

Perioperative Surgical Recommendations in Patients with Lupus

Donovan Diego Ruiz Baltazar¹, Mariana García Morales², Julie Rosario Guadalupe Barruquin³, Jocelyn Anaid Landeros Fraire⁴, Francisco Javier Delgado Dávalos⁵, Sergio González Ramírez⁶, José Raúl Rodríguez Amparán⁷, Ernesto Fernando Montelongo Sedano⁸, José Manuel Villafuerte Hernández⁹, Ana Denisse Aboytes Bucio⁵, Carlos Mario González García¹⁰, Doryan Monroy Cordoba¹¹

¹Universidad Tominaga Nakamoto

²Universidad Autónoma del Estado de México

³Universidad de Guadalajara

⁴Universidad Autónoma de Zacatecas “Francisco García Salinas”, Zacatecas, México. ORCID: 0009-0008-4288-2095

⁵Universidad Autónoma de Guadalajara

⁶Universidad Juárez del Estado de Durango

⁷Universidad Autónoma de Chihuahua

⁸Universidad Autónoma de Aguascalientes ORCID: 0009-0002-1539-1262

⁹Universidad Michoacana de San Nicolás de Hidalgo

¹⁰Clínica Hospital ISSSTE Tuxtepec

¹¹Hospital Materno San Luis de La Paz

ABSTRACT

Systemic lupus erythematosus (SLE) is a long-lasting autoimmune condition that affects the connective tissues and has a varied and diverse range of symptoms. The severity of the disease varies greatly, with the majority experiencing less severe versions. However, it may be life-threatening depending on the extent of organ involvement. The ailment was identified as early as the Middle Ages, with the 12th-century physician Rogerius being the first to use the name lupus to describe the characteristic malar rash. In 1872, Moric Kaposi was the first to acknowledge the systemic aspect of the disease. During the perioperative period, systemic lupus erythematosus (SLE) may provide significant difficulties for the anesthesiologist due to the presence of accumulated organ damage, coagulation abnormalities, and intricate care protocols. This article focuses on the signs and therapies of adult systemic lupus erythematosus (SLE) that are relevant to anesthesiologists. It also discusses the perioperative care of these patients, who present unique challenges due to the complexity of their condition.

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INTRODUCTION

The incidence of systemic lupus erythematosus (SLE) varies from 7.4 to 159.4 cases per 100,000 individuals in the population. The greatest rates are seen among Afro-Caribbean individuals residing in the United Kingdom, as well as non-White groups in other regions. The reported ratio of females to males is 9:1, with the highest occurrence of symptoms seen between the ages of 15 and 40. However, instances may occur at any age, from infancy to old age, with a female-to-male

ratio of roughly 2:1 in advanced age. Individuals of the male gender and those who get the condition at a later stage in life often have more severe symptoms and have a less favorable outlook for recovery. The involvement of genetic variables in the development of lupus is indicated by a concordance rate of 24%–60% among monozygotic twins and 2%–5% among dizygotic twins.

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Table 1. Diagnostic Guidelines for Systemic Lupus Erythematosus

Criterion	Definition
Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
Arthritis	Nonerosive arthritis involving 2 or more peripheral joints, characterized by tenderness, swelling, or effusion
Serositis	(a) Pleuritis or (b) Pericarditis
Renal disorder	(a) Persistent proteinuria or (b) Cellular casts
Neurologic disorder	(a) Seizures or (b) Psychosis
Hematologic disorder	(a) Hemolytic anemia or (b) Leukopenia or (c) Lymphopenia or (d) Thrombocytopenia
Immunologic disorder	(a) Anti-dsDNA antibody or (b) Anti-Sm antibody or (c) Positive finding of antiphospholipid antibodies with either (i) abnormal serum IgG or IgM anti-cardiolipin antibody levels or (ii) positivity for lupus anticoagulant or (iii) false positive serological testing for syphilis
Antinuclear antibody	Abnormal ANA titer

Adapted from Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, Schaller JG, Talal N, Winchester RJ. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982;25:1271-7.

Pharmacotherapy refers to the use of medications to treat medical conditions.

The primary approach to treating SLE is addressing the symptoms with the use of NSAIDs, antimalarials, or aspirin. Additionally, immunosuppressive medications are used to attain a state of disease remission. Immunosuppression regimens vary depending on the affected organ, but often include the administration of corticosteroids, cyclophosphamide, azathioprine, methotrexate, and mycophenolate mofetil. These medicines may be used individually or in combination. Additional pharmacological agents are used to treat end-organ damage, such as in the cases of pulmonary hypertension, dyslipidemia, or accelerated coronary artery disease (CAD).

It is crucial to comprehend the toxicity profiles of these medications and their impact on perioperative treatment (Table 3). Determining whether symptoms are due to SLE activity or medication toxicity is challenging. However, making this distinction, along with consulting the patient's rheumatologist, enables more effective therapy options.

Cardiotoxicity is a known consequence of high-dose cyclophosphamide treatment. It may cause immediate decompensation and reversible decreases in systolic function. Although uncommon, similar instances have also been seen with hydroxychloroquine. Cardiac dysfunction associated with hydroxychloroquine may be caused by myotoxicity, which is consistent with a wider neuromyotoxicity seen in case studies. These reports indicate that the main finding is a proximal myopathy, with or without peripheral neuropathy or cardiomyopathy.

Azathioprine and methotrexate may both cause liver damage, leading to abnormal liver function tests (LFTs). Methotrexate, in particular, has a higher likelihood of causing severe liver fibrosis and cirrhosis. Methotrexate-induced pulmonary toxicity has been seen, often presenting as drug-induced pneumonitis accompanied by lung infiltrates. Mycophenolate mofetil is a newer medicine that is being used more often to treat lupus nephritis. It is an immunosuppressant that selectively targets lymphocytes and works by inhibiting purine production. Compared to prior medications, it has a

positive toxicity profile. However, like most other therapy agents, it might potentially produce medically significant myelosuppression.

Glucocorticoids are known to have extensively established negative consequences. Patients who have had long-term glucocorticoid medication should be carefully evaluated for potential hypothalamic-pituitary-adrenal axis suppression. Discontinuing glucocorticoids suddenly or experiencing the stress reaction after surgery might trigger an Addisonian crisis in these individuals. In addition, glucocorticoids induce hyperglycemia, hypercholesterolemia, osteoporosis, and hypertension.

Surveillance

In clinical practice, the monitoring of SLE involves distinguishing between disease activity and the accumulation of organ damage. Several disease activity indices have been developed, such as the SLEDAI (Systemic Lupus Erythematosus Disease Activity Index), SLAM (Systemic Lupus Activity Measure), BILAG (British Isles Lupus Assessment Group), and ECLAM (European Community Lupus Activity Measure). The BILAG index offers a comprehensive assessment of activity by including 8 organ systems, while the other indices give a broader evaluation of overall activity. Evaluation is determined by the patient's answers to comprehensive questionnaires and the findings of standard laboratory tests. The SLICC/ACR damage index measures the total damage that has occurred in 12 different organs or systems in the body. Inclusion requires the presence of changes for a minimum of 6 months.

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Table 2. Estimated Lifetime Prevalence of Major Systemic Lupus Erythematosus Manifestations

Condition	Estimated prevalence
Dermatologic	
Malar rash	50%
Chronic discoid lesions	25%
Neurologic	
Seizures	7%–20%
Cardiovascular	
Symptomatic pericarditis	25%
Pericardial tamponade	<2%
Myocarditis	5%–10%
Libman–Sacks endocarditis	10%
Valvular dysfunction	3%–4%
Raynaud's phenomenon	30%–40%
Pulmonary	
Pleuritis	35%
Pneumonitis	1%–10%
Diffuse alveolar hemorrhage	1%–5%
Pulmonary arterial hypertension	0.5%–14%
Renal	
Lupus nephritis	60%
End-stage renal disease	3%–12%
Hematology	
Anemia of chronic disease	40%
Autoimmune hemolytic anemia	5%–10%
Autoimmune thrombocytopenia	10%
Gastrointestinal	
Oral ulcers	7%–52%
Sjogren's syndrome	10%
Dysphagia	1%–13%
Acute abdominal pain	40%
Abnormal liver function tests	Up to 60%
Autoimmune hepatitis	2%–5%
Musculoskeletal	
Arthritis	15%–50%
Osteoporosis	23%
Fractures	12.5%
Asymptomatic atlantoaxial subluxation	8.5%

Table 3. Systemic Lupus Erythematosus (SLE) Pharmacotherapy and Significant Side Effects

Drug	Indication	Anesthetic implications
Anti-malarials (hydroxychloroquine)	Cutaneous SLE Pleuritis/pericarditis Arthritis	Retinotoxicity Neurotoxicity Cardiotoxicity
Corticosteroids (prednisone, methylprednisone, topical preparations)	Reduced renal flares Cutaneous SLE	Hyperglycemia
	Arthritis Nephritis Pleuritis/pericarditis Diffuse alveolar hemorrhage NPSLE Mesenteric vasculitis SLE pancreatitis	Hypercholesterolemia Hypertension Osteoporosis
Aspirin/NSAIDs	Antiphospholipid syndrome SLE arthritis	Peptic ulceration Platelet inhibition Renal impairment Fluid retention/electrolyte disturbance Hepatic dysfunction Bronchospasm
Cyclophosphamide	Nephritis NPSLE	Myelosuppression Pseudocholinesterase inhibition Cardiotoxicity Leucopenia Hemorrhagic cystitis
Azathioprine	Arthritis	Myelosuppression Hepatotoxicity
Methotrexate	Arthritis Cutaneous SLE	Myelosuppression Hepatic fibrosis/cirrhosis Pulmonary infiltrates/fibrosis
Mycophenolate mofetil	Nephritis Hemolytic anemia, thrombocytopenia	GI upset Pancytopenia

NPSLE = neuropsychiatric SLE; NSAID = nonsteroidal anti-inflammatory drugs; GI = gastrointestinal.

Regular laboratory testing is advised for the purpose of monitoring patients with Systemic Lupus Erythematosus (SLE). It is recommended to do a full blood count, erythrocyte sedimentation rate, C-reactive protein, urea and creatinine, liver function tests, and urinalysis. There is a strong desire to identify lupus biomarkers that are associated with disease activity, however the results have been inconsistent. However, a rise in anti-dsDNA titers may indicate the likelihood of lupus flares, particularly when accompanied by a decrease in complement levels. Typically, C3/C4 and anti-C1q are often assessed, but there is a possibility that testing for complement breakdown products, such as C3d or C4d, may become more prevalent in the future.

There has been a recent recognition of the heightened risk of cardiovascular disease (CVD) among these people. As a consequence, there is now increasing emphasis on monitoring and treating modifiable risk factors such as hypertension and hypercholesterolemia.

Considerations related to the period before, during, and after a surgical procedure.

The preoperative examination should specifically focus on determining if it is necessary to continue immunosuppressant medications and replace steroids throughout the surgical period. A comprehensive physical examination should be performed, which may uncover heart valvular abnormalities, pericarditis, pleural effusions, interstitial lung disease, or

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peripheral neuropathies. Referral for preoperative transesophageal echocardiography is recommended in cases of unexpected heart murmurs or results that are indicative of endocarditis. It is recommended to do laboratory testing for all patients. The levels of antibodies or complements might be helpful when assessed in reference to prior results and their correlation with disease activity. It is necessary to test for the existence of aPL antibodies in order to determine whether there is a higher chance of blood clot formation. In cases where there is a considerable risk of blood clot-related problems, such as orthopedic or vascular surgery, it is recommended to use preventive measures to reduce the risk of blood clots.¹³¹ A baseline 12-lead electrocardiogram is necessary due to the heightened risk of myocardial ischemia. Customized perioperative treatment is necessary to suit the specific needs of each patient. In order to ensure proper monitoring, it is advisable to incorporate a 5-lead ECG. This is because cases of unexpected intraoperative myocardial ischemia have been documented in patients with systemic lupus erythematosus (SLE). Given the heightened cardiac risk in this group, it is advisable to have a low threshold for inserting an arterial catheter in serious instances. When selecting an anesthetic strategy, it is important to consider the possible interactions between drugs used for immunosuppression, as well as the possibility of encountering a difficult airway due to subglottic stenosis or laryngeal edema, undetected cardiac ischemia, and the risk of blood clot formation. If the patient is using anticoagulant

medication, regional procedures may not be recommended, and it is important to prioritize the resumption of anticoagulation after the surgery. It is important to be cautious about the danger of infection and take appropriate measures such as using antibiotics to prevent it. Additionally, careful placement during surgery is necessary to avoid fractures in bones weakened by osteoporosis and compression of peripheral nerves. It is recommended to use strategies to preserve the kidneys, even if there is no obvious kidney damage.

It is important to evaluate the pharmacological interactions between anesthetic medications and immunosuppressant agents. Azathioprine, a kind of medication that inhibits the production of certain substances in the body's immune system, may have an effect on muscle relaxants. In one research, it was shown that increases in dosage of 37% for atracurium, 20% for vecuronium, and 45% for pancuronium were necessary when used in combination with azathioprine. Renal insufficiency counteracted the increases seen in the case of pancuronium and vecuronium. Cyclophosphamide functions as a pseudo-cholinesterase inhibitor, which might explain the increased likelihood of extended apnea after the administration of succinylcholine. Combining NSAIDs with methotrexate is known to have harmful consequences, as shown by several case reports of severe renal failure and pancytopenia. Furthermore, administering methotrexate close to nitrous oxide exposure might lead to bone marrow suppression.

Table 4. Recommended Guidelines for the Perioperative Management of Systemic Lupus Erythematosus (SLE) Patients

	Management issue	Comment
Preoperative	History	Review disease activity index, accrued organ damage, and drug history.
	Examination	Thorough examination of cardiovascular, respiratory, and neurological systems, including testing for atlantoaxial subluxation symptoms and signs.
	Full blood count	Test for anemia, thrombocytopenia, and leucopenia. Consider further testing for hemolysis if anemia is present.
	Serum electrolytes, creatinine, urea	Any abnormality requires further investigation for lupus nephritis.
	Liver function tests	Abnormalities should prompt review for autoimmune or drug hepatotoxicity.
	Coagulation studies	Elevated aPTT requires investigation for the presence of lupus anticoagulant.
	Anti-dsDNA, complement levels	May reflect lupus activity after comparison with previous baseline measurements.
	Urinalysis	Proteinuria, red cells, white cells, and cellular casts may indicate clinically silent disease and prompt further investigation.
	Electrocardiogram	Silent ischemia, myocarditis, pericarditis, and conduction abnormalities may be identified.
	Chest radiograph	Pleural effusion, interstitial pneumonitis, pericardial effusion, or subglottic stenosis may be seen.
Intraoperative	5-lead electrocardiography	Accelerated coronary artery disease, conduction abnormalities.
	Intra-arterial blood pressure monitoring	Case dependent, consider in presence of myocarditis, conduction abnormalities, valvular abnormalities, or autonomic dysfunction. Special care to be taken in the presence of Raynaud's phenomenon.
	Laryngeal mask airway if appropriate	Minimize airway manipulation due to risk of inflammation and postextubation airway edema.
	Difficult airway precautions with immediate access to smaller-size endotracheal tubes	Vocal cord paralysis, subglottic stenosis, or laryngeal edema may make intubation difficult.
	Standard antibiotic prophylaxis	Innate susceptibility to infection and immunosuppressive therapy predispose to infection risk.
	Caution with muscle relaxants	Azathioprine and cyclophosphamide may interact with muscle relaxants.
	Renal protective strategies	Maintain urine output, avoid hypoperfusion and hypotensive states, and use nephrotoxic drugs cautiously because of possibility of subclinical lupus nephritis.
	Careful patient positioning	Predisposition to peripheral neuropathies and osteoporosis.
	Antithrombotic prophylaxis	Institute mechanical and pharmacological measures early, especially in the presence of antiphospholipid antibodies. Patients with confirmed lupus anticoagulant and previous thromboembolic events warrant therapeutic anticoagulation in discussion with a hematologist.
	Eye protection and artificial tears/lubrication	Sjogren's Syndrome may predispose to corneal abrasions despite adequate eye taping.
Postoperative	Temperature monitoring	Hypothermic states may induce vasospasm in patients with Raynaud's phenomenon.
	Pain management	Consider side effects of systemic analgesics; regional techniques may be helpful if neuropathies, myelitis, and coagulopathies are excluded.
	Corticosteroid cover	Adrenal suppression may have resulted from long-term corticosteroid therapy with the need for a "stress dose" perioperatively.
	Pain management	Regular review and input by a specialist pain service to minimize systemic side effects.

aPTT = activated partial thromboplastin time; dsDNA = double-stranded DNA.

CONCLUSION

SLE is a multifaceted autoimmune condition characterized by a wide range of clinical symptoms and the accumulation of damage. The prognosis of SLE patients has consistently improved over time, leading to higher life rates and an increase in the number of patients seeking surgery. Consequently, anesthesiologists must possess a comprehensive understanding of the various difficulties they may face while providing care for SLE patients. Due to the diverse nature of this illness and its capacity to impact any organ in the body, the administration of anesthesia and care during the perioperative period relies on the clinician's expertise and comprehension of the medical factors involved in these patients.

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