Risk Factors for One-Year Hospital Readmissions in Patients with Systemic Lupus Erythematosus

Jinxia Chen (18666722726@163.com)
Affiliated Hospital of Guangdong Medical University https://orcid.org/0000-0001-8264-9759
Limin Zhang
Longhua Branch of Shenzhen People's Hospital
Liutao Huang
Affiliated Hospital of Guangdong Medical University
Shuxian Chen
Affiliated Hospital of Guangdong Medical University
Shuxian Xu
Affiliated Hospital of Guangdong Medical University
Huafeng Liu
Affiliated Hospital of Guangdong Medical University

Research Article

Keywords: Lupus Erythematosus, Systemic, Patient Readmission, Risk Factors, Serum Albumin, Cystatin C, Infection

Posted Date: October 25th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-989689/v1

Abstract

Objective: To reveal the characteristics and risk factors of systemic lupus erythematosus (SLE) patients with frequent readmission to intervene early and improve the quality of care during initial hospitalizations.

Methods: This was a single-center, retrospective case-control study involving 521 hospitalized patients with SLE from January 2014 to December 2016 in the Affiliated Hospital of Guangdong Medical University.

Results: A total of 521 patients were enrolled, including 400 patients who were hospitalized once and 121 patients who were hospitalized repeatedly, and 23.2% of the patients were readmitted within one year. The results showed that the age of onset (odds ratio [OR] 1.022, 95% confidence interval [CI] 1.007-1.036), serum albumin (OR 0.965, 95% CI 0.942-0.989), and cystatin C (OR 1.404, 95%CI 1.180 -1.670) were closely related to readmission. The most common causes of readmission were infections (52 cases, 27.08%), especially respiratory tract infections, and lupus activity or recurrence (45 cases, 23.4%).

Conclusion: Special attention should be paid to SLE patients with older age of onset, low serum albumin levels, and high cystatin C levels to avoid infection and recurrence with the aim of reducing the hospital readmission rate.

Background

Systemic lupus erythematosus (SLE) is a chronic and persistent autoimmune disease with a high heterogeneity and multiple organ involvement [1]. The prevalence of SLE is higher in Asia than in Europe [2]. In China, it is estimated that the prevalence of SLE is 30 to 37.56 cases per 100,000 in adults [3, 4]. Almost 60% of SLE patients suffer from persistently active disease or episodes of flare during the year, resulting in frequent hospitalization [5]. SLE is one of the diseases with the highest readmission rate of all chronic diseases [6]. It was reported that 20–25% of patients with SLE were hospitalized each year [7] and 17.6% of SLE patients were readmitted within 30 days after the first discharge from hospitals [6]. Frequent readmissions affect the quality of life of patients with SLE and impose a heavy financial burden on the health care system. Several studies have demonstrated that health care utilization and costs of SLE were significantly higher than those of non-SLE patients [7]. Identifying the characteristics of SLE patients with frequent readmission can help in identifying risk factors associated with readmissions. Additionally, these characteristics can promote early intervention and improve the quality of care during initial hospitalizations. Considering the limited amount of research in this area and that our previous study found western Guangdong to be a high-risk area for lupus [8], we aimed to conduct a retrospective study to uncover the characteristics and risk factors of frequent readmission in patients with SLE.

Materials And Methods

This was a single-center, retrospective case-control study involving 531 hospitalized patients with SLE from January 2014 to December 2016 in the Affiliated Hospital of Guangdong Medical University. These patients were diagnosed with SLE according to the 1997 American College of Rheumatology revised diagnostic criteria. Patients with one of the following conditions were excluded: patients with drug-induced lupus, mixed connective tissue disease, systemic sclerosis, polymorphic erythema, less than 18 years of age, pregnancy, died during the initial hospitalization, and incomplete data. The demographics, diagnosis, number of admissions, sex, age, duration of hospital stays, duration of illness, reason for admission, major clinical symptoms, comorbidities, laboratory findings, kidney pathology, and other information were collected through the electronic medical record system. Diagnoses were coded according to the International Classification of Diseases, 10th revision (ICD-10). The local gross domestic product (GDP) per capita results were obtained from the Internet (https://www.zhanjiang.gov.cn/tjj/index.html). The study protocol was approved by the Ethics Committee of the Affiliated Hospital of Guangdong Medical University and ethics approval number was 2020-104-01. Informed consent was obtained from patients.

Statistical analyses

The mean ± standard difference was used, and an independent-samples t-test was applied to compare the means between two groups in normal distribution measurement data. The skewed distribution measurement data were represented by the median (25%, 75%), and the comparison between the two groups was conducted using a non-parametric test. Categorical data were expressed as frequency and percentage, and comparisons between the two groups were conducted using the chi-square and non-parametric tests. Univariate logistic regression analysis was applied to define the risk factors for readmission in patients with SLE within 1 year. Multicollinearity analysis was performed among the screened risk factors, and multicollinearity among variables was established if variance inflation factor (VIF) > 10. Multivariable logistic regression models were used to estimate odds ratios (ORs) to define the related risk factors for readmission. A two-sided P-value <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp).

Results

The General and Socio-demographic characteristics

A total of 521 patients were enrolled, including 400 patients hospitalized once and 121 patients hospitalized repeatedly, and 23.2% of the patients were readmitted within one year. Hospital stays were longer in patients with readmission during the first hospitalization than in patients without readmission (11.0±8.4 vs. 9.0±6.0 days, *P*=0.007). Age at SLE onset and first hospitalization were higher in the readmission group (35.8±17.0 vs. 31.6±13.3 years, *P*=0.007; 40.3±16.4 vs. 35.5±13.6 years, *P*=0.015, respectively). In addition, gender, disease duration, payment method, hospitalization cost, local GDP per capita, and geographical distance from hospital were compared between the two groups, and the differences were not statistically significant (Table 1).

Clinical Characteristics

The incidence of kidney damage and hypertension in the SLE patients with readmission was significantly higher than that in the SLE patients without readmission (Table 2) (63.9% vs. 50.4%, *P*=0.01; 12.4% vs. 4.0%, *P*=0.001, respectively). There were no statistically significant differences in other clinical symptoms, including fever, alopecia, arthritis, edema, convulsion, erythra, dental ulcers, or other complications between the two groups (Table 2).

Laboratory Examination and Renal Pathology

Patients with SLE who were readmitted had lower hemoglobin and albumin levels than patients without readmission (P=0.005 and P<0.001, respectively) during initial hospitalization, and higher urea nitrogen, total cholesterol, cystatin C, serum creatinine, blood uric acid, and triglycerides levels than patients without readmission (all P <0.005) (Table 3). There were no statistically significant differences in white blood cell counts, platelet counts, aspartate aminotransferase, alanine aminotransferase, total bilirubin, complement, antinuclear antibody series, or urine protein levels between patients (Table 3). More patients underwent renal biopsy in SLE patients who were readmitted than patients without readmission (33.1% vs. 20.8%, P=0.006). Type IV lupus nephritis was common in both groups, but there was no statistically significant difference in renal pathological types between the groups.

Analysis of risk factors associated with readmission and reasons for readmission in SLE patients within 1 year

Univariate logistic regression analysis was applied to define the risk factors for readmission in patients with SLE within 1 year in general and in relation to sociodemographic characteristics, clinical characteristics, laboratory examination results, and renal pathology. Finally, the onset age, duration of the first hospitalization, the hemoglobin, albumin, urea nitrogen, total cholesterol, cystatin C, serum creatinine, uric acid, blood triglycerides levels, and kidney damage were confirmed to be statistically significant. Multicollinearity analysis was performed among the screened risk factors, and the results showed VIF < 10, suggesting that there was no multicollinearity among these risk factors. However, cystatin C, urea nitrogen, and serum creatinine are highly correlated, and cystatin C is reported to be more sensitive. The screened risk factors excluding serum creatinine and urea nitrogen were enrolled, and multivariate logistic regression analysis was applied. The results showed that the age of onset (OR 1.022, 95%CI 1.007-1.036), albumin (OR 0.965, 95%CI 0.942-0.989), and cystatin C (OR 1.404, 95%CI 1.180 -1.670), were closely related to readmission (Table 4).

The most common causes of readmission were infection (52 cases, 27.08%), lupus activity or recurrence (45 cases, 23.4%), review and consolidation treatment (16 cases, 8.3%), and readmission due to cardiovascular and cerebrovascular diseases (12 cases, 6.25%) (Table 5).The most common infection factors in readmitted SLE patients were respiratory tract infection (29, 60%), followed by herpes zoster (8,14%), skin and soft tissue infection (7,12%), urinary tract infection (4,7%), and other factors such as nervous system infection, acute peritonitis, and pelvic inflammatory mass (Table 5).

Discussion

Our study demonstrated that 23.2% of the SLE patients were readmitted within 1 year and revealed that age of onset, albumin, and cystatin C were closely related to readmission. The most common causes of readmission were infection, especially respiratory tract infection.

The readmission rate in SLE patients in our study was lower than that reported by Teh et al. (35%) [9]. As the study by Teh et al. was conducted in 2008, the improvement of treatment may explain the lower readmission rate in our study. A study by Yazdany et al. showed that readmission is more likely to occur in young patients and those with publicly funded health insurance [6]. However, our data suggested that SLE patients with readmission tended to be older, and multivariate logistic regression analysis suggested that the age of onset was closely related to readmission. In addition, these patients did not show any difference in payment methods. The reason why our results are different from others may be related to different races, national conditions, and different study designs. It has been reported in previous literature that the incidence of SLE is higher among people belonging to race/ethnic minorities in remote areas and low socioeconomic status [10]. A study of non-whites showed that poverty had a greater impact on SLE mortality than race/ethnicity [11]. However, our study showed that the per capita GDP of SLE patients, the geographical distance from the research center, and the payment method did not affect readmission. This may be related to the hierarchical medical system in China. With the improvement of primary medical care, more patients can receive timely and high-quality medical treatment in rural areas.

Lupus nephritis is one of the most common and serious organ complications of SLE and a major factor affecting the long-term survival of the patients and their kidneys. Clinical characteristics and laboratory examination also indicated that SLE patients with readmission were more likely to suffer from kidney damage, and multivariate logistic regression analysis confirmed that albumin and cystatin C were closely related to readmission. It is suggested that patients with low serum albumin levels and high cystatin C levels have an increased risk of readmission. Our results were consistent with those of Yazdany et al [6]. A higher incidence of hypertension in the SLE patients with readmission was probably associated with renal damage. Prevalent renal involvement led to a high proportion of SLE patients receiving renal biopsy in the readmission group. Lupus IV nephritis was common in both groups, but there was no difference in the distribution of renal pathological types between the groups.

Our data indicated that infection, especially respiratory tract infection, is the most common cause of readmission in SLE. SLE patients are susceptible to infection due to immune abnormalities and long-term treatment with glucocorticoids and immunosuppressive agents. Studies have reported that more than 20% of hospitalizations are caused by infections, and bacterial infections are commonly reported in SLE. These infections affect multiple organs such as the respiratory tract, urinary tract, skin, and soft tissue [12], which is consistent with our findings. Infection is considered to be an important factor triggering lupus activity and a common cause of death in SLE [13]. Remission and recurrence alternations are one of the characteristics of SLE. This study found that lupus activity or recurrence is the second leading cause of readmission in patients with SLE. The results indicated that necessary medical intervention and

close follow-up should be offered to patients with SLE with low serum albumin levels and high cystatin C levels to protect themselves from infections. Subsequently, this will contribute in reducing readmission.

There are several limitations to our study that need to be addressed. This was a single center, retrospective study. Moreover, different cultural, race, economical, and geographical factors may influence the results and restrict the generalizability of the findings. Readmissions in other hospitals may be neglected.

Conclusions

Older age at onset, low serum albumin level, and high cystatin C level in SLE patients were risk factors for readmission within 1 year. Infection, disease activity, or recurrence was the main causes of readmission. We should pay attention to SLE patients with older age of onset, low serum albumin levels, and high cystatin C levels to avoid infection and recurrence with the aim of reducing the hospital readmission rate.

Declarations

Funding: This research was funded by the Zhanjiang Science and Technology Project (grant numbers 2019A01027).c

Conflicts of Interests: The authors have no conflicts of interest to declare that are relevant to the content of this paper.

Compliance with ethical standards: This study protocol was approved by the Ethics Committee of the Affiliated Hospital of Guangdong Medical University (ethics approval number: 2020-104-01). Informed consent was obtained from the patients.

Author Contributions: Jinxia Chen designed the study; Limin Zhang and Liutao Huang collected and analyzed the data; Limin Zhang wrote the first draft of the manuscript; Jinxia Chen,and Liutao Huang edited the manuscript; Huafeng Liu and Yongzhi Xu supervised the study.

References

1. Dörner T, Furie R. Novel paradigms in systemic lupus erythematosus. Lancet. 2019;393:2344–58. https://doi.org/10.1016/S0140-6736(19)30546-X.
2. Wang YF, Lau YI, Yang W. Genetic studies on systemic lupus erythematosus in east asia point to population differences in disease susceptibility. Am J Med Genet C Semin Med Genet. 2019;181:262–8. https://doi.org/10.1002/ajmg.c.31696.
3. Li R, Sun J, Ren LM, et al. Epidemiology of eight common rheumatic diseases in china: A large-scale cross-sectional survey in beijing. Rheumatology. 2012;51:721–9. https://doi.org/10.1093/rheumatology.

4. Zou YF, Feng CC, Zhu JM, et al. Prevalence of systemic lupus erythematosus and risk factors in rural areas of Anhui Province. Rheumatol Int. 2014;34:347–56. https://doi.org/10.1007/s00296-013-2902-1.
5. Nikpour M, Urowitz MB, Ibañez D, Gladman DD. Frequency and determinants of flare and persistently active disease in systemic lupus erythematosus. Arthritis Rheum. 2009;61:1152–8. https://doi.org/10.1002/art.24741.
6. Yazdany J, Marafino BJ, Dean ML, et al. Thirty-day hospital readmissions in systemic lupus erythematosus: predictors and hospital- and state-level variation. Arthritis Rheumatol. 2014;66:2828–36. https://doi.org/10.1002/art.38768.
7. Elixhauser A, Steiner C. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project. In: Readmissions to U.S. Hospitals by diagnosis. United States, 2010. Rockville: Agency for Healthcare Research and Quality; 2013. Statistical brief no.153.
8. Pan Q, Li Y, Ye L, et al. Geographical distribution, a risk factor for the incidence of lupus nephritis in china. BMC Nephrol. 2014;15:67. https://doi.org/10.1186/1471-2369-15-67.
9. Teh CL, Chan GYL, Lee J. Systemic lupus erythematosus in a tertiary, east malaysian hospital: admission, readmission and death. IntJ Rheum Dis. 2008;11:24–9. https://doi.org/10.1177/0961203308096661.
10. Feldman CH, Hiraki LT, Liu J, et al. Epidemiology and sociodemographics of systemic lupus erythematosus and lupus nephritis among us adults with medicaid coverage, 2000-2004. Arthritis Rheum. 2013;65:753–63. https://doi.org/10.1002/art.37795.
11. Walsh SJ, Gilchrist A. Geographical clustering of mortality from systemic lupus erythematosus in the United States: contributions of poverty, hispanic ethnicity and solar radiation. Lupus. 2006;15:662–70.
12. Jung JY, Suh CH. Infection in systemic lupus erythematosus, similarities, and differences with lupus flare. Korean J Intern Med. 2017;32:429–38. https://doi.org/10.3904/kjim.2016.234.
13. Wang Z, Wang Y, Zhu R, Tian X, Xu D, Wang Q. Long-term survival and death causes of systemic lupus erythematosus in China: a systemic review of observational studies. Medicine. 2015;94:e794.

Tables

Table 1.Comparison of Socio-demographic characteristics between SLE patients with non-readmission and readmission

Subject	non-readmission （n=400）	readmission (n=121)	p-value
Female n（%）	349（87.3）	102（84.3）	0.404
The duration of the first hospitalization （day）	9.0±6.0	11.0±8.4	0.007
age of SLE onset（year）	31.6±13.3	35.8±17.0	0.007
The age of first hospitalization（year）	35.5±13.6	40.3±16.4	0.015
<1year	169（42.3）	45（36.3）	
1year~5year	126（31.5）	29.0	
5year~10year	75（18.8）	28（22.6）	
＞10year	30（7.5）	15（12.1）	
Payment method			0.817
Residents’ health care n (%)	259（64.8）	79（65.3）	
Employee health care *n* (%)	51（12.8）	15（12.4）	
Rural Cooperative Medical Insurance n (%)	13（3.3）	6（5.0）	
Self-paying *n* (%)	77（19.3）	21（17.4）	
cost（median （25%，75%）	3877.55 （2258.26-6503.75）	4216.4 （2804.23-6582.66）	0.139
Per-capita GDP			0.283
10000~30000yuan *n* (%)	171（42.8）	40（33.1）	
31000~6000 yuan *n* (%)	161（40.3）	55（45.5）	
61000~90000 yuan *n* (%)	19（4.8）	7（5.8）	
＞90000 yuan *n*(%)	49（12.3）	19（27.9）	
geographical distance			0.393
1~30 km *n* (%)	113（28.2）	42（34.7）	
30~100 km *n* (%)	216（54）	60（49.6）	
＞100 km *n*(%)	71（17.8）	19（15.7）	

GDP: Gross Domestic Product.

Table 2. Comparison of Clinical Characteristics between SLE patients with non-readmission and readmission

Subject	non-readmission group (*n*=400)	readmission group (*n*=121)	p-value
Fever *n* (%)	97（24.4）	30（25.0）	0.888
Alopecia *n* (%)	82（20.7）	17（14.3）	0.122
Arthritis *n* (%)	215（54.2）	70（58.8）	0.369
Edema *n* (%)	130（32.7）	49（40.8）	0.103
Convulsion *n* (%)	4（1.0）	2（1.7）	0.910
Erythra *n* (%)	197（49.6）	55（46.6）	0.611
Dental ulcer *n* (%)	34（8.6）	14（29.2）	0.296
Renal involvement *n* (%)	200（50.4）	76（63.9）	0.010
Neuropathy *n* (%)	8（4.3）	5（4.2）	0.959
Hematological impairment of lupus n (%)	255（63.7）	85（70.2）	0.188
comorbidities			
Thyroid disease n (%)	18（4.5）	3（2.5）	0.468
Infection *n* (%)	122（30.5）	40（33.1）	0.594
Heart-failure n (%)	8（2.0）	3（2.5）	1.000
Tumor *n* (%)	4（1.0）	4（3.3）	0.166
Osteoporosis n (%)	8（2.0）	7（5.8）	0.061
Hypertension n (%)	16（4.0）	15（12.4）	0.001
Diabetes n (%)	7（1.8）	5（4.1）	0.236

Table 3. Comparison of Laboratory examination results and renal pathological types between readmission group and non- readmission group

Subject	non-readmission group (*n*=400)	readmission group (*n*=121)	p-value
WBC（4×10^9/L *n*（%）	305(76.3)	95(78.5)	0.606
PLT（100×10^9/L *n*（%）	336(84.0)	100(82.6)	0.724
HGB（110g/L *n*（%）	207(51.7)	80(66.1)	0.005
Complement C3（0.79g/L *n*（%）	310(77.5)	96(79.3)	0.669
Complement C4（0.16g/L *n*（%）	269(67.3)	83(68.6)	0.782
ALB （30g/L n（%）	139（34.8）	65（53.7）	（0.001
AST （48U/L n（%）	44（11.0）	13（10.7）	0.937
ALT （50U/L n（%）	40（10.0）	8（6.6）	0.259
BUN （8.07mmol/l n（%）	85（21.3）	46（38.0）	（0.001
CHOL（5.7mmol/l n（%）	99（24.8）	48（39.7）	0.001
Cys C（1.25mg/l n（%）	136（34.0）	76（62.8）	（0.001
CREA（177umol/l n（%）	34（8.5）	25（20.7）	（0.001
SUA（420umol/l n（%）	115（28.7）	51（42.1）	0.006
TBIL（20umol/l n（%）	18（4.5）	7（5.8）	0.562
TG（2.0mmol/l n（%）	106（26.5）	55（45.5）	（0.001
24h-Proteinuria（g（n（%）			0.876
（3.5g n（%）	359（89.8）	108（89.3）	
（3.5g n（%）	41（10.3）	13（10.7）	
Urinary RBC（3/HP *n*（%）	265（66.3）	71（58.7）	0.127
ANA *n*（%）	315（78.8）	89（22.0）	0.230
Anti-SS-A/RO52KD antibody *n*（%）	155（38.8）	43（35.5）	0.524
Anti-SS-A/RO60KD antibody *n*（%）	207（51.7）	64（52.9）	0.826
Anti-Histones antibody *n*（%）	149（37.3）	45（37.2）	0.990
Anti-Nucleosomes antibody *n*（%）	162（40.6）	49（40.5）	0.983
Anti-ds-DNA *n*（%）	157（39.3）	52（43.0）	0.464
anti-ribosomal p protein antibody *n*（%）	93（23.3）	32（26.4）	0.471
Anti-SmD1 antibody *n*（%）	212（53.0）	62（51.2）	0.734
Anti-SnRNP antibody *n*（%）	134（33.5）	47（38.8）	0.279
Renal biopsy *n*（%）	82（20.8）	40（33.1）	0.006

Type II and Type III *n*（%）	12（14.6）	6（15.0）	0.072
Type IV *n*（%）	45（54.9）	19（47.5）	
Type IV+V *n*（%）	15（18.3）	10（25.0）	
Type V and Type VI *n*（%）	10（12.2）	5（12.5）	

WBC: White Blood Cells; PLT: Platelets; HGB: hemoglobin; ALB: Albumin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BUN, Blood Urea Nitrogen; CHOL, cholesterol; Cys C: cystatin C; CREA: Creatinine; SUA, serum uric acid; TBIL: total bilirubin; TG: triglycerides; RBC: Red blood cell.

Table 4.Multiple logistic regression analysis of risk factors for readmission

factor	β	SE	Wald	*P-value*	OR value	95%CI
ALB	-0.035	0.012	8.342	0.004	0.965	（0.942 -0.989）
cystatin C	0.339	0.089	14.657	0.000	1.404	（1.18-1.67）
Age of onset	0.021	0.008	8.890	0.003	1.022	（1.007-1.036）

ALB: Albumin.

Table 5. Reasons for readmission in SLE patients within 1 year

readmission	Readmission （192 times）	constituent ratio
nfection	52	27.1%
respiratory tract	31	16.1%
herpes zoster	7	3.7%
skin and soft tissue	6	3.1%
urinary tract	4	2.1%
others	4	2.1%
Lupus activity or recurrence	45	23.4%
Post-treatment review	16	8.3%
Cardio-cerebral-vascular disease	12	6.3%
Digestive tract disease	9	4.6%
Tumor	9	4.6%
Hemodialysis	9	4.6%
Renal biopsy	6	3.1%
Osteoporosis	5	2.6%
Pregnancy（premature birth（abortion）	3	1.6%
Others	9	4.6%