ORIGINAL ARTICLE

Predictors of outcome in 176 South African patients with peripartum cardiomyopathy

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ABSTRACT

Objective Identify novel prognostic factors for patients with peripartum cardiomyopathy (PPCM).

Design and setting Prospective cohort study conducted in a single tertiary care centre in South Africa.

Patients 176 African women with newly diagnosed PPCM were studied.

Interventions Clinical assessment, echocardiography and laboratory results were obtained at baseline and at 6 months.

Main outcome measures Poor outcome was defined as the combined end point of death, left ventricular (LV) ejection fraction (LVEF) < 35%, or remaining in New York Heart Association (NYHA) functional class III/IV at 6 months. Complete LV recovery was defined as LVEF ≥55% at 6 months.

Results Forty-five (26%) patients had a poor outcome. Multiple logistic regression analysis revealed that, after adjustment for age, NYHA functional class, LVEF and systolic blood pressure, increased left ventricular end systolic dimension (LVESD), lower body mass index (BMI) and lower total cholesterol at baseline were independent predictors of poor outcome (adjusted OR 1.09, 95% CI 1.04 to 1.15, p=0.001; OR 0.89, 95% CI 0.83 to 0.96, p=0.004, and OR 0.50, 95% CI 0.34 to 0.73, p=0.0004, respectively). Thirty (21%) of the 141 surviving patients with echocardiographic follow-up recovered LV function at 6 months. Multiple logistic regression analysis revealed that, after adjustment for NYHA functional class, LVEF and left ventricular end diastolic dimension, older age and smaller LVESD at baseline were predictors of LV recovery (OR 1.08, 95% CI 1.01 to 1.17, p=0.02 and OR 0.92, 95% CI 0.86 to 0.98, p=0.007, respectively).

Conclusions This study suggests that increased LVESD, lower BMI and lower serum cholesterol at baseline may be independent predictors of poor outcome in patients with PPCM, while older age and smaller LVESD at baseline appear to be independently associated with a higher chance of LV recovery.

INTRODUCTION

Peripartum cardiomyopathy (PPCM) is a potentially life-threatening disease that occurs in women of child-bearing age. This disease is characterised by new onset of heart failure between several months before and 6 months after delivery in previously healthy women. Although patients with PPCM have a higher rate of spontaneous recovery of left ventricular (LV) function than patients with other forms of non-ischaemic cardiomyopathy,[1] normalisation of LV function at 6 months has been reported to occur in only 23–54% of them.[1–5]

Factors predicting poor outcome in case series include degree of LV systolic dysfunction[2 3 6 7] and LV dilatation[2 8 9] on presentation, as well as LV thrombus.[8] Identifying additional prognostic factors, particularly factors that may be easily and relatively inexpensively assessed, would be beneficial in providing optimal care for patients with PPCM.

Body mass index (BMI) has been shown to be a predictor of outcome in patients with chronic heart failure,[10–13] as well as acute decompensated heart failure,[14] but this association has not previously been assessed in patients with PPCM. Renal and liver dysfunction have also both been shown to predict poor outcome in patients with heart failure, but, again, this association has not previously been investigated in patients with PPCM. Inflammation has been implicated in the pathogenesis and prognosis of PPCM,[5 15] and, while it has been shown that lipoproteins play a role in regulating cytokine production and the associated inflammatory response,[16] an association between cholesterol and outcome in patients with PPCM has not previously been reported. We sought to determine whether these variables, among others, may be predictors of outcome in patients with PPCM.

METHODS

Study design and patient recruitment

The study was conducted at Chris Hani Baragwanath (CHB) Hospital, Soweto, South Africa. Patients were referred from local clinics, secondary hospitals and the Department of Obstetrics at CHB Hospital. History of pre-existing cardiac signs or symptoms, pre-eclampsia or eclampsia and mode of delivery were obtained from the patient and confirmed by examining the obstetric card carried by each patient. Signs and symptoms were recorded during first presentation at the cardiac unit at CHB Hospital (baseline) and after a follow-up period of 6 months. Clinical assessment, echocardiography and blood analysis were performed at baseline and at 6 months.

Inclusion criteria were: (1) age ≥16 and ≤40 years; (2) symptoms of congestive heart failure that developed in the last month of pregnancy or during the first 5 months post partum; (3) no other identifiable cause of heart failure; (4) LV ejection fraction (LVEF) ≤45% by transthoracic echocardiography; and (5) sinus rhythm. Exclusion criteria were: (1) significant organic valvular heart disease;

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(2) systolic blood pressure >160 mm Hg or diastolic blood pressure >100 mm Hg; (3) clinical conditions other than cardiomyopathy that could increase plasma levels of inflammatory markers; (4) severe anaemia (haemoglobin <9 g/dl); and (5) any clinical condition that, according to the investigators, precluded inclusion in the study, such as ischaemic heart disease or malignancy.

Among the 176 patients included in the study, 164 (93%) received treatment with furosemide and 141 (80%) were treated with an ACE inhibitor. Digoxin was being taken by 113 (64%) of the 176 patients. Patients with an LVEF < 25% or LV thrombus were treated with warfarin. Carvedilol was initiated in 100 (57%) of the 176 patients after resolution of overt heart failure. ACE inhibitor and carvedilol doses were titrated upward as tolerated throughout the 6-month study period. Furosemide dose was titrated upward or downward as indicated according to clinical assessment. This study was approved by the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg, South Africa and complies with the Declaration of Helsinki. All study participants gave written informed consent before study entry. A total of 176 consenting consecutive patients diagnosed with PPCM and fulfilling the inclusion criteria were enrolled in the study. All women were of African descent.

Echocardiography, assessment of New York Heart Association (NYHA) functional class, and non-invasive blood pressure measurements

Two-dimensional and targeted M-mode echocardiography with Doppler colour flow mapping were performed using either a Hewlett Packard Sonos 5500 (Royal Philips Electronics, Amsterdam, Netherlands) or a VIVID i (General Electric Company, Fairfield, Connecticut, USA) echocardiography machine. Systolic and diastolic LV dimensions were measured according to the American Society of Echocardiography (ASE) guidelines. LV dimensions and function were determined using the mean of three or more cycles. Echocardiography was taped on video or CD and stored within the Soweto Cardiovascular Research Unit Division for further reference and audit purposes.

NYHA functional class of each patient at baseline and follow-up visits was evaluated by a physician, who was provided with clinical data but blinded to the protocol and unaware of the results of the laboratory tests. Blood pressure and heart rate were measured non-invasively with a Critikon Dinamap vital signs monitor 1846 and calculated as mean values from five readings. Measurements were made after a 30 min resting period in the sitting position with 2 min intervals between successive measurements.

Research-specific blood tests

Between 10 am and 12 noon, 8 ml blood was withdrawn from an antecubital vein and collected in prechilled tubes containing ethylenediaminetetra-acetic acid or clot activator and mixed rapidly. Plasma or serum was separated by centrifugation at 2500 rpm for 7 min within 10 min of collection. Aliquots were stored at −80°C. Full blood count, liver function, renal function and total cholesterol were assessed.

Outcomes

Poor outcome was defined as the combined end point of death, LVEF <35%, or remaining in NYHA functional class III/IV at 6 months. Complete LV recovery was defined as LVEF ≥55% at 6 months.

Statistical analysis

Database management and statistical analyses were performed with SAS V.9.2 software. Continuous data are expressed as mean ±SD or median (range). Comparison of means and proportions between groups at baseline was performed by independent t test and χ^2 statistics or Fisher exact test, respectively. A Wilcoxon rank-sum test was used where data were not normally distributed. Differences in class variables and continuous data between baseline and 6 months were assessed by a McNemar test and a paired t test or sign test (data not normally distributed), respectively.

Univariate and stepwise multiple logistic regression analyses were performed to establish independent predictors of poor outcome and LV recovery with cholesterol, blood pressure and echocardiographic variables in separate models after adjustment for age and BMI. Univariate logistic regression was used to examine associations with death. Significance was assumed at a two-sided p value of <0.05.

RESULTS

Baseline characteristics

Baseline clinical characteristics are listed in table 1. Notably, the mean age was 30.7±6.9 years, mean parity was 2 (range 1–7),

Table 1 Baseline characteristics of study population (n=176)

Clinical characteristic	Value
Age (years)	30.7±6.9
Parity, n (range)	2 (1–7)
BMI (kg/cm^2)	25.6±5.2
Systolic blood pressure (mm Hg)	111±17
Diastolic blood pressure (mm Hg)	72±13
Heart rate (beats/min)	97.3±19.1
NYHA functional class, n (%)	
I/II	33 (18)
III/IV	143 (82)
Echocardiography	
LVEDD (mm)	59.5±7.3
LVESD (mm)	51.8±7.6
Ejection fraction (%)	27.1±8.1
E velocity (m/s)	0.89±0.25
A velocity (m/s)	0.49±0.20
E/A	2.02±0.89
Deceleration time (ms)	134.5±63.2
LV thrombus, n (%)	19 (11.1)
Laboratory	
Haemoglobin (g/dl)	12.1±1.8
Creatinine (mmol/l)	84.1±20.5
Urea (mmol/l)	5.4±2.9
Total protein (g/l)	77.9±11.4
Albumin (g/l)	40.1±18.5
Total bilirubin (μmol/l)	17.3±26.8
Direct bilirubin (μmol/l)	9.2±23.2
Indirect bilirubin (μmol/l)	8.2±7.3
Alkaline phosphatase (U/l)	117.9±51.0
AST (U/l)	45.0±46.8
ALT (U/l)	54.7±67.1
GGT (U/l)	72.4±49.4
Total cholesterol (mmol/l)	4.0±1.1

Values are mean±SD unless otherwise specified.
ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; GGT, γ-glutamyl transpeptidase; LV, left ventricular; LVEDD, LV end diastolic diameter; LVESD, LV end systolic diameter; NYHA, New York Heart Association.

Table 2 Clinical, echocardiography and laboratory variables at baseline and 6 months among survivors (n=141)

Variable	Baseline*	6 months*	p Value
Clinical			
Systolic blood pressure (mm Hg)	111±17	113±17	0.18
Diastolic blood pressure (mm Hg)	72±13	72±12	0.65
NYHA functional class, n (%)			
I/II	30 (21)	128 (91)	<0.001
III/IV	111 (79)	13 (9)	
Echocardiography			
LVEDD (mm)	58.9±7.3	54.0±8.6	<0.0001
LVESD (mm)	51.3±7.6	42.3±9.5	<0.0001
Ejection fraction (%)	27.3±8.1	43.3±12.5	<0.0001
E velocity (m/s)	0.91±0.26	0.80±0.22	<0.0001
A velocity (m/s)	0.49±0.20	0.57±0.18	0.0002
E/A	2.01±0.86	1.51±0.65	<0.0001
Deceleration time (ms)	140.0±66.1	185.1±67.9	<0.0001
LV thrombus, n (%)	17 (12)	0	<0.0001
Laboratory			
Haemoglobin (g/d)	12.2±1.77	12.8±1.52	0.0004
Creatinine (mmol/l)	84.8±19.8	76.4±23.5	<0.0001
Urea (mmol/l)	5.2±2.5	4.4±1.6	0.002
Total protein (g/l)	77.8±11.5	82.2±8.9	0.003
Albumin (g/l)	40.4±19.8	43.7±13.5	<0.0001
Total bilirubin (μmol/l)	15.1±18.6	11.0±8.6	0.006
Direct bilirubin (μmol/l)	7.3±13.7	4.5±4.9	0.02
Indirect bilirubin (μmol/l)	8.0±7.3	6.1±4.4	0.002
Alkaline phosphatase (U/l)	118.2±51.5	97.4±36.4	<0.0001
AST (U/l)	42.0±33.5	26.4±12.9	<0.0001
ALT (U/l)	52.9±56.6	24.5±14.0	<0.0001
GGT (U/l)	74.6±50.3	52.8±40.8	<0.0001
Total cholesterol (mmol/l)	4.0±1.1	NR	NR

*Values are mean±SD unless otherwise specified.
ALT, alanine transaminase; AST, aspartate transaminase; GGT, γ-glutamyl transpeptidase; LV, left ventricular; LVEDD, LV end diastolic diameter; LVESD, LV end systolic diameter; NYHA, New York Heart Association; NR, not reported.

Table 3 Univariate logistic regression analysis of predictors of poor outcome (n=162)

Predictor	Unadjusted OR	95% CI	p Value
Clinical characteristic			
Age (years)	1.02	0.95 to 1.07	0.52
Parity (number)	0.89	0.65 to 1.13	0.38
BMI (kg/cm^2)	0.95	0.89 to 1.02	0.17
Systolic blood pressure (mm Hg)	0.97	0.95 to 0.99	0.02
Heart rate (beats/min)	1.01	0.99 to 1.03	0.16
NYHA functional class	1.43	0.85 to 2.43	0.18
Medication			
Carvedilol (yes, no)	0.67	0.31 to 1.45	0.31
ACE inhibitors (yes, no)	0.71	0.38 to 1.34	0.29
Furosemide (yes, no)	0.81	0.24 to 2.78	0.74
Digoxin (yes, no)	1.31	0.68 to 2.52	0.42
Echocardiography			
LVEDD (mm)	1.05	1.00 to 1.11	0.052
LVESD (mm)	1.07	1.02 to 1.12	0.009
Ejection fraction (%)	0.95	0.91 to 0.99	0.019
E/A	2.09	1.29 to 3.39	0.003
Deceleration time (ms)	0.99	0.99 to 1.01	0.09
LV thrombus	0.97	0.37 to 2.53	0.95
Laboratory			
Haemoglobin (g/dl)	0.86	0.12 to 1.05	0.15
Creatinine (mmol/l)	1.01	0.99 to 1.03	0.35
Urea (mmol/l)	1.09	0.95 to 1.25	0.22
Total protein (g/l)	0.99	0.96 to 1.02	0.37
Albumin (g/l)	0.99	0.96 to 1.02	0.35
Total bilirubin (μmol/l)	1.01	0.99 to 1.03	0.29
Direct bilirubin (μmol/l)	1.01	0.99 to 1.04	0.37
Indirect bilirubin (μmol/l)	1.03	0.99 to 1.08	0.30
Alkaline phosphatase (U/l)	0.99	0.99 to 1.00	0.28
AST (U/l)	1.01	1.00 to 1.02	0.033
ALT (U/l)	1.01	1.00 to 1.02	0.03
GGT (U/l)	1.00	0.99 to 1.01	0.73
Total cholesterol (mmol/l)	0.53	0.36 to 0.77	0.001

Stepwise multiple logistic regression analysis revealed that, after adjustment for variables including age, systolic blood pressure, medications, LVEF and NYHA functional class, increased LVESD, lower BMI and lower total cholesterol at baseline were independent predictors of the prespecified poor outcome (adjusted OR 1.09, 95% CI 1.04 to 1.15, p=0.001; OR 0.89, 95% CI 0.83 to 0.96, p=0.004; and OR 0.50, 95% CI 0.34 to 0.73, p=0.0004, respectively).
ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; GGT, γ-glutamyl transpeptidase; LV, left ventricular; LVEDD, LV end diastolic diameter; LVESD, LV end systolic diameter; NYHA, New York Heart Association.

mean BMI was 25.6±5.2 kg/m^2, and most of the women (82%) presented with NYHA functional class III or IV symptoms.

Baseline versus 6-month characteristics among survivors

Table 2 lists the characteristics of the survivors among the study population at baseline and 6 months. Mean LV end systolic dimension (LVESD) decreased significantly from 51.3±7.6 mm to 42.3±9.5 mm (p<0.0001), while mean LV ejection fraction (LVEF) increased significantly from 27.3±8.1% to 43.3±12.5% (p<0.0001). Mitral inflow E/A decreased significantly from 2.01±0.86 to 1.51±0.65, and mitral inflow deceleration time increased significantly from 140.0±66.1 ms to 185±67.9 ms (p<0.0001 for both). Haemoglobin, renal function and liver function test results had all improved at 6 months. Total cholesterol results were not obtained in most of the study population at 6 months; hence these results were not tabulated.

Combined measure of poor outcome

During the 6-month study period, nine patients were lost to follow-up, three patients moved to remote areas where follow-up could not occur, and two patients did not undergo LVEF assessment at 6 months. Of the remaining 162 patients, 45 (28%) met the prespecified combined end point of death (21 patients, 13%), remaining in NYHA functional class III or IV (13 patients, 9%) or LVEF <35% at 6 months (40 patients, 25%).

Predictors of poor outcome

Univariate analysis revealed that predictors of the prespecified poor outcome include decreased systolic blood pressure, increased LVESD, decreased LVEF, increased mitral inflow E/A, decreased mitral inflow deceleration time, increased aspartate transaminase and alanine transaminase, and decreased total cholesterol (table 3).

Predictors of LV recovery

Thirty (21%) of the 141 surviving patients had fully recovered LV function (LVEF ≥55%) at 6 months. Baseline characteristics of patients who fully recovered versus patients who did not are listed in table 4. Univariate analysis revealed that predictors of LV recovery included older age, decreased LV end diastolic

Table 4 Baseline characteristics for patients with complete recovery of LVEF versus patients with non-recovery of LVEF (n=141)

Characteristic	Recovered LVEF (n=30)*	Non-recovered LVEF (n=111)*	p Value
Clinical			
Age (years)	33.2±5.9	30.4±6.6	0.035
Parity, n (range)	3 (1–4)	2 (1–7)	0.053
BMI (kg/cm^2)	26.5±6.0	25.8±5.4	0.66
Systolic blood pressure (mm Hg)	117±17	110±17	0.08
Diastolic blood pressure (mm Hg)	75±13	72±12	0.17
NYHA functional class, n (%)			
I/II	29 (97)	98 (89)	0.054
III/IV	2 (3)	12 (11)	
Echocardiography			
LVEDD (mm)	56.2±6.5	59.6±7.4	0.07
LVESD (mm)	48.1±6.3	52.2±7.8	0.026
Ejection fraction (%)	28.7±8.4	26.9±8.0	0.22
E velocity (m/s)	0.88±0.28	0.91±0.25	0.77
A velocity (m/s)	0.52±0.17	0.49±0.21	0.13
E/A	1.73±0.69	2.10±0.89	0.03
Deceleration time (ms)	141.5±59.2	139.7±68.0	0.74
LV thrombus, n (%)	6 (20)	11 (10)	0.20
Laboratory			
Haemoglobin (g/dl)	12.8±1.8	12.0±1.8	0.035
Creatinine (mmol/l)	73.8±19.5	87.8±18.8	0.0005
Urea (mmol/l)	5.0±3.5	5.3±2.2	0.09
Total protein (g/l)	79.1±10.5	77.5±11.7	0.28
Albumin (g/l)	46.7±30.8	38.8±15.4	0.02
Total bilirubin (μmol/l)	12.6±7.8	15.8±20.6	0.88
Direct bilirubin (μmol/l)	5.3±4.6	7.9±15.3	0.97
Indirect Bilirubin (μmol/l)	7.4±4.5	8.1±7.9	0.83
Alkaline phosphatase (U/l)	132.2±63.2	114.4±47.4	0.33
AST (U/l)	36.6±18.7	43.5±46.4	0.93
ALT (U/l)	45.8±31.8	54.8±61.6	0.64
GGT (U/l)	79.1±47.9	73.4±51.1	0.40
Total cholesterol (mmol/l)	4.1±1.2	4.0±1.1	0.60

*Values are mean±SD unless otherwise specified.
ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; GGT, γ-glutamyl transpeptidase; LV, left ventricular; LVEDD, LV end diastolic diameter; LVESD, LV end systolic diameter; NYHA, New York Heart Association.

Table 5 Univariate logistic regression analysis of predictors of LV recovery (n=141)

Predictor	Unadjusted OR	95% CI	p Value
Clinical characteristics			
Age (years)	1.07	1.00 to 1.15	0.04
Parity (number)	1.26	0.96 to 1.65	0.09
BMI (kg/cm^2)	1.02	0.95 to 1.10	0.54
Systolic blood pressure (mm Hg)	1.02	0.99 to 1.05	0.07
Heart rate (beats/min)	0.98	0.96 to 1.00	0.06
NYHA functional class	0.74	0.41 to 1.35	0.33
Medication			
Carvedilol (yes, no)	0.80	0.35 to 1.80	0.58
ACE inhibitor (yes, no)	0.93	0.34 to 2.57	0.89
Furosemide (yes, no)	2.25	0.27 to 18.75	0.45
Digoxin (yes, no)	0.95	0.42 to 2.16	0.90
Echocardiography			
LVEDD (mm)	0.93	0.88 to 0.99	0.025
LVESD (mm)	0.93	0.87 to 0.98	0.01
Ejection fraction (%)	1.03	0.98 to 1.08	0.27
E/A	0.56	0.31 to 1.02	0.057
Deceleration time (ms)	1.00	0.99 to 1.01	0.90
LV thrombus	1.93	0.60 to 6.25	0.27
Laboratory			
Haemoglobin (g/dl)	1.33	1.05 to 1.69	0.02
Creatinine (mmol/l)	0.96	0.93 to 0.98	0.0008
Urea (mmol/l)	0.94	0.79 to 1.13	0.51
Total protein (g/l)	1.01	0.98 to 1.05	0.51
Albumin (g/l)	1.02	0.99 to 1.04	0.10
Total bilirubin (μmol/l)	0.99	0.95 to 1.02	0.42
Direct bilirubin (μmol/l)	0.98	0.92 to 1.03	0.40
Indirect bilirubin (μmol/l)	0.99	0.93 to 1.05	0.64
Alkaline phosphatase (U/l)	1.01	0.99 to 1.01	0.11
AST (U/l)	0.99	0.98 to 1.01	0.33
ALT (U/l)	0.99	0.99 to 1.01	0.45
GGT (U/l)	1.00	0.99 to 1.01	0.73
Total cholesterol (mmol/l)	1.10	0.76 to 1.61	0.61

ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; GGT, γ-glutamyl transpeptidase; LV, left ventricular; LVEDD, LV end diastolic diameter; LVESD, LV end systolic diameter; NYHA, New York Heart Association.

dimension (LVEDD), decreased LVESD, higher haemoglobin and lower creatinine (table 5). Stepwise multiple logistic regression analysis showed that, after adjustment for NYHA functional class, medication, LVEF and LVEDD, older age and smaller LVESD were predictors of LV recovery (adjusted OR 1.08, 95% CI 1.01 to 1.17, p=0.02 and OR 0.92, 95% CI 0.86 to 0.98, p=0.007, respectively).

Predictors of death

Univariate analysis showed that predictors of death included younger age (OR 0.93, 95% CI 0.87 to 1.00, p=0.04), lower BMI (OR 0.83, 95% CI 0.72 to 0.95, p=0.007), increased LVEDD (OR 1.08, 95% CI 1.01 to 1.15, p=0.02), increased LVESD (OR 1.07, 95% CI 1.01 to 1.14, p=0.02), and higher NYHA functional class (OR 2.35, 95% CI 1.12 to 4.94, p=0.02). The mean age of the patients who died (n=21) was 27.8±8.6 years, while the mean age of the patients who survived but were not lost to follow-up (n=141) was 31.0±6.6 years. The mean BMI of the patients who died was 22.6±3.3 kg/m^2, while the mean BMI of the patients who survived but were not lost to follow-up was 25.9±5.5 kg/m^2.

DISCUSSION

This prospective single-centre study of 176 newly diagnosed patients with PPCM summarises data on clinical, echocardiographic and laboratory characteristics at the time of diagnosis and after 6 months of standard clinical care. We confirmed previous findings in our collective[5] that a relatively high percentage of patients (79%) had failed to normalise LV function at 6 months compared with collectives from the USA.[3 8] Increased LVESD, lower BMI and lower total cholesterol were identified as potential novel predictors of poor outcome on stepwise multivariate logistic regression analysis. Older age appears to be a novel predictor of LV recovery, while younger age, lower BMI, increased LVEDD, increased LVESD and higher NYHA functional class all seem to be predictors of mortality.

Numerous factors predicting morbidity and mortality in patients with PPCM have previously been proposed but not validated. These factors include degree of decreased LVEF and LV dilatation at diagnosis,[2 7 8 17 18] presence of LV thrombus,[8] and

being of African descent.[8 19] Previous studies performed at our own institution have shown that NYHA functional class,[5] N-terminal prohormone of brain natriuretic peptide,[20] and increased plasma markers of inflammation and apoptosis[5 20] at diagnosis are predictors of poor outcome as well.

The present analysis, using a much larger sample size than in most previous analyses, reveals different findings with regard to some predictors of morbidity and mortality, but confirms other findings. As previously reported,[2] increased LVESD at diagnosis was a significant predictor even when adjusted for other variables in multivariate analysis. In contrast with previous reports, LVEF and LVEDD at diagnosis,[2 3 6 8 9] NYHA functional class[5] and presence of LV thrombus[8] were not predictors of poor outcome. A novel finding in the present study was that lower BMI and lower total cholesterol at baseline were both associated with poor outcome.

Previous studies have shown that increased BMI is associated with decreased all-cause mortality in patients with chronic heart failure.[10 12 13] The potentially beneficial effect of being overweight or obese has been termed the 'obesity paradox'. Several hypotheses have been proposed to account for this paradox, including the suggestions that overweight and obese patients may have higher metabolic reserve, reduced cytokine and neuroendocrine activation, higher blood pressure, which may allow more aggressive upward titration of medication, and higher serum lipid levels. An association between higher BMI and improved survival in patients with acute decompensated heart failure has also been shown. An analysis of more than 100 000 patients enrolled in the Acute Decompensated Heart Failure National Registry showed that higher BMI was associated with lower in-hospital mortality.[14] The mechanisms by which a higher BMI may be protective for patients with either acute or chronic heart failure remain unclear.

Several studies have reported an inverse relationship between cholesterol and mortality in patients with chronic heart failure.[21–23] Rauchhaus and colleagues were among the first to demonstrate this paradox in a derivative/validation study in 417 patients with chronic heart failure whereby lower serum total cholesterol was independently associated with worse prognosis.[24] A more recent study demonstrated that higher serum high-density lipoprotein (HDL) cholesterol and higher serum triglycerides were associated with lower mortality in a cohort of 833 outpatients with chronic heart failure due to various aetiologies.[25] In contrast with the results of these studies, Christ and colleagues found that, in patients with idiopathic dilated cardiomyopathy, low cholesterol levels are dependent on the severity of cardiac disease and do not independently predict adverse outcomes in these patients.[26]

Low cholesterol has also been shown to be a predictor of adverse outcomes in acute heart failure. Findings from the Acute Heart Failure Database main registry show that low total cholesterol was one of several predictors for in-hospital mortality in patients admitted for acute heart failure.[27] In a cohort of 207 older patients, low cholesterol was associated with increased length of hospital stay and was among the best predictors of in-hospital mortality.[28]

Although the pathophysiological basis for the association of low cholesterol and impaired prognosis has not been fully elucidated, an 'endotoxin–lipoprotein' hypothesis has been proposed.[16] Patients with chronic heart failure have increased cytokine activation, which depends, at least in part, on exposure to bacterial endotoxins due to mesenteric venous congestion.[24 29] Lipoproteins serve as natural buffers because they bind to endotoxins. This, in turn, leads to reduced lipopolysaccharide activity and diminished immune activation.[16]

We have previously shown that patients with PPCM display increased cytokine levels and that failure to decrease interferon γ was associated with poor outcome.[5 20] On the basis of the results of the present study, low total cholesterol at diagnosis may be a marker for increased immune activation in patients with PPCM and portend a poor prognosis.

Predictors of LV recovery

In this study, only 21% of surviving patients had attained complete LV recovery at 6 months. Predictors of LV recovery were older age and smaller LVESD at diagnosis, confirming a previous study that reported that smaller LVESD at diagnosis is associated with better LV recovery.[2] Other studies have reported that smaller LVEDD,[8 9] higher LVEF,[2 6 19] higher fractional shortening[9] and absence of LV thrombus[8] at diagnosis may predict LV recovery, but none of these factors predicted LV recovery in our patient population. Of note, the LV recovery rate at 6 months in this study was quite low compared with a previous study of patients with PPCM in the USA, of whom only 19% were black, which reported an overall LV recovery rate of 54%.[3] More recently, another study from the USA in which 14 of 39 patients with PPCM were black reported that normalisation of LV function at 6 months occurred in 56% of white patients but only 30% of black patients.[1] The LV recovery rate in our study of black African patients with PPCM is even lower than that reported for black patients living in the USA, but similar to that reported in patients living in Haiti[4] and Turkey.[2] These findings suggest that patients of African ancestry with PPCM may be less likely to normalise their LV function at 6 months than patients of other racial or ethnic backgrounds.

Differences in nutrition between patients from various ethnic and sociodemographic backgrounds have not been evaluated and may also play a role. Fett and colleagues[30] have shown that, among 32 Haitian patients with severe heart failure, only 6% had recovered at 6 months, but 100% had recovered by 48 months. The long-term recovery rate of the patients with PPCM in the present study has not been assessed, but it may be that predictors of late LV recovery may differ from predictors of early LV recovery. This issue merits further investigation.

Age has not previously been reported as a predictor of LV recovery. The reason(s) why older patients with PPCM in this study had better LV recovery than younger patients remains unclear. It is possible that younger patients mounted a more severe immune response than older patients, resulting in more extensive myocardial damage, thereby decreasing the probability of functional recovery.

Predictors of mortality

Of the 162 patients with follow-up, 21 (13%) died within 6 months of diagnosis. Similar to previous reports, degree of LV dilatation[2] and higher NYHA functional class[5] at diagnosis were predictors of mortality in univariate analysis. Lower BMI and younger age at diagnosis seemed to be independent predictors of mortality, which are novel findings. Because of the relatively low number of deaths in the current cohort, multiple logistic regression analysis of mortality was not performed. Studies including larger numbers of patients with PPCM are warranted to further elucidate and validate predictors of death among this patient population.

Limitations

Total cholesterol was measured at baseline for all patients, but was not assessed at 6 months in the majority of patients, thus not allowing comparison of change over time. In addition, only

total cholesterol was measured, so data on the levels of various types of cholesterol including HDL, low-density lipoprotein, triglycerides and non-HDL are not available. Assessment of cholesterol types at baseline and at follow-up may provide additional information in future studies. Finally, follow-up concluded at 6 months. Longer follow-up would probably increase our knowledge about predictors of poor outcome as well as LV recovery in patients with PPCM.

CONCLUSION

In this study, larger LVESD and low total cholesterol were found to be associated with a composite poor outcome in a large cohort of African women with PPCM, while smaller LVESD and older age were found to be associated with a better chance of LV recovery. These results confirm and expand upon previous findings by our group and others and merit further investigations on potential pathophysiological mechanisms underlying these findings.

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Predictors of outcome in 176 South African patients with peripartum cardiomyopathy

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