1.017; $P < 0.001$), male gender (OR = 1.498, 95%CI: 1.264-1.776; $P < 0.001$), ECI (OR = 1.036, 95%CI: 1.025-1.046; $P < 0.001$), hemoglobin (OR = 1.067, 95%CI: 1.020-1.116; $P = 0.005$), MV use in the first day of ICU admission (OR = 1.003, 95%CI: 1.000-1.006; $P = 0.041$), and diabetes (OR = 1.538, 95%CI: 1.298-1.823; $P < 0.001$) were risk factors for SIC (Table 4). SBP (OR = 0.983, 95%CI: 0.977-0.989; $P < 0.001$) and liver failure (OR = 0.340, 95%CI: 0.251-0.459; $P < 0.001$) were protective factors for SIC (Table 4).

Furthermore, the multivariate logistic regression analysis showed that lactate level (OR = 1.107, 95%CI: 1.038-1.180; $P = 0.002$), SAPS-II score (OR = 1.035, 95%CI: 1.021-1.049; $P < 0.001$), sepsis type (OR = 1.386, 95%CI: 1.066-1.801; $P = 0.015$), and BUN (OR = 1.009, 95%CI: 1.003-1.015; $P = 0.006$) were risk factors for hospital death of SIC patients (Table 5). SBP (OR = 0.986, 95%CI: 0.973-1.000; $P < 0.001$) and platelet level (OR = 0.998, 95%CI: 0.997-1.000; $P < 0.001$) were protective factors for hospital death of

Table 4 Multivariate logistic analysis of risk factors for sepsis-induced cardiomyopathy

Covariate	OR	95%CI	*P* value
Age	1.012	1.006-1.017	0.000
Male	1.498	1.264-1.776	0.000
ECI	1.036	1.025-1.046	0.000
Hemoglobin	1.067	1.020-1.116	0.005
MV use[1]	1.003	1.000-1.006	0.041
Diabetes	1.538	1.298-1.823	0.000
Liver failure	0.340	0.251-0.459	0.000
SBP	0.983	0.977-0.989	0.000

[1]MV use means mechanical ventilation use in the first day of intensive care unit admission. ECI: Elixhauser comorbidity index, and we used the modified van Walraven Elixhauser comorbidity score in our study, which consists of 30 comorbidity disease and ranges from -19 to 89 points, with higher scores indicating a greater risk of hospital mortality; OR: Odds ratio; SBP: Systolic blood pressure.

Table 5 Multivariate logistic regression analysis for risk factors of hospital death in sepsis-induced cardiomyopathy patients

Covariate	OR	95%CI	*P* value
Lactate	1.107	1.038-1.180	0.002
SAPS-II score	1.035	1.021-1.049	0.000
Sepsis types	1.386	1.066-1.801	0.015
BUN	1.009	1.003-1.015	0.006
SBP	0.986	0.973-1.000	0.044
Platelet level	0.998	0.997-1.000	0.031

SAPS-II: Simplified acute physiologic score-II; Sepsis types included sepsis, severe sepsis, and septic shock; the hospital mortality level in the sepsis group was set as baseline level and was set as 0, severe sepsis was set as 1, and septic shock was set as 2 in this multivariate logistic analysis. OR: Odds ratio; BUN: blood urea nitrogen; SBP: Systolic blood pressure.

SIC patients (Table 5).

DISCUSSION

A total of 3530 patients with sepsis who met the inclusion criteria were included in the present study. Among them, 997 patients met the SIC diagnostic criteria. The incidence of SIC was 28.20% (95%CI: 26.80%-29.70%). We searched the PubMed, EMBASE, and Web of Science databases, and the current epidemiological studies of SIC are mainly small studies[13-20]; large-scale studies are still lacking. To the best of our knowledge, the current study is the largest scale research with regard to the clinical characteristics of SIC.

Prior to this study, reports on the incidence of SIC varied greatly. Jardin and colleagues studied 90 patients with sepsis (aged 55 ± 18 years), 60% of whom had Gram-positive bacteremia, and monitored cardiac systolic and diastolic function by transthoracic echocardiography (TTE). Their results showed that 51% of patients had cardiac function depression[37]. Narváez *et al*[13] screened 57 patients with sepsis or septic shock who were admitted to the ICU from May 2014 to October 2015; of these, 13 patients met the diagnostic criteria for SIC, and the incidence of SIC was 22.8%. Sato *et al*[14] screened 210 patients with sepsis or septic shock who were admitted to the ICU in Japan; a total of 29 of those patients had SIC, with an incidence of SIC of 13.8%. Vieillard-Baron *et al*[17] screened 67 sepsis patients who had no previous cardiac disease and survived more than 48 h after being admitted to the ICU, and the results showed that the incidence of SIC was 60%. Other studies have reported an SIC incidence between 24%-40%[15,16,18,19]. Our study showed that the incidence of SIC

was 28.20% (95%CI: 26.80%-29.70%), which was in the middle of the range reported in previous studies. We considered that the reasons for the varied SIC incidences reported among the different studies were related to the following factors: First, there is still no gold standard or unified consensus for the diagnosis of SIC. The diagnostic criteria for SIC in various studies were mainly based on the exclusion of previous cardiac diseases combined with cardiac ultrasound indicators, especially LVEF. However, the LVEF cut-off value for diagnosing SIC varied among studies. Some studies used LVEF < 45% as the diagnostic criterion, and some other studies used LVEF < 50%[13-16,18-20]. Vieillard-Baron *et al*[17] used LVEF < 40% and cardiac index < 3 L/min/m^2 as diagnostic criteria. The above different diagnostic criteria might affect the epidemiological results of SIC. The criteria used in our research were based on previous studies and international cardiac failure guidelines[27-29]; the cut-off value of LVEF for diagnosing SIC in our study was < 50%. Second, since left ventricular diastolic dysfunction and right ventricular dysfunction (isolated or concurrent) are common in elderly and critically ill patients[38,39], it is difficult to directly attribute the above ventricular dysfunctions to sepsis. Therefore, the definition of SIC in our study was restricted to systolic dysfunction of the LV, which may explain why the incidence of SIC in our study is lower than that in some previous studies. Third, our study was a large sample study based on analysis of the MIMIC-III database, which included information on all patients who entered Beth Israel Deaconess Medical Center between 2002 and 2011, and we rigorously excluded patients with concomitant cardiac disease. As a result of the more rigorous inclusion and exclusion criteria, the research results were more reliable in our study.

In terms of secondary outcomes, our study showed that more patients in the SIC group than in the non-SIC group received MV and vasopressor therapy. The results were consistent with those after PSM. Sato *et al*[14] also reported that more patients in the SIC group received norepinephrine and vasopressin. In the study by Pulido *et al*[18], more patients in the SIC group received norepinephrine. Our results were consistent with those of previous studies.

We further studied the risk factors for SIC and the multivariate logistic regression analysis revealed that age, male, ECI, hemoglobin level, diabetes and MV use in the first day of ICU admission were risk factors for SIC (Table 4). Sato *et al*[14] reported that gender and age were risk factors for SIC, which was consistent with our findings. However, due to the limitation of the sample size, Sato *et al*[14] obtained few risk factors through logistic regression analysis. Based on the large sample size compared with previous studies, the risk factors for SIC in our study were more comprehensive.

Some previous studies showed that the mechanism of SIC was related to chemical mediators, such as endotoxins and cytokines[1,43]. Interestingly, we found that liver failure might be a protective factor against SIC. Estrogen has an inhibitory effect on cytokines[44], and the level of estrogen is usually high in liver failure. Further studies are warranted to determine the role of estrogen and liver failure in the pathogenesis of SIC.

There were some limitations in our study that should also be noted. First, this study was based on analysis of the MIMIC-III database, making this be a single-center retrospective study. Due to the nature of the research, there was unavoidable risk of bias. To decrease the influences of bias, our study adjusted for the baseline characteristics between the SIC and non-SIC groups using PSM method, and we further studied the primary outcomes through multiple subgroup analyses. Ultimately, the results were still consistent, which demonstrated that our results were reliable. Second, due to the lack of widely accepted diagnostic criteria for SIC, the cut-off values of LVEF used among studies varied widely[13-20]. Therefore, inconsistent SIC diagnostic criteria may influence the comparability of results between different studies. Third, the diagnosis of SIC in our study was mainly dependent on TTE. However, TTE is subjective and dependent on the operator's technique and level of experience, and the interpretation of the results may vary among operators, which might partly influence our results. Recently, researchers reported that using two-dimensional speckle tracking echocardiography to evaluate patients' cardiac function is more sensitive[45]. Therefore, future studies using more sensitive ultrasound techniques may increase the ability to evaluate cardiac function and improve the sensitivity of SIC diagnosis.

CONCLUSION

Our study showed that the incidence of SIC in patients with sepsis is 28.20% (95%CI: 26.80%-29.70%). Hospital mortality is higher in the SIC patients compared with the

non-SIC patients.

ARTICLE HIGHLIGHTS

Research background

Sepsis-induced cardiomyopathy (SIC) is a complication of sepsis and septic shock. The current epidemiological studies of SIC are mainly small ones.

Research motivation

At present, large-scale studies on the clinical characteristics of SIC, such as the incidence, prognosis, and risk factors, are lacking. The present study was intended to investigate these characteristics.

Research objectives

This study aimed to evaluate the SIC incidence rate and hospital mortality rate, as well as mechanical ventilation or renal replacement therapy use during hospital stay, the use of vasopressors (including norepinephrine, dopamine, epinephrine, and vasopressin), the length of intensive care unit (ICU) stay, and the length of hospital stay.

Research methods

Based on the analysis of the MIMIC-III public database, we performed a large-scale retrospective study involving sepsis patients who were admitted to the ICU and had no concomitant cardiac disease. We used propensity score matching analysis and multivariate logistic regression to ensure the robustness of the results.

Research results

In the present study, we included 3530 sepsis patients. The incidence of SIC was 28.20% (95% confidence interval: 26.80%-29.70%). Compared to patients in the non-SIC group, patients in the SIC group had a significantly older age and higher SAPS-I score, SAPS-II score, and Elixhauser comorbidity index (ECI). Hospital mortality was higher in the SIC group than in the non-SIC group. For the secondary outcomes, more patients in the SIC group received mechanical ventilation and vasopressors. Multivariate logistic regression analysis showed that age, male sex, ECI, hemoglobin level, diabetes, and mechanical ventilation use on the first day of ICU admission were risk factors for SIC.

Research conclusions

Our study showed that the incidence of SIC in patients with sepsis is 28.20%. Hospital mortality is higher in the SIC patients than in the non-SIC patients.

Research perspectives

The current study is the largest-scale study with regard to the clinical characteristics of SIC. The incidence of SIC is high. The hospital mortality is higher in the SIC group than in the non-SIC group. Clinicians should pay more attention to these patients. Further multicenter large scale studies with regard to SIC are needed.

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