

Clinical characteristics and one-year all-cause mortality outcomes in Africans with dilated cardiomyopathy[☆]

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ABSTRACT

Aims: Dilated cardiomyopathy (DCM) is a common cause of heart failure in sub-Saharan Africa (SSA). The affected individuals present with new-onset heart failure with reduced ejection fraction and no identifiable primary or secondary aetiology. We aim to describe the clinical characteristics of participants with heart failure of unknown origin.

Methods: We screened 161 participants with heart failure of unknown origin and prospectively excluded primary and secondary causes of DCM. All study participants were subjected to laboratory biochemical testing, echocardiography, cardiovascular magnetic resonance (CMR) imaging and invasive coronary angiography.

Results: The study comprised 93 participants with a mean age of 47.5 SD 13.1 years. Forty-six (56.1%) participants had evidence of late gadolinium enhancement (LGE) on imaging, and LGE was visualised in the mid wall in 28 (61.0%) of these participants. After a median duration of 13.4 months [interquartile range (IQR): 8.8–28.9 months], 18 (19%) participants died. Non-survivors had a higher median left atrial volume index (44.9 mL/m² (IQR: 34.4–58.7) compared to survivors [32.9 mL/m² (IQR: 24.5–47.0), $p = 0.017$]. The rate of all-cause rehospitalisation was 29.3%, of which 17 of the 22 re-hospitalisations were heart failure related.

Conclusion: Dilated cardiomyopathy in Africans primarily affects young males. In our cohort, this disease was associated with an all-cause mortality of 19% in one year. In SSA, large multicenter studies are required to investigate this disease's pathogenesis and outcomes.

1. Introduction

In sub-Saharan Africa (SSA), heart failure is common and has a high six-month mortality rate of 18% [1]. Many patients with heart failure do not have an identifiable aetiology. Dilated cardiomyopathy (DCM) is characterised by left ventricular or biventricular dilatation and systolic dysfunction not explained by abnormal loading conditions or coronary artery disease sufficient to cause global systolic impairment [2]. This definition excludes valvular heart disease, congenital heart disease and hypertensive heart disease, which cause chronic abnormal loading

conditions leading to myocardial dilatation and dysfunction [2].

In a prospective registry of 1006 patients from nine African countries with acute heart failure, the leading diagnoses were hypertension (45.4%) and idiopathic dilated cardiomyopathy (IDCM) in 18.8% of patients [1]. Also, IDCM has been reported in >30% of patients presenting with clinical signs and symptoms of heart failure with reduced ejection fraction (HFrEF) [3]. Furthermore, the prevalence of IDCM in African countries is 13.8% (interquartile range: 11.0–19.6%) [4].

Despite the high prevalence of DCM in Africa, little is known about this disease's clinical manifestations and outcomes, particularly after the

[☆] All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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availability of novel heart failure therapeutic molecules and intracardiac device therapy. This study aimed to describe the contemporary clinical characteristics and one-year all-cause mortality outcomes in a carefully phenotyped cohort of Africans with DCM.

2. Methods

2.1. Study design and participants

From July 2015 to December 2018, we screened 161 patients with a clinical diagnosis of heart failure without an identifiable cause. The study enrolled de novo acute heart failure, acute decompensated chronic heart failure, and stable chronic heart failure patients. These patients were recruited from the cardiac admission wards and outpatient heart failure clinic at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), a tertiary academic state-owned institution in South Africa.

We recruited patients with a left ventricular ejection fraction (LVEF) less than or equal to 40%, based on the biplane Simpson's method on echocardiography. Study participants with concomitant chronic organic valvular heart disease, hypertension, coronary artery disease, human immunodeficiency virus (HIV) infection, endocrine or metabolic conditions, pregnancy or peripartum state, and myocarditis were excluded from the study.

A comprehensive clinical history was obtained from all study participants. In addition, a physical examination focused on clinical signs and symptoms of heart failure was performed on study enrolment. Obstructive coronary artery disease was excluded in all patients by invasive coronary angiography. Clinical investigations in all patients recruited into the study included a 12-lead electrocardiogram (ECG) and a 2D transthoracic echocardiogram (General Electric Vivid 9 4D). These assessments were done to evaluate for arrhythmias and myocardial structural abnormalities, respectively. Furthermore, cardiovascular magnetic resonance (CMR) imaging was performed to exclude infiltrative conditions and myocardial fibrosis.

2.2. Cardiovascular magnetic resonance imaging

Cardiovascular magnetic resonance imaging was performed with a Philips 1.5 Tesla whole-body scanner. An ECG-triggering device was used, and respiratory bellows were placed on the patient's abdomen throughout imaging. After the acquisition of localisation images, continuous short-axis cine images of the left ventricle were obtained by steady-state free precession sequence at end-expiration.

Ventricular volumes, as well as left and right ventricular ejection fractions were calculated using four-chamber and short-axis slice summation. Images depicting late gadolinium enhancement (LGE) were acquired approximately 15 min after administering 0.1 mmol/kg of gadobenate dimeglumine (Bracco) at 2 mL per second injection rate. The presence of LGE was evaluated on inversion-recovery prepared segmented gradient echo sequence images. The images were visually analysed for the presence and extent of LGE. Two radiologists were available for image interpretation, and a single radiologist independently reviewed each set of CMR images. The visual scoring method was based on the 17-segment model. The percentage of the myocardium with LGE was calculated by counting the number of segments with LGE and dividing by 17. The imaging protocol and reporting of CMR imaging findings were guided by the Society for Cardiovascular Magnetic Resonance reporting guidelines [5].

2.3. Outcomes data

Cardiac patients seen at the CMJAH are routinely followed up in the cardiology department with minimal loss of follow-up. Study outcomes (all-cause mortality, number of rehospitalisations and occurrence of thrombo-embolic complications) were collected telephonically and from the electronic health record system that captures data of all CMJAH

cardiac inpatients. Approval to conduct the study was granted by the University of the Witwatersrand Human Research Ethics Committee (Ethics Clearance certificate number: M150467). The study complied with the Declaration of Helsinki, and informed consent was obtained from all study participants.

2.4. Sample size calculation

To construct a 95% confidence interval with a margin of error of 5%, the study had to recruit a minimum sample size of 80 study participants. The sample proportion was estimated at 5.5%, based on a previously reported one-year all-cause mortality rate in DCM patients [6].

3. Statistical analyses

Quantitative variables with a normal distribution were summarised as the mean and standard deviation. The median and interquartile ranges (IQR) were used to summarise continuous variables with a non-normal distribution. Categorical variables are expressed as numbers and percentages, and Pearson's chi-square test or Fisher's exact test, where appropriate, were applied to compare categorical variables. We compared continuous variables with a normal distribution using the Student's *t*-test, and the Wilcoxon rank-sum (Mann-Whitney) test was used to compare medians for non-normal data. Univariable and multivariable logistic regression analyses were used to assess the relationship between all-cause mortality and explanatory variables after adjusting for confounders such as age and gender. Odds ratios were calculated at 95% confidence interval levels, and differences were considered statistically significant at a *p*-value <0.05. Statistical analyses were conducted using Stata SE Version 17.0 (StataCorp, Texas).

4. Results

4.1. Demographics and clinical presentation

After carefully screening 161 patients, 100 study participants with DCM were recruited. We further excluded seven patients from the data analysis whose survival could not be confirmed after one year of follow-up from the time of recruitment (Fig. 1). The final DCM cohort comprised 93 study participants. At the time of recruitment into the study, the cohort had a mean age of 47.5 SD 13.1 years. However, the mean age was 43.9 SD 12.0 years at prior index-diagnosis of heart failure. The youngest age at diagnosis of heart failure was 15 years. More than half (58%) of the study participants reported a history of gradual onset of heart failure symptoms at diagnosis. The rest of the patients reported acute onset of heart failure symptoms. The complete demographic and clinical characteristics of the cohort are presented in Table 1.

At the time of recruitment into the study, 85% of patients had at least two symptoms suggestive of congestive cardiac failure. Dyspnea was the most common symptom (62%), followed by orthopnea (58%), decreased effort tolerance (49%), and paroxysmal nocturnal dyspnea (42%). On clinical examination, 40 (44%) patients had grade one pedal oedema, 7 (8%) had pulmonary crepitations, and only 6 (7%) had ascites. The New York Heart Association (NYHA) functional class was not specified in one patient, with 37 (40%), 36 (39%), 16 (17%), and 3 (3%) patients in NYHA functional classes 1,2,3, and 4, respectively.

A clinical history of a previous thromboembolic disease was reported by 14 (15%) patients, and 4% had a previous lower limb deep vein thrombosis (DVT). Three patients had implanted cardiac resynchronisation therapy (CRT) devices - two cardiac resynchronisation defibrillation therapy (CRT-D) and one cardiac resynchronisation pacemaker (CRT-P) inserted for complete heart block. Among the 68 patients with complete iron studies, absolute iron deficiency (serum ferritin level < 100 µg/L) was detected in 19 (28%) patients, and 16 (24%) had relative iron deficiency. There were no statistically significant differences in

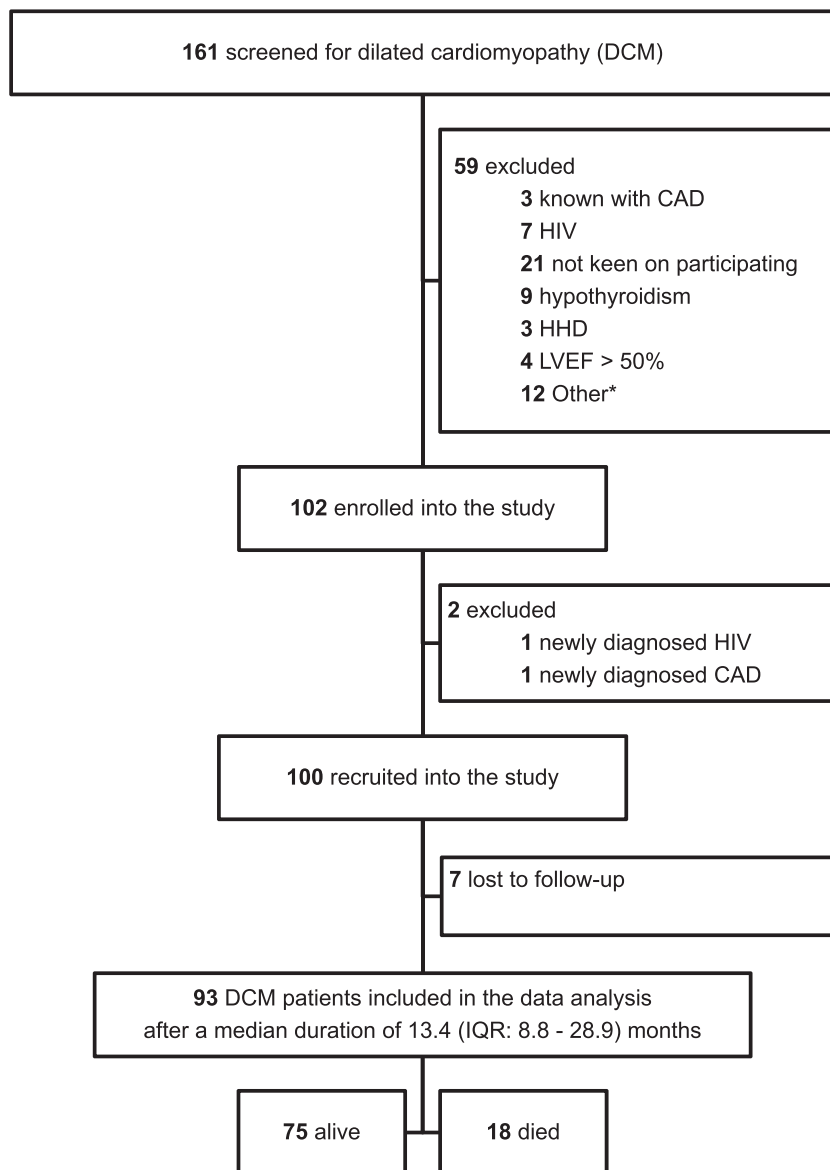


Fig. 1. Flow chart showing patients screened and enrolled in the study. CAD = coronary artery disease, DCM = dilated cardiomyopathy, HHD = hypertensive heart disease, HIV = Human immunodeficiency virus, IQR = interquartile range, LVEF = Left ventricular ejection fraction. *Other: peripartum cardiomyopathy (n = 1), malignancy (n = 2), organic valvular heart diseases (n = 2), pacemaker in-situ (n = 1), end-stage renal impairment (n = 3), recreational substance abuse (n = 1), unstable patient (n = 1), dilated cardiomyopathy precipitated by supraventricular tachycardia (n = 1).

serum ferritin levels between survivors and non-survivors.

4.2. Echocardiogram and electrocardiogram parameters

Non-survivors had a higher median left atrial volume index [44.9 mL/m² (IQR: 34.4–58.7) compared to survivors [32.9 mL/m² (IQR: 24.5–47.0), *p* = 0.017]. The baseline median LVEF was 25% (IQR: 16–37), and 75% of the participants had a LVEF <35%. The mean LVEF was comparable between survivors and non-survivors (26% SD 12.6 vs 25% SD 10.8, *p* = 0.838). The ratio between the E-wave and A-wave (E/A ratio) was above 2.0 in 9 (69.2%) patients that demised and did not differ significantly between survivors and non-survivors (*p* = 0.061). In total, 33 (48.5%) patients had an E/e ratio above 15.0, and none of the non-survivors had an E/e ratio <8.0 (*p* = 0.225).

The ECG revealed sinus rhythm in 94% of the participants. The median PR interval was 177 milliseconds (ms) (IQR: 158–201), and the median QRS duration was 108 ms (IQR: 94–149). Only 31 (33.3%) study patients had a QRS duration ≥120 ms, and six (19.3%) of these patients died within one year of follow-up (*p* = 0.576).

4.3. Cardiovascular magnetic resonance imaging findings

Among the 93 DCM patients described, CMR imaging findings were available in 82 (88.0%) patients. Cardiovascular magnetic resonance imaging was contraindicated in four patients (bullet in-situ, *n* = 1, and intracardiac devices, *n* = 3). One patient could not lie supine due to severe symptoms of congestive heart failure, and two patients died before imaging. The remaining patients (*n* = 4) were lost to follow-up before CMR imaging. The CMR imaging parameters are reported in Table 2.

Forty-six (56.1%) participants had evidence of LGE on imaging. Late gadolinium enhancement was visualised in the mid-wall in 28 (61%) participants. The most common site for LGE was the basal anteroseptal, mid inferoseptal and mid anteroseptal segments in 85, 70 and 53% of patients, respectively. A transmural LGE pattern was visualised in three (6.5%) participants, and two (4.3%) patients had areas of focal LGE. None of the patients with a transmural LGE pattern had any evidence of obstructive epicardial disease on coronary angiography, suggesting that the transmural LGE pattern might suggest the presence of underlying subendocardial ischaemia. There was no evidence of infiltrative disease, tumours or congenital anomalies on CMR imaging. Features of left

Table 1

Baseline clinical characteristics of participants with dilated cardiomyopathy stratified according to all-cause mortality.

	All patients		All-cause mortality		p-value
	(n = 93)	Yes (n = 18)	No (n = 75)		
Age (years), mean (SD)	47.5 (13.1)	44.2 (14.4)	48.3 (12.7)		0.240
Male sex	60 (64.5)	13 (72.2)	47 (62.7)		0.447
Ethnicity					
Black	86 (92.5)	15 (83.3)	71 (94.7)		0.102
White	2 (2.1)	1 (5.6)	1 (1.3)		0.267
Asian	3 (3.2)	2 (11.1)	1 (1.3)		0.035
Mixed Ancestry	2 (2.2)	0 (0)	2 (2.7)		0.484
Body mass index, kg/m ²	26.9 (23.5–30.9)	24.8 (23.1–27.0)	27.7 (23.7–31.2)		0.086
Family history of DCM	5 (5.4)	0 (0)	5 (6.7)		0.260
Smoking	16 (17.2)	7 (38.9)	9 (12.0)		0.007
NYHA functional class					
1	37 (40.2)	2 (11.8)	35 (46.7)		0.004
2	36 (39.1)	8 (47.1)	28 (37.3)		0.093
3	16 (17.4)	6 (35.3)	10 (13.3)		0.013
4	3 (3.3)	1 (5.9)	2 (2.7)		0.098
Vital signs, mean (SD)					
Resting heart rate	82.9 (17.0)	88.2 (22.7)	82 (15.3)		0.155
Systolic BP, mmHg	118 (19.8)	113 (17.8)	119 (20.2)		0.246
Diastolic BP, mmHg	77 (15.2)	75 (15.5)	77 (15.2)		0.585
MAP, mmHg	91 (17.5)	88 (19.5)	92 (17.1)		0.379
Laboratory tests					
Haemoglobin, g/dL	13.9 (1.7)	13.8 (1.7)	14.0 (1.7)		0.647
Platelet count	232 (201–280)	207 (178–264)	232 (205–282)		0.236
Sodium, mmol/L	140 (138–143)	140 (138–141)	141 (139–143)		0.183
Potassium, mmol/L	4.4 (0.6)	4.5 (0.8)	4.4 (0.5)		0.256
GFR, mL/min (MDRD)	70.4 (49–92.9)	60 (48.4–92.9)	75.3 (49–92.5)		0.595
Pro BNP, ng/L	2066 (739–4598)	6278 (2434–8592)	1626 (505–3097)		0.001
C-reactive protein*, mg/L	2.6 (0.6)	3.0 (0.8)	2.5 (0.5)		0.000
Troponin*, ng/L	2.9 (1.0)	3.2 (1.0)	2.8 (1.0)		0.089
TSH, mmol/L	1.8 (1.2–2.6)	1.9 (1.3–3.5)	1.8 (1.1–2.5)		0.419
Free T4, pmol/L	16.9 (14.8–19.4)	18.1 (15.7–21.5)	16.5 (14.4–18.7)		0.131
Cholesterol, mmol/L	4.1 (1.1)	3.7 (0.6)	4.2 (1.2)		0.109
LDL	2.6 (0.8)	2.2 (0.6)	2.7 (0.9)		0.042
HDL	1.0 (1.0–1.4)	1.0 (0.9–1.2)	1.0 (0.8–1.4)		0.944
HbA1c	6.2 (6.0–6.7)	6.4 (5.6–6.7)	6.2 (6.0–6.7)		0.816
INR	1.1 (1.0–1.5)	1.3 (1.1–1.8)	1.1 (1.0–1.4)		0.066
ECG					
PR interval	177 (158–201)	192 (163–222)	175 (157–196)		0.338
QRS interval	108 (94–149)	109 (95–144)	107 (94–149)		0.791
Echocardiogram					
LVEF, %	25 (16–37)	24 (17–30)	25 (16–37)		0.839
LVIDd, mm	64 (56–70)	66 (61–72)	61 (55–69)		0.225
LVIDs, mm	56 (44–64)	59 (50–66)	54 (43–62)		0.342

Values are expressed as n (%) unless stated otherwise. BNP = Brain natriuretic peptide; BP = blood pressure; DCM: dilated cardiomyopathy; eGFR = estimated glomerular filtration rate; HbA1c = glycated haemoglobin; HDL = high density lipoprotein; HR = heart rate; INR = international normalised ratio; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; LVIDd = left ventricular internal diameter during diastole; LVIDs = left ventricular internal diameter during systole; MAP = mean arterial pressure; NYHA = New York Heart Association; SD = standard deviation; TSH = thyroid stimulating hormone. Estimated eGFR calculated with the Modification of Diet in Renal Disease (MDRD) equation. *Values log-transformed.

Table 2

Cardiovascular magnetic resonance imaging findings in patients with dilated cardiomyopathy.

	All patients (n = 82)
LVEF (%)	24 (18–34)
LVEDV (mL)	226 (189–297)
LVESV (mL)	176 (122–239)
LVEDVI (mL/min)	125 (96–152)
LVESVI (mL/min)	93 (63–126)
LV stroke volume (mL)	56.5 ± 17.9
LV stroke volume index (mL/m ²)	30.2 ± 10.0
LVED wall mass (g)	133 (107–161)
LVED wall mass index (g/m ²)	74 (54–89)
LV total mass (g)	195.4 ± 57.9
LV mass index (g/m ²)	99 (85–116)
RVEDV (mL)	145 (110–224)
RVESV (mL)	92 (61–169)
RVEF (%)	33.8 ± 16.4
RVEDVI (mL/m ²)	74 (59–112)
RVESVI (mL/m ²)	46 (33–85)
RV stroke volume (mL)	48 (30–68)
RV ED wall mass (g)	139 ± 47.8
Cardiac output (L/min)	4.1 (3.1–5.3)
Cardiac index (L/min/m ²)	2.4 (2.1–3.5)
Cardiac density (g/mL)	1.0 (1.0–1.0)

Values are expressed as mean ± standard deviation and median (interquartile range) ED = end diastolic; LV = left ventricle; LVEDV = left ventricular end diastolic volume; LVEDVI = left ventricular end diastolic volume index; LVEF = left ventricular ejection fraction; LVESV = left ventricular end systolic volume; LVESVI = left ventricular end systolic volume index; RVEDV = right ventricular end diastolic volume; RVEDVI = right ventricular end diastolic volume index; RVEF = right ventricular ejection fraction; RVESV = right ventricular end systolic volume.

ventricular non-compaction were found in 5 (10.9%) participants with LGE, while 9 (11.0%) and 8 (9.7%) patients had pericardial and pleural effusions, respectively.

4.4. Medication

At recruitment, 85 (97%) subjects were on oral beta-blocker therapy, with a median total daily dose of carvedilol at 12.5 (IQR: 6.25–50) mg. Angiotensin-converting enzyme inhibitors (ACE-I) were prescribed to 73% of the cohort, and only ten patients were on angiotensin receptor blockers (ARB). Mineralocorticoid receptor antagonists were prescribed to 89% of all study participants, with 88% of these patients on 25 mg daily. Oral loop diuretics were prescribed to 84 (93%) patients (Fig. 2). Only three participants were prescribed digoxin. There were no statistically significant differences in total daily dosages for all medications among survivors and non-survivors.

4.5. Outcomes

Outcomes were measured after one year of follow-up from the time of recruitment (median 13.4 months, IQR: 8.8–28.9). Among the 93 participants recruited, 18 (19%) died. Six of these patients were in-patients that died after a pump failure admission. To determine the cause of death in the remaining 12 deceased participants, we used information from family members and in-hospital medical records where accessible. We could not validate the exact cause or nature of death in the participants who had demised outside our hospital.

The rate of all-cause rehospitalisation was 29.3%. A total of 17 of the 22 re-admissions were heart failure related. A single admission was documented for nine patients, while three participants were admitted twice. One participant was admitted three times, and only one patient had five episodes of hospitalisations during the study follow-up period. Complications were uncommon and reported by three study participants. Each study participant had a cerebrovascular event, pulmonary embolism, and deep vein thrombosis.

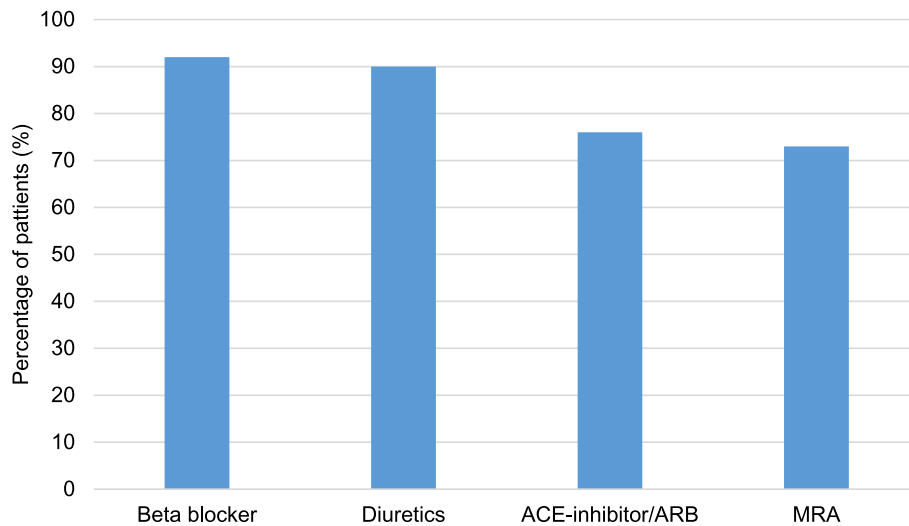


Fig. 2. Graph showing oral heart failure medication prescribed to patients with dilated cardiomyopathy at recruitment. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; MRA, mineralocorticoid antagonist.

Among the patients who died, 7 (39%) were smokers. Nearly half of the survivors (47%) were in NYHA functional class 1, while 88% of non-survivors were in NYHA functional class 2 or higher at study recruitment. After adjusting for age and gender on the univariable logistic regression analysis, smokers were five times more likely to demise, OR = 4.99 (CI: 1.422–17.488, $p = 0.012$). However, on multivariate logistic regression analysis, none of these parameters were independent predictors of all-cause mortality (Table 3).

5. Discussion

We report on the clinical characteristics and one-year all-cause mortality rate for 93 subjects with a working diagnosis of DCM. These participants were prospectively enrolled from a large academic tertiary centre in Johannesburg, South Africa. The clinical characteristics of this cohort revealed a younger mean age of onset for heart failure (44 years) and male dominance. At one year follow-up (median 13.4 months, IQR: 8.8–28.9), 19% of the participants had died.

In clinical practice, DCM patients are often given a working diagnosis of IDC to emphasise the lack of an identifiable secondary cause for the cardiomyopathy.

There are limited data from SSA reporting on clinical outcomes in patients with DCM. Contemporary studies have reported all-cause

mortality rates in patients with dilated cardiomyopathy, non-ischaemic dilated cardiomyopathy (NIDCM) or heart failure due to any cause. The one-year all-cause mortality rate in NIDCM ranges between 4% and 5% [6,7]. However, Tyminska et al. studied 312 patients with NIDCM and reported a higher mortality rate of 10% [8]. In South Africa, eighty patients with IDC had a five-year mortality rate of 40% [9]. In the International Congestive Heart Failure (INTER-HEART) multicentre cohort study involving 1294 participants with heart failure from five African countries, the one-year all-cause mortality rate was 26.4% [10]. The South African subgroup had 169 heart failure patients, and among these patients, 11.7% died within one year [10].

Current guideline-recommended therapy for HFrEF, such as sodium-glucose cotransporter-2 inhibitors, sacubitril valsartan, cardiac resynchronisation therapy, and heart transplantation services, are still not readily available in South Africa, particularly in the state-funded sector. Furthermore, out of the four heart transplantation centres in South Africa, only one is in a state-funded hospital. The limited access to heart failure device therapeutic interventions and transplant services may have reduced survival in our cohort. Also, considering that our hospital offers tertiary-level care, there may have been a delay in the referral of patients, such that our patients were already at advanced stages of heart failure upon presentation to our hospital.

Some of the predictors of mortality in IDC patients reported in the

Table 3
Univariable and multivariable logistic regression analysis for predictors of all-cause mortality.

	Univariable			Multivariable		
	Odds Ratio*	95% CI	p-value	Odds Ratio*	95% CI	p-value
Smoking	4.99	1.422–17.488	0.012	8.28	0.888–77.19	0.063
Indian race	7.96	0.647–97.896	0.105			
Body mass index	0.92	0.822–1.031	0.150			
NYHA class 1	0.15	0.032–0.736	0.019	0.72	0.072–7.265	0.784
NYHA class 2	1.73	0.579–5.225	0.324			
NYHA class 3	2.89	0.810–10.375	0.102			
NYHA class 4	2.41	0.194–29.869	0.493			
C-reactive protein	1.06	1.006–1.120	0.028	1.08	0.992–1.176	0.075
LDL cholesterol	0.50	0.238–1.057	0.070			
Troponin ^f	1.58	0.883–2.820	0.123			
N-terminal Pro BNP	1.00	1.000–1.000	0.029	1.00	0.999–1.000	0.101
INR	1.47	0.785–2.749	0.229			
LA volume index	1.03	1.001–1.075	0.043	0.98	0.925–1.040	0.528
E/A ratio	1.05	0.427–2.591	0.912			

* Adjusted for age and gender. ^fLog-transformed. BNP = brain natriuretic peptide; CI = confidence interval; E/A ratio = ratio between the E-wave and A-wave; INR = international normalised ratio; LA = left atrial; LDL = low density lipoprotein; NYHA = New York Heart Association.

literature are functional mitral regurgitation, a higher NYHA functional class and an increased left atrial size [11]. Low and high serum levels of low-density lipoprotein cholesterol (LDL-C) are associated with an increased risk of all-cause mortality in the general population and patients with advanced heart failure [12,13]. Also, markers of inflammation, such as c-reactive protein (CRP), which are usually elevated in heart failure patients, may contribute to disease progression [14]. In our study, a high CRP, smoking, a high NYHA functional class and an increased left atrial volume index were associated with mortality on univariable logistic regression analysis. However, none of these covariates independently predicted one-year all-cause mortality.

N-terminal pro-brain natriuretic peptide (pro-BNP) is a hormone released predominantly by cardiac myocytes in reaction to stretching of the ventricular wall [15] and is a sensitive biomarker of myocardial dysfunction. In our study, pro-BNP levels were almost six times higher in non-survivors. When increased, pro-BNP levels are prognostic of poor outcomes in heart failure [16,17] and the general healthy population [18]. The precise role of these clinical parameters in independently predicting mortality could be better delineated in large cohorts of meticulously phenotyped DCM patients.

Several studies have reported a higher prevalence of DCM in males [19,20]. Although our population demonstrated similar results where 64% of the DCM cohort were males, the actual burden of DCM may be underestimated in females since we only recruited females who were not pregnant and those who presented with heart failure beyond the peripartum phase. Moreover, recently published data suggest that peripartum cardiomyopathy could be a variant of DCM [21].

An endomyocardial biopsy (EMB) is the gold standard for the histological evaluation of cardiac tissue. It is indicated in patients with fulminant myocarditis and/or acute myocarditis presenting with cardiogenic shock or acute heart failure with left ventricular dysfunction, with or without malignant ventricular arrhythmias [22]. In the setting of DCM, EMB may be considered in patients with acute onset or decompensated heart failure with moderate-to-severe left ventricular dysfunction and in patients with heart failure refractory to standard therapy. Also, in patients with DCM, an EMB may be indicated for excluding other specific aetiologies, particularly in patients with a negative family history or negative results after genetic testing for cardiomyopathy [22]. In our study, 42% of the cohort reported an acute onset of heart failure symptoms. However, none of these patients had a clinical presentation nor elevated cardiac biomarker levels, and CMR imaging findings to suggest myocarditis. Furthermore, none of the study participants were refractory to acute heart failure therapy.

The goal of therapeutic strategies in DCM is to improve the quality of life, reduce the symptom burden, slow disease progression and improve survival [23]. All patients in our cohort were optimally treated with available guideline-mandated medical therapy. >80% of patients were on guideline-recommended oral heart failure therapy. This is comparable to other centres managing DCM patients. For example, in a study involving 603 IDCM patients in Italy, the prescription rate of beta blockers, ACE-I/ARB and loop diuretics in 2011 was 86%, 97% and 77%, respectively [11]. In 2016, a retrospective chart review of 1441 IDCM patients in China showed lower prescription rates of 69%, 67% and 64%, respectively [20]. However, the relatively low total daily dosage of these therapies results from many of our study participants being in the up-titration phase of therapy at the time of recruitment into the study. Furthermore, some therapies may have been temporarily down-titrated or stopped in a small proportion of patients, especially in acutely decompensated chronic heart failure patients.

While the study recruitment was focused on acute de novo or acute heart failure patients, those in NYHA class 3 and 4 were allowed to participate in the study once they had recovered within the same hospitalisation. This allowed all study investigations to be carried out without compromising the patient's clinical state. Therefore, the clinical parameters reported in the study were collected at the time of recruitment. As a result, 40% of participants were in NYHA class 1 at study

recruitment. However, it is worth noting that structured symptom or quality of life assessment tools such as the Kansas City Cardiomyopathy Questionnaire (KCCQ) and The Minnesota Living with Heart Failure Questionnaire (MLHFQ) were not routinely administered to patients during recruitment.

The classification of dilated cardiomyopathies is complex and, at times, clinically challenging because of the interplay between genetic and environmental factors implicated in the pathogenesis of this condition. By its true definition, IDCM refers to a primary myocardial disease of unknown cause, despite genetic testing. Furthermore, the absence of an identifiable genetic cause does not necessarily indicate a diagnosis of IDCM, considering the vast variation in gene mutations implicated in and causing DCM. Current recommendations are to use polygenic testing panels when screening patients suspected of having a DCM genetic cause. However, these gene panels are derived from non-African cohorts and may fail to identify pathogenic or likely pathogenic gene polymorphisms in patients of African ancestry.

6. Limitations

There are a few limitations that apply to this study. The sample size was relatively small, probably reducing the statistical power of the analyses. However, this was a very well-characterised cohort, reflecting an accurate phenotype of DCM in an African population. Although the study was in a single centre, the spectrum of participants represents individuals from various regions in Southern Africa. Furthermore, an EMB was not performed in any of our study participants. However, none of the participants had CMR imaging findings that necessitated histological correlation. Our study participants' heart failure symptoms were not objectively evaluated using the KCCQ or the MLHFQ during enrolment. Furthermore, we did not routinely measure clinical parameters such as the LVEF or objectively evaluate heart failure disease progression during the follow-up period.

7. Conclusion

Dilated cardiomyopathy in Africans primarily affects young males. In our cohort, this disease was associated with an all-cause mortality of 19% in one year. In SSA, large multicenter studies are required further to investigate this disease's pathogenesis and contemporary outcomes.

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CRedit authorship contribution statement

Nqoba Tsabedze: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Visualization, Writing – original draft, Writing – review & editing. **Dineo Mpanya:** Writing – original draft, Writing – review & editing. **Claude Bailly:** Writing – original draft, Writing – review & editing. **Samantha Nel:** Writing – original draft, Writing – review & editing. **Sacha Grinter:** Writing – original draft, Writing – review & editing. **Michele Ramsay:** Writing – original draft, Writing – review & editing. **Amanda Krause:** Writing – original draft, Writing – review & editing. **Quinn Wells:** Writing – original draft, Writing – review & editing. **Pravin Manga:** Conceptualization, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

NT is a cardiologist and has received consultation fees from Acino

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