

Conference Proceedings

Improving cardiovascular outcomes for patients with heart failure in sub-Saharan Africa: conference proceedings of the 2022 Nigerian Cardiovascular Symposium

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Abstract

The Nigerian Cardiovascular Symposium is an annual conference held in partnership with cardiologists in Nigeria and the diaspora to provide updates in cardiovascular medicine and cardiothoracic surgery with the aim of optimising cardiovascular care for the Nigerian population. This virtual conference (due to the COVID-19 pandemic) has created an opportunity for effective capacity building of the Nigerian cardiology workforce. The objective of the conference was for experts to provide updates on current trends, clinical trials and innovations in heart failure, selected cardiomyopathies such as hypertrophic cardiomyopathy and cardiac amyloidosis, pulmonary hypertension, cardiogenic shock, left ventricular assist devices and heart transplantation. Furthermore, the conference aimed to equip the Nigerian cardiovascular workforce with skills and knowledge to optimise the delivery of effective cardiovascular care, with the hope of curbing 'medical tourism' and the current 'brain drain' in Nigeria. Challenges to optimal cardiovascular care in Nigeria include

workforce shortage, limited capacity of intensive care units, and availability of medications. This partnership represents a key first step in addressing these challenges. Future action items include enhanced collaboration between cardiologists in Nigeria and the diaspora, advancing participation and enrollment of African patients in global heart failure clinical trials, and the urgent need to develop heart failure clinical practice guidelines for Nigerian patients.

Keywords: cardiomyopathy, heart failure, pulmonary hypertension, advanced heart failure, cardiac amyloidosis, hypertrophic cardiomyopathy, cardiogenic shock, left ventricular assist device, heart transplantation, Nigeria, sub-Saharan Africa

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Heart failure (HF) is the final common pathway for many cardiovascular disorders and remains a significant global problem. In Nigeria and the rest of sub-Saharan Africa (SSA), HF care and research is plagued by limited population or registry-based data, limited training of the cardiovascular (CV) workforce, and the 'brain drain'. This is further compounded by inadequate availability of medications, and CV diagnostic and therapeutic resources. Additionally, the population afflicted by HF in SSA tends to be younger than in other parts of the world. A report from the SSA survey of HF revealed that acute HF in SSA affects younger patients (mean age 52.3 years), mainly due to preventable/treatable aetiologies such as hypertension (43.9%), rheumatic heart disease (RHD) (15%) and dilated cardiomyopathy (19.5%).^{1,2}

Despite advancements in medical, device-based and surgical management of HF, disparities in treatment patterns and outcomes persist, even in Western countries,³ and these advances may not be readily accessible to patients with HF in SSA. Moreover, clinical practice guidelines are routinely developed in the United States and Western Europe, based on clinical trials that may not be reflective of the reality of the African patient with HF.⁴ In order to develop relevant SSA HF clinical practice guidelines, the continental variation in aetiopathogenesis of HF, access to CV diagnostics, and timely initiation of evidence-based HF therapeutics must be considered. Other considerations include the younger HF population in Africa, and lack of funds and credible health insurance policies, which may lead to poor adherence to medications.

To bridge these treatment disparities, the Cardiovascular Education Foundation (a US-based non-profit organisation) has organised the Nigerian Cardiovascular Symposium in collaboration with the Nigerian Cardiac Society. This symposium is a series of hybrid didactic (virtual) lectures over four weekends and practicum sessions where the diaspora-based faculty spend one to two weeks in Nigeria training and performing diagnostic and interventional procedures (percutaneous interventions and electrophysiology procedures) with Nigerian colleagues. The aim of the symposium is to educate the CV workforce, facilitate capacity building and teach advanced CV diagnostic and interventional skills to the cardiovascular workforce in Nigeria.

The purpose of this article is to highlight a summary of the pivotal points presented at the HF and cardiomyopathies session of the annual Nigerian Cardiovascular Symposium, which took place virtually on 11 September 2022. The session covered a wide range of topics: diagnosis and management of HF with reduced ejection fraction (HFrEF) and HF with preserved ejection (HFpEF), cardiomyopathies and pulmonary hypertension (PH). The symposium concluded with the care of the critically ill cardiac patient with advanced HF or cardiogenic shock (CS) who may benefit from left ventricular assist devices (LVAD) and/or heart transplantation (HT).

The American College of Cardiology (ACC)/ American Heart Association (AHA) 2022 HF guidelines: applicability to the Nigerian patient with HF

The presentation started by highlighting the significant HF burden in SSA due to a younger population being affected. HF hospitalisation is a marker for poor outcomes where rates

of rehospitalisation remain high, about 30% within 60 to 90 days of discharge.⁵ The definition of HF, which emphasises the symptoms/signs of HF caused by a structural and/or functional cardiac abnormality corroborated by elevated natriuretic peptide levels or evidence of cardiogenic pulmonary or systemic congestion was highlighted.⁶ The stages in the development/progression of HF from stage A (at risk for HF), stage B (pre-HF), stage C (symptomatic HF) to stage D (advanced HF) were emphasised.⁴ In addition, left ventricular (LV) ejection fraction (EF) categories were reviewed: HF with mildly reduced EF (HFmrEF) (LVEF 41–49%) and HF with improved EF (HFimpEF), a baseline LVEF of $\leq 40\%$, a ≥ 10 -point increase from baseline LVEF, and a second measurement of LVEF $> 40\%$.⁶

The top 10 take-home messages are: (1) guideline-directed medical therapy (GDMT) for HFrEF includes four medication classes that include sodium-glucose co-transporter-2 inhibitors (SGLT2i), angiotensin receptor neprilysin inhibitor (ARNI), angiotensin converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB), beta-blocker (BB) and mineralocorticoid receptor antagonist (MRA), (2) SGLT2i are highly recommended in HFmrEF over other GDMT, (3) recommendations for SGLT2i, MRA and ARNI in HFpEF (2b recommendation), (4) improved LVEF refers to HFrEF where LVEF is now $> 40\%$; these patients should continue HFrEF treatment, (5) value statements for recommendations for interventions/therapies with published high-quality, cost-effectiveness studies, (6) recommendations for amyloid heart disease treatment, (7) evidence supporting the importance of increased filling pressures for diagnosis of HF if LVEF $> 40\%$, (8) recommendation for palliative care or advanced HF therapies for patients with advanced HF who wish to prolong survival, (9) primary prevention of HF was emphasised by restaging HF as those at risk for HF (stage A) or pre-HF (stage B), (10) recommendations are provided for patients with HF and iron deficiency anaemia, hypertension, sleep disorders, type 2 diabetes mellitus, atrial fibrillation (AF), coronary artery disease (CAD) and malignancy.

African patients are almost non-existent in HF clinical trials, which may limit generalisability in Nigerian patients. Furthermore, cost and access may be a barrier to adequate evidence-based guideline-directed quadruple HF therapy. Ajuluchukwu *et al.* reported that BB and MRA were under-prescribed and that physician adherence to GDMT was influenced by the patient's age.⁷

HF with preserved EF: much commoner than we think

The conference emphasised that, despite having a younger population, HFpEF is common in Africa, as was seen in the INTER-CHF trial where 28.8% of patients had EF $> 50\%$.⁸ HFpEF accounts for HF in 50% of the US population and is primarily a disease of aging. It is estimated that $> 70\%$ of patients with HF over 65 years have HFpEF.⁹ The five-year mortality of HFpEF is approximately 75%, similar to that of HFrEF.¹⁰

Diagnosis of HFpEF entails having a high pretest probability corroborated by physical examination. Cardiac tests such as natriuretic peptides (may be low due to smaller LV size, increased clearance by adipocytes), electrocardiogram, echocardiogram and

coronary angiogram are confirmatory. The role of provocative testing using exercise or saline loading during right heart catheterisation (RHC) or invasive cardiopulmonary stress test can help confirm the diagnosis in cases of diagnostic equipoise. The importance of excluding differential diagnosis such as infiltrative cardiomyopathies, hypertrophic cardiomyopathy (HCM), hypertensive cardiomyopathy, valvular heart disease, constrictive pericarditis and myocarditis was emphasised.¹⁰ A common but underappreciated presentation of HFpEF is patients with unexplained dyspnoea, and two clinically useful diagnostic scoring systems, the H2FPEF score and the HFA-PEFF may aid in the diagnosis of HFpEF.^{11,12}

Treatment of HFpEF involves symptom management, defining the HFpEF phenotype, and treatment of associated co-morbidities. Lifestyle modification (exercise training, and weight loss for obese patients) is also important. For medical therapy, the efficacy of standard HFrEF GDMT is limited due to pathophysiological heterogeneity of HFpEF. BB may be tried for patients with concomitant AF and CAD; however, caution must be exercised with use as many of these patients have concomitant chronotropic incompetence. Decongestive therapies with loop diuretics are key but HFpEF patients are more prone to azotaemia. Other agents indicated for HFpEF include spironolactone (in selected patients) based on the TOPCAT trial and ARNI based on the PARAGON-HF trial.^{13,14} Empagliflozin is approved for HFpEF based on the strength of the EMPEROR-Preserved trial.¹⁵ Data from the DELIVER trial using dapagliflozin has shown similar benefits and will likely soon be approved for use in HFpEF.¹⁶

Cardiomyopathies: focus on HCM and cardiac amyloidosis

A presentation on all cardiomyopathies was beyond the scope of the symposium and the presentation started with an overview of the cardiomyopathies such as genetic, mixed aetiology or acquired cardiomyopathies. Nigeria has the highest incidence of peripartum cardiomyopathy in the world, which is characterised by late presentation, high mortality rates and low rates of myocardial recovery.¹⁷ However, due to recent advances in management options, the focus was on HCM and restrictive cardiomyopathy [cardiac amyloidosis (CA)].

Hypertrophic cardiomyopathy

HCM is the most common hereditary heart disease in the USA and affects persons regardless of age, gender or ethnicity.^{18,19} HCM is largely caused by dysfunction in the sarcomere, which may be due to genetic mutations but many patients with HCM lack pathogenic mutations. It is characterised by left ventricular hypertrophy (LVH), hypercontractility, impaired relaxation, increased energy consumption and reduced compliance.

The pathophysiology of symptoms for HCM can be characterised by the presence or absence of dynamic narrowing of the LV outflow tract (LVOT), by the systolic anterior motion of the mitral valve, or in cases of severe LVH, by dynamic mid-cavity obliteration in systole. A LVOT gradient > 30 mmHg is diagnostic of obstruction. The natural history of HCM is characterised by clinical stability with normal longevity in most patients, but some patients have disease progression manifesting

as symptoms of AF/stroke, sudden death, progressive HF, or 'burnt out' end-stage advanced HF.

Treatment includes avoidance of dehydration and extreme physical activity, but moderate-level exercise as part of a healthy lifestyle is permissible. Traditional medical therapy includes BB or non-dihydropyridine calcium channel blockers such as verapamil or diltiazem and anticholinergic agents such as disopyramide. Mavacamten represents a new therapeutic option for obstructive HCM patients. In the phase 3 EXPLORER-HCM trial, treatment with mavacamten improved exercise capacity (peak VO_2 +1.4 ml/kg/min, 0.6–2.1; $p = 0.0006$), LVOT obstruction, New York Heart Association (NYHA) functional class, and health status in patients with obstructive HCM.²⁰ The VALOR-HCM showed that in patients with obstructive HCM with severe symptoms, mavacamten significantly reduced the fraction of patients meeting guideline criteria for septal reduction therapy after 16 weeks.²¹

In the context of Nigerian patients, although genetic testing may play a role in family screening and identification of HCM phenocopies,²² we do not recommend this routinely. This is because identified mutations may have unclear significance and do not predict future risk of adverse clinical events, prognosis or sudden death. It is also expensive and can lead to genetic discrimination. Although mavacamten has beneficial effects, its cost to patients in SSA with limited health insurance coverage may make it logistically difficult to become the standard of care for HCM patients in SSA.

Cardiac amyloidosis

The presentation started by highlighting the high prevalence of CA, especially the isoleucine 122 (V122I) variant of transthyretin amyloidosis (ATTR) in patients of African ancestry.^{23–25} Variant transthyretin V122I has an autosomal dominant pattern of inheritance and is carried by 3.43% of blacks in the USA.²⁵ It is associated with isolated cardiac involvement in patients over the age of 60 years, with male predominance (men:women in a ratio of 6:1).²³ The gene frequency and implications of transthyretin ATTR V122I in West African populations such as Nigeria is unknown and needs to be better understood.²⁶ This is an important unknown because the geographic emergence of the ATTR V122I is likely an initial mutation from West Africa. The Atlantic slave trade led to population dislocations that transported subjects to the Americas, Caribbean and parts of Western Europe. Cardiac ATTR V122I amyloidosis is a common but under-appreciated cause of HF in elderly (7th decade) patients of African origin, with persistent fluid overload despite diuretic use. Survival in ATTR V122I is poor.²⁶

CA is a common cause of HFpEF and a high index of suspicion is required to confirm this diagnosis.²⁷ The two major sub-types of CA are immunoglobulin light-chain, amyloid light-chain (AL) amyloidosis or transthyretin (TTR) amyloidosis (senile CA). Cardiac involvement manifests as HF (most common), AF, conduction disease, orthostatic hypotension and ventricular arrhythmias.²⁸

Amyloid cardiomyopathy is a disease of diastole, and rapid rise of filling pressures leads to low end-diastolic volume and consequently reduction in stroke volume and reduced cardiac output. Compensatory tachycardia is often necessary to maintain cardiac output. Low systolic pressures (< 100 mmHg) are

common due to low stroke volume and peripheral tone. Peripheral neuropathy and carpal tunnel syndrome are uncommon in other forms of HFpEF but are seen in many patients with CA. A history of carpal tunnel syndrome is seen in almost half of the patients and this should be considered a red flag for ATTR V122I CA among older patients of African ancestry with HF.²⁹

From a diagnostic perspective, an electrocardiogram may show low voltage in the limb leads or pseudo-infarction pattern. However, 44.3% of patients with ATTR V122I CA have normal or increased voltage and an abnormal electrocardiogram may not be reliable for the diagnosis of ATTR V122I CA cases.³⁰ Echocardiography typically reveals thickened walls, which may be interpreted as demonstrating hypertrophy, either related to hypertension or HCM, both common conditions in African patients.

The three most important studies for a patient with suspected CA (with HFpEF and any degree of wall thickening on echocardiogram) are (1) serum-free light-chain assay (kappa and lambda light chains to assess monoclonality as determined by an abnormal ratio), (2) serum and immuno-fixation to assess for the presence of a monoclonal protein, and (3) technetium pyrophosphate scan for myocardial uptake of ATTR. Abnormal monoclonal protein and consistent echocardiographic features are highly suspicious for AL amyloidosis. An abnormal free light-chain kappa/lambda ratio is found in > 90% of patients with untreated AL amyloidosis. All patients with suspected AL amyloidosis should have a bone marrow biopsy to determine the percentage of plasma cells and rule out co-existing multiple myeloma. Biomarker values of NT-proBNP, troponin T, and free light chains have prognostic value in AL amyloidosis.

The presence of a positive pyrophosphate scan is highly sensitive for the diagnosis of ATTR CA.³¹ In the absence of a monoclonal protein, a scan that is graded 2 or 3 in uptake is considered diagnostic of ATTR CA without biopsy.³² However, the presence of a monoclonal protein and a positive technetium pyrophosphate scan makes a tissue biopsy necessary to establish a diagnosis. Many patients with ATTR CA have a detectable abnormality of immunoglobulins. All patients with suspected ATTR CA based on a pyrophosphate scan should have genetic testing and counselling offered for abnormal results. Diagnosis of CA requires a high degree of clinical suspicion due to its ability to mimic other cardiac diseases such as hypertensive heart disease and that there is no single confirmatory diagnostic test.

Therapy for AL amyloidosis includes steroids (dexamethasone), proteasome inhibitors (bortezomib) and/or chemotherapy (cyclophosphamide).³⁴ Tafamidis is an oral stabiliser administered once daily that was tested in wild-type and mutant ATTR CA in the ATTR-ACT trial. This trial demonstrated lower all-cause mortality and cardiovascular-related hospitalisations with tafamidis compared to placebo, leading to its approval. It has a very favourable toxicity profile.

Gene-silencing medications are either small interfering RNAs or antisense oligonucleotides: patisiran and inotersen. They demonstrated improvement in neurological impairment and quality of life when compared with a 15- to 18-month placebo arm in phase 3 trials in mutant TTR peripheral neuropathy,^{35,36} and are currently being tested in amyloid cardiomyopathy.

Supportive management of ATTR CA includes reduction of preload with loop diuretics; either high-dose furosemide > 80 mg daily or torsemide due to superior absorption ±

metolazone (can cause hypokalaemia or hypotension). Patients with advanced ATTR CA require higher intravascular fluid volumes and have higher filling pressures and may tolerate diuretics poorly. Tachycardia is compensatory and required to maintain cardiac output. Beta-blockade to reduce the heart rate may result in worsening of symptoms. For patients with supraventricular tachyarrhythmias, digoxin is preferred to metoprolol or carvedilol.

Atrial arrhythmias occur commonly in ATTR CA, and cardioversion may be attempted although its efficacy is limited in this patient population. Pacemaker implantation can be beneficial in patients with significant bradycardia, but the value of implantable cardiac defibrillators remains controversial as many patients die with electrical mechanical dissociation, and the efficacy of the defibrillator impulse capture in an amyloid-involved ventricle is uncertain. Orthostatic hypotension is common in patients with amyloidosis and may be due to progression of the disease with moderate/severe cardiac involvement, autonomic failure, or aggressive diuretic therapy.

Pulmonary hypertension

The conference acknowledged that causes of PH may be different in SSA than in other parts of the world. In SSA, PH may be more commonly due to untreated congenital heart diseases or HIV (WHO group I PH) or group II related to RHD, mitral valve disease or cardiomyopathies or other WHO groups such as PH secondary to schistosomiasis or sickle cell disease.³⁷ PH is classified into five WHO class groups based on aetiology. A distinction needs to be made between pulmonary arterial hypertension (PAH) defined by mean pulmonary artery pressure (mPAP) > 20 mmHg, pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg and pulmonary vascular resistance (PVR) > 2 wood units and pulmonary hypertension secondary to left heart disease.³⁸

PAH is a rare orphan disease and affects approximately two to 3% of patients with PH. However, PH secondary to left heart disease (WHO group II PH), defined as mPAP > 20 mmHg, PAWP > 15 mmHg and PVR < 2 wood units but with PVR > 3 wood units for combined pre- and post-capillary PH, is commoner.^{38,39} The pathophysiology of PAH involves pulmonary vascular proliferation mediated by the endothelin, nitric oxide and prostacyclin pathway but that of WHO group II PH is due to passive venous congestion.

Echocardiogram and right heart catheterisation are important diagnostic tools for diagnosis. In SSA, Doppler-derived echocardiogram measurement of mPAP remains the main method for PH diagnosis although there are some data that Doppler-derived pressures correlate poorly with invasive PA pressures and may be unreliable for making a diagnosis of PH.⁴⁰ Echocardiogram features such as right ventricular (RV) or right atrial (RA) enlargement, septal straightening, loss of inferior vena cava, respiratory collapse, tricuspid regurgitation and signs of RV systolic dysfunction are shown.

Right heart catheterisation is required for confirmatory diagnosis for almost all patients with suspected PH. It measures PAWP or left ventricular end-diastolic pressure (LVEDP), confirms the diagnosis, establishes severity and prognosis, and can be used to monitor progress and test for vasodilatory response for patients with PAH. A vasodilator responder meets the three haemodynamic criteria on right heart catheterisation

(RHC): (1) fall in mean PA pressure of 10 mmHg, (2) to a value of < 40 mmHg, and (3) no change of increase in cardiac output. Inhaled nitric oxide, adenosine and epoprostenol are commonly used to evaluate for vasodilator response.

Treatment of PAH involves pulmonary vasodilators, which are not indicated and may cause harm in patients with WHO group II PH due to left heart disease. Calcium channel blockers are indicated for patients with a positive vasodilator response. Three classes of pulmonary vasodilators are indicated for PAH: (1) prostacyclins, (2) oral endothelin receptor antagonists, and (3) mediators of the nitric oxide system such as phosphodiesterase inhibitors and soluble guanylate cyclase inhibitors. The treatment for group II PH involves treating the underlying left heart disease.

A key take-away message from this section is the distinction between WHO groups of PH and the role of RHC in diagnosis, recognising the limited cardiac catheterisation capacity in most of SSA.

Advanced heart failure, cardiogenic shock and LVAD

The presentation started by defining advanced HF as a clinical syndrome characterised by persistent or progressive symptoms of HF and ventricular dysfunction despite GDMT. Data remain sparse but the INTER-CHF showed about 20.9% of African patients were NYHA class IV HF.⁸ Advanced HF can have a highly unpredictable clinical course and can challenge even the most experienced clinician to correctly identify the optimal timing of referral to an advanced cardiomyopathy/HF specialist.⁴¹ Patients with advanced HF are typically ACC/AHA stage D HF, NYHA class IV or INTERMACS profile 1–4 (critical cardiogenic shock and inotrope dependence).

A useful mnemonic is 'I NEED HELP' where I = inotropes, previous or current need for inotropes; N = NYHA III/IV/natriuretic peptides, persisting NYHA III–IV symptoms or increased NT-proBNP; E = end-organ dysfunction, deteriorating kidney and/or liver function; E = ejection fraction, severely depressed left ventricular function (EF < 20%); D = defibrillator shocks, repeated ICD shocks; H = hospitalisations, more than one admission for HF in the last 12 months; E = oedema/escalating diuretics, persisting congestion or increasing diuretic dose; L = low blood pressure, consistent low systolic blood pressure (< 90–100 mmHg); P = prognostic medication, cannot up-titrate, inability to titrate evidence-based medication (ACE inhibitor/ARB/BB/MRA or ARNI). Many patients with advanced HF may progress to acute decompensated HF cardiogenic shock (CS).⁴²

The 'shock pyramid' system describes stages of CS from A–E based on physical examination, biochemical markers and haemodynamics.⁴³ The stage A 'at risk' patient may have non-ST-segment myocardial infarction (STEMI), prior MI or decompensated HFrEF or HFpEF with normal laboratory results and physical examination. The stage B 'beginning CS' patient has clinical evidence of relative hypotension [systolic blood pressure (SBP) < 90 mmHg or mean arterial pressure (MAP) < 60 mmHg or > 30 mmHg drop from baseline) or tachycardia without hypoperfusion. Stage C is the 'classic' CS, a patient with hypoperfusion that requires initial interventions (inotropes, pressor, mechanical support) beyond volume resuscitation to restore perfusion. Laboratory findings may include impaired kidney function, elevated lactate, brain natriuretic peptide,

and/or liver enzymes. Invasive haemodynamics (if available) demonstrate the classic depressed cardiac index that is associated with CS. Stage D, 'deteriorating or doom' CS, describes a patient who has failed to stabilise despite initial efforts, further escalation is required and 30 minutes have elapsed, but the patient has not responded with resolution of hypotension or end-organ hypoperfusion. Stage E: 'extremis' CS is the patient with circulatory collapse, frequently (but not always) in refractory cardiac arrest with ongoing cardiopulmonary resuscitation or is being supported by multiple simultaneous acute interventions, including extracorporeal membrane oxygenation.

LVADs represent a therapeutic option for patients with Stage D HFrEF who may not be candidates for HT and provide improved survival rates, functional capacity and quality of life. General cardiologists and internists may encounter LVAD patients in routine practice. With the withdrawal of the Medtronic Heartware, the Abbott Heartmate 3 (HM3) is the only US Food and Drug Administration approved LVAD that is commercially available.

The basic LVAD design, regardless of manufacturer, consists of internal components such as the inflow cannula, implantable pump and outflow graft, and external components such as the driveline exiting the abdominal wall, the controller: a smartphone-sized 'computer' that gives the patients and clinician basic diagnostics and triggers alarms in certain dangerous scenarios, and an energy source connected to a controller that comes from batteries or an AC power source.

Warfarin and aspirin therapy are required by all patients because of the interaction of blood along the surface of the LVAD, and the subsequent development of thrombus. The recommended international normalised ratio (INR) goal is 2.0–3.0 and the recommended dose of aspirin is 325 mg for patients with an HMII or HeartWare device, and 81 mg for an HM3. Blood pressure measurement for LVAD patients is best achieved with a Doppler device by evaluating the pressure at which the Doppler sound returns during cuff deflation (which corresponds to the MAP). Most patients with LVAD have a narrow arterial pulse pressure and their pulses may be absent or intermittent on palpation.

In case of arrest for the LVAD patient, the first step is to listen over the chest to see if there is an LVAD hum, then an assessment of end-organ perfusion must be done. In patients without an LVAD hum, or with signs of impaired end-organ perfusion, LVAD connections should be assessed to ensure adequate connection between the driveline and controller and that flows are maintained. In patients with constant low-flow alarms as well as evidence of end-organ dysfunction, such as marked hypotension (MAP < 50 mmHg), or an end-tidal carbon dioxide tension (PetCO₂) value of < 20 mmHg, routine advanced CV life support and basic life support protocols should be followed as recommended by current guidelines.^{44,45}

Atrial and ventricular arrhythmias are common in LVAD patients, due to pre-existing cardiomyopathy, alterations in electrical conduction system post-LVAD, scar tissue with previous myocardial ischaemia, scar around the LVAD inflow cannula, suction events (because of LV underfilling or high pump speed), or changes in the QT interval secondary to LV unloading.⁴⁶ Treatment includes anti-arrhythmic agents (BB, especially propranolol), ventricular tachycardia ablation and stellate ganglion block in refractory cases.

Complications of LVADs include bleeding, pump thrombosis, stroke and right heart failure. Bleeding is a common adverse event in the early (< 90 days) postoperative period following LVAD implantation and is a frequent complication in the late period (≥ 90 days), with nearly one-third of patients experiencing a major bleeding episode by one year.⁴⁷ Late bleeding is most commonly due to gastrointestinal bleeding, which accounts for nearly 60% of all LVAD-associated bleeding. Antiplatelet and anticoagulation therapies, an acquired Von Willebrand syndrome and the development of angiodysplasias are believed to be contributory to gastrointestinal bleeding in LVAD patients. Cessation of antiplatelet and/or anticoagulation therapy as well as reversal with vitamin K, fresh frozen plasma, or prothrombin complex concentrate is useful. Procedurally based strategies during an acute bleed include cauterisation, arterial embolisation, and, in extreme cases, surgical intervention.

LVAD thrombotic events have decreased over the past few years due to innovations in LVAD pump design, especially with the HM3. The incidence of suspected or confirmed LVAD thrombosis at two years was significantly lower with the HM3 than the HMII device, occurring in seven (1.4%) versus 70 patients (13.9%) ($p < 0.001$).⁴⁸ Treatment for suspected LVAD thrombosis includes increased antithrombotic and antiplatelet therapies and early LVAD exchange, LVAD explantation (in case of significant myocardial recovery), or consideration of urgent HT.

External driveline exit-site abdominal wall infections represent the majority of LVAD infections. Excellent driveline hygiene is important for infection prevention. Infections with cellulitis and drainage may be managed with oral antibiotics but intravenous antibiotics and surgical debridement may also be used. In extreme cases, complete pump exchange or explant and even HT may be needed.

Haemorrhagic and ischaemic stroke remain a significant source of morbidity associated with LVADs because of their catastrophic effect on functional capacity and quality of life. In many cases it makes patients ineligible for HT. Ischaemic and haemorrhagic strokes occur after LVAD implantation, with an incidence ranging from five to 30%, varying by device type.⁴⁹⁻⁵² Risk factors for stroke vary by device type and include age, presence of infections, antiplatelet and anticoagulant therapies, and elevated blood pressure.^{48,53-55} Haemorrhagic strokes are thought to be related to hypertension with anticoagulation, high-velocity intracranial flow, and/or haemorrhagic conversion from prior thromboembolic stroke.

Right heart failure (RHF) is a source of morbidity and mortality in patients in the early (< 30 days) and late (> 30 days) period following LVAD placement.⁵⁶ Late RHF has been associated with higher risk of hospitalisation, gastrointestinal bleed, stroke, infection and worse quality of life.⁵⁶ Therapies for this condition are limited and include high doses of diuretics, continuous inotrope infusions and HT in eligible patients.^{56,57}

HT: updates and general care of the HT patient

HT remains the gold-standard treatment for end-stage (D) HF with more than 6 000 heart transplants performed annually worldwide, with one-year post-transplant survival > 90%.⁵⁸ Although the first HT in the world was performed by Dr Christian Bernard in South Africa in 1967 and the patient

died of rejection a few days later, HT is rarely performed in SSA, with the majority being done in North America and Western Europe.^{58,59} The average life expectancy is 13 years but many patients live over 20 years, and some patients live for more than 30 years. Limited intensive care capacity, lack of surgical expertise, and lax or non-existent organ donation laws are postulated reasons why HT is unlikely to be performed in Nigeria or SSA. However, emphasising heart disease prevention with evidence-based medications and lifestyle changes may be a more cost-effective measure.

Short-term complications include allograft rejection and infections. Immunosuppressants (calcineurin inhibitors, antimetabolites and steroids) are commonly used to suppress the immune system to prevent cardiac allograft rejection. HT recipients are also prone to infection because of immunosuppressants. Cardiac allograft rejection can be acute cellular rejection (and the risk of occurrence is highest in the first year post transplant) or antibody-mediated rejection. It is treated with high-dose steroids, plasmapheresis, intravenous immunoglobulin ± rituximab. Surveillance of allograft rejection has traditionally involved endomyocardial biopsies although the role of non-invasive graft surveillance using donor-derived cell-free DNA is now emerging.⁶⁰ Infections usually occur within the first six months post transplant and can be common community-acquired infections.

Long-term complications of HT include cardiac allograft vasculopathy, hypertension, renal dysfunction, diabetes mellitus, malignancies, infections, and medication side effects. Cardiac allograft vasculopathy is a late complication of HT characterised by a unique form of accelerated coronary disease affecting both intramural and epicardial coronary arteries and veins. It is a common cause of re-transplantation. Hypertension post HT is multifactorial and due to steroids, which can accelerate underlying atherosclerotic disease, calcineurin inhibitors and renal dysfunction. Malignancies, usually skin malignancies and post-transplant lymphoproliferative disorder, are common.

Future directions

Future directions include the need for enhanced collaboration between the cardiologists in Nigeria and the diaspora to ensure diffusion of best practices and identification of areas of unmet need as targets for future conferences. These include:

- Bolstering capacity of the cardiology workforce through cardiovascular competency training for cardiology trainees and improving intensive care unit availability and cardiac catheterisation laboratory services. These are still major challenges, despite the rising burden of ischaemic cardiomyopathy.
- Improving access to medications through 'fair pricing' to ensure that medications are obtained at 'discontinued' cost and increasing the role of health insurance programmes for HF to prevent catastrophic out-of-pocket medical expenditures.⁶¹ Accumulating evidence regarding the efficacy of the polypill may diminish the pill burden, which has the potential to assist adherence to GDMT.^{62,63}
- Implementing strategies to improve enrollment of African patients in contemporary HF clinical trials to advance diversity of trial participants and ensure that medications are available to the populations that they will eventually be marketed to.

- Developing HF clinical practice guidelines for the SSA cardiovascular community that are applicable and congruent to practical HF care in SSA.

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