Prognostic factors for the short-term mortality of patients with rheumatoid arthritis admitted to intensive care units

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Abstract

Background Patients with rheumatoid arthritis (RA) have high mortality risk and are frequently treated in intensive care units (ICUs).

Materials and Methods This study included 67 patients (20 males, 47 females) with RA who were admitted at the ICU of our institution for ≥48 h between January 2008 and March 2018. We analyzed the 30-day mortality of these patients and the investigated prognostic factors in RA patients admitted to our ICU.

Results Upon admission, the mean age was 68 years, and RA duration was 14 years. The 30-day, 90-day, and 1-year mortality rates were 22%, 27%, and 37%, respectively. The major reasons for ICU admission were cardiovascular complications (24%) and infection (40%) and the most common ICU treatments were mechanical ventilation (69%), renal replacement (25%), and vasopressor (78%). In the 30-day mortality group, infection led to a fatal outcome in most cases (67%), and nonsurvivors were associated with a significantly higher prednisone dose, Charlson's comorbidity index, and acute physiology and chronic health evaluation (APACHE) II score. Blood data at ICU admission showed that lower platelet number and total protein and higher creatinine and prothrombin time international normalized ratio (PT-INR) indicated significantly poorer prognosis. Multivariate analysis revealed that dose of prednisone, high APACHE II score, and prolonged PT-INR indicated a higher risk of 30-day mortality.

Conclusion Our study revealed that high prednisone dose, elevated APACHE II score, and coagulation abnormalities predicted poorer prognosis in RA patients admitted to the ICU.

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune inflammatory disorder that promotes the production of inflammatory cytokines, which leads to the destruction of joints and systematic complications [1]. Immunosuppressive treatment for RA using glucocorticoids, conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biologic disease-modifying antirheumatic drugs (bDMARDs), and targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs; e.g., JAK inhibitors) significantly improves disease activity and joint destruction; however, numerous comorbidities and complications, including infection, malignancy, and organ failure (cardiovascular disease [CVD], respiratory distress, and renal failure) remain associated with the increased mortality of RA patients compared with the general population [2–4]. Novel biological treatments have transformed the evolution of joint disease and its complications, such as serious infection [5]. Worsening comorbidities and complications in RA patients require advanced therapy, thus leading to admission into intensive care units (ICUs) [6–9].

A previous study reported that the reasons for the ICU admission of RA patients included CVD and serious infection and showed that RA patients have increased one-year mortality compared with the general population [8]. The prognostic factors for mortality in RA patients admitted to the ICU included admission

for infection, higher acute physiology and chronic health evaluation (APACHE) II score [10], and necessity for mechanical ventilation or renal replacement therapy [6–9, 11–14]. Furthermore, the risk factors for the admission of RA patients to an ICU included older age and comorbidities such as chronic obstructive pulmonary disorder (COPD) or chronic kidney disease (CKD) [15]. Considering that patients with systemic rheumatic disease (RD) frequently require ICU treatment for their condition, it is important to understand the prognostic factors [16]. Despite the elevated risk of ICU admission and higher mortality in RA patients, few studies have investigated the prognostic factors for RA patients requiring ICU treatment. Furthermore, most studies included multiple autoimmune RDs, such as RA, connective tissue diseases, vasculitis, spondyloarthritis, and other autoimmune disorders, which display different causes of ICU admissions and outcome. A recent study of 43 RA patients admitted to the ICU reported that the risk factors for 30-day mortality included heart failure, liver failure, elevated sequential organ failure assessment (SOFA) score, and vasopressor treatment [17].

RA patients require hospitalization for surgery and various systemic medications owing to joint destruction, flare, or complications and have a high incidence of ICU admission. Thus, this study investigated the prognostic factors for short-term mortality in RA patients after ICU admission.

Materials And Methods

Patients

This single-center retrospective study reviewed the medical records of all consecutive patients with RA admitted to the ICU of Kyushu University Hospital for ≥48 h between January 1, 2008, and December 31, 2017. Kyushu University Hospital is a 1275-bed national university teaching hospital located at Fukuoka in the south of Japan. This hospital has a critical and emergency care center for patients with severe disorders and/or multiple traumas, as well as an organ transplant center. Our ICU has 10 beds for critical and emergency care and 10 beds for postsurgical and nosocomial severe patients. To identify patients who require intensive care, we excluded patients who were admitted overnight for postoperative observation and analyzed patients who were admitted for ≥48 h. No RA patients died within 48 h after ICU admission in our study. RA diagnosis was established according to the classification criteria of the American College of Rheumatology[18], and patients were examined and verified by a rheumatologist using medical reports or other medical documents in our electronic database. The underlying status of RA at ICU admission included sex, age, RA duration, Steinblocker stage and class, medication (tsDMARDs, bDMARDs, csDMARDs, and glucocorticoid), and comorbidities to predict mortality by classifying or weighting comorbid conditions according to the updated Charlson's comorbidity index (CCI) [19, 20]. Daily glucocorticoid dose at ICU admission was calculated as prednisone dose. The reasons for ICU admission were grouped as cardiovascular complications, infectious complications, liver failure, respiratory disorder, gastrointestinal tract disorder, neurological disorder, renal failure, or other (e.g., trauma and addiction). Complete laboratory data were evaluated at ICU admission and the following day. The APACH II score, which predicts the risk of death, was calculated using age, previous health status, and routine

physiological measurements during the first 24 h after ICU admission [21]. Disseminated intravascular coagulation (DIC) score [22, 23] at ICU admission was made by the Japanese Association for Acute Medicine DIC scoring system using prothrombin time international normalized ratio (PT-INR) and fibrin degradation product [24]. Several intensive treatments were performed for organ failure such as mechanical ventilation, renal replacement therapy, plasma exchange therapy, vasopressors, and/or antibiotic therapy. The duration of each ICU and hospital stay was documented. This retrospective study was approved by the Ethics Committee of Kyushu University Hospital (approval number: 30-478).

Outcome measures

The primary outcomes were the 30-day, 90-day, and 1-year survival rates of all patients included in the study. Information on patient survival was obtained from medical records at our hospital and/or changing hospital after 30 days, 90 days, and 1 year. A total of 67 patients were followed up at 30 and 90 days, but 5 patients were lost to follow-up 1 year after ICU admission because the patients changed hospital or did not return to the hospital.

Statistical analysis

Statistical analysis was performed using JMP pro 13.0.0 (SAS Institute, Cary, NC). Categorical variables were compared using Pearson's chi-squared test, and continuous variables were analyzed by the Mann–Whitney *U* test. Multivariable logistic regression analysis was performed to identify the independent predictors of mortality. Statistical difference was defined as $P < 0.05$ for all comparisons. Data represent the mean ± standard deviation.

Result

Baseline characteristics of patients

This study included 67 consecutive patients with RA (n = 67) who were admitted to the ICU at Kyushu University Hospital between January 1, 2008, and December 31, 2017 (Table 1). Six of the patients were readmitted to the ICU more than once during this period but were only analyzed at the first ICU admission. The mean age at ICU admission was 68 ± 13 years old (range, 33–96, median, 70), the median RA duration was 14 ± 15 years (range, 0–61, median, 10), and the average follow-up duration was 863 ± 987 days (range, 3–3988). Kaplan–Meier survival curve analysis revealed that the median overall survival after the first ICU admission was 824 days (Fig. 1), and the 30-day, 90-day, and 1-year mortality rates were 22% (15/67), 27% (18/67), and 37% (23/67), respectively (Table 1). Given that the majority of nonsurvivors died within the first 30 days, we investigated the prognostic factors of 30-day mortality by using univariate analysis. Table 1 shows the characteristics associated with RA status at baseline. There was no statistical difference between the 30-day mortality at baseline of survivors and nonsurvivors. Treatment with bDMARDs ($P = 0.1680$) or csDMARDs ($P = 0.4493$) immediately prior to ICU admission showed no statistical difference, whereas the use of glucocorticoids ($P = 0.0239$) was associated with poorer prognosis in nonsurvivors in the 30-day mortality group in a prednisone dose-dependent manner

(P = 0.0095). After ICU admission, patients who were able take csDMARDs and/or prednisone continued with this medication, whereas those who were unable to take anything by mouth were administered a corresponding amount of prednisone without csDMARDs via injection until they could take oral medicine. Treatment with bDMARDs was temporally discontinued during the ICU stay. Most patients, who had been recovered from critical condition and could take orally, has begun taking same amount of DMARDs again. No patient had been treated with tsDMARDs.

Comorbidities with RA patients at ICU admission

The comorbidities of the RA patients were calculated using updated CCI, which predicts hospital mortality by classifying or weighting comorbidities [19, 20] (Table 2). The total CCI score (P = 0.0001), including the liver disease (P = 0.0004) and renal disease scores (P = 0.0009), was significantly increased in nonsurvivors compared with survivors.

Reasons for ICU admission and treatments

The analysis of ICU scores revealed that high APACHE II scores were significantly associated with 30-day mortality (P = 0.0029). The duration of ICU stay showed no difference between two groups, whereas hospitalization was statistically shorter in the 30-day mortality group owing to death within 30 days. The main reason for ICU admission was infection (40%; 27/67) (sepsis, 2; gastrointestinal, 4; skin & soft tissue, 5; respiratory, 8; other infection, 8) ,followed by cardiovascular complications (24%; 16/67) (acute myocardial infarction, 3; acute aortic dissection, 2; post heart operative management, 11), respiratory disorder (13%; 9/67) (acute adult respiratory distress syndrome, 3; others, 6), neurological disorder (6%; 4/67) (cerebral infarction, 2; intracerebral hemorrhage, 1; transient cerebral ischemia, 1), renal failure (4%; 3/67) (post renal transplant, 3), liver failure (3%; 2/67) (post hepatic transplant, 2), gastrointestinal tract disorder (1%; 1/67) (post esophageal cancer operative management, 1), and others (7%; 5/67). Among these reasons, infection was the leading cause of death in the 30-day mortality group (67%; 10/15). ICU treatments included mechanical ventilation (69%; 47/67), renal replacement therapy (25%; 17/67), plasma exchange therapy (3/67; 4%), vasopressor, therapy (52/67; 78%), and antibiotic therapy (39/67; 58%) in the survivor and nonsurvivor groups. Renal replacement therapy for renal failure associated with infection or other organ failures was statistically elevated in nonsurvivors compared with survivors (P = 0.0005) (Table 2).

Biomarkers at ICU admission

To identify the prognostic biomarkers at ICU admission, we performed univariate analysis to compare the difference between survivors and nonsurvivors in the 30-day mortality groups by using blood tests at the first and second days after ICU admission. Mann–Whitney analysis revealed that the nonsurvivors in the 30-day mortality group showed significantly lower platelet number, total protein, and albumin and higher blood urea nitrogen, creatinine, and PT-INR. In particular, lower platelet number and PT-INR were significant on both the first and second days (Table 3). Furthermore, DIC score was higher in the nonsurvivors than in the survivors according to the coagulation abnormalities (Table 2).

Prognostic factors for 30-day mortality in RA patients transferred to the ICU

Table 4 shows the multivariate analysis of 30-day mortality after ICU admission. Multivariate logistic regression analysis was used to estimate the odds of 30-day mortality at ICU admission. The prednisone dose (odds ratio [OR], 1.22; 95% confidence interval [CI], 1.04–1.54; *P* = 0.0286), high APACHE II score (OR, 1.31; 95% CI, 1.09–1.75; *P* = 0.0168), and extended PT-INR (OR, 47.40; 95% CI 2.55–4439.41; *P* = 0.0370) were associated with increased odds of 30-day mortality in the ICU.

Discussion

This study retrospectively analyzed the prognosis of 67 RA patients after ICU admission and identified the predictive factors of 30-day mortality. We revealed that the prognostic factors of 30-day mortality for RA patients included high prednisone dose, high APACHE II score, and prolonged PT-INR at ICU admission.

Previous studies have examined the risk factors and mortality of RA patients after ICU treatment [6–9, 11–15, 17, 25, 26]. The short-term fatal outcome of RD, including RA, tended to be worse in RA patients than in the general population [9, 17, 25], and the long-term (1–3 years) mortality of RA patients was significantly increased after ICU admission [8, 25]. In our institution, the 30-day, 90-day, and 1-year mortalities after ICU admission were 21%, 27%, and 37%, each. This is likely due to the tertiary nature of our hospital and because our study design excluded mild cases. Furthermore, Peschken et al. reported that the most common reasons for ICU admission were CVD and infection [8]. A French cohort study involving patients with RD demonstrated that infection and RD exacerbation were the most common causes for ICU admission [13]. Barrett et al. reported higher rates of severe sepsis and poorer prognosis in RA patients than in the general population [25]. RA patients have an increased a risk of infection [2–4, 15, 17]. A previous study demonstrated that the risk factors for the ICU admission of RA patients due to infection included the non-use of csDMARDs, old age, and comorbidity with COPD or CKD [15]. The current study found that the majority of the 30-day mortality group admitted to our ICU due to infection was nonsurvivors. Immunosuppressive treatment, including bDMARDs, csDMARDs, and glucocorticoids, is reportedly associated with infection [15, 27–32], whereas the use of bDMARDs and/or csDMARDs was not found to be a risk factor for mortality. In line with previous reports, multivariate analysis showed that the dose of prednisone was a strong risk factor in the 30-day mortality group in our study [6, 15, 17, 29, 32, 33]. Treatment with glucocorticoids increased the incidence and hazard of adverse effects in RA patients, such as diabetes mellitus, osteoporosis, thrombotic stroke, CVD, serious infection, and death [34–36]. Two studies previous showed that the use of glucocorticoids for RD led to poorer prognosis in short-term outcome after ICU admission [26, 37]. Therefore, our findings in RA patients indicate that the use of higher prednisone doses may be a risk factor for short-term mortality in these patients. Increased doses of prednisone may have been used in patients with higher disease activity who could not be treated with csDMARDs and/or b/tsDMARDs; however, we were unable to accurately analyze disease activity in patients because of disturbed consciousness or intensive care. Several studies have reported high disease activity and early

presence of joint damage as poor prognostic factors for RA [38–40]. Therefore, it seems reasonable to treat patients with DMARDs and avoid the use of glucocorticoids as possible. In this study, most of the patients with RA (79%) had been treated with glucocorticoid due to various severe complication, such as heart, liver, and renal failure, suggesting that the patients who had been hard to decrease the amount of glucocorticoid for their disease activity and severe complication might be poorer prognosis of 30-day ICU survival.

RA patients often have several comorbidities, and previous studies have reported the risk factors for ICU admission and mortality, such as pulmonary disorder, renal dysfunction, and hypertension [6, 13, 15]. To evaluate comorbidities, we calculated the updated CCI, which can be used to predict hospital mortality [20]. Univariate analysis showed that the updated CCI, particularly the liver and renal failure scores, was higher for nonsurvivors in the 30-day mortality group than for survivors (Table 2) [6, 13, 15, 17]. In the current study, the majority of RA patients were treated with mechanical ventilation and vasopressor therapy after IUC admission. Similar to another study [12], there was a significantly greater use of renal replacement therapy in the nonsurvivors of the 30-day mortality group than in the survivors. Renal replacement therapy was frequently used for worsened liver failure and renal disease among comorbidities and was increased in the nonsurvivors of the 30-day mortality group. Together with the findings from previous reports [12, 41], our data indicate that ICU patients requiring renal replacement therapy showed poorer prognosis. Previous studies reported that other organ replacement therapies, including mechanical ventilation and vasopressors, were associated with a higher mortality in the ICU population [12, 17, 37, 42, 43]. By contrast, the present study did not find any difference in the 30-day mortality groups probably because our study only included RA patients and did not include those with other collagen diseases, such as systemic lupus erythematosus, dermatomyositis, Sjögren's disease, progressive systemic sclerosis, mixed connective tissue disease, or vasculitis.

Some studies have reported that the prognostic factors of ICU mortality in patients with RD included high APACHE II and SOFA scores, serious infection, mechanical ventilation, vasopressor, renal replacement therapy, and glucocorticoid dose [6, 7, 9, 11, 12, 17, 26]. In the present study, multivariate analysis showed that the predictive factors for prognosis in RA patients admitted to the ICU were use of higher prednisone doses, elevated APACHE II score, and prolonged PT-INR. Previous studies in the general population reported that APACHE II and SOFA scores were predictive factors of ICU mortality in RA patients [6, 7, 11, 12, 14, 21]. Considering that the APACHE II scores of RD patients were shown to be approximately equal to those of the general population [14, 17], the results of the current study show that the APACHE II score in RA patients was also a prognostic factor of ICU mortality. Blood test analysis showed that coagulation abnormalities were a prognostic biomarker associated with poor outcome in all ICU mortality [44]. Multivariate analysis showed that prolonged PT-INR at ICU admission could predict ICU mortality by using a routine coagulation test. Therefore, PT-INR should be extended to the ICU admission of patients treated with an anticoagulation agent for their comorbidity. The DIC scores and PT-INR on the day after ICU admission were significantly elevated in the nonsurvivors of the 30-day mortality group, thus suggesting that PT-INR, as a representative of DIC, is a useful biomarker for ICU survival.

This study has several limitations. First, clinical data were retrospectively analyzed. Second, this study used a small cohort from a single institution and did not include a control group. However, the characteristics of the patients treated at the ICU vary between different institutions. Our study was able to analyze an RA population with more critical comorbidities and complications because our institution treated patients with more severe disorders, such as organ transplantation, compared with other institutions around this area. Third, we did not analyze the disease activity of all RA patients, and this approach may have affected the interventions and outcomes of the patients. However, it was difficult to identify disease activity because our study included patients with impaired consciousness and/or are immobile.

Conclusion

In summary, our study showed that patients admitted to the ICU have high 30-day (21%), 90-day (27%), and 1-year (37%) mortality of RA. Comorbidities, such as liver disease and renal failure, increased the risk of mortality, and most patients requiring renal replacement therapy had a fatal outcome. Infectious complications were the highest in the nonsurvivors of the 30-day mortality group, and prednisone use, elevated APACHE II score, and prolonged PT-INR led to poorer prognosis in RA patients admitted to the ICU.

Abbreviations

RA: Rheumatoid arthritis; RD: Rheumatic disease; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; bDMARDs: biologic disease-modifying antirheumatic drugs; tsDMARDs: targeted synthetic disease-modifying antirheumatic drugs; CVD: cardiovascular disease; ICU: intensive care unit; APACHEII: acute physiology and chronic health evaluation II; CCI: Charlson's comorbidity index; DIC: disseminated intravascular coagulation; PT-INR: prothrombin time international normalized ratio;

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of Kyushu University Hospital (approval number: 30-478).

Consent for publication

Not applicable.

Availability of data and material

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All the authors declare that they have no conflict of interest.

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Authors' contributions

TF, KT, KM, HT, YA, SI, JF, JM, NK, TA, TT, and YN conceptualized and designed study. TF and KT contributed to data curation and analysis. TA, TT, and YN supervised the study. TF and KT wrote the original draft. All authors read and approved the final manuscript.

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Tables

Table 1 Rheumatoid arthritis characteristics of the 30-day mortality group at ICU admission

Characteristic	All patients (n = 67)	30-day mortality		
		Survivors (n = 52)	Nonsurvivors (n = 15)	*P*-value
Age (years)	68.3 ± 13.5	66.9 ± 14.4	73.1 ± 8.5	0.1484
Sex (female/male)	47/20	39/13	8/7	0.1062
RA duration (years)	13.9 ± 15.0	14.1 ± 15.7	12.9 ± 12.9	0.7120
Steinblocker				
Stage (I/II/III/IV)	9/19/18/21	9/15/14/17	2/4/4/5	0.9975
Class (1/2/3/4)	7/16/38/6	8/14/29/4	1/3/9/2	0.8407
Medication				
bDMARDs	6 (9%)	6 (12%)	0 (0%)	0.1680
csDMARDs	37 (55%)	30 (57.7%)	7 (46.7%)	0.4493
MTX	19 (28%)	17 (33%)	2 (13%)	0.1428
Others	24 (36%)	18 (35%)	6 (40%)	0.7016
Glucocorticoids	53 (79%)	38 (73.1%)	15 (100%)	**0.0239**
prednisone dose (mg)	5.3 ± 5.3	4.5 ± 5.0	8.1 ± 5.8	**0.0095**
30-day mortality	15 (22%)			
90-day mortality	18 (27%)			
1-year mortality	23 (37%)			

Data represent mean ± SD.

bDMARDs, biologic disease-modifying anti-rheumatic drugs; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; MTX, methotrexate; RA, rheumatoid arthritis.

Table 2 The comorbidities and status of RA patients in ICU admission

		30-day mortality		
	All patients (n = 67)	Survivors (n = 52)	Nonsurvivors (n = 15)	*P*-value
Updated CCI				
Congestive heart failure (0/2)	0.3 ± 0.7	0.2 ± 0.6	0.5 ± 0.9	0.0904
Dementia (0/2)	0.09 ± 0.4	0.04 ± 0.3	0.3 ± 0.7	0.0617
Chronic pulmonary disease (0/1)	0.3 ± 0.5	0.3 ± 0.5	0.4 ± 0.5	0.5056
Rheumatologic disease (0/1)	1	1	1	ns
Liver disease (0/2/4)	0.6 ± 1.3	0.2 ± 0.8	1.7 ± 2.0	**0.0004**
Diabetes with chronic complications (0/1)	0.2 ± 0.6	0.2 ± 0.6	0.1 ± 0.5	0.5896
Hemiplegia/paraplegia (0/2)	0.2 ± 0.6	0.2 ± 0.6	0	0.1712
Renal disease (0/1)	0.3 ± 0.5	0.2 ± 0.4	0.7 ± 0.5	**0.0009**
Malignancy (0/2/6)	0.3 ± 0.9	0.3 ± 0.7	0.4 ± 1.5	0.5383
AIDS/HIV (0/4)	0	0	0	ns
Total CCI (0–24)	3.3 ± 2.0	2.7 ± 1.4	5.1 ± 2.5	**0.0001**
APACHE II (0–71)	16.2 ± 7.1	14.6 ± 5.6	21.7 ± 9.2	**0.0029**
ICU stay (days)	7.3 ± 7.7	6.6 ± 7.5	9.4 ± 8.4	0.1153
Hospitalization (days)	42.1 ± 35.1	46.2 ± 36.5	27.8 ± 25.6	**0.0302**
DIC score	3.6 ± 2.6	2.8 ± 1.9	6.4 ± 2.9	**<0.0001**
Reason for ICU admission				0.3239
Cardiovascular disease	16 (24%)	15 (29%)	1 (7%)	
Infection	27 (40%)	17 (33%)	10 (67%)	
Liver failure	2 (3%)	1 (2%)	1 (7%)	
Respiratory disorder	9 (13%)	7 (13%)	2 (13%)	
Gastrointestinal tract disorder	1 (1%)	1 (2%)	0 (0%)	
Neurological disorder	4 (6%)	4 (8%)	0 (0%)	
Renal failure	3 (4%)	3 (6%)	0 (0%)	
Others	5 (7%)	4 (8%)	1 (7%)	
ICU treatment				
Mechanical ventilation	46 (69%)	34 (65%)	12 (80%)	0.2824
Renal replacement therapy	17 (25%)	8 (15%)	9 (60%)	**0.0005**
Plasma exchange therapy	3 (4%)	1 (2%)	2 (13%)	0.0598
Vasopressor therapy	52 (78%)	40 (77%)	12 (80%)	0.8012
Antibiotic therapy	39 (58%)	27 (52%)	12 (80%)	0.0521

Data represent mean ± SD.

AIDS, acquired immunodeficiency syndrome; APACHE II, acute physiology and chronic health evaluation II; CCI, Charlson's comorbidity index; DIC, disseminated intravascular coagulation; HIV, human immunodeficiency virus; ICU, intensive care unit; ns, not significant.

Table 3 Blood test biomarkers at ICU admission

	30-day mortality					
	ICU admission day 1			ICU admission day 2		
	Survivors (n = 52)	Nonsurvivors (n = 15)	*P*-value	Survivors (n = 52)	Nonsurvivors (n = 15)	*P*-value
White blood cell (/μL)	10346 ± 5830	13549 ± 7284	0.0810	11433 ± 5106	13577 ± 8145	0.4890
Hemoglobin (g/dL)	10.5 ± 2.2	10.5 ± 2.2	0.6572	10.2 ± 1.7	10.3 ± 2.3	0.9281
Platelet ($\times 10^3$/μL)	178 ± 120	113 ± 93	**0.0365**	159 ± 110	98 ± 63	**0.0446**
C-reactive protein (mg/dL)	6.3 ± 7.6	11.6 ± 15.0	0.1552	10.1 ± 8.0	11.6 ± 15.2	0.6410
Total protein (g/dL)	6.0 ± 1.1	5.0 ± 1.3	**0.0063**	5.5 ± 0.9	5.0 ± 0.8	0.0540
Albumin (g/dL)	3.2 ± 0.8	2.4 ± 0.8	**0.0016**	3.0 ± 0.7	2.7 ± 0.6	0.3947
Blood urea nitrogen (mg/dL)	27.9 ± 18.0	44.6 ± 34.7	0.0758	28.8 ± 17.8	46.5 ± 30.3	**0.0139**
Creatinine (mg/dL)	1.5 ± 1.5	2.5 ± 2.4	0.0665	1.4 ± 1.2	2.3 ± 1.6	**0.0101**
Total bilirubin (mg/dL)	0.9 ± 0.7	3.6 ± 4.5	0.4973	1.1 ± 0.9	3.7 ± 4.4	0.1398
Lactate dehydrogenase (U/L)	367.3 ± 249.6	506.3 ± 413.7	0.1011	348.8 ± 166.4	604.0 ± 583.9	0.1027
PT-INR	1.2 ± 0.2	1.7 ± 1.0	**0.0003**	1.2 ± 0.5	1.4 ± 0.4	**0.0171**

Data represent mean ± SD.

ICU, intensive care unit; PT-INR, prothrombin time international normalized ratio.

Table 4 Multivariate logistic regression analysis of prognostic factors of 30-day mortality after ICU admission

		OR	95% CI	*P*-value
Patients	Age (year-old)	1.03	0.93–1.17	0.5245
	RA duration (years)	1.01	0.94-1.09	0.7651
Medication	DMARDs (yes/no)	0.73	0.08–6.72	0.7802
	Prednisone (mg/day)	1.22	1.04–1.54	**0.0286**
Status in ICU admission	Total CCI	1.98	0.93–6.63	0.1511
	APACHE II	1.31	1.09–1.75	**0.0168**
Blood data on day of ICU admission	Platelet ($\times 10^3/\mu L$)	1.10	0.77–1.02	0.1614
	PT-INR	47.40	2.55–4439.41	**0.0370**

CCI, Charlson's comorbidity index; 95% CI, 95% confidence interval; ICU, intensive care unit; OR, odds ratio; PT-INR, prothrombin time international normalized ratio; RA, rheumatoid arthritis.

Figures

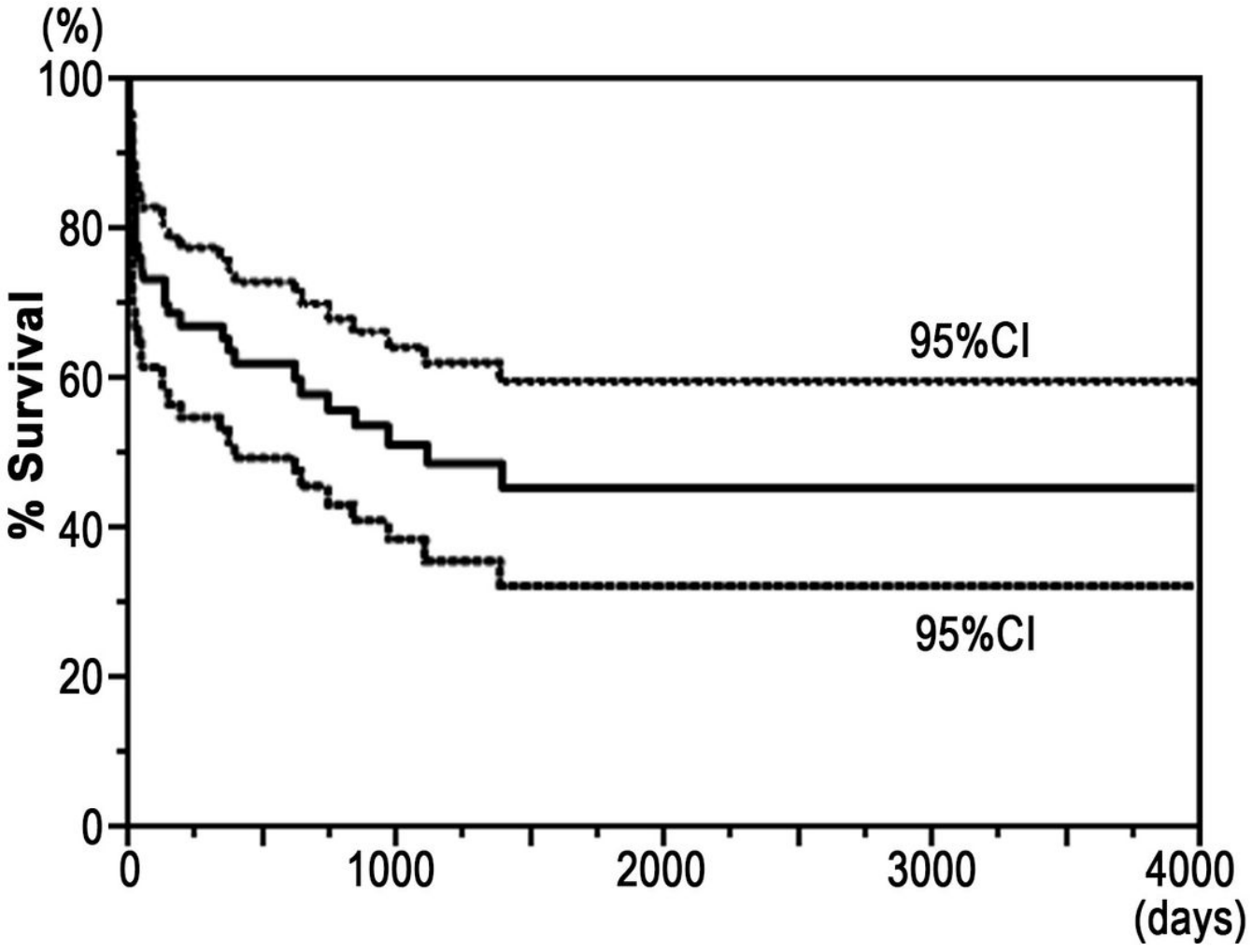

Figure 1

Overall survival of 67 patients after first admission to our ICU. The mean survival was 824 days. Overall survival is represented by a solid line, and 95% CIs are represented by broken lines.