

Echocardiographic Findings in HIV Disease and AIDS

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There are 40 million people in the world infected with the human immunodeficiency virus (HIV).¹ New treatments for HIV have allowed these patients to live longer and cardiac manifestations are becoming more evident. Echocardiographic abnormalities can be found in up to 44% of patients infected with HIV.² These findings include pericardial effusion (PE), left ventricular (LV) dysfunction, dilated cardiomyopathy (DCM), infective endocarditis (IE), pulmonary arterial hypertension (PAH), and cardiac masses such as lymphoma and Kaposi's sarcoma of the heart. In addition, highly active antiretroviral therapy (HAART) has been associated with the development of ischemic heart disease and LV diastolic abnormalities. This review discusses these findings in the adult and pediatric population, as they relate to the echocardiographer.

Pericardial Effusion

Pericardial effusion (PE) is one of the most common echocardiographic findings in HIV patients. The likelihood of finding a PE in the HIV patient increases with advancing stages of the disease. The incidence in patients with acquired immunodeficiency syndrome (AIDS) can be as

high as 11% per year. The majority of these PEs detected by echocardiography are small and asymptomatic; hence they rarely progress to cause hemodynamic compromise. Nevertheless, the presence of a PE in a patient infected with HIV usually is associated with advanced disease and has been found to be an independent predictor of increased mortality.^{2,3}

The etiology of most PEs in HIV patients is unknown, even after extensive diagnostic testing. When a specific cause is found, it is usually an opportunistic infection or an underlying malignancy. The HIV virus itself also can cause PE through the induction of circulating cytokines and an increased capillary leak. In these cases pleural effusions and ascites are commonly seen as well.³⁻⁵

Because most PEs are small and a treatable etiology is found only in a minority of patients, an aggressive diagnostic approach is not routinely indicated. Pericardiocentesis and operative drainage with a pericardial window should be reserved for large symptomatic PEs, recurrent effusions, and those that progress to tamponade.⁶ The typical signs of right ventricular and atrial diastolic collapse may be absent in those HIV patients with tamponade physiology and underlying PAH due to increased pressures of the right cardiac chambers. In rare cases, LV diastolic collapse may be seen.⁷

Pericarditis with a fibrinous, serous, hemorrhagic, or purulent PE may also develop in HIV patients. Fibrinous pericarditis is the most common type seen in HIV patients and usually

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has a benign course resolving without complications. A variable number of fibrinous strands can be noted in the pericardial space by echocardiography. Bacterial pericarditis tends to follow a more aggressive course and may lead to constrictive physiology.⁵ Therefore, it is important for echocardiographer to assess for pericardial constriction and tamponade physiology in these patients.

Left Ventricular Dysfunction and Dilated Cardiomyopathy

Compared to the general population, HIV patients have a higher incidence of both asymptomatic and symptomatic LV dysfunction. In a study of 69 HIV-infected patients without clinical cardiac disease, the prevalence of global hypokinesia with decreased ejection fraction (<45%) was 14.5%.⁸ Barbaro et al. reported a decrease of 20% in the mean LV ejection fraction in 1236 asymptomatic HIV patients compared to healthy controls.⁹

DCM also is a frequent finding on echocardiogram. The prevalence of DCM can range from 5% to 23% in patients with AIDS. Evidence of myocarditis by endomyocardial biopsy is found in the majority of cases, suggesting that myocarditis may play a significant role in the development of DCM in patients infected with HIV.^{5,10} Various viral agents (including the HIV virus), fungal organisms such as *Candida albicans* and *Cryptococcus neoformans*, atypical mycobacteria, and *Toxoplasma gondii* have been implicated.^{4,11}

Echocardiographic findings typically include four-chamber enlargement, diffuse hypokinesia, and a reduced LV ejection fraction. Concomitant mitral and tricuspid regurgitation due to annular dilation may be also seen. LV dilatation with eccentric hypertrophy is more commonly seen than concentric hypertrophy in HIV patients. Pathology usually reveals an enlarged, globular-shaped, flabby heart with pale myocardium, and increased weight.⁵ As with other echocardiographic findings in HIV patients, DCM and a depressed LV ejection fraction is more common in those with advanced AIDS and lower CD4 counts.^{8,12}

Other studies also have found diastolic abnormalities suggestive of abnormal relaxation and filling impairment of the LV in HIV patients. In the study by Barbaro et al., the HIV group had a 35% reduction in the mean E/A ratio and a 19.7% increase in the isovolumic relaxation time compared to healthy controls.⁹ Two other

studies also have found a significant decrease in the peak E velocity, a decrease in E/A ratio, and increases in the deceleration half-time of the early filling period and isovolumic relaxation time. All the patients in these two studies were asymptomatic and had preserved LV systolic function.^{13,14}

Endocarditis

Patients with HIV do not appear to be at higher risk for developing IE compared to the non-HIV population.¹⁵ Almost 90% of IE in patients with HIV is associated with intravenous drug use.¹⁶ The clinical presentation is similar to that of non-HIV patients, with *Staphylococcus aureus* isolated in the majority of cases. Cases involving less common organisms such as *Streptococcus bovis*, *Serratia marcescens*, *Salmonella* sp, *Aspergillus fumigatus*, *Cryptococcus neoformans*, and *Candida* sp have also been reported.^{10,16}

Because IE in HIV patients is most often associated with intravenous drug abuse, the tricuspid valve is frequently involved, with left-sided valves involved in about one-third of the cases.^{4,15,16} Typical vegetations with or without destruction of the affected valve(s) usually can be seen by transthoracic echocardiography. Workup and therapy of bacteremic HIV patients should be the same as in their HIV negative counterparts. Patients with advanced HIV disease and the lowest CD4 counts appear to have the highest mortality, which may reflect their overall poor medical condition and high number of comorbidities.¹⁵

Nonbacterial thrombotic endocarditis (NBTE) is seen mostly in patients with advanced disease or HIV wasting syndrome. It has been found in up to 5% of AIDS patients on autopsy. It is characterized by friable, noninfected vegetations comprised of platelets and fibrin that have a tendency to embolize. The vegetations of NBTE appear as mobile echodensities attached to a normal appearing valve. Usually, these lesions are found on left-sided valves. However, patients with HIV have a significant number on the tricuspid valve as well (Fig. 1).⁴

Cardiac Tumors

Kaposi's sarcoma and malignant lymphoma are found with a much higher frequency in patients with HIV than in the general population.

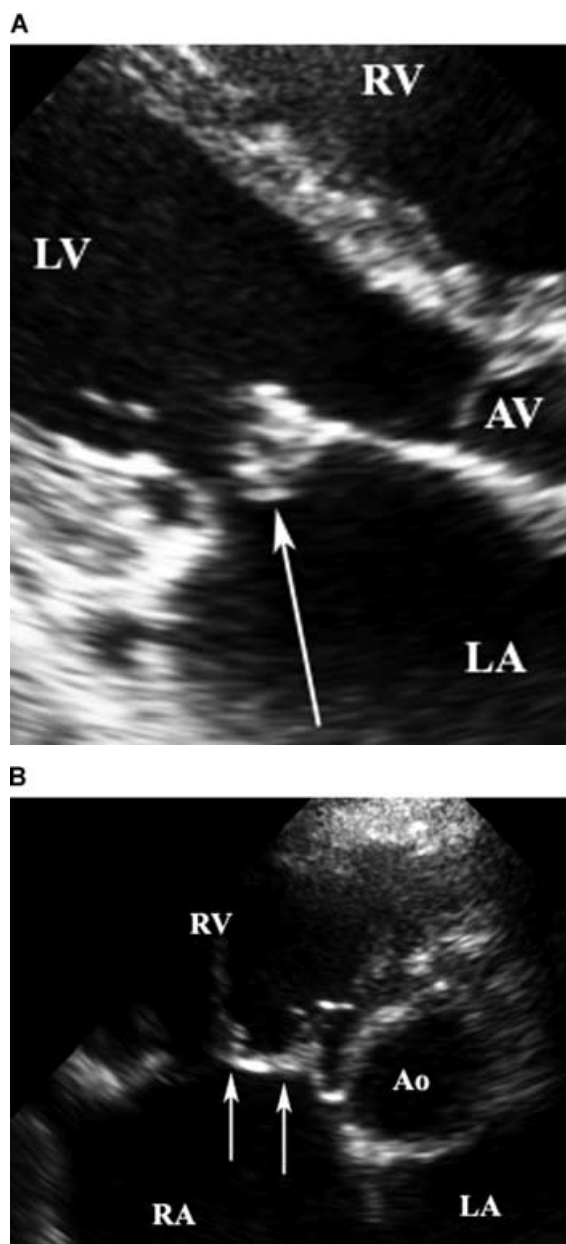


Figure 1. Transthoracic echocardiography performed in a patient with AIDS and an atypical mycobacterium lung disease. The patient had progressive lung disease and weight loss. **A.** Modified parasternal short axis imaging revealed a somewhat mobile mass (arrow) attached to the atrial surface of the anterior leaflet of the mitral valve. Mild-moderate mitral regurgitation was present. **B.** Parasternal short-axis image at the level just above the aortic valve (Ao) reveals a diffusely thickened septal leaflet of the tricuspid valve (arrows). Diffuse thickening of a valve leaflet is a pattern that may be found with NBTE. Although these findings were not confirmed histologically, the clinical scenario and echo appearance is consistent with NBTE. AV = aortic valve; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

Kaposi's sarcoma is the most common tumor found in the heart of patients with AIDS. These patients usually have disseminated disease. It usually presents as small focal masses involving the epicardium, pericardium, and the adventitia of the aorta and pulmonary trunk. Pericardiocentesis should be avoided in patients with PE and suspected Kaposi's sarcoma, as there is an increased risk of hemorrhagic tamponade.^{4,5}

Lymphoma is the second most common tumor involving the heart in HIV patients and has a frequency 25–60 times higher than the general population.¹⁰ Most cases are high-grade non-Hodgkin B cell derived lymphomas. The majority of patients present with disseminated disease rather than with a primary cardiac tumor. By echocardiography, the lesions appear as multilobulated or nodular masses within the myocardium, frequently involving the right atrium and right ventricle. Tumor of left-sided chambers or pericardial involvement with PE may also be noted (Fig. 2).⁵ Generally, the prognosis of patients with cardiac lymphoma is poor.

Three cases of left atrial myxoma and one case of papillary fibroelastoma have been reported in association with HIV disease.^{17–19} With almost 40 million HIV-infected people in the world, it is more likely that these tumors simply coexisted with HIV infection than having a direct etiologic relationship. Other infrequent causes of cardiac masses found in HIV-infected patients may be due to a variety of opportunistic pathogens including mycobacteria, *Cryptococcus*, and *Aspergillus*. Compared to the general population, AIDS patients have an increased incidence of extrapulmonary tuberculosis, which tend to form granulomatous lesions and may appear as a pericardial mass by echocardiography.^{5,18}

Pulmonary Arterial Hypertension

Patients infected with HIV have an increased risk for the development of PAH, with an incidence of 0.5%. HIV-associated PAH is thought to be mediated through a variety of virus-induced humoral factors that lead to the remodeling of pulmonary resistance vessels.^{20,21} HIV-associated PAH is more frequently seen in young male patients with a ratio of 1.5:1, in contrast to primary PAH, which is more common in women. The clinical presentation is no different in patients with HIV and includes progressive dyspnea, right-sided heart failure, fatigue, cough, and syncope. The echocardiographic

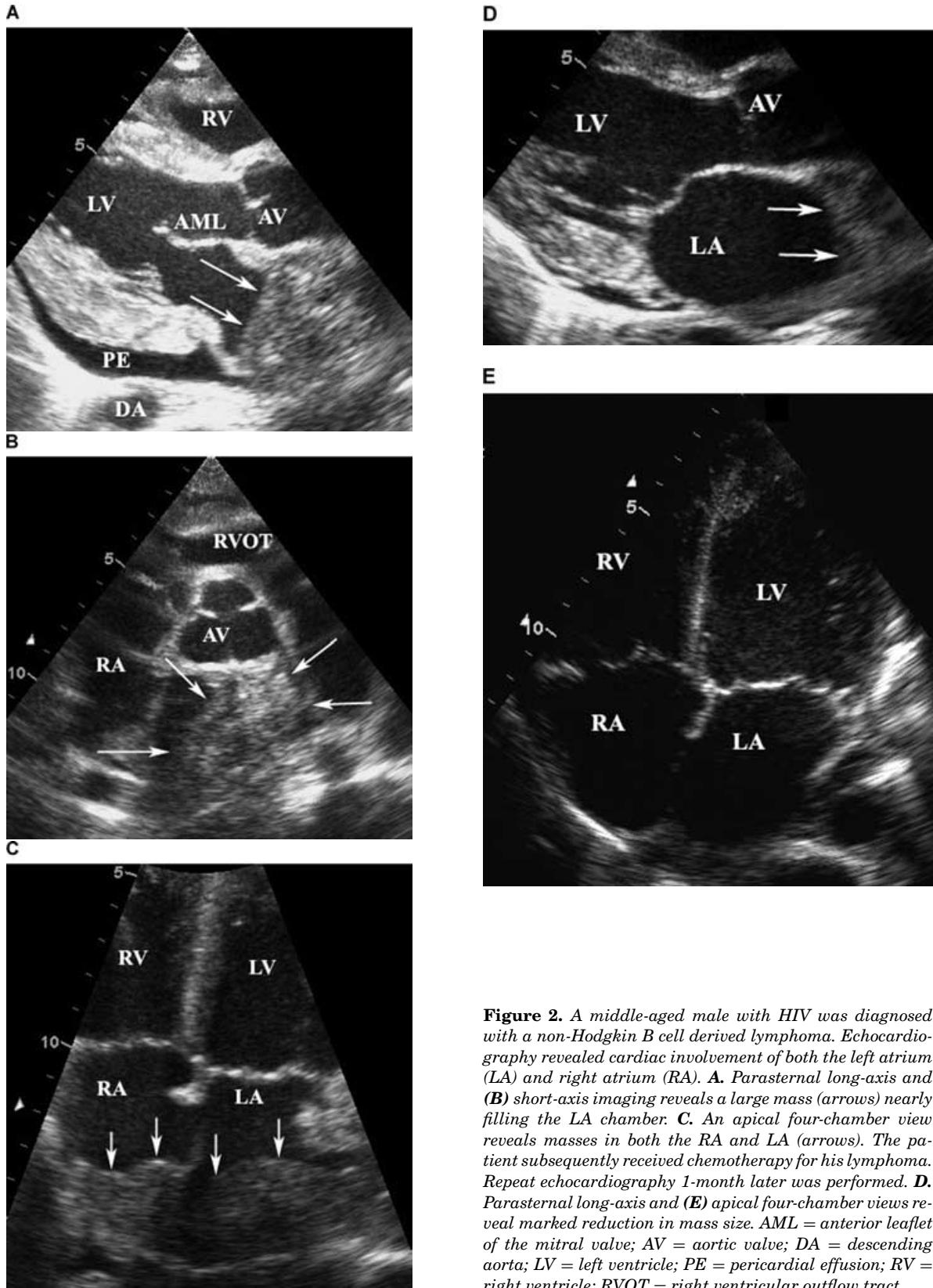


Figure 2. A middle-aged male with HIV was diagnosed with a non-Hodgkin B cell derived lymphoma. Echocardiography revealed cardiac involvement of both the left atrium (LA) and right atrium (RA). **A.** Parasternal long-axis and **(B)** short-axis imaging reveals a large mass (arrows) nearly filling the LA chamber. **C.** An apical four-chamber view reveals masses in both the RA and LA (arrows). The patient subsequently received chemotherapy for his lymphoma. Repeat echocardiography 1-month later was performed. **D.** Parasternal long-axis and **(E)** apical four-chamber views reveal marked reduction in mass size. AML = anterior leaflet of the mitral valve; AV = aortic valve; DA = descending aorta; LV = left ventricle; PE = pericardial effusion; RV = right ventricle; RVOT = right ventricular outflow tract.

features of PAH are similar to those of patients without HIV disease.²⁰

In a large study of HIV patients with PAH, mean systolic and diastolic pulmonary artery pressures were 67 and 40 mmHg, respectively.²¹ LV diastolic abnormalities are not uncommon in these patients.²⁰ There are reports of hemodynamic improvement in patients with HIV-associated PAH after treatment with HAART.²² Echocardiography may be a useful way to follow response to therapy.

Effect of Antiretroviral Therapy

The use of HAART, especially with protease inhibitors, is associated with insulin resistance and hyperlipidemia. In addition, these drugs appear to accelerate atherosclerosis and increase the risk of coronary artery disease.^{4,23} Echocardiographic findings of segmental wall motion abnormalities in HIV patients taking HAART should prompt the physician to pursue an appropriate ischemic workup. A number of drugs used in the treatment of HIV disease and related opportunistic infections may also lead to cardiovascular toxicity. Amphotericin B, doxorubicin, and foscarnet have been reported to cause LV dysfunction.⁴ Zidovudine (AZT) has been associated with a rare form of cardiomyopathy by exerting a toxic effect on the mitochondria which leads to myocardial damage in susceptible patients.²⁴

An increase in LV wall thickness and diastolic abnormalities has been found in asymptomatic HIV patients taking protease inhibitors. These changes were seen independent of age, sex, body mass index, and blood pressure.²⁵ Whether these subclinical echocardiographic findings have any prognostic significance is not yet known. However, it seems prudent to follow these patients by echocardiography at regular intervals for disease progression.

Cardiac Manifestations in Children

Worldwide, more than 2.5 million children under the age of 15 are infected with the HIV virus. Since most of these patients live in underdeveloped areas of Africa and Southeast Asia they lack access to appropriate therapy.¹ LV dysfunction, increased LV mass, myocarditis, and PE are the most common echocardiographic findings in these children infected. Echocardiographic abnormalities are less common during infancy than in older children, as the majority succumb to infectious causes without appro-

priate antiretroviral treatment. However, the frequency of HIV-related cardiac disease increases with age in surviving children.²⁶

The 5-year cumulative incidence for development of LV systolic dysfunction can be as high as 28%, with a 1-year mortality of 52% after presentation with clinical heart failure.²⁷ Myocarditis is a common cause of LV dysfunction, due to a wide variety of infectious agents including the HIV virus itself. However, in children, adenovirus and cytomegalovirus are the pathogens most frequently isolated. PE is also very common in HIV-infected children with a prevalence of 16–26%. As in adults, the majority of these effusions are small and asymptomatic.²⁶ A number of congenital cardiac malformations have been described in HIV-infected children, but the overall incidence does not appear to be significantly different from HIV-negative controls.²⁶

Summary

As the HIV epidemic grows and the new treatments allow patients to live longer, cardiac manifestations of this disease are increasing. Echocardiography is a useful tool, which can diagnose many of these cardiac abnormalities. It is important for the echocardiographer to recognize these HIV-related cardiac abnormalities, and to assess for them when performing and interpreting studies in this group of patients.

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