JACC Vol. 13, No. 5
April 1989:1030–6

Cardiac Manifestations of Human Immunodeficiency Virus Infection: A Two-Dimensional Echocardiographic Study

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To determine the prevalence of cardiac abnormalities in patients with human immunodeficiency virus (HIV) infection, two-dimensional Doppler echocardiography was performed on 70 consecutive patients with HIV infection, including 51 with acquired immunodeficiency syndrome (AIDS), 13 with AIDS-related complex and 6 with asymptomatic HIV infection. Of the 70 patients, 36% were hospitalized and 64% were ambulatory at the time of evaluation. The average age was 37 years; 93% were homosexual men.

Echocardiographic findings included dilated cardiomyopathy in eight patients (11%), pericardial effusions in seven patients (10%) (one with impending tamponade), pleural effusion in four patients (6%) and mediastinal mass in one patient (1%). Among the 25 hospitalized patients, echocardiographic abnormalities were noted in 16 (64%), whereas among the 45 ambulatory patients, the only abnormality noted was mitral valve prolapse in 3 patients (7%) ($p < 0.0001$). Dilated cardiomyopathy was the only echocardiographic lesion more common in the 25 hospitalized patients than in 20 hospitalized control patients with acute leukemia. Symptoms of congestive heart failure responded to conventional therapy. Cardiac lesions were associated with active *Pneumocystis carinii* pneumonia and low T helper lymphocyte counts.

Dilated cardiomyopathy of unknown origin may be more common than was previously recognized in hospitalized, acutely ill patients with AIDS, but is uncommon in ambulatory patients with HIV infection. Echocardiography should be considered in the evaluation of dyspnea in hospitalized patients with HIV infection, especially those with dyspnea that is out of proportion to the degree of pulmonary disease.

(J Am Coll Cardiol 1989;13:1030–6)

With the increasing prevalence of acquired immunodeficiency syndrome (AIDS) and human immunodeficiency virus (HIV) infection, varied clinical manifestations of disease, including cardiac involvement, have been noted (1–11). Although pathologic studies and case reports of AIDS patients with dilated cardiomyopathy (1–7), pericardial effusion (7,8), Kaposi's sarcoma (9) and opportunistic infections (10,11) involving the heart have been described, the prevalence of cardiac abnormalities in living adults with HIV infection is unknown. To better define this prevalence, relate cardiac abnormalities to other manifestations of HIV-associated disease and compare the prevalence of cardiac abnormalities in hospitalized and ambulatory patients, we performed two-dimensional echocardiography with Doppler ultrasound studies on a series of consecutive patients with HIV infection.

Methods

Patient selection (Table 1). The study protocol was approved by the Committee for Human Research at the University of California, San Francisco. From September 1987 to September 1988, 82 consecutive patients from the AIDS clinic with known HIV infection were asked to participate in the study; of these patients, 70 (85%) were evaluated. Of the 70 study patients, 25 (36%) were hospitalized and 45 (64%) were ambulatory at the time of evaluation. There was no clinical or radiographic suspicion of cardiac disease in the ambulatory patients, all of whom were examined by one of the authors (D.N.C., H.H.). One patient with left ventricular

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Manuscript received September 18, 1988, revised manuscript received October 26, 1988, accepted November 11, 1988.

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0735-1097/89/$3.50

Table 1. Clinical Manifestations of Human Immunodeficiency Virus (HIV) Infection in 70 Patients

	Hospitalized HIV	Ambulatory HIV	Control
No. of patients	25	45	20
Age (yr)	35 ± 5	37 ± 7	36 ± 10
Weight (kg)	64 ± 8	73 ± 9*	69 ± 12
IBW (%)	96 ± 14	102 ± 16	103 ± 13
Systolic BP (mm Hg)	99 ± 12	113 ± 11*	117 ± 19*
Diastolic BP (mm Hg)	63 ± 11	73 ± 8*	70 ± 10
Serum albumin (g/liter)†	23 ± 4	35 ± 8*	27 ± 5
Hematocrit	0.31 ± 0.6	0.37 ± 0.6*	0.29 ± 0.5
T4 cell count (×10⁶/liter)	131 ± 186	333 ± 217*	NA
Major infections			
Pneumocystis carinii	18	14*	1*
Cytomegalovirus	2	5	2
Mycobacterial disease	3	1	1
Bacterial sepsis	1	0	6
Disseminated fungal disease	1	0	5
Neoplasms			
Kaposi's sarcoma	6	5	0*
Lymphoma	1	1	0
Zidovudine (AZT) therapy	11	14	0*

*$p < 0.05$ versus hospitalized patients with HIV; †conversion factor to mg/dl is 0.1. AIDS = acquired immunodeficiency syndrome; BP = blood pressure; IBW = predicted ideal body weight; NA = not available.

dysfunction and known significant left main coronary artery disease was excluded from the study.

Diagnoses according to criteria from the Centers for Disease Control (12) included AIDS in 51 patients, AIDS-related complex in 13 and asymptomatic HIV infection in 6. Of the 70 study patients, 43 (61%) had an AIDS-defining opportunistic infection, 12 (17%) had an AIDS-defining malignancy and 7 (10%) had both. The average age was 37 years (range 23 to 54); all but 3 patients were male. Risk factors for HIV infection included homosexuality in 65 patients (93%), blood transfusion in 3 (4%), intravenous drug abuse in 3 (4%) and heterosexual contact in 2 (3%); 4 patients had more than one risk factor. Clinical manifestations of HIV infection are listed in Table 1. Zidovudine (AZT) was being administered to 25 patients (36%) in the study, including 11 hospitalized patients.

Control patients (Table 1). The control patients were identified from a retrospective review of hospitalized patients with acute leukemia between the ages of 20 and 55 years who underwent echocardiography as a baseline test before the initiation of chemotherapy or bone marrow transplantation between 1982 and 1987. Hematologic diagnoses were based on the results of bone marrow biopsy in all patients; patients who were treated with anthracycline derivatives before the echocardiogram were excluded. Twenty patients who met these criteria served as control patients. Their mean age was 36 years, and 15 patients were male. Hematologic diagnoses were acute myelogenous leukemia in 12, accelerated phase of chronic myelogenous leukemia in 5 and acute lymphocytic leukemia in 3. Clinical information on these patients is listed in Table 1.

Chart review. Hospital and clinic charts on all study and control patients were reviewed for the following information: height and weight at the time of evaluation, physical examination, medications, opportunistic infections, serum albumin, hematocrit, chest radiograph and electrocardiogram (ECG). For study and control patients, predicted ideal body weight was also calculated.

T4 lymphocyte counts. T4 lymphocyte cell counts were performed on 60 of the HIV-infected patients. Lymphocytes expressing the T4 antigen (helper/inducer cells) were enumerated with the use of simultaneous dual immunofluorescence and flow cytometry (Becton-Dickinson Immunocytometry Systems) with mixed monoclonal antibodies (13). T4 lymphocyte counts in normal adult range from 459 to 1,535 × 10^6/liter by this technique in this laboratory.

Echocardiography

Imaging technique. Quantitative M-mode, two-dimensional and Doppler echocardiograms were performed on a phantom-calibrated IREX Meridian ultrasound machine. The subjects were placed in the 90° left lateral decubitus position, left ventricular chamber sizes were maximized in standard views and respiration was suspended before recording (14). Blood pressure was determined by sphygmomanometer at the end of the echocardiographic study with the patient seated.

Measurements and tracing. Echocardiographic measurements were made on a phantom-calibrated Diasonics computer-guided light-pen digitizing system. End-diastolic areas were traced on video frames at the peak of the R wave on the ECG or just after mitral valve closure; end-systolic areas were traced at the frame immediately preceding mitral valve opening.

Morphology. Mitral-septal separation was defined by M-mode echocardiography as the perpendicular distance between the E point of the anterior mitral leaflet and a tangent drawn to the most posterior point reached by the interventricular septum within the same cycle (15). Mitral-septal separation was measured at a level in which both mitral leaflets were well seen.

Average diastolic left ventricular wall thickness and left ventricular mass were calculated with use of a truncated ellipsoid formula (16). Previous work (17) indicates that mean left ventricular mass index by this technique in a normal adult man is 71 g/m^2; the upper limit of normal is 94 g/m^2.

Left ventricular volumes and ejection fraction were measured using a modification of Simpson's rule (18–20). End-systolic and end-diastolic endocardial areas were traced in the apical two and four chamber views to generate left

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ventricular end-diastolic volume, end-systolic volume and ejection fraction. According to previous work (20), mean left ventricular end-diastolic volume index by this technique in a normal adult man is 58 ml/m^2; the upper limit of normal is 80 ml/m^2.

Dilated cardiomyopathy was defined as the presence of diffuse left ventricular hypokinesia (ejection fraction ≤45%) and left ventricular dilation (left ventricular end-diastolic volume index >80 ml/m^2).

Doppler evaluation. Standard Doppler evaluations of all four cardiac valves in pulsed wave and continuous wave modes were performed. The presence and severity of valvular regurgitation were determined by standard methods (21).

Doppler localization of tricuspid insufficiency was performed in the pulsed mode, then maximized and measured in the continuous wave mode. By a modification of the Bernoulli formula (22), the peak pressure gradient (in mm Hg) between the right atrium and ventricle was estimated as the product of 4 and maximal tricuspid insufficiency velocity squared ($\Delta P = 4V^2$). Right ventricular systolic pressure was computed as the sum of this pressure gradient and right atrial pressure (right ventricular systolic pressure = $4V^2$ + right atrial pressure) (23). Subcostal views in all but four patients demonstrated >50% collapse of the diameter of the proximal inferior vena cava during deep inspiration. Right atrial pressure was assumed to be 5 mm Hg for these patients and 15 mm Hg for the four patients with <50% collapse of the inferior vena cava (24,25). By this method, the upper limit of normal for right ventricular systolic pressure in this laboratory is 30 mm Hg.

Statistical analysis. Data were evaluated by chi-square analysis and factorial analysis of variance. Upper limits of normal for left ventricular mass index and end-diastolic volume index in normal men determined in this laboratory (listed earlier) have previously been computed and reported (17,20) as the 90% upper confidence bounds for the 95th percentile. Comparisons were made between hospitalized and ambulatory patients with HIV infection and between hospitalized patients with HIV infection and control patients. Values are listed as mean ± standard deviation (SD). The null hypothesis was rejected at the 5% level.

Results

Clinical Data (Table 1)

Among the 70 patients with HIV infection, 25 were hospitalized and 45 were ambulatory at the time of evaluation.

Ambulatory versus hospitalized with HIV infection. Compared with the ambulatory patients, the hospitalized patients more frequently had a history of *Pneumocystis carinii* pneumonia and had significantly lower mean values for body weight, systolic and diastolic blood pressure, serum albumin, hematocrit and T4 lymphocyte count.

Table 2. Echocardiographic Findings in 70 HIV-Infected Patients

	Hospitalized HIV	Ambulatory HIV	Control
No. of patients	25 (24)	45 (27)	20
Dilated cardiomyopathy	8 (7)	0*	0*
Pericardial effusion	7 (7)	0*	6
Pleural effusion	4 (3)	0*	2
Mediastinal mass	1 (1)	0	0
Mitral valve prolapse	0	3 (1)	1

*$p < 0.05$ versus hospitalized patients with HIV; numbers in parentheses indicate patients with AIDS as opposed to AIDS-related complex or asymptomatic HIV infection. HIV = human immunodeficiency virus.

Hospitalized patients with HIV infection versus control patients. The control patients with acute leukemia and the hospitalized patients with HIV infection were similar in mean age, body weight, percent of ideal body weight, diastolic blood pressure, serum albumin and hematocrit. However, control patients had significantly higher values for systolic blood pressure. Compared with control patients, hospitalized patients with HIV infection also more frequently had a history of *Pneumocystis carinii* pneumonia, Kaposi's sarcoma and treatment with AZT.

Two-Dimensional Echocardiographic Findings (Table 2)

Echocardiographic lesions. Two-dimensional echocardiography demonstrated dilated cardiomyopathy, pericardial effusion, pleural effusion or mediastinal mass in 16 (64%) of the 25 hospitalized patients with HIV infection. In comparison, mitral valve prolapse was the only abnormality noted in 3 (7%) of the 45 ambulatory patients ($p < 0.0001$).

Of the echocardiographic lesions, only dilated cardiomyopathy was significantly more common in hospitalized patients with HIV infection than in control patients with acute leukemia. Dilated cardiomyopathy was demonstrated in eight study patients with HIV infection versus no control patient ($p < 0.05$), pericardial effusion in seven study patients versus six control patients (p = NS), pleural effusion in four study patients versus two control patients (p = NS) and mediastinal mass in one study patient versus no control patients (p = NS). All of these echocardiographic lesions were limited to patients with AIDS, except for one patient with AIDS-related complex who had dilated cardiomyopathy and a pleural effusion.

Dilated cardiomyopathy. Among the eight hospitalized patients with HIV infection and dilated cardiomyopathy, four were detected from the clinical evaluation and four were first recognized at the time of the echocardiogram. All eight patients had four chamber enlargement and diffuse left ventricular hypokinesia, with a mean ejection fraction of 33 ± 13% (range 10 to 45%), end-diastolic volume index of 96 ± 40 ml/m^2 and left ventricular mass index of 108 ± 23 g/m^2

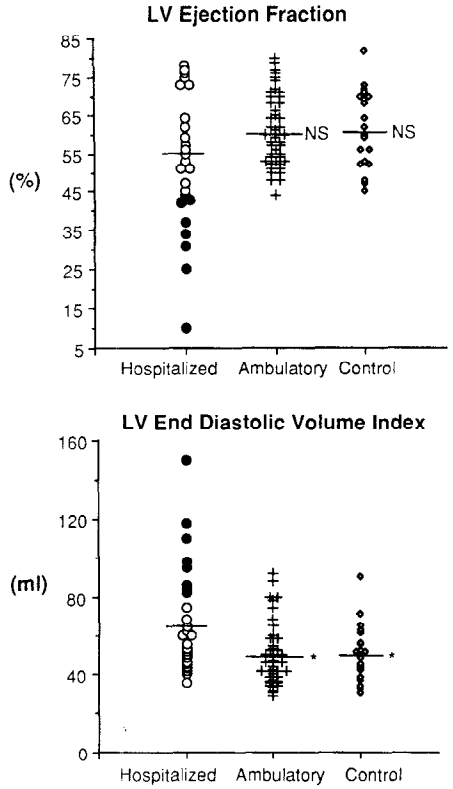

Figure 1. Comparison of left ventricular (LV) ejection fractions and end-diastolic volume indexes by two-dimensional echocardiography in 25 hospitalized patients with HIV infection, 45 ambulatory patients with HIV infection and 20 control patients with acute leukemia. The eight patients with dilated cardiomyopathy are indicated by **black circles** in the **first column**; the other 17 hospitalized patients by **open circles**. **Horizontal bars** indicate mean values. *$p < 0.05$ versus hospitalized patients with HIV infection. NS = no significant difference versus the same group.

(Fig. 1). Two patients presented with congestive heart failure at the time of a first AIDS-defining opportunistic infection; five other patients had previously known AIDS and one had previously known AIDS-related complex.

None of the patients with cardiomyopathy had had prior administration of cardiotoxic medications or a history of alcohol abuse, hypertension, diabetes or coronary disease; however, two patients did have a history of intravenous drug abuse and one had concomitant hepatic and renal failure. Two patients with AIDS who did not have cardiomyopathy were treated with anthracycline derivatives for Kaposi's sarcoma. Among the eight patients with cardiomyopathy, five had active *Pneumocystis carinii* pneumonia, one had Kaposi's sarcoma, one had tuberculosis and one had bacterial pneumonia; four patients with cardiomyopathy were receiving AZT therapy. The four patients with symptoms of congestive heart failure were successfully palliated with diuretic drugs, digoxin and an angiotensin-converting enzyme inhibitor. At 6 months follow-up after echocardiography, four of the patients with cardiomyopathy have died (two of progressive hypotension and dyspnea attributed to cardiac failure, and two of respiratory failure due to *Pneumocystis carinii* pneumonia). Autopsy in one patient revealed dilated cardiomyopathy without evidence of inflammatory myocarditis or cardiac opportunistic infection.

Pericardial effusion. In the seven patients with pericardial effusion, no effusion was suspected clinically. One of the seven patients had a moderate-sized effusion associated with mild right atrial collapse, consistent with impending tamponade (26); the patient refused pericardiocentesis and was treated with a nonsteroid anti-inflammatory drug. Follow-up study revealed a significant decrease in the size of the pericardial effusion with resolution of right atrial collapse. The other six patients had a small pericardial effusion without clinical or echocardiographic evidence of hemodynamic compromise. Among the seven patients, six were hospitalized for treatment of active *Pneumocystis carinii* pneumonia, one had a previous history of this infection, two had a history of Kaposi's sarcoma, one had pulmonary tuberculosis and one had non-Hodgkin's lymphoma; three of the patients also had dilated cardiomyopathy. The mean serum albumin concentration in these seven patients was 25 g/liter (2.5 g/dl); the lower limit of normal in this laboratory is 33 g/liter (3.3 g/dl).

Pleural effusion. In the four patients with pleural effusion by echocardiography (two with a large left pleural effusion, one with a small right effusion and one with a small bilateral effusion), the effusion had been previously documented by chest radiograph with decubitus films. Manifestations of AIDS in these four patients included *Pneumocystis carinii* pneumonia in three, mycobacterial infection in two, cardiomyopathy in two and Kaposi's sarcoma in one. In the two patients with a large effusion and dyspnea, thoracentesis was performed, with sympomatic benefit.

Mediastinal mass. One patient who had lymphadenopathic Kaposi's sarcoma presented with dyspnea and decreased exercise tolerance. Echocardiography showed an 8 cm anterior mediastinal mass that compressed the right ventricle. Computed tomography confirmed the presence of a water density mass and also revealed diffuse mediastinal and axillary lymphadenopathy. Biopsy of the mediastinal mass was declined.

Doppler findings. Comparison of the hospitalized and ambulatory patients with HIV infection revealed no significant differences in the incidence of regurgitation of the mitral (52% versus 45%), tricuspid (74% versus 67%) or aortic (4% versus 0%) valve, respectively (all p = NS). Although no patient in the study had severe mitral or tricuspid insufficiency, the eight patients with dilated cardiomyopathy usually had mild to moderate valvular regurgitation by Doppler study that was associated with a murmur on physical examination, whereas the other patients had absent, trivial or mild regurgitation that was usually not associated with a murmur. Peak pulmonary systolic pressure was significantly higher in

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Table 3. Echocardiographic Measurements in 70 HIV-Infected Patients

	Hospitalized HIV (n = 25)	Ambulatory HIV (n = 45)	Control (n = 20)
E point (cm)	0.9 ± 0.6	0.4 ± 0.1*	0.5 ± 0.2*
LVEDVI (ml/m^2)	67 ± 29	50 ± 16*	51 ± 15*
LVESVI (ml/m^2)	34 ± 23	20 ± 6*	24 ± 7*
LVEF (%)	54 ± 18	60 ± 8	61 ± 10
LVMI (g/m^2)	78 ± 24	67 ± 21	72 ± 25
AWT (cm)	1.1 ± 0.2	0.9 ± 0.3*	1.1 ± 0.2
LAVI (ml/m^2)	43 ± 21	34 ± 10*	34 ± 9*

*$p < 0.05$ versus patients hospitalized with HIV. AWT = average diastolic left ventricular wall thickness; E point = mitral-septal separation; HIV = human immunodeficiency virus; LAVI = left atrial volume index; LVEDVI = left ventricular end-diastolic volume index; LVEF = left ventricular ejection fraction; LVESVI = left ventricular end-systolic volume index; LVMI = left ventricular mass index.

hospitalized than in ambulatory patients with HIV infection (37 ± 11 versus 22 ± 4 mm Hg, respectively, $p < 0.05$).

Quantitative Planimetry (Table 3)

Hospitalized versus ambulatory patients with HIV infection (Fig. 1). Compared with the ambulatory patients with HIV infection, hospitalized patients with HIV infection had significantly higher echocardiographic values for mean mitral-septal separation, left ventricular end-diastolic and end-systolic volume indexes, average wall thickness and left atrial volume index (Fig. 1). There were no significant group differences for mean left ventricular ejection fraction or mass index.

Hospitalized patients with HIV infection versus control patients (Fig. 1). Compared with control patients, hospitalized patients with HIV infection also had significantly higher values for mitral-septal separation, left ventricular end-diastolic and end-systolic volume indexes and left atrial volume index. Mean left ventricular ejection fraction, mass index and average wall thickness were not significantly different between these two groups.

Discussion

To determine the prevalence of cardiac lesions, we evaluated a series of HIV-infected patients by two-dimensional echocardiography with Doppler ultrasound. The patients in the study were mainly symptomatic homosexual men. Of the 70 study patients with HIV infection, eight (11%) were found to have dilated cardiomyopathy, seven (10%) had pericardial effusion, four (6%) had pleural effusion and one (2%) had a mediastinal mass.

Selection of control patients. Although it is difficult to select an appropriate control group for adults hospitalized with AIDS, we chose young patients with acute leukemia who had baseline echocardiography before the administration of anthracycline derivatives. Like the hospitalized HIV-infected patients, the control patients were relatively young and systemically ill. Of the echocardiographic lesions demonstrated, only dilated cardiomyopathy was statistically more common in hospitalized patients with HIV infection than in control patients. These results in consecutively studied patients, plus the diagnosis of dilated cardiomyopathy in four other patients with AIDS in this laboratory over the 3 years before this study, suggest an association between dilated cardiomyopathy and AIDS.

Comparison with previous reports. The prevalence of dilated cardiomyopathy in this study was nearly identical to that in a recent necropsy series of patients with AIDS (2). Pericardial tamponade has also been reported previously in patients with AIDS (7). One of our seven patients with pericardial effusion had incipient tamponade that improved after therapy with a nonsteroid anti-inflammatory drug; the remaining six patients had a small, hemodynamically insignificant effusion. The origin of the pericardial effusion in this study was not clear; however, hypoalbuminemia and contiguous pneumonitis may have been contributing factors. We have previously described (27) a patient with AIDS with a large mediastinal mass.

Findings in hospitalized versus ambulatory patients. We observed a striking difference in the incidence and severity of echocardiographic findings between hospitalized and ambulatory patients with HIV infection. Among the 25 hospitalized HIV-infected patients, cardiac and thoracic abnormalities were noted in 16; in contrast, among the 45 ambulatory patients, the only abnormality noted was mitral valve prolapse in three patients. Our data in living subjects confirm previous pathologic reports (1–5) that dilated cardiomyopathy and other cardiac abnormalities are fairly common in hospitalized, acutely ill patients with AIDS. However, we have also shown that cardiac lesions are uncommon in ambulatory patients with HIV infection, despite prior major opportunistic infections in one-third of patients.

Comparing the hospitalized with the ambulatory patients with HIV infection, the former had larger, thicker hearts and higher peak pulmonary systolic pressures. The differences between these groups were mainly due to the hospitalized patients with dilated cardiomyopathy. Although hospitalized patients had a lower hematocrit than ambulatory patients, cardiac enlargement has been reported (28) to develop only in association with severe anemia. Left ventricular hypertrophy could not be attributed to hypertension because hospitalized patients had significantly lower values for systolic and diastolic blood pressure than did outpatients with HIV infection or control patients.

In the ambulatory HIV-infected study patients, values for mean left ventricular mass and end-diastolic volume were lower than normal, but still in the normal range reported for healthy adult men (17,20). After correction for body surface

area, these variables were closer to mean normal values; thus, we attributed this difference in cardiac size to cachectic habitus. Mild or moderate pulmonary hypertension was noted in the patients with dilated cardiomyopathy and in two additional hospitalized patients who had active *Pneumocystis carinii* pneumonia.

Prognosis of dilated cardiomyopathy. Among the eight HIV-infected patients with dilated cardiomyopathy, four had a rapidly fatal acute course. Despite this poor outcome, symptoms of congestive heart failure due to dilated cardiomyopathy often initially responded to conventional treatment. Therapy with AZT did not appear to prevent the development of cardiomyopathy because four of the eight patients had been given this drug.

Pathogenesis of dilated cardiomyopathy. The history of each patient with cardiomyopathy was negative for exposure to known cardiotoxins. AZT and trimethoprim-sulfamethoxazole, the two most commonly administered drugs in this study, have not been reported to cause myocarditis or congestive heart failure in AIDS or non-AIDS patients (29,30). Although many of the hospitalized patients with AIDS were underweight or even cachectic at the time of evaluation, nutritional deficiency seems unlikely as an etiologic factor, since hospitalized patients with HIV infection and control patients were comparably abnormal in percent of predicted ideal body weight and serum albumin. Similar to previous studies (1–7), the patients studied were nearly all homosexual men without a history of intravenous drug abuse. Thus, cardiac abnormalities associated with addiction, such as valve vegetations, valvular sclerosis and cardiac abscesses, were not demonstrated. It is unknown whether patients with AIDS secondary to intravenous drug abuse have a greater or lesser incidence of cardiac lesions, including dilated cardiomyopathy.

We found an association between the presence of active Pneumocystis carinii pneumonia infection and cardiac abnormalities. Neither the organism nor the drugs employed in treatment have been reported to cause myocarditis or myocardial depression. There was no correlation with other active opportunistic infections such as cytomegalovirus. We speculate that the most immunologically compromised patients with AIDS may be predisposed to develop multiple complications of immunocompromise, including myocarditis. Although this concept is supported by significantly lower T4 cell counts in hospitalized than in ambulatory study patients with HIV infection (31), T4 counts did not differ between patients with dilated cardiomyopathy and other hospitalized patients with HIV infection.

Recent reports (1–7) suggest that the most likely origin of dilated cardiomyopathy in patients with HIV infection is infectious myocarditis. Several autopsy studies in adult and pediatric patients with AIDS (1–5) have demonstrated that focal myocarditis is a common and often asymptomatic cardiac lesion. Although various cardiac pathogens have been identified by necropsy in patients with AIDS (including cytomegalovirus, *Toxoplasma gondii*, *Crytococcus neoformans*, *Candida albicans*, *Mycobacterium tuberculosis* and *Histoplasma capsulatum*), there is no clear relation between the presence of an opportunistic pathogen and the severity of myocarditis (3). Alternatively, myocardial dysfunction may be caused by direct myocyte infection by HIV. In one report (32), HIV was cultured from an endomyocardial biopsy sample in a living patient with myocarditis. Our findings in patients with dilated cardiomyopathy are limited by the lack of myocardial tissue by either endomyocardial biopsy or autopsy. Further clinicopathologic research is required to confirm the diagnoses and provide information about the pathogenesis of the disease.

Clinical implications. Many patients with AIDS develop multiple opportunistic pulmonary infections, so that dyspnea is often assumed to be of pulmonary origin. Our findings suggest that cardiac abnormalities should also be considered in the evaluation of dyspnea in these patients. Palliative therapy for dyspnea due to congestive heart failure or pericardial effusion in this setting is efficacious, and differs from therapy for pulmonary processes. In addition, the detection of occult cardiomyopathy in AIDS may have relevance for the choice of antibiotic and tumor therapy. For example, intravenous trimethoprim-sulfamethoxasole must be administered in a large volume of fluid to avoid crystallization of drug in the renal tubules (33); this fluid load might not be well tolerated by a patient with cardiac compromise. Likewise, anthracycline derivatives, which are used as chemotherapeutic agents for Kaposi's sarcoma, could lead to further deterioration of cardiac function if administered to a patient with cardiomyopathy. The use of echocardiography should be considered in the evaluation of dyspnea in hospitalized patients with AIDS, especially those who have shortness of breath that is out of proportion to their diagnosed pulmonary disease.

We are indebted to Salvatore Geraci, RDMS for performing most of the echocardiographic studies, and to Melvin Cheitlin, MD and Robert Wachter, MD for reviewing the manuscript.

References

1. Cohen IS, Anderson DW, Virmani R, et al. Congestive cardiomyopathy in association with the acquired immunodeficiency syndrome. N Engl J Med 1986;315:628–30.
2. Anderson DW, Virmani R, Reilly JM, et al. Prevalent myocarditis at necropsy in the acquired immunodeficiency syndrome. J Am Coll Cardiol 1988;11:792–9.
3. Lafont A, Marche C, Wolff M, et al. Myocarditis in acquired immunodeficiency syndrome (AIDS): etiology and prognosis (abstr). J Am Coll Cardiol 1988;11:196A.
4. Lipschutz SE, Canock S, Sanders SP, Coan SD, Perez-Atayde A, McIntosh K. Cardiac manifestations of pediatric human immunodeficiency virus infection (abstr). Circulation 1987;76(Suppl IV):IV-515.

5. Stewart JM, Kaul A, Gromisch DS, Woolf PK, Gweitz MH. Congestive heart failure in children with human immunodeficiency virus infection (abstr). Circulation 1987;76(Suppl IV):IV-515.

6. Corboy JR, Fink L, Miller WT. Congestive cardiomyopathy in association with AIDS. Radiology 1987;165:139–41.

7. Fink LI, Reichek N, St. John Sutton MG. Cardiac abnormalities in acquired immune deficiency syndrome. Am J Cardiol 1984;54:1161–4.

8. Cammarosano C, Lewis W. Cardiac lesions in acquired immune deficiency syndrome (AIDS). J Am Coll Cardiol 1985;5:703–6.

9. Silver MA, Macher AM, Reichert CM, et al. Cardiac involvement by Kaposi's sarcoma in acquired immune deficiency syndrome (AIDS). Am J Cardiol 1984;53:983–5.

10. Henochowicz, S., Mustafa M, Lawrinson WE, Pistole M, Lindsay J Jr. Cardiac aspergillosis in acquired immune deficiency syndrome. Am J Cardiol 1985;5:1239–40.

11. Laws W, Lipsick J, Cammarosano C. Cryptococcal myocarditis in acquired immune deficiency syndrome. Am J Cardiol 1985;55:1240.

12. Centers for Disease Control. Revision of the CDC case surveillance case definition for acquired immunodeficiency syndrome. Morbid Mortal Weekly Rep 1987;36(Suppl 1S):1S–15S.

13. Stites DP, Cassavant CH, McHugh TM, et al. Flow cytometric analysis of lymphocyte phenotypes in AIDS using monoclonal antibodies and simultaneous immunofluorescence. Clin Immunol Immunopathol 1986;38:161–77.

14. Schiller NB, Gutman JM. Quantitative analysis of the adult left heart by two-dimensional echocardiography. In: Giuliani ER, ed. Two-Dimensional Real-Time Ultrasonic Imaging of the Heart. Amsterdam: The Netherlands: Martinus Nijhoff, 1985:135–45.

15. Massie BM, Schiller NB, Ratshin RA, Parmley WM. Mitral-septal separation: new echocardiographic index of left ventricular function. Am J Cardiol 1977;39:1008–16.

16. Schiller NB, Skiodebrand C, Schiller E, et al. Canine left ventricular mass estimation by two-dimensional echocardiography. Circulation 1983;68: 210–6.

17. Byrd BF III, Wahr DW, Wang YS, Bouchard A, Schiller NB. Left ventricular mass and volume/mass ratio determined by two-dimensional echocardiography in normal adults. J Am Coll Cardiol 1985;6:1021–5.

18. Schiller NB, Acquatella H, Ports TA, et al. Left ventricular volume from paired biplane two-dimensional echocardiographs. Circulation 1979;60: 547–52.

19. Silverman NH, Ports TA, Snider AR, Schiller NB, Carlsson E, Heilbron DC. Determination of left ventricular volume in children: echocardiographic and angiographic comparisons. Circulation 1980;62:548–57.

20. Wahr D, Wang Y, Schiller N. Clinical quantitative echocardiography. II. Left ventricular volume in a normal adult population. J Am Coll Cardiol 1983;1:863–9.

21. Feigenbaum H. Echocardiography. 4th ed. Philadelphia: Lea & Febiger, 1986:188–224.

22. Hatle L, Angelsen B. Doppler Ultrasound in Cardiology: Physical Principals and Clinical Applications. 2nd ed. Philadelphia: Lea & Febiger, 1985:23.

23. Yock PG, Popp RL. Noninvasive estimation of right ventricular systolic pressure by Doppler ultrasound in patients with tricuspic regurgitation. Circulation 1984;70:657–62.

24. Kircher B, Himelman RB, Schiller NB. Estimation of right atrial pressure by two-dimensional echocardiography of the respiratory behavior of the inferior vena cava (abstr). Circulation 1988;78(Suppl II):II-550.

25. Simonson JS, Schiller NB. Sonospirometry: a new method for noninvasive estimation of mean right atrial pressure based on two-dimensional echographic measurements of the inferior vena cava during measured inspiration. J Am Coll Cardiol 1988;11:557–64.

26. Gillam LD, Guyer DE, Gibson TC, Etta King M, Marshall JE, Weyman AE. Hemodynamic compression of the right atrium: a new echocardiographic sign of cardiac tamponade. Circulation 1983;68:294–301.

27. Himelman RB, Schiller NB. Diagnosis of mediastinal lesions by two-dimensional echocardiography. Echocardiography 1988;5:219–25.

28. Graettinger JS, Parsons RL, Campbell JA. A correlation of clinical and hemodynamic studies in patients with mild and severe anemia with and without congestive failure. Ann Intern Med 1963;58:617–26.

29. Gordin FM, Simon GL, Wofsy CB, Mills J. Adverse reactions to trimethoprim-sulfamethoxazole in patients with the acquired immunodeficiency syndrome. Ann Intern Med 1984;100:495–9.

30. Richman DD, Fischl MA, Grieco MH, et al. The toxicity of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. N Engl J Med 1987;317:192–7.

31. Kornfeld H, Vande Stouwe RA, Lange M, Reddy MM, Grieco MH. T-lymphocyte subpopulations in homosexual men. N Engl J Med 1982;307:729–31.

32. Calabrese LH, Proffitt MR, Yen-Lieberman B, Hobbs RE, Ratliff NB. Congestive cardiomyopathy and illness related to the acquired immunodeficiency syndrome (AIDS) associated with isolation of retrovirus from myocardium. Ann Intern Med 1987;107:691–2.

33. Mandell GL, Sande MA. Antimicrobial agents: sulfonamides, trimethoprim-sulfamethoxazole, and urinary tract antiseptics. In: Gilman AG, Goodman LS, Gilman A, eds. The Pharmacological Basis of Therapeutics. 7th ed. New York: Macmillan, 1985:1095–115.