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REVIEW

Echocardiography in Infiltrative Cardiomyopathy

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Left ventricular (LV) wall thickening can occur due to both physiological and pathological processes. Some LV wall thickening is caused by infiltrative cardiac deposition diseases — rare disorders from both inherited and acquired conditions, with varying systemic manifestations. They portend a poor prognosis and are generally not reversible except in rare circumstances when early diagnosis and treatment may alter the outcome (e.g., Fabry disease). Cardiac involvement is variable and depends on the degree of infiltration and type of infiltrate. These changes often lead to the development of abnormalities in both the relaxation and contractile function of the heart ultimately resulting in heart failure. Echocardiography is generally the first investigation of choice as it is easily available and gives valuable information about the thickness of the ventricular walls as well as systolic and diastolic function. It is also able to identify unique, characteristic features of the disease as well as detecting any haemodynamic sequelae. This review looks at the role of echocardiography in the diagnosis and prognosis of infiltrative cardiac deposition diseases.

Keywords Left ventricular hypertrophy • Infiltrative cardiomyopathy • Echocardiography • Amyloidosis • Sarcoidosis • Fabry disease

Introduction

Many patients have the phenotype of left ventricular hypertrophy (LVH), which may occur due to: chronic afterload increases — aortic stenosis (AS) or systemic hypertension (HTN); genetic conditions — hypertrophic cardiomyopathy (HCM); or, cardiac infiltrative deposition diseases — amyloid, sarcoid, Anderson-Fabry disease or haemochromatosis. Differentiation of the aetiology of the LVH is important so that appropriate, disease specific treatment can be initiated. The aim of this review is to demonstrate the usefulness of echocardiography in the differentiation of patients with abnormal thickening of the LV walls due to cardiac involvement in infiltrative deposition diseases.

Amyloidosis

Pathophysiology

Amyloidosis is a clinical disorder that results from the extracellular deposits of abnormal fibrils in various organs including the heart [1]. More than 30 different unrelated proteins can form amyloid fibrils but many of these are rare and do not affect the heart [2].

Cardiac amyloidosis is the involvement of the heart by amyloid deposition and may be cardiac specific or more commonly part of systemic amyloidosis. Light-chain or primary (AL), familial or senile (ATTR) and secondary (AA) amyloidosis are the three most common types of amyloidosis. These amyloid types differ in disease profile and long

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term outcome [3]. The most common form of cardiac amyloid disease is systemic AL (primary amyloidosis), where the protein deposited is monoclonal immunoglobulin light chain. In the majority of cases, this occurs in the setting of multiple myeloma, with 15%–30% of myeloma patients developing AL cardiac amyloidosis [4]. Signs and symptoms of cardiac involvement occur in up to 50% of patients with AL amyloidosis compared to less than 5% of patients with AA amyloidosis [5]. Regardless of the degree of left ventricular (LV) wall thickness, AL amyloidosis has an aggressive clinical course. In fact, despite advances in treatment and improvement in overall survival over time, the 1-year mortality is 45% [6]. AL requires early diagnosis and prompt treatment for the underlying condition. Unlike AL amyloidosis, systemic AA amyloidosis (secondary amyloidosis) rarely involves the heart. Wild-type ATTR amyloidosis (ATTRwt) is caused by an increase in the accumulation of wild-type transthyretin (TTR) —a protein that is produced in the liver; whereas, familial or mutant ATTR (ATTRm) is due to a mutation in the TTR gene leading to misfolding of the protein. Cardiac involvement varies with the type of mutation and there are over 100 different mutations that have been described in ATTR amyloidosis [7]. Cardiac mutations of ATTR amyloidosis can be associated with significant increase in LV wall thickness (especially senile systemic amyloidosis, SSA). Haemodynamic alterations are less common and the disease runs a less aggressive course compared to AL amyloidosis. Early diagnosis becomes increasingly important as new treatments have recently been tested in ATTR cardiac amyloidosis showing promising results [8].

Left Ventricular Wall Thickness

The most common finding in amyloidosis is increased LV wall thickness with a global wall thickening the usual scenario; however rarely there may be a more regional distribution (Figure 1A). This increase in wall thickness is due to myocardial infiltration and not due to true myocyte hypertrophy, and therefore the term LVH should be used with caution. The walls of the ventricles often reveal myocardial speckling (a sparkling or granular appearance); however this is not a diagnostic sign of cardiac amyloid [6] with reasonable specificity of up to 81% [9,10] but low sensitivity (up to 36%) [10–13]. The specificity of increased LV wall thickness on its own is low for cardiac amyloidosis as this finding can be found in many other conditions, like HCM, hypertensive heart disease and other infiltrative cardiomyopathies. The combination of increased LV mass in the absence of high electrocardiograph (ECG) voltages may be more specific for cardiac infiltrative diseases, of which amyloidosis is the most common Table 1.

Diastolic Dysfunction

Left ventricular diastolic dysfunction occurs early in the course of cardiac amyloid and correlates with disease severity. As the disease progresses the diastolic function deteriorates which can progress to a restrictive pattern in later stages (Figure 2), with up to 88% of late stage cardiac amyloid patients demonstrating a restrictive filling pattern [14–16]. Moreover, a restrictive filling pattern is associated with 50% mortality at 12 months [16]. Early diastolic filling velocities (E′) measured at four mitral annular sites using Tissue Doppler imaging (TDI) demonstrated impairment in both early and late cardiac amyloidosis [17,18]. The E′ velocity at all four mitral annular sites was normal in patients with non-cardiac amyloid, mildly impaired in patients with cardiac amyloid but no clinical evidence of heart failure, and severely impaired in patients with cardiac amyloid and heart failure despite preserved LV systolic function in all three groups [18].

Systolic Dysfunction

Left ventricular systolic dysfunction in the form of reduced LV ejection fraction (LVEF) appears only late in the disease

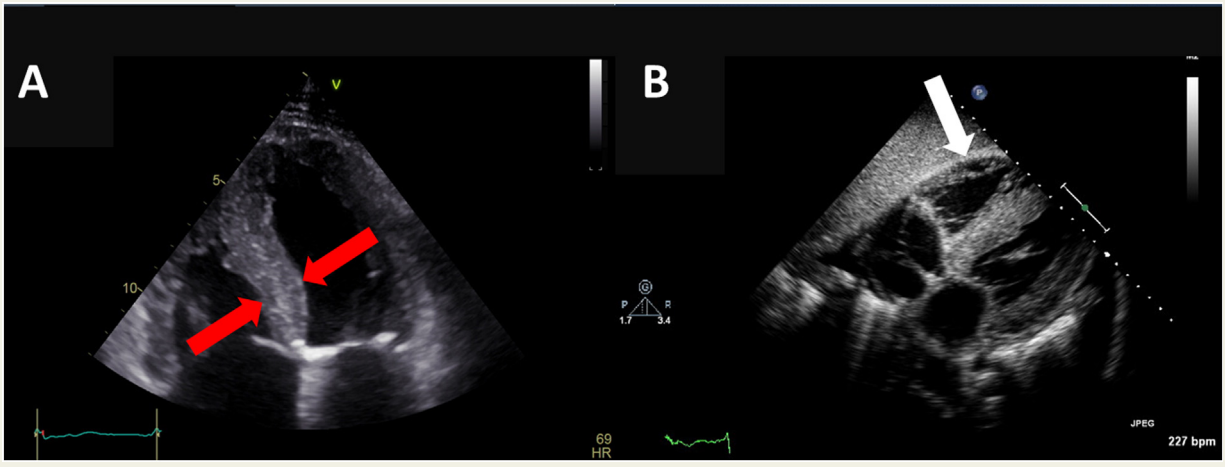

Figure 1 Apical four-chamber (A) and subcostal four-chamber (B) two-dimensional (2D) echocardiographic images from two different patients with cardiac amyloidosis, showing increased left ventricular wall thickness (red arrows) and pericardial effusion (white arrow).

Table 1 Clinical and echocardiographic features of the Common Infiltrative Cardiomyopathies, adapted from Shah et al. [90].

	Clinical presentation	Echocardiogram	Myocardial deformation imaging
Amyloidosis	Diastolic heart failure Right heart failure	Increased LV wall thickness Diastolic dysfunction (+/- Restrictive filling pattern) Atrial enlargement Systolic dysfunction in advanced stage Pericardial effusion	Impaired LV strain Relative apical sparing pattern on longitudinal strain imaging
Sarcoidosis	Conduction abnormalities CCF SCD	Basal Interventricular septal thinning Regional wall motion abnormalities not associated with coronary artery distribution LV systolic and diastolic dysfunction	Impaired LV strain not associated with coronary artery distribution (no 'typical' pattern observed)
Anderson-Fabry disease	Unexplained left ventricular hypertrophy CCF Conduction abnormalities	Increased wall thickness Abnormal diastology	Impaired LV strain Regional strain abnormality in the basal inferolateral region

Abbreviations: LV, left ventricular; CCF, congestive cardiac failure; SCD, sudden cardiac death; LVH, left ventricular hypertrophy.

and portends a poor prognosis. However, myocardial deformation imaging such as TDI and speckle tracking strain are able to detect systolic impairment prior to overt dysfunction. Koyama et al. demonstrated reduced TDI systolic mitral annular velocities (S') in patients with cardiac amyloid and preserved LV systolic function compared to patients with non-cardiac amyloid [18]. There was, however, no difference in the S' between the heart failure and non-heart failure cardiac amyloid patients, indicating that abnormalities in the systolic TDI velocities occur early in the disease process and prior to overt heart failure. Echocardiographic strain studies have shown subtle impairment even early in the course of the disease [19].

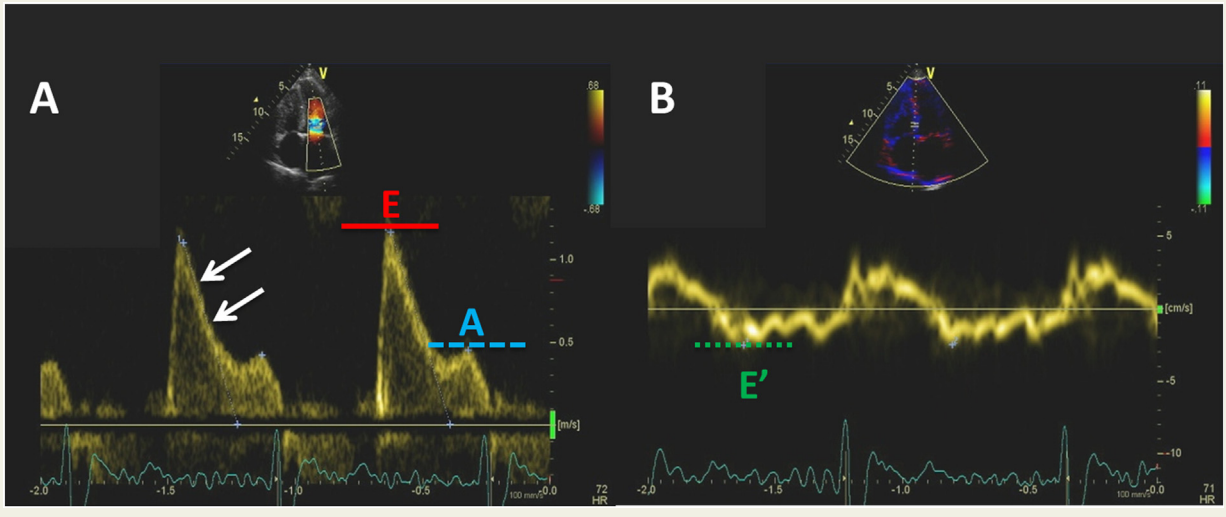

Figure 2 Spectral Doppler of mitral inflow of the same patient with cardiac amyloidosis as seen in Figure 1A demonstrating shortened deceleration time (DT) (white arrows) and increased E:A ratio (red and blue lines), suggestive of restrictive physiology (A) and the corresponding tissue Doppler recording at mitral septal annulus of the same patient demonstrating significantly reduced E' velocity (green line) and elevated E/E' corresponding to pronounced reduction in myocardial longitudinal function and elevated left sided filling pressures, respectively (B).

Moreover, in patients with wild type ATTR amyloidosis, the mitral annular plane systolic excursion (MAPSE) was a predictor of survival in the total cohort regardless of rhythm and LV ejection fraction [20].

Advanced Echocardiographic Imaging

Strain and strain rate are sensitive in assessing early LV systolic dysfunction in amyloid heart disease. It is now well recognised that there is a specific strain 'pattern' demonstrated in cardiac amyloidosis, with a severe impairment of basal longitudinal strain (LS) along with preserved strain in the apical regions [21]. This relative apical sparing pattern observed along with the apical-to-base gradient in longitudinal strain parallels the larger extent of amyloid infiltration at basal level compared to the apex (Figure 3) [22,23]. Moreover, this apical sparing pattern is observed in both AL and ATTR (hereditary and wild type) cardiac amyloid and the basal-to-apical LS abnormalities are similar across both types, reflecting the amyloid burden. A loss of this apical sparing has been shown to predict major adverse cardiac events [23]. Furthermore, Phelan et al. have demonstrated that the pattern of relative apical sparing has a high accuracy to differentiate cardiac amyloidosis from other causes of LVH [24]. In their study, a relative apical LS (defined as average apical LS/[average basal LS + mid-LS]) of 1.0 was 93% sensitive and 82% specific in differentiating cardiac amyloidosis from LVH due to HCM or aortic stenosis.

Additionally, the systolic basal LS on its own has been shown to be a predictor of clinical outcomes. The basal LS is more severely impaired in ATTRwt and AL amyloidosis when compared to ATTRm amyloidosis [25] with a corresponding increase in death and heart failure hospitalisation rates.

Studies have also demonstrated a dissociation between radial and longitudinal systolic strain in patients with cardiac amyloidosis [21]. With this in mind a ratio comparing the LVEF to the global longitudinal strain (GLS), known as Ejection Fraction Strain Ratio (EFSR) has been developed [26]. The EFSR is higher in cardiac amyloid patients (5.7 ± 1.7) in comparison to the other groups (3.7 ± 0.6 for HCM patients and 3.2 ± 0.3 for normal participants). A cut-off of EFSR = 4.1 was able to differentiate cardiac amyloidosis from HCM [27]. In fact, Di Bella et al. found a decrease in LV longitudinal function with increasing myocardial amyloid deposition as detected by ^{99m}Tc-Diphosphonate Imaging in TTR related amyloidosis, with a compensatory increase in both radial and circumferential strain [28].

Right Ventricular Involvement

Amyloid deposition in the right ventricle (RV) occurs later than the LV and portends a worse prognosis. A reduction in the RV free wall systolic tissue velocity and LS is observed in AL amyloid patients compared to normal controls [29]. Furthermore, RV LS is a predictor of all-cause mortality [29,30].

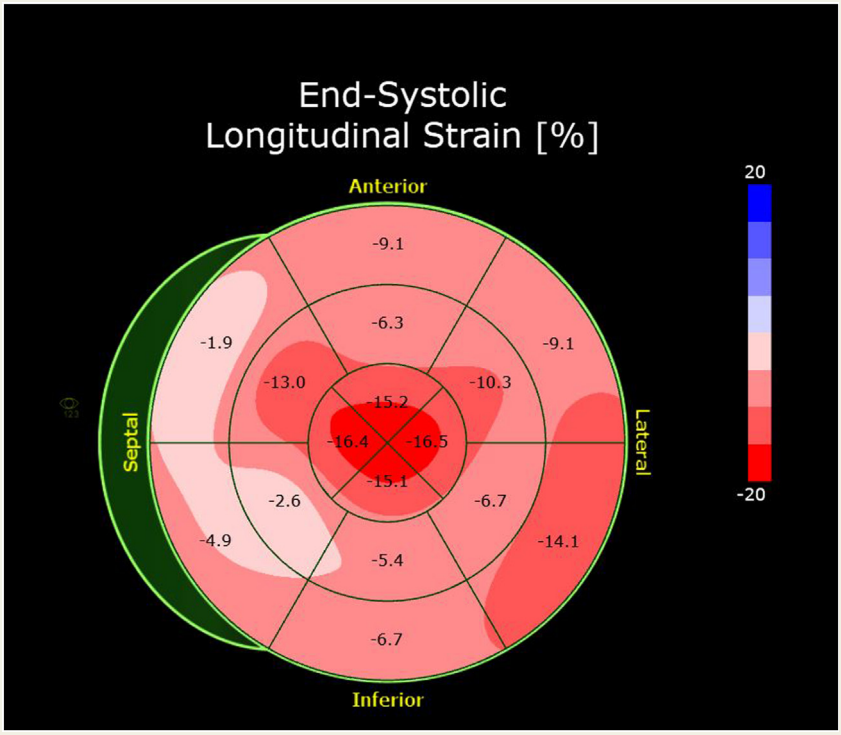

Figure 3 Global strain analysis (using speckle tracking echocardiography) in the same patient with cardiac amyloidosis as Figure 1A and 2 demonstrating reduced regional strain in the basal and mid region of the left ventricle (pale colour), with relative sparing of the apical segments (darker colour).

Other Findings

Amyloid protein deposition may cause the cardiac valves to be thickened with or without significant dysfunction. Atrial involvement can lead to atrial dilatation (Figure 1) and dysfunction. Mohty et al. found that a decrease in 3D derived peak atrial LS is associated with worse outcome, independently of left atrial (LA) volume [31]. Pericardial effusion (Figure 1B) may also be observed, however it is generally only small to moderate in size without haemodynamic compromise.

Sarcoidosis

Pathophysiology

Sarcoidosis is an idiopathic disease associated with the collection and progression of inflammatory cells in the form of granulomas that affect several organs of the body, disrupting normal organ function. It results in non-caseating granulomatous infiltration (the histopathological hallmark of the disease). Although the cause of sarcoidosis is unknown, it is likely that it results from an immunological response to an unidentified antigen in genetically susceptible individuals [32]. There are three sequential stages of the disease—oedema, granuloma formation and fibrosis leading to scar formation. Various organs, including the heart, can be affected and the involvement may be focal or diffuse. Cardiac involvement is generally underdiagnosed with autopsy and advanced imaging studies suggesting cardiac involvement in more than 25% of the patients despite only 5% of patients with systemic sarcoidosis reporting cardiac symptoms [33]. Although rare, cardiac sarcoidosis has significant morbidity and mortality, with mortality rates of up to 60% reported in some registries [34]. Often the first symptom of cardiac sarcoidosis can be malignant arrhythmias resulting in sudden cardiac death (SCD). Symptoms have been related to the degree and location of granuloma formation and subsequent scarring, and can range from no symptoms to severe heart failure. Sarcoidosis can produce granulomatous inflammation in any area of the heart, including the endocardium, myocardium, pericardium, conduction system, coronary arteries, and vena cava. Most research has focussed on cardiac findings in patients with known extra-cardiac sarcoidosis, therefore very little is known about patients with isolated cardiac sarcoidosis.

Cardiac sarcoidosis is a condition with a poor prognosis [35]. Cardiac death is generally due to heart failure or SCD [35]. Cardiac sarcoid is difficult to diagnose due to the focal nature of the disease with endocardial biopsy findings only 20–30% sensitive for positive diagnosis [36]. Several diagnostic criteria have been proposed for the diagnosis of cardiac sarcoidosis, including the Japanese Ministry of Health and Welfare (JMHW) criteria (originally published in 1993 and modified in 2006) and the Heart Rhythm Society (HRS) 2014 Expert Consensus Statement [37]. Due to the rarity of the disease none of the diagnostic criteria are supported by randomised data or prospective studies.

Two-Dimensional Echocardiography

Echocardiography serves an important role as the initial imaging modality in suspected or known cardiac sarcoidosis. Any abnormalities depend on the extent of myocardial involvement and may be absent in many patients [38]. There may be global hypokinesia of one or both ventricles or a regional pattern of dysfunction depending upon the extent of myocardial involvement (Figure 4). In patients with dilated cardiomyopathy the presence of basal interventricular septal thinning is suggestive of cardiac sarcoid [39]. Other more rare findings include LV wall thickening, aneurysms and diastolic dysfunction, although these abnormalities are variable and are only seen in 14 to 67% of patients with cardiac sarcoidosis [40–42]. The published diagnostic echocardiography criteria include basal thinning of the interventricular

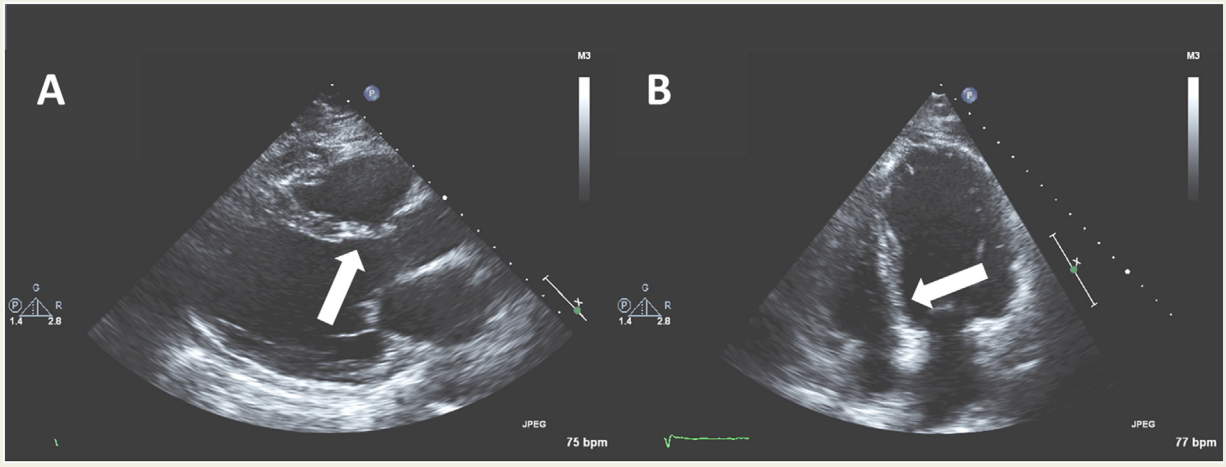

Figure 4 A parasternal long axis (A) and apical four-chamber image of a patient with late stage cardiac sarcoidosis (B). Note the thinning of the basal interventricular septum (arrow).

septum, reduced LVEF < 50%, wall motion abnormalities, wall thickening or thinning outside of a coronary distribution pattern and LV dilatation.

Whilst diastolic dysfunction is invariably present in cardiac sarcoid it is not a specific sign of cardiac involvement [43]. Generally standard echocardiography abnormalities are variable and non-specific. Any abnormalities considered cardiac sarcoid-specific detected on echocardiography have been shown to have 62% sensitivity but only 29% specificity for confirmed cardiac sarcoidosis [44]. Only 25% of patients with cardiovascular magnetic resonance (CMR) or 18F-FDG-PET evidence of cardiac sarcoid had 'typical' abnormalities in their echocardiogram [38]. Notwithstanding this, an abnormal echocardiographic result can assist in suggesting the presence of cardiac sarcoid. A reduction in LVEF predicts mortality in patients with cardiac sarcoid [41,45]. Moreover, corticosteroid treatment for patients has been shown to be more effective prior to reduction in LVEF, however it was the New York Heart Association (NYHA) symptomatic class that was the strongest predictor of mortality in this study [45]. Myocardial deformation imaging in the form of LS, has been demonstrated as a better assessment of cardiac involvement in sarcoidosis and shows promise in diagnosis and prognosis.

Advanced Echocardiographic Imaging

Global longitudinal strain has been shown to be reduced in patients with extra-cardiac sarcoidosis but without overt evidence of cardiac involvement, indicating pre-clinical cardiac involvement prior to any reduction in LVEF or other ECG/echocardiographic abnormalities [46,47] (Figure 5). Moreover, this reduction in GLS has also been associated with poorer outcomes, including all-cause mortality, heart failure hospitalisation and malignant ventricular arrhythmias [46–49]. Furthermore, GLS is able to differentiate between patients with extra-cardiac ($-19.6 \pm 1.9\%$) and cardiac sarcoid ($-14.7 \pm 2.4\%$) with virtually no overlap between the two groups [50]. Reduced GLS was found to correlate with the presence and extent of CMR late gadolinium enhancement (LGE) in the cardiac sarcoid patients [50] (Figure 6), indicating that this represents both oedema and replacement fibrosis. Three-dimensional derived radial strain was found to differentiate cardiac sarcoid vs dilated cardiomyopathy in one study [51], however other studies found that only longitudinal and circumferential strain could do this [52]. Furthermore, a study looking at multiple strain measurements in all cardiac chambers in patients with diagnosed cardiac sarcoidosis found that GLS, LV radial and circumferential strain, LV twist and untwist as well as RV GLS and LA and RA reservoir functions were significantly impaired in patients compared with controls [53]. Although more research is required, speckle tracking strain shows promise in detection of cardiac sarcoidosis, particularly for patients who do not have access to or have a contraindication to CMR or positron emission tomography (PET).

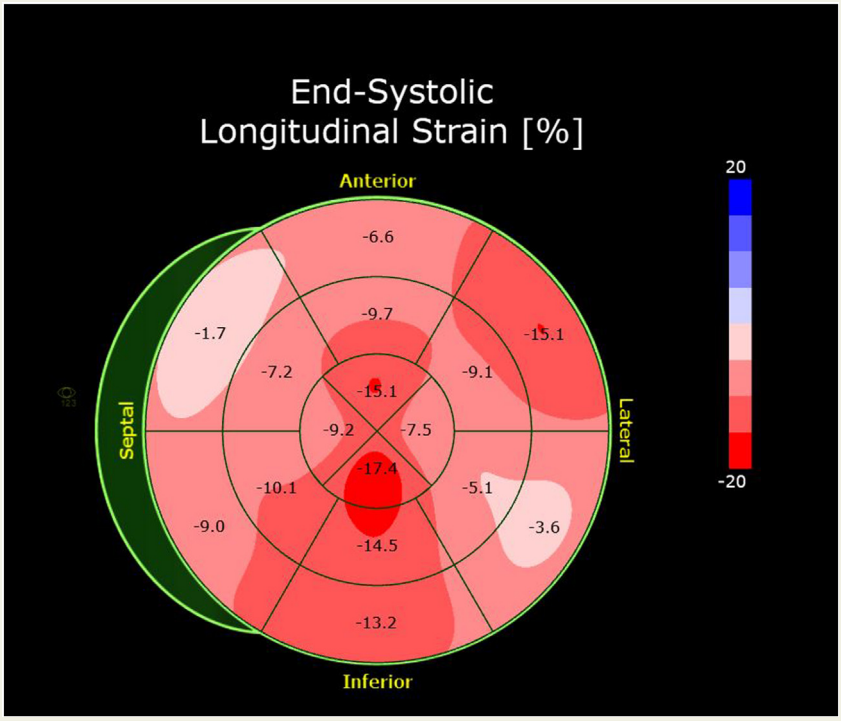

Figure 5 Global strain analysis (using speckle tracking echocardiography) in the same patient with cardiac sarcoidosis seen in Figure 4 demonstrating reduced global longitudinal strain (GLS) and regional strain pattern that does not correspond to coronary artery distribution.

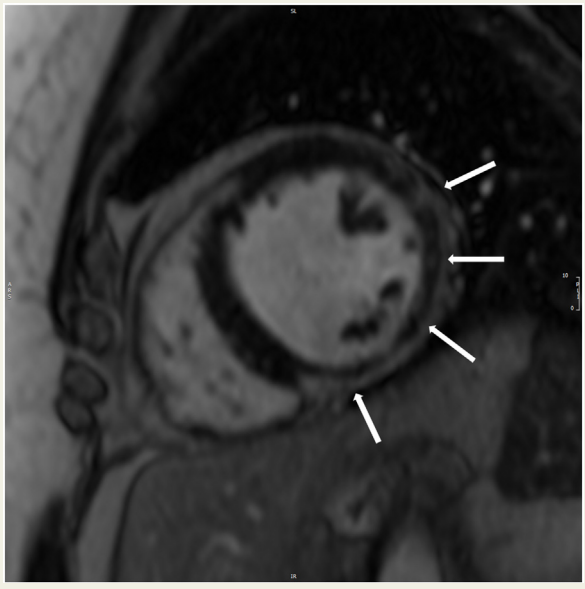

Figure 6 Cardiac magnetic resonance late gadolinium enhancement imaging of the same patient with cardiac sarcoid seen in Figures. 4 and 5. Note the patchy appearance of the late gadolinium enhancement (white arrows) that does not correspond to coronary artery distribution.

Fabry Disease

Pathophysiology

Anderson-Fabry disease (AFD) is a rare X-linked inherited metabolic disorder, which results in a deficiency or absence of the enzyme ∝- galactosidase leading to the accumulation of glycosphingolipids in various cells and organs including the heart. The deposition of sphingolipids in the vascular endothelium of the heart, kidney, skin, and brain leads to tissue and organ damage and ultimately failure. Cardiac involvement is common [54] and results in LV wall thickening and regional fibrosis [55]. Clinically, patients may present with heart failure and conduction abnormalities which account for the most common cause of death in these patients. However, many patients present with unexplained LVH on routine echocardiography and may remain undiagnosed due to this non-specific finding. The diagnosis is primarily based on direct testing of the ∝- galactosidase level, genetic mapping, and endomyocardial biopsy.

Unlike other infiltrative cardiomyopathies, AFD has the potential of reversibility with treatment by enzyme replacement therapy (ERT) or chaperone therapy, especially if diagnosed early [56]. Whilst still rare, AFD is not as rare as initially thought and may be difficult to distinguish from other forms of infiltrative or hypertrophic cardiomyopathies. Most studies have focussed on males, as they tend to demonstrate the phenotype of LV wall thickening earlier and are thought to have more cardiovascular complications. However, due to the pattern of heredity, over two-thirds of patients with AFD are females and symptoms may range from negligible to severe. Chimenti et al. tested female patients with HCM and discovered that 12% of female patients, in fact, have AFD on myocardial biopsy [55] whereas in a similar population of male patients with HCM the rate was lower at 6.3% [57]. In patients with unexplained LVH, a prevalence of AFD up to 3% has been shown [58]. Autopsy and histopathology studies have demonstrated glycolipid deposition in the LV, RV and LA [59–61].

Two-Dimensional Echocardiography

The main echocardiographic finding in AFD is concentric LV wall thickening usually with preserved systolic function in the early stages of the disease process (Figure 7). As with other infiltrative cardiomyopathies, abnormal diastolic filling patterns may be observed. There may be some thickening of the cardiac valves; however, severe dysfunction is rare.

Left ventricular wall thickening is a more common finding in males than females with AFD [62,63] with males displaying increase LV mass at a younger age then females [63]. The presence of increased LV wall thickening has been associated with more cardiovascular symptoms, arrhythmias and valvular disease in AFD [63]. Right ventricular hypertrophy (RVH) is also seen in AFD patients with varying prevalence between 31–71% [64–66]. The presence of RVH is not gender specific as is the case with LVH, is more frequent with increasing age and the severity is correlated with the severity of co-existing LVH [65]. However, overt RV systolic dysfunction is rare, even in the presence of RVH [64].

Prominent papillary muscles have been observed in patients with AFD. An echocardiographic ratio of papillary muscle size to LV circumference was higher in AFD patients compared to patients with Friedreich ataxia, hypertensive heart disease and cardiac amyloidosis [67]. This prominence of the papillary muscles has been confirmed with CMR in patients with and without LV wall thickening [68].

Diastolic dysfunction is more prevalent in AFD patients with increased LV mass (79% vs 7% without LV wall thickening) [69]. Furthermore, there was decreased LA compliance in patients with AFD compared with normal controls using TDI irrespective of the degree of LV mass [69].

The utility of the binary sign or endocardial 'stripe' as seen in echocardiography has been investigated as a hallmark of the disease. The binary sign is the appearance of a bright, hyper-echogenic region in the LV myocardium adjacent to a relatively low echo intensity region giving a clear black/white interface. Pieroni et al. found a binary sign in 83% of patients with AFD [70] leading to further research by other groups, however all other studies have demonstrated a much lower prevalence of approximately 20% and have noted that the binary sign occurs more frequently in patients with LVH, which may partially account for this discrepancy [71,72].

Advanced Echocardiographic Imaging

Tissue Doppler imaging has been shown to identify early stages of AFD [73]. Weidemann et al. found that TDI strain and strain rate was reduced in AFD patients compared with normal controls. Furthermore, this abnormal strain and strain rate improved with ERT, but only in those without

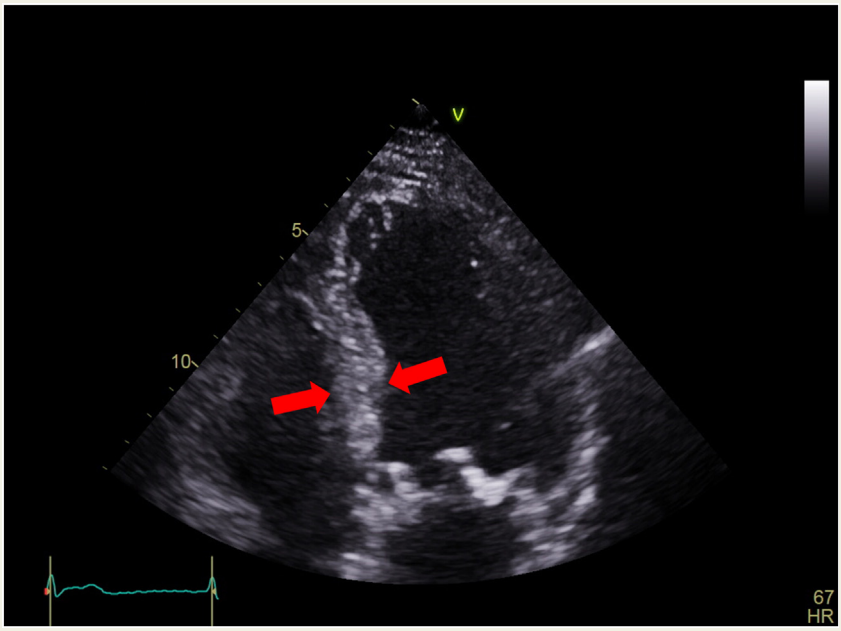

Figure 7 An apical four-chamber image of a patient with genetically diagnosed Anderson-Fabry disease. Note the mild to moderate increase in left ventricular wall thickness (red arrows).

fibrosis as defined by LGE on CMR. This would indicate that improvement in LV subclinical function with ERT is dependent on the degree of fibrosis [56,74]. Zamorano et al. expanded on this, demonstrating that only 33% of patients on ERT, compared with 80% of patients not on ERT, developed abnormal TDI strain parameters [75]. All three studies concluded that TDI strain may be an indicator for AFD cardiomyopathy progression and may assist with the decision for early intervention with ERT.

Speckle tracking strain has more recently been shown to identify AFD, independently of LVH with greater sensitivity and specificity than TDI [76]. Reduced strain and strain rate has been shown to correlate to myocardial regions on CMR with LGE [77]. In fact Niemann et al. demonstrated that the development of myocardial fibrosis as detected by LGE on CMR does not require LV wall thickening in female patients which clearly impacts how the AFD cardiomyopathy should be defined [78]. Furthermore, Saccheri et al. demonstrated that regional longitudinal LV strain was impaired in at least one or more segments in all patients with AFD, regardless of the presence of LV wall thickening [79].

Whilst some studies have demonstrated a decrease in GLS this reduction is generally due to a regional decrease in strain in the basal inferolateral regions (Figure 8) [77,80,81]. Furthermore, the circumferential strain is also reduced in patients with AFD with a decrease in both the global circumferential strain and a loss of the normal base to apex gradient [77,80].

Longitudinal strain has also been reported as being reduced in the RV [82] and LA [82–84] in patients with AFD and may also provide information on cardiac glycolipid accumulation prior to the development of abnormal LV wall thickening and cardiac symptoms.

Haemochromatosis and Iron Overload Cardiomyopathy

There are two main types of iron overload cardiomyopathy (IOC), a familial idiopathic IOC and secondary haemochromatosis from iron overload [85]. This results in excessive iron in various organs, including the heart, liver and pancreas, leading to damage and impairment. Whilst CMR is the gold standard for non-invasive imaging in patients with or with suspected IOC due to its ability to determine myocardial iron content; echocardiography is a valuable tool for screening and follow-up of these patients. Patients may present with different phenotypes depending of the degree of iron overload which may include diastolic dysfunction, increased LV wall thickness, dilated cardiomyopathy and/or restrictive cardiomyopathy [86,87].

Advanced Echocardiographic Imaging

Both speckle tracking strain and TDI have demonstrated regional systolic LV and RV abnormalities in patients with IOC due to beta thalassaemia [88]. Moreover, in asymptomatic patients with IOC due to thalassaemia major, LV rotation was impaired prior to the development of overt systolic dysfunction [89]. Further research is required in IOC to better define the role of echocardiographic myocardial imaging in these patients.

Other Infiltrative Diseases

Other, rarer infiltrative diseases may also present as an LVH phenotype. These include glycogen storage diseases (GSD) which includes Danon disease. These patients clinically present with skeletal myopathy, mental retardation and heart failure.

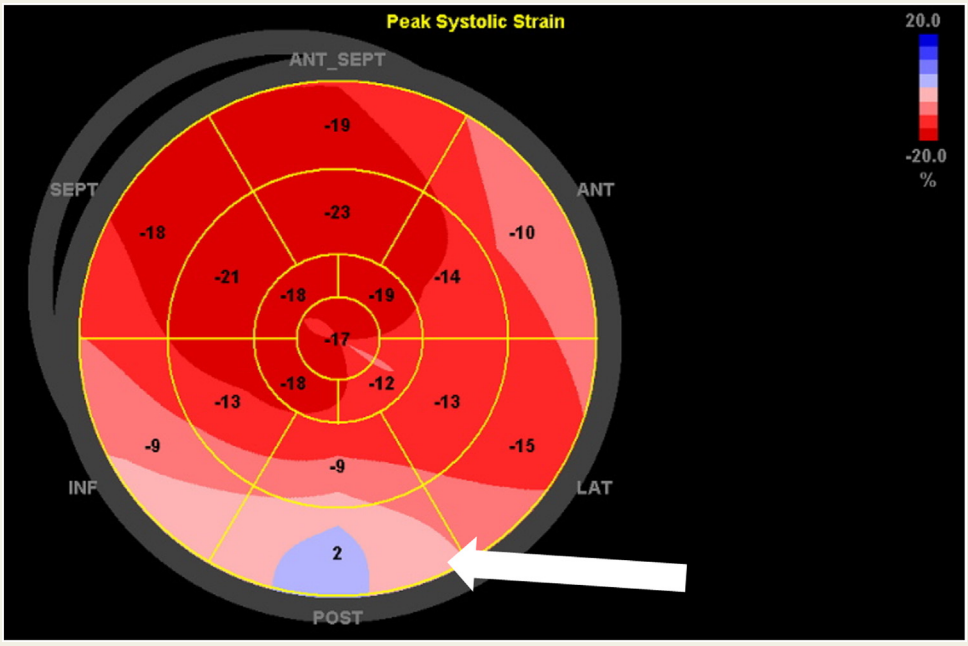

Figure 8 Global strain analysis (using speckle tracking echocardiography) in the same patient as Figure 7 with Anderson-Fabry disease demonstrating reduced regional strain in the basal inferolateral region of the left ventricle (pale red and blue colour, shown with white arrow), with normal regional strain elsewhere (darker colour).

Echocardiography often demonstrates LVH and LV outflow tract obstruction however these findings are not diagnostic.

Friedreich's ataxia is an autosomal recessive disorder. Echocardiography initially demonstrates increased interventricular septal thickness however as the disease progresses the main finding is that of a dilated cardiomyopathy.

Conclusions

Diagnosis of infiltrative cardiomyopathies from a patient presenting with the LVH phenotype is clinically challenging. The addition of advanced myocardial imaging techniques (strain analysis) to standard echocardiography may give a better indication of the disease aetiology and lead to further non-invasive and invasive diagnostic testing. Accurate diagnosis requires integration of clinical assessment, multimodality cardiac imaging and endomyocardial biopsy.

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