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Outcomes and organ dysfunctions of critically ill patients with systemic lupus erythematosus and other systemic rheumatic diseases

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Abstract

Our objective was to compare the pattern of organ dysfunctions and outcomes of critically ill patients with systemic lupus erythematosus (SLE) with patients with other systemic rheumatic diseases (SRD). We studied 116 critically ill SRD patients, 59 SLE and 57 other-SRD patients. The SLE group was younger and included more women. Respiratory failure (61%) and shock (39%) were the most common causes of ICU admission for other-SRD and SLE groups, respectively. ICU length-of-stay was similar for the two groups. The 60-day survival adjusted for the groups' baseline imbalances was not different (P = 0.792). Total SOFA scores were equal for the two groups at admission and during ICU stay, although respiratory function was worse in the other-SRD group at admission and renal and hematological functions were worse in the SLE group at admission. The incidence of severe respiratory dysfunction (respiratory SOFA >2) at admission was higher in the other-SRD group, whereas severe hematological dysfunction (hematological SOFA >2) during ICU stay was higher in the SLE group. SLE patients were younger and displayed a decreased incidence of respiratory failure compared to patients with other-SRDs. However, the incidences of renal and hematological failure and the presence of shock at admission were higher in the SLE group. The 60-day survival rates were similar.

Key words: Critical illness; Rheumatic diseases; Systemic lupus erythematosus; Intensive care units; Multiple organ failure; Patient outcome assessment

Introduction

Systemic rheumatic diseases (SRDs) are common in the general population (1,2). In addition, they are one of the leading causes of death among young and middle-aged women (1). Approximately 10 to 25% of all patients with SRDs visiting Emergency Departments require hospital admission, and 30% of these patients are admitted to the intensive care unit (ICU) (3). The mortality of critically ill rheumatologic patients is higher than for the general ICU population with similar disease severity (2,4-6).

Multiple organ dysfunction syndrome (MODS) is the most common cause of death in the ICU population (7). The severity of MODS measured by the sequential organ failure assessment (SOFA) score, as well as SOFA-derived variables, are strongly associated with clinical outcomes (8,9). Currently, there are few data regarding MODS evaluation in

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critically ill rheumatologic patients (2). Moreover, the accuracy of other physiologically based severity scores, such as the acute physiology and chronic health evaluation II (APACHE II), in predicting clinical outcomes in these patients is unclear (5,10,11).

Patients with systemic lupus erythematosus (SLE) usually present polymorphic manifestations. In view of this complexity, we hypothesized that SLE patients might have worse outcomes than other-SRD patients. Therefore, the primary aim of this study was to determine whether critically ill patients with SLE have the same incidence and severity of organ dysfunction as critically ill patients with other-SRDs and to compare their clinical outcomes. Secondarily, we attempted to determine the prognostic factors in a general sample of SRD patients and to report the incidence of organ dysfunctions and outcomes in this population.

Patients and Methods

Study design and sampling

This was a single-center cohort study consisting of 1780 consecutive critical patients admitted to the clinical ICU of the Emergency Department, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HCFMUSP), in Brazil. Data were retrieved from April 2003 to January 2010, and all variables were collected prospectively; however, hypotheses were generated before data analysis and after data collection. The present study was approved by the Ethics Committee (CAPPesq) of Hospital das Clínicas, Universidade de São Paulo. Due to its strictly observational design, informed consent was waived.

All patients with the diagnoses of SRD were eligible for inclusion, and only the first ICU admission was considered. Only patients with SRDs diagnosed either before or during the ICU stay were retrieved. The SRDs analyzed in the present study were as follows: SLE (12), polymyositis/dermatomyositis (13), Wegener's granulomatosis (14), rheumatoid arthritis (15), mixed connective tissue disease (16), spondyloarthritis (17), systemic sclerosis (18), Sjögren syndrome (19), primary antiphospholipid syndrome (20), pulmonary-renal syndrome (21), Takayasu's arteritis (22), Behçet's disease (23), Churg-Strauss syndrome (24), and adult-onset Still's disease (25). The exclusion criteria were as follows: SRDs induced by drugs and paraneoplastic syndromes, and rheumatic diseases that were irrelevant to our purpose, such as fibromyalgia, osteoarthritis, rheumatic fever, gout, and undefined SRD.

We included 116 critically ill patients with SRD from the 1780 admitted patients (7%). Patients were clustered into SLE (59 patients) and other-SRD (57 patients) groups.

Data collection

Data were extracted from our database, including demographics (age, gender, ethnicity), co-morbidities (systemic arterial hypertension, diabetes mellitus, chronic renal failure, chronic obstructive pulmonary disease, chronic liver disease, chronic heart failure, infection, previous thrombotic event), admission diagnosis, source of admission, type of admission, use of noninvasive positive pressure ventilation (NPPV), mechanical ventilation (MV), renal replacement therapy (RRT), or vasoactive drugs. The follow-up of patients was extended to death or hospital discharge, and the ICU and hospital length of stay (LOS) were recorded.

Definitions

Infections. Defined by microbiologically documented processes (bacteriological and opportunistic) or suspicious (e.g., suggested by radiographic, clinical and/or laboratory findings). Sepsis syndrome, severe sepsis and septic shock were defined according to the Consensus Conference (26).

Activity of rheumatic disease (*flare*). Acute exacerbation attributable to SRD, after the exclusion of infections, drug reactions, metabolic disturbances, and hypervolemia based on laboratory and clinical data.

Infection and flare. Defined when it was not possible to characterize only one of the previous conditions.

Adverse reaction from treatment drugs. Life-threatening severe reactions to drugs used in the treatment of the respective SRD.

Thrombotic event. Defined as deep vein thrombosis, arterial thrombosis and/or pulmonary embolism. Each of these diagnoses required radiographic or pathological documentation.

Bleeding. Gastrointestinal tract or central nervous system bleeding (e.g., intracranial hemorrhage or acute subarachnoid hemorrhage) as well as alveolar hemorrhage, which was diagnosed according to established criteria (27).

Shock. In this category, we included all patients with cardiovascular dysfunction (systolic blood pressure <90 mmHg refractory to 20-30 mL/kg of crystalloid volume infusion or need for vasopressor therapy).

Acute renal failure. Defined as a creatinine increase >0.3 mg/dL between two measurements up to 48 h apart, acute RRT requirement at any time (e^{-1} for 6 consecutive hours. Patients with chronic renal failure were considered in this

definition (acute renal failure exacerbating chronic dysfunction) if creatinine was increased 1.5-fold from baseline (28).

Respiratory failure. Patients with an oxygen saturation <90% or PaO_2 <60 mmHg at room air, patients with a P/F ratio <300 or need for mechanical ventilation due to respiratory causes (excluding neurological events and anesthesia for surgery).

Central nervous system disturbances. Patients with stroke, intracranial hemorrhage, meningitis, seizures, or coma.

Organ function and severity scores

Clinical and laboratory data for the APACHE II were reported as the worst value within 24 h after admission (29). A daily evaluation of any degree of organ dysfunction according to the SOFA score was performed (30), with the worst value for each of the six organ systems (neurological, cardiovascular, respiratory, renal, hepatic, and hematological) being collected on admission and every 24 h thereafter. Severe dysfunction was defined as a SOFA score higher than 2 for the organ in question (30). SOFA-derived variables were calculated as follows: total SOFA was calculated as the sum of each organ score daily during the ICU stay for each patient; maximum SOFA was the highest score of total SOFA during the ICU stay; mean SOFA was calculated as the arithmetic mean of total SOFA values during the ICU stay; total maximum SOFA (TMS) was calculated as the sum of the worst score for each organ independent of the day, and delta SOFA was the difference between the maximum SOFA and total SOFA at admission. We also recorded the day of the ICU stay during which the maximum SOFA occurred (9,30).

Statistical analysis

The normality of variables was tested using the Kolmogorov-Smirnov goodness-of-fit model. Data are reported as means ± SD or median and 25th and 75th percentiles if they were parametrically or non-parametrically distributed, respectively. Baseline characteristics of the SLE and other-SRD groups were compared using the Mann-Whitney or the unpaired *t*-test as appropriate. The Fisher exact test or chi-square statistics (with Yates correction) were used for dichotomous variables. The Kaplan-Meier curve was used to evaluate the survival of both groups; the probability of survival was compared using the log-rank test. To compare the effect of imbalances (age, gender, chronic renal failure, chronic lung disease, admission syndrome, and hemorrhage evidence) between SLE and other-SRD patients, the Cox proportional hazard analysis was used.

To evaluate the prognostic factors for in-hospital mortality among all 116 patients, we performed a binary logistic regression. After univariate analysis, variables with P values less than 0.2 were included in multivariate analysis with likelihood-ratio backward elimination. The P values used as entry and removal criteria in the backward elimination were 0.05 and 0.10, respectively. Single colinearity was evaluated with the Pearson's correlation with the independent variable, and multicolinearity was evaluated with the variance inflation factor (VIF). To explore the impact of organ dysfunction severity on in-hospital mortality, three models were developed: 1) a model using admission SOFA; 2) a model using maximum SOFA, and 3) a model using TMS (to explore the impact of the worst function of each organ on in-hospital mortality irrespective of the time of occurrence). Significance was considered as $P < 0.05$ (two-tailed). All statistical tests were performed using the commercial package SPSS 13.0 for Windows (USA).

Results

The general features of all 116 patients (59 SLE and the 57 other-SRD patients) enrolled in the study are shown in Table 1. Data regarding only SLE patients such as autoantibodies, immunosuppression and time from SLE diagnosis to ICU admission are shown in Table 2. Table 3 indicates whether life support was used on the patients during the ICU stay as well as other diagnoses and outcomes. Eleven patients had adverse reactions to treatment drugs: severe acute pancreatitis in 4 patients, cumarinic poisoning in 3 patients, toxic epidermal necrolysis in 2 patients, myelosuppression in 1 patient, and acute pulmonary edema secondary to intravenous human immunoglobulin in 1 patient.

The 60-day probability of survival is shown in Figure 1. Panel A shows the probability of crude survival of SLE *vs* other-SRD patients, and Panel B shows the probability of survival of SLE *vs* other-SRD patients adjusted for age, gender, chronic renal failure, chronic obstructive pulmonary disease, admission syndrome, and any hemorrhage evidence. The characterization of organ dysfunctions observed at admission and during the ICU stay, using the SOFA score, is shown in Table 4.

The univariate and multivariate analyses of data associated with the in-hospital mortality of the whole group of critically ill rheumatologic patients are shown in Table 5. To explore the impact of the occurrence of non-synchronic organ dysfunction on in-hospital mortality, we constructed a third model using TMS instead of the maximum SOFA as an independent variable to measure organ dysfunction. In this new multivariate model, age [odds ratio (OR) = 1.05, 95% confidence interval (CI) = 1.02-1.09, P = 0.004, VIF = 1.060)], total maximum SOFA (OR = 1.32, 95%CI = 1.19-1.47, P

< 0.001, VIF = 1.056) and admission from the emergency unit (OR = 0.19, 95%CI 0.05-0.64, P = 0.007, VIF = 1.011) were independently associated with in-hospital mortality.

Discussion

Few studies have analyzed the clinical features, prognosis and outcome of critically ill SRD patients in the ICU (2,4-6). In the present study, we report one of the largest samples in the current literature analyzing these patients. Moreover, to our knowledge, this is the first study comparing SLE and other-SRD patients and also analyzing the SOFA score for the diagnosis and quantification of organ dysfunction in this setting.

The ICU and in-hospital mortality rates were similar to the most recent reports (5,11) and lower than in previous studies (4,6,31) (Table 3). This fact may reflect advances in ICU management and rheumatologic care. Godeau et al. (4,6) have shown that the mortality of critically ill SLE patients is lower than that of other-SRD patients. In contrast, Ansell et al. (31) have suggested that SLE patients have a particularly poor survival rate. However, these studies were not designed to evaluate this issue. The present study demonstrated that the mortality of the SLE group did not differ from that of the other-SRD patient group, which does not support the pre-study hypothesis (Figure 1). The crude mortality was lower in the SLE group despite several features classically associated with worse outcomes, such as major incidence of chronic renal failure (32), higher LOS in the hospital and higher incidence of shock at admission to the ICU (33). However, SLE patients were predominantly young women, a factor strongly associated with better outcome (29,34). Ultimately, the balance of these characteristics resulted in a similar mortality rate.

The association of alveolar hemorrhage, pneumonia, chronic obstructive pulmonary disease, and SRD with pulmonary involvement in the other-SRD group could explain the higher respiratory SOFA at admission. In this group, the occurrence of severe respiratory dysfunction (respiratory SOFA >2) was also higher than in the SLE group (Table 4). However, during the ICU stay the incidence of severe respiratory dysfunction was similar between groups. Furthermore, the need for noninvasive and invasive MV was similar for all groups, which may indicate a higher ICU incidence of adverse events in the SLE group. It is interesting to note that our incidence of MV (52%) was lower than reported for other case series (68-87%) (10,31). A possible explanation for this fact was the use of NPPV (40% of patients), a factor classically associated with fewer intubations in patients with hypoxemic respiratory failure (35). SLE patients had more chronic renal failure before ICU admission, which could explain the higher renal SOFA score on admission and during the ICU stay. Renal failure is common in SLE and strongly related to clinical outcome (3,31). However, in our patients, when taking into account only severe renal failure (renal SOFA >2) on ICU admission and during the ICU stay, the occurrence was similar for all groups, as was the need for RRT. The development of acute renal failure associated with critical illness in other-SRD patients could explain the similar severe renal dysfunction and the need for RRT in both groups. Moreover, the frequency of thrombocytopenia has been reported to be as high as 40%, and is strongly associated with mortality in SLE (36). In this setting, the marked occurrence of hematological dysfunction in the SLE group during the ICU stay may represent not only disease activity but also dysfunction secondary to other critically ill injuries (37).

Analysis of the group as a whole (116 patients) showed that our patients are younger than those in other studies on SRDs in the literature (4,6) (Table 1). This may be related to the current recognition of milder forms of SRD and the prevalence in the cited studies (4,6) of patients with diagnoses of rheumatoid arthritis and systemic vasculitis, diseases typically diagnosed in older patients (1). Respiratory failure was the main cause of ICU admission in our study, a finding similar to other samples of SRD (4) and SLE (10) patients. Regarding the etiology of ICU admission syndrome, infection and flare were common. Moreover, in 22% of our patients the etiologic diagnosis of ICU admission syndrome was related to infection plus flare, which highlights the difficulty in distinguishing between the two diagnoses (Table 1). The differential diagnosis between infection and flare is a challenge in general SRD patients, mainly because the therapeutic approaches are antagonistic. Thus, the treatment instituted often includes empirical antibiotic treatment plus systemic immunosuppression (38).

Regarding the prognostic factors (Table 5), the APACHE II score was not independently associated with in-hospital mortality, which agrees with previous studies showing that the APACHE II is not associated (10,31) or weakly associated (5,11) with mortality. Therefore, it seems that the APACHE II score is not a good tool for predicting mortality in SRD patients. This is probably related to the small number of SRD patients used in the validation of the score (29) and to the fact that SRD patients are generally younger than the general population of critically ill patients. In our study age was independently and consistently associated with in-hospital mortality as well as admission from the emergency room. This result agrees with the current literature, in which young age and emergency room admission (when compared to admission from the ward) are protective factors in general critically ill patients (39). Bleeding was common in our patients, and it has been related to poor outcomes in critically ill patients with SLE (10). In contrast, we did not find it as an outcome factor in multivariate analysis, probably because the incidence of bleeding in the SLE group was lower than in

the other-SRD patients. Moreover, alveolar hemorrhage, the most common site of bleeding in our sample, was directly associated with the need for MV, which was one of the main factors associated with outcome. We found that the SOFA score was a good predictor of in-hospital mortality in SRD patients, as it was in other specific critically ill patients (40). However, admission SOFA was not associated with in-hospital mortality in the multivariate analysis, probably because severe respiratory dysfunction requiring MV was a stronger mortality predictor in the same analysis. Therefore, a worsening of other organ functions during ICU stay (maximum SOFA) was independently associated with in-hospital mortality, suggesting that the process leading to death is preceded by more severe MODS (7).

This study has several limitations. First, our sample was retrieved from a single tertiary hospital and, thus, our findings may not be applicable to other settings. Second, it is a retrospective analysis, and therefore we did not have access to some variables, such as the assessment of SRD activity using specific scores. Third, we did not evaluate long-term quality of life in our patients, an important outcome in view of the fact that SRD and critical illness are chronically debilitating processes.

In this large cohort of critically ill rheumatologic individuals, SLE and other-SRD patients had similar 60-day mortality. SLE patients were younger, had more renal and hematological failure, less respiratory failure and an increased incidence of shock at admission. The major dysfunctions in the total sample at admission and during ICU stay were respiratory and renal. Older patients and those with a need for MV and an increased number of failed organs were more susceptible to poor outcomes. In our sample, APACHE II was not an adequate mortality predictor. However, further prospective studies with these patients should be performed.

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Table 1. Characteristics of all patients at admission.

	Whole group (N = 116)	Other-SRDs (N = 57)	SLE (N = 59)
Characteristics			
Age, years (mean ± SD)	41 ± 17	50 ± 16	32 ± 12*
Female/male gender, N (%)	97 (84)/19 (16)	16 (72)/41 (28)	56 (95)/3 (5)**
Race (black/white), N (%)	19 (25)/87 (75)	10 (18)/47 (82)	19 (32)/40 (68)
APACHE II score (mean ± SD)	18.62 ± 7.98	18.81 ± 7.38	18.43 ± 8.58
Medical/surgical patients, N (%)	101 (87)/15 (13)	48 (84)/9 (16)	53 (90)/6 (10)
Origin of patients, N (%)			
Ward	70 (60)	36 (64)	34 (58)
Emergency room	37 (32)	17 (30)	20 (34)
Other ICU	5 (4)	2 (4)	3 (5)
Operating room	4 (3)	2 (4)	2 (3)
Rheumatologic diagnosis, N (%)			
SLE	59 (51)	-	59 (100)
Wegener's granulomatosis	10 (9)	10 (18)	-
Dermatomyositis/polymyositis	10 (9)	10 (18)	-
Rheumatoid arthritis	7 (6)	7 (12)	-
Mixed connective tissue disease	7 (6)	7 (12)	-
Spondyloarthritis	5 (4)	5 (9)	-
Systemic sclerosis	3 (3)	3 (5)	-
Sjögren syndrome	3 (3)	3 (5)	-
Antiphospholipid syndrome	3 (3)	3 (5)	-
Pulmonary-renal syndrome	3 (3)	3 (5)	-
Takayasu's arteritis	2 (2)	2 (4)	-
Behçet's disease	2 (2)	2 (4)	-
Churg-Strauss syndrome	1(1)	1(2)	-
Adult-onset Still's disease	1(1)	1(2)	-
Co-morbid conditions, N (%)			
Systemic arterial hypertension	54 (47)	29 (51)	25 (42)
Diabetes mellitus	7 (6)	3 (5)	4 (7)
Chronic renal failure	29 (25)	9 (16)	20 (34)**
Chronic heart failure	17 (15)	7 (12)	10 (17)
Chronic obstructive pulmonary disease	5 (4)	5 (9)	0 (0)**
Previous thrombotic event	26 (22)	13 (23)	13 (22)
Syndrome at admission, N (%)			
Respiratory failure	53 (46)	35 (61)	18 (31)**
Shock	31 (27)	8 (14)	23 (39)**
CNS disturbances	15 (13)	4 (7)	11 (19)
Renal failure	10 (9)	5 (9)	5 (9)
Postoperative status	7 (6)	5 (9)	2 (3)
Etiology of admission syndrome, N (%)			
Infection	42 (36)	23 (40)	19 (32)
Flare	36 (31)	19 (33)	17 (29)
Infection + flare	25 (22)	8 (14)	17 (29)
Other	13 (11)	7 (12)	6 (10)

Other-SRDs = other systemic rheumatic diseases; SLE = systemic lupus erythematosus; APACHE = acute physiological and chronic health evaluation score; CNS = central nervous system. *P < 0.05 compared to other-SRDs (unpaired *t*-test). **P < 0.05 compared to other-SRDs (Fisher exact test or chi-square statistics, as appropriate).

Table 2. Characteristics of patients with systemic lupus erythematosus.

	N (%)	
Autoantibodies[a]		
Antinuclear antibodies	55 (100)	
Anti-double-stranded DNA (anti-dsDNA)	30 (55)	
Anti-RNP	23 (42)	
Anti-Sm	14 (25)	
Anti-ribosomal P	13 (24)	
Anti-Ro/SS-A	21 (38)	
Anti-La/SS-B	2 (4)	
Anti-cardiolipin	6 (11)	
Time from SLE diagnosis to ICU admission - days, median [IQR]	1308 [30-3763]	
	Pre-ICU admission	During ICU stay[b]
Immunosuppressive drugs		
Chloroquine	23 (39)	1 (2)
Corticosteroids	51 (86)	53 (96)
Mycophenolate mophetil	7 (12)	1 (2)
Tacrolimus	1 (2)	0 (0)
Methotrexate	4 (7)	0 (0)
Cyclophosphamide	10 (17)	7 (13)
Azatioprine	14 (24)	0 (0)
Plasmapheresis	0 (0)	4 (7)
Gammaglobulin	0 (0)	6 (11)

[a]Data not available for 4 patients. [b]Data not available for 5 patients. IQR = interquartile range.

Table 3. Patient support in the ICU, secondary diagnosis and outcomes.

	Whole group (N = 116)	Other-SRDs (N = 57)	SLE (N = 59)
Support during ICU stay			
Non-invasive positive ventilation, N (%)	46 (40)	23 (40)	23 (39)
Mechanical ventilation, N (%)	60 (52)	32 (56)	28 (48)
Length of mechanical ventilation, median [IQR]	2.5 [1-5]	3.5 [1.3-6.8]	2 [1-4]
Renal replacement therapy, N (%)	26 (22)	10 (18)	16 (27)
Use of antibiotics, N (%)	81 (70)	37 (65)	44 (75)
Vasoactive drugs, N (%)	46 (40)	26 (46)	20 (34)
Septic syndrome, N (%)	67 (58)	31 (54)	36 (61)
Sepsis	14 (21)	5 (16)	9 (25)
Severe sepsis	31 (46)	13 (42)	18 (50)
Septic shock	22 (33)	13 (42)	9 (25)
Infection source, N (%)			
Lung	32 (48)	21 (68)	11 (31)*
Urinary tract	10 (15)	4 (13)	6 (17)
Skin/soft tissues	8 (12)	4 (13)	4 (11)
Abdominal	8 (12)	1 (3)	7 (19)
Blood infection	6 (9)	1 (3)	5 (17)
CNS	2 (3)	0 (0)	2 (6)
Articular	1 (2)	0 (0)	1 (3)
Evidence of hemorrhage, N (%)	33 (28)	20 (35)	13 (22)
Alveolar	21 (64)	15 (75)	6 (46)*
Abdominal	6 (18)	2 (10)	4 (31)
CNS	6 (18)	3 (15)	3 (23)
Evidence of activity of rheumatic disease, N (%)	61 (53)	27 (47)	34 (58)
New-onset rheumatic disease in the ICU, N (%)	6 (5)	2 (4)	4 (7)
Adverse reaction to drugs/treatment, N (%)	11 (9)	2 (4)	9 (15)
Outcomes			
LOS in ICU, median [IQR]	6 [3-8]	5 [2-7]	6 [3-11]
LOS in hospital, median [IQR]	15 [11-30]	12 [8-19]	22 [14-35]**
ICU mortality, N (%)	31 (27)	19 (33)	12 (20)
In-hospital mortality, N (%)	42 (36)	24 (42)	18 (31)
Unit after ICU discharge, N (%)			
Ward	61 (72)	27 (71)	34 (72)
Step-down unit	23 (27)	11 (29)	12 (26)
Other ICU	1 (1)	0 (0)	1 (2)
ICU re-admission, N (%)	18 (21)	7 (18)	11 (23)
One	11 (61)	4 (11)	7 (15)
Two or more	7 (39)	3 (8)	4 (9)

Other-SRDs = other systemic rheumatic diseases; SLE = systemic lupus erythematosus; CNS = central nervous system; LOS = length-of-stay. IQR = interquartile range. *P < 0.05 compared to other-SRDs (Fisher exact test or chi-square statistics as appropriate). **P < 0.05 compared to other-SRDs (Mann-Whitney test).

Table 4. Characterization of organ dysfunctions using the SOFA score at admission and during the ICU stay.

	Whole group (N = 116)	Other-SRDs (N = 57)	SLE (N = 59)
Admission SOFA, mean ± SD	5.5 ± 4.7	5.1 ± 4.1	5.9 ± 5.1
Neurological	0.8 ± 1.3	0.6 ± 1.1	0.9 ± 1.4
Cardiovascular	0.9 ± 1.4	0.9 ± 1.4	0.8 ± 1.4
Respiratory	1.5 ± 1.3	1.8 ± 1.4	1.2 ± 1.2*
Renal	1.3 ± 1.6	0.9 ± 1.4	1.6 ± 1.6*
Hepatic	0.3 ± 0.7	0.2 ± 0.6	0.4 ± 0.7
Hematological	0.8 ± 1.3	0.6 ± 1.2	1.0 ± 1.3*
Maximum SOFA, mean ± SD	7.4 ± 5.4	6.9 ± 5.3	7.8 ± 5.5
Neurological	1.4 ± 1.6	1.2 ± 1.5	1.5 ± 1.7
Cardiovascular	1.5 ± 1.7	1.5 ± 1.7	1.4 ± 1.6
Respiratory	2.0 ± 1.3	2.2 ± 1.5	1.8 ± 1.3
Renal	1.7 ± 1.7	1.4 ± 1.6	2.0 ± 1.7*
Hepatic	0.4 ± 0.7	0.3 ± 0.6	0.5 ± 0.8
Hematological	1.1 ± 1.4	0.8 ± 1.3	1.4 ± 1.5*
Total maximum SOFA, mean ± SD	8.0 ± 5.8	7.5 ± 5.6	8.6 ± 6.0
Mean SOFA, mean ± SD	5.3 ± 4.5	5.0 ± 4.3	5.6 ± 4.7
Delta SOFA, mean ± SD	1.9 ± 3.3	1.8 ± 3.6	1.9 ± 3.0
Day of maximum SOFA, median [IQR]	1 [1-3]	1 [1-3]	2 [1-3]
No. of dysfunctions at admission, median [IQR]	1 [0-2]	1 [0-2]	1 [0-2]
Occurrence of dysfunction at admission, N (%)			
Neurological	19 (16)	7 (12)	12 (20)
Cardiovascular	21 (18)	12 (21)	9 (15)
Respiratory	32 (28)	22 (39)	10 (17)**
Renal	28 (24)	10 (18)	18 (31)
Hepatic	1 (1)	0 (0)	1 (2)
Hematological	15 (13)	5 (9)	10 (17)
No. of dysfunctions during ICU stay, median [IQR]	1 [0-3]	1 [0-2]	1 [0.5-2.5]
Occurrence of dysfunctions during ICU stay, N (%)			
Neurological	34 (29)	14 (25)	20 (34)
Cardiovascular	37 (32)	20 (35)	17 (29)
Respiratory	50 (43)	27 (47)	23 (39)
Renal	42 (36)	16 (28)	26 (44)
Renal (attributable to disease activity)	19 (16)	4 (07)	15 (25)**
Hepatic	1 (1)	0 (0)	1 (2)
Hematological	25 (22)	8 (14)	17 (29)**

SOFA = sequential organ failure assessment score; Other-SRDs = other systemic rheumatic diseases; SLE = systemic lupus erythematosus; IQR = interquartile range. Organ dysfunction means SOFA >2. *P < 0.05 compared to other-SRDs (unpaired *t*-test). **P ≤ 0.05 compared to other-SRDs (Fisher exact test or chi-square statistics as appropriate).

Table 5. Univariate and multivariate analysis of variables associated with the in-hospital mortality of critically ill rheumatologic patients.

Variable	Univariate analysis[a]		Multivariate analysis[b]			Multivariate analysis[c]		
	OR (95%CI)	P	OR (95%CI)	P	VIF	OR (95%CI)	P	VIF
Age	1.05 (1.02-1.07)	0.001	1.05 (1.02-1.11)	0.002	1.053	1.05 (1.02-1.09)	0.005	1.060
APACHE II	1.07 (1.02-1.13)	0.008	-	-	-	-	-	-
Admission SOFA	1.20 (1.09-1.31)	<0.001	-	-	-	Not included	-	-
Maximum SOFA	1.38 (1.23-1.55)	<0.001	Not included	-	-	1.39 (1.22-1.59)	<0.001	1.011
No. of co-morbidities	1.48 (1.04-2.09)	0.028	-	-	-	-	-	-
SLE	0.60 (0.28-1.30)	0.195	-	-	-	-	-	-
Surgical patients	0.40 (0.11-1.50)	0.173	-	-	-	-	-	-
Emergency room admission	0.51 (0.22-1.20)	0.125	0.243 (0.08-0.75)	0.014	1.016	0.18 (0.05-0.63)	0.007	1.056
Infection	1.31 (0.60-2.83)	0.496	-	-	-	-	-	-
Disease activity	0.63 (0.29-1.35)	0.234	-	-	-	-	-	-
Bleeding	2.47 (1.08-5.64)	0.033	-	-	-	-	-	-
Need for MV	9.80 (3.81-25.18)	<0.001	6.94 (2.43-19.84)	<0.001	1.126	-	-	-
Need for RRT	3.18 (1.30-7.82)	0.012	-	-	-	-	-	-
Vasopressor	2.29 (1.05-4.98)	0.036	-	-	-	-	-	-

[a]Only variables with a P value <0.2 in the univariate analysis were used in the multivariate analysis; [b]Multivariate analysis including admission SOFA and not including maximum SOFA; [c]Multivariate analysis including maximum SOFA and not including admission SOFA; OR = odds ratio; CI = confidence interval; VIF = variance inflation factor; APACHE = acute physiological and chronic health evaluation score; SOFA = sequential organ failure assessment score; SLE = systemic lupus erythematosus; MV = mechanical ventilation; RRT = renal replacement therapy.

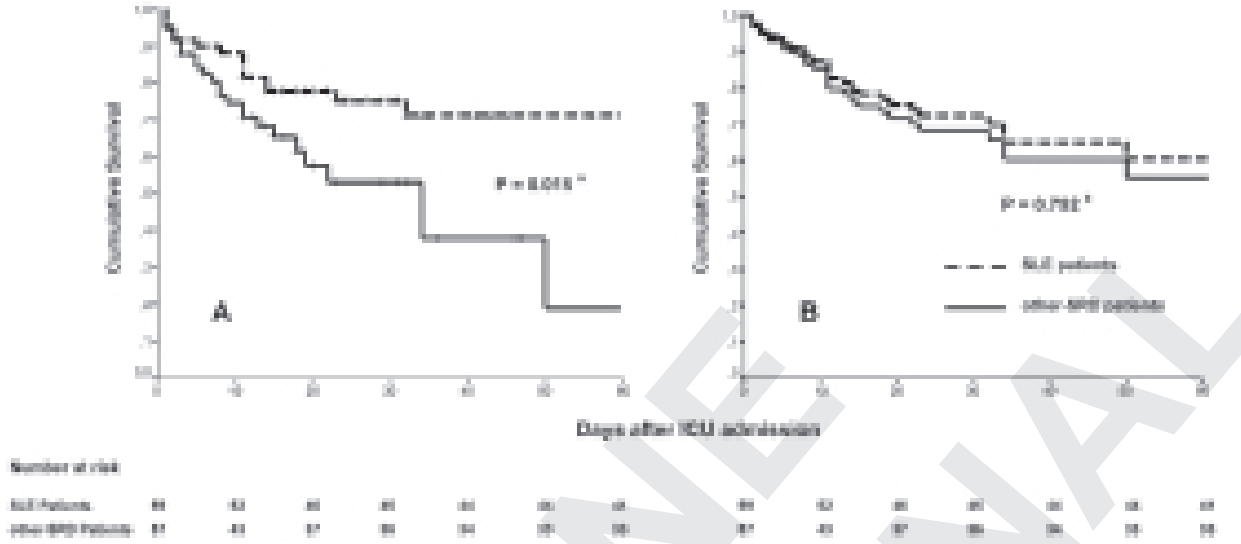

Figure 1. Actuarial 60-day survival among 116 rheumatologic patients with systemic lupus erythematosus (SLE) or other systemic rheumatologic diseases (SRD) after ICU admission. *Panel A* shows the Kaplan-Meyer probability of crude survival curve, and *Panel B* shows the 60-day probability of the survival curve adjusted for age, gender, chronic renal failure, chronic lung disease, admission syndrome, and hemorrhage evidence. [a]P value using the log-rank test. [b]P value using the Cox proportional-hazards regression model with the non-balanced variables between groups as covariates.