Myocardial and Pericardial Disease in HIV

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Opinion statement

Cardiovascular complications are frequently encountered in the HIV-infected population. Cardiac care providers should implement appropriate preventive, screening, and therapeutic strategies to maximize survival and quality of life in this increasingly treatable, chronic disease. All HIV-infected individuals should undergo periodic cardiac evaluation, including echocardiography, in order to identify subclinical cardiac dysfunction. Left ventricular (LV) dysfunction can result from, or be exacerbated by, a variety of treatable infectious, endocrine, nutritional, and immunologic disorders. Aggressive diagnosis and treatment of these conditions may lead to improvement or even normalization of myocardial function. Endomyocardial biopsy should be considered to direct etiology-specific therapy. Standard measures for the prevention and treatment of congestive heart failure are recommended for HIV-infected patients. Afterload reduction with angiotensin-converting enzyme inhibitors may be indicated for patients with elevated afterload and preclinical LV dysfunction diagnosed by echocardiogram. However, judicious drug selection and titration are necessary in this cohort of patients with frequent autonomic dysfunction, at risk for a number of potentially lethal drug interactions. Carnitine, selenium, and multivitamin supplementation should be considered, especially in those with wasting or diarrhea syndromes. Monthly intravenous immunoglobulin (IVIG) infusions have been demonstrated to preserve LV parameters in HIV-infected children; ventricular recovery has been documented in some children with recalcitrant HIV-related cardiomyopathy following IVIG infusion. We support the use of immuno-modulatory therapy in the pediatric population, and look forward to further study into the efficacy and broader application of this approach. Highly active antiretroviral therapy (HAART) may be associated with dyslipidemia and the metabolic syndrome. This should be treated with dietary and possibly with pharmacologic interventions. Drug interactions need to be considered when instituting pharmacologic therapies. Pericardial effusions are often seen in patients with advanced HIV infection. Asymptomatic effusions are most often nonspecific in nature, related to the proinflammatory milieu found in advanced AIDS. Nonspecific effusions are a marker of advanced disease and do not require exhaustive etiologic evaluation. In contrast, large or symptomatic effusions are often associated with infection or malignancy, and warrant thorough investigation and etiology-specific treatment.

Introduction

Cardiovascular manifestations of HIV infection have been clearly described since the early days of the AIDS pandemic. Cardiovascular involvement produces a vast spectrum of clinical findings, resulting from direct myocardial retroviral infection, opportunistic or viral infections, autoimmune, nutritional, and drug effects. Frequently encountered clinical entities include cardiomyopathy, myocarditis, and pericardial disease. Where available, the advent of highly active antiretro-viral therapy (HAART) markedly prolongs survival, while inducing lipid and metabolic abnormalities that may hasten the development of acquired atherosclerotic disease. Drug interactions exist with a number of HAART agents, which may lead to hazardous complications. Physicians caring for HIV-infected patients must remain suspicious of subclinical cardiovascular illness in order to provide appropriate preventive and therapeutic intervention.

Cardiomyopathy and left ventricular dysfunction

- The spectrum of HIV-associated cardiovascular disease is summarized in Table 1. Dilated cardiomyopathy is one of the most frequent complications encountered, developing in 8% to 15% of HIV-infected children and adults [1,6]. The prevalence of HIV-related cardiomyopathy is increasing as patients live longer. In vertically infected children followed with echocardiography, the cumulative incidence of symptomatic heart failure or cardiac medication use was 10% over 2 years of observation [6]. Cardiomyopathy is most often seen when the CD4 count falls below 400 cells/mL. Diverse mechanisms have been implicated, including infectious, autoimmune, nutritional, endocrine, and toxin-mediated etiologies. Currently, there are no prospective data regarding the impact of HAART on the development of HIV-associated cardiomyopathy. However, the improvement of overall health, immunologic state, and rate of opportunistic infections seen in HAART may lead to a beneficial effect toward lowering the incidence and severity of this HIV-related condition.

- Myocarditis has frequently been associated with the development of left ventricular (LV) dysfunction. Dilated cardiomyopathy may be related to direct HIV action on the myocardium or an HIV-induced autoimmune process, possibly augmented by viral coinfection [7]. Myocardial biopsy may be clinically helpful to guide specific, targeted therapy toward active myocarditis or opportunistic coinfections, such as cytomegalovirus, coxsackievirus group B, Epstein-Barr virus, fungal, mycobacterial, or bacterial pathogens. Endomyocardial biopsy may also detect abnormal mitochondria, which might support the need for an antiretroviral drug holiday.

- Therapeutic interventions are predicated on accurate diagnosis. We advocate routine echocardiographic screening of HIV-infected patients. These individuals often show some degree of exercise intolerance, fatigue, breathlessness, and fluid retention due to complications of their HIV status. Such symptoms may mask the gradual development compromising heart disease. Echocardiography allows for assessment of LV systolic function and degree of LV hypertrophy, two parameters that have been identified as independent predictors of all-cause mortality in the HIV-infected infant or child [8]. Echocardiography can also identify the presence of pericardial effusions, valvular disease, and endocarditis, all of which are associated with poor outcomes in the HIV-infected population. Echocardiographic data are also helpful in the setting of intracardiac thrombi or tumors, and can characterize right-sided dysfunction seen with HIV-associated pulmonary hypertension. Figure 1 outlines a suggested cardiac management scheme for monitoring LV function, pericardial effusion, intracardiac masses, or

Table 1. HIV-associated cardiovascular abnormalities

Type	Possible etiologies and associations	Incidence
Dilated cardiomyopathy	Infectious: HIV, *Toxoplasma gondii*, coxsackievirus, group B, Epstein-Barr virus, cytomegalovirus, adenovirus Autoimmune response to infection Drug-related: cocaine, possible nucleoside analogues, interleukin-2, doxorubicin, interferon Metabolic/endocrine: adrenal insufficiency, hyperinsulinemia, thyroid hormone, growth hormone Nutritional deficiency/wasting: selenium, B_{12}, carnitine Cytokines: TNF-α, nitric oxide, TGF-β, endothelin-1 Hypothermia Hyperthermia Autonomic insufficiency Encephalopathy AIDS HIV viral load, length of immunosuppression	Estimated annual incidence of 15.9/1000 asymptomatic HIV-infected persons [1]
Coronary heart disease	PI-induced metabolic, lipid, and coagulative disorders	Mostly limited to case reports [2]
Systemic arterial hypertension	HIV-associated endothelial dysfunction; leukoclastic vasculitis in small, medium, and large vessels; atherosclerosis secondary to HAART; PI-induced insulin resistance with increased sympathetic activity and sodium retention	20% [3]
Pericardial effusion	Bacterial, mycobacterial. Viral: HIV, herpes simplex virus, herpes simplex virus type 2, cytomegalovirus Other pathogens: *Cryptococcus, Toxoplasma, Histoplasma* Malignancy: Kaposi's sarcoma, non-Hodgkin's lymphoma Hypothyroidism Prolonged immunodeficiency: capillary leak/wasting/malnutrition	11%/y [4]
HIV-associated pulmonary hypertension	Recurrent pulmonary infections, pulmonary arteritis, microvascular pulmonary emboli due to thrombus or drug injection. Plexogenic pulmonary arteriopathy. Mediator release from endothelium	Rare

HAART—highly active antiretroviral therapy; PI—protease inhibitor; TGF—transforming growth factor; TNF—tumor necrosis factor. (*Modified from* Barbaro *et al.* [5]; with permission.)

vegetations in HIV-infected patients. We advocate serial echocardiography in HIV-infected patients with no evidence of cardiac involvement at the time of diagnosis and every 1 to 2 years thereafter. When cardiovascular abnormalities are identified, further follow-up is guided on a lesion-specific basis by the managing cardiologist.

HAART-associated complications

- Where available, the use of HAART markedly prolongs the life of patients with HIV, leading to a higher prevalence of associated chronic complications of the disease. Lipid abnormalities associated with HIV infection were described prior to the development of HAART. HIV infection leads to elevated triglyceride and total cholesterol levels, with an associated decrease of high-density lipoprotein (HDL) concentration [10•]. These lipid abnormalities may not be specific to HIV and AIDS, but may reflect a nonspecific response to chronic inflammation. Long-term HAART, specifically protease

inhibitor (*eg,* amprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir) and non-nucleoside reverse transcriptase inhibitor (*eg,* abacavir, didanoside, lamivudin, stavudine, zalcitabine, zidovudine) use, further increase serum triglyceride and cholesterol levels. Dyslipidemia was first reported with ritonavir, which induced a greater than 200% increase of serum triglyceride and a 30% to 40% increase of total cholesterol levels [11]. Triglyceride elevation may be extreme (> 1000 mg/dL), particularly with ritonavir. HAART is also associated with lipodystrophy, an abnormal fat accumulation in the abdomen and posterior neck ("buffalo hump") with reduced fat in the face and limbs. Insulin resistance and increased C-peptide levels are also seen. Cohort data support an increased incidence of myocardial infarction in HIV-infected patients, at least partially related to this altered lipid metabolism [2]. The exact mechanistic pathways remain to be elucidated, but it appears that protease inhibitors alter lipid metabolism by cross inhibition of homologous enzymes (cytoplasmic retinoic-acid binding protein 1, low-density lipoprotein receptor-related protein), leading to the clinically described dyslipidemias [12].

Dysautonomia

- Autonomic dysfunction has been described in the HIV-infected population [13]. Early clinical signs of dysautonomia include syncope or presyncope, diminished sweating, and diarrhea. Figure 2 demonstrates an approach toward the initial evaluation and treatment of autonomic dysfunction in this population. Rhythm abnormalities including sinus tachycardia, intraventricular conduction delay, and QTc prolongation appear to be more common in HIV-infected patients than in the general population. Kocheril *et al.* [14] documented a 29% incidence of prolonged QTc (> 440 msec) in a hospitalized cohort of HIV-infected patients. QTc prolongation may contribute to the development of torsades de points and refractory ventricular arrhythmias. Drug interactions may contribute to QTc prolongation and should be taken into consideration prior to the institution of specific therapies (Table 2). ECG algorithms have been proposed to determine baseline QTc values and to monitor for changes with the institution of specific drug therapy [15]. Pentamidine, an agent frequently used for *Pneumocystis carinii* pneuomonia prophylaxis, is an example of an agent that has been associated with QTc prolongation and the onset of torsades de point; Figure 2 demonstrates one monitoring approach aimed at limiting the risk for arrhythmia. An updated, thorough list of medications affecting the QT interval is regularly updated at http://www.torsades.org.

Pericardial disease

- Pericardial disease is frequently found in association with HIV infection. Pericardial effusions tend to develop in patients with AIDS, as opposed to those with asymptomatic HIV infection. Heidenreich *et al.* [16] reported a yearly incidence of pericardial effusion at 11% in adults with AIDS followed prospectively over a 5-year period. Pericardial effusions were small in 80% and asymptomatic in 87%. Children with vertically acquired HIV infection develop pericardial effusions less frequently; effusions in this pediatric population tend to be small and nonprogressive [6]. Symptomatic pericarditis or tamponade requiring therapeutic pericardiocentesis are rare, but can occur. Accordingly, HIV should enter into the differential diagnosis of unexplained pericardial effusion.
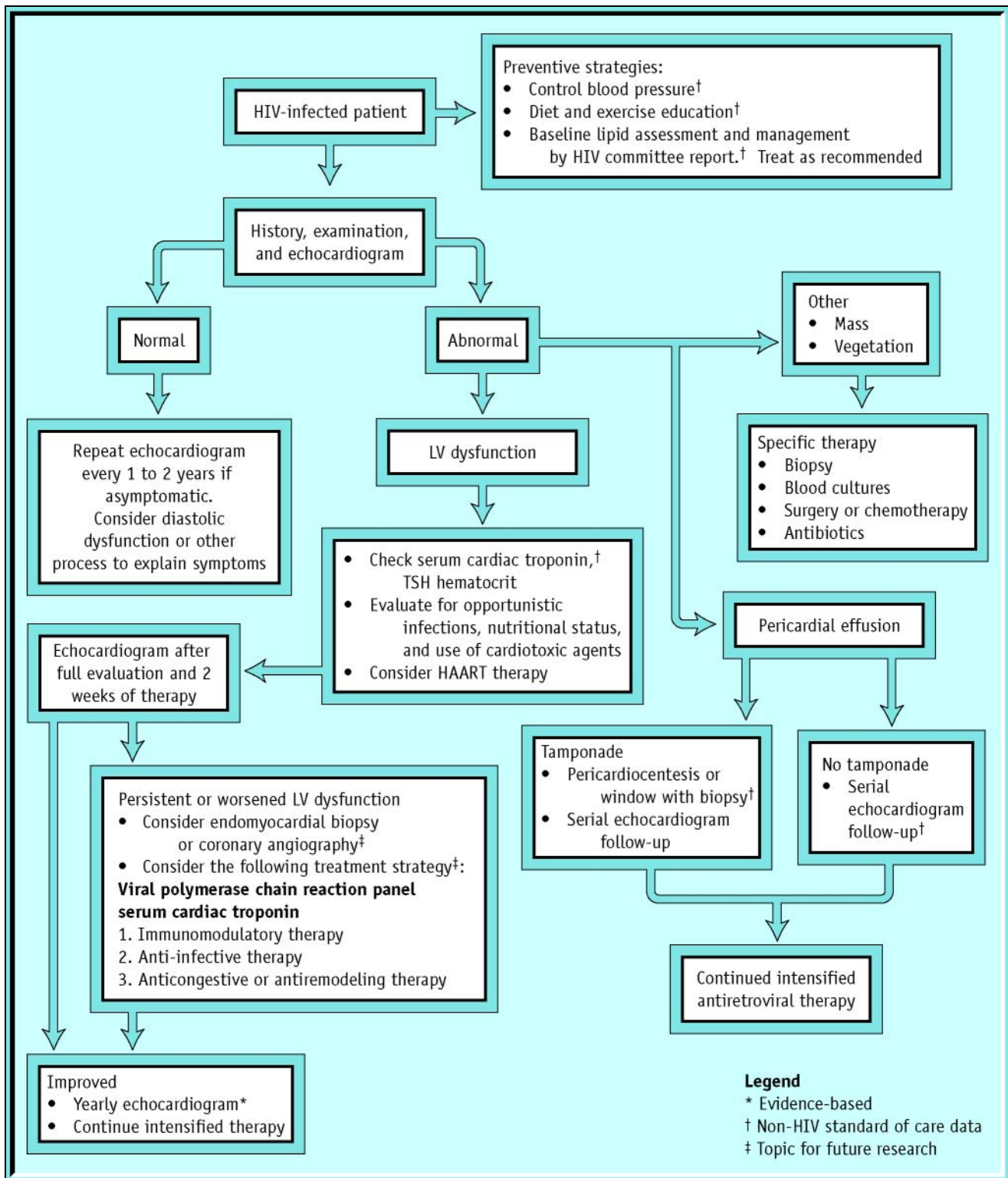
Figure 1. Screening, prevention, and treatment strategy for cardiac dysfunction commonly found in HIV infection. Echocardiography should be used at the initial evaluation. HAART—highly active antiretroviral therapy; LV—left ventricular; TSH—thyroid-stimulating hormone. (*Modified from* Dolin *et al.* [9]; with permission.)

- Pericardial effusions are seen in association with a number of conditions, including infectious (viral, fungal bacterial, mycobacterial) and malignant (Kaposi's sarcoma, lymphoma) etiologies. Tuberculous pericarditis is more frequently associated with HIV infection in Africa, and has been described
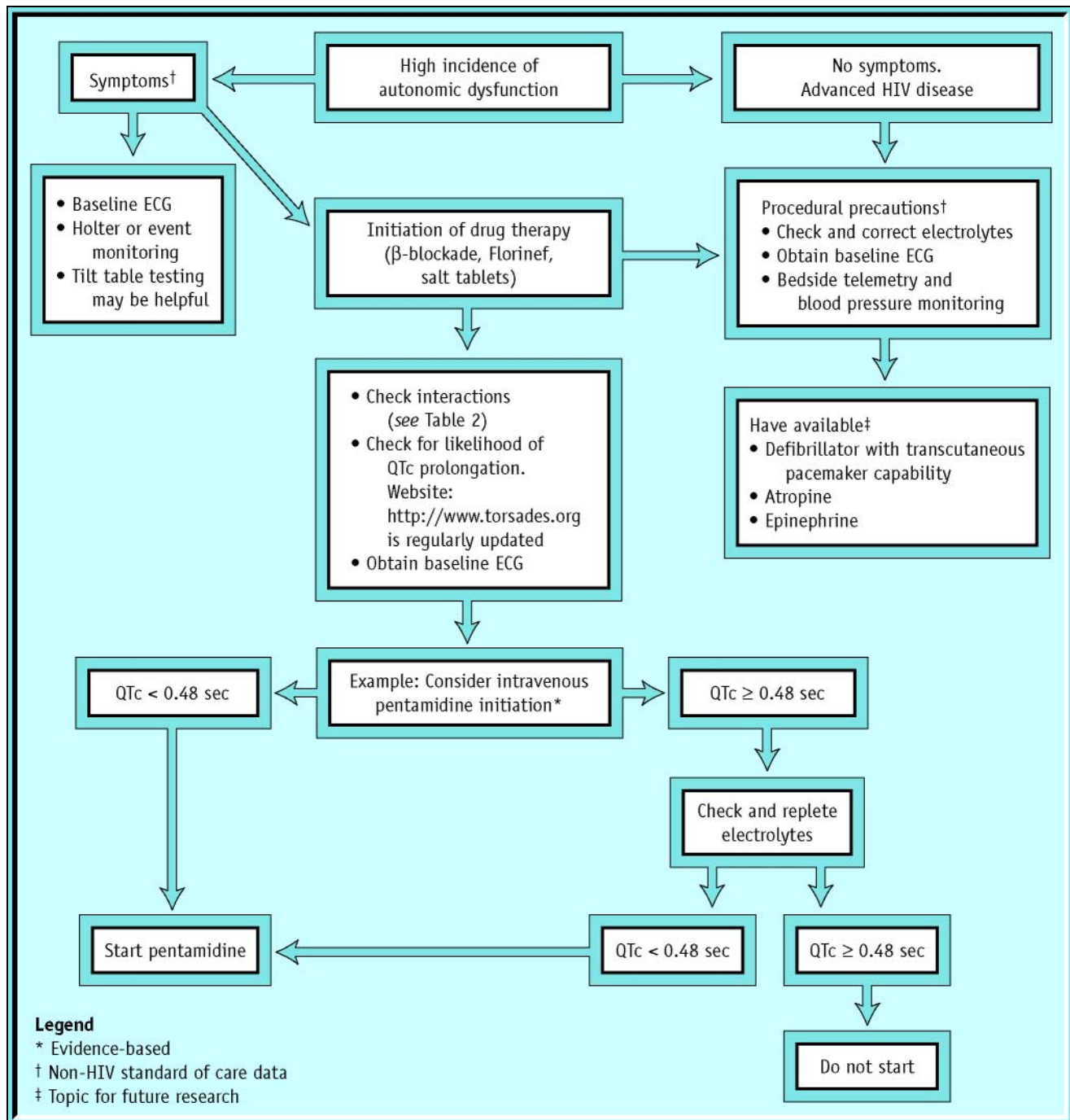
Figure 2. Diagnostic and treatment strategies for HIV-associated autonomic dysfunction. Dysautonomia is common in this population; caution is indicated with the institution of new drug therapy, sedation, or anesthesia. (*Modified from* Dolin *et al.* [9]; with permission.)

in intravenous drug users [4,17]. However, the majority of effusions found in HIV-infected patients are serous in nature and are not related to a specific etiology. These nonspecific effusions most often occur during the later stages of HIV disease. Those affected may have concurrent serous pleural effusions and ascites, findings suggestive of a more generalized "capillary leak" syndrome. This capillary leak likely stems from the generalized dysregulated, proinflammatory milieu described in advanced AIDS [18]. Nutritionally related hypoalbuminemia may also lower the serum oncotic pressure and contribute to the development of these serous effusions.

Table 2. Cardiovascular interactions of commonly used drugs in HIV patients

Class	Drugs	Cardiac drug interaction	Cardiac side effects
Antiretroviral			
Nucleoside reverse transcriptase inhibitors	Abacavir (Ziagen)		Rare: lactic acidosis. Skeletal muscle myopathy (mitochondrial dysfunction hypothesized, but not seen clinically)
	Zidovudine (AZT, Rescriptor)	Dipyridamole	
Non-nucleoside reverse transcriptase inhibitors	Delavirdine (Rescriptor)	Warfarin (class interaction); calcium channel blockers	
	Efavirenz (Sustiva)		
	Nevirapine (Viramune)	β-Blockers, nifedipine, quinidine, steroids, theophylline	
Protease inhibitors	Amprenavir (Agenerase)	All are metabolized by cytochrome P-450 and interact with sildenafil, amiodarone, lidocaine, quinidine, warfarin, "statins"	Implicated in premature atherosclerosis, dyslipidemia, insulin resistance, fat wasting, and redistribution (lipodystrophy)
	Indinavir (Crixivan)		
	Nelfinavir (Viracept)		
	Ritonavir (Norvir)	Calcium channel blockers, prednisone, quinine. Increases β-blocker levels 1.5 to 3 times	
	Saquinavir (Invirase, Fortovase)		
Anti-infective			
Antibiotics	Erythromycin	Cytochrome P-450 metabolism and interactions	Orthostatic hypotension, VT, torsades (drug interaction)
	Trimethoprim/ sulfamethoxazole (Bactrim)	Increases warfarin effects	Orthostatic hypotension, anaphylaxis, QT prolongation
Antifungal agents	Amphotericin B	Digoxin toxicity	Hypertension, arrhythmias, renal failure, hypokalemia, thrombophlebitis, bradycardia, angioedema, dilated cardiomyopathy
	Ketoconazole	Cytochrome P-450 metabolism and drug interaction increases levels of sildenafil, warfarin, "statins," nifedipine, digoxin	
	Itraconazole		
Antiviral agents	Foscarnet		Reversible cardiac failure, electrolyte abnormalities
	Ganciclovir	Zidovudine	VT, hypotension
Antiparasitic	Pentamidine (IV)		Hypotension, arrhythmias (torsades, VT), hyperglycemia, hypoglycemia, sudden death (Note: contraindicated if baseline QTc > 0.48)

IV—intravenous; VT—ventricular tachycardia.
(*Modified from* Barbaro *et al.* [5]; with permission.)

Table 2. Cardiovascular interactions of commonly used drugs in HIV patients *(Continued)*

Class	Drugs	Cardiac drug interaction	Cardiac side effects
Chemotherapy agents	Vincristine		Arrhythmia, myocardial infarction, cardiomyopathy
	Interferon-α		Orthostatic hypotension, myocardial infarction, ventricular and supraventricular arrhythmias, sudden death, atrioventricular block
	Interleukin-2		Hypotension, arrhythmia, sudden death, myocardial infarction, cardiac failure, capillary leak, thyroid alterations
	Doxorubicin (Adriamycin)	Decreases digoxin level	Myocarditis, cardiomyopathy, cardiac failure

IV—intravenous; VT—ventricular tachycardia.
(*Modified from* Barbaro *et al.* [5]; with permission.)

- Nonspecific pericardial effusions often resolve spontaneously. However, the presence of even a transient pericardial effusion has prognostic significance. Heidenreich *et al.* [16] reported a 36% survival 6 months following the onset of pericardial effusions, as compared with a 93% survival in those who never developed an effusion. In this series, the pericardial effusion was thought to contribute directly to death in only one patient with a large effusion and dilated cardiomyopathy. In the remainder of this patient cohort, pericardial effusion appeared to be an indicator of the advanced status of HIV infection. The impact of HAART on the development of pericardial effusion and prognosis awaits further study.

Indications for hospital admission of HIV-related cardiomyopathy

- Most individuals with HIV-associated cardiomyopathy are identified during outpatient screening. Hospitalization is indicated for acutely symptomatic heart failure per consensus guidelines [19]. These guidelines recommend admission for patients with clinical or ECG evidence of acute myocardial ischemia, pulmonary edema, severe respiratory distress, oxygen saturation below 90% (in the absence of pulmonary disease), anasarca, symptomatic hypotension or syncope, heart failure refractory to outpatient therapy, and those who have inadequate social support for safe outpatient management.

Treatment of HIV-related cardiomyopathy

- An algorithm for the cardiac management of HIV-infected patients is depicted in Figure 1.
- Routine therapy for HIV-associated cardiomyopathy is extrapolated from similar forms of nonischemic heart disease and have not been specifically studied in the HIV-infected population. American Heart Association (AHA) consensus practice guidelines have been published for the treatment of adults with, or at risk for developing, chronic heart failure [20•]. Asymptomatic HIV-infected patients should be considered at risk for the development of heart disease (AHA Stage A) and undergo appropriate risk assessment and screening.

- Consider empiric angiotensin-converting enzyme (ACE) inhibitor therapy in HIV-positive individuals with normal ventricular function on HAART. Prevention is the best therapy to treat heart failure. In the HOPE (Heart Outcome Prevention Evaluation) study [21], treatment with ramipril significantly decreased the incidence of cardiovascular morbidity and mortality in a broad range of high-risk patients not known to have a low ejection fraction or heart failure. Ramipril may be a cost-effective, clinically useful means of preventing ventricular dysfunction in this high-risk population.

Diet and lifestyle

- All HIV-infected patients should be educated regarding potential cardiac side effects, the potential for serious drug interactions, and the need for lifelong monitoring of heart function and coronary artery disease risks.
- Heart-healthy lifestyles should be encouraged in all patients living with HIV infection. Aerobic exercise can produce symptomatic, physiologic, and psychological benefits. Patients with LV compromise should be assessed for stable LV function with appropriate exercise testing prior to the institution of an exercise program [20•]. Heavy isometric exercise should be discouraged; if exercise is pursued, this should be under the direct supervision of a cardiologist and exercise physiologist.
- Dyslipidemia screening and treatment should be provided.
- Alcohol consumption and illicit drug use should be discouraged in patients with LV compromise, because they may further impair LV function.
- Restricting salt intake to 2.5 g/d and minimizing fluctuation in sodium intake may be beneficial to patients with symptomatic congestive heart failure.

When left ventricular dysfunction is identified

- Evaluate for opportunistic or other infections, because their treatment and cure may lead to improvement or even normalization of LV function.
- Obtain serum selenium and carnitine levels to guide nutritional supplementation.
- Evaluate thyroid function and growth hormone levels, with subsequent treatment, where deficient.
- Serum troponin assays are sensitive and specific indicators of ongoing myocardial injury, and may help guide the need for further evaluation by endomyocardial biopsy in order to characterize the ongoing inflammatory status and identify viral infection.
- General therapy for asymptomatic LV dysfunction includes treatment with ACE inhibitors and β-blockade. Symptomatic patients may require the addition of digitalis, loop diuretics, aldosterone antagonists, and dietary salt restriction.
- Drug interactions could complicate routine therapy. Table 2 summarizes cardiac drug interactions and side-effect profiles for a number of agents frequently used in HIV infection.

Pharmacologic treatment

ACE inhibitors

Standard dosage Enalapril maleate: Adult dosage: 2.5 mg daily; maintenance 10 to 14 mg daily (every day to twice a day). Pediatric dosage: 0.1 to 0.5 mg/kg/d (every day to twice a day); maximum: 0.5 mg/kg/d [21].

	Captopril: Initial adult dosage is 6.25 to 12.5 mg three times per day; maintenance dosage is 12.5 to 25 mg three times per day. Pediatric dosage is 0.15 to 0.5 mg/kg once or twice daily; maximum dosage is 6 mg/kg/d [22].
Contraindications	*Absolute:* Hypersensitivity reaction to ACE inhibitors, pregnancy, symptomatic hypotension. *Relative:* Renal insufficiency (dose reduction may be necessary in patients with creatinine clearance < 30 mL/min), systolic blood pressure less than 90 mm Hg, hyperkalemia, breast-feeding.
Main drug interactions	Blood pressure may fall drastically after ACE inhibitor therapy is initiated in some patients on diuretic therapy. ACE inhibitors may attenuate potassium loss caused by some thiazide-type diuretics. Patients taking lithium may develop lithium toxicity.
Main side effects	*Acute:* Hyperkalemia, angioedema. *Chronic:* Cough, rash.
Cost/cost-effectiveness	Enalapril: $77.29 per 100 tablets (2.5 mg) [23]. Captopril: $3.75 per 100 tablets (12.5 mg) [23].

β-Blockers

Standard dosage	Carvedilol (Coreg; GlaxoSmithKline, Research Triangle Park, NC): Adult dosage: Initial adult dosage is 3.125 mg twice a day for 2 weeks, titrated upwards every 2 weeks to a maximum of 25 to 50 mg twice a day [21]. Metoprolol: Adult dosage is 100 to 450 mg/kg/d in two or three divided doses. Pediatric dosage: 1 to 5 mg/kg/d in two divided doses [22].
Contraindications	*Absolute:* Hypersensitivity reaction, sinus bradycardia, second- and third-degree atrioventricular block, cardiogenic shock. *Relative:* Fatigue, dizziness, fainting, asthma, overt cardiac failure.
Main drug interactions	Catecholamine-depleting drugs (*eg,* reserpine) may have an additive effect when given with β-blockers, resulting in hypotension or marked bradycardia.
Main side effects	*Acute:* Dizziness, fainting, shortness of breath, bradycardia, bronchospasm, dyspnea. *Chronic:* Tiredness, mental depression, impotence.
Cost/cost-effectiveness	Carvedilol: $162.35 per 100 tablets (3.125 mg) [23]. Captopril: $6.45 per 100 tablets (50 mg) [23].

Immunomodulatory therapy for HIV-associated cardiomyopathy

- Many patients with HIV-associated LV dysfunction show evidence of ongoing myocarditis with increased CD3 and CD8 lymphocytic infiltrate. Cardiac-specific autoantibody formation has been demonstrated in the HIV-infected population [24], with the highest incidence (43%) in those with echocardiographic evidence of decreased LV function. These data support cardiac autoimmunity as a component of HIV-related heart disease, and suggest that cardiac autoantibody assay may represent a potential risk assessment/screening strategy worthy of further investigation. In HIV-infected children, there is evidence to support the use of intravenous immunoglobulin (IVIG) [25]. Monthly IVIG infusion (400 mg/kg) was associated with minimized LV dysfunction, shown by an increase in LV wall thickness and a reduction in peak LV wall stress on echocardiography. These data are summarized in Figure 3. LV recovery has also been demonstrated following IVIG treatment of recalcitrant HIV-related cardiomyopathy [26•]. The apparent effectiveness of IVIG further supports an antibody-mediated mechanism of cardiac injury that is responsive to immunomodulatory therapy. The efficacy of IVIG may stem from saturation of Fc receptors, preventing binding of cardiac-specific autoantibodies and resultant propagation of the inflammatory cascade. We continue to support the use of IVIG in the pediatric population, and await further study of this, and other, immunomodulatory therapies.
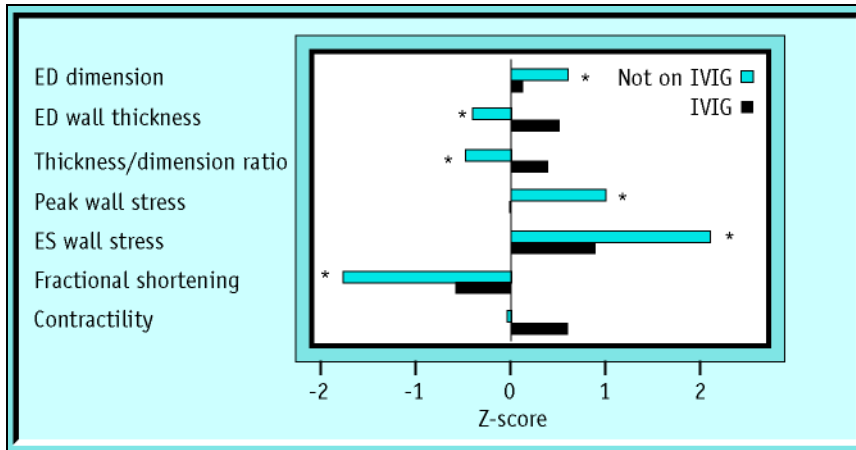
Figure 3. Monthly intravenous immunoglobulin (IVIG) therapy in HIV-infected patients without congestive heart failure is associated with more normal left ventricular (LV) size and function. Echocardiographic determination of LV structure and function in HIV-infected patients receiving monthly IVIG therapy (*black bars*) is compared with those not receiving IVIG therapy (*shaded bars*). Z-scores indicate the number of SDs above or below normal (Z-score = 0) for each parameter. *Asterisk* (*) indicates a value significantly different from normal. ED—end-diastolic; ES—end-systolic. (*Modified from* Lipshultz *et al.* [25]; with permission.)

Treatment of HAART-associated dyslipidemia

- Altering atherogenic lipid profiles lowers the rate of cardiovascular events in high-risk populations. Guidelines from the National Cholesterol Education Program (NCEP) have been recommended as the starting point for cholesterol control for HIV-infected patients [27], because studies in this population have not yet been conducted.

- The NCEP guidelines place emphasis on therapy for the "metabolic syndrome," a constellation of major risk factors for coronary artery disease. Components of the metabolic syndrome include abdominal obesity, atherogenic dyslipidemia (elevated triglyceride, small dense low-density lipoprotein [LDL] particles, low HDL), hypertension, glucose intolerance, insulin resistance, prothrombotic and proinflammatory states. These conditions are mimicked in many patients with HIV-infection and lipodystrophy receiving HAART.

- Dietary therapy and counseling as well as an aerobic exercise program should always be initial and concomitant therapies in this population. Low-dose HMG-CoA reductase administration may be helpful for the treatment of elevated LDL cholesterol or elevated LDL and triglyceride levels. Patients on protease inhibitors may be at increased risk for statin-induced myopathy and rhabdomyolysis due to medication interactions. For example, ritonavir with simvastatin can increase the simvastatin serum level up to 400-fold. Pravastatin or atorvastatin have been recommended based on their metabolic and side-effect profile. Colesevelam is a bile acid sequestrant that may be particularly well tolerated for treatment of elevated LDL as an alternate or combination therapy in this population.

- Fibric acid derivatives are indicated for marked hypertriglyceridemia and low HDL.

Treatment of HIV-associated pericardial effusion

- Based on the known data, patients with asymptomatic or incidentally detected pericardial effusion do not require exhaustive etiologic evaluation.

- When nonspecific serous effusions are found, intensification of antiretroviral therapy and nutritional support may be warranted.

- In contrast, an infectious or malignant etiology has been found in two thirds of HIV-infected patients presenting with symptomatic or large effusions, indicating the need for further diagnostic evaluation in this subset of individuals [18]. Therefore, pericardiocentesis is indicated for suspected malignancy or opportunistic infection, to drain large effusions, or in the setting of tamponade.
- Asymptomatic patients with HIV-associated pericardial effusions should be followed by repeat echocardiography on monthly intervals (Fig. 1). Unexplained dyspnea, jugular venous distention, or cardiomegaly on chest radiograph should prompt earlier evaluation with echocardiography.

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