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Predominance of Heart Failure in the Heart of Soweto Study Cohort

Emerging Challenges for Urban African Communities

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Background—There is a paucity of data to describe the clinical characteristics of heart failure (HF) in urban African communities in epidemiological transition.

Methods and Results—Chris Hani Baragwanath Hospital services the 1.1 million black African community of Soweto, South Africa. Of 1960 cases of HF and related cardiomyopathies in 2006, we prospectively collected detailed demographic and clinical data from all 844 de novo presentations (43%). Mean age was 55 ± 16 years, and women (479 [57%]) and black Africans (739 [88%]) predominated. Most (761 [90%]) had ≥ 1 cardiovascular risk. Mean left ventricular ejection fraction was $45 \pm 18\%$. Overall, 180 patients (23%) had isolated diastolic dysfunction, 234 (28%) tricuspid regurgitation, 121 (14%) isolated right HF, and 100 (12%) mitral regurgitation. The most common diagnoses were hypertensive HF (281 [33%]), idiopathic dilated cardiomyopathy (237 [28%]), and, surprisingly, right HF (225 [27%]). Black Africans had less ischemic cardiomyopathy (adjusted odds ratio, 0.12; 95% CI, 0.07 to 0.20) but more idiopathic and other causes of cardiomyopathy (adjusted odds ratio, 4.80; 95% CI, 2.57 to 8.93). Concurrent renal dysfunction, anemia, and atrial fibrillation were found in 172 (25%), 72 (10%), and 53 (6.3%) cases, respectively.

Conclusions—These contemporary data highlight the multiple challenges of preventing and managing an increasing and complex burden of HF in urban Africa. In addition to tackling antecedent hypertension, a predominance of young women and a large component of right HF predicate the development of tailored therapeutic strategies. (*Circulation*. 2008;118:2360-2367.)

Key Words: Africa ■ epidemiological transition ■ epidemiology ■ heart failure ■ population

The clinical syndrome of heart failure (HF) is a final common pathway of most forms of cardiovascular disease.¹ Affected patients typically experience poor quality of life, recurrent hospitalizations, and premature mortality.² A sustained epidemic of HF fueled by high levels of atherosclerosis and hypertension within the aging populations of high-income countries^{3,4} has necessitated the development of cost-effective preventative¹ and disease management programs.⁵ There is, however, a paucity of data describing the etiology and underlying cardiac structure and function associated with HF in low- to middle-income countries. In Africa, few clinical data are derived from echocardiography,^{6,7} and the single largest study of 1000 subjects emanates from the early 1960s.⁸ In sub-Saharan Africa, the conventional view is that HF is caused by untreated rheumatic heart valvular disease, peripartum and idiopathic cardiomyopathy, and hy-

pertension.⁹ However, in the Heart of Soweto Study of one of Africa's largest urban concentrations of black Africans, we demonstrated the potential emergence of more affluent forms of cardiovascular disease due to epidemiological transition.¹⁰ It is within this context that we describe, to our knowledge, the largest and most comprehensive study of HF in Africa to date.

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Methods

Study Setting

As described previously,^{10,11} the Heart of Soweto Study is investigating emergent heart disease in the townships of Soweto (1.1 million people), South Africa. Like other parts of sub-Saharan Africa, greater wealth has created the potential for an epidemiolog-

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ical transition toward more affluent disease in Soweto, and modifiable cardiovascular risks are now highly prevalent.¹² Alternatively, Soweto is being steadily populated by rural migrants in whom traditional lifestyles remain the norm. South Africa has a population of different ethnic backgrounds encompassing a predominance of black Africans, Europeans, Asians, and those with mixed ancestry (coloreds), and this is reflected in our study cohort.

Significantly, among the 4162 cases captured by the prospective Heart of Soweto Study clinical registry of established and de novo presentations to the Cardiology Unit of the 3500-bed Chris Hani Baragwanath Hospital in 2006 (all were subjected to echocardiography), 1960 cases (47%) were diagnosed with HF.¹⁰ This article provides a detailed description of the clinical and demographic characteristics of the 844 de novo cases of HF (18% of 2006 cases).¹⁰ Our objectives were to better understand any fundamental changes in the pathways to HF in the region and to develop effective public health programs that optimize early detection and treatment.¹³

Study Cohort

Because the hospital is the only provider of specialist cardiac services for Soweto, its case load represents a barometer of the underlying spectrum of cardiovascular disease (mild to severe).¹⁰ In 2006, the hospital managed 129 633 inpatients (35% via the Department of Medicine).

Currently, the Cardiology Unit manages 21 000 patients per annum and is staffed by internal medicine specialists in cardiology training and experienced cardiologists. Collectively, they apply advanced diagnostic investigations and gold-standard treatment to all patients seen via the cardiology outpatient department and Coronary Care Unit. The Cardiology Unit also manages patients referred from all other inpatient (eg, general medical ward) and outpatient (eg, diabetic clinic) units as well as those referred from 12 local primary care clinics.

Study Data

In addition to detailed demographic and clinical profiling (eg, Minnesota coding of 12-lead ECGs¹⁴), all patients with HF were subjected to a detailed echocardiographic assessment of ventricular function, valvular integrity and function, and regional wall abnormalities (specific measurements available in all but 67 of de novo cases [8%]). Two-dimensional targeted M-mode echocardiography with Doppler color flow mapping was performed with a Hewlett-Packard Sonos 5500 echocardiograph attached to a 2.5- or 3.5-MHz transducer by trained operators according to the American Society of Echocardiography guidelines.¹⁵ Diastolic mitral flow was assessed by pulsed-wave Doppler echocardiography from the apical 4-chamber view. The E wave deceleration time was measured as the interval between the peak early diastolic velocity and the point at which the steepest deceleration slope is extrapolated to the zero line.

To exclude ischemic etiology, every patient (regardless of age and including those ultimately diagnosed with idiopathic dilated cardiomyopathy) with clinical suspicion of coronary artery disease based on ECG (eg, pathological Q waves) and echocardiography (eg, regional wall motion abnormalities) is routinely subjected to a combination of stress testing, cardiac nuclear imaging, and cardiac catheterization; this involved \approx 350 nuclear perfusion scans and 550 coronary angiograms in 2006. Data availability and specific criteria applied are provided in table legends.

Clinical Diagnoses

Table 1 summarizes the criteria that were applied, via independent review and consensus agreement by K.S. and S.S., to stratify patients according to the probable etiology of HF. These are based on European Society of Cardiology guidelines¹ and the recent European Heart Survey.¹⁶

Ethical Considerations

This study was approved by the local ethical committee and relevant administrative bodies and conforms to the principles outlined in the Declaration of Helsinki. Each patient in the study was assigned a

Table 1. Study Definitions

Study Definition	Criteria
LV systolic dysfunction	LV ejection fraction \leq 45%
Diastolic dysfunction	Based on E/A ratio and deceleration time according to generally accepted criteria ¹⁵
Idiopathic dilated cardiomyopathy	LV ejection fraction \leq 45% and possibly LVEDD $>$ 55 mm of indeterminate origin (CAD excluded by coronary angiography)
Ischemic cardiomyopathy	LV ejection fraction \leq 45%, confirmed diagnosis of CAD (via coronary angiogram) and regional wall motion abnormality
Hypertensive HF	Documented blood pressure of $>$ 180/100 mm Hg accompanied by symptoms of HF, increased LV septal thickness ($>$ 1.3 mm), diastolic dysfunction, and/or LV systolic dysfunction
Valvular HF	HF secondary to primary underlying valve disease (eg, rheumatic heart disease or degenerative valve disease) as opposed to underlying valvular dysfunction (eg, mitral regurgitation) due to underlying cardiac dysfunction/failure
Right HF	HF secondary to right-sided pathology with increased jugular venous pressure and liver size, tricuspid regurgitation, and/or elevated right ventricular systolic pressure $>$ 35 mm Hg; usually accompanied by peripheral edema as unique or concomitant to left HF; isolated right HF excludes significant LV and valvular involvement (eg, rheumatic heart disease)
Other causes leading to HF	Includes congenital heart disease with delayed diagnosis made only in adulthood, hypertrophic obstructive cardiomyopathy, peripartum cardiomyopathy, endomyocardial fibrosis, submitral aneurysm, and HF secondary to HIV infection, tuberculosis, and infectious pericardial effusion

LV indicates left ventricular; LVEDD, LV end diameter at diastole; and CAD, coronary artery disease.

unique identifying code (9 digits), all documents were labeled accordingly to maintain anonymity, and each patient verbally agreed to participate at the time of data collection.

Statistical Analyses

All study data were documented and entered into the study database by a dedicated team of experienced cardiac nurses. Data were then verified and analyzed with SAS version 9.1 (SAS Institute Inc, Cary, NC). Normally distributed continuous data are presented as mean \pm SD and nongaussian distributed variables as the median plus interquartile range. Percentages are presented with 95% CIs where appropriate. Comparisons according to demographic and clinical profile involved χ^2 analysis with calculation of odds ratios and 95% CIs for discrete variables and the Student *t* test and ANOVA for normally distributed continuous variables. Multiple logistic regression analyses (entry model) were performed on age, sex, ethnic origin, and risk factors to derive adjusted odds ratios. Significance was accepted at the 2-sided level of 0.05.

The authors had full access to and take responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Clinical and Demographic Profile

In 2006, 1960 patients (163 cases per month) presented with a primary or secondary diagnosis of HF. Of these, 844 patients

Table 2. Sociodemographic and Clinical Profile of Study Cohort (n=844)

	Men (n=365) (43%)	Women (n=479) (57%)	<i>P</i>	Black (n=739) (88%)	Others Races (n=105) (12%)	<i>P</i>
Sociodemographic profile						
Mean age, y	57±14	54±17	0.009	55±16	57±15	0.089
No education/standard education	109 (30%)	152 (32%)	0.187	247 (95%)	14 (5%)	<0.0001
Risk factor profile						
Positive family history	77 (36%)	138 (64%)	0.028	170 (79%)	45 (21%)	<0.0001
Mean BMI	25±6	30±8	<0.0001	28±8	28±6	0.756
Obese (BMI >30 kg/m ²)	33 (26%)	96 (74%)	<0.0001	112 (87%)	17 (13%)	0.863
Former or current smoker, %	243 (61%)	153 (39%)	<0.0001	329 (83%)	67 (17%)	0.0005
Hypertension	209 (42%)	294 (58%)	0.439	442 (88%)	61 (12%)	0.900
Prior stroke	27 (40%)	30 (6%)	0.068	44 (66%)	13 (34%)	0.029
Prior diabetes	55 (41%)	79 (59%)	0.444	107 (80%)	27 (20%)	0.003
Clinical presentation						
Dyspnea (NYHA class II, III, or IV)	245 (39%)	386 (61%)	<0.0001	563 (89%)	68 (11%)	0.012
Mean heart rate, bpm	86±20	90±21	0.001	90±20	80±18	<0.0001
Mean systolic BP, mm Hg	128±26	128±27	0.791	128±27	130±24	0.463
Mean diastolic BP, mm Hg	76±16	72±16	0.019	74±17	73±15	0.309
Mean eGFR, mL/min per 1.73 m ²	80±36	81±34	0.715	82±35	72±33	0.009
Chest pain/angina pectoris	91 (38%)	146 (62%)	0.076	198 (84%)	39 (16%)	0.027
Peripheral edema	116 (36%)	209 (64%)	0.0005	294 (91%)	31 (9%)	0.043
Clinical profile						
Renal dysfunction	75 (44%)	97 (56%)	0.715	142 (83%)	30 (17%)	<0.001
Anemia	23 (32%)	49 (68%)	0.029	63 (88%)	9 (12%)	0.957
Mean potassium, mmol/L	4.4±0.8	4.1±0.8	0.0002	4.2±0.8	4.4±0.7	0.069
Etiologic profile						
Idiopathic dilated cardiomyopathy and other cardiomyopathy	135 (45%)	163 (55%)	0.266	285 (96%)	13 (4%)	<0.0001
Ischemic cardiomyopathy	49 (64%)	28 (36%)	<0.0001	41 (96%)	36 (4%)	<0.0001
Hypertensive HF	109 (39%)	172 (61%)	0.058	251 (89%)	30 (11%)	0.272
Right HF (all cases)	94 (42%)	131 (58%)	0.302	196 (87%)	29 (13%)	0.480
Valvular HF (degenerative/rheumatic)	25 (37%)	42 (63%)	0.298	63 (94%)	4 (6%)	0.094

Data are presented as mean±SD or proportions. Standard education is 1 to 5 years of schooling. Height and weight data were used to calculate body mass index (BMI) in 376 cases (211 women). NYHA indicates New York Heart Association; BP, blood pressure; eGFR, estimated glomerular filtration rate, calculated in 702 cases with the Modification of Diet in Renal Disease abbreviated formula ($\text{eGFR in mL/min per } 1.73 \text{ m}^2 = 186.3 \times (\text{serum creatinine, mg/dL})^{-1.154} \times (\text{age})^{-1.154} \times (0.742 \text{ if female sex}) \times (1.21 \text{ if black African})$) using serum creatinine concentrations ($\mu\text{mol/L}$) converted to mg/dL. Renal dysfunction is defined as $\text{eGFR} < 60 \text{ mL/min per } 1.73 \text{ m}^2$ (moderate to severe renal impairment). Anemia is defined as hemoglobin level $< 11 \text{ g/dL}$ in men and $< 10 \text{ g/dL}$ in women from 699 cases. Sodium and potassium levels were recorded in 702 and 656 cases, respectively.

(43%) were de novo presentations. Most patients were referred either from another outpatient clinic (384 [46%]) or as a hospital inpatient (350 [42%]); the remainder (96 cases [11%]) primarily were referred from a primary care clinic. Women (479 cases [57%]) and black Africans (739 cases [88%]) predominated. Black African women (n=437) were the largest patient subgroup of patients, representing 59% versus 40% of their ethnic grouping ($P < 0.0001$; odds ratio, 1.49; 95% CI, 1.25 to 1.78) and 52% of the entire cohort. Almost two thirds were from Soweto and lived there for a median of 40 (interquartile range, 30 to 52) years. Table 2 compares the broad characteristics of the cohort according to sex and race. Women were on average 3 years younger than men and had significantly increased odds of having a positive family history and to be obese. Men were at increased odds of

having a history of smoking. More women reported advanced symptoms of dyspnea and peripheral edema and had higher resting heart rates. Compared with other ethnic groups, black Africans had received less formal education, and fewer reported a positive family history or a personal history of smoking, stroke, or diabetes. On presentation, black Africans had substantially higher resting heart rates but more preserved renal function.

Risk Factor Profile

Overall, 761 patients (90%) had ≥ 1 cardiovascular risk, and 519 (62%) had multiple risks, the most common being diastolic and/or systolic hypertension (503 cases [60%]), a history of smoking (396 cases [47%]), obesity (129 cases [34%] of those with both height and weight data recorded),

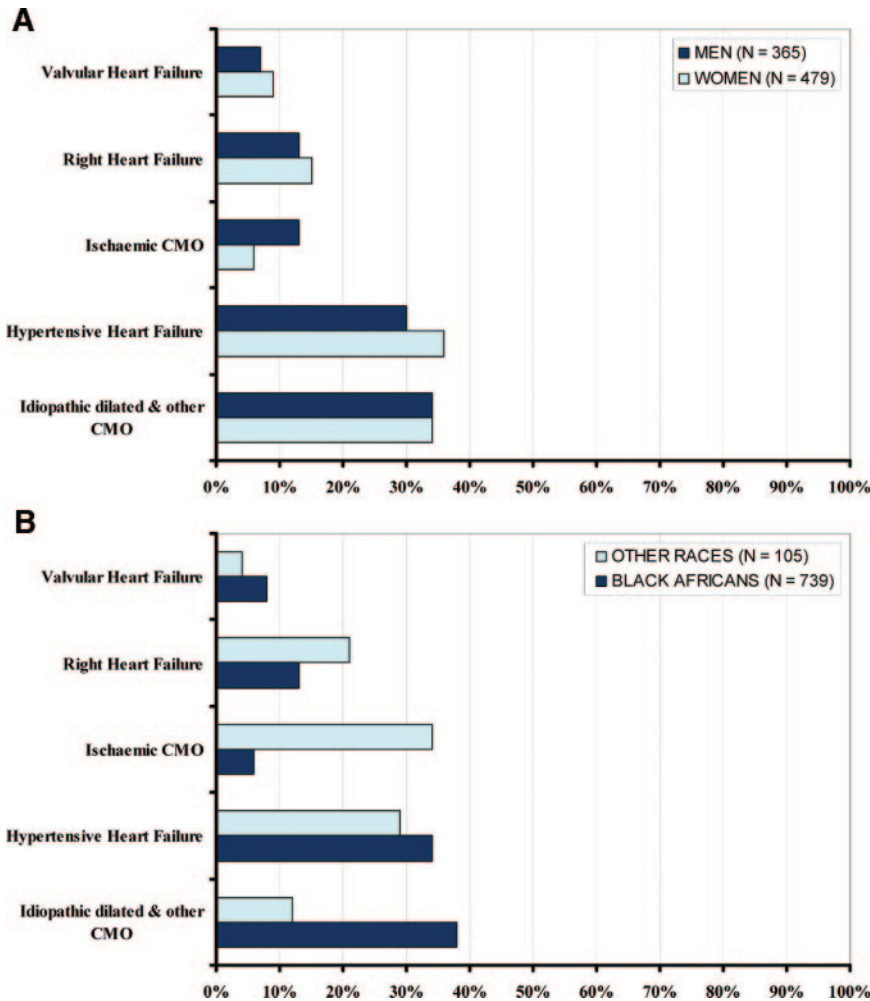


Figure. Underlying etiology of HF according to gender (A) and ethnic origin (B). CMO indicates cardiomyopathy.

and dyslipidemia (66 cases [19%] of those subject to fasting cholesterol tests).

Underlying Etiology

Five major forms of HF were diagnosed overall, with mixed left and right forms of HF found in 104 (12%) of cases: (1) 281 cases of hypertensive HF (33%; 95% CI, 30% to 36%); (2) 237 cases of idiopathic cardiomyopathy (28%; 95% CI, 25% to 31%); (3) 225 cases of right HF overall (27%; 95% CI, 24% to 30%) and 121 primary diagnoses of the same; (4) 77 cases of ischemic cardiomyopathy (9%; 95% CI, 7% to 11%); and (5) 67 cases of valvular HF (8%; 95% CI, 6% to 10%). A miscellaneous group of 61 cases of other discrete forms of HF (combined with idiopathic dilated cardiomyopathy in the tables and Figure) included 29 cases of peripartum cardiomyopathy, 29 cases of HIV-related cardiomyopathy (13 with concurrent tuberculosis), and 4 cases of hypertrophic obstructive cardiomyopathy.

The Figure shows clinically important differences in the etiology of HF according to gender and race. With adjustment for age, race, and risk factor profile (family history, smoking status, lipid profile, blood pressure, and diabetic status), the odds of a woman (predominantly black Africans) presenting with an ischemic cardiomyopathy (6% versus 13%; adjusted odds ratio, 0.49; 95% CI, 0.28 to 0.85; $P=0.011$) were

significantly lower compared with men. The odds of a black African presenting with an ischemic cardiomyopathy (6% versus 34%; adjusted odds ratio, 0.12; 95% CI, 0.07 to 0.20) were markedly lower than other ethnic groups. Conversely, black Africans had 5 times higher odds of presenting with an idiopathic dilated cardiomyopathy or other form of HF (38% versus 12%; adjusted odds ratio, 4.80; 95% CI, 2.57 to 8.93) compared with the rest ($P<0.0001$ for both comparisons).

Table 3 shows the clinical and demographic features of the 5 major groups of HF with some important differences evident. Those with idiopathic cardiomyopathy and other causes of HF were significantly younger than the rest ($P<0.001$). Only 10% of patients (72 cases) had concurrent anemia, and >10% had a history of stroke and/or atrial fibrillation (58 and 53 cases, respectively). Overall, 141 (20%) had an estimated glomerular filtration rate indicative of moderate to severe renal dysfunction. Black Africans were more likely to have preserved renal function (35% versus 23%; $P=0.009$) compared with the rest, which is partly explained by the fact that those with an ischemic cardiomyopathy had significantly lower estimated glomerular filtration rate than those with a dilated cardiomyopathy or right HF ($P<0.01$ for both comparisons).

Table 4 shows the echocardiographic features according to primary underlying etiology. Overall, 417 (54%) of those

Table 3. Clinical and Demographic Characteristics of 844 Cases of HF According to Primary Underlying Etiology

	Total Cohort	Idiopathic Dilated/Other Cardiomyopathy	Ischemic Cardiomyopathy	Hypertensive HF	Right HF	Valvular HF
Total (%)	844	298 (35%)	77 (9%)	281 (33%)	121 (14%)	67 (8%)
Mean age, y	55±16‡	50±16	58±12	61±15	57±15	53±18
Male	365 (43%)	135 (45%)	49 (64%)	109 (39%)	47 (39%)	25 (37%)
Black African	739 (88%)	285 (96%)	41 (53%)	251 (89%)	99 (82%)	63 (94%)
Risk factors						
Positive family history	215 (25%)	66 (22%)	26 (34%)	67 (24%)	34 (28%)	22 (33%)
Obese	129 (34%)*	41 (30%)	9 (28%)	58 (45%)	11 (9%)	10 (30%)
History of smoking	396 (48%)†	147 (51%)	45 (60%)	107 (39%)	67 (55%)	30 (47%)
Hypertension	467 (55%)‡	110 (37%)	40 (52%)	281 (100%)	6 (5%)	30 (45%)
Clinical presentation						
NYHA class III or IV	291 (34%)*	127 (43%)	22 (29%)	81 (29%)	40 (33%)	21 (31%)
Peripheral edema	325 (39%)	123 (41%)	21 (27%)	105 (37%)	49 (40%)	27 (40%)
Mean systolic BP, mm Hg	128±26‡	120±23	123±24	140±28	126±22	121±25
Mean diastolic BP, mm Hg	74±16‡	72±16	71±15	80±17	72±15	69±13
Mean eGFR, mL/min per 1.73 m ²	81±35‡	83±33	65±25	75±34	87±39	78±25
Comorbidity						
Coronary artery disease	83 (10%)‡	1 (0.3%)	77 (100%)	3 (1%)	0	2 (3%)
Acute myocardial infarction	18 (2%)‡	0	18 (23%)	0	0	0
Diabetes	86 (10%)‡	21 (7%)	18 (23%)	39 (14%)	3 (2%)	5 (7%)
Anemia	72 (10%)	28 (12%)	3 (5%)	22 (10%)	16 (13%)	3 (6%)
Stroke	58 (7%)‡	12 (4%)	7 (9%)	34 (12%)	1 (1%)	4 (6%)
Atrial fibrillation	53 (6%)*	13 (4%)	2 (3%)	25 (9%)	6 (5%)	7 (10%)
Renal dysfunction	172 (25%)*	54 (23%)	25 (39%)	60 (27%)	21 (20%)	12 (24%)

Data are presented as a mean±SD or proportions. NYHA indicates New York Heart Association; BP, blood pressure; and eGFR, estimated glomerular filtration rate. Test of mean values and distribution of cases according to primary diagnosis of HF: * $P<0.05$; † $P<0.01$; ‡ $P<0.001$.

with a quantified left ventricular ejection fraction had moderate to severe systolic dysfunction, and 225 (29%) had impaired diastolic function (180 [80%] with isolated diastolic dysfunction). In addition to those with primary valvular disease, patients with an idiopathic cardiomyopathy and right HF were most likely to have moderate to severe mitral or tricuspid regurgitation.

Case Complexity

There were many complex cases. For example, 237 patients were diagnosed with idiopathic dilated cardiomyopathy after exclusion of coronary artery disease and ongoing investigations for familial cardiomyopathy. Although prior hypertension was reported in 101 of these cases (43%), most were normotensive and had no evidence of left ventricular hypertrophy. In addition, 29 black African women presented with peripartum cardiomyopathy, and 24 cases were found to be HIV-related.

Right HF

Perhaps most significantly, there were many cases of right HF, either in its isolated form (ie, 121 patients without left-sided pathology, particularly valve disease, which could have explained their clinical state) or in combination with other forms of HF (104 cases). Beyond those with cor pulmonale (84 of 121 isolated right HF cases [69%]), there were a range of pathologies contributing to these cases. This

included 20 cases (9%) of rheumatic heart disease (primary etiology of valvular HF) and 13 cases (12 were women) of pulmonary hypertension secondary to connective tissue disorders (6%) in addition to 13 cases (6%) of pulmonary complications secondary to tuberculosis.

Initial Pharmacological Treatment

At clinical presentation, 517 patients (61%) were prescribed at least 1 form of HF-specific treatment (43% combination therapy) with no differences on the basis of race or gender. In those with systolic dysfunction (n=417), the 5 most commonly prescribed agents were loop or thiazide diuretic (85%), angiotensin-converting enzyme inhibitor (70%), β -blocker (64%), aldosterone inhibitor (60%), and digitalis (19%). In those with preserved systolic function (n=373), these were loop or thiazide diuretics (49%), angiotensin-converting enzyme inhibitor (44%), β -blocker (25%), aldosterone inhibitor (22%), and a calcium antagonist (18%).

Discussion

This study represents one of the largest and most comprehensive studies of HF in Africa focusing on cases derived from urban-dwelling black Africans in epidemiological transition. The volume and pattern of cases challenge a number of assumptions about the natural history of HF on the continent. Although resembling some aspects of the HF epidemic in

Table 4. Results of Echocardiographic and ECG Assessment According to Underlying Etiology of HF (n=844)

	All (n=844)	Idiopathic Dilated/Other Cardiomyopathy (n=298)	Ischemic Cardiomyopathy (n=77)	Hypertensive HF (n=281)	Right HF (n=121)	Valvular HF (n=67)
Systolic and diastolic function						
Mean LV ejection fraction, %	45±18‡	34±13	39±15	53±17	55±17	48±17
LVEDD, mm	50±12‡	59±11	53±9	46±11	44±12	52±13
LVESD, mm	38±14‡	49±11	42±11	32±11	32±12	40±15
IVSD >13 mm	254 (30%)‡	77 (26%)	11 (14%)	119 (42%)	30 (25%)	17 (25%)
RVSP >35 mm Hg	183 (22%)	51 (17%)	10 (13%)	28 (10%)	81 (70%)	13 (19%)
Preserved LV systolic function	373 (48%)‡	44 (15%)	19 (26%)	177 (66%)	101 (95%)	32 (50%)
Diastolic dysfunction	225 (29%)†	27 (9%)	15 (19%)	157 (56%)	2 (2%)	24 (36%)
Other echo parameters						
Mild/moderate/severe mitral regurgitation	59/27/14† (7%/3%/2%)	19/11/8 (6%/4%/3%)	7/1/0 (9%/1%/0%)	13/6/0 (5%/2%/0%)	9/1/0 (7%/1%/0%)	11/8/6 (16%/12%/9%)
Mild/moderate/severe tricuspid regurgitation	126/69/39‡ (15%/8%/5%)	25/26/11 (8%/8%/4%)	6/1/0 (8%/1%/0%)	12/4/3 (4%/1%/1%)	70/31/20 (58%/26%/17%)	13/7/5 (19%/10%/8%)
ECG findings						
LV hypertrophy	117 (15%)‡	64 (22%)	4 (6%)	36 (14%)	0	13 (22%)
Left or right bundle-branch block	56 (7%)	23 (8%)	8 (11%)	13 (5%)	8 (7%)	4 (6%)

Data are presented as mean±SD or proportions. Specific left ventricular (LV) ejection fraction values were recorded in 777 cases. LVEDD indicates LV end-diameter at diastole; LVESD, LV end diameter at systole; IVSD, intraventricular septum diameter at diastole; and RVSP, right ventricular systolic pressure (specific values recorded in 645 cases). Preserved systolic function=LV ejection fraction ≥45%.

Test of mean values and distribution of cases according to primary diagnosis of HF: † $P<0.01$; ‡ $P<0.001$.

high-income countries,³ the spectrum of documented cases represented a broad combination of traditional and affluent pathways to the syndrome in greater numbers than first anticipated. These data have important clinical and public health implications for Soweto and other populations in epidemiological transition.

Unlike the typical pattern of HF in high-income countries,^{2–4} this urban African cohort was dominated by young black African women, and we found a broad diversity of heart disease attributable to a combination of infectious and non-communicable diseases.¹⁰ The surprisingly high number of cases (while no doubt inflated by increased detection rates due to routine echocardiography) is indicative of a much higher prevalence of HF than previously suspected in urban Africans. Consistent with previous African reports, many cases were attributable to idiopathic dilated cardiomyopathy,¹⁷ HIV-related cardiomyopathy,¹⁸ peripartum cardiomyopathy,¹⁹ and endomyocardial fibrosis.²⁰ Equivalent studies from Nigeria (315 patients)²¹ and Cameroon (167 patients)²² have also highlighted the importance of communicable diseases and valve disease in the development of HF in Africa. Importantly, these data reinforce the central (and most probably increasing) role of hypertension (found in 60% of cases) in the development of HF,^{6,7} which represents a high-priority target for HF prevention in urban Africa. Fortunately, hypertension is readily identifiable,¹³ and 15% of patients had ECG evidence of left ventricular hypertrophy; although the progression from concentric left ventricular hypertrophy to HF has not been well defined in Africa, data from hypertensive African Americans suggest that this is a common outcome.²³

There is a clear need, therefore, to develop African-specific prevention programs that optimize the detection and management of hypertension in addition to targeting those most at risk of developing peripartum cardiomyopathy¹⁹ and HIV-related cardiomyopathy.¹⁸

These data also reaffirm that valvular disorders play a pivotal role in the development of HF in Africa, with 8% of de novo HF cases attributable to primary valve disease (mostly chronic rheumatic heart disease) and ≈25% of most forms of HF having concurrent valve dysfunction. Significantly, not a single case of acute rheumatic fever, a previously common diagnosis in the region,²⁴ was documented, most probably reflecting less overcrowding, better sanitation, and access to antibiotic therapy in children and young adults. However, children are managed elsewhere, and such cases remain high in rural areas of sub-Saharan Africa.⁶ Regardless, there is clear potential for early screening programs to detect rheumatic disease-related cardiac murmurs in urban communities. Furthermore, the latent potential for increasing numbers of cases with ischemic cardiomyopathy²⁵ is underscored by a near 5-fold difference (2% versus 9%) in reported cases compared with previous reports.⁶ With many so complex cases, it was essential to distinguish between primary versus functional valve disease (eg, idiopathic dilated cardiomyopathy resulting in annular dilatation). Surprisingly, few HF studies (eg, the EuroHeart Failure Survey II reported that 72% of de novo acute HF was complicated by mitral regurgitation) make such a distinction.¹⁶ In Africa, such distinctions are important given that the therapeutic approach to HF due to severe rheumatic mitral regurgitation (surgery)

versus functional mitral regurgitation (eg, in selected patients with idiopathic dilated cardiomyopathy who may benefit from a multisite pacemaker²⁶) will markedly differ. This highlights the challenge of adapting and prioritizing therapeutic strategies according to the changing etiology of HF.

The surprisingly high prevalence of isolated and concomitant right HF (21% of cases combined) relative to reports from high-income countries (only 3.2% in the EuroHeart Failure Survey II cohort¹⁶) is also worthy of comment. This disparity might reflect poor access to healthcare facilities; more than two thirds of right HF cases presented as “late” pulmonary complications. However, consistent with the BOLD Study showing that South Africa had a particularly high prevalence of chronic obstructive pulmonary disease,²⁷ ≈20% of right HF cases were of indeterminate origin. The high prevalence of right HF in individuals who never smoked requires further investigation, particularly in respect to the role of air pollution and potentially greater genetic susceptibility in certain individuals. Certainly, understanding and addressing the potentially preventable antecedents of right HF represent a major target for reducing the burden of HF in this population. Once again, this would require the development of specific treatments for a form of HF rarely reported and managed in high-income countries.

Our study has a number of limitations. First, this study cohort only reflects those who seek specialist care and therefore reflects those with more advanced forms of HF. These data undoubtedly underrepresent adults living with milder forms of HF, and we have no data on sudden fatal events secondary to undiagnosed HF. Unfortunately, there are no gold-standard methods for definitively categorizing the etiology and clinical characteristics of HF. We applied a clinically orientated approach based on published criteria.¹⁶ We acknowledge potential biases in our classification of cases despite our careful delineation of primary versus secondary valve disease/dysfunction. Finally, as a clinical registry we did not systematically validate diagnostic data but (wherever possible) have adhered to the recently published Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines in our reporting of study data.²⁸

In conclusion, this study provides important insights into the broadening range of causes (ie, beyond the traditional causes of HF in Africa) and characteristics of HF arising from a large urban population of black Africans in epidemiological transition. Although the current burden of HF in Soweto does not (yet) resemble that found in high-income countries, we have highlighted the emerging challenge of dealing with an expected rise of HF on the continent (particularly in relation to early prevention and treatment strategies). The complexity of cases has forced us to more critically examine case classifications beyond that typically reported. Ultimately, these data challenge us to recognize and respond to HF in Africa by recognizing unique aspects concerning its natural history (particularly antecedent hypertension and a major component of right HF) and the need for culturally sensitive interventions.

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Disclosures

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CLINICAL PERSPECTIVE

In one of the largest studies of heart failure (HF) in Africa, we studied 844 de novo cases in Soweto, South Africa. The results challenge a number of previous assumptions regarding the natural history of HF in Africa. Compared with more affluent countries, there was a higher prevalence of women (57%), and patients were younger (the mean age was 55 ± 16 years.) The unexpectedly high burden of HF was attributed to a combination of etiologies, with the expected cases of hypertensive HF, idiopathic dilated cardiomyopathy, and HF due to structural valve disease supplemented by right HF and ischemic heart failure. These data have important clinical and public health implications for urban African and other communities in epidemiological transition where old and new forms of HF will emerge. Treatment strategies need to keep pace with the changing etiology of HF, and preventative strategies need focus on both old (eg, late recognition of rheumatic heart disease) and new antecedents (eg, atherosclerosis) of HF. Hypertension, in particular, represents a traditional antecedent for HF in Africa that will gain even more clinical importance as a preventative target. Significantly, we found a surprisingly high burden of right HF (either in isolation or in combination with left HF). The increasing burden of HF in vulnerable populations in Africa and beyond will necessitate the development of relatively inexpensive but effective programs of care that provide treatments adapted to the local healthcare system and the specific population.