Constrictive pericarditis requiring pericardiectomy at Groote Schuur Hospital, Cape Town, South Africa: Causes and perioperative outcomes in the HIV era (1990-2012)

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Objective: The causes of constrictive pericarditis and predictors of perioperative outcome after pericardiectomy have not been clearly elucidated, especially in Africa, where the disease characteristics differ from those in developed countries. Furthermore, the effect of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) on pericardial constriction and outcomes after surgery is unknown. We investigated the causes of constrictive pericarditis, outcomes after pericardiectomy, and predictors of mortality in Cape Town, South Africa, during a 22-year period of high HIV/AIDS prevalence.

Methods: A retrospective review of the medical records of all patients who had undergone pericardiectomy for constrictive pericarditis at Groote Schuur Hospital from January 1, 1990 to December 31, 2012 was performed.

Results: Of 121 patients, 36 (29.8%) had proven tuberculosis, 74 (61.2%) had presumed tuberculosis, 6 (5%) had idiopathic causes, and 5 (4%) had miscellaneous causes of constrictive pericarditis. Seventeen patients (14%) died perioperatively with low cardiac output syndrome the main cause of mortality. On multivariable analysis, serum sodium (hazard ratio, 0.88; 95% confidence interval, 0.80-0.97; $P = .009$) and preoperative New York Heart Association class IV (hazard ratio, 3.42; 95% confidence interval, 1.29-9.08; $P = .014$; vs combined class I-III) were independent predictors of early mortality. Of the 121 patients, 14 (11.6%) were HIV positive, with a mean CD4 cell count of 284 ± 133 cells/ μ L. No early deaths occurred in the HIV-positive patients.

Conclusions: Tuberculosis is the main cause of constrictive pericarditis in South Africa. Despite its efficacy at relieving the symptoms of heart failure, pericardiectomy is associated with high perioperative mortality that was not influenced by HIV status. New York Heart Association functional class IV and hyponatremia predict for early mortality after pericardiectomy. (J Thorac Cardiovasc Surg 2014;148:3058-65)

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Constrictive pericarditis (CP) is a treatable cause of heart failure. Fibrosed, noncompliant parietal and visceral pericardium impede ventricular filling in diastole, thereby reducing the stroke volume and resulting in systemic venous congestion.¹ The causes of pericardial fibrosis vary,² with studies showing that infective causes are prevalent in the developing world.³⁻⁵ Pericardiectomy is the

standard method of relieving pericardial constriction.⁶ The outcomes after pericardiectomy and the predictors of mortality have been studied extensively in the developed world,⁷⁻⁹ but only a few small studies have examined the causes and outcomes of patients with constrictive pericarditis requiring pericardiectomy in Africa.^{5,10} Owing to differences in disease patterns and resource availability, the findings of studies conducted in the developed world might not be an accurate reflection of the experience of constrictive pericarditis requiring pericardiectomy in Africa.

During the past 20 years, South Africa has seen an increase in the prevalence of pulmonary and extrapulmonary tuberculosis (TB), largely driven by increases in the incidence and prevalence of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS).¹¹ The effect of the increase in HIV/AIDS on the clinical characteristics of constrictive pericarditis and the outcomes after pericardiectomy are not known.

We conducted a study to examine the causes and determinants of 30-day mortality, the functional outcomes, and the effect of HIV/AIDS on the clinical profile and outcomes after pericardiectomy at Groote Schuur Hospital in Cape Town, South Africa.

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Abbreviations and Acronyms

AIDS	= acquired immunodeficiency syndrome
CP	= constrictive pericarditis
HIV	= human immunodeficiency virus
HR	= hazard ratio
NYHA	= New York Heart Association
TB	= tuberculosis

METHODS

A retrospective review of the medical records of all patients who had undergone pericardiectomy for constrictive pericarditis at the Chris Barnard Division of Cardiothoracic Surgery of Groote Schuur Hospital was undertaken. The patients who had undergone pericardiectomy from January 1, 1990, and December 31, 2012, were eligible for the present study. The patient records were reviewed, and the data of interest (demographic information, clinical signs and symptoms, hemodynamic and laboratory data, operative techniques, and outcomes) were entered into a standardized data capture sheet. The patients whose records could not be found were excluded from the present study. The diagnosis of constrictive pericarditis was determined from typical clinical and echocardiographic findings, with confirmation of pericardial fibrosis and constriction intraoperatively.⁶ Commonly encountered clinical features included peripheral edema with hepatomegaly and ascites, pulsus paradoxus, and pleural effusions. Echocardiography typically revealed pericardial thickening, paradoxical septal motion, dilated inferior vena cavae, and typical respiratory variation in Doppler flow across the mitral and/or tricuspid valves. Cardiac catheterization and/or computed tomography were done in cases of diagnostic uncertainty to confirm pericardial thickening and constriction. All patients underwent surgery by way of a median sternotomy, with particular care taken to free up the entire ventricular epicardium, apex, and diaphragmatic surface of the heart. Once freed, the pericardium was removed anteriorly, extending laterally close to the phrenic nerves, with the posterior pericardium left in situ after being freed from the epicardium (total pericardiectomy). Any resection less than this was considered partial pericardiectomy. Cardiopulmonary bypass was used at the discretion of the surgeon or when hemodynamic instability prevented adequate exposure of the adherent pericardium. Presumed TB as a cause for constrictive pericarditis was defined as a history of pulmonary TB or the initiation of empiric antituberculous therapy by the attending physician, before pericardiectomy. Proven TB was defined as the presence of *Mycobacterium tuberculosis* in pericardial tissue or fluid or sputum by microscopy or culture. The presence of caseous pericardial tissue at surgery was also considered confirmatory of TB. Perioperative mortality was defined as death from any cause occurring during the index hospitalization or within 30 days of surgery, even if the patient had been discharged from the hospital. The University of Cape Town Human Research Ethics Committee approved the study (reference no. 558/2012).

Statistical Analysis

Categorical data were compared using the chi-square test and continuous data using the *t* test. The Kaplan-Meier method was used to calculate probabilities of death and the log-rank test to compare these probabilities by group. Cox proportional hazards regression models were fitted to determine the risk factors associated with mortality. In the present analysis, because of the small numbers, New York Heart Association (NYHA) classes I to III were combined and modeled as the baseline risk versus NYHA class IV. Variables significantly associated

with the outcome were included in the final model. The proportionality assumption of the Cox models was tested using $-\ln[-\ln(\text{survival})]$ curves and regression of scaled Schoenfeld residuals on the functions of time. All tests were 2-sided. Statistical analysis was conducted using the Statistical Package for Social Sciences, version 20, (SPSS, Chicago, Ill).

RESULTS

A total of 128 patients underwent pericardiectomy for constrictive pericarditis during the study period; 7 were excluded because of missing records. Of the 121 patients in the present study, 79 (65.3%) were men, and the mean age was 41.3 ± 16.1 years (range, 14-74). Two patients developed recurrent constriction requiring repeat pericardiectomy 2 months after the initial surgery. Total pericardiectomy was possible in 105 patients (88.2%), with 14 (11.8%) undergoing partial pericardiectomy. Five patients (4.1%) underwent concomitant mitral valve repair. One patient underwent concomitant aortic valve replacement with coronary artery bypass grafting. The baseline characteristics stratified by mortality status are listed in Table 1.

Of the 121 patients, 110 (90.9%) had constrictive pericarditis due to either proven (36; 29.8%) or presumed (74; 61.2%) TB. Of the remaining 11 patients, 6 (4.9%) had idiopathic constrictive pericarditis and 5 had other causes of pericarditis (Figure 1). The patient with radiation-induced constrictive pericarditis had undergone chest irradiation for Hodgkin's lymphoma 20 years previously, and the patient with Kaposi sarcoma was HIV negative. The causes of constrictive pericarditis reported in similar studies worldwide^{3,4,7-9,12-17} are listed in Table 2. Of the 121 patients, 63 (52.1%) underwent diagnostic cardiac catheterization, with only 1 case of coronary artery disease documented at coronary angiography. All 63 patients had elevation and equalization of diastolic pressures, with the dip-and-plateau configuration typical of constrictive pericarditis. A total of 18 patients (14.9%) underwent cardiac computed tomography scanning. The intraoperative complications included 27 cases (22.3%) of inadvertent myocardial wall or major vessel injury with bleeding, tachyarrhythmias requiring cardioversion ($n = 6$; 5%), and phrenic nerve injury ($n = 2$; 1.7%). Low output cardiac failure was the most common postoperative complication ($n = 80$; 66.1%), followed by sternal wound sepsis ($n = 9$; 7.4%), other site sepsis ($n = 9$; 7.4%), acute kidney injury ($n = 9$; 7.4%), repeat thoracotomy for bleeding ($n = 4$; 3.3%), repeat thoracotomy for placement of ventricular-assistive devices ($n = 2$; 1.7%), respiratory complications ($n = 6$; 5%), neuropsychiatric complications ($n = 5$; 4.1%), and tachyarrhythmias ($n = 3$; 2.5%). No intraoperative mortality occurred. Seventeen patients (14%) died postoperatively while still in hospital, 1 of whom had undergone concomitant mitral valve repair. Nine of these

TABLE 1. Baseline characteristics of study patients stratified by mortality status

Characteristic	All (n = 121)	Alive (n = 104)	Died (n = 17)	P value
Mean age (y)	41.3 ± 16.1	40.2 ± 16.1	47.6 ± 14.7	.08
Male sex	79 (65.3)	69 (66.3)	10 (58.8)	.546
Cause of constrictive pericarditis				.679
Tuberculosis	110 (90.9)	95 (91.3)	15 (88.2)	
Other	11 (9.1)	9 (8.7)	2 (11.8)	
Preoperative NYHA functional class				.001
I	3 (2.5)	2 (1.9)	1 (5.9)	
II	38 (31.4)	36 (34.6)	2 (11.8)	
III	57 (47.1)	52 (50.0)	5 (29.4)	
IV	23 (19)	14 (13.5)	9 (52.9)	
Symptom duration (mo)	12.5 ± 22.4	5.3 ± 4.4	13.7 ± 23.9	.154
HIV status				.274
Positive	14 (11.6)	14 (13.5)	0 (0.0)	
Negative	82 (67.8)	69 (66.3)	13 (76.5)	
Unknown	25 (20.6)	21 (20.2)	4 (23.5)	
Hypertension	12 (9.9)	9 (8.7)	3 (17.6)	.25
Diabetes mellitus	3 (2.5)	3 (2.9)	0 (0.0)	.478
Total daily diuretic dose* (mg)	119 ± 101	109 ± 71	174 ± 192	.014
Weight (kg)	65 ± 12	64.8 ± 12.2	66.1 ± 10.7	.715
SBP (mm Hg)	111 ± 15	112 ± 15	108 ± 13	.262
DBP (mm Hg)	70 ± 11	71 ± 11	68 ± 11	.288
Pulse rate (beats/min)	89 ± 16	88 ± 16	95 ± 14	.091
Pulsus paradoxus	77 (63.6)	68 (65.4)	9 (52.9)	.323
Ascites	92 (76)	77 (74)	15 (88.2)	.204
Diastolic knock	64 (52.9)	57 (54.8)	7 (41.2)	.297
Pleural effusion	96 (79.3)	83 (79.8)	13 (76.5)	.753
Hepatomegaly	108 (89.3)	95 (91.3)	13 (76.5)	.066
Pericardial calcification†	28 (23.1)	25 (24.0)	3 (17.6)	.562
Atrial fibrillation	10 (8.3)	7 (6.7)	3 (17.6)	.13
Low QRS amplitude	77 (63.6)	63 (60.6)	14 (82.4)	.084
LVEF (%)	57 ± 11	57 ± 11	58 ± 14	.704
Hemoglobin (g/dL)	13.1 ± 1.7	13.1 ± 1.7	13.0 ± 1.5	.759
Serum sodium (mmol/L)	137 ± 5	138 ± 4	133 ± 7	<.0001
Serum creatinine (μmol/L)	83 ± 23	81 ± 18	99 ± 38	.002
Total pericardiectomy‡	105 (88.2)	93 (90.3)	12 (75)	.077
Cardiopulmonary bypass	20 (16.5)	15 (14.4)	5 (29.4)	.123
Postoperative inotrope use	80 (66.1)	63 (60.6)	17 (100)	.001
Postoperative ICU stay (d)	3.4 ± 2.3	3.4 ± 1.8	3.5 ± 4.4	.96

Data presented as mean ± standard deviation for continuous variables and n (%) for categorical variables. NYHA, New York Heart Association; HIV, human immunodeficiency virus; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction (measured on echocardiogram or at cardiac catheterization); ICU, intensive care unit. *Furosemide. †Found on chest radiograph or at cardiac catheterization. ‡Anterior pericardium excised between phrenic nerves and posterior pericardium freed; pericardiectomy completeness could not be ascertained for 1 patient in each subgroup.

patients (52.9%) were in NYHA class IV before surgery. Low output cardiac failure was directly or indirectly responsible for the death of 11 patients, and acute kidney injury was implicated in the death of 6 patients. Postoperative sepsis was implicated in 4 deaths and postoperative bleeding, rapid atrial fibrillation, and respiratory failure in 1 each. One patient's death was sudden and unexplained, and the cause of death for 2 patients was not apparent from their medical records. Figure 2 shows the overall Kaplan-Meier survival plot for the study population. The 30-day survival rate in the present study was 86%. The

completeness of pericardiectomy did not have any effect on perioperative mortality (hazard ratio [HR], 1.74; 95% confidence interval [CI], 0.61-4.97; $P = .077$). The operative period did not affect perioperative mortality (1990-2000 mortality, 8 of 46 [17%]; 2001-2012 mortality, 9 of 75 [12%]; $P = .41$). No difference was seen in mortality between patients with proven versus those with presumed TB pericarditis ($P = .632$).

On univariable Cox proportional hazards regression analysis, the variables significantly associated with perioperative mortality were preoperative NYHA class (class IV,

FIGURE 1. Causes of constrictive pericarditis in 121 patients who underwent pericardiectomy (1990-2012). *TB*, Tuberculosis.

HR, 4.99; 95% CI, 1.92-13.03; $P = .001$, vs combined class I-III), preoperative total daily dose of diuretic (furosemide; HR, 1.003; 95% CI, 1.001-1.006; $P = .019$), preoperative serum creatinine (HR, 1.09; 95% CI, 1.01-0.03; $P = .002$), and preoperative serum sodium (HR, 0.86; 95% CI, 0.80-0.93; $P < .0001$). On multivariable analysis, serum sodium (HR, 0.88; 95% CI, 0.80-0.97; $P = .009$) and preoperative NYHA class (class IV, HR, 3.42; 95% CI, 1.29-9.08; $P = .014$, vs combined class I-III) were independent predictors of early mortality (Table 3).

Of the 96 patients tested, 14 (14.6%) were HIV positive on serology, and the HIV status of 25 of the 121 study patients (20.6%) was unknown. Most of the patients with an unknown HIV status had undergone pericardiectomy in the early 1990s before the advent of routine preoperative HIV testing. The baseline characteristics of the HIV-positive and HIV-negative patients are listed in Table E1. Women were overrepresented in the HIV-positive group (8 women [57.1%] vs 6 men [42.9%]; $P = .024$), and the hemoglobin (mean, 13.2 ± 1.7 vs 12.1 ± 2.0 g/dL; $P = .031$) and serum creatinine (mean, 86 ± 25 vs 68 ± 9 $\mu\text{mol/L}$; $P = .012$) were significantly lower in the HIV-positive patients than in the HIV-negative patients. No HIV-positive patients underwent surgery on cardiopulmonary bypass. The average CD4 count at surgery was 284 ± 133 cells/ μL (range, 50-435). Of the 14 HIV-positive patients, 9 (64.3%) were taking combination antiretroviral therapy at surgery. No perioperative deaths occurred in the HIV-positive group.

The preoperative and 30-day postoperative NYHA functional status was available for 73 (60.3%) of the 121 patients (Figure E1). Most showed improvement in functional status ($P < .0001$), with most changing from NYHA class II to class I ($n = 25$, 34.2%) and NYHA class III to class I ($n = 21$, 28.8%). Seven patients (9.6%) remained in the same functional class, and 2 (2.7%) had

experienced deterioration in their functional status at 30 days after pericardiectomy. Before surgery, most of the patients had NYHA class III symptoms ($n = 35$, 47.9%). However, postoperatively, most reported class I symptoms 30 days after surgery ($n = 50$, 68.5%).

DISCUSSION

We studied the etiology of constrictive pericarditis and early outcomes after pericardiectomy in 121 patients during a 22-year period at a single center from Sub-Saharan Africa. The period under review covered a time during which TB and HIV/AIDS were on the ascendency in this region. To the best of our knowledge, this is the first large study of the etiology and predictors of perioperative outcomes of constrictive pericarditis in the HIV/AIDS era in Africa. Our results have some variation from those reported in recent similar series covering the same subject.^{7-9,14,17,18}

Although our findings are relevant to practitioners in South Africa and other developing countries, the globalization of health implies that practitioners in North America and Europe are likely to treat increasing numbers of immigrants and refugees with TB and its sequelae, such as constrictive pericarditis.¹⁹

Of the 121 patients in our study, 110 (90.9%) had either proven or presumed TB as a cause of their constrictive pericarditis. This is greater than that reported in other series from China, Ghana, India, South Korea, and Turkey, where TB remains a major cause of constrictive pericarditis (Table 2). TB accounted for 65% of the patients undergoing pericardiectomy for constrictive pericarditis in a study from China,¹⁴ with studies from Ghana, India, South Korea, and Turkey revealing a prevalence rate of 63.6%, 61%, 42.4%, and 38%, respectively.^{3-5,13} Only 36 (32.7%) of the 110 patients had a proven diagnosis of tuberculous-constrictive pericarditis. This difference highlights the diagnostic difficulty faced by clinicians in resource-limited settings where TB is endemic—without recourse to advanced diagnostic techniques to determine the etiology of constrictive pericarditis, the clinician, armed only with knowledge of the background high prevalence of TB, is forced to treat empirically for TB to avoid the technical difficulty and associated morbidity and mortality that comes with performing pericardiectomy on patients with active or untreated tuberculous pericarditis.¹⁰ This common scenario is a likely contributor of the large number of cases of TB constrictive pericarditis seen in our series and might mean that TB has been overreported as a cause of constrictive pericarditis in South Africa. Fennell,¹⁰ in an earlier South African study, alluded to similar difficulties and a similar course of action in managing constrictive pericarditis. He had surmised that all 109 patients in his cohort had TB constrictive pericarditis.¹⁰ Histologic examination of most specimens recovered at pericardiectomy showed nonspecific chronic inflammation and did not solve this

TABLE 2. Causes of constrictive pericarditis, perioperative mortality, and determinants of mortality after pericardiectomy for constrictive pericarditis in a selection of large studies^{3,4,7-9,12-17}

Investigator	Country	Study period	Patients (n)	Constrictive pericarditis etiology	Perioperative mortality (%)	Predictors of perioperative mortality
Bashi et al ³	India	1954-1985	118	TB (61%)	16	Preoperative NYHA class III and IV
Bertog et al ⁸	USA	1977-2000	163	Idiopathic (46%), previous cardiac surgery (37%), after RT (9%), miscellaneous (8%)	6.1	—
Cinar et al ¹²	Turkey	1990-2005	70	TB (100%)	8.6	Ascites, symptom duration
Tokuda et al ¹⁶	Japan	2008-2012	346	—	10	Moderate-severe chronic lung disease, renal failure, preoperative NYHA class IV, previous cardiac surgery, CPB*
George et al ⁹	USA	1995-2010	98	Idiopathic (45%), previous cardiac surgery (31%), after RT (17%), tumor (3%), infection (1%), hemopericardium (1%), asbestos (1%)	7.1	CPB
Ling et al ⁷	USA	1985-1995	135	Idiopathic (33%), previous cardiac surgery (18%), pericarditis (16%), after RT (13%), connective tissue disease (7%), infection (3%), miscellaneous (10%)	6	—
McCaughan et al ¹⁵	USA	1936-1982	231	Idiopathic (73%), pericarditis (10%), infection (6%), after RT (5%), previous cardiac surgery (2%), connective tissue disease (2%), miscellaneous (2%)	14	Preoperative NYHA class IV
Szabo et al ¹⁷	Germany	1988-2012	89	Idiopathic (55%), previous cardiac surgery (23.6%), after RT (5.6%), TB (5.6%), uremia (4.5%), inflammatory (3.5%), after MI (2.2%)	7	—
Lin et al ¹⁴	China	2005-2010	51	TB (65%), idiopathic (25%), previous cardiac surgery (6%), connective tissue disease (2%), after trauma (2%)	3.9	—
Arsan et al ⁴	Turkey	1983-1993	105	TB (38%), malignancy (15%), uremia (11.4%), connective tissue disease (10.5%)	10.5	—
Kang et al ¹³	South Korea	1996-2010	85	Idiopathic (57.6%), TB (42.4%)	1.2	—

TB, Tuberculosis; NYHA, New York Heart Association; RT, radiotherapy; CPB, cardiopulmonary bypass; MI, myocardial infarction. *Predictors of perioperative mortality or major morbidity.

diagnostic dilemma.¹⁰ Despite the possibility that TB pericarditis as a cause of constrictive pericarditis might have been overreported in the present study, little doubt exists that TB remains the leading cause of effusive and subsequent constrictive pericarditis in South Africa. A local study found TB accounted for 69.5% of large pericardial effusions in this region of South Africa.²⁰ The use of imaging studies such as computed tomography or magnetic resonance imaging might help to reduce diagnostic uncertainty in situations in which active pericarditis or myopericarditis, such as can occur in active TB pericarditis, needs to be excluded.²¹ It is also worth noting the rarity with which

mediastinal irradiation, autoimmune diseases, and other causes of constrictive pericarditis commonly reported in developed countries are seen in our setting (Table 2).^{7,8,17} Only 1 patient had undergone pericardiectomy for radiation-induced constrictive pericarditis in 22 years at our center compared with 17 patients in 10 years in the study by Ling and colleagues.⁷

Our study found greater perioperative mortality than that reported in similar series worldwide. We have reported a 30-day mortality rate of 14%, but others have reported mortality rates in the range of 6% to 10%.^{7,12,16,17} The only recent study with similar perioperative mortality was that

FIGURE 2. Kaplan-Meier 30-day survival plot; 17 of 121 patients (14%) died within 30 days of pericardiectomy.

by Ariyoshi and colleagues,²² which reported 12.5% mortality but only among 16 patients. Also, McCaughan and colleagues¹⁵ reported a perioperative mortality rate of 14% in a cohort of 231 patients from 1932 to 1986. Bashi and colleagues³ reported a 16% perioperative mortality rate in 118 patients who had undergone surgery from 1954 to 1985. The mortality in our study was not influenced by the decade during which pericardiectomy was performed. Unlike Chowdhury and colleagues,²³ who found partial pericardiectomy to predict for perioperative mortality, we found no difference in outcomes between those who underwent total versus partial pericardiectomy using a surgical technique similar to that used by Chowdhury and colleagues.²³ Kang and colleagues,¹³ who reported on total and partial pericardiectomy just as we have, also found no difference in outcomes.

We found the preoperative NYHA class to be independently associated with perioperative mortality in our population. Compared with preoperative combined NYHA I to III functional status, patients with preoperative NYHA class IV symptoms had a greater risk of perioperative death. Other investigators have found a similar statistically significant association between preoperative NYHA IV status and early mortality. Tokuda and colleagues¹⁶ reported a 3.85 greater odds of early death ($P < .0001$), and Tirilomis

and colleagues²⁴ reported an increased risk of death with preoperative NYHA class IV symptoms ($P < .01$). Preoperative NYHA class IV signifies more severe disease with a greater degree of cardiac dysfunction that is more likely to result in perioperative morbidity and mortality. In studies of the long-term outcomes after pericardiectomy, preoperative NYHA class IV was also found to be a predictor of mortality.^{7,17}

We have also found preoperative serum sodium to be inversely associated with 30-day mortality, with lower serum sodium levels associated with increased early mortality. Bertog and colleagues⁸ also reported that low serum sodium was associated with greater overall mortality in their cohort of 163 patients. Low serum sodium is a reflection of severe fluid overload in the presence of gross heart failure (dilutional hyponatremia) or the use of higher doses of diuretic, such as occurred in our study, in patients with severe fluid overload. The latter assertion is supported by our finding that higher doses of diuretic (furosemide) and higher serum creatinine were also associated with mortality on univariable analysis—the 3 findings are likely to coexist in a patient with severe fluid overload; that is, a higher dose of diuretic (which is likely to cause low sodium and renal impairment with an increasing serum creatinine) will be used to treat a patient with severe fluid overload. Alternatively, hyponatremia reflects a generalized electrolyte imbalance as a marker of severe illness such as would occur in the syndrome of inappropriate antidiuretic hormone or sick cell syndrome.²⁵ Although not found in our study, other factors associated with 30-day mortality have included left ventricular dysfunction,²⁶ the use of cardiopulmonary bypass,^{9,16} and preoperative renal failure.¹⁶

Low output cardiac failure was a major contributor to mortality in our series, occurring in 11 (64.7%) of 17 patients who died. It was also found to be the predominant cause of perioperative death in other studies.^{7,8,14,27} Low output cardiac failure mainly results from the presence of myocardial atrophy and/or fibrosis, especially in cases of long-standing constriction.⁶ Despite the use of inotropes, intra-aortic balloon pump, and fluid resuscitation, a significant number of deaths associated with low output cardiac failure still occurred in our study.

TABLE 3. Univariate and multivariate Cox proportional hazards regression models of factors associated with mortality

Factor	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Serum sodium	0.86 (0.80-0.93)	<.0001	0.88 (0.80-0.97)	.009
Serum creatinine	1.09 (1.01-1.03)	.002	1.01 (0.99-1.03)	.089
Total daily dose (furosemide)	1.003 (1.00-1.006)	.02	1.00 (0.99-1.01)	.312
NYHA class		.001		.014
I-III	1		1	
IV	4.99 (1.92-13.03)		3.42 (1.29-9.08)	

HR, Hazard ratio; CI, confidence interval; NYHA, New York Heart Association.

Fourteen patients (11.6%) in our study had serologic evidence of HIV infection. To the best of our knowledge, this is the first study to document the prevalence, clinical characteristics, and outcomes of HIV-positive patients undergoing pericardiectomy for constrictive pericarditis. A recent nationwide study in the United States had <10 HIV-positive patients of a population of 3847 undergoing pericardiectomy.²⁸ The low frequency of HIV in our cohort might reflect the apparent protective effect of HIV infection on the progression to constrictive pericarditis.^{12,29-32} All the HIV-positive patients in our study had TB pericarditis as the cause of their constrictive pericarditis (6 proven TB, 8 presumed TB). The average CD4 count was 284 cells/ μ L, indicating some degree of immunologic integrity and thereby increasing the likelihood of progression to pericardial constriction. A CD4 count of 284 cells/ μ L is higher than what we commonly see in other cases of extrapulmonary TB and might have resulted from the use of combination antiretroviral therapy, which, at 64.3%, was greater than that seen in the background population during most of the study period.³³

The only significant differences between the HIV-positive and -negative populations were in sex (more female HIV-positive patients), a lower (but still largely normal) hemoglobin in the HIV-positive group, and a lower creatinine, which might reflect the reduced body habitus usually associated with HIV infection—these differences did not affect the outcomes between the 2 groups. No early deaths occurred in the HIV-positive population. The high prevalence of TB in our study and in the pre-HIV era study by Fennell¹⁰ suggests that the advent of HIV/AIDS did not affect the causality pattern of constrictive pericarditis in South Africa. Fennell¹⁰ reported in-hospital mortality of 3%, and we had 30-day mortality of 14%. The outcome results of our study and those from Fennell¹⁰ are not comparable because of differences in the methods of the 2 studies. The present study has shown that when TB constrictive pericarditis does occur in HIV-positive patients, the clinical characteristics and perioperative outcomes will be comparable to those for HIV-negative patients.

Despite the greater than commonly reported perioperative mortality, we have shown that most survivors experienced marked improvement in their effort tolerance, as measured by the NYHA classification. Most of our patients for whom data were available at both measurement points had improved from NYHA class II and III preoperatively to class I at 30 days after surgery ($P < .0001$). Ling and colleagues⁷ reported similar improvements in a cohort of 93 late survivors after pericardiectomy.

Study Limitations

Our study was limited by the small number of missing patient records and missing data from the available patient records owing to the retrospective study design. Despite these

limitations, we have identified the prognostic role of low serum sodium and NYHA functional class IV as predictors of outcome. Furthermore, the present study had a small number of HIV-infected patients and therefore could not provide definitive information on the effect of HIV infection in patients with constrictive pericarditis requiring pericardiectomy. Finally, the follow-up period included only the first 30 days after surgery. Longer term studies of the outcomes are required.

CONCLUSIONS

Our study has shown that although effective at relieving symptoms of constrictive pericarditis, pericardiectomy in Cape Town was associated with a high perioperative mortality of 14%, mainly related to low output cardiac failure. Preoperative NYHA class IV and hyponatremia have been shown to predict perioperative mortality. As expected, the prevalence of TB constrictive pericarditis was very high, although the possibility exists that TB as a cause of constrictive pericarditis was overreported. We have also shown that no major differences were present in the clinical profile and early outcomes of patients with and without HIV infection undergoing pericardiectomy for constrictive pericarditis. Our study has illustrated the need for early recourse to pericardiectomy before symptoms deteriorate to NYHA class IV or severe fluid overload, because a delay will result in probable myocardial atrophy from chronic myocardial constriction and lead to worse outcomes. Our findings also highlight the need to search for methods of reducing early mortality through improved management of postpericardiectomy low cardiac output syndrome and the need for better diagnostic techniques of constrictive pericarditis in our setting.

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FIGURE E1. Comparison of preoperative and 30-day postoperative New York Heart Association functional status in 73 patients ($P < .0001$). *NYHA*, New York Heart Association.

TABLE E1. Baseline characteristics of 96 study patients with known HIV status

Characteristic	HIV positive		P value
	No (n = 82)	Yes* (n = 14)	
Mean age (y)	40.2 ± 16.1	32.1 ± 7.2	.068
Male sex	60 (73.2)	6 (42.9)	.024
Cause of constrictive pericarditis			.256
TB	75 (91.5)	14 (100)	
Other	7 (8.5)	0 (0.0)	
Preoperative NYHA class			.724
I	2 (2.4)	0 (0.0)	
II	25 (31.7)	4 (28.6)	
III	36 (43.9)	8 (57.1)	
IV	18 (22.0)	2 (14.3)	
Symptom duration (mo)	12.6 ± 25.1	5.8 ± 5.1	.316
Hypertension	8 (9.8)	0 (0.0)	.222
Diabetes mellitus	2 (2.4)	0 (0.0)	.555
Total daily diuretic dose† (mg)	124 ± 115	126 ± 75	.953
Weight (kg)	64.5 ± 12.7	64.6 ± 10.4	.976
SBP (mm Hg)	111 ± 15	109 ± 12	.629
DBP (mm Hg)	70 ± 12	74 ± 9	.154
Pulse (beats/min)	89 ± 16	96 ± 16	.121
Pulsus paradoxus	53 (64.6)	7 (50)	.296
Ascites	65 (79.3)	11 (78.6)	.953
Diastolic knock	38 (46.3)	8 (57.1)	.455
Pleural effusion	63 (76.8)	13 (92.9)	.172
Hepatomegaly	71 (86.6)	13 (92.9)	.512
Pericardial calcification	17 (20.7)	3 (21.4)	.953
Atrial fibrillation	7 (8.5)	0 (0.0)	.256
Low QRS amplitude	52 (63.4)	10 (71.4)	.562
LVEF (%)	56 ± 11	60 ± 13	.241
Hemoglobin (g/dL)	13.2 ± 1.7	12.1 ± 2.0	.031
Serum sodium (mmol/L)	136 ± 5	137 ± 2	.721
Serum creatinine (μmol/L)	86 ± 25	68 ± 9	.012
Total pericardiectomy	71 (88.8)	13 (92.9)	.646
Cardiopulmonary bypass	17 (20.7)	0 (0.0)	.06
Postoperative inotrope use	56 (68.3)	8 (57.1)	.413
Postoperative ICU stay (d)	3.6 ± 2.6	3.2 ± 1.0	.564

Data presented as mean ± standard deviation for continuous variables and n (%) for categorical variables. *HIV*, Human immunodeficiency virus; *NYHA*, New York Heart Association; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *LVEF*, left ventricular ejection fraction; *ICU*, intensive care unit; *TB*, tuberculosis. *Mean CD4 count 284 ± 133 cells/μL. †Furosemide.