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Echocardiography in Systemic Lupus Erythematosus

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Abstract

Purpose of Review In patients with systemic lupus erythematosus (SLE), cardiovascular involvement is common and a major cause of morbidity and mortality. There have been few recent updates regarding the cardiac involvement in this clinical entity. The purpose of the review is to provide an update on the role of echocardiography in the management of these patients.

Recent Findings Echocardiography remains the imaging modality of choice and should be considered even in asymptomatic patients with SLE to detect cardiac abnormalities which are frequently not clinically apparent. Transesophageal echocardiography has higher sensitivity and specificity in identifying valvular lesions, and should be utilized in high risk patients when transthoracic echocardiography is negative. New advances such as speckle tracking echocardiography has shown promise in the detection of occult myocardial dysfunction, but more studies are needed to have a proper perspective of its role in SLE patients.

Summary SLE has protean cardiac manifestations. The most common involvement is pericarditis. Complicated pericarditis such as tamponade and constriction are rare but should be considered if the symptoms do not subside with treatment. Valvular involvement can take several forms. Libman-Sacks endocarditis is the most common form and is more prevalent in patients with high disease activity and with the presence of antisphopholipid antibodies. Myocardial involvement portends poor prognosis and should be sought and treated promptly to prevent morbidity and mortality.

Keywords Systemic lupus erythematosus · Echocardiography · Cardiac manifestations

Introduction

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease with multisystem involvement and a female preponderance. SLE has a wide range of cardiovascular manifestations and can involve any part of the heart. The symptoms and clinical findings are non-specific and mimic many other conditions, such that the diagnosis is based on multiple clinical factors and laboratory immunologic measures. Even though cardiac involvement is common in SLE, cardiac findings by themselves are insufficient in making the diagnosis. Cardiac involvement can occur as early as the neonatal period. Neonatal lupus is a congenital disorder linked to high circulating maternal anti-Ro/SS-A auto-antibodies which cross the placenta and result in complete heart block [1–4]. The leading cause of death in lupus patients with cardiac involvement is coronary artery disease (CAD) with the risk estimated to be at least doubled that of the general population [5]. Premature and accelerated atherosclerosis has been described as the main pathophysiology of CAD in lupus patients [5].

While it has been estimated in some studies that more than 50% of lupus patients have some sort of cardiovascular involvement, in only 10% of patients is cardiac involvement clinically evident [6, 7]. Indeed, valvular involvement may only be diagnosed after an embolic event which is usually a cerebral vascular event [8]. Echocardiography plays a major role in the non-invasive evaluation of cardiac involvement in lupus patients. Transthoracic echocardiography has been widely used but its sensitivity is limited. Transesophageal

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echocardiography has higher sensitivity and specificity, and thus should be used when the clinical suspicion remains high despite a negative transthoracic study [9]. In this review, we focus the discussion on the echocardiographic manifestations affecting the pericardium, the myocardium and the endocardium (Fig. 1). The prevalences of the different types of cardiac involvement have wide ranges largely due to the differences in patient population as to whether asymptomatic or symptomatic, the varying degree of disease activity and the presence or absence of antiphospholipid antibodies [1–4].

Pericardial Involvement

Pericarditis is the most common and first recognized cardiac manifestation of SLE. The prevalence of pericarditis is estimated between 12% and 48% [6]. Asymptomatic pericardial involvement is more frequent than clinical pericarditis. Lupus pericarditis presents in a similar fashion to classic pericarditis. Analysis of pericardial fluid shows exudative effusion with increased white blood cells count and predominant polymorphonuclear cells. Marked acidity with pH less than 7 may help in distinguishing lupus pericarditis from other etiologies [6]. Anti-nuclear antibodies should be requested and interpreted with caution as these antibodies are frequently positive in normal individuals. Lupus pericarditis is usually treated with a course of nonsteroidal anti-inflammatory agents and colchicine. The addition of corticosteroids may be required in refractory cases [6, 10].

Cardiac tamponade is uncommon in lupus patients. A series of more than 1300 SLE patients showed that the prevalence of tamponade is $<1\%$ [10]. A female predominance and insidious onset have been observed among lupus patients presenting with tamponade. Tamponade physiology may develop in circumferential as well as loculated effusion where regional tamponade develops that lacks the classical hemodynamic signs [11]. Although uncommon, large pericardial effusion or cardiac tamponade have been described as the first presentations of SLE [12–14]. Constrictive pericarditis is rare among SLE patients. Our experience suggests that constriction needs to be considered when there are marked inflammatory changes in the pericardial fluid evidenced by loculation, septation and multiple fibrin strands as demonstrated in our case in Fig. 2.

Myocardial Involvement

Myocarditis is the most distinctive feature of lupus-related myocardial involvement. However, in the recent era of corticosteroids and advanced immunomodulator therapy, clinical myocarditis is uncommon. Echocardiographic features include global hypokinesis in the absence of underlying coronary artery disease [15]. SLE has been associated with increased LV mass and diastolic dysfunction possibly secondary to inflammation-related arterial stiffness [16]. Moreover, SLE patients have impaired LV systolic function on the basis of LV ejection fraction compared to normal subjects. Advanced echocardiographic techniques like speckle tracking echocardiography (STE) may be used to measure LV global longitudinal strain (GLS) and detect myocardial dysfunction before the drop in ejection fraction occurs and may play a role in risk stratification [17].

SLE related cardiomyopathy, like almost all other cardiac manifestation, is a diagnosis of exclusion that can be made after ruling out more common causes like coronary artery disease and hypertensive heart disease. Etiology has not been clearly defined but may be related to microvascular damage and diffuse small vessel disease. The risk of heart failure morbidity and mortality is substantially increased in lupus patients. There is an estimated >2.5-fold increased risk of hospitalization and >3.5-fold increased risk of mortality among SLE patients with heart failure compared to

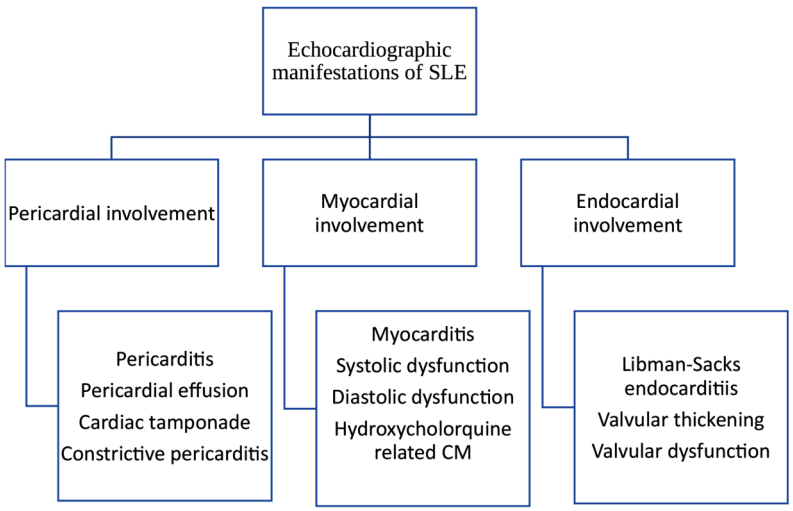

Fig. 1 Echocardiographic manifestations of Systemic Lupus Erythematosus (SLE). CM, cardiomyopathy

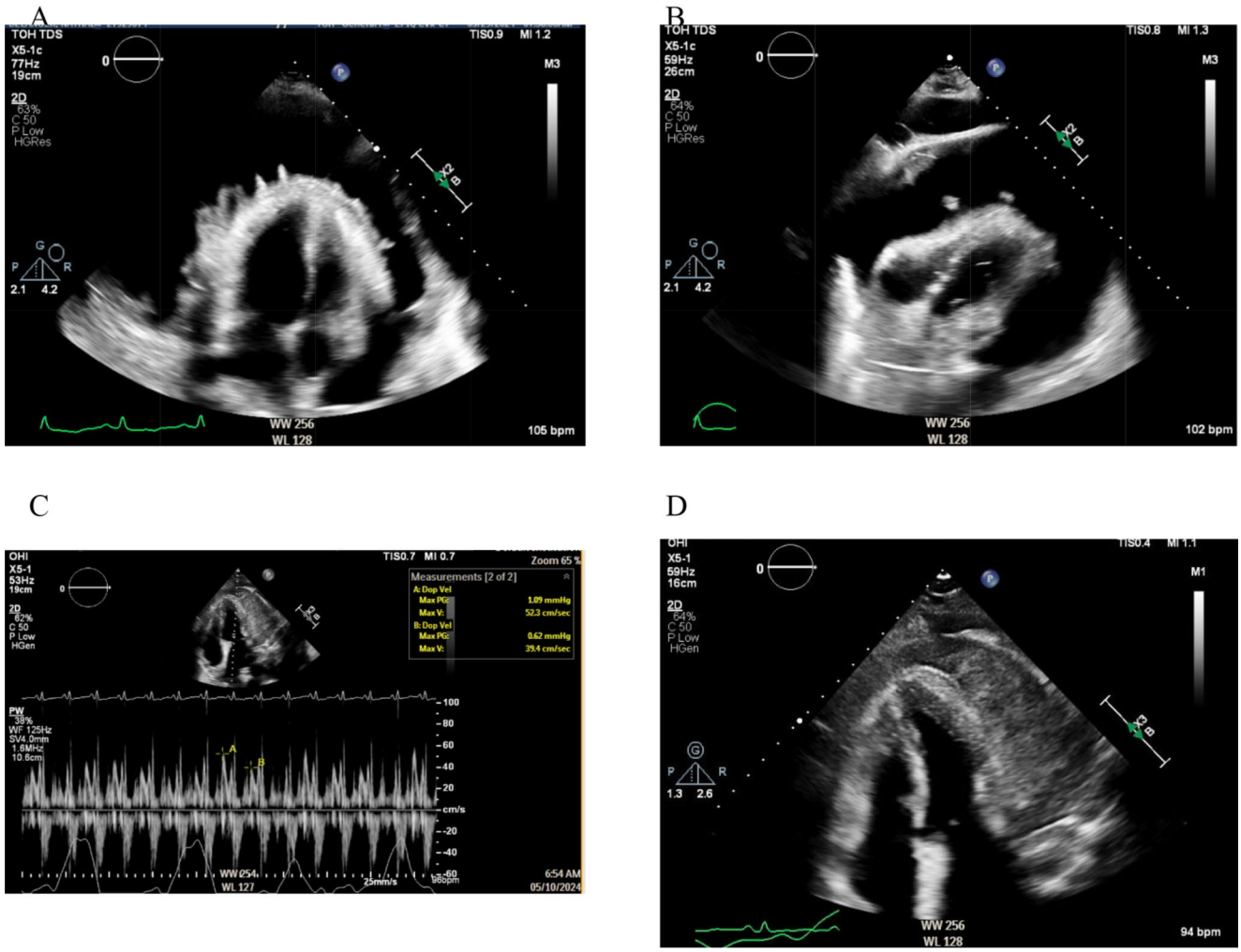

Fig. 2 **A**. Apical 4 chamber view in an SLE patient with chronic pericardial effusion showing large effusion (5 cm in diastolic diameter) with fibrin strands. **B**. Subcostal view of the same patient showing RV diastolic collapse. Other features (not shown) included significant respiratory flow variation and dilated, non-collapsible IVC consistent with the diagnosis of cardiac tamponade. **C** and **D**. Following pericardiocentesis, there is a significant respiratory inflow variation, pericardial thickening and leftward septal shift with inspiration. Other features (not shown) included septal bounce and annulus reversus (Septal e' > Lateral e') consistent with the diagnosis of effusive-constrictive pericarditis. The patient underwent surgical pericardiectomy. RV, right ventricle. IVC, inferior vena cava

general population with heart failure [18]. A reversible form of restrictive cardiomyopathy related to hydroxychloroquine therapy has been described. It is thought to be related to hydroxychloroquine toxicity which can be reversed with cessation of the drug [19]. It is safe to say that hydroxychloroquine toxicity is rare within the therapeutic dose range used in SLE patients.

Endocardial Involvement

The valvular dysfunction related to SLE can be categorized into masses or vegetations (Libman-Sacks endocarditis), valvular thickening, valvular regurgitation and infrequently valvular stenosis [20]. In 1924, Libman and Sacks described the first case of lupus-related sterile endocarditis. Libman-Sacks vegetations are non-infective thrombotic sterile vegetations which develop on the heart valves, most commonly mitral valve (Fig. 3), chordae tendinea or endocardial surfaces [21]. Transesophageal echocardiogram (TEE) produces high resolution images and is superior to transthoracic echocardiogram (TTE) in diagnosing these valve lesions [9, 22]. While the finding of Libman-Sacks endocarditis is quite common, estimated to be found in 10% of SLE patients, it is rarely related to clinically significant valve disease [23]. Infective endocarditis should always be in the consideration, because it is difficult to differentiate infective vegetation from Libman-Sacks vegetation based on the morphologic features. Nonetheless the latter is more likely if the vegetation is located at the leaflet base and not the closure line of the leaflet. Treatment of these vegetations

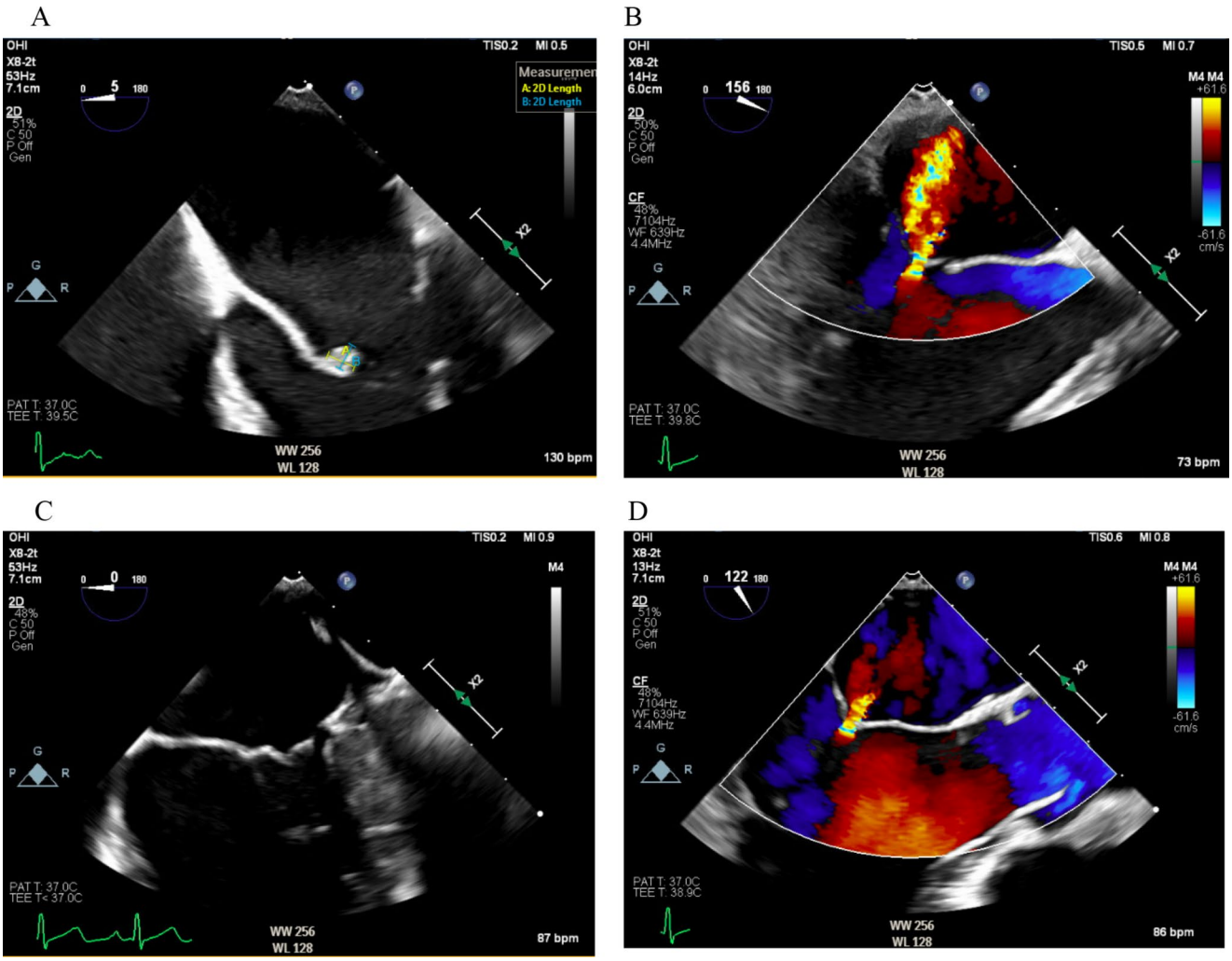

Fig. 3 **A**. TEE in a young patient with SLE and history of stroke shows a small mass [6×6 mm] attached to the atrial aspect of the distal anterior leaflet [A2 scallop) consistent with a Libman-Sacks vegetation. **B**. Mild to moderate mitral regurgitation. **C** and **D**. Repeated TEE following anticoagulation with warfarin and optimization of immunosuppressive therapy shows complete resolution of the mass and reduction in mitral regurgitation severity. TEE, transesophageal echocardiogram

includes starting anticoagulation for larger lesion or when embolic phenomena occur, and optimizing immunosuppression once infection has been excluded.

Other valvular manifestations include valvulitis with significant valve dysfunction in form of regurgitation or less commonly stenosis. The most affected valves are the mitral valve (Fig. 4) and the aortic valve [24]. The key feature in distinguishing SLE-related valve dysfunction from rheumatic involvement is the diffuse valve thickening and lack of fusion at the commissures.

A meta-analysis of 21 studies with a total of 2163 SLE patients, of which a quarter had valvular lesions, showed a significant association between anticardiolipin antibodies positivity with valvular dysfunction (relative risk of 1.55; confidence interval, 1.10–2.18) [25].

Discussion

As demonstrated in this review, SLE can involve all layers of the heart from pericardium to endocardium. Additionally, it involves the epicardial coronary arteries, conduction system and great vessels. Echocardiography reliably detects regional wall motion abnormalities due to coronary artery disease, but it cannot differentiate the underlying predisposing conditions [6]. Cardiac involvement tends to be subtle and non-specific with the majority of patients being asymptomatic. Therefore, a high index of suspicion is needed to make the diagnosis. As a rule of thumb, cardiac involvement of SLE is a diagnosis of exclusion which can be made once more common pathologies have been excluded.

Transthoracic echocardiography is a useful screening tool for cardiac manifestations of SLE as it covers a wide

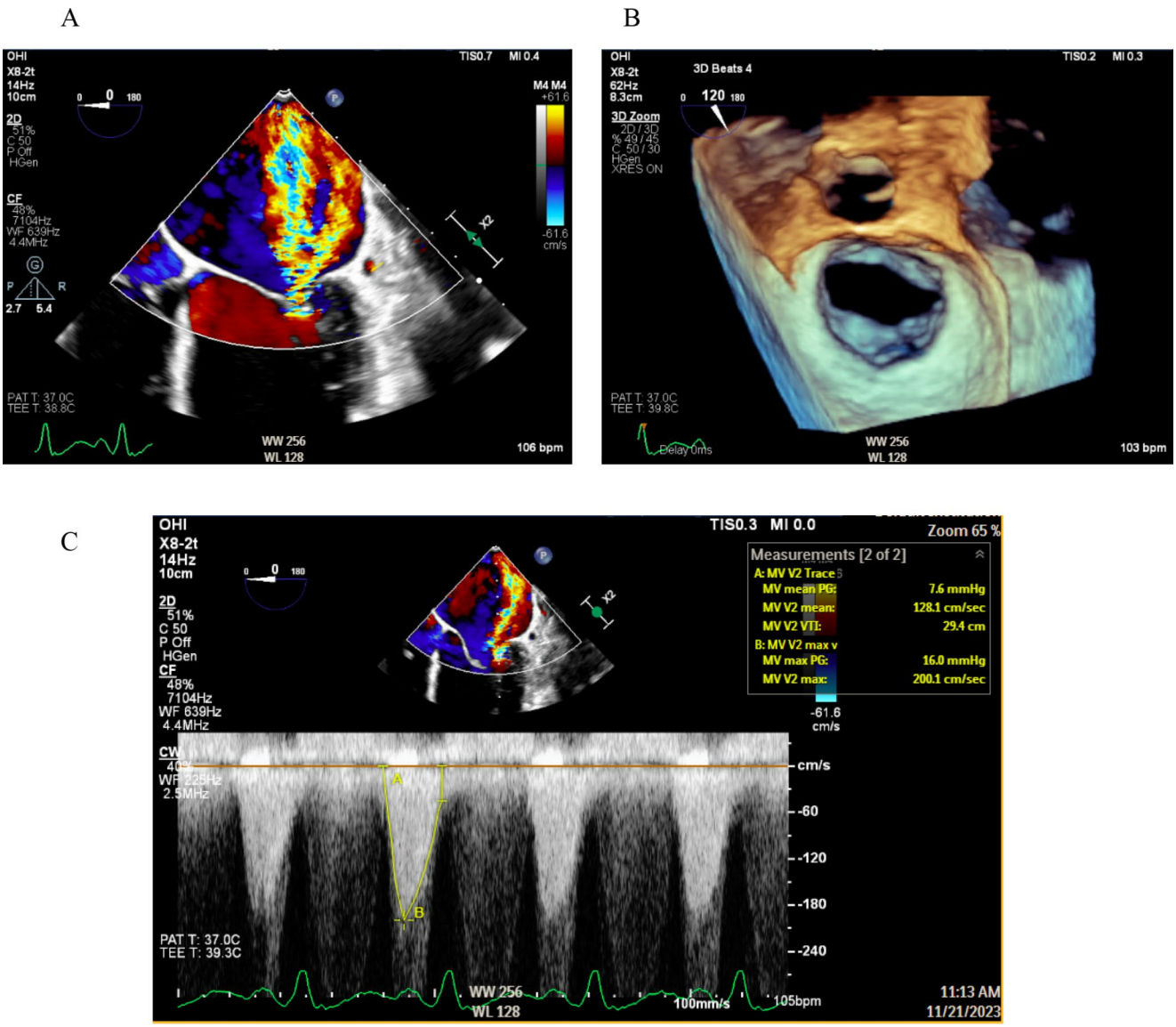

Fig. 4 **A**. TEE in a young patient with SLE showing restricted posterior mitral leaflet motion resulting in severe mitral regurgitation. **B**. 3D view of the mitral valve showing a restricted posterior mitral valve leaflet with no commissural fusion. **C**. Continuous wave Doppler of mitral inflow demonstrating increased transvalvular mitral gradients. The patient underwent surgical mitral valve replacement. TEE, transesophageal echocardiogram

range of these manifestations keeping in mind transesophageal echocardiogram has a better sensitivity and specificity for diagnosis of certain manifestations like Libman-Sacks vegetations. The role of periodic echocardiographic monitoring should be individualized based on the result of the initial examination and the patient's disease activity.

Management of SLE patients with cardiac involvement generally involves specific therapy for the heart along with optimizing SLE therapy for any evidence of active disease.

Conclusion

SLE patients can present with a wide range of cardiovascular manifestations. Echocardiography plays an important role in diagnosis, guiding management decisions and monitoring of cardiac involvement in lupus patients.

Author Contributions K.C. and M.A-Z. contributed equally.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Conflict of Interest Dr. Al-Zahir has nothing to disclose. Dr. Chan reports being on the Data Safety Monitoring Board of two trials (COPAS and EVOID-AS). COPAS is a pilot study initiated locally testing the effect of colchicine on progression of aortic stenosis, and EVOID-AS is a multi- center multinational study on the progression of aortic stenosis. He also reports being a member of task force on echo accreditation, Accreditation Canada and being a member of Cardiogenetics Expert Group, Ministry of Health, province of Ontario.

References

1. Siegel CH, Sammaritano LR. Systemic lupus erythematosus: a review. JAMA. 2024;331(17):1480–91. https://doi.org/10.1001/jama.2024.2315.
2. Miner JJ, Kim AH. Cardiac manifestations of systemic lupus erythematosus. Rheum Dis Clin N Am. 2014;40:51–60. https://doi.org/10.1016/j.rdc.2013.10.003.
3. Doria A, Iaccarino L, Sarzi-Puttini P, et al. Cardiac involvement in systemic lupus erythematosus. Lupus. 2005;14:683–6. https://doi.org/10.1191/0961203305lu2200oa.
4. Rao RV, Chan KL. Systemic Lupus Erythematosus in: ASE'S Comprehensive Echocardiograhy, Second Edition, an imprint of Elsevier Inc. 2016:757–760.
5. Schoenfeld SR, Kasturi S, Costenbader KH. The epidemiology of atherosclerotic cardiovascular disease among patients with SLE: A systematic review. Semin Arthritis Rheum. 2013;43(1):77–95. https://doi.org/10.1016/j.semarthrit.2012.12.002.
6. Moder KG, Miller TD, Tazelaar HD. Cardiac involvement in systemic lupus erythematosus. Mayo Clin Proc. 1999;74:275–284. https://doi.org/10.4065/74.3.275.
7. Crozier IG, Li E, Milne M, Gary Nicholls M. Cardiac involvement in systemic lupus erythematosus detected by echocardiography. Am J Cardiol. 1990;65:1145–8.
8. Bourré-Tessier J, Huynh T, Clarke AE, Bernatsky S, Joseph L, Belisle P, Pineau CA. Features associated with cardiac abnormalities in systemic lupus erythematosus. Lupus. 2011;20(14):1518–25. https://doi.org/10.1177/0961203311420318.
9. Roldan CA, Qualls CR, Sopko KS, et al. Transthoracic versus transesophageal echocardiography for detection of Libman-Sacks endocarditis: a randomized controlled study. J Rheumatol. 2008;35:224–9.
10. Cauduro AS, Moder KG, Tsang TS, Seward JB. Clinical and echocardiographic characteristics of hemodynamically significant pericardial effusions in patients with systemic lupus erythematosus. Am J Cardiol. 2003;92:1370–1372. https://doi.org/10.1016/j.amjcard.2003.08.036.
11. Maharaj S, Chang S. Pericardial effusions in systemic lupus erythematosus — Who is most likely to develop tamponade? Int J Cardiol. 2015;180:149–150. https://doi.org/10.1016/j.ijcard.2014.11.191.
12. Bilal A, Sulemankhil I, Chauhan R. et al. "Breaking Muscles and Hearts": Rhabdomyolysis and Pericardial Tampondate as Initial Manifestations of Systemic Lupus Erythematosuc. JACC. 2024;83(13_Supplement):3995. https://doi.org/10.1016/S0735-1097(24)05985-0.
13. Shalomi A, Ramesh R. Pericardial Effusion as the Initial Presentation of Systemic Lupus Erythematosus in a 37-Year-Old Female. Cureus. 2023;15(11):e49080. https://doi.org/10.7759/cureus.49080.
14. Creed K, Randhawa N, Siddiqui S, Wichmann A, Test V. Pericardial Effusion in a Middle Aged Woman as Initial Presentation of Systemic of Systemic Lupus Erythematous. CHEST. 160(4):A13. https://doi.org/10.1016/j.chest.2021.07.069.
15. Doherty N, Siegel R. Cardiovascular manifestations of systemic lupus erythematosus. Am Heart J. 1985;110:1257–65. https://doi.org/10.1016/0002-8703(85)90023-7.
16. Pieretti J. Systemic Lupus Erythematosus Predicts Increased Left Ventricular Mass. Circulation. 116(4). https://doi.org/10.1161/CIRCULATIONAHA.106.673319.
17. Gegenava T, Gegenava M, Steup-Beekman GM, Huizinga TWJ, Bax JJ, Delgado V, Marsan NA. Left ventricular systolic function in patients with systemic Lupus Erythematosus and its Association with Cardiovascular events. J Am Soc Echocardiogr. 2020;33(9):1116–22. https://doi.org/10.1016/j.echo.2020.04.018.
18. Ward MM. Premature morbidity from cardiovascular and cerebrovascular diseases in women with systemic lupus erythematosus. Arthritis Rheum. 1999;42(2):338–46.
19. Abbasi S, Tarter L, Farzaneh-Far R, Farzaneh-Far A. Hydroxychloroquine: a treatable cause of cardiomyopathy. J Am Coll Cardiol. 2012;60(8):786. https://doi.org/10.1016/j.jacc.2011.12.060.
20. Galve E, Candell-Riera J, Pigrau C, Permanyer-Miralda G, Garcia-Del-Castillo H, Soler-Soler J. Prevalence, morphologic types, and evolution of cardiac valvular disease in systemic lupus erythematosus. N Engl J Med. 1988;319(13):817–23. https://doi.org/10.1056/NEJM198809293191302.
21. Moyssakis I, Tektonidou M, Vasilliou VA, Samarkos M, Votteas V, Moutsopoulos H. Libman-Sacks endocarditis in systemic Lupus Erythematosus: Prevalence, associations, and evolution. Am J Med. 2007;120(7):636–42. https://doi.org/10.1016/j.amjmed.2007.01.024.
22. Roldan CA, Shively BK, Lau CC, Gurule FT, Smith EA, Crawford MH. Systemic lupus erythematosus valve disease by transesophageal echocardiography and the role of antiphospholipid antibodies. J Am Coll Cardiol. 1992;20(5):1127–34. https://doi.org/10.1016/0735-1097(92)90368-w.
23. Straaton KV, Chatham WW, Reveille JD, Koopman WJ, Smith SH. Clinically significant valvular heart disease in systemic lupus erythematosus. Am J Med. 1988;85(5):645–50. https://doi.org/10.1016/s0002-9343(88)80236-5.
24. Roldan CA, Shively BK, Crawford MH. An echocardiographic study of valvular heart disease associated with systemic lupus erythematosus. N Engl J Med. 1996;335(19):1424–30. https://doi.org/10.1056/NEJM199611073351903.
25. Hussain K, Gauto-Mariotti E, Cattoni HM, Arif AW, Richardson C, Manadan A, Yadav N. A Meta-analysis and Systematic Review of Valvular Heart Disease in Systemic Lupus Erythematosus and Its Association with Antiphospholipid Antibodies. J Clin Rheumatol. 2021;27(8):e525-e532. https://doi.org/10.1097/RHU.0000000000001464.

Key References

1. Siegel CH, Sammaritano LR. Systemic lupus erythematosus: a review. JAMA. 2024;331(17):1480–91. https://doi.org/10.1001/jama.2024.2315. The clinical and immunological features crucial to the diagnosis of systemic lupus erythematosus are presented.
2. Rao RV, Chan KL. Systemic Lupus Erythematosus in: ASE'S Comprehensive Echocardiograhy, Second Edition, 2016, an imprint of Elsevier Inc. pp. 757–760. A comprehensive discussion. of systemic lupus erythematosus focusing on the cardiac manifestations and their prevalences.

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