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Authors
Bruera, Sebastian
Lei, Xiudong
Blau, Brandon
et al.

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Postoperative Major Adverse Cardiac Events in Patients With Systemic Lupus Erythematosus

Sebastian Bruera,[1] Xiudong Lei,[2] Brandon Blau,[1] Hui Zhao,[2] Anita Deswal,[2] Jinoos Yazdany,[3] Sharon H. Giordano,[2] and Maria E. Suarez-Almazor[2]

Objectives. Patients with systemic lupus erythematosus (SLE) have a high risk of cardiovascular disease that could potentially increase postoperative major adverse cardiac events (MACE). We determined the rate of MACE in patients with SLE undergoing noncardiac surgery using national claims-based data.

Methods. This was a retrospective cohort study using Optum Clinformatics Data Mart from 2007 to 2020. We identified a cohort of patients with SLE who had undergone noncardiac surgeries using *Current Procedural Terminology* codes. We also identified two control cohorts without SLE, one with diabetes mellitus (DM) and one without DM. After matching cases and controls by age and sex, the odds of MACE were estimated using multivariable logistic regression models also including race and the Revised Cardiac Risk Index (RCRI) scores. We also examined use of preoperative cardiac testing.

Results. We identified 4750 patients with SLE, 496,381 DM controls, and 1,484,986 non-DM controls. After matching, the odds ratio (OR) for MACE in patients with SLE versus non-DM controls was 1.51 (95% confidence interval 1.09-2.08), which decreased after adjustment for RCRI score (OR: 0.97, 95% confidence interval 0.7-1.36). No significant differences were observed in the incidence of MACE between patients with SLE and DM controls (0.82 vs 1.04, $P = 0.16$). High-risk patients with SLE (RCRI score of ≥3) were less likely to receive preoperative cardiac testing than non-DM controls (42.7% vs 35.1%, $P < 0.05$).

Conclusion. Patients with SLE have an increased risk of postoperative MACE, which is driven by increased RCRI scores. Concerningly, high-risk patients received less cardiac testing 2 months before surgery than non-DM controls.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a risk factor for cardiovascular disease (CVD), which has emerged as a leading cause of death in this population (1–6). CVD can lead to major adverse cardiac events (MACE) after surgery. The American Heart Association has published guidelines for the preoperative management of patients with risk factors for CVD (7). These guidelines recommend that for patients with an increased risk of CVD by measurements such as the Revised Cardiac Risk Index (RCRI) and decreased functional status, preoperative cardiac testing (eg, pharmacologic stress testing) can be useful.

Several studies have used administrative claims data to investigate the relationship between RCRI scores, preoperative testing, and/or MACE during the perioperative period (8–13). Although there are limited data on patients with SLE undergoing surgery, prior studies showed that these patients had an increased risk of mortality during hospitalization after surgical procedures (14–16). However, prior studies had mixed results as to whether CVD was a contributing factor to increased MACE and

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[1]Sebastian Bruera, MD, Brandon Blau, MD: Baylor College of Medicine, Houston, Texas; [2]Xiudong Lei, PhD, Hui Zhao, MD, Anita Deswal, MD, Sharon H. Giordano, MD, MPH, Maria E. Suarez-Almazor, MD, PhD: The University of Texas MD Anderson Cancer Center, Houston; [3]Jinoos Yazdany, MD, MPH: Zuckerberg San Francisco General Hospital and University of California, San Francisco.

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Address correspondence to Maria E. Suarez-Almazor, MD, PhD, The University of Texas MD Anderson Cancer Center, Department of Health Services Research, Unit 1444, 1515 Holcombe Blvd, Houston, TX 77030. Email: msalmazor@mdanderson.org.

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did not use RCRI scores to stratify preoperative risk. Furthermore, no studies have examined the use of preoperative CVD testing among patients with SLE.

Our objective was to determine the risk of postoperative MACE in patients with SLE using a large claims data set.

METHODS

Data source. We queried the Optum Clinformatics Data Mart (Optum). Optum contains approximately 67 million privately insured patients and Medicare beneficiaries. Available data from Optum include demographic variables, diagnostic and procedure codes, prescription claims, and death. Optum does not include data for patients who are insured only by Medicaid or who are otherwise uninsured. All data are deidentified.

Cohort selection. *Noncardiac surgery.* We initially identified all patients who underwent moderate- to high-risk noncardiac surgery using *Current Procedural Terminology* (CPT) codes 20000-69955 from 2007 to 2020. Two internal medicine physicians (SB and BB) independently examined each CPT procedure code to exclude minor surgeries, including eye surgeries, gastrointestinal endoscopies, dental procedures, cystoscopies, minor dermatologic procedures, injections, fine-needle aspirations, insertion of catheters, orthopedic surgeries distal to the elbow or knee joints, and surgeries that are commonly conducted without general anesthesia. Afterward, any conflicts between reviewers were settled by consensus or by a third party (MESA) if consensus could not be reached.

SLE cases. We identified a cohort of patients with SLE who underwent noncardiac surgery. Only the first noncardiac surgery identified was included for analysis.

Inclusion criteria were the following:

1. Age 18 or older.
2. Two or more claims for SLE (*International Classification of Diseases, Ninth Revision* [ICD-9] code 710.0 or *International Classification of Diseases, 10th Revision* [ICD-10] codes M32.xx but not M32.0) on separate dates (inpatient or outpatient) within 1 year before the surgery.
3. Insurance coverage between 2 years before and 1 month after surgery.
4. Prescription claims for antimalarials, corticosteroids, biologics, and/or immunosuppressants for at least a 90-day supply within 2 years before the date of the first SLE code (Supplementary Table A1).

We excluded patients with two or more claims of 710.3 or M33.xx (dermatomyositis); 710.1 or M34.xx (systemic sclerosis); or 714.0, M05.xx, or M06.xx (rheumatoid arthritis) within 1 year before surgery.

Controls. To compare the rates of MACE in patients with SLE with that in other populations, we selected two cohorts of patients, matched by age and sex, who also underwent noncardiac surgery as defined above:

1. A cohort of patients with diabetes mellitus (DM) was identified with ICD-9 codes 250.x0, 250.x2, 583.81, and 360.2 or ICD-10 code E11 (type II DM). This population was selected because diabetes is a prevalent chronic disease that is recognized as a major risk for MACE after noncardiac surgery (17).
2. A control cohort excluding patients with SLE (or other connective tissue diseases as defined in Supplementary Table A2) and/or diabetes (non-DM).

Outcomes. The primary outcome was MACE (including myocardial infarction, ischemic stroke, or death from any cause) within 1 month of surgery. Deaths attributable to cardiovascular events are not available in Optum. The ICD and CPT codes used to define MACE are shown in Supplementary Table A3. We identified patients with MACE code(s) at discharge in the admission files. Only patients with dates of admission from 2 days before to 30 days after the first noncardiac surgery date were included. This was done to include patients who might have been admitted earlier than the surgery date (eg, a patient was admitted on a Saturday and underwent surgery on Monday). We excluded admissions prior to 2 days before the noncardiac surgery date because these patients could have been admitted for reasons other than the surgery.

Our secondary outcome was MACE within 3 months of surgery.

Covariates. *Demographics.* We categorized patients' ages at noncardiac surgery into six groups: 18 to 34, 35 to 44, 45 to 54, 55 to 64, 65 to 74, and 75 or older. Optum groups patients' race and ethnicity into White, Black, Hispanic, Asian, and unknown; race and ethnicity were categorized as White versus non-White in this analysis to ensure sufficient sample in each subgroup. Other demographic variables included sex and residence according to the US Census Regions.

RCRI score. The RCRI score includes six conditions ascertained within 1 year before the index surgery: ischemic heart disease, congestive heart failure, cerebrovascular disease, chronic kidney disease, insulin-dependent DM (≥30 days' supply of insulin within 3 months before the index date; Supplementary Table A4), and any moderate- or high-risk surgeries as the index surgery (18). Any of the above conditions contributes 1 point to the score. The RCRI score is the sum of total points and is categorized from 0 to 3 or higher. A score of 0 is typically low risk, a score of 1 is moderate risk, a score of 2 is high risk, and a score of 3 or higher is very high risk. The same process described earlier for the categorization of surgeries was used to generate CPT codes to identify noncardiac moderate- to high-risk surgeries (eg, intra-abdominal surgery, intrathoracic, oncologic, major joint replacement). These codes are shown in Supplementary Table A5.

Comorbidity score. In addition to the RCRI, we also used Charlson's comorbidity score to identify comorbidities that may not be captured by the RCRI, derived using ICD codes in the year before the index surgery date (19,20).

Garris score. For patients with SLE, we estimated disease activity within 1 year before the noncardiac surgery using the Garris score (21,22). The Garris index is an algorithm from administrative claims data with a sensitivity of 85.7%, specificity of 67.6%, positive predictive value (PPV) of 81.8%, and negative predictive value (NPV) of 73.5% for distinguishing moderate and/or severe from mild SLE when comparing administrative claims data to the SLE Disease Activity Index-2000 (21).

Cardiac testing. We identified preoperative cardiac tests performed within 2 and 6 months before surgery using CPT codes (Supplementary Table A6) for stress electrocardiogram, stress echocardiogram, stress nuclear test, stress magnetic resonance imaging, nonstress transesophageal echocardiography (TEE), and nonstress transthoracic echocardiography. Although TEEs are not used as preoperative risk stratification, we included them because practitioners may opt to use the results of a TEE conducted within 6 months before surgery for preoperative risk stratification.

Matching. We matched patients with SLE by age (per 5-year category) and sex with the diabetic and the nondiabetic control cohorts, with a 1:10 ratio and 1:40 ratio, respectively. For all cases and controls, the outcome was measured from day 0 of the index date (the date of surgery).

Statistical analysis. We compared baseline patient and clinical characteristics between the three unmatched and matched cohorts with χ^2 tests. We compared MACE rates within 1 and 3 months after surgery between all three cohorts using χ^2 tests and 95% confidence intervals (CI). We required insurance

Table 1. Baseline characteristics for matched cohorts

	SLE, n (%)	DM controls, n (%)	Non-DM controls, n (%)	*P*
Total, n	4749	46,885	189,760	
Age, years				
18-34	346 (7.3)	3394 (7.2)	13,840 (7.3)	0.99
35-44	656 (13.8)	6470 (13.8)	26,240 (13.8)	
45-54	1004 (21.1)	9785 (20.9)	40,080 (21.1)	
55-64	1195 (25.2)	11,790 (25.1)	47,680 (25.1)	
65-74	973 (20.5)	9716 (20.7)	38,920 (20.5)	
75+	575 (12.1)	5730 (12.2)	23,000 (12.1)	
Sex				
Female	4303 (90.6)	42,425 (90.5)	171,920 (90.6)	0.76
Male	446 (9.4)	4460 (9.5)	17,840 (9.4)	
Race				
White	2991 (63)	32,804 (70)	151,662 (79.9)	<0.001
Black	799 (16.8)	6644 (14.2)	15,554 (8.2)	
Hispanic	548 (11.5)	4844 (10.3)	12,528 (6.6)	
Asian	107 (2.3)	1025 (2.2)	3399 (1.8)	
Unknown	304 (6.4)	1568 (3.3)	6617 (3.5)	
Region				
Midwest	1000 (21.1)	14,689 (31.3)	69,821 (36.8)	<0.001
Northeast	385 (8.1)	4202 (9)	12,888 (6.8)	
South	2298 (48.4)	20,963 (44.7)	72,630 (38.3)	
West	1061 (22.3)	7001 (14.9)	34,304 (18.1)	
Unknown	5 (0.1)	30 (0.1)	117 (0.1)	
Low-income subsidy				
No LIS DUAL	2728 (57.4)	35,854 (76.5)	153,497 (80.9)	<0.001
MAPD DUAL	251 (5.3)	613 (1.3)	947 (0.5)	
MAPD LIS	180 (3.8)	271 (0.6)	423 (0.2)	
Other	618 (13)	1885 (4)	6900 (3.6)	
Unknown	972 (20.5)	8262 (17.6)	27,993 (14.8)	
RCRI score				
0	2356 (49.6)	22,943 (48.9)	121,997 (64.3)	<0.001
1	1685 (35.5)	17,751 (37.9)	61,688 (32.5)	
2	501 (10.5)	4653 (9.9)	5138 (2.7)	
3+	208 (4.4)	1538 (3.3)	937 (0.5)	
Comorbidity score				
0	26 (0.5)	9748 (20.8)	144,309 (76)	<0.001
1	1769 (37.2)	18,497 (39.5)	30,515 (16.1)	
2+	2955 (62.2)	18,640 (39.8)	14,936 (7.9)	

Abbreviations: DM, diabetes mellitus; DUAL, Medicaid/Medicare; LIS, low income subsidy; MAPD, medicare advantage prescription drug; RCRI, Revised Cardiac Risk Index; SLE, systemic lupus erythematosus.

coverage for 1 month as opposed to 3 months to maximize our sample size because MACE is a relatively rare outcome.

We conducted multivariable conditional logistic regression models to assess the association between the three cohorts and MACE. The analysis was performed in three steps to examine the effect of specific covariates on MACE outcomes: 1) model 1 included the matched cohorts as the sole variable, 2) model 2 adjusted for the RCRI scores, and 3) model 3 adjusted for race and ethnicity. Results were expressed as odds ratios (ORs) with 95% CI. In addition, we estimated the adjusted rates (ie, predicted marginals) from logistic regression models for the three cohorts while adjusting for RCRI score. We also examined use of cardiac testing prior to the index surgery in all three cohorts.

Among patients with SLE alone, we examined the association of patient and clinical factors with MACE within 1 month after surgery using logistic regression models. Given the small number of events (n = 39), our final model included age, RCRI score, and SLE disease activity by the Garris index (race and ethnicity could not be included).

Subgroup analysis. Analyses were repeated for patients who were 45 years or older.

Sensitivity analyses. As a sensitivity analysis, we also added the comorbidity score to the final logistic regression models because other comorbidities not specifically included in the RCRI could also increase the risk of MACE. We also performed a separate sensitivity analysis to include the year of surgery into the logistic regression model to account for potential differences in outcomes over time.

This study used deidentified data and was exempted by our institutional review board.

RESULTS

Baseline characteristics. We identified 4750 patients with SLE, 496,381 DM controls, and 1,484,986 non-DM non-SLE controls (Supplementary Table A7). Patients with SLE were younger, more commonly female, more likely to be Black, and had more comorbidities than the non-DM controls. About 67% of the patients were aged 64 or younger; 90% were women. The unadjusted rates for MACE 1 month after surgery were 0.8% for patients with SLE, 2% for DM controls, and 0.8% for non-DM controls.

The matched cohorts included 4749 patients with SLE, 46,885 DM controls, and 189,760 non-DM controls (Table 1). After matching for age and sex, there were differences in race (patients with SLE were more likely to be Black than general controls), geographic location (patients with SLE were more often in the South), and in RCRI scores (patients with SLE and DM had higher RCRI scores than non-SLE non-DM controls).

MACE outcomes. The percentages of MACE for the matched cohorts at 1 and 3 months for ages 18 and older and ages 45 and older are shown in Table 2. Patients with SLE had a statistically significant increase in MACE compared with non-DM controls at 1 and 3 months, both for ages 18 and older and 45 and older. The difference in MACE between SLE and diabetic controls was not statistically significant. At 1 month, the rate of MACE was 0.82% (95% CI 0.58%-1.08%) for patients with SLE, 0.55% (95%CI 0.52%-0.58%) for non-DM controls, and 1.04% (95% CI 0.96%-1.14%) for DM controls. Supplementary Table A8 shows the individual components of MACE. At 1 month, myocardial infarction was more likely in non-DM controls than in patients with SLE (P = 0.004). For 3-month outcomes, we likely underestimated MACE rates because 5.2% of the patients did not have complete follow-up at 3 months (5.0%, 5.9%, and 5.6% in non-DM, DM, and SLE, respectively). Because this is a binary end point (not a time-to-event end point), patients were not censored if lost to follow-up (eg, if a patient did not have insurance beyond 30 days, they were considered as not having a MACE event).

Multivariable logistic regression models. The first step of the multivariable conditional logistic regression model only included the three cohorts as a covariate. Patients with SLE had an increased risk of MACE at 1 month compared with non-DM controls (Table 3, model 1, OR 1.51, 95% CI 1.09-2.08). In step 2, after adjustment for the RCRI score, the OR was no longer statistically significant for SLE (model 2, 0.97, 95% CI 0.7-1.36), indicating that the increased risk was primarily driven by the comorbidities included in the RCRI score. The addition of race to the model did not change the results (model 3, OR 0.96, 95% CI 0.69-1.34). Multivariable conditional logistic regression models for those aged 45 and older showed similar results (Supplementary Table A9). At 3 months, after adjustment for RCRI, the risk of MACE was no

Table 2. Rates of MACE 1 and 3 months after surgery in matched cohorts

Outcome	SLE, rate % (95% CI)	DM controls, rate % (95% CI)	*P*	Non-DM controls, rate % (95% CI)	*P* (vs SLE)
Ages 18+					
MACE at 1 month	0.82 (0.58-1.08)	1.04 (0.96-1.14)	0.16	0.55 (0.52-0.58)	0.01
MACE at 3 months	1.45 (1.11-1.79)	1.53 (1.42-1.64)	0.74	0.79 (0.75-0.83)	<0.001
Ages 45+					
MACE at 1 month	1.04 (0.72-1.37)	1.26 (1.15-1.38)	0.26	0.67 (0.63-0.71)	0.01
MACE at 3 months	1.79 (1.36-2.21)	1.85 (1.71-1.99)	0.84	0.97 (0.92-1.02)	<0.001

Abbreviations: DM, diabetes mellitus; MACE, major adverse cardiac events; SLE, systemic lupus erythematosus.

longer statistically significant; however, the effect was much smaller (OR 1.28, 95% CI 0.99-1.65; Supplementary Table A9). Based on the multivariable model adjusting for RCRI score, we estimated the predicted marginals for MACE at 1 and 3 months. The predicted marginals of MACE at 1 month were 0.37% (95% CI 0.27%-0.51%) for patients with SLE, 0.52% (95% CI 0.46%-0.58%) for DM controls, and 0.47% (95% CI 0.44%-0.50%) for non-DM controls. The predicted marginals of MACE at 3 months were 0.70%, 0.81%, and 0.68%, respectively. These results indicate that about half of the risk for MACE in patients with SLE was associated with prior RCRI score. Sensitivity analyses were performed, adding the comorbidity score and year of surgeries to the final logistic models (Supplementary Tables A10 and A11). No significant additional decrease was observed in the OR for patients with SLE, indicating that increased risk of MACE in patients with SLE compared with non-DM controls was associated with RCRI factors rather than other comorbidities or surgical dates.

Preoperative cardiac studies. Table 4 shows the use of cardiac studies 2 months prior to surgery in patients aged 18 years and older and 45 years and older. Cardiac testing was generally low for all groups, although higher for the SLE cohort compared with the other two cohorts (15.2%). However, among the highest risk stratum (RCRI score of ≥3), patients with SLE were less likely to receive cardiac testing (35.1% vs 42.7% in non-DM controls). Similar results were seen for patients 45 years and older. Similar trends were observed for preoperative cardiac testing within 6 months of surgery; however, the differences among groups became nonsignificant (Supplementary Table A12).

Determinants of MACE among patients with SLE. Table 5 shows the logistic regression models for determinants of MACE in the SLE cohort at 1 and 3 months. No MACE were observed for Asian or Hispanic patients, so race and ethnicity could not be evaluated. No significant associations were observed between MACE and sex or with disease activity. Increasing RCRI scores and older age significantly increased the risk of MACE. Use of cardiac testing (within 2 or 6 months before surgery) was not significantly associated with MACE.

DISCUSSION

To our knowledge, this is the first study reporting the risk of postoperative MACE in patients with SLE according to RCRI

Table 3. Multivariable conditional logistic regression model for MACE 1 and 3 months after surgery in matched cohorts aged 18+

	Model 1, OR (95% CI)	*P*	Model 2, OR (95% CI)	*P*	Model 3, OR (95% CI)	*P*
Cohorts						
Non-DM control	1		1		1	
DM control	1.92 (1.7-2.1)	<0.001	1.26 (1.1-1.4)	<0.001	1.26 (1.1-1.4)	<0.001
SLE	1.51 (1.1-2.1)	0.013	0.97 (0.7-1.4)	0.88	0.96 (0.7-1.3)	0.82
RCRI						
0			1		1	
1			2.92 (2.6-3.3)	<0.001	2.92 (2.6-3.3)	<0.001
2			8.4 (7.2-9.8)	<0.001	8.35 (7.2-9.7)	<0.001
3+			12.72 (10.4-15.6)	<0.001	12.68 (10.4-15.5)	<0.001
Race						
White					1	
Black					1.26 (1.1-1.5)	0.005
Hispanic					0.65 (0.5-0.9)	0.002
Asian					1.3 (0.9-1.9)	0.18
MACE at 3 months						
Cohorts						
Non-DM control	1		1		1	
DM control	1.97 (1.8-2.15)	<0.001	1.33 (1.21-1.46)	<0.001	1.32 (1.2-1.45)	<0.001
SLE	1.87 (1.47-2.4)	<0.001	1.27 (0.99-1.63)	0.06	1.25 (0.97-1.61)	0.09
RCRI						
0			1		1	
1			2.58 (2.32-2.86)	<0.001	2.57 (2.32-2.86)	<0.001
2			6.97 (6.14-7.92)	<0.001	6.91 (6.09-7.85)	<0.001
3+			11.2 (9.45-13.28)	<0.001	11.1 (9.36-13.16)	<0.001
Race						
White					1	
Black					1.3 (1.14-1.49)	<0.001
Hispanic					0.79 (0.65-0.97)	0.026
Asian					1.12 (0.8-1.57)	0.51

Abbreviations: CI, confidence interval; DM, diabetes mellitus; MACE, major adverse cardiac events; OR, odds ratio; RCRI, Revised Cardiac Risk Index; SLE, systemic lupus erythematosus.

Table 4. Cardiac testing within 2 months before surgery stratified by RCRI score for matched cohorts

Cardiac testing within 2 months before surgery	SLE, n (%)	DM controls, n (%)	Non-DM controls, n (%)	*P*
Patients ≥18 years (n = 241,395)				
Yes	721 (15.2)	5938 (12.7)	13,786 (7.3)	<0.001
95% CI	15.0-15.3	12.5-12.8	7.2-7.4	
RCRI = 0 (n = 147,296)				
Yes	224 (9.5)	1933 (8.4)	6628 (5.4)	<0.001
95% CI	9.4-9.7	8.3-8.7	5.3-5.6	
RCRI = 1 (n = 81,124)				
Yes	282 (16.7)	2235 (12.6)	5315 (8.6)	<0.001
95% CI	16.5-17.0	12.4-12.8	8.4-8.8	
RCRI = 2 (n = 10,292)				
Yes	142 (28.3)	1176 (25.3)	1443 (28.1)	0.005
95% CI	27.5-29.2	24.4-26.1	27.2-28.9	
RCRI = 3+ (n = 2683)				
Yes	73 (35.1)	594 (38.6)	400 (42.7)	0.048
95% CI	33.3-36.9	36.8-40.5	40.8-44.6	
Patients ≥45 years (n = 190,449)				
Yes	13,033 (8.7)	5429 (14.7)	645 (17.2)	<0.001
95% CI	8.6-8.8	14.5-14.8	17.0-17.4	
RCRI = 0 (n = 117,026)				
Yes	6256 (6.5)	1786 (9.8)	213 (11.5)	<0.001
95% CI	6.3-6.6	9.7-10.0	11.3-11.7	
RCRI = 1 (n = 61,471)				
Yes	4974 (10.6)	1986 (14.9)	244 (18.9)	<0.001
95% CI	10.4-10.9	14.6-15.2	18.6-19.3	
RCRI = 2 (n = 9380)				
Yes	1409 (28.5)	1087 (27.1)	126 (29.7)	0.26
95% CI	27.6-29.4	26.2-28.0	28.8-30.6	
RCRI = 3+ (n = 2572)				
Yes	394 (42.7)	570 (38.7)	62 (34.6)	0.05
95% CI	40.8-44.7	36.9-40.6	32.8-36.5	

Abbreviations: CI, confidence interval; DM, diabetes mellitus; RCRI, revised cardiac risk index; SLE, systemic lupus erythematosus.

stratification, including a comparison with a cohort with a known chronic disease risk for MACE (diabetes) as well as general population controls, and also evaluating the use of preoperative cardiac testing. The risk of MACE in patients with SLE approached 1% and 1.5% at 1 and 3 months, respectively, despite 90% of the patients being women and more than two thirds being younger than 65. When compared with matched nondiabetic controls, patients with SLE had significant increases of 49% in MACE at 1 month (0.82% vs 0.55%) and 83% increase at 3 months (1.45% vs 0.79%). The risk of MACE for patients with SLE was similar to that for patients with diabetes.

We identified two other studies using US claims data evaluating cardiovascular outcomes after surgery in patients with SLE. Both studies evaluated the risk for complications during admission, and neither examined outcomes specifically at 1 and 3 months after surgery (14,15). Moreover, their criterion for diagnosis of SLE was a single diagnostic code, unlike our study, which required two codes and prior treatment to increase diagnostic specificity. Smilowitz et al (14), using data from the Healthcare Cost and Utilization Project's National Inpatient Sample, reported that patients with SLE were at higher risk of postoperative MACE during admission than general controls. Their rate of MACE in patients with SLE was higher (2.4%), probably reflecting a more selective population because they only included inpatient surgeries; also, it is unclear whether they excluded cardiac surgeries. In our study we included elective and ambulatory surgical procedures, and we excluded cardiac surgeries. We also omitted prolonged hospitalizations before the surgical index date because we only included patients hospitalized 2 days before the surgery. Babazade et al (15) analyzed data from seven states from the Instate Inpatient Databases and found an increase in in-hospital mortality and renal complications, but not in cardiovascular complications, in patients with SLE compared with controls (15,16). This study did not use a composite outcome and examined only individual components such as myocardial infarction. Finally, a study using data from Taiwan's National Health Insurance Research Database examined postoperative 30-day inpatient complications and found that patients with SLE compared with controls were more likely to experience various individual outcomes such as mortality, overall complications, stroke, and pulmonary embolism but did not include a composite outcome for MACE (16).

Table 5. Univariate and multivariable logistic regression model for MACE including death in 1 and 3 months after surgery among patients with SLE aged 18+

	Univariate, OR (95% CI)	*P*	Multivariable, OR (95% CI)	*P*
MACE at 1 month				
Age				
18-64	1		1	
65-74	4.56 (1.83-11.37)	0.001	3.8 (1.51-9.56)	0.005
75+	14.38 (6.3-32.82)	<0.001	11.02 (4.76-25.49)	<0.001
Sex				
Female	1		1	
Male	2.93 (1.38-6.22)	0.005	1.91 (0.88-4.13)	0.1
RCRI				
0	1		1	
1	1.54 (0.65-3.64)	0.32	1.3 (0.55-3.1)	0.55
2	5.76 (2.47-13.4)	<0.001	3.75 (1.58-8.87)	0.003
3+	6.97 (2.51-19.37)	<0.001	4.37 (1.54-12.45)	0.006
SLE disease activity				
Mild	1			
Moderate	0.51 (0.25-1.05)	0.07		
Severe	0.94 (0.41-2.18)	0.89		
Stress test within two months				
No	1			
Yes	1.68 (0.8-3.56)	0.17		
MACE at 3 months				
Age				
18-64	1		1	
65-74	2.63 (1.44-4.83)	0.002	2.16 (1.17-4)	0.014
75+	6.27 (3.57-11)	<0.001	4.62 (2.6-8.22)	<0.001
Sex				
Female	1		1	
Male	2.5 (1.38-4.54)	0.003	1.72 (0.93-3.17)	0.08
RCRI				
0	1		1	
1	1.97 (1.01-3.83)	0.046	1.78 (0.91-3.47)	0.09
2	6.83 (3.49-13.34)	<0.001	5.15 (2.61-10.18)	<0.001
3+	9.56 (4.41-20.7)	<0.001	7.13 (3.24-15.68)	<0.001
SLE disease activity				
Mild	1			
Moderate	0.91 (0.52-1.59)	0.73		
Severe	1.85 (1-3.45)	0.05		
Stress Pre 2m				
No	1			
Yes	2.32 (1.37-3.92)	0.002		

Abbreviations: CI, confidence interval; DM, diabetes mellitus; MACE, major adverse cardiac events; OR, odds ratio; RCRI, Revised Cardiac Risk Index; SLE, systemic lupus erythematosus.

The increased risk of MACE is likely driven by increased RCRI scores because after adjustment for RCRI score the OR decreased and was no longer statistically different from that of controls. This is consistent with the hypothesis that patients with SLE have increased underlying comorbidities that further increase the risk of MACE. Stratification by RCRI scores can easily be ascertained before surgery. Although, as a whole, our SLE cohort had more cardiac testing than the general cohort, use remained low (because most patients did not undergo testing), even for those 45 years and older. Concerningly, high-risk patients with SLE with an RCRI score of 3 or higher underwent less preoperative cardiac testing within 2 months than nondiabetic controls, suggesting that there may be a lack of awareness of the heightened cardiovascular risk in this population. Prior use of cardiac testing was not associated with MACE when added to the multivariate model. Several reasons could explain this finding. First, patients tested were those at highest risk, and second, we do not know whether other interventions were performed after testing in these patients that could improve MACE outcomes. It is unclear why the use of presurgical cardiac testing in high-risk patients with SLE was low. It would be expected that, given their cardiovascular comorbidities, patients with SLE should undergo equal if not greater testing that nondiabetic controls. One possible explanation is that the risk of CVD in people with SLE is underestimated by surgeons, anesthesiologists, and/or primary care physicians. Although rheumatologists may be more cognizant of the

increased cardiovascular risk of these patients, it is unclear how often patients with SLE will see their rheumatologist before undergoing surgery and whether they will receive specific recommendations for testing. Another potential explanation is that patients with SLE may undergo surgery more unexpectedly or emergently without the opportunity for preoperative testing. Further research is needed. General practitioners and rheumatologists should remain cautious and consider referral to cardiologists or ordering of preoperative tests, especially in patients at high risk.

The strengths of our study include a large national sample of patients with SLE who underwent noncardiac surgical procedures that we were able to match with a large sample of non-DM and DM controls. However, there are limitations to consider. First, administrative claims data do not include clinical variables such as functional status, which is important in risk stratifying patients preoperatively. However, we would not expect this to affect our results because we would expect patients with SLE to have more debilitation than general controls that may require increased stress testing. Second, we included patients with SLE who received hydroxychloroquine to increase specificity, so our results are not necessarily generalizable to untreated patients with SLE. Third, given the quantity of surgeries and procedure codes, we are unable to match or use propensity scores for specific surgeries. We would also not expect this to affect our results because the RCRI score has been validated and applied across different types of surgeries (23). Fourth, administrative claims data do not include uninsured patients and thus may not be reflective of the risk in patients with low socioeconomic status or those with limited health care status. Finally, for MACE, we could not include cardiac-specific mortality because this is not part of the Optum database. This may introduce bias that people with SLE may be dying from alternative causes (such as sepsis) that may be misclassified as MACE. Yet this is also a general limitation for most studies using claims to determine MACE in other populations.

Our study shows that SLE increases the risk of MACE after noncardiac surgery, likely because of increased comorbidities and CVD in patients with SLE. High-risk patients with SLE received less cardiac testing 2 months prior to surgery than the general population. Future studies should evaluate the impact of perioperative risk stratification and management on reducing MACE in patients with SLE.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Lei had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Bruera, Lei, Blau, Zhao, Deswal, Yazdany, Giordano, Suarez-Almazor.

Acquisition of data. Bruera, Lei, Blau, Suarez-Almazor.

Analysis and interpretation of data. Bruera, Lei, Blau, Deswal, Yazdany, Giordano, Suarez-Almazor.

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