Research article

Echocardiographic abnormalities in systemic lupus erythematosus patients at Kenyatta National Hospital

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Abstract

Background: The cardiovascular system is frequently affected in patients with Systemic Lupus Erythematosus (SLE). Involvement of the pericardium, endocardium, myocardium, coronary and pulmonary vessels has been found in several clinical and autopsy studies in patients with SLE; most of which can be detected by noninvasive two dimensional and Doppler echocardiography. More than half of SLE patients experience clinical cardiovascular manifestation during the course of the disease and cardiovascular complications are among the leading causes of morbidity and mortality in patients with SLE.

Objective: To determine the prevalence and spectrum of cardiac abnormalities; determined by echocardiography in SLE patients at Kenyatta National Hospital (KNH).

Methods: This was a cross-sectional descriptive study of SLE patients attending clinic at KNH. A targeted history and physical examination and a detailed trans-thoracic echocardiography were performed for all patients. The independent variables included; age, sex, duration of disease and medications. The echocardiogram outcome variables included; pericardial effusion, thickening and calcification, systolic and diastolic dysfunction, mitral valve thickening, stenosis and regurgitation, aortic valve thickening, stenosis and regurgitation, and pulmonary hypertension.

Results: Sixty three SLE patients participated in the study, the mean age was 36.7 years, with a female to male ration of 20:1 and a meadian duration of disease of 36 months. Over 70% of participants were on at least 2 disease modifying medication. The overall prevalence of echocardiographic abnormalities was 88.9%, the major drivers of this high prevalence being pericardial and valvular thickening. The single moast common cardiac lesion was pericardial thickening at 77.8%. The mitral valve was the most commonly affected valve with 69.8% and 30.2% having mitral thickening and regurgitation respectively. Aortic valve thickening and regurgitation was found in 25.4% and 6.3% of participants respectively. Diastolic dysfunction was found in 50.8% of participants and was found to be associated with older age at diagnosis. Pulmonary hypertension was found in 22.2% of participants.

Conclusion: The study demonstrates a high prevalence of cardiac abnormalities among SLE patients despite being on disease modifying medications. Even though the majority of these abnormalities comprised of clinically insignificant pericardial and valvular thickening, the prevalence of valvular insufficiency and pulmonary hypertension are substantially high and relatively higher than the prevalence seen in other studies in the case of pulmonary hypertension.

Introduction

Systemic lupus erythematosus is an autoimmune disorder resulting in multi-systemic inflammatory damage, the epidemiology of which is still largely undetermined in Africa. The general view had prevailed that the incidence of SLE in black Africans is low[1]. However recent studies by African researchers have clearly demonstrated that SLE may be common in Black Africans. Tikly *et al*[2] described the clinical features and antibody profile of 111 black South Africans with SLE and Adelowo *et al*[3] described a series of 66 SLE cases diagnosed at a Rheumatology clinic in Lagos Nigeria.

Cardiovascular disease is common among patients with SLE and has recently been acknowledged as a major cause of morbidity and mortality. A survey to determine the clinical spectrum and outcome of SLE in hospitalized Black Africans in Durban, South Africa, demonstrated a high mortality rate of 29% and the commonest causes of death

were renal, infection, neurological and cardiac[4]. The heart specifically is frequently affected in SLE and all its constituents can be involved from the pericardium to the endocardium.

The pericardium is the most commonly affected constituents of the heart, with pericarditis being one of the most characteristic manifestation of SLE and included in the American College of Rheumatology (ACR) classification of SLE[5]. Pericardial effusion occurs at some point in over half of patients with SLE and is the most frequent cause of symptomatic cardiac disease[6]. The course of pericarditis is benign in the large majority of cases however, it is usually associated with active disease in other organs[7].

Myocarditis is a rare but potentially fatal manifestation of SLE. It is often subclinical in nature, but 5 to 10% of all SLE patients develop symptomatic myocarditis[8]. Myocardial dysfunction may develop as a consequence of myocarditis and several other factors including; premature atherosclerosis, hypertension, renal failure, valvular disease and toxicity from medication[6,9].

Both anatomical and functional valvular abnormalities have been described in SLE. Libman-Sack endocarditis is the most characteristic lesion, though valvular thickening and regurgitation are more frequently observed. The clinical recognition of Libman-Sack endocarditis during life is extremely difficult, because valvular distortion is usually minimal even though large vegetation may be present. However verrucae may fragment and produce systemic emboli, leading to stroke and peripheral vascular disease. Furthermore infective endocarditis can develop in already damaged valve and has been reported in 7% of SLE patients with valvular heart disease[10]. Haemodynamically significant valvular lesions have been reported in 3 - 4% of SLE patients and only half of these require surgical treatment[10].

Pulmonary hypertension is a serious and potentially life threatening complication of SLE. The reported prevalence of pulmonary hypertension among SLE patients ranges from 0.5 to 14%[11,12]. Although pulmonary arterial hypertension is the most common cause of pulmonary hypertension in SLE, interstitial lung disease, thromboembolism, primary cardiac involvement and pulmonary veno-occlusive disease may be implicated in a minority of these cases. The onset of pulmonary hypertension in SLE does not correlate with disease duration or degree of extra-pulmonary manifestations[13] and may be the presenting feature before the diagnosis of SLE. It is the most severe form of lupus associated pulmonary involvement, with poor long term outcome despite therapeutic intervention and a mean survival from onset of 2 years[14].

Prevention of cardiovascular disease associated morbidity and mortality among these patients depends on early detection and close follow up of patients with cardiovascular disease. Data on the prevalence and spectrum of cardiac lesions among these patients would therefore be crucial to inform practice guide lines with regards to initial investigation and subsequent follow up of SLE patients. However prior to this study there were no studies documenting the prevalence and spectrum of cardiac lesions including pulmonary hypertension among SLE patients in our setting.

Materials and Methods

This was a cross sectional descriptive study. SLE patients fulfilling the ACR criteria were recruited from the Rheumatology clinic and medical wards over a period of 3 months. Participants were examined clinically to elicit clinical features attributable to SLE. All participants underwent a detailed transthoracic echocardiographic evaluation by a cardiologist, according to recommendations of the American Society of Echocardiography. All echocardiography studies were independently reviewed by a second cardiologist and discrepancies resolved by a joint review of the studies by the two cardiologists to reach a consensus. The results represent the consensus of the two cardiologists.

Pericardial effusion was defined as echo free space surrounding the heart and persistent throughout the cardiac cycle and pericardial thickening as a thickness greater that 3mm. The cutoff for systolic dysfunction was fractional shortening less than 29% and/or left ventricular ejection fraction less than 50%. Diastolic function was defined using mitral flow velocities, early mitral flow deceleration time and isovolumetric relaxation time. Using theses parameters diastolic dysfunction was graded as follows:

- Grade 1: Impaired relaxation; mitral E/A ‹ 1, DT › 200msec, IVRT › 100msec
- Grade 2: Pseudonormal pattern; E/A 0.8 – 1.5, DT 150 – 200msec, IVRT 60 – 100msec
- Grade 3: Restrictive reversible; E/A › 2, DT ‹ 160msec, IVRT ‹ 60msec and reversible on valsava manoeuvre
- Grade 4: Restrictive irreversible; same as Grade 3 but irreversible on valsava manoeuvre

Valvular thickening were defined as thickening greater than 3mm and 2mm for the mitral and aortic valves respectively. Mitral valve regurgitation was graded based on the extent of the regurgitant jet into the Left Atrium (LA) as follows; grade 1- jet extending up to proximal ¼ of the LA, grade 2 – ½ way up LA, grade 3 – up to ¾ of LA and grade 4 –beyond ¾ of LA. Pulmonary hypertension was classified into possible pulmonary hypertension when systolic pulmonary arterial pressure was between 37 and 50mmHg and likely pulmonary hypertension when systolic pulmonary pressure is greater than 50mmHg.

Data collected was coded, entered and managed in the statistical package for social sciences version 21.0 data sheet. Data cleaning, verification and analysis was done using the same programme. The study population was described using demographic and clinical characteristics. Continuous data (age, duration of disease) was analysed into means and medians while categorical data was analysed using percentages. Prevalence of cardiac abnormality was analyzed as a proportion with corresponding 95% confidence interval. Furthermore, various types of cardiac lesions were analyzed and presented as proportions. Associations between various cardiac lesions and demographic and clinical factors were analysed, using Student's t test to compare means and chi square test for categorical data associations. Criteria for statistical significance was set as a p value of less than or equal to 0.05.

Results

Between 22nd January and 23rd April 2015, 63 SLE patients were recruited into the study. The female to male ratio was 20:1, mean age of 36.7 years (SD ±9.8) and median duration of disease of 36 months (IQR 14.0 – 65.0). The predominat clinical manifestation was arthritis (55.6%) followed by Raynaud's phenomenon (28%). Over 70% of participants were on at least two disease modifying medication, the most commonly used medication being hydroxichloroquin (73%). Only 6.3% of participants were not on any disease modifying medication.

The overall prevalence of cardiac abnormalities was 88.9%, mostly driven by pericardial and valvular thickening. The most common echocardiographic abnormality was pericardial thickening detected in 77.8% of participants and none of these had features suggestive of constrictive pericarditis. Pericardial effusion was detected in only 1 (1.6%) participant, who was diagnosed with SLE at age 51, duration of disease was two years and was on prednesone, hydroxychloroquin and methotrexate at the time of evaluation.

There was generally good systolic function among participants with mean ejection fraction for the study population of 64.4 (SD 4.4). Only 11.1% had mild systolic dysfunction. On the other hand diastolic dysfunction was more prevalent, detected in 50.8% (Table 1). Diastolic dysfunction was found to be associated with age at diagnosis, the mean ages at diagnosis for participants with and without diastolic dysfunction were 36.7 (SD±9.1) and 28.7 (SD±8.5) respectively (p value 0.001).

Table 1: Myocardial dysfunction

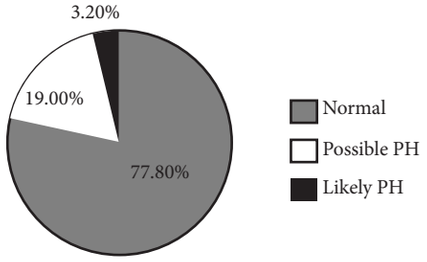
Variable		Frequency (%)
Diastolic dysfunction		32 (50.8)
Type	Type I	16 (25.4)
	Type II	12 (19.1)
	Type III	4 (6.3)

Valvular abnormalities were detected in 88.9% of participants (Table 2). The types of valvular abnormalities detected were valvular thickening and regurgitation, the mitral valve being the most commonly affected. No participant was found to have vegetation or stenosis of any valve. Multiple valve involvement was seen in 16 (25.4%); 15 (23.8%) had mitral and aortic involvement and 1 (1.6%) had mitral in pulmonary involvement. The tricuspid regurgitations encountered among participants were associated with raised pulmonary pressures from which the pulmonary pressures where derived.

Table 2: Valvular abnormalities

Variable	Frequency (%)
Valvular abnormalities	56 (88.9)
Mitral valve thickening	33 (52.4)
Mitral regurgitation	8 (12.7)
Mitral thickening and regurgitation	11 (17.5)
Aortic valve thickening	15 (23.8)
Aortic regurgitation	3 (4.8)
Aortic thickening and regurgitation	1 (1.6)
Pulmonary regurgitation	1 (1.6)

Figure 1: Pulmonary pressure



Pulmonary hypertension was found in 14 (22.2%) of participants (Figure 1). Two (3.2%) of participants were found to have likely pulmonary hypertension and one of these had clinical and echocardiographic features of right ventricular dysfunction.

Discussion

An overall prevalence of echocardiographic abnormalities in this population of SLE patients was found to be 88.9%. This represents a composite of pericardial, myocardial and valvular abnormalities as well as pulmonary hypertension. The whole spectrum of cardiac abnormalities that could be evaluated by echocardiography, to provide base line data that could serve as a frame work for documenting cardiac abnormalities in these patients was included. The high prevalence was mostly driven by clinically insignificant pericardial thickening and valve thickening. The pericardial and valvular thickening are described as clinically insignificant because none of the participants with pericardial thickening had any clinical or echocardiographic finding of constrictive pericarditis

and participants with valvular thickening had no clinical sequel resulting from valvular thickening. The overall prevalence of cardiac abnormalities in this study is similar to a study by Shazzad *et al*[15] that reported a prevalence of echocardiographic abnormalities among SLE patients of 80%, using similar echocardiographic modalities and covering a similar spectrum of cardiac abnormalities.

The pericardium is the most commonly affected cardiac constituent in SLE, with over half of patients having an episode of pericarditis during the course of their illness[6]. Being a sequel of pericarditis, it is not surprising that we found pericardial thickening in 77.8% of participants in this study. The pericardial thickening found in this cohort of SLE patients was not associated with any clinical or echocardiographic feature of constrictive pericarditis. This is in keeping with the natural history of pericarditis in SLE, which is usually acute, occurs during flairs and rarely progress to constrictive pericarditis[16]. Significant pericardial effusion was found in only 1.6% of the study participants, which is indicative of active pericarditis. This low prevalence of pericardial effusion could probably be explained by the fact that majority of the participants were on two or more disease modifying agents, with only 6.3% not on any disease modifying medication at the time of the study. In a study done in Egypt, Shahin *et al*[17] found pericardial effusion in 19% of SLE patients which is relatively high, however the medication profile of the participants was not reported.

In our study we found a generally good systolic function among SLE patients with only 11.1% with mild systolic dysfunction. Most of the systolic dysfunction was accounted for by subtle reduction in fractional shortening. This is comparable to a similar study in Bangladesh that reported systolic dysfunction in 8% of SLE patients[15]. Shahin *et al*[17] found an even lower prevalence of diastolic dysfunction at 4.8% among of SLE patients at a university clinic in Cairo. With regards to diastolic function, we found a higher prevalence at 50.8%. Diastolic dysfunction was found to be associated with older age at diagnosis of SLE. The high prevalence of diastolic dysfunction was not surprising considering the multiple risks for myocardial dysfunction associated with SLE including direct inflammation, hypertension and premature atherosclerosis. Shiruli *et al*[18] in a Master of Medicine thesis looked at cardiovascular risk factors in a cohort of SLE patients attending the same clinic and found a high prevalence of cardiovascular risk factors, namely; hypertension (42.5%), dyslipidemia (74.2%) and carotid plaque (22.9%). The high prevalence of diastolic dysfunction may represent a preclinical consequence of these multiple cardiovascular risk factors in this cohort of SLE patients.

In this study we found valvular lesions in 88.9% which was relatively high. The majority of these valvular lesions were valvular thickening with no associated valvular regurgitation. We used similar cut offs for valvular thickening as was used in a study done in Canada by Bourre-tessier *et al*[19] that found valvular abnormalities in only 40.1%. From our study we cannot determine the exact reason for this high prevalence of valvular thickening in this population. However, possible explanations include variation in disease phenotype and antibody profile, and concomitant subclinical rheumatic heart disease in this population. Rheumatic heart disease is prevalent in our setting and also predominantly affects the valves on the left side of the heart. There is no local data documenting the prevalence of subclinical rheumatic heart disease in Kenya. However, worldwide estimates demonstrate the highest prevalence of rheumatic heart disease in sub-Saharan Africa, at a rate of 5 to 7 per a thousand[20]. Okello *et al*[21] in a study done in Uganda to determine the burden, risk factors and outcome of rheumatic heart disease, found a prevalence of 14.6 per thousand which is twice the estimate for sub-Saharan Africa. The most commonly affected valve in our study was the mitral valve with 69.8% having mitral thickening and 30.2% having mitral regurgitation. Bourre-Tessier *et al*[19] also found the mitral valve to be the most commonly affected valve with mitral valve thickening found in 25.4% and mitral regurgitation in 25.8%.

Pulmonary hypertension was found in 22.2% of participants in our study, though majority of them are classified as possible pulmonary hypertension, this is a significant finding because of the substantial morbidity and mortality associated with pulmonary hypertension in patients with SLE. Pulmonary hypertension is the most severe form of lupus associated pulmonary involvement, with poor long term outcome despite a number of therapeutic interventions. The mean survival from onset of pulmonary hypertension is two years[14].

Conclusion

The study demonstrates a high prevalence of cardiac abnormalities among SLE patients despite being on disease modifying medications. Even though the majority of these abnormalities comprised of clinically insignificant pericardial and valvular thickening, the prevalence of valvular insufficiency and pulmonary hypertension are substantially high and relatively higher than the prevalence seen in other studies in the case of pulmonary hypertension.

Study limitations

Echocardiography is generally not the preferred imaging modality to assess pericardial or valvular thickness because of its inherent lack of accuracy for measurements less than 5mm, variable image quality and inter and intra observer variability.

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