Heart Failure in Sub-Saharan Africa

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Abstract

Heart failure is a growing problem in sub-Saharan Africa. This arises as the prevalence of risk factors for cardiovascular disease rises, life expectancy increases and causes of heart failure more common in Africa, such as rheumatic heart disease and endomyocardial fibrosis, continue to be a significant issue. Lack of access to diagnostics is an issue with the expense and technical expertise required for echocardiography limiting access. Biomarker strategies may play a role here. Access to essential medicines is also limited and requires a renewed focus by the international community to ensure that appropriate medications are readily available, similar to that which has been implemented for HIV and malaria.

Keywords

Heart failure, Africa, echocardiography, essential medicines, natriuretic peptides

Patients with heart disease in Africa commonly present with heart failure both for admission to hospital[1] and in the outpatient setting.[2] Recent data suggests that, in line with high-income countries, heart failure with preserved ejection fraction is also becoming more common.[3] Data from the 12 clinical studies performed before 2005 in eight sub-Saharan Africa (SSA) countries have shown that up to 75 % of cases of heart failure were non-ischaemic in origin.[1,4] A recent study showed that patients with heart failure in Africa were the youngest (mean [SE] = 53 [0.4] years), most likely to be illiterate (43 %), lack health insurance (66 %) and medication insurance (67 %), and most likely to be in New York Health Association functional class IV (21 %) compared with those from Asia, the Middle East and South America.[5]

Over the past several years a shift in the cardiovascular disease profile has been observed, which was reflected by recent clinical trial data derived from the largest multicentre registry for heart failure in Africa. The sub-Saharan Africa Survey of Heart Failure (THESUS-HF)[6] study characterised the causes, treatment and short-term outcome in 1006 Africans from nine SSA countries. Compared with data from prior to 2005, it highlighted hypertension as a rising cause of heart failure (from 23 % to 43 %), an increasing importance of cardiomyopathies (from 20 % to 29 %), a reduced recognition of rheumatic heart disease (from 22 % to 17 %), and a rise in ischaemic heart disease (from 2 % to 8 %) in the aetiology of heart failure.[4] Recent studies that have specifically looked for evidence of ischaemic heart disease have shown a higher prevalence than previously reported. A case-control study from Kenya recently suggested that ischaemic heart disease was the second most common cause of heart failure.[7] This is in line with the changing demographics in Africa and rise in risk factors, such as hypertension, diabetes and obesity (*Table 1*).

There are also causes of heart failure that are significantly more prevalent in Africa and rarely found outside low-income countries, such as rheumatic heart disease, endomyocardial fibrosis and HIV-related cardiomyopathy.

Rheumatic heart disease, caused by infection with group A *Streptococcus*, has been virtually eliminated in high-income countries but continues to be a significant problem in Africa. The prevalence of clinically silent rheumatic heart disease (21.1 per 1000 people; 95 % CI [14.1–31.4]) was about seven to eight times higher than that of clinically manifest disease (2.7 per 1000 people; 95 % CI [1.6–4.4]).[20] A recent study demonstrated the young age of patients with this condition (median age of 28 years) had a female preponderance (66.2 % female) and up to a quarter had evidence of left ventricular dysfunction.[21] Prevention of progression of valvular disease is currently based on regular penicillin prophylaxis.

Endomyocardial fibrosis is characterised by deposition of fibrous tissue on the endocardial surfaces and is the most common cause of restrictive cardiomyopathy. Its cause is unknown and there are no specific treatments for it. It is commonest within 15 degrees either side of the equator and commonly affects the young. A screening study in rural Mozambique showed a prevalence of 19.8 % with the highest prevalence among those aged 10–19 years.[22]

The pathophysiology of heart failure in HIV-infected persons is multifactorial and intimately related to the presence of traditional risk factors for coronary artery disease, myocardial inflammation, myocardial fibrosis, coronary artery disease and pericardial disease. The advent of antiretroviral therapy led to a dramatic reduction in this condition and, similar to heart failure of other aetiologies, heart failure with preserved ejection fraction is the most prevalent form of HIV-related cardiomyopathy in the era of highly-active antiretroviral therapy.[23,24]

Diagnosis of Heart Failure

The diagnosis of heart failure can pose significant challenges in Africa due to lack of access to appropriate diagnostics. Internationally, at least,

Clinical Syndromes

Table 1: Aetiology of Heart Failure in Sub-Saharan African Countries in the 21st Century

Study	Country	Study Size and Duration	Prevalence/Epidemiology
Kingue et al. 2005[9]	Cameroon	167 patients, single-centre, 3-year descriptive study	Main aetiologies of heart failure: hypertension (54.5 %), cardiomyopathies (26.3 %), rheumatic heart disease (24.6 %), valvular heart diseases (24.6 %), ischaemic heart disease (2.4 %)
Amoah et al. 2000[10]	Ghana	572 patients, single-centre, 4-year prospective study	Main causes of heart failure: hypertension (21.3 %), rheumatic heart disease (20.1 %), cardiomyopathy (16.8 %), congenital heart disease (9.8 %) and coronary artery disease (10.0 %) Commonest rheumatic valvular lesion: mitral regurgitation (78.0 %) Commonest cardiomyopathies: dilated cardiomyopathy (67.7 %), endomyocardial fibrosis (22.9 %), hypertrophic cardiomyopathy (9.4 %)
Oyoo et al. 1999[11]	Kenya	91 patients, single-centre, cross-sectional study	Main causes of heart failure: rheumatic heart disease (32.0 %), cardiomyopathy (25.2 %), hypertensive heart disease (17.6 %), pericardial disease (13.2 %), cor pulmonale (7.7 %), ischaemic heart disease (2.2 %), congenital heart disease (2.2 %)
Soliman et al. 2008[12]	Malawi	3,908 patients, single-centre, 5-year registry	Main causes of heart failure: valvular heart disease (mainly rheumatic heart disease; 34 %), hypertensive heart disease (24 %), cardiomyopathies (19 %), pericardial diseases (14 %), congenital heart disease (4 %), arrhythmias (4 %), other CVD (1 %)
Kennedy et al. 2013[13]	Malawi	250 children with an abnormal echocardiogram, single-centre, 2-year registry	Main causes of heart failure: 55.6 % congenital heart disease (24 % ventricular septal defect, 10 % tetralogy of Fallot, 7.2 % patent ductus arteriosus) and 44.4 % acquired heart disease (22.4 % rheumatic heart disease, 13.6 % dilated cardiomyopathy)
Karaye et al. 2013[14]	Nigeria	2 centres, 1-year registry of all patients Centre 1: patronised by high-income earners; Centre 2: patronised by low-income earners	Most common heart disease: hypertensive heart disease (56.7 %; more common in Centre 1), dilated cardiomyopathy (15.2 %) Second most common heart disease: ischaemic heart disease (8.7 %; more common in Centre 2) Third most common heart disease: rheumatic heart disease (8.3 %), peripartum cardiomyopathy (4.3 %; exclusively found in Centre 2)
Familoni et al. 2007[15]	Nigeria	82 patients, single-centre, 3-year descriptive study	Main causes of heart failure: hypertension (43.4 %), dilated cardiomyopathy (28.0 %), rheumatic heart disease (9.8 %), endomyocardial fibrosis (2.24 %), cor pulmonale (3.7 %), ischaemic heart disease (8.5 %), other (3.5 %)
Thiam et al. 2003[16]	Senegal	170 patients, single-centre, 6-month prospective study	Main causes of heart failure: hypertension (45.0 %), rheumatic heart disease (34.0 %), diabetes mellitus (11.8 %) Main aetiologies on ECG: LV hypertrophy (63.5 %), AF (16.6 %), valvular heart diseases (45.0 %), hypertension (34.0 %), unspecified (6.0 %)
Ismail et al. 2007[17]	Uganda	65 patients, single centre	Main causes of heart failure: dilated cardiomyopathy (47.7 %), rheumatic heart disease (35.4 %), cor pulmonale (4.6 %), ischaemic heart disease (4.6 %), endomyocardial fibrosis (1.5 %), pericardial disease (1.5 %), other (4.6 %)
Sliwa et al. 2008[18]	South Africa	844 patients (from 4,162 CVD patients, 85 % native Africans), single-centre, 1-year population study	Main causes for heart failure: hypertension (33.3 %), dilated cardiomyopathy (35.1 %), cor pulmonale (26.7 %), ischaemic heart disease (9.1 %), rheumatic heart disease (7.9 %), valvular heart disease (8 %)
Dokainish et al. 2016[5]	Africa	1,294 outpatients Nigeria (383 patients), South Africa (169 patients), Sudan (501 patients), Uganda (151 patients), Mozambique (90 patients)	Main causes for heart failure: hypertensive heart disease (35 %), ischaemic cardiomyopathy (20 %), idiopathic dilated cardiomyopathy (15 %), rheumatic valvular heart disease (7 %)
Abebe et al. 2016[3]	Ethiopia	850 patients admitted with acute heart failure	Main causes for heart failure: ischaemic heart disease (15.8 %), hypertensive heart disease (16.0 %), valvular heart disease (40.1 %), dilated cardiomyopathy (12.5 %), cor pulmonale (4.5 %), others (10.3 %)
Makubi et al. 2016[19]	Tanzania	411 patients >18 years of age from inpatient and outpatient setting	Medical history of: hypertension (47 %), dilated cardiomyopathy (23 %), ischaemic heart disease (10 %), diabetes (12 %), valve disease (1 %)

CVD = cardiovascular disease. Adapted from Glezeva, et al., 2015.[8]

six heart failure score methodologies based on symptoms and signs have been developed to help diagnose and assess the prevalence of heart failure in the non-hospitalised patient.[25] These generally include clinical history and examination, and chest X-ray at a minimum. A number of these criteria[26–28] were established before non-invasive techniques for assessing systolic and diastolic dysfunction became widely available. However, although the scores are useful in detecting manifest heart failure, objective measurements of cardiac function, such as echocardiography, appear necessary to reduce the false positive rate and accurately detect early stages of heart failure[25] and are now an essential part of European and North American guidelines on the diagnosis of heart failure.[29,30,3] However, echocardiography is

not widely available in Africa, where a reported survey in Kenya and Uganda showed functional and staffed radiography, ultrasound and ECG were available in less than half of hospitals in Kenya and Uganda combined; this did not specifically address echocardiography.[31] It has also been demonstrated that training nurses and mid-level providers in simplified echocardiographic protocols can be an effective strategy to improve heart failure diagnosis and management in SSA, but equipment remains relatively expensive for such resource-poor settings and training can be an issue.[32]

In the absence of sufficient resources, an effective approach to perform large-scale risk-profiling of patients would be the implementation of a point-of-care diagnostic test throughout SSA that could be used nationwide when echocardiography facilities are not available or readily accessible. Biomarker diagnostic tests are easy to perform as they do not require specific medical expertise and can be performed in any location as point-of-care tests, and are therefore practical in rural community settings that have limited access to hospitals or medical centres.

The use of natriuretic peptides (NPs) as a tool to rule out heart failure has been implemented in high-income countries[33] with success and these tests are also now available as point-of-care tests, which may prove a useful strategy in Africa. NPs are protein biomarkers with established clinical significance for diagnosis and prognosis of cardiovascular disease and heart failure.[34] Among them B-type natriuretic peptide (BNP) and N-terminal prohormone BNP (NT-proBNP) have consistently been shown to have the best diagnostic, prognostic and therapeutic clinical benefits in relation to both acute and chronic heart failure.[34–36] NPs have also been shown to be superior to echocardiography parameters in risk stratification in hypertension.[37] The strength of using inexpensive BNP and NT-proBNP tests for risk stratification of patients with high-risk factors for heart failure was also demonstrated by several clinical studies, including the recently published St Vincent's Screening to Prevent Heart Failure Study (STOP-HF)[38] and the NT-proBNP Selected Prevention of Cardiac Events in a Population of Diabetic Patients Without a History of Cardiac Disease (PONTIAC) study.[39] These studies used BNP and NT-proBNP, respectively, to identify a high-risk cohort in a group of individuals with cardiovascular disease or risk factors. By targeting care to these individuals (mostly through enhanced use of renin–angiotensin–aldosterone system modifying therapies and beta-blockers, which are also the keystone therapies in the management of heart failure with reduced ejection fraction, these studies were able to achieve a significant reduction in new onset heart failure and other major adverse cardiovascular events.

In low- and middle-income countries where access to expensive and technical cardiac imaging is likely to remain limited and confined to large population centres there is a potential for NPs to aid in the diagnosis and management of heart failure, particularly in combination with point-of-care echocardiography.

Management of Stable Heart Failure

Following diagnosis, it is important that access to appropriate medical therapies is available for patients with heart failure. The World Health Organization has targeted that medicines to prevent recurrent cardiovascular disease be available in 80 % of communities and used by 50 % of eligible individuals by 2025. However, a recent analysis of the Prospective Urban Rural Epidemiology Study (PURE) data sought to determine the availability of four key cardiovascular medications: aspirin, statin, angiotensin-converting enzyme (ACE) inhibitor and beta-blockers.[40] It found that all four medications were available in 62 % of urban and 37 % of rural communities in lower middle-income countries, and in 25 % of urban and one of 30 (3 %) rural communities in low-income countries. The four cardiovascular disease medicines were potentially unaffordable for 0.14 % of households in high-income countries (14 of 9,934 households) but unaffordable for 60 % of low-income countries studied.[40]

A survey of Kenya and Uganda showed that ACE inhibitors were only available in 51 % of Kenyan and 79 % of Ugandan hospitals. Almost one-third of the hospitals in each country had a stock-out of at least one of the medication classes in the prior quarter.[31] A study looking at medication availability in Uganda showed that ACE inhibitors were available in 22.2 % of health facilities overall, varying from 75 % of hospitals to significantly less in health centres (0–75 % depending on area) and private clinics (36.5 %) (p<0.001).[41]

Prognostic Variables

A recent analysis of the Symptoms and Signs of Heart Failure at Admission and Discharge and Outcomes in the Sub-Saharan Acute Heart Failure (THESUS-HF) data demonstrated that in acute heart failure patients in SSA, symptoms and signs of heart failure improve throughout admission, and simple assessments, including oedema, rales, oxygen saturation, respiratory rate, and asking the patient about general well-being, are valuable tools in patients' clinical assessments.[42] Interestingly echocardiographic parameters had limited prognostic benefit. Heart rate and left atrial size predicted death within 60 days or readmission. Heart rate, left ventricular posterior wall thickness in diastole, and presence of aortic stenosis were associated with the risk of death within 180 days. Echocardiographic variables, especially those of left ventricular size and function, were not found to have additional predictive value in patients admitted for acute heart failure.[43]

Conclusion

Heart failure in SSA is an increasing issue. There is a need to explore new diagnostic strategies that are implementable in low-income countries with a predominantly rural population. There is also a need to explore management strategies and, in particular, medication supply. Further research is also required in conditions particular to the African region, such as rheumatic heart disease and endomyocardial fibrosis, to ensure these conditions can be effectively managed. ∎

1. Damasceno A, Cotter G, Dzudie A, et al. Heart failure in sub-Saharan Africa: time for action. *J Am Coll Cardiol* 2007;**50**:1688–93. DOI: 10.1016/j.jacc.2007.07.030; PMID: 17950152.
2. Tefera YG, Abegaz TM, Abebe TB, Mekuria AB. The changing trend of cardiovascular disease and its clinical characteristics in Ethiopia: hospital-based observational study. *Vasc Health Risk Manag* 2017;**13**:143–51. DOI: 10.2147/VHRM.S131259; PMID: 28461753.
3. Abebe TB, Gebreyohannes EA, Tefera YG, Abegaz TM. Patients with HFpEF and HFrEF have different clinical characteristics but similar prognosis: a retrospective cohort study. *BMC Cardiovasc Disord* 2016;**16**:232. DOI: 10.1186/s12872-016-0418-9;

PMID: 27871223.
4. Mayosi BM. Contemporary trends in the epidemiology and management of cardiomyopathy and pericarditis in sub-Saharan Africa. *Heart* 2007;**93**:1176–83. DOI: 10.1136/hrt.2007.127746; PMID: 17890693.
5. Dokainish H, Teo K, Zhu J, et al. Heart failure in Africa, Asia, the Middle East and South America: the INTER-CHF study. *Int J Cardiol* 2016;**204**:133–41. DOI: 10.1016/j.ijcard.2015.11.183; PMID: 26657608.
6. Damasceno A, Mayosi BM, Sani M, et al. The causes, treatment, and outcome of acute heart failure in 1006 Africans from 9 countries. *Arch Intern Med* 2012;**172**:1386–94. DOI: 10.1001/archinternmed.2012.3310; PMID: 22945249.

7. Bloomfield GS, DeLong AK, Akwanalo CO, et al. Markers of atherosclerosis, clinical characteristics, and treatment patterns in heart failure: a case-control study of middle-aged adult heart failure patients in rural Kenya. *Glob Heart* 2016;**11**:97–107. DOI: 10.1016/j.gheart.2015.12.014; PMID: 27102027.
8. Glezeva N, Gallagher J, Ledwidge M, et al. Heart failure in sub-Saharan Africa: review of the aetiology of heart failure and the role of point-of-care biomarker diagnostics. *Trop Med Int Health* 2015;**20**:581–8. DOI: 10.1111/tmi.12461; PMID: 25598183.
9. Kingue S, Dzudie A, Menanga A, et al. [A new look at adult chronic heart failure in Africa in the age of the Doppler echocardiography: experience of the medicine

department at Yaounde General Hospital]. *Ann Cardiol Angeiol (Paris)* 2005;**54**:276–83 [in French]. DOI: 10.1016/j.ancard.2005.04.014; PMID: 16237918.

10. Amoah AG, Kallen C. Aetiology of heart failure as seen from a National Cardiac Referral Centre in Africa. *Cardiology* 2000;**93**:11–8. DOI: 10.1159/000006996; PMID: 10894901.

11. Oyoo GO, Ogola EN. Clinical and socio demographic aspects of congestive heart failure patients at Kenyatta National Hospital, Nairobi. *East Afr Med J* 1999;**76**:23–7. PMID: 10442143

12. Soliman EZ, Juma H. Cardiac disease patterns in northern Malawi: epidemiologic transition perspective. *J Epidemiol* 2008;**18**:204–8. DOI: 10.2188/jea.JE2008006; PMID: 18753734.

13. Kennedy N, Miller P. The spectrum of paediatric cardiac disease presenting to an outpatient clinic in Malawi. *BMC Res Notes* 2013;**6**:53. DOI: 10.1186/1756-0500-6-53; PMID: 23388520.

14. Karaye KM, Sani MU. The impact of income on the echocardiographic pattern of heart diseases in Kano, Nigeria. *Niger J Med* 2008;**17**:350–5. PMID: 18788267.

15. Familoni OB, Olunuga TO, Olufemi BW. A clinical study of pattern and factors affecting outcome in Nigerian patients with advanced heart failure. *Cardiovasc J Afr* 2007;**18**:308–11. PMID: 17957325.

16. Thiam M. [Cardiac insufficiency in the African cardiology milieu]. *Bull Soc Pathol Exot* 2003;**96**:217–8 [in French]. PMID: 14582299.

17. Ismail Y, Andia I, Byaruhanga S, et al. Echocardiographic features of cardiac failure in Uganda. *Trop Doct* 2007;**37**:267–8. DOI: 10.1258/004947507782332900; PMID: 17988510.

18. Sliwa K, Wilkinson D, Hansen C, et al. Spectrum of heart disease and risk factors in a black urban population in South Africa (the Heart of Soweto Study): a cohort study. *Lancet* 2008;**371**:915–22. DOI: 10.1016/S0140-6736(08)60417-1; PMID: 18342686.

19. Makubi A, Hage C, Sartipy U, et al. Heart failure in Tanzania and Sweden: comparative characterization and prognosis in the Tanzania Heart Failure (TaHeF) study and the Swedish Heart Failure Registry (SwedeHF). *Int J Cardiol* 2016;**220**:750–8. DOI: 10.1016/j.ijcard.2016.06.239; PMID: 27393861.

20. Rothenbühler M, O'Sullivan CJ, Stortecky S, et al. Active surveillance for rheumatic heart disease in endemic regions: a systematic review and meta-analysis of prevalence among children and adolescents. *Lancet Glob Health* 2014;**2**:e717–26. DOI: 10.1016/S2214-109X(14)70310-9; PMID: 25433627.

21. Zühlke L, Engel ME, Karthikeyan G, et al. Characteristics, complications, and gaps in evidence-based interventions in rheumatic heart disease: the Global Rheumatic Heart Disease Registry (the REMEDY study). *Eur Heart J* 2015;**36**:1115-22a. DOI: 10.1093/eurheartj/ehu449; PMID: 25425448.

22. Mocumbi AO, Ferreira MB, Sidi D, Yacoub MH. A population study of endomyocardial fibrosis in a rural area of Mozambique. *N Engl J Med* 2008;**359**:43–9. DOI: 10.1056/NEJMoa0708629; PMID: 18596273.

23. Pugliese A, Isnardi D, Saini A, et al. Impact of highly active antiretroviral therapy in HIV-positive patients with cardiac involvement. *J Infect* 2000;**40**:282–4. DOI: 10.1053/jinf.2000.0672 PMID: 10908024.

24. Cerrato E, D'Ascenzo F, Biondi-Zoccai G, et al. Cardiac dysfunction in pauci symptomatic human immunodeficiency virus patients: a meta-analysis in the highly active antiretroviral therapy era. *Eur Heart J* 2013;**34**:1432–6. DOI: 10.1093/eurheartj/ehs471; PMID: 23335603.

25. Mosterd A, Deckers JW, Hoes AW, et al. Classification of heart failure in population based research: an assessment of six heart failure scores. *Eur J Epidemiol* 1997;**13**:491–502. DOI: 10.1023/A:1007383914444; PMID: 9258559.

26. Carlson KJ, Lee DC, Goroll AH, et al. An analysis of physicians' reasons for prescribing long-term digitalis therapy in outpatients. *J Chronic Dis* 1985;**38**:733–9. DOI: 10.1016/0021-9681(85)90115-8; PMID: 4030999.

27. Harlan WR, Oberman A, Grimm R, Rosati RA. Chronic congestive heart failure in coronary artery disease: clinical criteria. *Ann Intern Med* 1977;**86**:133–8. DOI: 10.7326/0003-4819-86-2-133; PMID: 835934.

28. McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. *N Engl J Med* 1971;**285**:1441–6. DOI: 10.1056/NEJM197112232852601; PMID: 5122894.

29. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2016;**18**:891–975. DOI: 10.1002/ejhf.592; PMID: 27207191.

30. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J AM Coll Cardiol* 2013;**62**:e147–239. DOI: 10.1016/j.jacc.2013.05.019; PMID: 23747642.

31. Carlson S, Duber HC, Achan J, et al. Capacity for diagnosis and treatment of heart failure in sub-Saharan Africa. *Heart* 2017;**103**:1874–9. DOI: 10.1136/heartjnl-2016-310913; PMID: 28490619.

32. Kwan GF, Bukhman AK, Miller AC, et al. A simplified echocardiographic strategy for heart failure diagnosis and management within an integrated noncommunicable disease clinic at district hospital level for sub-Saharan Africa. *JACC Heart Fail* 2013;**1**:230–6. DOI: 10.1016/j.jchf.2013.03.006; PMID: 24621875.

33. Mant J, Doust J, Roalfe A, et al. Systematic review and individual patient data meta-analysis of diagnosis of heart failure, with modelling of implications of different diagnostic strategies in primary care. *Health Technol Assess* 2009;**13**:1–207. DOI: 10.3310/hta13320; PMID: 19586584.

34. Maisel A, Mueller C, Adams K, Jr., et al. State of the art: using natriuretic peptide levels in clinical practice. *Eur J Heart Fail* 2008;**10**:824–39. DOI: 10.1016/j.ejheart.2008.07.014; PMID: 18760965.

35. de Lemos JA, McGuire DK, Drazner MH. B-type natriuretic peptide in cardiovascular disease. *Lancet* 2003;**362**:316–22. DOI: 10.1016/S0140-6736(03)13976-1; PMID: 12892964.

36. Clerico A, Fontana M, Zyw L, et al. Comparison of the diagnostic accuracy of brain natriuretic peptide (BNP) and the N-terminal part of the propeptide of BNP immunoassays in chronic and acute heart failure: a systematic review. *Clin Chem* 2007;**53**:813–22. DOI: 10.1373/clinchem.2006.075713; PMID: 17384013.

37. Gallagher J, Watson C, Zhou S, et al. B-type natriuretic peptide and ventricular dysfunction in the prediction of cardiovascular events and death in hypertension. *Am J Hypertens* 2018;**31**:228–34. DOI: 10.1093/ajh/hpx153; PMID: 29036547.

38. Ledwidge M, Gallagher J, Conlon C, et al. Natriuretic peptide-based screening and collaborative care for heart failure: the STOP-HF randomized trial. *JAMA* 2013;**310**:66–74. DOI: 10.1001/jama.2013.7588; PMID: 23821090.

39. Huelsmann M, Neuhold S, Resl M, et al. PONTIAC (NT-proBNP selected prevention of cardiac events in a population of diabetic patients without a history of cardiac disease): a prospective randomized controlled trial. *J Am Coll Cardiol* 2013;**62**:1365–72. DOI: 10.1016/j.jacc.2013.05.069; PMID: 23810874.

40. Khatib R, McKee M, Shannon H, et al. Availability and affordability of cardiovascular disease medicines and their effect on use in high-income, middle-income, and low-income countries: an analysis of the PURE study data. *Lancet* 2016;**387**:61–9. DOI: 10.1016/S0140-6736(15)00469-9; PMID: 26498706.

41. Musinguzi G, Bastiaens H, Wanyenze RK, et al. Capacity of health facilities to manage hypertension in Mukono and Buikwe districts in Uganda: challenges and recommendations. *PloS One* 2015;**10**:e0142312. DOI: 10.1371/journal.pone.0142312; PMID: 26560131.

42. Sani MU, Cotter G, Davison BA, et al. Symptoms and signs of heart failure at admission and discharge and outcomes in the sub-Saharan acute heart failure (THESUS-HF) registry. *J Card Fail* 2017;**23**:739–42. DOI: 10.1016/j.cardfail.2016.09.016; PMID: 27664511

43. Sani MU, Davison BA, Cotter G, et al. Echocardiographic predictors of outcome in acute heart failure patients in sub-Saharan Africa: insights from THESUS-HF. *Cardiovasc J Afr* 2017;**28**:60–7. DOI: 10.5830/CVJA-2016-070; PMID: 28262911.