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Septic shock among patients with systemic lupus erythematosus: Short and long-term outcome. Analysis of a French nationwide database

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SUMMARY

Objectives: We aimed to assess the characteristics, outcomes and costs of septic shock complicating Systemic Lupus Erythematosus (SLE).

Methods: Characteristics of SLE patients experiencing a septic shock in France from 2010 to 2015 were analyzed through the French medico-administrative database. Factors associated with the 1-year post-admission mortality were analyzed, the crude 1-year survival of SLE patients experiencing septic shock was compared to those admitted for another reason, and we compared the 1-year outcome associated with SLE septic shock survival to a matched SLE ICU control population.

Results: Among 28,522 SLE patients, 1068 experienced septic shock. The 1-year mortality rate was 43.4%. Independently of the severity, an associated Sjögren syndrome was the only specific SLE phenotype associated with mortality (HR 1.392[1.021–1.899]). Within one year, post-septic shock survivors ($n = 738$) were re-admitted 6.42[17.3] times with total cost of € 14,431[20,444]. Unmatched analysis showed that the outcome of patients admitted in ICU for septic shock was poorer than that of patients admitted in ICU or hospital for another disease. However, 1-year healthcare use of septic shock survivors was not different from the other ICU survivors when matched on severity.

Conclusions: Septic shock is a frequent and severe complication among SLE patients even if it is not associated with more healthcare use than another episode of same severity.

Introduction

Systemic lupus erythematosus (SLE) is one of the most frequent, widespread, auto-immune connective tissue diseases. In addition to specific and nonspecific disease complications, SLE patients are prone to infection, as well as septic shock, either because of immunosuppressive treatment or intrinsic dysregulation of the immune system.[1] For patients with inflammatory systemic disorders, infectious diseases are the first reason for ICU admission.[2]

In France, from 2000 to 2009, among patients with SLE whose death was due to another disease, 10.2% died from infection.[3] A meta-analysis showed that the standardized mortality risk due to infection in SLE is nearly five times greater than in the general population.[4] Furthermore, recent studies showed that SLE-associated mortality has not improved over the past decades.[5]

Survivors experience a worsening of chronic health conditions, with increased healthcare use and up to 30% mortality in the year following septic episode.[6] However, very few is known about the burden of septic shock complicating SLE, including specific characteristics, risk factors and prognosis. We wanted to clarify if SLE specific characteristics have an impact on septic shock outcomes and how much healthcare use is modified after a septic shock episode in SLE population. Therefore, we conducted an analysis of a French nationwide database to assess the number, main characteristics, outcome, prognosis and the associated costs of septic shock complicating SLE.

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Materials and methods

Study population and data source

Exhaustive data for all patients admitted in French hospitals with at least one SLE diagnosis from January 2009 to December 2015 were collected from the national medical administrative database, the PMSI (Programme de Médicalisation des Systèmes d'Informations, Information System Medicalization Program). PMSI database provides a summary with diagnosis and individual medical conditions at discharge of any public or private French healthcare facilities. Information covers both medical and administrative data. Each facility produces its own anonymous standardized set of data, which are then compiled at the national level. Despite the fact that these data are anonymous, the system allows to follow all hospital stays for each individual patient. Routinely collected medical data include main diagnosis, secondary diagnoses, and performed procedures. Administrative data include age, gender, year, duration of hospital stay, and location of the hospital. In-hospital death is also reported. Diagnoses identified during the hospital stay are coded according to the International Classification of Diseases, tenth revision (ICD-10). Procedures performed during the hospital stay are coded according to the "Classification Commune des Actes Médicaux" (CCAM, French Common Classification of Medical Procedures). Since 2004, each hospital's budget depends on the medical activity described in this specific program. Regular checks are made by the social insurance authority to ensure that data are correctly imputed. In Intensive Care Units (ICU), severity at admission is measured by the Simplified Acute and Physiology Score II (SAPS II) and all procedures are recorded. The reliability and validity of PMSI data have been assessed elsewhere.[7,8]

To select the SLE population, we first extracted from the PMSI database all records of patients for whom at least one ICD-10 M32 diagnosis was reported. We excluded patients younger than 15 years old and patients admitted to hospital only for scheduled sessions (chronic hemodialysis, radiotherapy, chemotherapy). We also excluded the hospital stays identified with an error code ($n = 12{,}190$; 6%).

Definitions

We defined septic shock as the combination of at least one diagnosis of infection (ICD-10 code A00-B99 + others listed in supplementary data) with one diagnosis among the followings: R57.2 "septic shock", R57.8 "other shock", R 57.9 "shock without precision" or CCAM procedure code EQLF0010 and EQLF0030 which refers to the use of vasopressor agents. We considered only the first septic shock, and stays containing or following a M32 diagnosis code to ensure the SLE diagnosis. End-stage renal disease (ESRD) was defined as having received a renal transplant or having required chronic hemodialysis. For the exhaustive description of diagnosis and procedures codes used, see electronic supplementary materials. To determine SLE phenotype, we used all the specific diagnostic codes reported during or before the stay of interest.

Analysis 1: characteristics, outcome and costs of septic shock in the overall SLE population

We described the demographic characteristics, diagnosis and procedures associated with septic shock. For the determinant of the 30-day and 1-year post-ICU admission mortality, we used univariate and multivariate Cox proportional hazard models. The first day in ICU defined Time 0. For stays without ICU admission we considered the first day in hospital. For multivariate Cox models, we used gender, chronic kidney disease (CKD) and all variables that had a significance level <0.20 as covariates. Hazard ratios are presented as HR [CI95]. One-year healthcare use and hospital costs were assessed for survivors for at least 30 days after sepsis.

Analysis 2: crude comparisons of the 1-year survival in case of septic shock vs. patients with ICU stay without any septic shock

In a second analysis, we performed a crude comparison of the 1-year survival rate of SLE patients experiencing septic shock versus SLE patients without any septic shock in ICU and versus SLE patients not admitted in ICU. We used Kaplan–Meier method to represent their 1-year survival taking time 0 as first hospital admission. We then used a univariable Cox proportional hazard model to estimate hazard ratio of 1-year death among these populations.

Analysis 3: comparison of the survival rate and associated costs between SLE septic shock survivors and matched SLE non-septic shock survivors

We performed a 1:1 exposed/non-exposed propensity score matched study where we selected the exposed patients where the SLE patients with a septic shock from January 2010 to December 2014 and discharged alive from ICU. Eligible controls were defined as all the SLE patients without any septic shock and discharged alive from ICU. To build the propensity score we used a logistic regression model with several covariables including gender, Charlson-age adjusted comorbidity index, type of medical facility (university, general public, or private), use of invasive mechanical ventilation and the magnitude of the Simplified Acute Physiology Score II (SAPS II). We used a greedy algorithm to perform the matching. Further details of the matching procedure are available within the electronic supplementary materials.

On this matched population, we compared several outcomes during the year following time 0 (defined here as the day of hospital discharge): survival with Kaplan–Meier method, healthcare use (number, duration and cost of following hospitalizations), number of stays in a rehabilitation center, and diagnosis of an end-stage renal disease (ESRD).

Statistical analysis

The median value of the SAPSII was imputed to the 57 (0.5%) missing data. Categorical variables are presented as number (percentage). Quantitative variables are presented as mean [standard deviation]. In the matched analysis we performed a conditional logistic regression procedure adjusted on the propensity score and on the presence of lupus nephritis to test for significance. All tests were two-sided, and P values < 0.05 were considered to indicate a significant association.

All analyses were performed using SAS © software version 9.4 (SAS Inc, Cary NC). Kaplan–Meier curves were made with R software version 3.4.4, library "survival".

Ethical statement

In accordance with French legislation on non-interventional studies with anonymous data, signed informed consent of the participants was not needed (Law no 2012-300).

Results

Analysis 1: characteristics, outcome and costs of septic shock in the overall SLE population (Tables 1 and 2)

We extracted 1068 patients experiencing a first episode of septic shock among the whole population of 25,228 SLE patients over

Table 1
Characteristics and factors associated with the 1-year mortality of septic shocks among SLE overall population admitted in ICU.

	$n = 1068$	Univariate HR	p	Multivariate HR	p
*Age***	55.9 (+/−16.4)	1.023 (1.017–1.030)	<0.0001	–	–
Sex (F/M)	810/258 (75.8/24.2%)	0.962 (0.7880–1.188)	0.7211	1.116 (0.900–1.385)	0.3173
Associated condition					
Chronic kidney disease (eGFR <60 mL/min*)*	273 (25.6%)	1.181 (0.966–1.444)	0.1044	1.041 (0.848–1.278)	0.704
*Cancer***	112 (10.5%)	1.660 (1.279–2.155)	0.0001	–	–
*Diabetes mellitus***	128 (12.0%)	0.933 (0.704–1.217)	0.631	–	–
Cardiovascular history **	454 (42.5%)	1.221 (1.017–1.465)	0.0323	–	–
Charlson – age adjusted comorbidity index	4.0 (+/−1.8)	1.122 (1.164–1.283)	<0.001	1.166 (1.106–1.228)	<0.0001
Associated SLE disease					
Lupus nephritis	281 (26.3%)	0.922 (0.748–1.136)	0.4466	–	–
Serositis	241 (22.6%)	0.973 (0.782–1.211)	0.8064	–	–
Antiphospholipid syndrome	103 (9.6%)	0.793 (0.569–1.105)	0.1708	0.816 (0.584–1.142)	0.235
Sjögren syndrome	87 (8.2%)	1.328 (0.976–1.806)	0.0708	1.392 (1.021–1.899)	0.0365
Number of previous stay with SLE diagnosis	4.5 (+/−7.9)	1.005(0.995–1.015)	0.3207	–	–
Characteristics of the shock					
*SAPS II**	47.0 (+/−21.6)	1.024 (1.020–1.029)	<0.0001	1.022 (1.017–1.026)	<0.0001
Infection site:					
Bacteriemia	317 (29.7%)	1.205 (0.992–1.463)	0.06	1.071 (0.871–1.318)	0.516
Endocarditis	57 (5.3%)	1.235(0.853–1.787)	0.2643	–	–
Lower Respiratory tract	498 (46.6%)	0.899 (0.749–1.080)	0.2551	0.881 (0.726–1.070)	0.2
Urinary/genital tract	257 (24.1%)	0.753 (0.599–0.946)	0.0149	0.701 (0.553–0.889)	0.0034
Abdomen	224 (21.0%)	1.186 (0.955–1.472)	0.1218	1.116 (0.895–1.393)	0.3297
*CNS**	51 (4.8%)	1.110 (0.736–1.674)	0.6179	–	–
Bones and joints	37 (3.5%)	1.281(0.818–2.005)	0.2788	–	–
Skin	54 (5.1%)	0.878(0.567–1.360)	0.5604	–	–
Pathogens:					
Gram positive cocci	345 (32.3%)	0.982(0.809–1.192)	0.8511	–	–
Staphylococcus aureus	140 (9.7%)	1.078 (0.804–1.446)	0.6145	–	–
Streptococcus pneumoniae	61 (5.7%)	0.470 (0.246–0.799)	0.0054	–	–
Gram negative bacilli	465 (43.5%)	0.847 (0.704–1.020)	0.0798	–	–
Fungi	146 (13.7%)	1.309 (1.026–1.670)	0.0301	1.371 (1.056–1.781)	0.0179
Influenza virus	24 (2.3%)	0.598 (0.283–1.261)	0.2124	–	–
Viruses	145 (13.6%)	0.961 (0.736–1.256)	0.771	–	–
Parasites	23 (2.2%)	1.405 (0.809–2.440)	0.2267	–	–
Pneumocystis jirovecii	12(1.1%)	1.452 (0.688–3.064)	0.3275	–	–
Documented Infection	703 (65.8%)	0.940 (0.776–1.138)	0.5243	0.926 (0.752–1.141)	0.4723

Categorical variables are presented as n (%). quantitative variables are presented as mean (+/–sd).
* SAPS II: Simplified Acute Physiology Score; CNS Central Nervous System.
** Age. cancer. diabetes and cardiovascular history are considered to be part of Charlson – age adjusted index and germ variables to be part of documented infection so these variables were not used in multivariate analysis.

6 years. Sex ratio was (F/M) 75.8/24.2% and 25.6% ($n = 273$) of these patients had chronic kidney disease (CKD). Most of these stays took place in university hospitals (56.8%), followed by general hospitals (39.3%), whereas only 3.9% were in private for-profit hospitals (Table 1). The most common associated SLE phenotype was lupus nephritis (26.3%, $n = 281$). The lower respiratory tract was the main site of infection ($n = 498$; 46.6%) and a high proportion of patients had bacteremia ($n = 317$; 29.7%). Gram-negative bacilli were the most frequent pathogens identified ($n = 465$; 43.5%). Of note, 102 patients (9.6%) had infections due to vaccine-preventable pathogens (e.g., *Influenza* virus, *Streptococcus pneumoniae, Neisseria meninigitidis* or *Haemophilus influenza*). Patients were seriously ill with a mean [SD] SAPS II score of 47 [21.6]. Overall, 913 (85.6%) patients required vasopressive drugs (epinephrine, norepinephrine), 369 (34.6%) invasive mechanical ventilation and 342 patients (32.0%), renal replacement therapy for Acute Kidney Injury (AKI). Patients spent 11.6 [15.6] days in the ICU and 32.8 [32.1] in the hospital, and the mean associated cost was € 25,327 [23,396]. The 30-day and 1-year post admission mortality rates were 30.9% ($n = 330$) and 43.4% ($n = 463$), respectively. In- and out-of-hospital outcomes are presented on Table 2.

Determinants of the 1-year mortality are listed in Table 1. Patients' illness severity was the main determinant of mortality. In the univariate analysis, the various SLE phenotypes such as lupus nephritis (HR 0.922 [0.748–1.136]) or serositis (HR 0.973 [0.782–1.211]) were not significantly associated with the prognosis at 1 year. An associated Sjögren syndrome was at the limit of significance for an adverse effect: HR 1.328 [0.976–1.806].

In the multivariate analysis, at 1-year after ICU admission, independently of the acute illness severity and comorbidities, an associated Sjögren syndrome (HR: 1392 [1021–1899]) was significantly associated with death. Interestingly, the only infectious characteristic associated with increased mortality was fungal infection. In contrast, urinary tract infection was associated with survival (HR 0.701[0.553–0.889]), confirming findings observed in general ICU population with septic shock.[9]

The analysis of the 30-day post-septic shock mortality are presented in ESM and yielded similar results.

Within one year, post-septic shock survivors ($n = 738$) were readmitted 6.42[17.3] times for 64.1 [48.9] days with a total cost of € 14,431 [20,444], and 12 (1.6%) patients required the initiation of chronic hemodialysis (Table 2).

Analysis 2: crude comparisons of the 1-year survival in case of septic shock vs. patients with ICU stay without any septic shock

We identified 20,315 SLE patients without ICU admission and 3845 SLE patients with ICU stay without any septic shock that we compared to the 1068 SLE patients admitted in ICU and experiencing septic shock. At one year, taking people who were not admitted in the ICU and did not experience a septic shock as reference, SLE patients had a hazard ratio [CI 95] of 1-year death of 51 [37–61] and 269 [198–365] if they were experiencing a stay in ICU without septic shock or a septic shock, respectively. The 1-year survival was significantly poorer among ICU SLE patients with septic shock ($p < 0.0001$, Fig. 1).

Table 2
Healthcare use and outcome of SLE patients experiencing septic shock.

Septic shock stay ($n = 1068$):	
Duration of the stay in hospital (days)	32.8 (+/32.1)
ICU admission	1011 (94.7%)
Duration of the stay in ICU (days) ($n = 1\ 011$)	11.6 (+/15.6)
Cost of the hospital stay (€)	25,327 (+/−23 396)
Use of pressor amines	913 (85.6%)
Mechanical ventilation	369 (34.6%)
Renal replacement therapy for AKI	342 (32.0%)
Short and long-term outcome ($n = 1\ 068$):	
Death at 30 days post admission	330 (30.9%)
Death at 1 year post admission	463 (43.4%)
One-year healthcare use for 30 days post sepsis survivors ($n = 738$):	
Number of hospitalizations	6.42 (+/17.3)
Total cost (€)	14,431 (+/20 444)

Categorical variables are presented as *n* (%), quantitative variables are presented as mean(+/−sd).

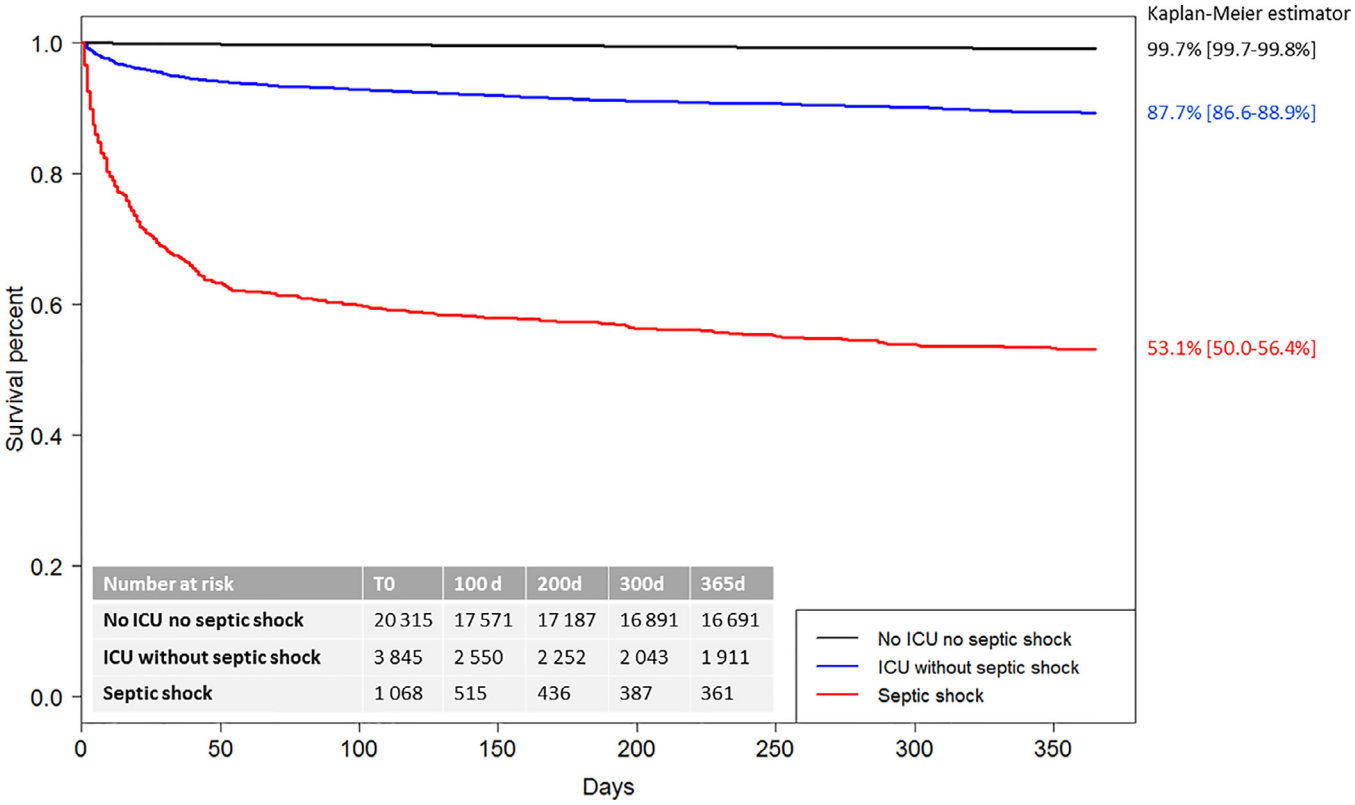

Fig. 1. One-year survival of SLE patients experiencing septic shock in ICU vs. SLE patients admitted in ICU without septic shock and vs. SLE patients admitted for standard hospitalization (time0 = first admission). Kaplan-Meier estimator at day 365 is presented with CI95 for each group.

Analysis 3: comparison of the survival rate and associated costs between SLE septic shock survivors and matched SLE non-septic shock survivors

Based on the initial illness severity, we were able to match 404 SLE ICU survivors with septic shock with 404 SLE ICU survivors without any septic shock (Table 3). SLE patients experiencing septic shock had a longer stay in ICU, and in hospital after the ICU, than matched controls. However, as shown in Fig. 2, there was no difference in the 1-year mortality between these groups (stratified Log–Rank test, $p = 0.46$). In the septic shock group, 57 patients people died within 1 year vs. 53 in the matched control group. We found no significant difference in 1-year hospital costs (€ 18,346 [23,250] in case of septic shock vs. € 18,460 [23,362] for controls, $p = 0.3276$), as well as their rate of healthcare use (Table 4). More patients in the control group required the initiation of chronic hemodialysis ($n = 39$; 9.7%) than in the septic shock group ($n = 11$ (2.7%), $p < 0.001$).

Discussion

In a large nationwide exhaustive cohort of SLE patients, we observed that septic shock was associated with a worsened morbidity and mortality. After taking into account the severity of the acute illness and comorbidities, an associated Sjögren syndrome was a factor of poor prognosis. For survivors, the onset of a septic shock appears as a turning point with heavily increased mortality, hospital costs, and healthcare use. However, the outcome of SLE septic shock survivors was not different from that of matched SLE ICU survivors of other diseases.

In our population of SLE patients, septic shock had a poor prognosis among SLE patients: mortality rates and associated costs were higher than in general population at short term[10–13] and long-term.[14] Indeed, SLE patients, mostly when treated with steroids or immunosuppressive drugs, can be considered as immunocompromised, clearly a determinant of poor prognosis in case of septic shock.[15] The ICU mortality rate of SLE patients with

Table 3
Baseline characteristics of SLE septic shock survivors and matched SLE ICU survivors.

	Septic shocks (n = 404)	*Controls (n = 404)*
Age	52.0 (+/−16.2)	51.1 (+/−16.3)
*Sex (F/M)**	313/91 (77.5/22.5%)	317/87 (78.5/21.5%)
Associated condition		
Chronic kidney disease (eGFR <60 mL/min)	107 (26.5%)	147 (36.4%)
End-stage renal disease	50 (12.4%)	63 (15.6%)
Cancer	28 (6.9%)	28 (6.9%)
Diabetes mellitus	51 (12.6%)	36 (8.9%)
Cardiovascular history	153 (37.9%)	141 (34.9%)
Charlson – age adjusted comorbidity index *	3.6 (+/−1.7)	3.5 (+/−1.6)
Characteristics of the stay		
*Kind of medical facility (University/General/Private)**	236/156/12 (58.4/38.6/3.0%)	259/134/11 (64.1/33.2/2.7%)
Time interval between ICU admission and ICU discharge (days)	11.1 (+/−13.5)	7.0 (+/−8.1)
Time interval between ICU discharge and hospital discharge (days)	16,1 (+/− 21,7)	11,4 (+/−14,7)
Time interval between ICU admission and hospital discharge (days)	27.2 (+/−23.0)	18.4 (+/−15.8)
Cost of the hospital stay (€)	27 794 (+/− 24 218)	17 819 (+/− 13 396)
Associated SLE phenotypes		
Lupus nephritis	61 (15.1%)	83 (20.5%)
Serositis	24 (5.9%)	19 (4.7%)
Antiphospholipid syndrome	24 (5.9%)	19 (4.7%)
Sjögren syndrome	13 (3.2%)	10 (2.5%)
Characteristics of the shock		
SAPS II *	39.4 (+/−14.8)	39.3(+/−13.8)
Use of pressor amines	371 (91.8%)	66 (16.3%)
Invasive mechanical ventilation *	103 (25.5%)	98 (24.3%)
Renal replacement therapy for AKI	101 (25.0%)	99 (24.5%)

Categorical variables are presented as *n* (%), quantitative variables are presented as mean (+/−sd).
* variables used to build the propensity score.

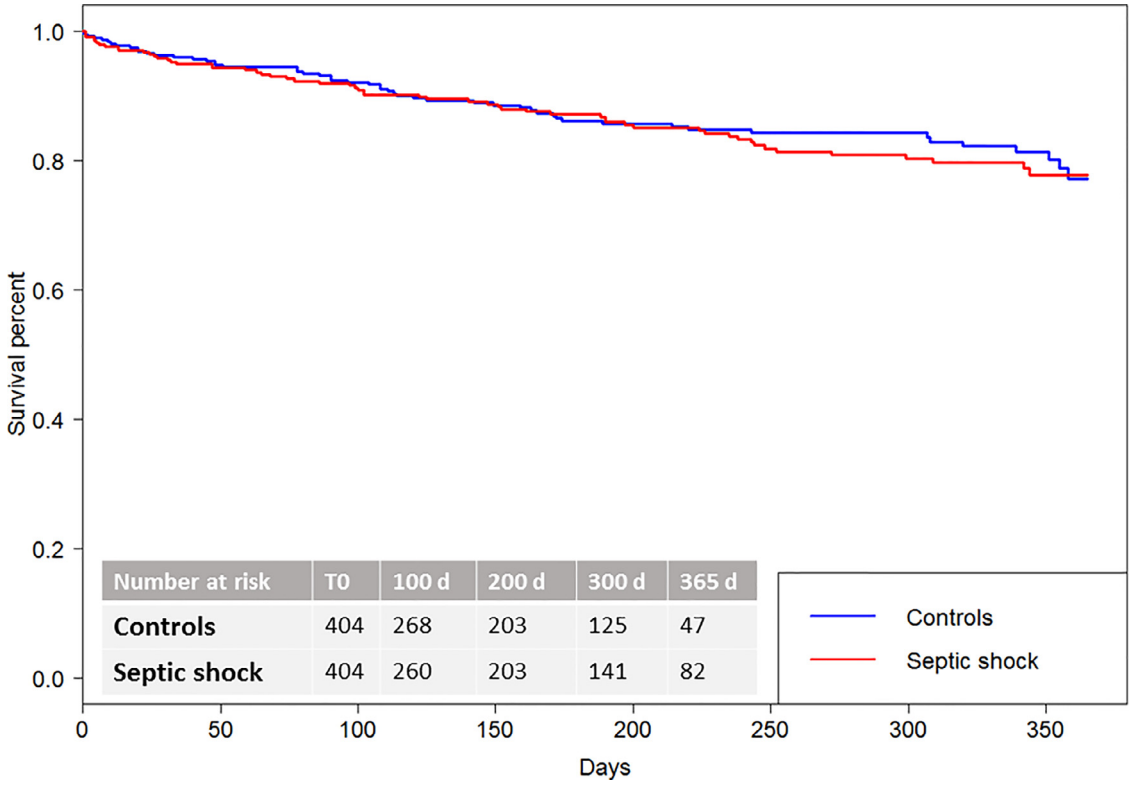

Fig. 2. One-year survival of SLE ICU patients survivors after a septic shocks vs. matched control SLE ICU survivors without any septic shock.

septic shock in France was higher than that previously observed probably because of selection bias in retrospective monocentric studies.[2,16–,22] Compared to patients from the general population experiencing septic shock, our SLE patients were younger and more often female. Infection characteristics were similar, except for fungal infections which seemed more frequent among SLE patients.[11]

The observed 1-year costs were higher than previously reported in hospitalized patients with SLE.[23] In comparison to the article of Prescott et al. [24] who evaluated the 1-year healthcare use in survivors of severe sepsis in a cohort extracted from general population, we observed more healthcare resources used within one year after septic episode in SLE patients. Several reasons could explain this difference: we selected patients only with septic shock,

Table 4
One-year outcome, healthcare use and costs of SLE septic shock ICU survivors and matched SLE ICU survivors without any septic shock.

	Septic shocks (n = 404)	*Controls (n = 404)*	*p**
Death	57 (14.1%)	53 (12.9%)	0.6015
Number of hospitalizations:			
Total	11.2(+/−26.4)	15.2 (+/−32.1)	0.1915
Standard hospitalizations	2.9 (+/−6.7)	3.3 (+/−5.4)	0.296
*Sessions***	6.8 (+/−26.0)	10.5 (+/−30.8)	0.2268
ICU	1.6 (+/−1.0)	1.5 (+/−0.8)	0.2168
Days spent in a hospital facility:	45.8 (+/−67.5)	54.2(+/−86.2)	0.3897
Total healthcare-associated cost for one patient:			
With initial stay's cost	46 141 (+/−34 764)	36 274 (+/−27 120)	<0.0001
Without initial stay's cost	18 346 (+/−23 250)	18 460(+/−23 362)	0.3276
Number of stays in a rehabilitation center	0.33 (+/−0.7)	0.30 (+/−0.6)	0.3080
Apparition of ESRD	11 (2.7%)	39 (9.7%)	0.0003

Categorical variables are presented as *n* (%), quantitative variables are presented as mean (+/−sd).
* *p* value is adjusted on the initial presence of lupus nephritis and on the propensity score.
** "Sessions" means a planned visit that last less than a day.

whereas Prescott et al. selected also patients with severe sepsis. In addition, all of our patients had SLE, which can be considered as a severe co-morbidity.[5]

In the matched comparison, SLE patients with septic shock had a prolonged hospital stay and increased in-hospital costs. But the post-ICU mortality and costs were not different between SLE ICU survivors with septic shock vs. those without septic shock. This finding is in contradiction with the study from Prescott et al. who observed a significant increase in the 1-year healthcare use between severe sepsis survivors and matched controls in a general population. The difference might be due to the impact of the underlying SLE disease on the 1-year healthcare consumption. Indeed, the rate of patients requiring chronic hemodialysis was higher in the SLE survivors without septic shock. It may also be related to the absence of adjustment on illness severity on ICU admission in the study of Prescott.[24]

Interestingly, we observed that, independently of the severity of the acute illness, associated Sjögren syndrome was a main determinant of the 1-year mortality. In contrast, other reported SLE features and, for example, associated antiphospholipid syndrome were not associated with a poorer 1-year survival. In a large SLE cohort, Sjögren syndrome had already been described as deleterious on damage scores and mortality.[25] To the best of our knowledge, the outcome of in-ICU Sjögren patients had never been evaluated. Sjogren's syndrome is associated with a specific risk of interstitial and cystic lung disease, which could affect both incidence and severity of lower respiratory tract infection.[26] We can postulate that Sjogren's syndrome can adversely affect ICU procedures, especially the invasive mechanical ventilation. Furthermore, infection was reported as the second cause of death among Sjögren patients, meaning that these patients were probably seriously affected by infectious diseases[27]

This study has some limitations. Because it is a hospital database, we had no access to the out-of-the-hospital mortality, healthcare resource use and costs. However, among SLE patients overall, Thomas et al. showed that in France between 2000 and 2009, the mortality was mostly (67.9%) in-hospital.[3] Though, the only possibility for a patient to get lost to follow up is that he died outside of a hospital or he moved abroad. Another limitation is that PMSI is based on coding diagnosis and procedures and this system might not be always sufficiently accurate. For example, the prevalence of CKD is higher than the one of lupus nephritis, even if it is a population of mostly young women without any other reason to develop a CKD. This can be explained by the fact that lupus nephritis may be encoded only for the hospital stay dealing with its management whereas CKD is encoded for all the hospital stay as a comorbidity. Therefore, non- or under-measured confounding factors, especially under-estimated SLE phenotypes (both number and types) could have biased our results. Besides, we can postulate that the coding process is overestimating the prevalence of septic shock in administrative database.[28] Nevertheless, regarding the severity and the outcome of our selected population, we considered that the septic shock definition was reliable.

We believe that this work has also several strengths. First, because of the French Health Insurance System, PMSI gather exhaustive data of all French hospitals, meaning that our data include every patient with at least one diagnosis of SLE hospitalized in France for six years. Severity scores at ICU admission using a well-recognized general ICU severity score and organ dysfunction daily scores were also exhaustively recorded. The selected population had SLE characteristics (i.e., prevalence, sex ratio, age) consistent with previously published large SLE epidemiologic studies in France.[29] Thanks to the chaining between the successive hospitalization episodes, we were able to examine all records of one individual patient and to assess the 30-day and 1-year outcome. Our matched study enabled us to perform comparisons of SLE patients with matched illness severity and matched levels of comorbidities.

Conclusions

Septic shock is a major concern for SLE patients with heavy associated short- and long-term morbidity and mortality. In order to improve SLE prognosis, significant efforts should be made to prevent infectious diseases in this immunocompromised population. Vaccination is clearly an issue since we observed in our cohort almost 10% of septic shock associated with vaccine-preventable pathogens.

Conflict of interest statements

Arthur Mageau: none; Karim Sacré: none; Anne Perozziello: none; Stéphane Ruckly: none; Claire Dupuis: none; Lila Bouadma: none; Thomas Papo: none; Jean-François Timsit: none.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2019.04.005.

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