

# Outcome of Patients with Systemic Sclerosis in the Intensive Care Unit

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**ABSTRACT. Objective.** Patients with systemic sclerosis (SSc) are prone to disease-specific or treatment-related life-threatening complications that may warrant intensive care unit (ICU) admission. We assessed the characteristics and current outcome of patients with SSc admitted to the ICU.

**Methods.** We performed a single-center retrospective study over 6 years (November 2006–December 2012). All patients with SSc admitted to the ICU were enrolled. Short-term (in-ICU and in-hospital) and longterm (6-mo and 1-yr) mortality rates were studied, and the prognostic factors were analyzed.

**Results.** Forty-one patients with a median age of 50 years [interquartile range (IQR) 40–65] were included. Twenty-nine patients (72.5%) displayed diffuse cutaneous SSc. The time from diagnosis to ICU admission was 78 months (IQR 34–128). Twenty-eight patients (71.7%) previously had pulmonary fibrosis, and 12 (31.5%) had pulmonary hypertension. The main reason for ICU admission was acute respiratory failure in 27 patients (65.8%). Noninvasive ventilation was first attempted in 13 patients (31.7%) and was successful in 8 of them, whereas others required endotracheal intubation within 24 h. Altogether, 13 patients (31.7%) required endotracheal intubation and mechanical ventilation. The overall in-ICU, in-hospital, 6-month, and 1-year mortality rates were 31.8%, 39.0%, 46.4%, and 61.0%, respectively. Invasive mechanical ventilation was the worst prognostic factor, associated with an in-hospital mortality rate of 84.6%.

**Conclusion.** This study provides reliable prognostic data in patients with SSc who required ICU admission. The devastating outcome of invasive mechanical ventilation in patients with SSc requires a reappraisal of indications for ICU admission and early identification of patients likely to benefit from noninvasive ventilation. (First Release July 1 2015; J Rheumatol 2015;42:1406–12; doi:10.3899/jrheum.141617)

**Key Indexing Terms:**  
SYSTEMIC SCLEROSIS  
OUTCOME

INTENSIVE CARE UNIT  
MECHANICAL VENTILATION

Systemic sclerosis (SSc) is a rare multisystem disease characterized by vascular hyperreactivity and fibrosis in the skin and other organs. Patients with SSc are classified according to the extent of skin involvement: limited SSc (lSSc) with no detectable skin involvement, limited cutaneous SSc (lcSSc) with skin involvement essentially limited to the hands and face, and diffuse cutaneous SSc (dcSSc) with proximal skin

involvement<sup>1</sup>. Visceral involvement is uncommon in patients with lSSc and lcSSc, and their prognosis is less severe than for patients with dcSSc<sup>2</sup>. Indeed, patients with dcSSc are prone to develop cardiopulmonary and renal involvement early in the course of the disease, complications that are responsible for reduced life expectancy<sup>3,4,5,6,7</sup>. Cardio-pulmonary manifestations are common and include inter-

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Presented in part at the 40th Congress of the French Intensive Care Society (Société de Réanimation de Langue Française), Paris, France (January 18–20, 2012).

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Accepted for publication April 23, 2015.

stitial lung disease (ILD), as well as pulmonary arterial hypertension (PAH)<sup>2,8,9</sup>. Scleroderma renal crisis (SRC) is a rare complication of SSc related to microangiopathic acute renal failure that may often result in dialysis-dependent chronic renal insufficiency<sup>5</sup>. Over the past 2 decades, advances in the understanding of the disease process and in the management of visceral manifestations have resulted in improved survival of patients with SSc<sup>6,10,11</sup>.

Because of specific organ dysfunctions and immunosuppressive treatments, patients with SSc are prone to life-threatening complications that may warrant ICU admission<sup>3</sup>. Yet, data on the prognosis of patients with SSc in the ICU are scarce and mostly derived from heterogeneous cohorts of critically ill patients with systemic autoimmune diseases, including connective tissue diseases and systemic vasculitis, in which patients with SSc are underrepresented<sup>12,13,14,15,16,17,18,19</sup>. However, indications and outcome of intensive care in patients with SSc would be best addressed by taking into account the specific prognosis of the disease. To address the current prognosis of patients with SSc requiring ICU admission, we performed a retrospective study within a tertiary care center.

## MATERIALS AND METHODS

**Patients and setting.** All patients with a previously known diagnosis of SSc who were admitted to our medical ICU from November 2006 to December 2012 were eligible for inclusion. In our unit, diagnosis coding was consistent and exclusively performed by senior physicians. All patients with SSc were coded using the International Classification of Diseases, 10th ed, code "systemic sclerosis" and could then be easily retrieved. A complete collection of data was ensured by the electronic patient data management system. Patients with SSc were excluded if they were admitted for the management of invasive procedures (e.g., fiberoptic bronchoscopy), central venous access adjustment, or intermittent hemodialysis for chronic renal failure. ICU admission decisions were made by both the intensivist and the referring physician. For patients who were admitted more than once to the ICU, only the first episode was analyzed. The study was conducted in compliance with the Declaration of Helsinki principles and with the French regulation of clinical research. Patients with SSc who were regularly followed at our institution were systematically proposed to be enrolled into a registry for research purposes. Constitution of this cohort of patients with SSc was approved by the local institutional review board and followed the principle of nonopposition after information. Accordingly, this retrospective observational study required neither specific ethical approval nor additional informed consent.

**Data collection.** Characteristics of SSc included organ involvement prior to the acute complication and longterm treatment with glucocorticoids and/or immunosuppressive drugs. ILD was diagnosed by chest high-resolution computed tomography showing 1 or more of isolated ground-glass opacities, honeycombing and concurrent presence of ground-glass attenuation, and traction bronchiectasis and/or bronchiolectasis in association with forced vital capacity (FVC) and DLCO. PAH was defined by either mean pulmonary artery pressure (PAP) > 25 mmHg on right-heart catheterization or by estimated systolic PAP > 50 mmHg on echocardiography when right-heart catheter measurements were not available<sup>20,21</sup>. SRC was defined as new-onset or accelerated-phase hypertension with evidence of renal impairment, microangiopathic hemolysis, and/or significant end-organ damage in the context of SSc<sup>22</sup>. Creatinine clearance was calculated using the Modification of the Diet in Renal Disease (MDRD) formula.

The Simplified Acute Physiology Score 2 (SAPS2) and Sequential Organ Failure Assessment (SOFA) severity scores were computed based on the first

24 h following ICU admission<sup>23,24</sup>. Patients with acute respiratory failure were eligible for noninvasive ventilation (NIV) in the absence of contraindications. Endotracheal intubation and mechanical ventilation were performed in case of refractory hypoxemia, respiratory arrest, inefficacy of NIV (as assessed by nonimprovement or deterioration of respiratory symptoms, or dependency for more than 12 h per day), unstable circulatory condition, or deterioration of neurologic status. Intubated patients were mechanically ventilated using a protective strategy with low tidal volume of 6 ml/kg and limitation of plateau pressure to 30 cm H<sub>2</sub>O whenever possible<sup>25</sup>. Patients with severe sepsis were treated according to the Surviving Sepsis Campaign guidelines<sup>26</sup>.

Endpoints were short-term (in-ICU and in-hospital) and longterm (6-mo and 1-yr) mortality rates. Longterm followup was obtained through the individual medical files of patients.

**Statistical analysis.** Results are reported as median (interquartile range) or number (%) as appropriate. Categorical variables were compared with chi-square or Fisher's exact tests, and continuous variables were compared with the Mann-Whitney U test. Survival curves were obtained using the Kaplan-Meier method and compared using the log-rank test.

## RESULTS

**Patients' characteristics.** During the 6-year study period, 41 patients with SSc were admitted to the ICU. SSc had been diagnosed within a median of 78 months (34–128) prior to ICU admission (Table 1). Most patients (72.5%) presented with dcSSc. Digestive tract disorders were present in all but 2 patients, and were almost exclusively manifested by gastroesophageal reflux. ILD with pulmonary fibrosis was detected in most patients and accounted for marked reduction of FVC < 55% and severe impairment in DLCO diffusion < 55% in 42.4% and 85.7% of patients, respectively. Twelve patients (31.5%) had PAH, as assessed by right heart catheter (n = 7) or echocardiography only (n = 5). Altogether, cardiopulmonary involvement resulted in severe impairment in respiratory functional status [New York Heart Association (NYHA) stage 3–4] in 20 patients. Eight patients had already known chronic renal failure with MDRD-estimated creatinine clearance < 50 ml/min, 1 patient being under chronic hemodialysis. Two patients had already experienced 1 episode of SRC. Twenty-seven (65.8%) and 12 (29.2%) patients were treated with longterm glucocorticoids [median daily dose 0.16 (0.13–0.24) mg/kg] and/or other immunosuppressive drugs, respectively.

**Acute complications and organ failures.** The main cause of admission into the ICU was acute respiratory failure (65.8% of patients; Table 2). Pulmonary infection was diagnosed in 14 patients (34.1%), and the causing pathogen was identified in 5 patients. An NIV trial was first attempted in 13 patients (31.7%) and was successful in 8 of them, whereas 5 subsequently required endotracheal intubation within 24 h. Overall, 13 patients (31.7%) required endotracheal intubation and mechanical ventilation, of whom 5 patients exhibited moderate to severe hypoxemia as assessed by a PaO<sub>2</sub>/FiO<sub>2</sub> ratio below 200. Duration of invasive mechanical ventilation was 3 days (2–9).

**Outcomes and prognostic factors.** Twenty-eight patients (68.2%) were discharged from the ICU and 25 (61%) were

Table 1. Baseline characteristics of patients with SSc, both in-hospital survivors and those who died. Values are n (%) or median (IQR) unless otherwise specified.

Variable	All Patients, n = 41	Survived, n = 25	Died, n = 16	p*
Age, yrs	50 (40–65)	47 (38–58)	59 (42–69)	0.10
Female	33 (80.5)	18 (72)	15 (93.7)	0.12
BMI, kg/m <sup>2</sup>	23 (18.8–25.8)	23 (17.4–26.4)	22.9 (19.4–25)	0.66
Non-SSc significant comorbidities	10 (24.4)	6 (24)	4 (25)	0.94
Cardiovascular diseases	7 (17)	5 (20)	2 (12.5)	
Others**	3 (7.3)	1 (4)	2 (12.5)	
Features of SSc				
Time since diagnosis, mos, n = 40	78 (34–128)	72 (45–105)	97 (21–187)	0.68
Type of SSc, n = 40				0.27
Diffuse cutaneous	29 (72.5)	20 (80)	9 (56.2)	
Limited cutaneous	11 (27.5)	5 (20)	6 (37.5)	
mRSS, n = 35	19 (5–30)	20 (7–30)	19 (3–28)	0.60
Digestive involvement	39 (95)	25 (100)	14 (87.5)	0.14
Pulmonary involvement				
NYHA stage 3–4, n = 37	20 (48.7)	11 (44)	9 (56.2)	0.59
Pulmonary fibrosis on CT scan, n = 39	28 (71.7)	17 (68)	11 (68.7)	0.48
DLCO, %, n = 35	41 (25–52)	40 (23–50)	45 (30–55)	0.37
< 70%	32 (91.4)	20 (80)	12 (75)	0.32
< 55%	30 (85.7)	19 (76)	11 (68.7)	0.62
FVC, %, n = 36	62 (48–77)	59 (47–75)	71 (38–81)	0.58
< 70%	21 (58.3)	15 (60)	6 (37.5)	0.49
< 55%	14 (42.4)	10 (40)	4 (25)	0.72
PAH, n = 38	12 (31.5)	7 (28)	5 (31.2)	0.72
Renal involvement				
Serum creatinine level, $\mu$ mol/l, n = 39	84 (63–105)	77 (52–89)	90 (85–118)	0.009
Creatinine clearance, ml/min, n = 39	69.7 (54.6–97.7)	89 (61–125)	61.4 (42–73.6)	0.03
Immunological features				
ANA, n = 38	38 (100)	25 (100)	13 (81.2)	0.19
ACA, n = 38	5 (13.1)	2 (8)	3 (18.7)	0.31
Antitopoisomerase I antibodies, n = 38	13 (34.2)	7 (28)	6 (37.5)	0.32
Anti-RNP antibodies, n = 36	5 (13.8)	4 (16)	1 (6.2)	0.64
Anti-PM/Scl antibodies, n = 37	1 (2.7)	1 (4)	0 (0)	1
Anti-RNA Pol III antibodies, n = 36	1 (2.7)	1 (4)	0 (0)	1
Current immunosuppressive treatment				
Glucocorticoids	27 (65.8)	16 (64)	11 (68.7)	0.75
Immunosuppressive drugs†	12 (29.2)	7 (28)	5 (31.2)	1

\* Comparisons were made between survivors and those who died. \*\* Breast cancer in complete remission for > 5 years (n = 1), endstage renal insufficiency because of obstructive nephropathy and requiring chronic hemodialysis (n = 1), liver transplantation for fulminant viral hepatitis 15 years ago (n = 1). † Mycophenolate mofetil (n = 6), weekly low-dose methotrexate (n = 2), monthly pulse of cyclophosphamide (n = 2), azathioprine (n = 1), tacrolimus (n = 1). SSc: systemic sclerosis; IQR: interquartile range; BMI: body mass index; mRSS: modified Rodnan Skin score; NYHA: New York Heart Association; CT: computed tomography; FVC: forced vital capacity; PAH: pulmonary arterial hypertension; ANA: antinuclear antibodies; ACA: anticentromere antibodies; PM/Scl: polymyositis/scleroderma.

discharged from hospital. Causes of death in the ICU included septic shock (n = 7), cardiogenic shock (n = 2), massive pulmonary embolism (n = 2), myocarditis with refractory ventricular arrhythmia (n = 1), and meningeal hemorrhage (n = 1). Twenty-two (53.6%) and 16 (39%) patients remained alive at 6 months and 1 year, respectively (Figure 1). Those patients who died displayed a higher number of severe organ failures, or failures that were more

severe, during the first 24 h of ICU admission, as assessed by higher SAPS2 and SOFA scores. The invasive mechanical ventilation requirement carried the worst prognostic value (Figure 2). Hence, only 2 mechanically ventilated patients survived the hospital stay. In the first case, acute respiratory failure was related to *Pneumocystis jirovecii* pneumonia associated with congestive heart failure, and the patient could be extubated after 5 days. In the second case, the patient was

Table 2. Intensive care management of patients with SSc, including in-hospital survivors and those who died. Data were available for all 41 patients. Values are n (%) or median (IQR) unless otherwise specified.

Variable	All Patients, n = 41	Survived, n = 25	Died, n = 16	p*
Time from hospital to ICU admission, days	1 (0–4)	1 (0–2)	1 (0–11)	0.58
Reasons for ICU admission				0.42
Acute respiratory failure	27 (65.8)	16 (64)	11 (68.7)	
Acute renal failure	6 (14.6)	5 (20)	1 (6.2)	
Others	8 (19.5)	4 (16)	4 (25)	
Main diagnosis				0.07
Pulmonary infection**	14 (34.1)	7 (28)	7 (43.7)	
Cardiovascular complications†	8 (19.5)	3 (12)	5 (31.2)	
Scleroderma renal crisis	7 (17)	5 (20)	2 (12.5)	
Others‡	12 (29.2)	10 (40)	2 (12.5)	
Admission characteristics				
Mean arterial pressure	88 (77–104)	92 (81–105)	79 (71–98)	0.03
Glasgow coma scale	15 (15–15)	15 (15–15)	14 (7–15)	0.01
Serum protein level, g/l	69 (59–73)	70 (63–76)	59 (52–68)	0.002
Serum creatinine level, $\mu\text{mol/l}$	88 (56–160)	72 (52–204)	101 (90–170)	0.10
Serum bilirubin level, $\mu\text{mol/l}$	7.5 (4–11.7)	6 (3–9)	12 (5–27)	0.007
Admission severity scores				
SAPS2, points	38 (23–53)	26 (22–36)	55 (41–89)	< 0.001
SOFA, points	4 (4–7)	4 (2–5)	7 (5–11)	< 0.001
Life-sustaining interventions				
Noninvasive ventilation	13 (31.7)	6 (24)	7 (43.7)	0.30
Invasive mechanical ventilation	13 (31.7)	2 (8)	11 (68.7)	< 0.001
Vasopressors	13 (31.7)	1 (4)	12 (75)	< 0.001
Renal replacement therapy	12 (29.2)	3 (12)	9 (56.2)	0.002
In-ICU length of stay, days	3 (2–7)	2 (2–3)	5 (3–11)	0.005

\* Comparisons were made between survivors and those who died. \*\* Microbiological documentation in 5 patients: *Streptococcus pneumoniae* (n = 2), *Escherichia coli* and *Klebsiella pneumoniae* (n = 1), *Pseudomonas aeruginosa* (n = 1), *Pneumocystis jirovecii* (n = 1). † Cardiovascular complications: acute pulmonary edema (2), myocarditis (2), pulmonary embolism (2), out-of-hospital cardiac arrest (1), acute right ventricular failure (1). ‡ Others: acute respiratory failure without any definite diagnosis (5), drug-induced pneumonitis (1), DRESS syndrome (1), meningeal hemorrhage (1), acute cytolytic hepatitis (1), pneumothorax (1). SSc: systemic sclerosis; IQR: interquartile range; ICU: intensive care unit; SAPS2: Simplified Acute Physiology Score 2; SOFA: Sequential Organ Failure Assessment; DRESS: Drug Reaction with Eosinophilia and Systemic Symptoms.

intubated for 24 h in the setting of threatening ventricular cardiac arrhythmia related to SSc-related myocarditis. Of note, the extent of prior pulmonary involvement was not predictive of endotracheal intubation (Table 1).

## DISCUSSION

Several studies have addressed the prognosis of patients with systemic diseases hospitalized in the ICU<sup>12,13,14,15,16,17,18,19,27,28,29</sup>. Inaugural complications and acute exacerbations directly related to the underlying disease represent the main reasons warranting ICU admission in these cohorts. While rheumatoid arthritis, systemic lupus erythematosus, and necrotizing vasculitis account for a large majority of patients in these studies, it is noteworthy that few patients had SSc, making it difficult to draw any firm conclusions about their specific prognosis. Only 1 study specifically investigated the outcome of 9 patients with SSc admitted to the ICU between 1991 and 2002<sup>27</sup>. Nevertheless, analysis of those reports highlights the poor prognosis of patients with SSc in the ICU. Considering patients with SSc from the

above-mentioned studies, a total of 58 patients have been studied. The vital status was available in the publication for 41 patients and showed a gross in-hospital mortality rate of 68.2%<sup>12,13,14,15,16,17,18,19,27</sup>. Further analysis from these studies is limited by the availability of data, and therefore justifies constituting a homogeneous cohort of patients with SSc.

SSc is a very severe disease responsible for multiple organ involvement that may result in organ failures likely to require advanced life support in the ICU<sup>3</sup>. Although the treatment of the disease remains challenging, a few studies have emphasized the improvement in the overall outcome of patients with SSc over time. Thus, the 5-year survival rate of dcSSc increased from 69% to 84% between 2 periods, 1990–1993 and 2000–2003, possibly as a consequence of better management of specific organ involvement<sup>11</sup>. Likewise, a large study reported the trends in mortality and in the causes of deaths between 1972 and 2002. The overall prognosis was improved because the 10-year survival rate increased steadily from 54% to 66% over the study period as a result of changes in



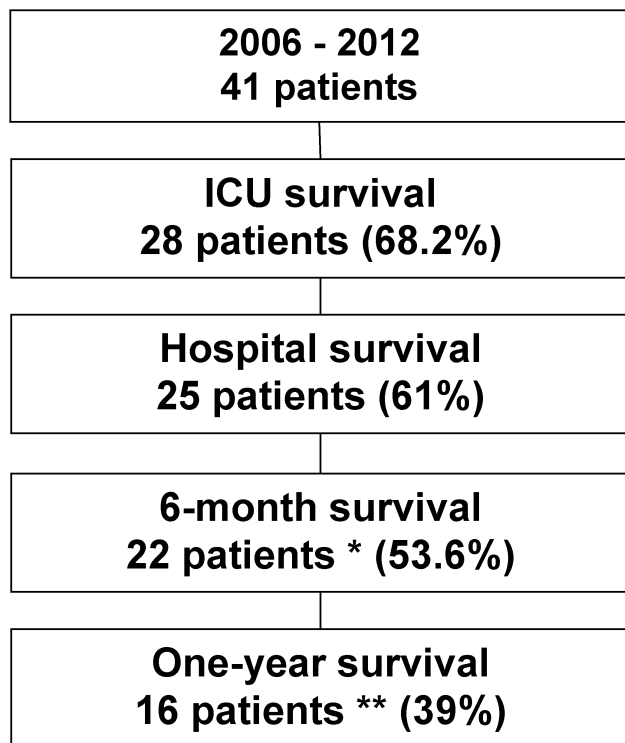


Figure 1. Short-term and longterm vital status. \*One additional patient lost to followup. \*\*Three additional patients lost to followup. ICU: intensive care unit.

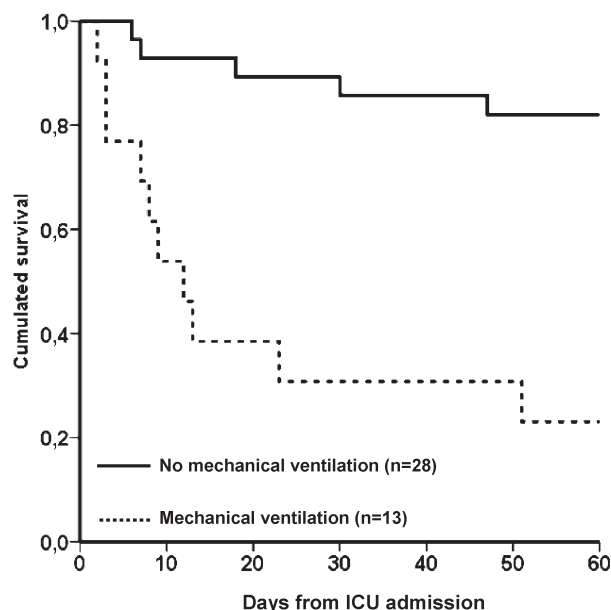


Figure 2. Survival according to the requirement of endotracheal intubation and mechanical ventilation. Log-rank test  $p < 0.001$ . ICU: intensive care unit.

the causes of death<sup>6</sup>. The number of scleroderma-related deaths tended to decrease within the recent period while more patients died from nonscleroderma-related disorders<sup>6</sup>.

However, the subject is still a matter of debate, and in a metaanalysis including 9 studies, Elhai, *et al* reported that survival did not improve in patients with SSc during the last 40 years<sup>7</sup>.

Whereas SRC was the main cause of death in patients with SSc in the 1970s and the early 1980s, it accounted for less than 10% of deaths in the 1990s. Indeed, the prognosis of SRC dramatically improved over the last 2 decades as a result of better recognition and demonstration of the undisputed efficacy of angiotensin-converting enzyme inhibitors. Guillemin, *et al* reported a large French multicenter series of 91 patients with SRC and updated the current outcome of this complication. Although it is unclear whether these patients were managed in general ICU, in nephrology units, or in general wards, 53.8% of them required dialysis that was definitive for the majority. In these patients, the 6-month and 1-year mortality rates were 20.9% and 40.7%, respectively<sup>5</sup>. In a prospective international study of 87 patients with SRC, 36% of them died at 1 year<sup>30</sup>. In our current study, the short-term outcome of patients admitted for SRC was relatively good, with 5 out of 7 discharged from hospital.

As a result, ILD and PAH now account for the main causes of death in SSc<sup>6,31</sup>. Indeed, 50–70% of patients with SSc develop ILD<sup>8</sup>, and 5–10% develop PAH<sup>2,9,32</sup>. PAH remains a severe complication and a leading cause of morbidity and mortality of the disease. General improvements in the management of PAH, including prostanoids, endothelin receptors antagonists, and phosphodiesterase-5 inhibitors, lead to improved survival of patients with SSc, although the median survival remains around 3 years. Thirteen patients from our cohort (31%) were identified as having PAH prior to ICU admission, and their in-hospital mortality rate was 54%.

The main cause of admission to our general ICU was acute respiratory failure, and it is striking that all but 2 invasively ventilated patients died. Likewise, 8 out of 9 mechanically ventilated patients from the study by Shalev, *et al* died<sup>27</sup>. This is in line with the poor prognosis of patients with pulmonary fibrosis undergoing mechanical ventilation<sup>33</sup>. Our results raise the question of indications of NIV in patients with SSc with acute respiratory failure, and avoiding endotracheal intubation should be considered a major therapeutic goal in this setting. This discussion is reminiscent of what we have been discussing over the last 2 decades for the high-risk subgroup of patients with hematological malignancies, in whom invasive mechanical ventilation used to be associated with mortality rates of 80% and higher<sup>34,35</sup>. Since then, the outcome of acute respiratory failure in patients with cancer has dramatically improved because of the efficacy of NIV to avoid endotracheal intubation<sup>36</sup> and to the improvement in survival of patients who required invasive mechanical ventilation<sup>37</sup>. Interestingly, NIV was attempted in 13 of our patients and was successful, permitting the avoidance of intubation in 8 patients. This suggests that some patients with SSc with mild to moderate acute respiratory failure may

benefit from early ICU admission for the application of NIV to prevent deterioration to terminal respiratory insufficiency and to secure at-risk diagnostic procedures, such as fiberoptic bronchoscopy and bronchoalveolar lavage. Early identification of such patients clearly represents an area of improvement in the management of patients with SSc. However, the potential benefit of NIV in patients with SSc with acute respiratory failure should not disregard the risks related to delayed intubation. Although some patients with undisputed indications for NIV, such as decompensated chronic obstructive pulmonary disease and cardiogenic pulmonary edema, may be successfully managed by intensive NIV during several days, we learned from hematological patients that delayed intubation could be associated with worse outcome than first-line intubation<sup>38,39</sup>. So management of hypoxemic acute respiratory failure with NIV in immunocompromised patients remains highly controversial<sup>40</sup>. Rules of paramount importance in applying a cautious NIV trial in patients with SSc are identification of patients at the early phase of respiratory deterioration, respect of contraindications, careful management of NIV by a trained team, and rapid conversion to endotracheal intubation in case of worsening respiratory distress and/or dependency on NIV (e.g., inability to avoid NIV for longer than 2 h).

Our study has several limitations. Although it reports the largest series published so far, the number of patients remains limited because of the rarity of the disease. The design was retrospective, but data collection was accurate through the database of the National Referral Center and the computerized patient data management system in the ICU. However, some important data might have been omitted, such as the functional status prior to the acute complication. Besides the NYHA classification, a functional scale such as the Performance Status would certainly be more accurate. In the same way, the nutritional status might also be of importance in these patients and could only be grossly assessed through the body mass index and the serum protein level at the time of ICU admission. Most importantly, patients admitted to the ICU were probably carefully selected upstream, but we did not assess whether and how many patients with endstage disease were declined ICU admission by their referring physicians. Finally, the study was carried out in a single center that can be considered a privileged environment for patients with SSc. Indeed, the internal medicine and rheumatology departments share a particular expertise in the acute and chronic management of the disease, and the ICU team is experienced in the treatment of immunocompromised patients with malignancies or systemic diseases. Attending physicians and intensivists are used to collaborating in all steps of the decision-making processes, including early assessment of patients with new-onset organ dysfunctions.

Our study provides reliable prognostic data for patients with SSc who required ICU admission. Acute respiratory failure is the leading cause of ICU admission. The devas-

tating outcome associated with invasive mechanical ventilation calls for early identification of patients likely to benefit from an NIV trial, assuming no contraindications, to prevent respiratory deterioration and to secure invasive diagnostic investigations. This will be best achieved through close collaboration between attending physicians in the wards and intensivists.

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