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BRIEF COMMUNICATION

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Association between SLICC/ACR damage index and outcomes for lupus patients after cardiac valve surgery

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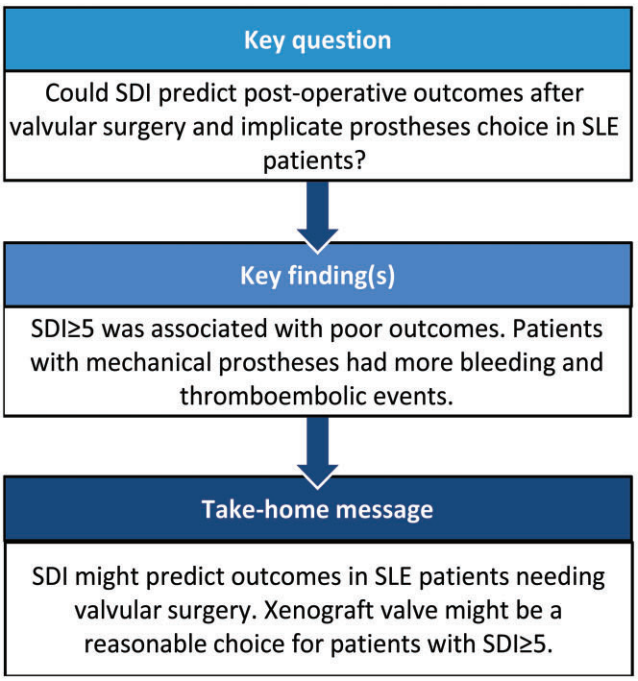

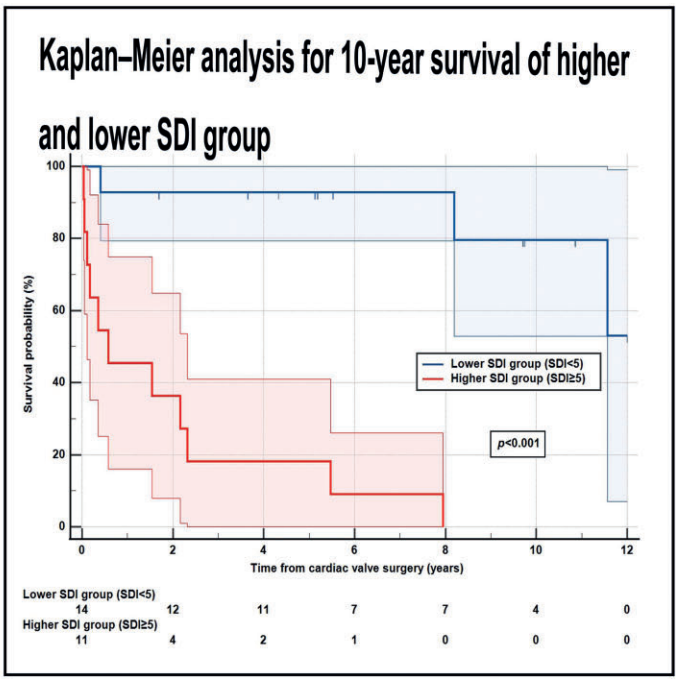

Abstract

Systemic lupus erythematosus (SLE) is associated with multi-organ damage including cardiac valve, which may need valvular operation. However, methods for outcome prediction and prosthetic valve selection are unclear in SLE patients undergoing cardiac valve surgery. Twenty-five SLE patients receiving valvular operation in a single institute between 2002 and 2020 were enrolled. Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index (SLICC/ACR damage index, SDI) was applied to evaluate the damage severity. Clinical outcomes were compared between patients with different SDI. The hospital survival rate was 88%, and long-term survival rate was 59.5% and 40.2% at 5 and 10 years. The median SDI was 4 (interquartile range 3–6) in our study, patients were then grouped into higher SDI (defined as SDI $\geq$ 5, $n = 11$) and lower SDI group (defined as SDI < 5, $n = 14$). The in-hospital survival rate (72.2% vs 100%, $P = 0.074$) and 5-year survival rate (18.2% vs 92.9%, $P < 0.001$) were lower in higher SDI group, compared to lower SDI group. SDI score was associated with long-term outcome for SLE patients receiving cardiac valve surgery. SDI $\geq$ 5 was associated with very poor long-term outcomes. This finding implicates that xenograft might be a reasonable choice for SLE patients with SDI $\geq$ 5.

Keywords: Systemic lupus erythematosus • Cardiac valves • Cardiac valve prostheses • Follow-up study

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease with multiple organ involvement. Prognosis is poor in patients presenting with organ damage caused by SLE disease progression, related treatment or other concomitant diseases [1, 2]. However, the association between the severity of SLE organ damage and outcomes after cardiac valve surgery in these patients was not been reported before. The aim of the present study was to evaluate the short-term and long-term outcomes in SLE patients receiving cardiac valve surgery and the association between the severity of organ damage and to assess whether Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index (SLICC/ACR damage index, SDI) [1] could be applied as a useful indicator for valve choice in this patient group.

METHODS

Ethical statement

The study was approved by the National Taiwan University Hospital Institutional Review Board (NTUH-201811037RIN).

Patients and study design

From January 2002 to June 2020, patients with a diagnosis of SLE were retrospectively identified from hospital electronic records and open-heart database by the following International Classification of Diseases (ICD) codes: ICD-9:710.0 or ICD-10: M3210-15, M3219, M328, M329, and was ensured that only those who fulfilled the 1997 American College of Rheumatology Revised Criteria for Classification of SLE were enrolled [3]. Patients with concomitant coronary artery disease with functional mitral regurgitation and insufficient data recording were excluded.

The SDI [1] was applied to assess the severity of organ damage. Other clinical variables including end-stage renal disease, EuroSCORE II [4] and medication use were also recorded.

The selection of prosthetic valve was made with a joint discussion between the surgeons and the patients according to the current valve surgery guideline, clinical condition, anticoagulant compliance and the patients' subjective willing. The target international normalized ratio (INR) for patients with mechanical prostheses replacement was controlled between 2.0 and 2.5 for mitral position and between 1.5 and 2.5 for aortic position, controlled directly by the surgeon and the rheumatologist [5]. For patients receiving xenograft prostheses, Vitamin-K antagonist was prescribed for 3 months after the operation. For patients with antiphospholipid syndrome and already been prescribed with Vitamin-K antagonist before operation, the target INR will be controlled to 2–3, and would be titrated if further thromboembolism episode occurred.

All continuous variables were presented as median value and interquartile range (IQR), the valve-related complication was calculated as linearized rate and the confidence interval was calculated based on the Poisson distribution. Survival outcomes were modelled using the Kaplan–Meier method and compared with log-rank test. Statistical significance was defined as P-value <0.05. All statistical analyses were performed using MedCalc® Statistical Software version 20 (MedCalc Software Ltd, Ostend, Belgium).

RESULTS

Twenty-five SLE patients underwent cardiac valve operation were retrospectively included in this study.

The median age of the study cohort was 60 years (IQR: 34–72), and the median SDI was 4 (IQR: 3–6). There were 68% of the patients had renal involvement, including 7 patients had already been on dialysis (Table 1).

Regarding the surgical procedures, 2 patients received mitral valve repair. Twenty-three patients received valve replacement, including 16 mechanical and 7 xenograft prostheses. Other detailed information regarding study flowchart, demographic data, operative procedures, postoperative outcomes and follow-up echocardiography data were listed in Supplementary Material (see Supplementary Material, Fig. S1 and Tables S1–S3).

There were three in-hospital mortalities, including mediastinitis ($n = 1$, SDI = 6) and postoperative heart failure ($n = 2$, SDI = 5 and 7), accounting for an in-hospital mortality rate of 12%, which was higher than the estimated EuroSCORE II (3.81%).

The follow-up duration ranged from 0 to 12 years, with a median of 4.75 years. Overall survival rates for the study cohort were 72 ± 9%, 59.5 ± 9.9% and 40.2 ± 11.4% at 1, 5 and 10 years, respectively (Fig. 1A). The causes of death during the follow-up period included heart failure ($n = 2$), infection (pneumonia = 4, catheter-related bacteraemia = 1, urosepsis = 1), pulmonary haemorrhage ($n = 1$), intracranial haemorrhage ($n = 1$) and SLE flare-up ($n = 1$). Variables associated with overall mortality were listed in Supplementary Material, Table S3.

There were 3 patients with mechanical prostheses complicated with ischaemic stroke (INR = 2.1, 2.0 and 1.9 upon the episode), and 3 patients complicated with bleeding (intracerebral haemorrhage = 1, INR = 3.5; pulmonary haemorrhage = 1, INR = 4.2; and gastrointestinal bleeding = 1, INR = 3.1, upon the episode). None of the patients receiving xenograft prostheses had complicated with bleeding or thrombo-embolism events after the operation. The linearized rate of thrombo-embolism and bleeding event rate between mechanical and xenograft prostheses were 2 (95% confidence interval = 0.9–6.6) vs 0 per 100 patient-years ($P = 0.16$); and 1.56 (95% confidence interval = 0.6–5.8) vs 0 per 100 patient-years ($P = 0.24$). However, one patient with xenograft had complicated with prostheses infectious endocarditis and received reoperation at 3 years after the primary operation. For the remaining 2 patients who received mitral valve repair, one died due to heart failure after operation, the other patient lived without any adverse events during the follow-up period.

The median SDI was 4(IQR 3–6), therefore, we grouped our patients into higher SDI (defined as SDI ≥ 5, $n = 11$) and lower SDI group (defined as SDI < 5, $n = 14$). Compared to lower SDI group, patients in higher SDI group had higher percentage of renal involvement (100% vs 43%, $P < 0.001$), end-stage renal disease needing dialysis (64% vs 0%, $P < 0.001$) and Prednisolone use (100% vs 43%, $P = 0.029$).

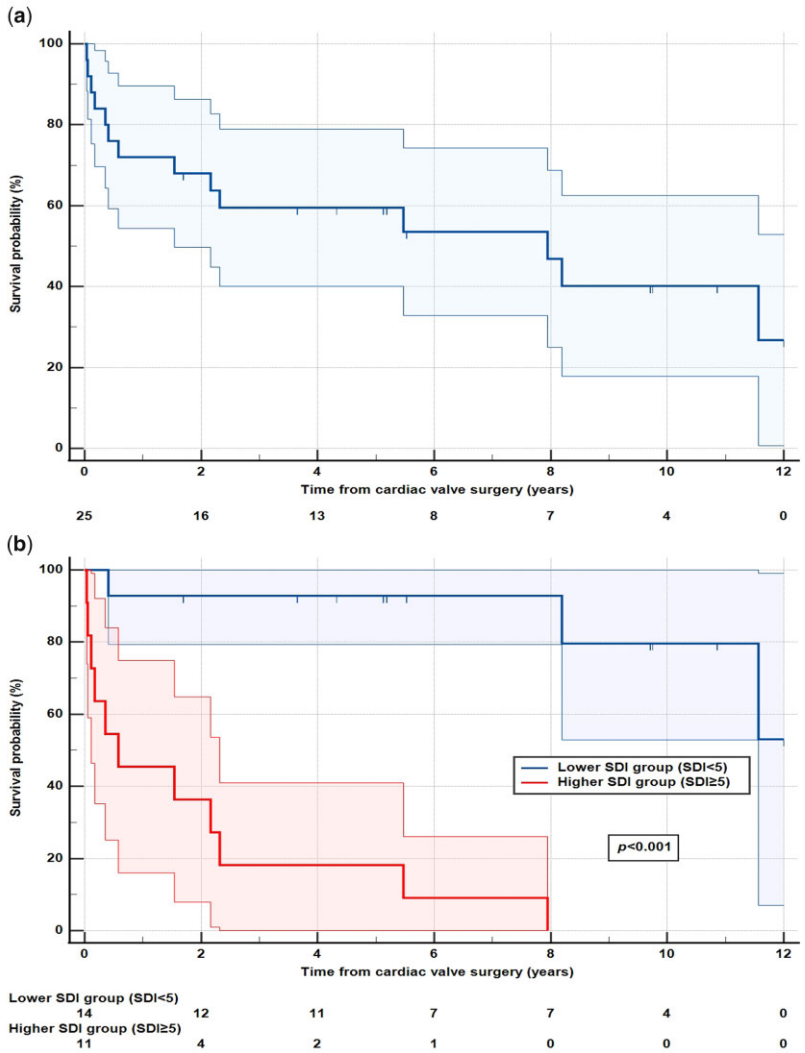

Figure 1: Kaplan–Meier analysis for long-term probability survival of the study patients (**A**) and of higher SDI and lower SDI group (**B**). SDI: SLICC/ACR damage index.

The in-hospital outcome was poorer in higher SDI group as compared with that in lower SDI group, including longer mechanical ventilation days (28.5, IQR: 1–80 vs 1, IQR: 1–1.25, $P < 0.001$), longer ICU days (7, IQR: 5–41 vs 4, IQR: 4–5, $P < 0.001$), longer hospital days (32, IQR: 18–42 vs 13, IQR: 11–17, $P = 0.031$) and higher infection rate (55% vs 7%, $P = 0.014$).

Eight patients died in the higher SDI group during follow-up, including infection ($n = 5$), heart failure ($n = 2$) and SLE flare-up ($n = 1$); 3 patients died in the lower SDI group, including infection ($n = 1$) and bleeding (pulmonary = 1, intracranial = 1). The overall survival probability for higher SDI group was 45.5 ± 15%, 18.2 ± 11.6% and 0.0 ± 0% at 1, 5 and 10 years, which was significantly lower than that for lower SDI group (92.9 ± 6.8%, 92.9 ± 6.8% and 79.6 ± 13.6% at 1, 5 and 10 years, $P < 0.001$, Fig. 1B).

DISCUSSION

Preoperative SDI is a good indicator in predicting postoperative outcomes in SLE patients undergoing cardiac valve surgery. SDI ≥ 5 is associated with poor in-hospital and long-term survival rates. In our study, patients in higher SDI group had significant higher renal involved rate, long-term dialysis rate and Prednisolone usage rate, and mostly died from serious infection events after operation. Impaired renal function is known as a major cause of mortality due to the high burden of serious infection for SLE patients [6]. In addition to renal impairment, immunological abnormalities related to SLE and glucocorticoid use [7] could also contribute to the vulnerability of severe infection in SLE patients.

The selection of mechanical or xenograft prostheses in SLE patients is controversial. Mechanical valve is preferred for the relatively young age, needing concomitant anticoagulant therapy for SLE, and preventing end-stage renal disease-related accelerated structural failure in xenograft [8, 9]. However, xenograft is also advocated for the easier and safer management of anticoagulants to lower the thrombo-embolism and bleeding complications in SLE patients [10]. In our study, we found that the postoperative survival in SLE patients with SDI ≥ 5 was very poor, however, no mortality was directly related to prosthetic valve failure, and no bleeding or thrombo-embolism events occurred in patients receiving xenograft. These results implicated that xenograft prostheses might be a reasonable choice for patients with SDI ≥ 5 to avoid life-long anticoagulants use, drug-related bleeding complications and the mechanical valve-related thrombo-embolism.

Table 1: Characteristics of the study patients stratified by lower and higher SDIs

	All ($n = 25$)	Lower SDI group (SDI < 5, $n = 14$)	Higher SDI group (SDI ≧ 5, $n = 11$)	*P*-value
SDI (IQR)	4 (3–6)	3 (2–4)	6 (5–9)	0.019
SDI distribution, *n* (%)				
Ocular	3 (12)	0	3 (27)	0.073
Neuropsychiatric	6 (24)	3 (21)	3 (27)	1
Renal	17 (68)	6 (43)	11 (100)	<0.001
Pulmonary	15 (60)	8 (57)	7 (64)	1
Cardiovascular	25 (100)	14 (100)	11 (100)	
Peripheral vascular	1 (4)	0	1 (9)	0.44
Gastrointestinal	2 (8)	1 (7)	1 (9)	1
Musculoskeletal	5 (20)	2 (14)	3 (27)	0.60
Skin	1 (4)	0	1 (9)	0.44
Diabetes under treatment	6 (24)	1 (7)	5 (46)	0.058
Premature gonadal failure	0	0	0	
Malignancy	2 (8)	1 (7)	1 (9)	1
Baseline preoperative characteristics				
Male gender, *n* (%)	7 (28)	4 (29)	3 (27)	0.65
EuroSCORE II (%, IQR)	3.81 (2.21–6.49)	2.58 (1.72–3.85)	6.1 (4.35–8.59)	0.36
Age (year, IQR)	60 (34–72)	52.5 (31.8–67.8)	65 (37–73)	0.52
Dialysis, *n* (%)	7 (28)	0	7 (64)	<0.001
Old cerebrovascular accident, *n* (%)	4 (16)	3 (21)	1 (9)	0.39
Combine APS, *n* (%)	8 (32)	6 (43)	2 (18)	0.19
Urgency, *n* (%)	9 (36)	4 (29)	5 (46)	0.33
Prednisolone use, *n* (%)	17 (68)	6 (43)	11 (100)	0.029
DMARDs use, *n* (%)	23 (92)	13 (93)	10 (91)	0.69
Prostheses type, *n* (%)				0.080
Mechanical	16 (70)	11 (85)	5 (50)	
Xenograft	7 (30)	2 (15)	5 (50)	

APS: antiphospholipid syndrome; DMARDs: disease-modifying anti-rheumatic drugs; IQR: interquartile range; SDI: SLICC/ACR damage index.

Due to retrospective study design, limited patient numbers and case discrepancy between mechanical and xenograft prostheses, further prospective study is required for definite outcome prediction in SLE patients undergoing cardiac valve surgery and prostheses selection.

CONCLUSIONS

SDI ≥ 5 was associated with very poor outcomes for SLE patients receiving valvular surgery. Xenograft prostheses might be a reasonable choice for SLE patients with SDI ≥ 5 who needs a cardiac valve replacement.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

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Conflict of interest: none declared.

Data availability

All relevant data are within the manuscript and its Supporting Information files.

Reviewer information

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