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Research article

Efficacy of the treatment for elderly emergency patients with sepsis

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ABSTRACT

Objectives: We evaluated the impact of age in septic patients admitted through the ER on clinical outcome and cost.

Methods: Patients with sepsis admitted to the intensive care unit (ICU) through the emergency room in our hospital between January 2013 and December 2018 were analyzed. They were divided into three groups according to their age: <65 years (group Y); 65–79 years (group M); and ≥80 years (group E). The duration of ICU and hospital stay, prognosis, and total hospital costs were compared among the three groups.

Results: During this period, 1,392 patients were admitted to the ICU through the emergency room, and 174 patients with sepsis were analyzed. There were 49, 79, and 46 patients in groups Y, M, and E, respectively. There was no significant difference in ICU stay. Group E exhibited the shortest hospital stay and the lowest total hospital cost with statistically significant difference ($p = 0.010$ and $p = 0.007$, respectively). However, group E showed the highest rate of hospital mortality (30.4%) compared to groups Y and M (14.3% and 21.5%, respectively; $p = 0.163$).

Conclusions: Elderly (aged ≥80 years) emergency patients with sepsis require shorter hospital stay and are associated with lower total hospital cost. However, it may be difficult for these patients to maintain the hospital mortality equivalent to those observed in patients aged <80 years.

1. Introduction

Life expectancy in developed countries has increased considerably. Currently, Japan has the highest rate of aging population worldwide [1]. The National Institute of Population and Social Security Research in Japan reported that the proportion of the population aged ≥65 years in 2017 was 27.7%. It is estimated that this proportion will increase to approximately 33% and 40% by 2036 and 2065, respectively [2]. The rapid increase in the aging population, combined with the diminishing number of children and prolongation of the mean lifespan, leads to an acute inclining trend in medical care expenses for citizens (especially the elderly) in Japan, which is expected to continue in the future [3]. For example, in 1987, the medical care expenses of Japan were 165 billion USD. In 2027, this number will increase to 384 billion USD [3]. In addition, emergency ambulance dispatches to assist elderly individuals have increased in parallel with the aging Japanese population. The 2019 annual report of the Fire and Disaster Management Agency in Japan indicated that the percentage of assistance to elderly individuals aged ≥65 years in all emergency ambulance dispatches increased from 33.9% in 1997 to 60.0% in 2019 [4].

Among those emergency patients, many require intensive care. Sepsis is a leading cause of admission to the intensive care unit (ICU), mortality, and morbidity in both developed and developing countries [5, 6].

We hypothesized that the length of ICU and hospital stay is longer, the prognosis is poorer, and the total hospital cost is higher for elderly patients with sepsis admitted to the ICU through the emergency room (ER). The purpose of this study was to evaluate the impact of age in septic patients admitted through the ER on clinical outcome and cost.

2. Patients and methods

The protocol of this retrospective study was approved by the research ethics board of Gunma University Hospital (Maebashi, Japan) without the need for informed consent (#2016-044). The conduct of this study was announced on the website of our university.

Patients with sepsis who were admitted to the ICU directly or after operation through the ER in our hospital between January 2013 and

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December 2018 were analyzed. Sepsis and septic shock were defined according to The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2016 (J-SSCG2016) [7]. Patients aged <18 years, with terminal-stage malignant disease, and those who underwent cardiopulmonary resuscitation due to cardiopulmonary arrest on arrival were excluded from this study.

Patients were divided into three groups according to their age: <65 years (group Y); 65–79 years (group M); and ≥80 years (group E). The reasons for categorizing the patients into three age groups were as follows: 1) elderly people are generally considered as those aged ≥65 years [5, 6]; and 2) there is an evidence indicating that life expectancy in developed countries has considerably increased in parallel with rapid aging during the past few decades [8, 9]. In addition, the United States of America (USA) Central Intelligence Agency in 2017 published The World Factbook reporting that the average lifespan of individuals in developed countries is ≥ 80 years (e.g., 80.0 years in the USA; 80.80 years in the United Kingdom and Germany; 81.90 years in France; and 85.30 years in Japan) [10]. Comorbidities of patients, suspected sites of infection, sequential organ failure assessment (SOFA) score at the ER, the presence of septic shock at the ER, duration of ICU and hospital stay, hospital mortality, and total hospital cost were compared among the three groups.

2.1. Statistical analysis

Data are presented as the median and interquartile ranges (IQR) for age, ICU and hospital days because Shapiro-Wilk test showed that data were not normally distributed. Costs and other parameters are expressed as numbers and/or percentage. Comparisons of continuous variables among the three groups were performed using the Kruskal–Wallis test; subsequently, post-hoc analyses were conducted to assess the differences between the three groups. Comparisons of categorical variables among the three groups were performed using the chi-squared test. A p-value of <0.05 indicated statistically significant differences. Statistical analysis was performed using the SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA) software.

3. Results

A total of 1,392 patients were admitted to the ICU. Of these patients, 188 patients met the inclusion criteria of sepsis. Fourteen patients were excluded based on the exclusion criteria, and 174 patients were finally enrolled in this study (Figure 1). The median of age of the patients was 72 (63, 80) years. The median of the durations of ICU and hospital stay, and the total hospital cost linked to the patients were 6.0 (4.0, 11.0) days, 20.0 (11.3, 38.7) days, and 17,281 [10,137, 32,753] USD, respectively. The total hospital mortality rate was 21.8% (38/174 patients). The comparisons between survival and nonsurvival groups are shown in Table 1. As shown in Table 1, there were no significant differences in age, the duration of ICU stay, and the total hospital cost, however, the duration of hospital stay was significantly longer in the survival group than in the nonsurvival group. Septic shock was found in 60 patients (34.5%). There were no significant differences in the durations of ICU stay (6.0 [4.0, 12.3] days in patients with septic shock vs. 6.0 [3.3, 9.8] days in those without septic shock; p = 0.162) and hospital stay (28 [12.3, 49.5] days in patients with septic shock vs. 18.0 [10.4, 33.0] days in those without septic shock; p = 0.069). However, the hospital mortality was significantly higher in patients with septic shock (33.3%) than in those without septic shock (15.8%, p = 0.008).

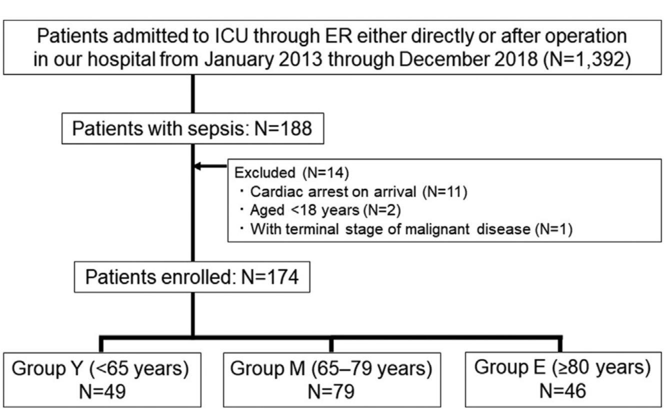

Figure 1. Flow diagram of the study. ER, emergency room; ICU, intensive care unit.

Groups Y, M, and E included 49, 79, and 46 patients, respectively (Figure 1). Age, male/female ratio, and comorbidities are shown in Table 2. Of note, there was some overlap in comorbidities among the groups. There was no significant difference in the male/female ratio among the three groups. Regarding comorbidities, there was a significant difference in the rate of chronic kidney disease (pairwise analysis showed that there were significant differences between group Y and E and between group M and E).

Table 3 shows the focus of infection, SOFA score at ER, and the presence of septic shock at ER. There were no significant differences in these parameters among the three groups. Moreover, there was no significant difference in the duration of ICU stay among the three groups (group Y: 7 [3, 11] days; group M: 6 [4, 14] days; and group E: 5 [3, 9] days, p = 0.333) (Figure 2a). However, group E exhibited the shortest duration of hospital stay (15 [10, 24] days) among the three groups (group Y: 20 [11, 40] days; and group M: 30 [12, 56] days) with a significant difference (p = 0.010) (Figure 2b).

The rate of ICU mortality in group E (15.2%) was similar to that noted in group M (15.2%) and higher than that recorded in group Y (6.1%), without a significant difference (p = 0.269) (Figure 3a). The hospital mortality in group E (30.4%) was the highest among the three groups without a significant difference (p = 0.163) (Figure 3b).

Group E was associated with the lowest total hospital cost (12,037 [7,368, 23,345] USD) among the three groups with a significant difference (17,007 [11,068, 29,183] USD in group Y; 23,236 [12,131, 37,186] USD in group M; p = 0.007) (Figure 3c). In patients who was discharged from our hospital or transferred to other hospital (that means patients who survived in our hospital), total hospital cost in group E (n = 32, 11,539 [7,368, 19,364] USD) was also the lowest among the three groups with a significant difference (17,044 (10,965, 25,996) USD in group Y [n = 42]; 21,457 [15,801, 35,627] USD in group M [n = 62]; p = 0.001) (Figure 3d). There was no significant difference in the cost/patient day (dividing total hospital cost by hospital days) among the three groups (832 [572, 1,260] USD in group Y; 749 [563, 1,179] USD in group M; 867 [667, 1,252] USD in group E; p = 0.826).

4. Discussion

In the present study, no significant differences were found among the three examined groups in terms of the focus of infection, SOFA score at ER, and the proportion of patients with septic shock at ER. These findings indicate that the severity at ER was similar in all three groups. There was no significant difference in the duration of ICU stay; however, group E had the shortest duration of hospital stay and the lowest total hospital cost, with a significant difference. However, the hospital mortality rate in group E was the highest among the three groups without a significant difference.

Our hospital, situated in Maebashi in Gunma Prefecture, is located approximately 100 km north of Tokyo. Maebashi has higher rates of aging population and exhibits a higher aging tendency than that observed in urban areas. Therefore, the analysis of the present conditions in our hospital is important to identify future tendencies in developed countries worldwide.

Vast expenditure is required for the treatment of sepsis worldwide. In Germany, sepsis is linked to a significant national socioeconomic burden, and it has been estimated that severe sepsis generates costs between 3.6

Table 1. Comparisons between survival and nonsurvival groups.

	All (n = 174)	Survival group (n = 136)	Non-survival group (n = 38)	p value
Age (years)	72 (63, 80)	72 (61, 79)	74 (68, 82)	0.068
The duration of ICU	6.0 (4.0, 11.0)	6.0 (4.0, 9.3)	5.0 (2.0, 14.5)	0.692
The duration of hospital stay	20.0 (11.3, 38.7)	22.0 (13.0, 44.4)	12.0 (2.0, 29.6)	0.002*
The total hospital cost (USD)	17,281 (10,137, 32,753)	17,539 (10,806, 30350)	13,204 (7,796, 35,372)	0.315

ICU, intensive care unit; USD, United States dollar.
Data are shown as the median (IQR), *p < 0.05.

Table 2. Comparisons among the three patient groups.

	Group Y (N = 49)	Group M (N = 79)	Group E (N = 46)	p-value
Age (years)	56 (44, 61)	73 (69, 75)	84 (81, 86)	<0.001
Male/Female	34/15	43/36	21/25	0.059
Comorbidities (overlapping)				
Heart disease	10 (20.4%)	23 (29.1%)	18 (39.1%)	0.134
Hypertension	13 (26.5%)	30 (38.0%)	18 (39.1%)	0.334
Neurological disease	5 (10.2%)	7 (8.9%)	10 (21.7%)	0.094
Diabetes mellitus	14 (28.6%)	21 (26.6%)	7 (15.2%)	0.249
Respiratory disease	4 (8.2%)	12 (15.2%)	6 (13.0%)	0.507
Hepatic disease	6 (12.2%)	8 (10.1%)	5 (10.9%)	0.933
Cerebrovascular disease	2 (4.1%)	5 (6.3%)	4 (8.7%)	0.653
Blood disease	4 (8.2%)	2 (2.5%)	3 (6.5%)	0.335
Malignancy (solid)	2 (4.1%)	7 (8.9%)	2 (4.3%)	0.454
Chronic kidney disease	9 (18.4%)	12 (15.2%)	1 (2.2%)	0.039*
Autoimmune disease	7 (14.3%)	6 (7.6%)	1 (2.2%)	0.093
Endocrine disease	2 (4.1%)	5 (6.3%)	0	0.221

Data are shown as the median (IQR), number and/or percentage, *p < 0.05.

Table 3. Comparison among the three groups.

	Group Y (N = 49)	Group M (N = 79)	Group E (N = 46)	p-value
Focus of infection				0.642
Respiratory	21	35	23	
Abdominal	13	14	13	
Urogenitald	7	14	7	
Bones/soft tissue	4	8	2	
Others	4	8	1	
SOFA score at ER	6 (4, 9)	6 (4, 8)	5 (4, 7)	0.287
Septic shock at ER	17 (34.7%)	29 (36.7%)	14 (30.4%)	0.776

SOFA, Sequential Organ Failure Assessment; ER, emergency room.
Data are presented as median (IQR) or numbers (%).

and 7.7 billion EUR annually [11]. The cost for the management of sepsis in hospitals in the USA ranks highest among those for all diseases. In 2013, sepsis accounted for >24 billion USD in hospital expenses, representing 13% of the total hospital costs in the USA [12]. In Korea, the standardized average cost per sepsis case increased from 422.5 × 10,000 KRW in 2005 to 741.7 × 10,000 KRW in 2012. Furthermore, the estimated total national expenditure on sepsis was tripled (311.8%) during the same period, with the estimated total amount of expenditure at 13, 226.5 × 100,000,000 KRW in 2012 [13]. In addition, a systematic review of the hospital-related cost of sepsis (including 37 articles/studies) showed that the total hospital cost per patient ranged between 13,292 USD and 75,015 USD [14]. In our study, the total hospital costs for groups Y and M were within this range. However, the total hospital cost for group E was lower. Estimates of the hospital-related cost of sepsis varied considerably across the included studies, depending on the method used for the calculation of cost, the type of sepsis, and the population examined. The evaluation of both outcome and costs for the treatment of sepsis is necessary, and the construction of a standard model may improve the quality of studies investigating the cost of sepsis [14].

The relationship between aging and sepsis has been previously reported. Knoop et al. analyzed patients with sepsis in Norwegian hospitals and reported that sepsis is, in particular, a disease of the elderly. They also stated that the impact of sepsis on healthcare will continue to increase in parallel with the aging population [15]. Kim et al. investigated patients with sepsis in Korea and reported that the increase in the number of patients with sepsis was higher among the elderly population. They concluded that the burden of sepsis in Korea was high and expected to increase further considering the aging population [13]. In a nationwide study in Taiwan, Lee et al. determined the incidence of sepsis in individuals aged ≥85 years to be 9,414 cases per 100,000 population. This

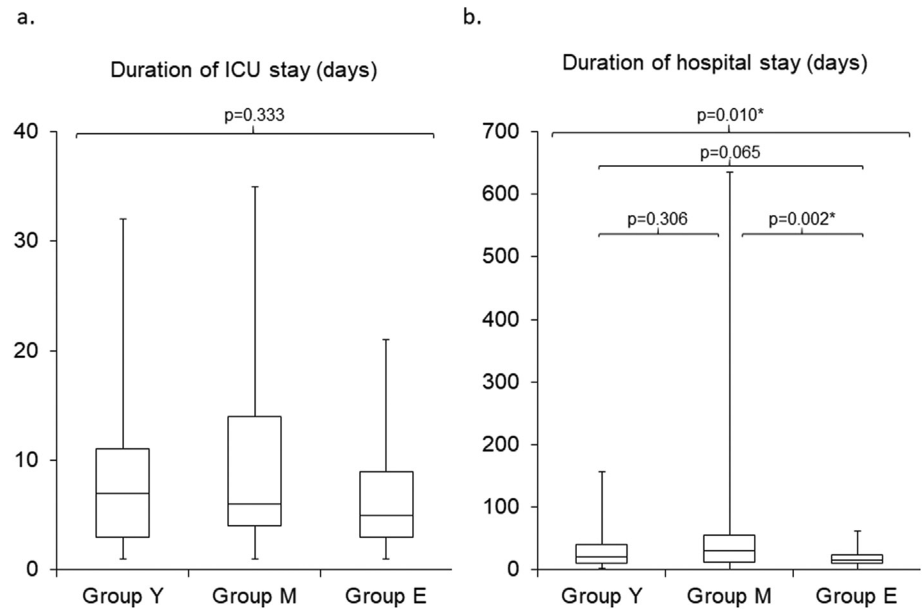

Figure 2. Comparison of the duration of ICU (a) and hospital stay (b). a. There was no significant difference in the duration of ICU stay among the three groups ($p = 0.333$). ICU, intensive care unit. b. The duration of hospital stay in group E was the shortest among the three groups with a significant difference. The results of post-hoc analyses are also shown. *$p < 0.05$.

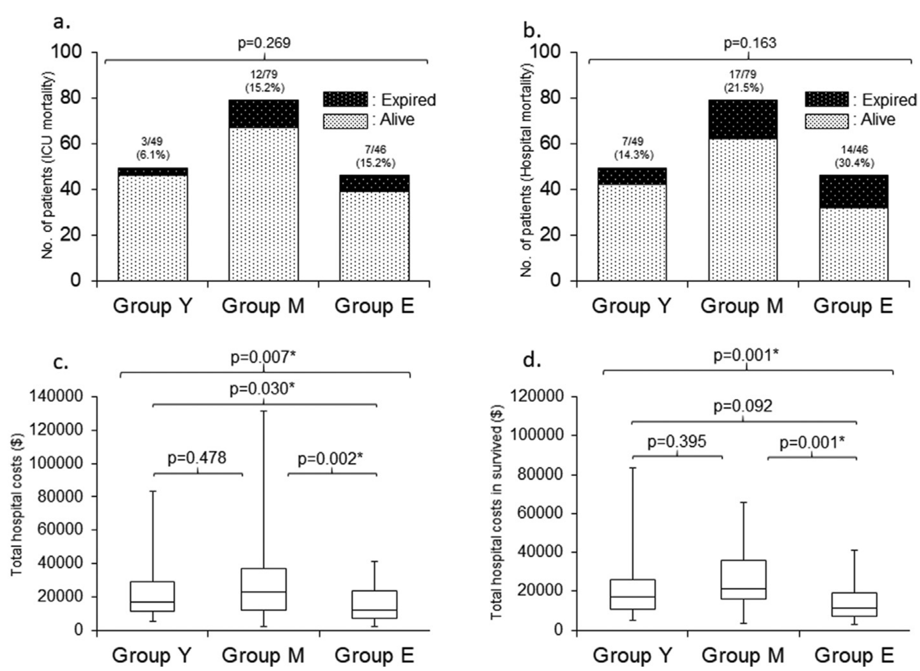

Figure 3. Comparison of ICU mortality (a), hospital mortality (b), total hospital costs (c), and total hospital costs in survived (d). ICU, intensive care unit.

represents a 31- and three-fold higher incidence than that reported in patients aged 18–64 years (303/100,000) and 65–84 years (2,980/100,000), respectively [6].

Among patients admitted to hospitals and the ICU, critically ill elderly patients have a higher mortality rate than younger patients [16]. Our previous study also showed that elderly patients with trauma (aged ≥80 years) require long-term treatment (including ICU stay and higher cost) and are associated with higher hospital mortality versus young patients with trauma [17]. In addition, some researchers found that advanced age is an independent predictor of death in patients with sepsis [13, 18, 19]. Nasa et al. reported that the risk of death from severe sepsis is considerably higher in elderly (60–80 years) and very elderly (>80 years) patients, with age being an independent risk factor for mortality [19]. On the other hand, Chelluri et al. [20] reviewed the literature on outcomes of intensive care for elderly patients with regard to ICU utilization, mortality, hospital costs and charges, and quality of life after intensive care. They concluded that age alone was not an acceptable predictor of critical illness with regard to mortality and the quality of life of survivors. Marik [21] reported that functional elderly patients have a favorable "long-term" outcome after admission to the ICU, and age alone should not be used in making ICU triage decisions. We recently investigated patients aged ≥90 years who were admitted to our department through the ER, and 77.6% of those were discharged from our hospital [22]. Two population-based studies of elderly patients admitted to a hospital or ICU found that a somewhat surprising proportion of elderly patients survived critical illness, were discharged from the hospital, and were able to function independently [16, 23]. Atramont et al. analyzed data extracted from the French national health system database and reported that long-term mortality was high in young surviving patients, but not in elderly patients, compared to the general population matched by age and sex. Nevertheless, aging was associated with an increased risk of mortality within 3 years after discharge from the hospital that included admission to an ICU, with a sharp increase noted in patients aged ≥80 years [24]. However, functional status, markers of quality of life, and long-term prognosis were not assessed in that study.

Kaarlola et al. [25] emphasized that advanced age alone was not a valid reason to refuse intensive care. Nevertheless, the benefits obtained by intensive care appeared to decrease with aging. Our study also revealed that it may be difficult for elderly emergency patients with sepsis requiring intensive care to achieve therapeutic effects equivalent to those reported in younger patients. We supposed that two factors influenced our results. First, the primary disease that caused sepsis was not treatable due to the decreased physiologic reserve [26]. Second, the preexisting chronic medical conditions and comorbidities were associated with prognosis [27]. Therefore, a possibility of getting worse again is high in elderly patients. When conditions of elderly patients get worse again, it is suggested that medical professionals and/or their relatives refrain from positive medical treatment for elderly patients. Brummel and Ferrante insisted that we urgently need to integrate the principles of geriatrics into critical care [28]. They advocated entrustable professional activities overlapping between geriatrics and critical care. These activities consist of the following five factors: (1) facilitate family meeting, including discussion of advanced directives and end-of-life decisions; (2) lead multidisciplinary healthcare teams; (3) provide palliative and end-of-life care; (4) teach patients, families, and multidisciplinary team; and (5) improve quality and safety at the individual and system levels.

4.1. Limitations

This study was retrospective, performed at only one institution, and the sample size was small. The evaluation of acute organ dysfunction during hospitalization and long-term prognosis was not performed. In addition, the lack of functional capacity at discharge and depending on age alone rather than a frailty score are also limitations of the study. A multicenter study is warranted to further clarify the appropriate treatment for elderly emergency patients with sepsis.

5. Conclusion

Elderly emergency patients with sepsis require shorter hospital stay and are associated with lower hospital cost. However, it may be difficult for these patients to maintain the hospital mortality equivalent to those observed in patients aged <80 years.

Declarations

Author contribution statement

Yuta Isshiki and Kiyohiro Oshima: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Jun Nakajima and Yusuke Sawada: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Yumi Ichikawa, Kazunori Fukushima and Yuto Aramaki: Performed the experiments.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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