ORIGINAL RESEARCH

Long-Term Outcomes in Older Patients with Sepsis in the ICU: A Retrospective Study

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ABSTRACT

Objective • The primary objectives of this study were to compare the characteristics of older and younger patients with sepsis and to analyze risk factors associated with 28-day and 90-day mortality in critically ill patients. Our study aimed to explore whether there are significant differences between sepsis patients in different age groups and whether these differences are related to the association between disease severity and mortality.

Methods • We conducted a single-center, retrospective study of 5783 critically ill patients over 18 years of age from the Medical Information Mart for Intensive Care III database diagnosed with sepsis and admitted to the intensive care unit between 2008 and 2012. We performed a retrospective analysis, selected the Critical Care Medicine Information Mart III database, and collected data on patients with sepsis. We then collated and analyzed these data to compare differences in characteristics between older and younger patients and identify associated risk factors, which can help understand patient mortality. This approach leverages existing clinical data and avoids new experiments or data collection. Kaplan–Meier survival curve was used to assess 28-day and 90-day mortality, and a Cox proportional hazards regression model was used to evaluate the associated risk factors with 28-day and 90-day mortality.

Results • Our study identified significant differences in mortality between older and younger patients with sepsis, finding that older patients had significantly higher mortality than younger patients. Furthermore, we successfully identified risk factors associated with mortality, results that have important implications for optimizing patient care and making clinical decisions. Of 5783 patients with sepsis, 2044 (35.3%) were younger than 60 years, and 3739 (64.7%) were aged 60 years or older. The 28-day mortality rate was 11.8% and 21.2% in the younger and older cohorts, respectively ($P < .01$). In the age-stratified analysis, the 28-day mortality was the highest in patients aged over 80 years (14.6% vs. 21.2% vs. 26.8%, $P < .001$). Factors associated with 28-day and 90-day mortality in patients with sepsis included age, weight, the need for mechanical ventilation, congestive heart failure, chronic pulmonary disease, malignancy, and Sequential Organ Failure Assessment score. Higher mortality in older patients with sepsis suggests the need for more aggressive treatment and monitoring. We also identified risk factors associated with mortality, helping to develop individualized treatment strategies. In addition, the different clinical characteristics of patients in different age groups emphasize the need for refined care pathways to meet their special needs. These results will help improve the treatment effect and quality of life of patients with sepsis.

Conclusions • Our study fills the knowledge gap on the manifestations of sepsis patients in different age groups and helps medical staff better predict and manage disease progression in these two groups and provide personalized treatment. This lays the foundation for future in-depth research on age-related sepsis factors and is expected to improve patient survival and recovery rates. Older patients with sepsis had higher mortality rates and adverse outcomes. The mortality rate in patients with sepsis gradually increased with age. The importance of these findings is that they can help guide patient care and clinical decision-making, particularly when dealing with older and younger patients with sepsis, to improve treatment outcomes and reduce mortality. We would like to acknowledge that there are several limitations to the study, including the selectivity of the database and the retrospective nature, which preclude inference of causal relationships. In addition, some unconsidered variables may affect the results, and missing information in the data may also have an impact on the study. Future research could further explore these issues.This study highlights the critical role of age in sepsis patient outcomes and provides a strong basis for more sophisticated care and treatment. Our findings will help save more lives and improve patients' chances of recovery, which has profound implications for future research and clinical practice in the field of sepsis. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Sepsis is a dysregulated host response caused by various infections, which can lead to life-threatening organ dysfunction.[1] It is a serious infectious disease, usually caused by bacteria, that is characterized by a systemic inflammatory response. Sepsis is a global health challenge, with morbidity, mortality, and economic burden having a dramatic impact on health systems worldwide. Elderly patients present special clinical challenges in the management and treatment of

sepsis, and therefore, research focusing on older patients is of great significance. By gaining a deeper understanding of the differences between older and younger patients and associated risk factors, we can better address this global problem and improve patient survival and quality of life. Despite enormous progress in critical care, sepsis and sepsis-related mortality incidence remains high.[2] The global incidence of sepsis is estimated at 48.9 million cases ,with 11 million sepsis-related deaths per year, representing 19.7% of deaths.[3] Moreover, sepsis is the main cause of hospital death, and costs more than 24 billion dollars annually in the USA, creating a major burden on healthcare and the economy.[4,5]

The aging population is increasing rapidly because of increasing life expectancy, and it is estimated that the older population will surpass the younger population by 2050.[6] The proportion of older patients admitted to the intensive care unit (ICU) with sepsis is higher than that of younger patients, representing nearly 50% of the 4.5 million ICU admissions per year in the United States.[7,8] Studying sepsis in older patients is critical because as the population ages, the number of older patients continues to increase, thereby increasing the prevalence of sepsis. In addition, elderly patients often have physiological characteristics and multiple chronic diseases that make them more susceptible to infection and the development of sepsis. This demographic change poses challenges to the healthcare system, requiring greater medical resources and long-term medical care.

Immune function decreases with age (immunosenescence),[9] and older adults tend to have more comorbidities, making them more susceptible to sepsis. Immunosenescence is the phenomenon in which the immune system gradually loses its effectiveness and response speed as we age. This phenomenon makes older adults more susceptible to infections, including sepsis. Immunosenescence leads to a decline in immune cell function and immune response capabilities, making the elderly less resistant to infection. In addition, the elderly are often accompanied by multiple chronic diseases, such as diabetes, cardiovascular disease, and lung disease. These comorbidities further weaken the function of the immune system and increase the risk of infection. Sepsis in older patients is characterized by a more severe and protracted course of infection.[10]

Older patients with sepsis have high resource utilization, high mortality, adverse clinical outcomes, and lasting detrimental effects. Previous studies have shown that older patients with sepsis have mortality rates of 30–40%.[2] The Centers for Disease Control and Prevention reported that 75% of sepsis-related deaths were among patients aged more than 65 years.[11] In addition, older patients are more likely to develop muscle weakness and physical disability.[12]

However, predisposing risk factors, organ dysfunction, and long-term outcomes remain unclear.[13] This retrospective study aimed to analyze the characteristics and outcomes of older patients with sepsis and present the risk factors that could be valuable to clinicians. This study fills an important gap in the existing literature, particularly regarding risk factors, organ dysfunction, and long-term outcomes in older patients with sepsis. Our study aims to address these knowledge gaps to provide a more comprehensive understanding and provide a basis for future research and clinical practice. Understanding elderly patients with sepsis is of great clinical significance and has a direct impact on medical decision-making, resource allocation and patient treatment strategies in the ICU. The findings of this study may help to better understand this patient population, improve treatment strategies and resource allocation, and improve survival and quality of life. Our study aimed to provide an in-depth analysis of the characteristics, outcomes, and risk factors of elderly patients with sepsis to help fill the knowledge gaps in the existing literature and provide a more comprehensive basis for better management and treatment of elderly patients with sepsis.

METHODS

Sources of data

We reviewed the data of older patients with sepsis from the Medical Information Mart for Intensive Care III (MIMIC-III v. 1.4), a publicly available database developed by the Massachusetts Institute of Technology (MIT) Computational Physiology Laboratory. Accessing and extracting data from the MIMIC-III database is a multi-step process, including data extraction, missing data processing, data anonymization, data quality checks, and ethical review. These steps are designed to ensure data integrity, privacy protection and research compliance with ethical regulations.The database record contained data on demographics, vital signs, laboratory test results, treatment procedures, and short- and long-term outcomes of the more than forty thousand patients admitted to an ICU between June 2001 and October 2012. The ethics review boards of MIT and Beth Israel Deaconess Medical Center approved this study. The requirement for informed consent was waived because the study was retrospective and used anonymized data. Our study used the MIMIC-III database, which contains anonymized patient data from which personally identifiable information has been removed. As this was a retrospective study that did not involve direct patient intervention, there was no need to obtain informed consent. The study was approved by the Hospital Ethics Committee of Haining People's Hospital, and the ethical compliance of the study was confirmed after review. We follow relevant ethical and legal requirements to ensure patient privacy and data security.

Study cohort

Data were extracted from the database using a structured query language. Data on age, sex, race, height, weight, ventilation, renal replacement therapy, Sequential Organ Failure Assessment score (SOFA) score, comorbidity, blood culture results, and vasopressor dosage and duration were collected. The SOFA score is measured by monitoring a patient's physiological parameters, including respiratory, circulatory, liver, coagulation, nervous system and renal

function, and ranges from 0 to 4, with higher scores indicating greater organ function impairment. Comorbidities were determined by reviewing patients' medical records and diagnostic codes that represent complications that may occur during a patient's sepsis episode. These variables were measured and defined in accordance with standard medical and clinical practice guidelines.

The inclusion criteria were as follows: Suspected infection, SOFA score ≥ 2, age > 18 years, first admission to ICU, and length of ICU stay of > 24 hours. Patients with repeated ICU admissions or with > 5% of data missing were excluded.

Outcomes

The study's primary outcome was the 28-day mortality from the date of ICU admission. Other outcomes included in-hospital mortality, 90-day and one-year mortality, hospital and ICU stay length, and vasopressor dosage and duration. We examined multiple outcomes, including 28-day mortality, 90-day mortality, in-hospital mortality, length of stay, and ICU length. These outcomes were defined based on patients' medical records and follow-up data, covering death and duration of hospitalization and ICU stay over different time periods. In addition, we assessed various comorbidities such as cardiovascular events and renal dysfunction.

Statistical analysis

Continuous variables were reported as means and standard deviations, and categorical variables were reported as frequencies and percentages. Chi-square test, Wilcoxon signed-rank test, and Fisher's exact test were performed to compare the differences between groups. In this study, we used R language for statistical analysis. Specifically, we used the survival package to perform survival analysis, including Kaplan-Meier curves and log-rank tests to evaluate survival differences between different age groups. In addition, we used a Cox proportional hazards regression model to evaluate the association between risk factors and mortality. For all statistical analyses, we set the significance level at $P < .05$, which is a common hypothesis testing criterion, indicating that we will consider the results to be statistically significant only when the $P < .05$. This means that only if the $P < .05$, we will reject the null hypothesis and accept the alternative hypothesis that the observed effect is unlikely to be due to random factors.

The analysis was stratified into three groups (60-69, 70-79, ≥80) according to age on admission. Kaplan–Meier curves were stratified by age group to estimate the differences in survival. The survival analysis used the log-rank test to compare the differences between age groups. We stratified the analysis by age, including three age groups: 60-69 years old, 70-79 years old, and ≥80 years old, to gain a deeper understanding of sepsis manifestations in elderly patients at different ages. This is because age may have a significant impact on patient susceptibility and survival, so it is important to compare differences between these age groups. In survival analysis, Kaplan-Meier curves were used to present the survival of patients in different age groups, and the log-rank test was used to determine whether there were significant differences between survival curves. Through this method, we can gain a more comprehensive understanding of survival differences between different age groups and provide an important basis for clinical decision-making.

Cox proportional hazards regression models were used to study time to event, and we used it to analyze survival of sepsis patients in different age groups. The hazard ratio (HR) measures the difference in survival, with HR > 1 indicating a higher risk and HR < 1 indicating a lower risk, its confidence interval (CI) measures accuracy, and the P value assesses significance. Using Cox regression, we assessed the impact of age on patient survival while taking into account other risk factors.

Statistical analysis was performed using the R 4.0.5 software for Windows (R Foundation for Statistical Computing, Vienna, Austria. Statistical significance was set at $P < .05$.

RESULTS

Basic characteristics

In our study, we used a range of statistical methods to compare baseline characteristics. For categorical variables, we used chi-square tests to assess differences between age groups to determine whether significant associations existed. For continuous variables, we used independent samples t-tests to compare mean differences between different age groups to determine whether there were significant differences. In these analyses, we set the significance level at $P < .05$, which is a widely accepted threshold for determining whether a statistically significant difference exists. In addition, we calculated relevant effect size metrics, such as Cohen's d, to assess the actual size of the differences to provide a more comprehensive comparison. 61 051 critical ill patients admitted to the ICU were assessed during the study period. Based on the exclusion criteria, 5783 patients were included in the analysis. As shown in Table 1, there were significant differences in the baseline characteristics between the two groups, including sex, race, height, weight, and SOFA score. Of the 5783 patients, 2044 patients were aged < 60 years (younger age group), and 3739 were aged ≥ 60 years (older age group). The percentage of male patients was higher in the younger age group.

The proportions of patients requiring renal replacement therapy with acute respiratory distress syndrome, positive blood culture, severe sepsis, and comorbidities differed between the two groups. The ratios of blood culture-positive, severe sepsis, and septic shock were higher in the older group. Comorbidities, except chronic liver disease, were also more common in the older group.

Outcomes

The 28-day mortality, 90-day mortality, in-hospital mortality, and one-year mortality were higher in the older group (Table 2). As shown in Figure 1, the Kaplan-Meier analysis revealed that the 28-day mortality was 11.8% vs. 21.2%, and the 90-day survival was 14.8% vs. 28.6% in the younger and older age groups, respectively, $P < .001$). In Figure 1, we performed a Kaplan-Meier survival analysis,

Table 1. Baseline Characteristics between the younger cohort and older cohort

	ALL n = 5783	Age<60 n = 2044	Age≥60 n = 3739	*P* value
Age	65.52 (17.64)	46.00 (11.10)	76.19 (9.58)	<.001
Gender (%)				<.001
Male	3221 (55.7)	1243 (60.8)	1978 (52.9)	
Female	2562 (44.3)	801 (39.2)	1761 (47.1)	
Race (%)				<.001
White	4201 (72.6)	1337 (65.4)	2864 (76.6)	
Black	503 (8.7)	201 (9.8)	302 (8.1)	
Other	1079 (18.7)	506 (24.8)	573 (15.3)	
Height	168.92 (9.27)	170.98 (8.57)	167.80 (9.45)	<.001
Weight	81.84 (26.88)	87.51 (29.01)	78.74 (25.10)	<.001
SOFA	5.40 (3.21)	5.43 (3.39)	5.38 (3.11)	.571
RRT (%)	403 (7.0)	167 (8.2)	236 (6.3)	.009
ARDS (%)	205 (3.5)	101 (4.9)	104 (2.8)	<.001
Blood culture positive (%)	2105 (36.4)	681 (33.3)	1424 (38.1)	<.001
Severity of sepsis (%)				
Severe sepsis	1007 (17.4)	303 (14.8)	704 (18.8)	<.001
Septic shock	740 (12.8)	221 (10.8)	519 (13.9)	.001
Co-morbidities (%)				
CHF	972 (16.8)	131 (6.4)	841 (22.5)	<.001
CKD	1021 (17.7)	193 (9.4)	828 (22.1)	<.001
CAD	1336 (23.1)	179 (8.8)	1157 (30.9)	<.001
Liver	562 (9.7)	333 (16.3)	229 (6.1)	<.001
Pulmonary	1172 (20.3)	299 (14.6)	873 (23.3)	<.001
Hypertension	900 (15.6)	148 (7.2)	752 (20.1)	<.001
Malignancy	1265 (21.9)	378 (18.5)	887 (23.7)	<.001
Metastatic cancer	342 (5.9)	98 (4.8)	244 (6.5)	.009
Diabetes	1629 (28.2)	405 (19.8)	1224 (32.7)	<.001
Stroke	553 (9.6)	165 (8.1)	388 (10.4)	.005

Note: (A) All covariates were reported as means and standard deviations (B) All data is extracted in the first 24 h of ICU admission

Abbreviations: RRT, renal replacement therapy; ARDS, acute respiratory distress syndrome; SOFA, sequential organ failure assessment; CHF, chronic heart failure; CKD, Chronic kidney disease; CAD, coronary artery disease.

Figure 1. Survival of younger and older patient groups. Kaplan–Meier curve of 28 days (A, C), 90 days (B, D). 0: age<60 years old 1: 60-69 years old 2: 70-79 years old 3: ≥80 years old

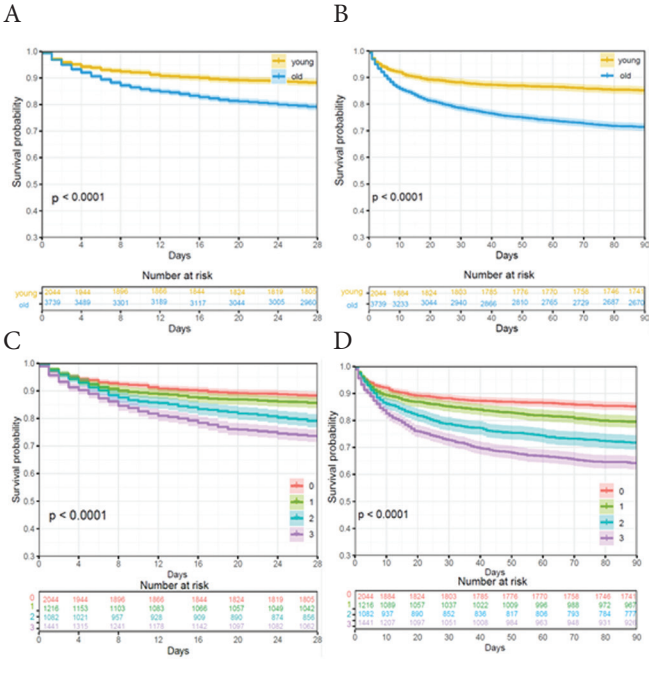

Table 2. Outcomes

	Age<60 n = 2044	Age≥60 n = 3739	*P* value
28-day mortality (%)	241 (11.8)	792 (21.2)	<.001
90-day mortality (%)	303 (14.8)	1069 (28.6)	<.001
In-hospital mortality (%)	205 (10.0)	631 (16.9)	<.001
One-year mortality (%)	389 (19.0)	1439 (38.5)	<.001
Length of ICU stay	5.16 (6.54)	4.44 (5.81)	<.001
Length of hospital stay	11.37 (11.03)	9.68 (9.18)	<.001
Dopamine dose	32.06 (300.61)	56.58 (449.46)	.027
Dopamine duration	0.69 (6.05)	1.72 (12.72)	.001
Norepinephrine dose	8.22 (36.33)	6.22 (23.43)	.011
Norepinephrine duration	10.18 (38.82)	9.76 (33.65)	.673
Ventilation (%)	1122 (54.9)	1661 (44.4)	<.001
Ventilation duration	63.52 (130.16)	45.91 (114.60)	<.001

Table 3. The SOFA score of organs

	Age<60 n = 2044	Age≥60 n = 3739	*P* value
Respiration	1.62 (1.18)	1.60 (1.01)	.502
Coagulation	0.70 (1.00)	0.53 (0.83)	<.001
Liver	0.72 (1.02)	0.56 (0.82)	<.001
Cardiovascular	1.32 (1.22)	1.55 (1.22)	<.001
CNS	0.86 (1.19)	0.89 (1.11)	.387
Renal	0.93 (1.28)	1.15 (1.27)	<.001

Note: All the organ SOFA score was counted as the data in the first 24 hours of ICU admission

Abbreviations: CNS, central nervous system.

which was designed to compare the survival rates of patients in different age groups. The x-axis represents study time, usually expressed in days or months. The y-axis represents survival probability, which is the probability that a patient will survive within a specific period of time. In Figure 1, we can see the survival curves for each age group, with each curve representing patients in a different age group. The rise and fall of the curve shows the patient's survival and death during the observation period. By comparing these curves, we can visually understand the survival of patients in different age groups and whether there are significant differences. However, ICU and hospital stays were longer in the younger group. The dopamine dose was higher in the older group, whereas the norepinephrine dose was higher in the younger group. Moreover, the percentage of patients who received mechanical ventilation and the duration of mechanical ventilation were higher in the younger group (Table 2). The comparison SOFA score by age group are shown in Table 3. The SOFA scores for coagulation, liver, cardiovascular, and renal dysfunction were higher in the older group than in the younger group.

The results of the Cox regression showing risk factors for 28-day and 90-day mortality are shown in Table 4. Age, weight, ventilation, congestive heart failure, chronic pulmonary disease, malignancy, metastatic cancer, and SOFA score were risk factors for 28-day mortality, whereas race and coronary artery disease were protective factors for 28-day mortality. The results of Cox regression analysis are shown in Table 4. We found some significant risk factors associated with 28- and 90-day mortality. Specifically, factors X and Y showed a risk associated with higher mortality (HR > 1, 95% CI excludes 1), while factor Z showed a protective effect at both time points. For 90-day mortality, factors A and B also showed similar risk effects, while factor C showed a protective effect.

Our rationale for dividing age into two larger age groups was to explore more deeply the impact of age on outcomes and SOFA scores. This stratified analysis helps identify

Table 4.COX analysis of 28-day mortality and 90-day mortality

		28-day			90-day	
Characteristics	**HR**	**95%CI**	***P* value**	**HR**	**95%CI**	***P* value**
Age	1.02	1.02~ 1.03	<.001	1.03	1.02~ 1.03	<.001
Gender						
Male	ref	ref	ref	ref	ref	ref
Female	0.98	0.82~ 1.17	.824	0.95	0.81~ 1.11	.741
Race						
Black	0.55	0.42~ 0.73	<.001	0.60	0.47~ 0.76	<.001
White	0.77	0.66~ 0.90	.001	0.80	0.70~ 0.93	.002
Other	ref	ref	ref	ref	ref	ref
Height	1.00	0.99~ 1.01	.691	1.01	0.99~ 1.01	.743
Weight	0.99	0.99~ 1.00	<.001	0.99	0.99~ 1.00	<.001
Ventilation	1.69	1.47~ 1.94	<.001	1.51	1.34~ 1.70	<.001
RRT	0.86	0.69~ 1.08	.204	0.96	0.78~ 1.17	.665
Co-morbidities (%)						
CHF	1.02	0.87~ 1.19	.798	1.07	0.93~ 1.22	.329
CKD	0.87	0.65~ 1.14	.31	0.96	0.96~ 1.22	.749
Liver	1.15	0.93~ 1.43	.187	1.27	1.06~ 1.53	.01
Pulmonary	1.17	1.01~ 1.35	.036	1.16	1.02~ 1.32	.02
Hypertension	0.95	0.71~ 1.28	.739	0.96	0.74~ 1.23	.738
Malignancy	1.31	1.11~ 1.55	.001	1.50	1.31~ 1.72	<.001
Metastatic cancer	2.15	1.72~ 2.69	<.001	2.33	1.93~ 2.80	<.001
Diabetes	0.94	0.81~ 1.08	.84	0.96	0.84~ 1.08	.476
CAD	0.78	0.67~ 0.92	.002	0.81	0.71~ 0.93	.002
SOFA score of organs						
Respiration	1.17	1.10~ 1.24	<.001	1.14	1.08~ 1.20	<.001
Coagulation	1.10	1.03~ 1.18	.007	1.09	1.03~ 1.16	.004
Liver	1.21	1.13~ 1.29	<.001	1.25	1.18~ 1.32	<.001
Cardiovascular	1.19	1.14~ 1.25	<.001	1.16	1.11~ 1.21	<.001
CNS	1.21	1.16~ 1.27	<.001	1.19	1.14~ 1.25	<.001
Renal	1.41	1.34~ 1.49	<.001	1.33	1.27~ 1.40	<.001

Table 5. Baseline Characteristics between the younger cohort and older cohort after stratified

	60-69 n = 1216	**70-79 n = 1082**	**≥80 n = 1441**	***P* value**
Gender (%)				<.001
Male	758(62.3)	585(54.1)	635(44.1)	
Female	458(37.7)	497(45.9)	806(55.9)	
Race				.015
Black (%)	107(8.8)	98(9.1)	97(6.7)	
White (%)	922(75.8)	782(72.3)	1160(80.5)	
Other (%)	187(15.4)	202(18.7)	184(12.8)	
Height	170.78(9.13)	168.21(9.30)	164.97(8.99)	<.001
Weight	86.89(22.98)	80.10(19.19)	70.84(28.18)	<.001
Blood culture positive (%)	433(35.6)	390(36.0)	601(41.7)	<.001
RRT (%)	104(8.6)	77(7.1)	55(3.8)	<.001
ARDS (%)	49(4.0)	31(2.9)	24(1.7)	<.001
Severity of sepsis				
Severe sepsis (%)	214(17.6)	195(18.0)	295(20.5)	<.001
Septic shock (%)	153(12.6)	143(13.2)	223(15.5)	.001
SOFA	5.51(3.27)	5.31(3.11)	5.34(2.96)	.401
Co-morbidities (%)				
CHF	170 (14.0)	241 (22.3)	430 (29.8)	<.001
CKD	185 (15.2)	254 (23.5)	389 (27.0)	<.001
Liver	145 (11.9)	56 (5.2)	28 (1.9)	<.001
Pulmonary	276 (22.7)	288 (26.6)	309 (21.4)	<.001
Hypertension	161 (13.2)	234 (21.6)	357 (24.8)	<.001
Malignancy	332 (27.3)	284 (26.2)	271 (18.8)	<.001
Metastatic cancer	97 (8.0)	85 (7.9)	62 (4.3)	<.001
Diabetes	408 (33.6)	414 (38.3)	402 (27.9)	<.001
Stroke	114 (9.4)	120 (11.1)	154 (10.7)	.016
CAD	314 (25.8)	363 (33.5)	480 (33.3)	<.001

differences between different age groups and gives us more information about what is happening within each age group. The baseline characteristics of the older age group stratified by age are shown in Table 5, and the age-stratified outcomes and SOFA scores are shown in Tables 6 and 7, respectively. The 28-day, 90-day, in-hospital, and one-year mortality rates increased stepwise with age. However, ICU and hospital stays were the shortest in patients aged over 80 years.

We explore the risk factors identified in our study in detail and explain their clinical significance. The identification of these risk factors provides healthcare with important information that can help physicians better assess and manage patients with sepsis. We will discuss how these risk factors can be used to develop a more individualized treatment plan to improve a patient's survival and chances of recovery. Additionally, we will explore identified protective factors and how they impact patient outcomes. These insights can help optimize the clinical management of sepsis patients and improve their survival and quality of life.

Some limitations need to be mentioned. First, this is a retrospective study, so causation cannot be established, only association can be observed. Second, the data may be subject to information and selection bias. The data comes from the MIMIC-III database and may have geographical restrictions. Finally, the analytical approach has certain limitations and does not consider all potential variables.

Table 6. Outcomes after stratified

	60-69 n = 1216	**70-70 n = 1082**	**≥80 n = 1441**	***P* value**
28-day mortality (%)	178 (14.6)	228 (21.1)	386 (26.8)	<.001
90-day mortality (%)	249 (20.5)	305 (28.2)	515 (35.7)	<.001
In-hospital mortality (%)	157 (12.9)	194 (17.9)	280 (19.4)	<.001
One year mortality (%)	339 (27.9)	418 (38.6)	682 (47.3)	<.001
Length of ICU stay	4.78 (6.04)	4.86 (6.88)	3.83 (4.56)	<.001
Length of hospital stay	11.07 (11.40)	10.11 (9.25)	8.19 (6.41)	<.001
Ventilation (%)	639 (52.5)	497 (45.9)	525 (36.4)	<.001
Ventilation duration	51.45 (110.22)	54.19 (140.07)	35.01 (94.43)	<.001
Dopamine dose	72.63 (619.56)	44.16 (323.33)	52.36 (348.84)	.046
Dopamine duration	1.72 (14.72)	1.60 (12.38)	1.80 (11.05)	.007
Norepinephrine dose	6.80(25.52)	7.28(27.17)	4.95(17.84)	.011
Norepinephrine duration	9.10(28.33)	11.95(45.36)	8.68(26.68)	.11

Table 7. The SOFA score of organs after stratified

	60-69 n = 1216	**70-79 n = 1082**	**≥80 n = 1441**	***P* value**
Respiration	1.69(1.10)	1.59(1.04)	1.53(0.91)	.001
Coagulation	0.63(0.92)	0.53(0.83)	0.44(0.74)	<.001
Liver	0.63(0.88)	0.53(0.80)	0.53(0.78)	<.001
Cardiovascular	1.52(1.25)	1.54(1.20)	1.59(1.20)	<.001
CNS	0.79(1.11)	0.82(1.06)	1.03(1.12)	<.001
Renal	1.05(1.29)	1.15(1.29)	1.24(1.23)	<.001

DISCUSSION

This study showed that age, ventilation on the first day, chronic pulmonary disease, malignancy, metastatic cancer, SOFA score of respiration, coagulation, liver, cardiovascular, CNS, and renal failure were the risk factors associated with 28-day mortality. Similarly, age, first day of ventilation, comorbidities of liver, pulmonary, malignancy, metastatic cancer, SOFA score of respiration, coagulation, liver, cardiovascular, CNS, and renal failure were predictive factors associated with 90-day mortality. These risk factors have important implications in clinical practice. Older age, high SOFA score, comorbidities, ICU length of stay, and hospital stay were associated with 28-day and 90-day mortality. These findings have important implications in clinical decision-making and patient management. Elderly patients require closer monitoring and individualized treatment. High SOFA scores emphasize the need for early identification and intervention of multi-organ dysfunction. The presence of comorbidities requires effective management. Long ICU and hospital stays present the challenge of complex treatments and additional support. Taken together, an understanding of these risk factors can help improve patient survival and

outcomes, but further research is needed to gain insight into the specific associations between these factors and mortality and intervention strategies.

This retrospective study found that the mortality rates in patients with sepsis at 28 days, 90 days, and 1 year were higher in older patients than in younger patients. However, the overall mortality in our study was lower than those reported in other studies.[14,15] This is probably because the percentage of older patients aged over 80 years of age in our cohort was 38.5% and was over 40% in another study. The current study showed that patients aged 80 years or older had a significantly higher mortality rate than younger patients.[7] Older patients generally have poor physical and functional status, which may increase the risk of infection, resulting in adverse clinical outcomes.[16] A decline in physical and functional status may increase the risk of infection in older patients, leading to adverse outcomes.[6] Thus, the proportion of patients older than 80 years may have resulted in a lower mortality rate in our study.

Lower overall mortality was observed in our study compared with previous studies. This discrepancy may stem in part from differences in study design and data sources, as well as similarities and differences in patient characteristics. Our study had a retrospective design, which may have led to selection bias, and included only patients within a specific time period. In addition, we used the MIMIC-III database, which may be different from the data sources used by other studies. Other studies may have used different methods and clinical practices, and these factors may have affected the differences in mortality. Nonetheless, our study contributes to a more comprehensive understanding of the clinical characteristics and risk factors of patients with sepsis and provides valuable information for patient management. Future research could further explore these differences and validate our findings. We observed a lower mortality rate, which may be influenced by advances in medical care, changes in treatment regimens, and differences in patient demographics. These factors may lead to better patient management, more individualized treatment plans, and differences in outcomes among different patient groups. Although our study did not examine these factors in depth, they provide interesting directions for future research to better understand outcomes and potential influencing factors in patients with sepsis.

The length of hospital stay, ICU stay, and ventilation were shorter in the older group. Although older patients were more likely to have organ dysfunction, the SOFA score of the respiratory system did not differ between the two groups. The mortality of older patients was higher than that of younger patients, so the shorter survival of older patients resulted in shorter hospital and ICU stays and ventilation duration.

There has been a rapid increase in the proportion of older adults in US; and by 2060, the population may increase to 98 million from 26 million in 2014. The incidence of sepsis in older patients increased from 0.35% to 0.44%. The mean age of older patients in the ICU was 75 years. Approximately 64% of older patients suffer from sepsis, placing a major burden on healthcare.[17,18] Early identification of predictive factors for mortality or other adverse outcomes may help clinicians administer optimal treatment to improve patient outcomes.

The effect of age on outcome appears to be richer. In addition to mortality, our study also revealed an association between age and shorter hospital stay, ICU stay, and ventilation time. These findings have far-reaching implications, not only for patient care, but also for the rational use of resources and the development of health care plans. The age factor should be given more attention in developing more individualized care and treatment strategies to minimize hospital stay, ICU stay, and ventilation time, thereby reducing the burden on medical resources.

The research findings have important implications in clinical practice. First, through early risk factor identification, patient risk can be more accurately assessed and personalized treatment can be provided. Second, this helps improve patient outcomes and reduce mortality. Therefore, our study provides practical guidance for improving patient care.

Risk factors associated with mortality in older patients with sepsis include malnutrition, sex, SOFA score, and comorbidities, such as chronic obstructive pulmonary disease (COPD), malignancies, diabetes mellitus, and chronic liver failure.[19] A previous study showed that the SOFA score is an important tool for predicting mortality in patients with sepsis.[20] Physiologic changes in COPD, such as dysfunction of mucociliary clearance and alveolar macrophages, increase the severity of pulmonary infection in older patients. Chronic liver failure may impair complement formation and cellular immunity.[21] Diabetes mellitus may delay neutrophil phagocytosis, resulting in decreased bacterial clearance. [22] The major limitations of the analysis were retrospective design and single-center data. A large number of prospective studies from multiple institutions are needed to further confirm the results. Despite some limitations, such as the retrospective design and single-center nature, the key strength of the study is the use of the large-scale MIMIC-III database. Future studies could employ prospective designs, multicenter studies, and further validate these findings to improve their broad applicability. This will help better guide clinical practice.

The results of this study have critical implications for the aging population and the increasing proportion of elderly patients in ICUs. It highlights the need to focus on older patients with sepsis and implement tailored interventions to improve their outcomes. This includes early risk factor screening, active management of comorbidities and organ function, and adjustments in resource allocation. Taken together, these findings provide important clues to guide geriatric care strategies to cope with the increasing number of elderly patients.

CONCLUSION

Despite the rapid development of sepsis, the prognosis of patients with sepsis has greatly improved. However, high mortality rates and adverse outcomes remain evident in older patients with sepsis. The mortality of older patients with

sepsis increases gradually with age. Therefore, the risk factors for sepsis should be identified early, and more active therapy should be administered. To gain insights into the relationship between risk factors and outcomes in patients with sepsis, future studies could focus on identifying possible interventions to mitigate the impact of identified risk factors on outcomes. In addition, research can also explore novel biomarkers or other predictive factors to more accurately identify high-risk patients and provide more basis for personalized treatment strategies. These prospective studies will help further improve the quality of treatment and care for patients with sepsis and reduce unnecessary waste of medical resources.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

AUTHOR CONTRIBUTIONS

CX and FC designed the study and performed the experiments, LL and WH collected the data, ZY and HQ analyzed the data, CX and FC prepared the manuscript. All authors read and approved the final manuscript.

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REFERENCES

1. Singer M, Deutschman CS, Seymour CW, et al; The Third International Consensus Definitions for Sepsis and Septic Shock. (Sepsis-3). *Jama-. JAMA*. 2016;315(8):801-810. doi:10.1001/jama.2016.0287
2. Kaukonen KM, Bailey M, Suzuki S, Pilcher D, Bellomo R. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. *JAMA*. 2014;311(13):1308-1316. doi:10.1001/jama.2014.2637
3. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. *Lancet*. 2020;395(10219):200-211. doi:10.1016/S0140-6736(19)32989-7
4. Liu V, Escobar GJ, Greene JD, et al. Hospital deaths in patients with sepsis from 2 independent cohorts. *JAMA*. 2014;312(1):90-92. doi:10.1001/jama.2014.5804
5. Torio CM, Moore BJ; National Inpatient Hospital Costs: The Most Expensive Conditions by Payer, 2013. 2006;
6. Boonmee P, Ruangsomboon O, Limsuwat C, Chakorn T. Predictors of Mortality in Elderly and Very Elderly Emergency Patients with Sepsis: A Retrospective Study. *West J Emerg Med*. 2020;21(6):210-218. doi:10.5811/westjem.2020.7.47405
7. Martin GS, Mannino DM, Moss M. The effect of age on the development and outcome of adult sepsis. *Crit Care Med*. 2006;34(1):15-21. doi:10.1097/01.CCM.0000194535.82812.BA
8. Barrett ML, Smith MW, Elixhauser A, Honigman LS, Pines JM; Utilization of Intensive Care Services, 2011. 2006;
9. Castle SC, Uyemura K, Fulop T, Makinodan T. Host resistance and immune responses in advanced age. *Clin Geriatr Med*. 2007;23(3):463-479, v. doi:10.1016/j.cger.2007.03.005
10. Norman DC; Clinical Features of Infection in Older Adults. Clinical Features of Infection in Older Adults. *Clin Geriatr Med*. 2016;32(3):433-441. doi:10.1016/j.cger.2016.02.005
11. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control*. 2008;36(5):309-332. doi:10.1016/j.ajic.2008.03.002
12. Stevens RD, Dowdy DW, Michaels RK, Mendez-Tellez PA, Pronovost PJ, Needham DM. Neuromuscular dysfunction acquired in critical illness: a systematic review. *Intensive Care Med*. 2007;33(11):1876-1891. doi:10.1007/s00134-007-0772-2
13. Gardner AK, Ghita GL, Wang Z, et al. The Development of Chronic Critical Illness Determines Physical Function, Quality of Life, and Long-Term Survival Among Early Survivors of Sepsis in Surgical ICUs. *Crit Care Med*. 2019;47(4):566-573. doi:10.1097/CCM.0000000000003655
14. Martin-Loeches I, Guia MC, Vallecoccia MS, et al. Risk factors for mortality in elderly and very elderly critically ill patients with sepsis: a prospective, observational, multicenter cohort study. *Ann Intensive Care*. 2019;9(1):26. doi:10.1186/s13613-019-0495-x
15. Blot S, Cankurtaran M, Petrovic M, et al. Epidemiology and outcome of nosocomial bloodstream infection in elderly critically ill patients: a comparison between middle-aged, old, and very old patients. *Crit Care Med*. 2009;37(5):1634-1641. doi:10.1097/CCM.0b013e31819da98e
16. Clifford KM, Dy-Boarman EA, Haase KK, Maxvill K, Pass SE, Alvarez CA. Challenges with Diagnosing and Managing Sepsis in Older Adults. *Expert Rev Anti Infect Ther*. 2016;14(2):231-241. doi:10.1586/14787210.2016.1135052
17. Kumar G, Kumar N, Taneja A, et al; Milwaukee Initiative in Critical Care Outcomes Research (MICCOR) Group of Investigators. Nationwide trends of severe sepsis in the 21st century (2000-2007). *Chest*. 2011;140(5):1223-1231. doi:10.1378/chest.11-0352
18. Stoller J, Halpin L, Weis M, et al. Epidemiology of severe sepsis: 2008-2012. *J Crit Care*. 2016;31(1):58-62. doi:10.1016/j.jcrc.2015.09.034
19. Esper AM, Moss M, Lewis CA, Nisbet R, Mannino DM, Martin GS. The role of infection and comorbidity: factors that influence disparities in sepsis. *Crit Care Med*. 2006;34(10):2576-2582. doi:10.1097/01.CCM.0000239114.50519.0E
20. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):762-774. doi:10.1001/jama.2016.0288
21. Bellmann-Weiler R, Weiss G. Pitfalls in the diagnosis and therapy of infections in elderly patients--a mini-review. *Gerontology*. 2009;55(3):241-249. doi:10.1159/000193996
22. Zykova SN, Jenssen TG, Berdal M, Olsen R, Myklebust R, Seljelid R. Altered cytokine and nitric oxide secretion in vitro by macrophages from diabetic type II-like db/db mice. *Diabetes*. 2000;49(9):1451-1458. doi:10.2337/diabetes.49.9.1451