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Research Article

Hepatic and Renal Outcomes in Systemic Lupus Erythematosus Patients following Coronary Artery Bypass Grafting: A Study from the National Inpatient Sample

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Background and Aim of the Study. While several studies have suggested a relationship between adverse postoperative outcomes and systemic lupus erythematosus (SLE) in major surgical settings, no study to date has explored postoperative outcomes of SLE patients undergoing coronary artery bypass grafting (CABG). This study aimed to compare the characteristics and outcomes of SLE patients compared to non-SLE patients undergoing CABG. *Methods.* We utilized the Nationwide Inpatient Sample (NIS) data from 2008–2018 for CABG patients ≥18 years old. Patients were divided into two groups based on SLE status (confirmed SLE diagnosis or no SLE present). Primary outcomes were in-hospital mortality, favorable discharge, and length of stay (LOS). Secondary outcomes included acute kidney injury (AKI), acute liver injury (ALI), hemodialysis, acute myocardial infarction (AMI), and cardiogenic shock. Patient characteristics including age, sex, race, and preexisting comorbidities were considered. Multivariable models, adjusting for confounding variables, were utilized. *Results.* Data from a total of 352,772 patients who underwent CABG were analyzed. 980 patients had a diagnosis code for SLE. SLE and non-SLE patients had similar rates of in-hospital mortality (OR = 0.92, [0.63–1.35]), nonhome discharge (OR = 1.09, [0.95–1.24]), and LOS (OR = 1.02, [0.99–1.06]). SLE patients developed AKI at a higher rate (OR = 1.50, [1.05–1.48]) and ALI at a lower rate (OR = 0.35, [0.16–0.74]). Both groups had similar rates of hemodialysis (OR = 1.19, [0.98–1.44]), AMI (OR = 0.93, [0.81–1.06]), and cardiogenic shock (OR = 0.8, [0.61–1.05]). *Conclusion.* These findings suggest that SLE patients undergoing CABG have similar mortality, discharge disposition, and LOS compared to non-SLE patients. However, SLE patients are at increased risk of AKI and decreased risk of ALI than non-SLE patients. These associations warrant further investigation to elucidate their physiologic basis.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder with heterogeneous presentation, having systemic effects on organ systems including the cardiovascular, nervous, and urogenital systems. SLE patients represent a small but significant minority in the United States with a prevalence of 72.8 cases per 100,000 person-years, [1] disproportionally affecting female patients of child-bearing age and patients of African, Hispanic, and Asian descent [2–4]. In the absence of complications, the ten-year survival rate of this patient population is approximately 82% [5]. However, the mortality rate increases with the development of cardiovascular disease, renal disease, and systemic infection [6]. SLE patients also experience additional life costs, including decreases in mental acuity, pharmaceutical costs,

and altered career trajectories due to painful symptoms [7]. The pathophysiology and etiology of SLE are complex and are triggered by many factors resulting in a variety of clinical presentations. Briefly, SLE is characterized by systemic inflammation and organ injury caused by B cell hyperactivity secondary to antigen stimulation and T cell activation in response to faulty apoptotic somatic cells [2]. The faulty apoptosis of somatic cells, caused by defects in phagocytes, causes intracellular receptors to be exposed to immune cells which falsely recognize them as threats [8]. This causes a proliferation of antibodies specific to the body's own cells, with the anti-DNA antinuclear antibodies (ANA) the most prominent among them [9]. It is the collection of these autoantibodies combined with the buildup of improperly phagocytosed cells that cause the widespread microvascular inflammation of SLE. The etiology of SLE is complex and involves a wide range of genetic and environmental factors. Multiple genetic loci have been identified as potential regions for genetic susceptibility for SLE, with the prevalence of each mutation varying by ethnicity [10–13]. Additionally, epigenetic factors, particularly DNA methylation, have been implicated in the onset and progression of SLE [14, 15]. Environmental factors implicated in SLE development include UV radiation, air pollution, alcohol, Epstein–Barr virus infection, and heavy metals, among others [16]. The different contributing factors involved in the progression of SLE make it a disease of many faces, causing varying clinical presentations ranging from skin and renal disease to significant cardiovascular dysfunction [17].

The prevalence of cardiovascular disease (CVD) in patients with SLE is significantly higher than that in the general population, with complications arising from widespread microvascular inflammation and blockages as well as atherosclerosis in late-stage disease [18, 19]. In the cardiovascular system, antibodies to lipoproteins and a systemic influx of inflammatory cytokines cause damage to endothelial linings and lead to inflammatory injury [20]. Common secondary cardiovascular complications of SLE include pericarditis, myocarditis, heart valve dysfunctions, and lupus aortitis, leading to myocardial infarction (MI), stroke, heart failure, and transient ischemic attack (TIA) [21–24]. The exact CVD prevalence in SLE patients is unknown. However, SLE patients demonstrate a twofold to tenfold higher risk of suffering MI and a twofold higher risk of suffering stroke when compared to the general population [25]. SLE patients, especially those with late-stage cardiovascular complications, often require invasive cardiac procedures including aortic and mitral valve repairs and replacements, heart transplantation, and coronary artery bypass grafting (CABG) [26–31]. However, the frequency and outcomes of these surgeries in SLE patients have not been studied. Existing data suggest that SLE patients with MI and both ischemic and hemorrhagic stroke are at a higher risk of in-hospital mortality [26]. In percutaneous coronary interventions, patients with SLE have similar initial intervention success but significantly poorer one-year outcomes and are at higher risk of MI at one-year post-intervention [32]. Additionally, it has been reported that SLE patients undergoing noncardiac surgery are at increased risk for perioperative and postoperative major adverse cardiac events, including MI and death, with these results disproportionately affecting patients under the age of fifty [33]. However, epidemiological data suggesting an association between SLE diagnosis and adverse outcomes following cardiac surgery remain scant. Specifically, no large-scale multicenter study has yet examined the relationship between SLE diagnosis and adverse outcomes after CABG procedures. We performed a retrospective cohort analysis of the nationwide inpatient sample (NIS) using data from January 2008–December 2018 to examine the relationship between SLE and outcomes following CABG procedures and to compare resource utilization between CABG patients with and without SLE.

2. Methods

The methods for this study were adapted from a similar study, Del Re et al., which was completed by this same research team [34]. The study carried out by Del Re et al.. looked at the effect of major depressive disorder on CABG outcomes whereas this study looks at the effect of SLE on CABG outcomes.

2.1. Data Source. We queried the national inpatient sample (NIS) from January 2008 to December 2018. The NIS, developed for the Healthcare Cost and Utilization Project (HCUP), is the largest publicly available database of inpatient admissions in the United States containing 7 million yearly admissions representing a 20% sample of all inpatient admissions in the United States [35]. The present study was deemed exempt from IRB review (IRB# 1753188-6).

2.2. Study Population. We conducted a retrospective study of patients older than eighteen years of age who underwent CABG. Exclusion criteria were patients with a diagnosis of primary antiphospholipid syndrome or other connective tissue disorders. CABG and systemic lupus erythematosus (SLE) diagnoses were ascertained through the International Classification of Diseases ninth revision (ICD-9) and tenth revision (ICD-10) codes (ICD codes listed in Supplementary Table 1). Patients diagnosed with SLE were compared to those without the diagnosis. Patient characteristics including age, sex, race, median household income quartile, comorbidities (hypertension, diabetes mellitus, heart failure, prior coronary artery disease, prior myocardial infarction, prior CABG; complete list found in Supplementary Table 1), weekend admission, hospital location/teaching status, and hospital bed size (small, medium, and large) were collected and included in the model.

2.3. Variables and Outcomes. Our primary outcomes were in-hospital mortality, favorable discharge, and LOS. Secondary outcomes were the following inpatient complications: acute myocardial infarction, acute kidney injury, cardiogenic shock, infection, transient ischemic attack/stroke, acute liver injury, acute limb ischemia, and

hemodialysis. These complications were identified using ICD-9 and ICD-10 diagnostic codes as listed in Supplementary Table 1.

2.4. Statistical Analysis. All analyses were performed using Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC. The *svy* command was used to apply weights and make national estimates using the methodology outlined by HCUP [33]. Multivariable logistic regression models were used for binary outcomes. Careful attention was placed to adjust for confounding variables, avoid collinear variables, and avoid overfitting in each model. Model covariates were chosen a priori in order to avoid bias. We adjusted all models for age, smoking, anxiety, dyslipidemia, obesity, heart failure, hypertension, prior coronary artery disease, prior mesenteric ischemia, prior percutaneous coronary intervention, prior CABG, prior TIA/stroke, atrial fibrillation, peripheral artery disease, anemia, chronic pulmonary diseases, liver disease, coagulopathy, fluid and electrolyte disorders, and cancer. We adjusted the control group to match the experimental group to eliminate demographic differences using propensity matching. We conducted gamma regression with a log-link function for LOS given the right-skewed distribution nature of this variable. We reported adjusted odds ratios (ORs) and 95% confidence limits for binary outcomes and β-coefficients for LOS. β-coefficient denotes a percent change in the outcome (ex.-coefficient = 1.09 indicates a 9% increase). An alpha level of significance (p) was set as priori at 0.05.

3. Results

3.1. Population Characteristics. A total of 354,852 patients underwent CABG, of which 1,100 patients were excluded due to comorbid primary antiphospholipid syndrome (APS) or other connective tissue diseases. Among the remaining CABG patients, 0.27% ($n = 880$, mean age = 62.2 years) had a diagnostic code for SLE while 99.73% ($n = 322{,}226$, mean age = 66.08 years) did not have any SLE-related diagnostic codes. Among the CABG patients with a diagnosis of SLE, 74.0% were women, 16.9% were Black, and 16.7% had a median household income in the bottom 25th percentile nationally (compared to 26.0% women, 6.4% Black, and 19.3% in the 25th percentile of national income in CABG patients without SLE). Patient demographics are listed in Table 1.

3.2. Primary Outcomes. CABG patients with a comorbid SLE diagnosis had statistically similar odds of in-hospital mortality when compared to non-SLE CABG patients (OR = 0.92, $p = 0.671$). Among the surviving CABG patients, no significant differences were found in nonhome discharge (OR = 1.06, $p = 0.395$) or length of hospital stay ($p = 0.130$) (Table 2).

3.3. Secondary Outcomes. CABG patients with a comorbid SLE diagnosis had significantly increased odds of postoperative acute kidney injury (OR = 1.27, $p = 0.009$) and significantly decreased odds of acute liver injury (OR = 0.36, $p = 0.012$) when compared to CABG patients without an SLE diagnosis. No significant difference was found in hemodialysis (OR = 1.16, $p = 0.166$), AMI (OR = 0.94, $p = 0.413$), cardiogenic shock (OR = 0.76, $p = 0.072$), PCI (OR = 0.83, $p = 0.378$), transient ischemic attack (TIA)/stroke (OR = 0.98, $p = 0.903$), infections (OR = 1.02, $p = 0.931$), acute limb ischemia (OR = 0.75, $p = 0.713$), or mechanical circulatory support (OR = 0.91, $p = 0.408$) (Table 3).

4. Discussion

This study utilizing the NIS database is the first to our knowledge to investigate the relationship between the preoperative diagnosis of SLE and inpatient outcomes following CABG. The results of our investigation reveal that CABG patients with a preoperative diagnosis of SLE are at 27% increased odds of postoperative acute kidney injury when compared to CABG patients without an SLE diagnosis. It is well-understood that kidney disease is an inherent risk for patients with SLE. The most common renal complication of SLE continues to be lupus nephritis (LN), a condition defined by the SLE autoimmune response targeted towards renal cells, causing considerable kidney inflammation and damage [36, 37]. LN is widespread in SLE patients, affecting up to fifty percent of patients [37]. Wong and Goral report that up to thirty percent of all SLE patients will progress to end-stage kidney disease (ESKD) while Parikh et al. report a five-year mortality rate of up to twenty-five percent for patients with proliferative LN and ESKD secondary to SLE [38, 39]. Present studies exploring a variety of patient databases in the United States and internationally have demonstrated that SLE-related renal damage contributes to adverse postoperative outcomes in kidney transplantations, Caesarian sections, vascular surgery, and other minimally invasive and invasive procedures [40–43]. It is, therefore, not surprising that postoperative outcomes for individuals with SLE undergoing cardiac surgery such as CABG are affected by their renal health. Other studies examining noncardiac surgery postoperative outcomes for SLE patients seem to corroborate our results. In a study of 4,321 Taiwanese SLE patients undergoing invasive surgery, Bartoszko and Karkouti found that patients who had received SLE-related clinical care within six months of their procedure had 7.23 times greater odds of postoperative renal failure within 30 days than patients who had not received the same care [44]. While Lin's study does not clarify which procedures are undertaken, the effects of SLE on postoperative adverse renal outcomes are clear.

One potential explanation for our results is the use of cardiopulmonary bypass (CPB) during CABG procedures. While substantial advances have been made in the field of tissue perfusion during surgery, adverse outcomes including coagulopathy, hypoperfusion, and widespread inflammation continue to be major concerns for patients on CPB [45]. These complications, in turn, are known to adversely affect the kidneys; systemic inflammatory responses caused by the patient's blood entering the foreign environment of the

Table 1: Patient demographics among systemic lupus erythematosus (SLE) using patients undergoing CABG in the national inpatient sample (NIS 2008–2018).

Characteristic	SLE patients $n = 880$ % (n)	Non-SLE patients $n = 322{,}226$ % (n)	p value for difference*	95% CI*	% bias*
Age (years ± SD)	62.20 ± 8.47	66.08 ± 8.89			
Gender					
Male	26.0 (229)	74.0 (238,522)	<0.001	[0.64–0.74]	0.0
Female	74.0 (651)	26.0 (83,685)			
Race					
White	64.3 (566)	73.4 (236,598)	0.604	[−0.06–0.10]	0.0
African American	16.9 (149)	6.4 (20,670)	<0.001	[0.30–0.49]	0.0
Income					
1st quartile	29.7 (261)	27.5 (88,702)	0.148		
2nd quartile	28.3 (249)	27.0 (87,042)			
3rd quartile	23.3 (205)	24.1 (77,568)			
4th quartile	16.7 (147)	19.3 (62,319)			
Comorbidities					
Smoking status	39.2 (345)	44.6 (143,570)	0.045	[−0.10–−0.001]	0.0
Anxiety disorders	15.5 (136)	9.5 (30,634)	0.045	[0.002–0.13]	0.0
Dyslipidemia	61.3 (539)	75.6 (243,743)	<0.001	[−0.21–−0.11]	0.0
Hypertension	66.6 (586)	69.7 (224,436)	0.029	[−0.10–−0.01]	0.0
Obesity	24.0 (211)	23.9 (76,958)	<0.001	[−0.16–−0.06]	0.0
Diabetes mellitus	35.6 (313)	44.2 (142,562)	<0.001	[−0.26–−0.16]	0.0
Prior CAD	17.7 (156)	17.5 (56,537)	0.572	[−0.04–0.08]	0.0
Prior MI	19.0 (167)	15.5 (50,096)	0.001	[0.03–0.16]	0.0
Prior CABG	1.4 (12)	1.9 (6,064)	0.314	[−0.29–0.09]	0.0
Prior PCI	10.7 (94)	10.1 (32,561)	0.571	[−0.05–0.10]	0.0
Peripheral artery disease	14.4 (127)	12.7 (41,055)	0.072	[−0.01–0.12]	0.0
Prior TIA/stroke	11.5 (101)	7.4 (23,900)	<0.001	[0.06–0.21]	0.0
Atrial fibrillation/flutter	22.5 (198)	27.7 (89,211)	0.763	[−0.05–0.06]	0.0
Anemia	20.0 (176)	13.7 (44,282)	0.001	[0.04–0.16]	0.0
Chronic pulmonary diseases	41.9 (369)	30.6 (98,549)	<0.001	[0.08–0.18]	0.0
Liver disease	4.5 (40)	2.2 (7,130)	<0.001	[0.12–0.36]	0.0
Coagulopathy	25.8 (227)	20.8 (66,983)	<0.001	[0.08–0.18]	0.0
Fluid and electrolyte disorders	40.3 (355)	32.1 (103,328)	<0.001	[0.04–0.14]	0.0
Pulmonary circulation disorders	9.5 (84)	5.9 (19,088)	0.001	[0.06–0.22]	0.0
Cancer	0.80 (7)	1.1 (3,465)	0.911	[−0.23–0.26]	0.0

Table 2: Length of stay and disposition for systemic lupus erythematosus (SLE) patients compared to non-SLE patients after coronary artery bypass grafting (CABG) surgery.

Resource	SLE patients $n = 880$ Mean (median)	Non-SLE patients $n = 322{,}226$ Mean (median)	95% CI	p value
Length of stay (days)	11.1 (9)	9.8 (8)	0.99–1.07	0.130
Disposition		Odds ratio		
Nonhome care facility		1.06	0.92–1.22	0.395

perfusion pump cause inflammation and microemboli formation in the kidneys [46]. The most immediate consequences are vasoconstriction and renal ischemia, resulting in a decreased glomerular filtration rate [47]. In practice, this can lead to decreased or disrupted kidney function, presenting as acute kidney injury (AKI) and less commonly ESKD requiring the use of dialysis (e.g., patients without SLE) [48]. In patients with SLE, whose kidneys may already be compromised through the widespread inflammatory effects of SLE and LN, the potential for renal complications increases further. Our findings regarding the increased association of postoperative acute kidney disease corroborate the relationship between SLE and kidney disease. There appeared to be a trend towards increased risk of postoperative hemodialysis in patients with SLE, though this did not reach statistical significance.

Our study also revealed that CABG patients with a preoperative diagnosis of SLE are at 64% decreased odds of postoperative acute liver injury. There has been significantly less research performed on the pathophysiology of hepatic conditions in patients with SLE. While the liver is not traditionally noted as an organ of interest in the progression of SLE, several cohort and case studies have made light of the potential for hepatic complications in SLE patients. Takahashi et al. demonstrated in a study of 206 Japanese patients with SLE that liver dysfunction of varying degrees was

Table 3: Outcomes for systemic lupus erythematosus (SLE) patients compared to non-SLE patients after coronary artery bypass grafting (CABG) surgery.

Outcome	SLE patients $n = 880$ % (n)	Non-SLE patients $n = 322{,}226$ % (n)	OR (95% CI)	p value
Death	3.3 (29)	2.4 (7,787)	0.92 (0.63–1.35)	0.671
Acute kidney injury	20.9 (184)	16.9 (54,543)	1.27 (1.06–1.53)	**0.009**
Acute myocardial infarction	46.5 (409)	44.5 (143,476)	0.94 (0.82–1.09)	0.413
Transient ischemic attack/stroke	5.9 (52)	5.6 (17,925)	0.98 (0.74–1.31)	0.903
Percutaneous coronary intervention	2.7 (24)	2.9 (9,205)	0.83 (0.55–1.25)	0.378
Mechanical circulatory support	10.8 (95)	9.6 (30,908)	0.91 (0.73–1.14)	0.408
Hemodialysis	16.9 (149)	12.6 (40,662)	1.16 (0.94–1.44)	0.166
Infections (defined as septicemia/septic shock, postoperative infection, central venous catheter-related infection, transfusion-related infection, or cardiac device-related infection)	4.0 (35)	2.8 (9,024)	1.02 (0.71–1.45)	0.931
Cardiogenic shock	6.3 (55)	5.9 (19,121)	0.76 (0.57–1.02)	0.072
Acute liver injury	0.91 (8)	1.3 (4,110)	0.36 (0.16–0.80)	**0.012**
Acute limb ischemia	0.34 (3)	0.27 (886)	0.75 (0.17–3.38)	0.713

OR: odds ratio, CI: confidence interval. The bold values indicate that $p < 0.05$.

evident in 123 patients, or 59.7% of patients overall [49]. While this number is considerable, Takahashi points out that of the patients with liver dysfunction, it was more likely that the dysfunction was drug-induced (30.9%) than a manifestation of SLE (28.5%). A study by Kübel et al. on 172 SLE patients, additionally, found elevated liver enzymes that are indicative of liver injury in 63.4% of the population, with abnormal liver ultrasound findings in 19.8% [50]. The study fails to provide a causative agent for the observed hepatic abnormalities, however, focusing instead on potential steps for healthcare providers to track changes in hepatic function for SLE patients. Hepatic prognosis in SLE patients, meanwhile, is largely positive; a study by Chowdary et al. revealed that in a cohort of forty patients with SLE, 93% of patients did not have any hepatic disease onset five-year postdiagnosis [51]. Collectively, hepatic pathology in SLE patients is largely nonspecific, with the prevalence of hepatic complications largely attributable to nonimmunologic causes such as hepatotoxic drugs, alcohol use, or preexisting hepatic conditions. Our finding of decreased acute liver injury in SLE patients after CABG is difficult to explain based on the existing literature and therefore warrants further investigation.

One demographic feature of note in our cohort is the increased percentage of SLE patients undergoing CABG who were women (74.0%) and Black (16.9%) when compared to non-SLE patients undergoing CABG (26.0% women and 6.4% Black). These findings are in line with statistics reported by Maidhof et al. that demonstrated Asian, Afro-Caribbean, Afro-American, and Hispanic backgrounds, as well as women of child-bearing age, were more likely to develop SLE [2]. The demographics of our cohort allow us to, in part, retroactively validate that our selected population is characteristic of the SLE patient population at large.

Our study contains a few noteworthy limitations. First, the NIS allows us to investigate trends but does not allow us to investigate detailed clinical variables such as imaging, laboratory test results, and medication use. Moreover, this study relied heavily on the ICD-9 and ICD-10 coding standards to develop our SLE and non-SLE populations, which makes the results of this study prone to medical coding errors by healthcare professionals as patients were entered into the NIS database. Lastly, our study lacked a balanced sample size for the cohort of CABG patients with SLE, with 880 SLE patients versus 322,226 non-SLE patients in the cohort of CABG patients without SLE. This is a function of the rarity of SLE in the general American population, but it is noteworthy nonetheless for the imbalance of sample sizes.

5. Conclusion

Our study demonstrates that patients with a preoperative diagnosis of SLE had a higher association with postoperative acute kidney injury and a lower association with acute liver injury following CABG. In line with other studies investigating the involvement of the kidneys in SLE, our results may reflect the prevalence of renal complications present in SLE patients. Our results also encourage further investigation into the causes of positive hepatic outcomes and mitigating factors for negative renal outcomes in SLE patients undergoing CABG.

Data Availability

The data used to support the findings of this study are obtained from the National Inpatient Registry, which was developed for the Healthcare Cost and Utilization Project (HCUP).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Supplementary Materials

Tables include ICD-9 and ICD-10 Procedure and Diagnosis Codes. (*Supplementary Materials*)

References

[1] P. M. Izmirly, H. Parton, L. Wang et al., "Prevalence of systemic lupus erythematosus in the United States: estimates from a meta-analysis of the centers for disease control and prevention national lupus registries," *Arthritis & Rheumatology*, vol. 73, no. 6, pp. 991–996, 2021.

[2] W. Maidhof and O. Hilas, "Lupus: an overview of the disease and management options," *Pharmacy and Therapeutics*, vol. 37, no. 4, pp. 240–249, 2012.

[3] A. Gcelu, "Rheumatic diseases and pregnancy," *South African Medical Journal*, vol. 104, no. 9, p. 643, 2014.

[4] G. Stojan and M. Petri, "Epidemiology of systemic lupus erythematosus: an update," *Current Opinion in Rheumatology*, vol. 30, no. 2, pp. 144–150, 2018.

[5] C. Gordon, "Long-term complications of systemic lupus erythematosus," *Rheumatology*, vol. 41, no. 10, pp. 1095–1100, 2002.

[6] Y. H. Lee, S. J. Choi, J. D. Ji, and G. G. Song, "Overall and cause-specific mortality in systemic lupus erythematosus: an updated meta-analysis," *Lupus*, vol. 25, no. 7, pp. 727–734, 2016.

[7] J. Dixon, F. S. Cardwell, A. E. Clarke, and S. J. Elliott, "Choices are inevitable: a qualitative exploration of the lifecosts of systemic lupus erythematosus," *Chronic Illness*, vol. 18, no. 1, pp. 125–139, 2022.

[8] L. E. Munoz, U. S. Gaipl, S. Franz et al., "SLE--a disease of clearance deficiency?" *Rheumatology*, vol. 44, no. 9, pp. 1101–1107, 2005.

[9] A. Rahman, "Autoantibodies, lupus and the science of sabotage," *Rheumatology*, vol. 43, no. 11, pp. 1326–1336, 2004.

[10] J. A. Kelly, K. L. Moser, and J. B. Harley, "The genetics of systemic lupus erythematosus: putting the pieces together," *Genes and Immunity*, vol. 3, no. S1, pp. S71–S85, 2002.

[11] T. M. Järvinen, A. Hellquist, M. Zucchelli et al., "Replication of GWAS-identified systemic lupus erythematosus susceptibility genes affirms B-cell receptor pathway signalling and strengthens the role of IRF5 in disease susceptibility in

a Northern European population," *Rheumatology*, vol. 51, no. 1, pp. 87–92, 2012.

[12] A. L. Sestak, B. G. Fürnrohr, J. B. Harley, J. T. Merrill, and B. Namjou, "The genetics of systemic lupus erythematosus and implications for targeted therapy," *Annals of the Rheumatic Diseases*, vol. 70, no. 1, pp. i37–i43, 2011.

[13] J. B. Harley, M. E. Alarcón-Riquelme, L. A. Criswell et al., "Genome-wide association scan in women with systemic lupus erythematosus identifies susceptibility variants in ITGAM, PXK, KIAA1542 and other loci," *Nature Genetics*, vol. 40, no. 2, pp. 204–210, 2008.

[14] B. M. Javierre, A. F. Fernandez, J. Richter et al., "Changes in the pattern of DNA methylation associate with twin discordance in systemic lupus erythematosus," *Genome Research*, vol. 20, no. 2, pp. 170–179, 2010.

[15] C. M. Lanata, S. A. Chung, and L. A. Criswell, "DNA methylation 101: what is important to know about DNA methylation and its role in SLE risk and disease heterogeneity," *Lupus Science & MedicineLupus Science & Medicine*, vol. 5, no. 1, Article ID e000285, 2018.

[16] G. Gulati and H. I. Brunner, "Environmental triggers in systemic lupus erythematosus," *Seminars in Arthritis and Rheumatism*, vol. 47, no. 5, pp. 710–717, 2018.

[17] G. Murphy and D. Isenberg, "Effect of gender on clinical presentation in systemic lupus erythematosus," *Rheumatology*, vol. 52, no. 12, pp. 2108–2115, 2013.

[18] D. P. Symmons and S. E. Gabriel, "Epidemiology of CVD in rheumatic disease, with a focus on RA and SLE," *Nature Reviews Rheumatology*, vol. 7, no. 7, pp. 399–408, 2011.

[19] J. Frostegård, "Systemic lupus erythematosus and cardiovascular disease," *Lupus*, vol. 17, no. 5, pp. 364–367, 2008.

[20] M. B. Urowitz, D. Gladman, D. Ibañez et al., "Atherosclerotic vascular events in a multinational inception cohort of systemic lupus erythematosus," *Arthritis Care & Research*, vol. 62, no. 6, pp. 881–887, 2010.

[21] R. Alghareeb, A. Hussain, M. V. Maheshwari, N. Khalid, and P. D. Patel, "Cardiovascular complications in systemic lupus erythematosus," *Cureus*, vol. 14, no. 7, Article ID e26671, 2022.

[22] A. Torres, A. D. Askari, and C. J. Malemud, "Cardiovascular disease complications in systemic lupus erythematosus," *Biomarkers in Medicine*, vol. 3, no. 3, pp. 239–252, 2009.

[23] M. Akiyama, Y. Kaneko, and T. Takeuchi, "Lupus aortitis: a fatal, inflammatory cardiovascular complication in systemic lupus erythematosus," *Lupus*, vol. 29, no. 12, pp. 1652–1654, 2020.

[24] A. Joshi, J. Lerman, T. Aberra et al., "Increased clinical and financial burden of heart failure hospitalizations in patients with rheumatoid arthritis: insights from the national inpatient sample," *Journal of the American College of Cardiology*, vol. 71, no. 11, p. A903, 2018.

[25] S. R. Schoenfeld, S. Kasturi, and K. H. Costenbader, "The epidemiology of atherosclerotic cardiovascular disease among patients with SLE: a systematic review," *Seminars in Arthritis and Rheumatism*, vol. 43, no. 1, pp. 77–95, 2013.

[26] C. H. Lin, M. L. Lee, and R. B. Hsu, "Cardiac surgery in patients with systemic lupus erythematosus," *Interactive Cardiovascular and Thoracic Surgery*, vol. 4, no. 6, pp. 618–621, 2005.

[27] H. Dajee, E. J. Hurley, and R. J. Szarnicki, "Cardiac valve replacement in systemic lupus erythematosus," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 85, no. 5, pp. 718–726, 1983.

[28] J. Tejeda-Maldonado, L. Quintanilla-González, J. Galindo-Uribe, and A. Hinojosa-Azaola, "Cardiac surgery in systemic lupus erythematosus patients: clinical characteristics and outcomes," *Reumatología Clínica*, vol. 14, no. 5, pp. 269–277, 2018.

[29] N. Bozbuğa, V. Erentuğ, E. Kaya, E. Akinci, and C. Yakut, "Coronary artery bypass grafting in patients with systemic lupus erythematosus," *Journal of Cardiac Surgery*, vol. 19, no. 5, pp. 471-472, 2004.

[30] M. Ura, R. Sakata, Y. Nakayama, Y. Ohtsuka, and T. Saito, "Coronary artery bypass grafting in patients with systemic lupus erythematosus," *European Journal of Cardio-Thoracic Surgery*, vol. 15, no. 5, pp. 697–701, 1999.

[31] K. Maksimowicz-McKinnon, F. Selzer, S. Manzi et al., "Poor 1-year outcomes after percutaneous coronary interventions in systemic lupus erythematosus: report from the National Heart, Lung, and Blood Institute Dynamic Registry," *Circulation: Cardiovascular Interventions*, vol. 1, no. 3, pp. 201–208, 2008.

[32] A. Ehsan, A. Del Re, K. Rivera Perla, G. Aghagoli, K. Bellam, and F. Sellke, "Trends and outcomes of coronary artery bypass grafting in patients with major depressive disorder: a perspective from the national inpatient sample," *Heart Mind*, vol. 6, no. 2, pp. 62–69, 2022.

[33] N. R. Smilowitz, G. Katz, J. P. Buyon, R. M. Clancy, and J. S. Berger, "Systemic lupus erythematosus and the risk of perioperative major adverse cardiovascular events," *Journal of Thrombosis and Thrombolysis*, vol. 45, no. 1, pp. 13–17, 2018.

[34] Hcup Databases, *Healthcare Cost and Utilization Project (HCUP)*, Agency for Healthcare Research and Quality, Rockville, MD, USA, 2021.

[35] L. Oni, R. D. Wright, S. Marks, M. W. Beresford, and K. Tullus, "Kidney outcomes for children with lupus nephritis," *Pediatric Nephrology*, vol. 36, no. 6, pp. 1377–1385, 2021.

[36] N. I. Maria and A. Davidson, "Protecting the kidney in systemic lupus erythematosus: from diagnosis to therapy," *Nature Reviews Rheumatology*, vol. 16, no. 5, pp. 255–267, 2020.

[37] S. V. Parikh, S. Almaani, S. Brodsky, and B. H. Rovin, "Update on lupus nephritis: core curriculum 2020," *American Journal of Kidney Diseases*, vol. 76, no. 2, pp. 265–281, 2020.

[38] T. Wong and S. Goral, "Lupus nephritis and kidney transplantation: where are we today?" *Advances in Chronic Kidney Disease*, vol. 26, no. 5, pp. 313–322, 2019.

[39] L. Quintanilla-González, G. Torres-Villalobos, and A. Hinojosa-Azaola, "Risk factors for development of early infectious and noninfectious complications in systemic lupus erythematosus patients undergoing major surgery," *Lupus*, vol. 27, no. 12, pp. 1960–1972, 2018.

[40] J. C. Ramirez-Sandoval, H. Chavez-Chavez, M. Wagner, O. Vega-Vega, L. E. Morales-Buenrostro, and R. Correa-Rotter, "Long-term survival of kidney grafts in lupus nephritis: a Mexican cohort," *Lupus*, vol. 27, no. 8, pp. 1303–1311, 2018.

[41] S. R. Ke, C. W. Liu, Y. W. Wu et al., "Systemic lupus erythematosus is associated with poor outcome after acute myocardial infarction," *Nutrition, Metabolism, and Cardiovascular Diseases*, vol. 29, no. 12, pp. 1400–1407, 2019.

[42] J. M. López-Morales, L. Quintanilla-González, J. C. Ramírez-Sandoval, and A. Hinojosa-Azaola, "Early outcomes in kidney transplant recipients with systemic lupus erythematosus," *Rheumatology International*, vol. 39, no. 3, pp. 479–487, 2019.

[43] J. A. Lin, C. C. Liao, Y. J. Lee, C. H. Wu, W. Q. Huang, and T. L. Chen, "Adverse outcomes after major surgery in patients with systemic lupus erythematosus: a nationwide population-based study," *Annals of the Rheumatic Diseases*, vol. 73, no. 9, pp. 1646–1651, 2014.

[44] J. Bartoszko and K. Karkouti, "Managing the coagulopathy associated with cardiopulmonary bypass," *Journal of Thrombosis and Haemostasis*, vol. 19, no. 3, pp. 617–632, 2021.

[45] M. Vives, A. Hernandez, F. Parramon et al., "Acute kidney injury after cardiac surgery: prevalence, impact and management challenges," *International Journal of Nephrology and Renovascular Disease*, vol. 12, pp. 153–166, 2019.

[46] T. Bove, F. Monaco, R. D. Covello, and A. Zangrillo, "Acute renal failure and cardiac surgery," *HSR Proceedings in Intensive Care and Cardiovascular Anesthesia*, vol. 1, no. 3, pp. 13–21, 2009.

[47] J. J. Chen, C. H. Chang, V. C. Wu et al., "Long-Term outcomes of acute kidney injury after different types of cardiac surgeries: a population-based study," *Journal of the American Heart Association*, vol. 10, no. 9, Article ID e019718, 2021.

[48] A. Takahashi, K. Abe, R. Saito et al., "Liver dysfunction in patients with systemic lupus erythematosus," *Internal Medicine*, vol. 52, no. 13, pp. 1461–1465, 2013.

[49] D. Kübel, M. Tiller, T. Mühling et al., "Hepatopathie bei systemischem Lupus erythematodes–Ergebnisse einer explorativen Beobachtungsstudie [Liver disease in systemic Lupus erythematodes-results of an explorative observational study]," *Zeitschrift für Gastroenterologie*, vol. 56, no. 10, pp. 1257–1266, 2018.

[50] V. R. Chowdhary, C. S. Crowson, J. J. Poterucha, and K. G. Moder, "Liver involvement in systemic lupus erythematosus: case review of 40 patients," *Journal of Rheumatology*, vol. 35, no. 11, pp. 2159–2164, 2008.

[51] S. Patel, M. Demory Beckler, and M. M. Kesselman, "Lupus and the liver: a case study," *Cureus*, vol. 11, no. 8, Article ID e5477, 2019.