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Role of Echocardiography in Research into Neglected Cardiovascular Diseases in Sub-Saharan Africa

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1. Introduction

Echocardiography is a non-invasive imaging technique that has been important in improving the quality and reliability of cardiovascular diagnosis, but access to it remains limited in most developing countries in Africa due to the costs of the technique and the lack of highly specialized personnel to perform it. Training in echocardiography is part of the postgraduate residency training requirements in cardiology in most African countries, despite the absence of an accreditation process such as that designed in Europe and United States of America (Ogah et al., 2006). While the use of transthoracic echocardiography has been spreading slowly around the continent, transesophageal echocardiography is still limited to few centers.

Barriers to obtaining ultrasound services in Sub-Saharan Africa include distance, time, cost of transfers and ultrasound charges (Shah et al., 2008). However, compared to other diagnostic imaging modalities echocardiography is safe, portable and inexpensive, uses simple power supply, and requires minimal maintenance. These characteristics make it the most suitable imaging technique for low-resource areas of Sub-Saharan Africa, where the introduction of smaller and battery-powered ultrasound machines is being used to reach out for people living in remote areas that traditionally did not have access to specialized cardiovascular diagnosis and care.

While witnessing an increasing awareness of the epidemic of cardiovascular disease, encompassing conditions such as hypertension, acute coronary syndrome, stroke and chronic heart failure, Sub-Saharan Africa still has a high burden of several infectious-related cardiovascular diseases and specific conditions such as cardiomyopathies. These neglected cardiovascular diseases include amongst others rheumatic heart disease (RHD) and endomyocardial fibrosis (EMF), both representing a considerable source of burden to the communities and playing a major role in determining premature mortality around the continent. Having recognized the potential of echocardiography as a research tool, African scientists have been using this technique to describe the epidemiology and profile of neglected cardiovascular conditions, as well as to bring new insights into the main causes of heart failure in both pediatric and adult populations (Mocumbi et al., 2008; Sani et al., 2007; Jaiyesimi & Antia, 1981a, b; Marijon et al., 2007; Adesanya 1979).

RHD and EMF have been the subject of community- and hospital-based research using echocardiography. This has resulted in an increase in the number of publications from Africa in indexed medical journals during the last decade. However, the increase is far from the desirable as the number of epidemiological and clinical studies using echocardiography augmented from 6 to 15 for RHD and from 2 to 4 for EMF (Figure 1).

In this chapter we review the recent use of transthoracic echocardiography worldwide for advancing knowledge about the pathogenesis and natural history of RHD and EMF, focusing on the modalities most readily available in low-resource settings, namely bidimensional, M-mode, pulsed and continuous Doppler. Finally, we discuss the specific role of echocardiography in fostering research into these two endemic diseases in Africa, and present the current challenges and opportunities of the use of this technique in Sub-Saharan Africa.

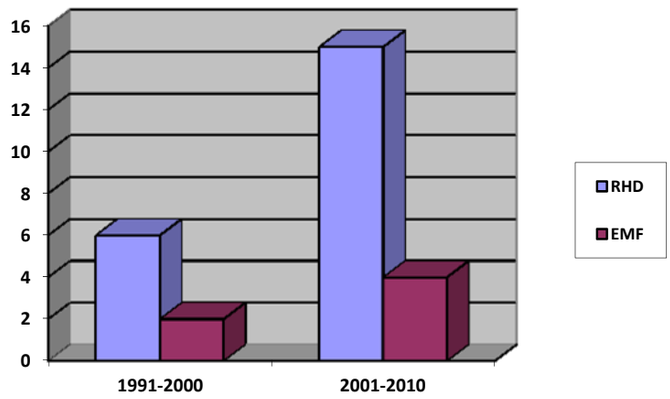

Fig. 1. Number of publications in indexed journals that reported hospital or community-based epidemiological and clinical studies using echocardiographic diagnosis for Rheumatic Heart Disease (RHD) and Endomyocardial Fibrosis (EMF) in the last two decades in Africa.

2. Endomyocardial fibrosis

EMF is a restrictive cardiomyopathy of unknown etiology characterised by progressive fibrous thickening of the ventricular endocardium, leading to restrictive physiology associated with atrioventricular valve dysfunction. Most of our knowledge of this condition comes from hospital-based studies in endemic areas of Uganda, Cote d'Ivoire, Nigeria, India and Brazil. Data on its exact epidemiology are scarce, but variations in geographical and ethnic distribution have been reported, stimulating the search for both environmental factors and genetic factors.

EMF is thought to be the commonest restrictive cardiomyopathy worldwide (Somers, 1990), affecting mainly children and adolescents of low-income communities from tropical regions of Africa, Asia and South America. Established and advanced disease can be easily diagnosed by clinical examination in endemic areas, but the finding of relatively asymptomatic individuals who present important echocardiographic abnormalities is not rare (Mocumbi et al., 2008; Salemi et al., 2005). The characterisation of early stages of the

disease has not been systematically done, leading to major gaps in our knowledge of its pathogenesis and natural history.

The use of echocardiography for diagnosis of EMF, started almost half a century ago, has contributed to characterization of the disease and better understanding of its pathophysiology, resulting in improvements in management and prognosis. Several authors from different parts of the world have described the clinical and echocardiographic findings in EMF (Acquatella et al., 1979; Gonzalez-Lavin et al., 1982; Vijayaraghavan et al., 1983; Okereke et al., 1991; Rashwan et al.,1995), and more recently there have been attempts to use this technique for understanding its epidemiology (Mocumbi et al., 2008) as well define prognostic criteria prior to surgery (Mady et al., 2004).

2.1 Echocardiographic features

The hallmark of established EMF is the presence of thickened endocardium, ventricular obliteration and dilated atria. The typical image of restrictive cardiomyopathy is that of inversion of the size of heart cavities with small obliterated ventricles and dilated atria (Hassan et al., 2005; Berensztein et al., 2000). The wide spectrum of distribution and severity of the fibrotic lesions, as well as the changes in heart shape and distortion mandate a careful and comprehensive echocardiographic evaluation of each patient, using the usual and less conventional views.

The most characteristic echocardiographic features of EMF are large endocardial plaques, patchy endocardial thickening, obliteration of ventricular apices or valve recesses, ventricular and atrial thrombi, ventricular cavity volume reduction, enlarged atrium, restricted mobility of the atrioventricular valve leaflets, fusion of the papillary muscles to the wall and abnormalities of the ventricular regional wall motion (Okereke et al., 1991; Mady et al., 2005; Hassan et al., 2005; Berensztein et al., 2000). Less specific echocardiographic abnormalities include diffuse atrioventricular valve leaflet thickening, enhanced echodensity of the moderator band or trabeculae, abnormal movement of the interventricular septum and/or posterior LV wall, and presence of thickened left ventricular "false tendon" (Mocumbi et al., 2008). Moderate to massive pericardial effusion is a frequent finding in both left and right forms of EMF (George et al., 1982; Lowenthal & Teeger, 2000). Occasionally, endocardial calcification may be seen in the ventricles (Lowenthal & Teeger, 2000; Morrone et al., 1996; Trigo et al., 2010).

The pattern of distribution of the morphological and hemodynamic abnormalities allows the classification of EMF in different forms according to exclusive or predominant distribution of structural lesions in one or both sides of the heart. Hence the description of right, left and bilateral EMF.

2.1.1 Endocardial thickening

Thickening of the endocardium is the most characteristic feature of established EMF (Ojereke et al., 1991; Connor et al., 1967). It may consist of large plaques affecting one or both ventricles, as well as patchy endocardial thickening evenly distributed in the ventricular walls or affecting exclusively the interventricular septum. These abnormalities can be assessed by both bidimensional and M-mode. The most striking and constant

features are increased amplitude echos at the right ventricular trabecular region, left ventricular apex and the region of the posterior mitral valve leaflet (Vijayaraghavan et al., 1983).

2.1.2 Ventricular thrombosis

Spontaneous contrast and ventricular thrombi are frequently seen in normally contracting ventricles in early stages of EMF, as part of the initial process that leads to endocardial fibrosis (Berensztein et al., 2000). The presence of ventricular thrombi, calcified or not, is a major determinant of management and prognosis.

2.1.3 Ventricular obliteration

This characteristic abnormality of EMF consists in partial or complete exclusion of a portion of the ventricle from the circulation (Figure 2). In right EMF the trabecular portion of the ventricle is separated from the remaining cavity by a large fibrotic endocardial plaque, underneath which there is myocardium of apparently normal texture (Trigo et al., 2010). Left ventricular obliteration affects both the apex and the recesses of the posterior mitral valve leaflet excluding these parts from the ventricular cavity (Berensztein et al., 2000). It is thought that obliteration by thrombi and subsequent scarring fibrosis are the mechanisms involved (Connor et al., 1967), both leading to reduction of the diastolic properties of the ventricles. Also, thrombi may involve the sub-valvar apparatus, leading to scarring and fusion of leaflets to the ventricular wall, therefore resulting in leaflet movement restriction and severe atrioventricular valve dysfunction.

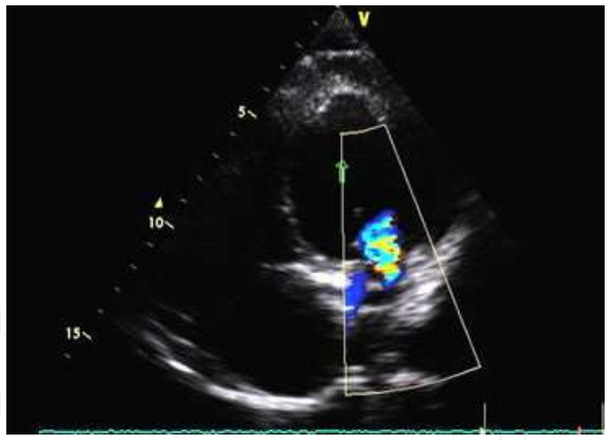

Fig. 2. Left-sided EMF with obliteration and endocardial thickening at the ventricular apex. The atypical mitral regurgitation jet is frequent in moderate disease.

With progression of the disease to more advanced stages cavity retraction occurs with further reduction of the effective ventricular cavity volume, seemingly due to progressive organization and fibrosis of the mural thrombi and adjacent endocardium. Particularly in the right ventricle, this process is associated with pulling of the wall by the retracted tricuspid valve apparatus, resulting in the distinctive finding of advanced right-sided EMF called "apical notch" (Figure 3). The apical notch gives the heart a shape that resembles the map of Africa, hence the designation "Heart of Africa" (Davies, 1960). On the left side the

ventricular apex is never retracted; it becomes thicker leading to considerable reduction of the longitudinal diameter of the ventricle, resulting in a spherical ventricular shape.

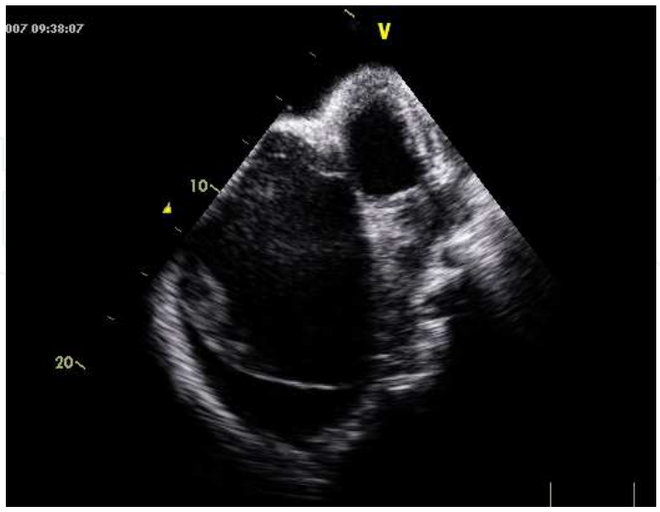

Fig. 3. Transthoracic image obtained during field research using a portable ultrasound machine showing retraction of the trabecular portion of the right ventricle with reduction of cavity size and aneurysmal right atrium in which a thrombus can be seen.

2.1.4 Diffuse leaflet thickening

Diffuse thickening of the atrioventricular valve leaflets occurs in some patients with EMF. This pattern helps differentiating left-sided EMF with predominant valvular lesion from chronic rheumatic disease of the mitral valve in endemic areas for both diseases. In chronic rheumatic mitral regurgitation leaflet thickening is usually restricted to or exaggerated at the tip of the valve, extends to the chordae, and is never associated to obliteration of the contralateral ventricle (Saraiva et al., 1999; Metras et al., 1983).

2.1.5 Septal motion abnormalities

The restricted movement of the fibrotic left ventricular apex and its obliteration are accompanied by compensatory contractile mechanism that results in exaggerated and distinctive motion of the basal portion of the left ventricle, the so-called Merlon sign (Vijayaraghavan et al., 1983; Berensztein et al., 2000). On M-mode the interventricular septum has a rapid anterior movement in early diastole (Acquatella et al., 1979) assuming an M-shaped movement. In some patients the septal motion may be reversed (paradoxical septal movement).

2.1.6 Restrictive filling pattern

A tall E wave with E/A ratio greater than 2, deceleration time less than 120ms and isovolumic relaxation time inferior to 160ms are the criteria used to define the presence of ventricular restrictive filling pattern. This evaluation is usually compromised by the presence of severe mitral regurgitation. The brisk early diastolic filling with poor filling in the remainder of diastole, the absence of respiratory changes, the presence of normal

pericardium and the usual association to pericardial effusion, enable distinction from constrictive pericarditis.

2.1.7 Atrioventricular valve regurgitation

Mild mitral regurgitation is found in initial stages of left EMF. The jet is atypical and seems to start inside the ventricular cavity (figure 2). In severe left EMF thickening and scarring of the valve leaflets and the mitral valve apparatus lead to severe mitral regurgitation that is usually eccentric, due mainly to restricted movement of the posterior leaflet. The regurgitation has a high velocity jet directed to the posterior wall of the left atrium, reaching the pulmonary veins in most cases (Figure 4).

The tricuspid valve apparatus is distorted in EMF with restricted movement of the leaflets in early phases of the disease. In severe right EMF there is massive tricuspid annulus dilatation and non-turbulent low velocity regurgitant jet, witnessing the absence of pressure gradient between the two right cavities. In these cases the right filling pressures are very high, leading to severe dilatation of the cava system and reflux from the right atrium towards the supra-hepatic veins, a phenomenon easily accessed using pulsed and color Doppler.

2.1.8 Atrial dilatation

Both the restriction to ventricular filling and the atrioventricular valve regurgitation result in increase in atrial pressure, leading to progressive atrial dilatation. The consequence is further increase in atrioventricular valve annulus dilatation perpetuating the cycle and being responsible for the frequent finding of aneurysmal atria (Hassan et al., 2005; Berensztein et al., 2000). Annular dilatation, leaflet retraction and fibrosis of the sub-valvar apparatus lead to non-coaptation and free tricuspid valve regurgitation (Okereke et al., 1991), this later seen as a non-turbulent low velocity jet on color Doppler.

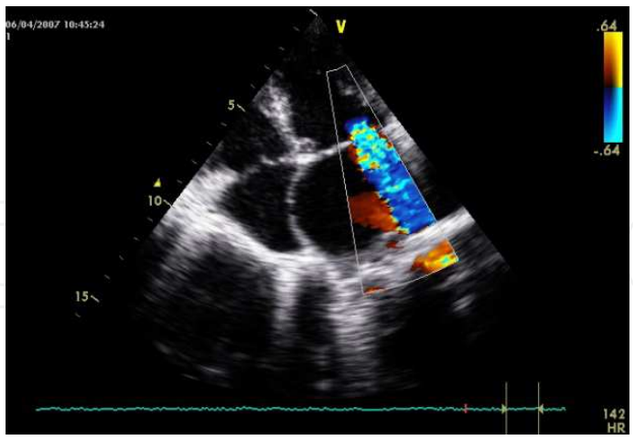

Fig. 4. Mitral regurgitation and left atrial dilatation on a patient with left EMF evaluated using portable ultrasound machine during a community-based study.

2.1.9 Semilunar valve abnormalities

The pulmonary valve is usually spared from structural abnormalities but there is often pulmonary regurgitation that allows estimation of the mean and diastolic pulmonary

pressures. In severe cases due to the lack of pressure gradient between the atrium, the ventricle and the pulmonary artery, there is often diastolic opening of the pulmonary valve. The aortic valve is almost always normal, but in few cases there may be thickening of the cusps.

2.1.10 Abnormalities of the left side of the heart

Early left-sided EMF is characterized by thickening of the mitral leaflets, presence of apical thrombus, and/or obliteration of the apex or the recess between the posterior leaflet and the posterior wall. Thrombi may be found in the sub-valvar apparatus involving the free edges of both papillary muscles or in the apex. There is moderate left atrial dilatation but the valve remains non-regurgitant. The flow across the mitral valve reveals early diastolic filling followed by restriction pattern.

In the established left-sided EMF endocardial thickening is prominent in interventricular septum, the apex and posterior wall behind the recess of the posterior mitral leaflet, the ventricular cavity assumes a spherical shape and there is increased contractility at its basal portion. The left ventricular ejection fraction is usually not calculated due to the presence of mitral regurgitation and left ventricular distortion. The heart distortion and change in the position of the heart in the chest explains the fact that contractility is often graded using a visual scale. In patients without severe distortion of the left ventricular shape and no mitral regurgitation, the LV end-systolic and end-diastolic volumes and ejection fraction can be determined from the apical 4-chamber view according to the modified Simpson's rule or the Teicholz method (Feigenbaum, 1994**)**.

Although in rare patients the mitral valve may be stenotic, most patients present an eccentric mitral regurgitation with signs of passive pulmonary hypertension. The left atrium maximal linear dimensions at the end of left ventricular systole are increased in all plans and, in severe cases the cavity may be aneurysmal. However, there is rarely left atrial thrombus.

Regarding the mitral valve there is leaflet thickening and shortage, leading to non-coaptation and severe mitral regurgitation. The posterior mitral valve leaflet appears to be tethered down to the left ventricular posterior wall, with reduced mobility during diastole. In severe cases the leaflet, its chordae and papillary muscle are completely adherent to the wall leading to massive regurgitation**.**

2.1.11 Abnormalities of the right side of the heart

The initial lesions on the right side consist of thickening of the moderator band. In the longitudinal view of the right ventricle and short axis of the left ventricle at the level of the aorta a stretched moderator band is seen, while in 4 chambers-view the ventricular cavity is separated into two cameras. There may be thickening of the tricuspid leaflets and the analysis of the tricuspid inflow by pulsed Doppler reveals abnormal compliance.

Right ventricular trabecular cavity obliteration is thought to start by separation of the trabecular chamber of the right ventricle from the rest of the cavity, as seen in 4-chambers view (Figure 5). It is usually accompanied by mild to moderate tricuspid regurgitation caused by restriction to the movement of the anterior and septal leaflets of the tricuspid

valve. The leaflets may present attachments to the wall leading to an echocardiographic picture that may mimic "Ebstein Malformation" (Vaidyanathan et al., 2009), namely with dilatation of the tricuspid annulus, tricuspid regurgitation with jet originating from the level of non-cooptation of the leaflets, which is dislocated to the trabecular portion of the ventricle. The right ventricular systolic function, evaluated through a visual semi-quantitative scale using two-dimensional guided M-mode in several incidences (four-chambers, parasternal long axis, parasternal short axis and sub-costal views), is globally normal, but may be reduced when there are large endocardial plaques and cavity retraction.

Advanced right EMF is defined by retraction of the ventricular cavity due to elimination of the trabecular portion of the cavity, resulting in the pathognomonic finding of an "apical notch". The right ventricular outflow tract is dilated and hyperdynamic to compensate the loss of the trabecular portion, and the interventricular septal motion may be reversed.

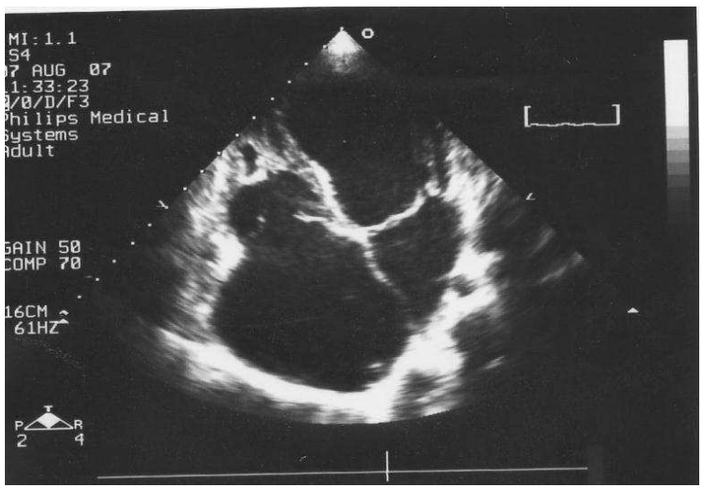

Fig. 5. Right EMF seen in 4-chambers view showing separation of the cavity in two portions, a feature that is characteristic prior to complete obliteration of the trabecular cavity.

Severe tricuspid regurgitation with no turbulence is characteristically associated to restriction of leaflet movements caused by involvement of the papillary muscles in the fibrotic process and to dilatation of the annulus that results from severe right atrial dilatation. At this stage most patients have spontaneous contrast inside the right atrium extending to the inflow tract of RV and also to the inferior vena cava and dilated supra-hepatic veins. Multiple thrombi may be found some moving freely and others attached to the atrial wall. The dilated inferior vena cava and supra-hepatic veins, usually with dynamic echos indicating stasis, do not show the normal respiratory changes, indicating increased systemic venous pressure. Pericardial, pleural and peritoneal effusions are also frequently present in patients in heart failure, best seen in subcostal view.

The colour Doppler is used for semi-quantitative estimation of tricuspid regurgitation severity, taking into account the width and depth of regurgitant jet inside the atrium seen from different views (four-chambers, short-axis and sub-costal). One criteria used to define severe tricuspid regurgitation is the lack of aliasing of the jet and its large width at origin, especially when there is non-coaptation of the tricuspid valve leaflets. The aneurismal right atrium results in heart distortion and compression of the left cavities making it difficult to

evaluate the presence of mitral dysfunction. Abundant pericardial effusion and compression of left cavities compromise an adequate evaluation of the left ventricular function.

The lateral and supero-inferior dimensions of the right atrium are always increased and an aneurysmal atrium is usually found. The high pressure inside the atrial cavity pushes the interatrial septum towards the left side opening the *foramen ovale* in many occasions, and allowing a certain degree of right –to-left shunt that causes mild cyanosis. Compression of the left cavities by the severely dilated atrium and tense right ventricle at the level of the admission chamber may impede adequate ventricular filling as well as mask mitral regurgitation. On M-mode these findings are associated with interventricular paradoxical septal motion and small left ventricular cavity.

2.2 Pathological correlation

Surgery can be used to assess the accuracy of transthoracic echocardiography in determining the severity of EMF. This has been achieved by performing standardized transthoracic echocardiography on EMF patients prior to surgery, followed by detailed intra-operative examination of the abnormalities and histopathological evaluation of tissue obtained from excised biopsies (Mocumbi et al., 2010). In this series of patients from Mozambique the echocardiographic description coincided with the intraoperative findings in more than 80% of patients, the concordance being absolute for the most important pathological lesions of EMF, namely fusion of the posterior papillary muscle and leaflet to the wall, left ventricular apical fibrosis, thickening of the atrioventricular leaflets, right ventricular obliteration, right ventricular retraction and ventricular thrombi. This suggested that transthoracic echocardiography can be used in isolation for diagnosis and surgical management of chronic EMF in low-resource endemic areas.

2.3 Challenges and opportunities

Echocardiography can make a confident non-invasive diagnosis of EMF (Vijayaraghavan et al., 1983; Mocumbi et al., 2010), has been useful in determining patients who can benefit from surgery and allows evaluation of the response to treatment. Access to hand-carried echocardiography battery-operated systems has allowed for the first time the design and implementation of epidemiological research in a remote area in Mozambique. In this community, known to have a high attack rate of the disease from previous hospital-based data (Ferreira et al., 2002), 1063 individuals of all ages were randomly selected and submitted to transthoracic echocardiography using a standardized protocol (Mocumbi et al., 2008). A prevalence of 19.8% was found, with the majority of the individuals being asymptomatic and having mild or moderate disease.

For such disease with so many gaps in knowledge there is need to build regional or continental registries starting with phenotypic characterization of individuals in early stages of EMF through echocardiography, using standardized criteria that can be validated on follow-up studies in several endemic areas. This may contribute to uncover aspects related to its natural history, and constitute cohorts to test differences in genetic and to biological profile between healthy individuals and those affected by the disease in endemic areas. Follow-up of individuals with well-established echocardiographic phenotype may also be important to identify predictors of outcome using different disease management strategies.

3. Rheumatic heart disease

RHD is the most important form of acquired cardiovascular disease in children and adolescents in Africa. It is the only chronic sequelae of rheumatic fever (RF), a systemic disease that results from group A streptococcal infections.

Rheumatic Heart Disease (RHD) is still a major concern in Africa (World Health Organization, 2007) despite the dramatic declines in the incidence and prevalence of this condition that have occurred over the last 150 years in the developed world (Gordis, 1985). It is a disease traditionally associated with poverty and overcrowding, and this decline was achieved through improvement in living conditions and widespread use of penicillin for the treatment of streptococcal pharyngitis. The unacceptably high rates of RF/RHD in Sub-Saharan Africa lead to considerable use of health-care resources and a major impact on the patients, their families and the society as a whole.

Although RHD is still a neglected disease, there has been a new surge on research on this condition. This has been centered in developing countries and those populations within middle- and high-income countries where high burdens of disease still exist. Echocardiography is considered the adequate tool for identifying early stages of heart valve disease (Carapetis & Zuhlke, 2011).

3.1 Echocardiographic diagnosis

Echocardiography is an essential tool in diagnosis and management of RF and RHD. Several structural and hemodynamic abnormalities are important for classifying valve lesions, both in the acute and chronic phases of the disease. Even before the advent of colour Doppler flow imaging several studies had already highlighted the utility of echocardiography for the diagnosis of rheumatic carditis, and emphasized its value in defining the mechanisms of valve disease and heart failure associated with severe attacks of carditis (Vansan et al., 1996; Narula et al., 1999). Colour flow Doppler imaging was then considered a useful method of identifying subclinical mitral and aortic valvar disease at all stages of rheumatic fever when carditis cannot be otherwise detected (Folger et al., 1992). Regarding chronic rheumatic heart disease, echocardiography may be used to track the progression of valve abnormalities and to help determine the time for surgical intervention.

3.1.1 Acute carditis

In acute rheumatic disease Doppler-echocardiography identifies and quantifies valve abnormalities, ventricular dysfunction and pericardial effusion (Narula et al., 1999; Folger et al., 1992). The valve most commonly affected is the mitral, followed by the aortic valve (Folger et al., 1992). In the African context, severe pure rheumatic mitral regurgitation is as prevalent as pure stenosis but has an entirely different time course, surgical anatomy, and relation to disease activity, suggesting a separate pathophysiologic mechanism (Marcus et al., 1994).

The usual features of acute rheumatic valvulitis are annular dilatation, elongation of the chordae to the anterior leaflet, and postero-laterally directed mitral regurgitation jet (Vansan et al., 1996; Narula et al., 1999; Folger et al., 1992). Nodular thickening of valve leaflets also occurs (Vansan et al., 1996), and may represent echocardiographic equivalents of rheumatic

verrucae seen universally at autopsy in patients who died of acute rheumatic fever (Baggenstoos & Titus., 1968) and noted macroscopically at surgery in a substantial proportion of patients subjected to valve surgery during the acute phase (Kinsley et al., 1981). When acute carditis courses with chordal thickening (Vijayalakshmi et al., 2008), it suggests acute rheumatic fever recurrence in patients with established rheumatic heart valve disease. Mild mitral regurgitation present during the acute phase usually resolves weeks to months after. In contrast, patients with moderate-to-severe carditis have persistent mitral and/or aortic regurgitation.

Valve insufficiency due to endocarditis, rather than myocardial dysfunction caused by myocarditis, is the dominant cause of heart failure in acute rheumatic fever, related to ventricular dilatation and/or restriction of leaflet mobility (Vansan et al., 1996). This has been supported by demonstration of the absence of cTnI elevations during rheumatic fever (Kamblock et al., 2003; Essop et al., 1993). The left ventricle is dilated with preserved or increased fractional shortening in most cases, but variable degree of ventricular dysfunction is not rare in the African setting probably due to the high prevalence of predisposing factors such as anemia.

3.1.2 Chronic rheumatic heart disease

Isolated mitral regurgitation or combined mitral and aortic regurgitation are the most common abnormalities found in chronic RHD (Vansan et al., 1996; Folger et al., 1992; Marcus et al., 1994). Several morphological abnormalities have been considered features of chronic mitral RHD namely (a) valve and/or chordal thickening; (b) restrictive leaflet motion due to chordal thickening, shortening or fusion, commissural fusion and leaflet calcification or thickening; and (c) chordal elongation, rupture or prolapse (Marijon et al., 2007; Paar et al., 2010; Namboodiri et al., 2009; Wilkins et al., 1988). In mitral regurgitation the posterior mitral leaflet is shortened and immobile because its submitral complex is also thickened, fused and shortened, resulting in a gap or non-coaptation of the two leaflets in many patients (Okubo et al., 1984). Mitral stenosis occurs when the leaflets of the affected valves become diffusely thickened, with fusion of the commissures and chordae tendineae, as well as increased echodensity of the mitral valve that may signify calcification. However, valvular calcification is rare in juvenile rheumatic heart disease, frequently seen in Africa (Yuko-Jowi et al., 2005). Left atrial thrombus is a common finding in mitral stenosis.

There are few studies of characterization of aortic valve abnormalities in rheumatic heart disease. Rheumatic aortic valve disease is usually diagnosed in combination with mitral disease, and after exclusion of congenital disease, mainly bicuspid aortic valve. Echocardiographic diagnosis has been based on morphological changes such as the presence of thickened leaflets, rolled leaflet edges, coaptation defect, deformed leaflets, commissural fusion, leaflet retraction, abnormal leaflet mobility, systolic doming of leaflet, hyperechogenicity of leaflet edges and prolapse are used (Marijon et al., 2007; Paar et al., 2010). For community studies a more accurate case-definition and assessment of severity is needed since follow up of patients with RHD shows that those with no or mild aortic valve disease at the time of mitral valve intervention rarely develop severe aortic valve disease, and seldom require aortic valve surgery over the long-term follow up, while the presence of mild aortic stenosis at baseline is predictive of relatively more rapid progression in the minority of cases (Namboodiri et al., 2009).

Two-dimensional echocardiographic criteria of organic rheumatic tricuspid valve disease include thickened leaflets with restriction in motion, diastolic doming, and encroachment of the leaflet tips on the wall of the ventricular inlet (Guyer et al., 1984; Meira et al., 2006). Since pulmonary hypertension is predominant in mitral valve disease, there is commonly annulus dilatation that results from right cavities dilatation and leads to tricuspid regurgitation. This must be differentiated from organic valve disease, which has usually morphological changes similar to that described above for the mitral valve.

3.1.3 Major valvular abnormalities

3.1.3.1 Restrictive or excessive leaflet motion

Restrictive leaflet motion is evident in most patients with established RHD requiring surgery MR (Chavaud et al., 2001), nearly one third of patients with acute RF (Vijayalakshmi et al., 2008; Marcus et al., 1989) and all those with rheumatic mitral stenosis (Wilkins et al., 1988; Naito et al., 1980; Prasad & Radhakrishnan, 1992; Van der Bel-Kahn & Becker, 1986). It is caused by chordal shortening, thickening and fusion, commissural fusion, and leaflet calcification and thickening (Chavaud et al., 2001; Van der Bel-Kahn & Becker, 1986; Carpentier, 1983). The terms used to characterize the abnormal and restricted mobility of the mitral leaflets include elbow, dog-leg and hockey-stick deformity (Paar et al., 2010; Webb et al., 2009; Steer et al., 2009; Reeves et al., 2011; Carapetis et al., 2008) (Figure 6).

Chordal elongation and rupture of the primary chords are the mechanisms responsible for mitral valve prolapse in RHD. These changes must be carefully looked for as they influence the surgical management (Chavaud et al., 2001; Marcus et al., 1989; Carpentier, 1983).

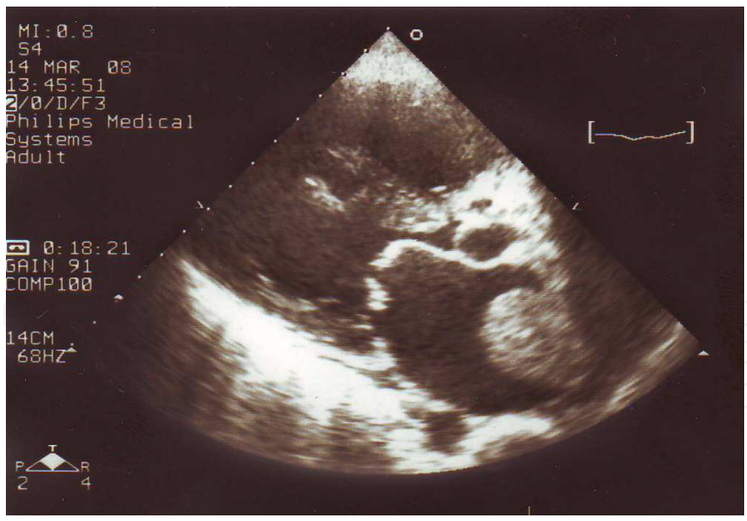

Fig. 6. Long axis parasternal view of a patient with mitral stenosis due to RHD showing thickening of the mitral and aortic valves, as well as restricted motion of the mitral leaflets. Notice a large left atrial thrombus.

3.1.3.2 Valve thickening

The rheumatic valve is fibrotic and firm, with thickening and fusion of leaflets and commissures (Van der Bel-Kahn & Becker, 1986), mostly seen in stenotic valves. Thickening

of the mitral valve, especially the anterior mitral leaflet, appears to be a consistent feature of RHD (Figure 6), which can be adequately assessed in the parasternal long axial view where the anterior mitral valve because the ultrasound beam is perpendicular to the leaflet. Regarding the aortic valve both the parasternal and subcostal views allow adequate evaluation. Valve thickness of both mitral and aortic valves increases with age, based on an autopsy study (Sahsakul et al., 1988). However, in populations where RHD is prevalent there are very few additional conditions that are associated with increased thickness of the mitral valve in the age groups affected by RHVD, except for endemic areas for both RHD and EMF (Mocumbi et al., 2008).

3.2 Recent advances and research needs

The knowledge gap regarding epidemiology, pathogenesis and natural history of RF/RHD in Africa is related to several factors. First, group A streptococcal infections that precede RHD are subclinical, and most of the clinical cases are of a minor nature compared with other diseases afflicting children in this setting. Secondly, RF/RHD is not notifiable in most African countries and its impact is underestimated. Thirdly, many children are not brought to medical care when they complain of sore throat or a skin lesion. Finally, the diagnosis of rheumatic fever/carditis, requires clinical sophistication that exceeds the expertise available at many local hospitals that are manned by nurses or trained health care workers.

The echocardiographic diagnosis of RHD is not standardized and there are few studies looking systematically at criteria for diagnosing valve disease using modern echocardiographic tools. However, due to the persisting burden of the disease in some areas of the world echocardiography has been used in community studies in Mozambique and Cambodia (Marijon et al., 2007), Tonga (Carapetis et al., 2008), Nicaragua (Paar et al., 2010), Fiji (Steer et al., 2009; Reeves et al., 2011), Kenya (Anabwani et al., 1996), India (Thakur et al., 1996; Bhaya et al., 2010), Pakistan (Sadiq et al., 2009; Rizvi et al., 2004) and China (Zhimin 2006). These studies applied different inclusion and diagnostic criteria, raising the issue about the need for standardization of the definition of rheumatic heart valve disease by echocardiography.

Patients from African series present severe abnormalities at early ages (Sliwa et al., 2010; Marijon et al., 2008). Because rheumatic heart valve disease has an initial latent stage that can be detected by appropriate tests (among which echocardiography), has adequate affordable therapy, and may have its prognosis improved by interventions at an early stage, it should be the target of screening as a tool of preventive medicine.

3.2.1 Developing guidelines for echocardiographic screening

Early detection of “subclinical” rheumatic valve disease by echocardiography is vital, as it presents an opportunity for case detection at a time when prophylactic penicillin – to prevent recurrent episodes – can stop progression to important valve disease. This is very important in Africa, where most new patients admitted to hospitals have already advanced and complicated rheumatic valvular lesions (Sliwa et al., 2010), often resulting in heart failure and/or arrhythmia that cannot be adequately managed due to unavailability of open heart surgery. A current challenge for African scientists is therefore to make echocardiographic screening reliable, affordable and feasible in low-resource settings, using

diagnostic criteria that are clear, simple, robust and reproducible. This would allow their incorporation in protocols for performing, reading and interpreting echocardiograms, in order to avoid over- and under-diagnosis.

Researchers from Africa have been involved in continental efforts to assess the epidemiology of RHD using echocardiography. This has started with the "**A**wareness, **S**urveillance, **A**dvocacy and **P**revention Strategy" lounged by the Pan African Society of Cardiology in 2005, which aims at reducing the burden of RF/RHD in the continent (Mayosi et al., 2006). More recently African researchers have been taking part in a global initiative aiming at standardization of echocardiographic screening that is led by the World Heart Federation (World Heart Federation, 2011).

3.2.2 Disseminating echocardiographic screening

The use of highly trained specialists for large scale echocardiographic screening of RHD in endemic areas of Africa is not practical (Figure 7) but the diffusion of ultrasound technology to nontraditional users has been rapid and far-reaching in the last years (Shah et al., 2008). Experiences for dissemination of echocardiography to non-traditional users in Rwanda and Tanzania have been designed aiming at the evaluation of pericardial effusion, rheumatic heart disease, congestive heart failure and estimation of global left ventricular function (Shah et al., 2008; Adler et al., 2008). The impact of this technology diffusion is being quantified, but early results show that ultrasound is a teachable skill, leads to accuracy of diagnosis, helps in management of common cardiovascular conditions, and improves professional satisfaction of local health providers (Shah et al., 2009). The role of task-shifting inside the health systems to allow non-cardiologists to perform echocardiographic screening for RHD must therefore be studied. However, there is need to carefully choose the health providers to be trained and implement measures of quality assessment and sustainability.

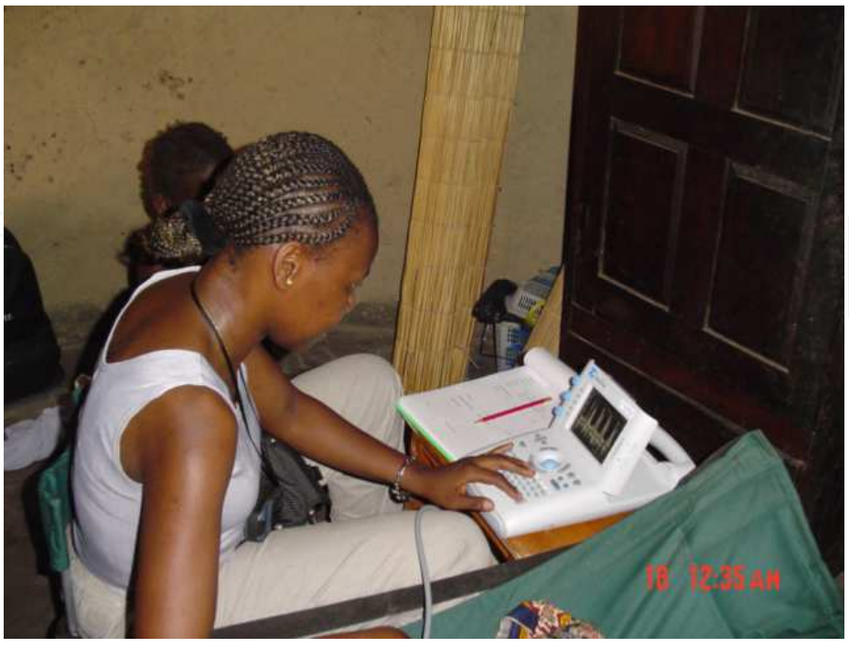

Fig. 7. Photograph of a researcher performing echocardiography in an Africa rural setting.

3.2.3 Definition of curricula and selection of ultrasound machines

Considering the unique pattern of cardiovascular disease in Africa, there is need for designing *curricula* and training materials tailored to the local needs, taking into consideration the differential diagnosis with conditions such as cardiomyopathy, which are also highly prevalent in the continent. In the particular conditions of health care provision in Africa the choice of the ultrasound machines is also of paramount importance. Machine specificities that are suitable for the African environment include durability, portability, battery-operated machines and high two-dimensional image quality. In portable machines a storage bag with room for gel, towels, probe covers and cleaning supplies is recommended (Shah et al., 2008).

4. Conclusions

There has been an increase in scientific publications from African researchers and institutions with the dissemination of echocardiography. Echocardiographic-driven research into neglected diseases such as endomyocardial fibrosis and rheumatic heart disease have contributed to uncover epidemiology and clinical profile of these conditions in the continent, confirming the role for this imaging technique in fostering research and improving quality of care in cardiovascular diseases in resource-deprived areas of Africa. Echocardiography may also help to quantify the health impact of certain neglected cardiovascular diseases in Africa, as well as assist in design and implementation of programs for surveillance, prevention and control of such conditions.

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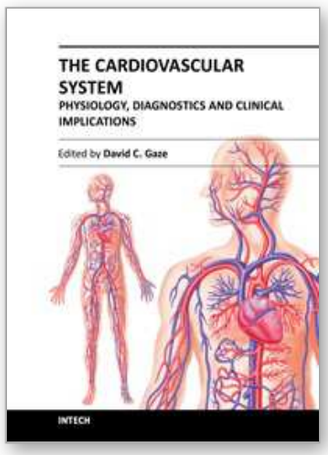

The Cardiovascular System - Physiology, Diagnostics and Clinical Implications

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The cardiovascular system includes the heart located centrally in the thorax and the vessels of the body which carry blood. The cardiovascular (or circulatory) system supplies oxygen from inspired air, via the lungs to the tissues around the body. It is also responsible for the removal of the waste product, carbon dioxide via air expired from the lungs. The cardiovascular system also transports nutrients such as electrolytes, amino acids, enzymes, hormones which are integral to cellular respiration, metabolism and immunity. This book is not meant to be an all encompassing text on cardiovascular physiology and pathology rather a selection of chapters from experts in the field who describe recent advances in basic and clinical sciences. As such, the text is divided into three main sections: Cardiovascular Physiology, Cardiovascular Diagnostics and lastly, Clinical Impact of Cardiovascular Physiology and Pathophysiology.

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