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Outcomes in Critically Ill Patients With Systemic Rheumatic Disease

A Multicenter Study

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BACKGROUND: Patients with systemic rheumatic diseases (SRDs) may require ICU management for SRD exacerbation or treatment-related infections or toxicities.

METHODS: This was an observational study at 10 university-affiliated ICUs in France. Consecutive patients with SRDs were included. Determinants of ICU mortality were identified through multivariable logistic analysis.

RESULTS: Three hundred sixty-three patients (65.3% women; median age, 59 years [interquartile range, 42-70 years]) accounted for 381 admissions. Connective tissue disease (primarily systemic lupus erythematosus) accounted for 66.1% of SRDs and systemic vasculitides for 26.2% (chiefly antineutrophil cytoplasm antibodies-associated vasculitides). SRDs were newly diagnosed in 43 cases (11.3%). Direct admission to the ICU occurred in 143 cases (37.9%). Reasons for ICU admissions were infection (39.9%), SRD exacerbation (34.4%), toxicity (5.8%), or miscellaneous (19.9%). Respiratory involvement was the leading cause of admission (56.8%), followed by shock (41.5%) and acute kidney injury (42.2%). Median Sequential Organ Failure Assessment (SOFA) score on day 1 was 5 (3-8). Mechanical ventilation was required in 57% of cases, vasopressors in 33.9%, and renal replacement therapy in 28.1%. ICU mortality rate was 21.0% (80 deaths). Factors associated with ICU mortality were shock (OR, 3.77; 95% CI, 1.93-7.36), SOFA score at day 1 (OR, 1.19; 95% CI, 1.10-1.30), and direct admission (OR, 0.52; 95% CI, 0.28-0.97). Neither comorbidities nor SRD characteristics were associated with survival.

CONCLUSIONS: In patients with SRDs, critical care management is mostly needed only in patients with a previously known SRD; however, diagnosis can be made in the ICU for 12% of patients. Infection and SRD exacerbation account for more than two-thirds of these situations, both targeting chiefly the lungs. Direct admission to the ICU may improve outcomes.

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ABBREVIATIONS: AKI = acute kidney injury; ARF = acute respiratory failure; CTD = connective tissue disease; IQR = interquartile range; SOFA = Sequential Organ Failure Assessment; SRD = systemic rheumatic disease

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Multiorgan systemic rheumatic diseases (SRDs) are infrequent and heterogeneous disorders. They share an immunologic substrate, frequent multiorgan involvement, chronic inflammation, and a natural history with acute exacerbations.[1] During the last decade, outcome has improved dramatically, particularly because of advances in the understanding of the pathophysiologic mechanisms leading to organ dysfunction and improved use of immunosuppression and immunomodulation.[2,3] However, various life-threatening conditions requiring ICU management can occur at any stage of the SRD course.[4] Data suggest that overall, up to 25% of patients with SRDs need ICU admission when presenting to the ED, and up to one-third may require life-sustaining support.[5] Despite advances in the management of patients with critical illnesses, mortality remains as high as 50% in this population.[6,7] To date, little attention has been given to critically ill patients with SRDs. Most of those studies include a limited number of patients managed in single centers[7,8] or cohorts of patients with a single disease, warranting further research in this area. Moreover, because patients may be admitted to the ICU with various conditions (SRD exacerbation, infection, toxicity, or decompensating comorbidity), data are needed to optimally guide the patient's management. For instance, intensivists need to know how and when they need to treat sepsis and at the same time rule out SRD exacerbation or ascribe an organ dysfunction to drug-related toxicity.

We sought to describe the use of intensive care in patients with SRDs. To that aim, we included a large cohort of patients with SRDs requiring ICU admission to 10 ICUs between 2009 and 2013. Factors associated with ICU mortality were analyzed, with particular attention to the respective contributions of SRD exacerbation and infection. In addition, we attempted to determine the factors associated with SRD exacerbation so as to maintain a high level of awareness so that urgent immunosuppressive therapy and lifesaving interventions can be initiated.

Materials and Methods

This study was carried out in 10 medical ICUs in France. All patients with an SRD admitted between January 1, 2009, and January 1, 2013, were identified by computerized ICU summaries and were included retrospectively. We reviewed the medical charts of all patients. The diagnoses were established according to American College of Rheumatology classification criteria and the Chapel Hill 2012 consensus conference nomenclature[9] for systemic vasculitides. Behçet disease was diagnosed according to international Behçet disease criteria.[10] The diagnostic criteria for rheumatologic diseases fulfilled the previous published classifications.[1] We excluded recipients of hematopoietic stem cell transplants. At the time of the study, in accordance with French law, a formal approval from an ethics committee was not required for this kind of project (retrospective methodology).

Data Collection

The data reported in Tables 1 to 4 were collected retrospectively from patients' charts. Sequential Organ Failure Assessment (SOFA) score was computed within 24 h of admission. Shock and acute respiratory failure (ARF) were defined according to previously published criteria.[11,12] Acute kidney injury (AKI) was diagnosed when patients fulfilled the Kidney Disease Improving Global Outcome criteria.[13] We defined neurologic dysfunction by coma (ie, Glasgow Coma Score < 9), altered mental status, seizures, or motor paralysis. Vascular emergencies included pulmonary embolism, life-threatening arrhythmia, pericardial effusion, myocardial infarction, malignant hypertension, thrombotic thrombocytopenic purpura, serious coagulopathy such as catastrophic antiphospholipid syndrome, or cardiac arrest. Cardiovascular risks factors were defined as hypertension, peripheral arterial obstructive disease, coronary heart disease, or diabetes.

Diffuse alveolar hemorrhage and ARDS were diagnosed based on previously published criteria.[14,15] Connective tissue disease (CTD) with associated interstitial lung disease diagnosis was defined according to British Thoracic Society guidelines[16] after exclusion of alternative causes (ie, infection, medication, pulmonary edema). Glomerulonephritis was diagnosed in patients with acute renal failure and kidney biopsy-proven glomerular involvement or proteinuria > 1 g/d, hematuria, or both. Scleroderma renal crisis was defined by rapidly progressive oliguric renal insufficiency with no other explanation, rapidly progressive hypertension occurring during the course of systemic sclerosis, or both.[17] Catastrophic antiphospholipid syndrome was defined according to the Asherson findings.[18] Direct admission to the ICU was defined as being when a patient was admitted from the ED or emergency ambulance service.

The use of life-sustaining therapies throughout the ICU stay was reported. We also recorded the specific SRD treatments initiated in the ICU (ie, high-dose/pulse steroids, IV immunoglobulins, cyclophosphamide, rituximab, or plasma exchange). ICU-acquired infections were defined as recommended previously.[19]

At ICU discharge, patients were classified retrospectively by the ICU physician in each center by using the medical form as follows: SRD exacerbation (manifestations directly attributable to the systemic disease, based on clinical, immunologic, or histologic findings according to the diagnosis criteria described previously), infectious disease (clinically or microbiologically documented bacterial or nonbacterial disease), drug-related toxicities (adverse event caused by therapies used to treat underlying disease), and other diseases (if situations were not

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TABLE 1] Clinical Characteristics of the 363 Critically Ill Patients With SRD

Variable	Patients	No. Missing[a]
Age, median (IQR), y	59 (42-70)	3
Female sex	237 (65.3)	1
Diagnosis of SRD before first ICU admission	318 (88.1)	2
Time from SRD diagnosis to first ICU admission, median (IQR), y	7 (2-16)	45
Geographic origin		100
White	146 (55.5)	
African	54 (20.5)	
North African	45 (17.1)	
Asian	15 (5.7)	
South America	3 (1.1)	
At least one connective tissue disease[b]	240 (66.1)	…
Systemic lupus erythematous	98 (27.0)	
Systemic sclerosis	64 (17.6)	
Rheumatoid arthritis	35 (9.6)	
Secondary Sjögren syndrome	21 (5.8)	
Primary Sjögren syndrome	13 (3.6)	
Inflammatory myopathies[c]	20 (5.5)	
Others	12 (3.3)	
Multisytemic vasculitides	95 (26.2)	…
ANCA-associated vasculitides	51 (14.0)	
Giant cell arteritis	19 (5.2)	
Mixed cryoglobulinemia	6 (1.7)	
Polyarteritis nodosa	3 (0.8)	
Others	19 (5.2)	
Antiphospholipid syndrome	34 (9.4)	…
Sarcoidosis	20 (5.5)	…
Major comorbidities		
Cardiovascular risk factors (one or more)	168 (46.3)	…
Tobacco dependence	88 (24.3)	1
Chronic kidney disease	70 (19.3)	…
Others[d]	81 (22.3)	…

Data are presented as No. (%) unless indicated otherwise. ANCA = antineutrophil cytoplasm antibody; IQR = interquartile range; SRD = systemic rheumatic disease.

[a]No. missing observations, unless Ø.

[b]Some patients had more than one SRD or more than one major comorbidity.

[c]Inflammatory myopathies: dermatomyositis, n = 13; polymyositis, n = 4; others, n = 3.

[d]Solid cancer, n = 34; pulmonary hypertension, n = 13; chronic respiratory insufficiency, n = 12; solid organ transplant, n = 8; viral hepatitis, n = 11; HIV, n = 3.

caused by one of these mains reasons, mostly from decompensating comorbidities).

Statistical Analysis

Quantitative parameters are presented as median (interquartile range [IQR]) and qualitative parameters as number (%). Categorical variables were compared using Fisher exact tests, and continuous variables using Wilcoxon rank-sum tests.

Our primary end point was ICU mortality. The second outcome was SRD exacerbation. To identify associations between patients' characteristics and ICU mortality or SRD exacerbation, we performed logistic regression analyses. In these analyses, each admission (ie, patients hospitalized more than once) was considered to be an independent observation. Factors included in the multivariate regression model were selected for their clinical relevance among variables yielding P values $< .10$ in the univariate analyses. Missing values of covariates were handled by multiple imputations with a chained equation, based on $M = 30$ imputed complete datasets.[20,21] The final multivariate model was selected by a backward stepwise procedure based on P value.

All tests were two sided, and P values $< .05$ were considered to indicate a significant association. Analyses were performed using R statistical software, version 2.14.0 (available online at http://www.R-project.org).

TABLE 2] Description of the Causes of Admissions of the 381 ICU Stays

Variable	No. (%)	No. Missing[a]
No. admissions	381	…
Cause of admission		…
Infection	152 (39.9)	
SRD exacerbation	131 (34.4)	
Treatment-related complication	22 (5.8)	
Comorbid condition	76 (19.9)	
Respiratory failure, including[b]	216 (56.8)	1
Pneumonia	94 (44.5)	5
Pulmonary edema	50 (23.7)	…
Diffuse alveolar hemorrhage	25 (11.8)	…
CTD-ILD	14 (6.6)	…
Others	45 (21.3)	…
Shock, including	158 (41.5)	
Septic	90 (57.0)	…
Cardiogenic[c]	43 (27.2)	…
Hypovolemic	17 (10.8)	2
Others	8 (5.0)	…
AKI, including	160 (42.2)	1
Acute tubular necrosis	71 (44.9)	…
Transient AKI	36 (22.8)	…
Glomerulonephritis	28 (17.7)	1
Scleroderma renal crisis	8 (5.1)	4
Others	15 (9.5)	2
Neurologic, including	75 (19.7)	
Seizures	15 (21.1)	…
Toxic	10 (14.1)	3
Stroke	9 (12.7)	…
Meningitides	6 (8.5)	8
Metabolic	3 (4.2)	…
Others	28 (39.4)	…
Vascular, including	91 (24.1)	
TTP	11 (13.3)	…
Cardiac arrest	11 (13.3)	…
Acute coronary syndrome	11 (13.3)	…
Cardiac tamponade	9 (10.8)	…
CAPS	8 (9.6)	1
Pulmonary embolism	7 (8.4)	…
Endocarditis	6 (7.2)	…
Malignant hypertension	5 (6.0)	…
Others	15 (18.1)	…
Urgent surgery[d]	28 (7.4)	…

AKI = acute kidney injury; CAPS = catastrophic antiphospholipid syndrome; CTD-ILD = connective tissue disease-associated interstitial lung disease; TTP = thrombotic thrombocytopenic purpura. See Table 1 legend for expansion of other abbreviation.

[a]No. missing observations, unless Ø.

[b]Some patients had more than one cause of respiratory failure.

[c]Specific heart involvement: n = 19.

[d]Urgent cardiac surgery: valve replacement, n = 6 (infective endocarditis, n = 3; Libman-Sachs endocarditis, n = 2; other, n = 1); pericardial drainage, n = 4; coronary artery bypass, n = 1; heart transplant, n = 2; mechanical circulatory support device implant, n = 1.

Results

Three hundred sixty-three patients were included (237 women, 126 men; median age, 59 years [IQR, 42-70 years]). Patients' characteristics and SRD types at baseline are listed in Table 1. Forty-three patients (11.9%) had a diagnosis of previously unknown SRD established in the ICU. Among the remaining patients, the time since SRD diagnosis was 7 years (IQR, 2-16 years) before first ICU admission. CTD, primarily systemic lupus, constituted 66.1% of the population, vasculitides (primarily antineutrophil cytoplasm antibodies-associated vasculitides) accounted for 26.2%, sarcoidosis for 5.5%, and antiphospholipid syndrome for 9.4% of the cohort. In contrast, among newly established diagnoses, vasculitides (18%) are more frequently diagnosed than is CTD (11%) (systemic lupus erythematosus, n = 14; systemic sclerosis, n = 4). Details on SRDs and previous organ involvement are shown in e-Table 1.

Systemic nature of illness was sustained by a median of three (one to four) organs' involvements. Among the 336 cases with previously diagnosed SRD, 70.2% received long-term steroids at admission with a median dose of 10 mg/d (IQR, 7-20 mg/d). In addition, cytotoxic drugs or immunosuppressive therapy were given in 66 cases (19.6%) and 56 cases (16.7%), respectively. Nineteen cases had been treated previously with biotherapies (rituximab or tumor necrosis factor-α blockers) (e-Table 1).

Table 2 describes the patients' management throughout the ICU stay. ICU admission was required primarily for infection (152 cases, 39.9%), followed by SRD exacerbation (131 cases, 34.4%), and drug-related toxicities (22 cases, 5.8%). Decompensating comorbid conditions accounted for 19.9% of ICU admissions. Among clinically or microbiologically documented infections, the pulmonary

TABLE 3] Infection Details

Variable	No. (%)
No. admissions	381
Infection	152 (39.3)
Pneumonia	94
Bacteremia	17
GI tract infection	13
Urinary tract infection	10
Endocarditis	6
Central nervous system infection	6
Skin/soft-tissue infection	4
Unknown origin	2
Microbial agents	
Bacteria	69
Cocci Gram[a]	55
Clostridium difficile	4
TB	3
Listeria monocytogenes	2
Legionella pneumophila	5
Viruses	9
Fungi	18
Pneumocystis jirovecii	7
Invasive pulmonary aspergillosis	8
Candida	3
Patients with presumed infection without microbiologic documentation	65

[a]Gram-negative, n = 32; gram-positive, n = 23.

focus was the leading site of infection (94 cases, 24.7%). Table 3 discloses infection sites and documented pathogens and shows that community-acquired and nonopportunistic infections were more common than hospital-acquired or opportunistic infections.

Respiratory failure was the leading cause of ICU admission (n = 216, 56.8%) and was related to infectious pulmonary involvement (44.5%), cardiogenic pulmonary edema (23.7%), diffuse alveolar hemorrhage (11.8%), or CTD-related interstitial lung involvement (21.3%). Among the 158 cases with shock (41.5%), 90 (57.0%) had septic shock and 43 (27.2%) cardiogenic shock, and the 25 (15.8%) remaining had hypovolemic, anaphylactic, or mixed shock. Nineteen patients had cardiogenic shock believed to be ascribable to the SRD itself. Among the 160 cases (42.2%) with AKI, 71 (44.9%) had persistent AKI, 36 (22.8%) had transient AKI, and 36 (22.8%) had SRD-related AKI. The 15 remaining (9.5%) had kidney injury from vascular, immune nephritis, or obstructive origins. The information was not available for two patients.

TABLE 4] Characteristics Throughout the 381 ICU Stays and Outcome

Variable	No. (%) or Median (IQR)	No. Missing[a]
No. admissions	381	…
SOFA at day 1	5 (3-8)	84
Direct admission to ICU	143 (37.9)	4
Life-sustaining treatments during ICU stay		
Mechanical ventilation including	217 (57.0)	
First-line MIV	150 (69.1)	…
NIV only	29 (13.4)	…
NIV followed by MIV	38 (17.5)	…
Length, MIV-d	6 (2-11.25)	…
Vasopressive drugs	129 (33.9)	
Length, d	2 (1-6)	…
Inotropic drugs	57 (15.0)	
Length, d	4 (2-8)	2
Renal replacement therapy	107 (28.1)	
Length, d	3 (1-10)	1
Specific treatment introduced in ICU		
Initiation of corticosteroids	62 (16.4)	2
Pulse	79 (20.7)	…
Cyclophosphamide	40 (10.5)	1
Plasma exchange	45 (11.8)	…
Rituximab	15 (3.9)	…
IVIG	12 (3.1)	…
Median duration of ICU stay, d	6.0 (3.0-12.0)	2
ICU mortality	80 (21.0)	…

IVIG = IV immunoglobulin; MIV = mechanical invasive ventilation; NIV = noninvasive ventilation; SOFA = Sequential Organ Failure Assessment. See Table 1 legend for expansion of other abbreviation.
[a]No. missing observations, unless Ø.

Specifically, 81 patients had both AKI and shock. Among them, the majority (62 patients) had AKI clinically consistent with acute tubular necrosis caused by hemodynamic failure, 16 had prerenal AKI, one had glomerulonephritis, and two had vascular nephropathies.

In 28 cases (7.4%), urgent surgery was required: cardiac surgery (14 patients), GI surgery (eight patients), and neurologic/soft tissue surgery (six patients). Details on urgent cardiac surgery are mentioned in the Table 2 footnotes.

Median SOFA score at admission was 5 (IQR, 3-8). As shown in Table 4, mechanical ventilation was needed in

217 cases (57.0%) (29 were noninvasive only and 38 noninvasive followed by invasive, and 150 received first-line invasive ventilation), vasoactive drugs in 149 (39.1%), renal replacement therapy in 107 (28.1%), and extracorporeal membranous oxygenation in six (1.6%). The durations of life-sustaining therapies are reported in Table 4.

In 112 cases, an immunosuppressive treatment was started in the ICU. Namely, 62 patients (16.4%) received newly prescribed corticosteroids, 79 (20.7%) received high-dose pulse steroids (ie, 500 mg-1 g/d for 3 days), 40 (10.5%) cyclophosphamide, 45 (11.8%) plasma exchanges, and 15 (3.9%) rituximab (Table 4).

The median ICU length of stay was 6 days (IQR, 3-12 days). ICU-acquired infections occurred in 72 cases (18.9%). The crude ICU mortality rate was 21.0% (80 deaths). Forty-two patients died of multiorgan failure with any primary cause. Infection was the main cause of death (40 patients, 50.0%), followed by SRD exacerbation (24 deaths, 30%), and iatrogenic complications (three deaths, 3.8%). Finally, 13 deaths (16.2%) were related to miscellaneous causes.

Tables 5 and 6 discloses independent determinants of ICU mortality by multivariate analysis and determinants of SRD exacerbation. Results of univariate analysis are shown in e-Tables 2 and 3. Factors associated with ICU mortality were shock and SOFA score ($P < .05$). Direct ICU admission was associated with significantly reduced mortality. Among variables depicting the nature, extent, or any characteristics related to SRDs or comorbidities, none was associated with ICU mortality.

As shown in Tables 5 and 6, the probability of SRD exacerbation decreases with advanced age or when a patient presents with shock at admission ($P < .001$). Conversely, among patients with newly diagnosed SRD (during the ICU stay), SRD exacerbation was the most likely reason for ICU admission.

Fourteen patients were admitted to the ICU more than once, corresponding to a total of 32 admissions. Ten of these 14 patients were admitted twice in the period of the study and four patients were admitted three times. We did not find any statistical differences in patient characteristics and causes of admissions between patients with more than one admission and others. The most frequent causes of admission in patients with readmissions were infection (31%) and SRD exacerbation (47%). Among the 10 patients with two admissions, six had the same cause of admission: Three were admitted twice for infection and three for SRD exacerbation. Among the four patients with three admissions, none had the three same causes of admission, but all had two out of the three admissions with the same cause. AKI was more frequent in patients with only one admission (44.4%) compared with patients with more than one admission (18.6%) ($P = .005$). We did not find statistical differences in other causes of admission between the two groups. Among the 14 patients with ICU readmissions, five ICU deaths were observed, corresponding to a crude ICU mortality rate of 36% (95% CI, 13%-65%).

Discussion

This study reports the results from the largest cohort on critically ill patients with SRD. Patients' severity and organ dysfunction were mostly related to infectious complications and SRD exacerbation. This study, which enrolled 363 patients (381 ICU admissions), identified two important and novel findings, namely, that mortality was not related to SRD characteristics, but was significantly reduced by an early admission to the ICU.

In our study, the most common SRD was systemic lupus erythematosus, in agreement with the findings of several other reports.[7,22,23] This is different from older reports, in which rheumatoid arthritis was the most common.[6,24-26] This change in epidemiology has remained unchanged

TABLE 5] Final Multivariate Logistic Regression for ICU Death as Admission Cause-Results From 30 Imputed Datasets

	Observed Figures		Imputed Figures	
Variables	No	Yes	OR (95% CI)	*P* Value
No. admissions	301	80	…	…
Model 1[a]				
Shock, No. (%)	97 (32.2)	61 (76.2)	3.77 (1.93-7.36)	.0001
Direct admission in ICU, No. (%)	122 (41.1)	21 (26.2)	0.52 (0.28-0.97)	.04
SOFA score, median (IQR)	4.0 (2.5-7.0)	8.5 (5.2-12.0)	1.19 (1.10-1.30)	.00005

See Table 1 and 4 legends for expansion of abbreviations.
[a]Adjusted for disease conditions (iatrogenic complication or others/infection/SRD exacerbation).

TABLE 6] Final Multivariate Logistic Regression for SRD Exacerbation as Admission Cause-Results From 30 Imputed Datasets

Variables	SRD Exacerbation		Imputed Figures	
	No	Yes	OR (95% CI)	*P* Value
No. admissions	250	131	...	...
Model 2				
SRD diagnosis in ICU, No. (%)	2 (0.8)	41 (31.5)	42.0 (9.4-187.4)	<.00001
Age at ICU admission, median (IQR), y	63.0 (50.0-73.2)	45.0 (29.0-59.0)	0.96 (0.94-0.97)	<.00001
Shock diagnosis during ICU, No. (%)	119 (47.6)	39 (29.8)	0.39 (0.22-0.68)	.0009

See Table 1 legend for expansion of abbreviations.

since the 2000s.[4] Furthermore, systemic vasculitides were less frequent than CTD, according to the differences observed in distribution among the general population.[27,28] However, systemic vasculitides were more often newly diagnosed in the ICU than was CTD (18.4% and 10.4%, respectively). Severe specific organ involvement requiring urgent supportive therapy could explain this result.

In this large cohort study, infection was the first cause of ICU admission. Sepsis, particularly septic shock, was also the leading cause of death. This finding is consistent with other studies[6,24,29] that identified infection as the primary cause of death. This reflects the key role of the immunosuppressive state in these patients. Interestingly, we noted that opportunistic agents were not as common as expected in immunocompromised patients. Regarding this, *Pneumocystis* pneumonia has been recognized as a major complication in patients with SRDs undergoing induction therapy.[30,31] However, we found a limited number of *Pneumocystis* pneumonia (n = 7) in contrast to the importance of the immunosuppressive regimen at admission. An important message is to consider these patients at high risk of overwhelming infection.

SRD exacerbation was the second most common reason for admission, occurring in one-third of admitted patients. Indeed, for 11.9% of patients, SRD was newly diagnosed in the ICU. This is important for internists and critical care physicians who must maintain a high level of suspicion toward SRD exacerbation among differential diagnoses in unexplained systemic manifestations, in particular with renal injuries, pulmonary injuries, or both. Because SRDs can be responsible for death from severe organ dysfunction, it is necessary to consider starting immunosuppressive treatment as early as possible. Thus, ICU management should include at the same time organ support therapy and specific treatment, a situation that was observed in almost 30% of the patients.

This is even more relevant in newly diagnosed SRD. Conversely, immunosuppression intensification should be carried out with caution in case of shock or in older patients for whom SRD exacerbation is less likely to occur.

This study underlines the various possible reasons for ICU admission in patients with SRDs. One striking finding was that ARF was among the most prevalent symptoms. This is consistent with previously published studies in which pneumonia was the first cause of ARF ahead of acute pulmonary edema or CTD with associated interstitial lung disease and diffuse alveolar hemorrhage.[32,33] Previous studies reported disease activity or diffuse alveolar hemorrhage to be the most common reason for ARF, particularly in small-vessel vasculitides.[33,34] It is important to keep this finding in mind among differential diagnoses of lung infiltrates in critically ill patients with SRD. ARF was associated with a very severe course of disease: Mechanical ventilation was required in up of 81% of patients.[34,35] In keeping with our results, 57% of patients needed mechanical ventilation. Studies on the best possible ventilator strategy in the immunocompromised are warranted, given the high case fatality in this subgroup of patients.[7,36]

Overall, the crude mortality rate in our study was 21.0%. This is in agreement with the mortality rate expected based on the values of the severity scores (SOFA at day 1). This short-term mortality was lower than generally estimated (25%-50%).[4] In their study of 187 patients, Godeau et al[6] reported an ICU mortality rate of 33%. On the contrary, in their large study of 149 critical ill patients with SRD, Faguer et al[37] found a 28-day mortality rate of 16%. Major advances in the care of critically ill could explain our result.[11,12,38] Moreover, this study identified a new target for further reducing mortality in patients with SRDs. Namely, we found that direct admission to the ICU was independently associated with survival.

Thus study has some limitations, however. First, the retrospective design may have influenced the quality of the data collection and the results. However, SRDs have a low incidence, and this study reports a constant number of patients from 10 centers. Second, the fact that the study was performed in tertiary hospitals with SRD reference centers may preclude the generalizability of the results. However, such patients are usually managed in highly specialized and skilled centers, making these results similar to those which may be expected in other settings. Last, various underlying SRDs were included. This could make it difficult to assess the influence of each SRD on mortality. However, based on the respective incidence of SRDs, collecting data on a large number of patients with each single SRD does not seem realistic. Moreover, this study did not show any association between SRD characteristics and outcomes.

Conclusions

In summary, in patients with SRDs, both infection and disease exacerbation are leading reasons for ICU admission. ARF and sepsis are the leading causes of admission and may be associated with high morbidity and mortality. Intensivists must keep in mind that SRD exacerbation may require immunosuppressive agents along with life-saving interventions, particularly in newly diagnosed SRDs. The association between direct admission to the ICU and survival suggests that delays in a patient's management should be avoided and warrants further interventions in these patients.

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Additional information: The e-Tables can be found in the Supplemental Materials section of the online article.

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