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Maastricht University

Faculteit Geneeskunde en Levenswetenschappen
School voor Levenswetenschappen
master in de biomedische wetenschappen

Masterthesis

The epidemiological profile of heart failure patients in Lubumbashi, DR Congo

Stef Thonissen

Scriptie ingediend tot het behalen van de graad van master in de biomedische wetenschappen, afstudeerrichting klinische biomedische wetenschappen

PROMOTOR :
Prof. dr. Virginie BITO

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The epidemiological profile of heart failure patients in Lubumbashi, DR Congo

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ABSTRACT

Despite continuously increasing cases of heart failure (HF) and other non-communicable diseases (NCD) in Sub-Saharan Africa, epidemiological data on these conditions remain scarce. In Lubumbashi (Democratic Republic of Congo), numerous cardiovascular risk factors related to lifestyle, genetics and the environment are progressively more prevalent. In this epidemiological study, some of these elements are brought to light. The primary aim of our study was to estimate the prevalence of diabetes mellitus (DM) in a HF population in Lubumbashi, since these two conditions frequently appear together. Indeed, their co-occurrence has therapeutical and prognostic implications as the presence of diabetes is associated with a worse HF severity. DM was diagnosed retrospectively using patient records and HF in compliance with the ESC guidelines. HF severity was established by examining the left ventricular ejection fraction (LVEF) by echocardiography. Overall, we hypothesised that patients with DM have lower LVEF than those without. In this study, a prevalence of 10 % DM was found, which corresponds to data previously reported in literature. However, no significant difference in LVEF between patients with and without DM was found ($p = 0.651$), which might be a consequence of the rather small sample size ($n = 40$) and the large amount of missing data. Yet, our data provide preliminary but useful epidemiological data on HF risk factors as this is poorly reported in the developing world.

INTRODUCTION

Heart failure (HF) is a complex, multi-factorial, clinical syndrome that affects around 64.3 million people worldwide at this moment (1-4). This generates an enormous burden on clinical, societal and economic systems (2). HF is characterized by the inability of the heart to provide sufficient blood to the rest of the body to meet our metabolic demands (3). It is considered the final and most severe manifestation of nearly every form of cardiac disease (5), such as hypertension, coronary heart disease, valvular heart disease, cardiac arrhythmias, myocarditis and congenital heart disease. Yet, diabetes mellitus (DM) also significantly increases the risk of developing HF (3). Indeed, the 20-year Framingham cohort study on cardiovascular disease (CVD) and DM has shown a 2-fold and 5-fold increased risk of HF in DM patients in respectively men and women (6). It is thus essential to determine the aetiology since HF therapy is often based on treating the underlying conditions. Traditionally, HF is classified into three categories, based on the left ventricular ejection fraction (LVEF). Patients with an LVEF of ≤ 40 % have HF with reduced ejection fraction (HFrEF). Patients suffer from HF with a mildly reduced ejection fraction (HFmrEF) if the LVEF is between 41 and 49 %. Finally, an LVEF ≥ 50 % and objective evidence of structural and / or functional

cardiac abnormalities and / or raised natriuretic peptides (NP) indicates HF with a preserved ejection fraction (HFpEF) (1,4). The condition of the heart can be objectively and subjectively classified based on respectively the LVEF (7) and the New York Heart Association (NYHA) functional classification (3).

In most cases, the condition is characterised by specific symptoms (i.e. dyspnoea, fatigue and ankle swelling) and clinical signs of HF (i.e. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) (4). These can occur in an acute or chronic setting. In acute heart failure (AHT), the patient abruptly develops symptoms that require hospitalisation or a visit to the emergency department. Chronic heart failure (CHF) is a progressive condition that develops gradually over years (4,8). Throughout the development of CHF, the body attempts to adapt via numerous compensatory mechanisms to maintain cardiac output (CO). These include changes in myocardial structure and function, but also neurohormonal alterations. However, a perpetuating cycle of increased neurohormonal stimulation and hemodynamic and myocardial responses leads to the further deterioration of the condition of the heart, also called decompensated HF (3,9).

Besides, there has also been found a direct linear relationship between the prevalence of HF and the socio-economic index. This implies that the healthcare systems of middle- and low-income countries are affected by the surge of HF and other non-communicable diseases (NCD) even more (2). As a matter of fact, there has been a noteworthy shift from communicable to non-communicable diseases (e.g. CVDs, cancers, respiratory diseases and DM) in developing Sub-Saharan African countries, such as the Democratic Republic of Congo (DRC) for the past few decades (10-12). CVDs make up more than 50 % of these NCDs (11). It is estimated that NCDs will surpass HIV as the leading cause of mortality in Sub-Saharan Africa over the following decade (12). In part, this shift can be attributed to a growing incidence of cardiovascular risk factors (11). These can be for a part related to lifestyle (e.g. smoking, excessive alcohol consumption, obesity, overconsumption of salty food, etc.). Yet, environmental and genetic components also seem to play an important role (e.g. black race, nutritional deficiencies, psychological stress, environmental pollution, etc.). In Lubumbashi, heavy metal (HM) pollution due to poorly regulated mining areas further worsens the development of CVDs and DM-associated HF (13). Moreover, according to the Global Burden of Disease Study 2017, comorbidities, such as HF and DM, are likely to be an important aspect of NCD epidemiology in sub-Saharan Africa (14). The substantial presence of DM in HF patients has already been shown. According to the European Society of Cardiology, the prevalence of DM in symptomatic HF patients lies between 12 and 30 % (15). The pathophysiological relationship between the two has already been established. Hyperglycaemia, insulin resistance and hyperinsulinemia are all parameters characterising DM that pose significant risks for HF and considerably contribute to its progression (16,17). DM in hospitalized HF patients has been shown to lead to a higher post-discharge CVD mortality and HF hospitalisation rate (18), longer hospital length of stay (LOS) and increased all-cause rehospitalisation (19). However, even if well established in Europe, data on the prevalence of DM as a comorbidity in HF patients in the DRC, and in particular in Lubumbashi, are not available. This is important since it appears that HF aetiologies vary significantly between high- and low-income countries (10) and its characteristics are bound to unique regions in developing countries (20).

In addition, a general lack of organization of health care, limited resources, poor health literacy, certain beliefs of cultures or religions, lack of covering insurance and low incomes combined with high hospitalisation costs further add to poor health outcomes in the developing world (13,21). As a result, the treatment of HF in Sub-Saharan countries still faces substantial challenges. There is limited access to surgical medicine and nonpharmacological remedies are rather unavailable. Currently, medicinal treatment is one of the only therapies HF patients receive in the developing world (13). Due to a lack of resources and poor health care organisation, patients often resort to traditional medicine. However, folk medicine is mainly based on beliefs and scientific proof is often missing and can be even dangerous for the patients trying to cure themselves. Altogether, morbidity and mortality related to CVD in developing countries are high. A study has

revealed an in-hospital HF mortality rate of 19 % in Lubumbashi (13).

However, next to comorbidities, there are other, less obvious factors, which could also play a critical role in HF epidemiology in the DRC. Multiple studies and meta-analyses have already disclosed that HF patients in Sub-Saharan Africa have only little knowledge about their condition and prescribed medication (21-23). This phenomenon is called health literacy, which is defined as the degree to which individuals can obtain, process, and understand the basic health information and services they need to make appropriate health decisions (24). A systematic review by Cajita *et al*. has demonstrated that, even in developed countries, where medical care and education are more accessible to people, 39 % of HF patients in the United States have low health literacy (23). Furthermore, low health literacy has been associated with low health knowledge (25), low medication knowledge (26), high health care costs (27), low self-reported health status (28), and most importantly a greater risk of hospitalisation (29) and mortality (30). Thus, an increased knowledge level of the disease could conceivably improve HF patient's health, since they would be able to better understand care instructions, recognize signs and symptoms that necessitate a visit by the cardiologist and increase their self-management abilities by acting upon lifestyle-related risk factors of HF (23,31).

Finally, the anarchic urbanization and the gradual switch from the traditional African diet to a Western diet rich in saturated fats and sugar, likely play a pivotal role in the increasing prevalence of HF and other NCDs (32). It is not a hidden fact that diets high in fatty and processed meats, saturated fats, refined grains, salt and sugars; but lacking in fresh fruits and vegetables are significantly associated with an increased risk of CVD and all-cause mortality (33) and an increased risk of chronic diseases in general (34). Furthermore, the food chain is severely polluted in the region around the Copperbelt Mining Area (CMA), where Lubumbashi resides (35,36). The excessive leakage of HMs in the soil, lakes and rivers and in this way in locally grown and caught crops and fish inevitably also has a significant impact on public health (37,38).

Hence, there still is a major knowledge gap on the prevalence of DM in HF patients, as well as about the effect of this condition on the development and progression of HF in Lubumbashi. It is thus crucial to investigate this, since both diseases worsen each other's patient outcomes and are projected to increase in prevalence over time, especially in the developing world (16). Therefore, the core aim of this study was to investigate the prevalence of DM as a comorbidity in HF patients in Lubumbashi, DRC. Thus, the primary objective of our study was to determine the prevalence of DM in HF patients visiting the department of internal medicine or who come for an outpatient visit at Clinique Universitaire de Lubumbashi between the 29th of November 2021 and the 27th of May 2022. In addition, we hypothesised that patients with DM had a worse HF severity than those without. Finally, we also examined health literacy concerning HF and dietary habits and investigated whether these two factors also increase HF disease severity.

EXPERIMENTAL PROCEDURES

Study design – This is an academic, observational, cross-sectional, epidemiological study, initiated by Clinique Universitaire de Lubumbashi, and executed between the 29th of November 2021 and the 27th of May 2022. The study was approved by the medical ethics committee of Clinique Universitaire de Lubumbashi. The protocol meets the ethical guidelines imposed by the 1975 Declaration of Helsinki. The envisaged sample size was 137 patients. However, due to a limited timeframe and inadequate hospital organization, only 40 patients were included. All data were gathered from the medical file of the patients and two questionnaires and entered into an electronic case report form (eCRF). This eCRF included patient's characteristics, indications, laboratory results, aetiology, medication, transthoracic echocardiography (TTE), follow-up and the results of the two surveys (table 1).

Patient recruitment – All patients admitted to the department of internal medicine or coming for a consultation and diagnosed with new-onset or recurrent HF at Clinique Universitaire de Lubumbashi were asked to participate. Inclusion criteria are a diagnosis of new-onset or recurrent HF and exclusion criteria are being younger than 18 years, not being able to sign and understand the

Table 1: Collected data.

Categories	Details
Patient characteristics	Age, sex, length, weight, BMI, alcohol abuse, smoking status, health insurance, place of residence, city of origin, ethnicity, medical history, etc.
Indications	Symptoms (e.g. leg oedema, dyspnoea, fatigue, etc.) and NYHA score
Laboratory results	Relevant laboratory values on three time points
Aetiology	Conclusion of echocardiography (e.g. DCM, PPCM, PAH, etc.)
Medication	Medication intake before and during / after admission
Echocardiography	HR, SV, CO, LVEF, LVEDd, LVESd, LVSF, AWT, PWT, LVEDV, LVESV and E/A ratio
Follow-up	Date of admission, discharge and mortality, duration in hospital / ICU and all-cause in-hospital mortality
Health literacy results	Atlanta Heart Failure Knowledge Test
Dietary habits results	Epidemiological questionnaire validated on Congolese population

Abbreviations: BMI, body mass index; NYHA, New York Heart Association; DCM, dilated cardiomyopathy; PPCM, peripartum cardiomyopathy; PAH, pulmonary arterial hypertension; HR, heart rate; SV, stroke volume; CO, cardiac output; LVEF, left ventricular ejection fraction; LVEDd, left ventricular end diastolic diameter; LVESd, left ventricular end systolic diameter; LVFS, left ventricular fractional shortening; AWT, anterior wall thickness; PWT, posterior wall thickness; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume.

informed consent and not being able to speak French or Swahili. Upon approval, the questionnaires regarding dietary habits and health literacy took place. Additionally, laboratory and TTE results, medication intake and demographical data were extracted from patient records. The necessary examinations for HF diagnosis were done for a subset of patients (TTE, electrocardiography (ECG), blood analysis, etc.). Since the echocardiograms were done by different cardiologists with multiple devices, it is impossible to give details on the TTE methods.

Heart failure diagnosis – To diagnose HF, the required examinations were done according to ESC guidelines for a subset of patients. At admission, they underwent anamnesis and physical examination in which the patient's characteristics and medical history, the manifestation of symptoms and / or signs of HF and objective evidence of cardiac dysfunction were assessed. Based on the results of these examinations, diagnostic tests were whether or not done, dependent on the patient's resources. Subsequently, a blood sample was taken to assess relevant blood values, of which the plasma NT-proBNP value should stay below 125 pg / ml. Other substances (i.e. serum urea and electrolytes, creatinine, full blood count and liver and thyroid function markers) were also measured to better evaluate and guide the patient's pathophysiological state and differentiate HF from other conditions. Finally, a TTE was executed to assess the function and structure of the heart. This is the key investigation to diagnose HF, determine its severity and identify the aetiology (4).

Sample size calculation – The sample size was calculated based on the primary research question (prevalence quantification). It was done based on the desired precision around the point estimate. The hypothesized prevalence was 15 % and a precision of 6 % was used. We aspired to include at least 137 patients during a study period of 6 months.

Outcomes and outcome measures – To assess the prevalence of DM, we adopted a retrospective approach. Patient records were reviewed to determine whether the patient had the condition. Diagnosis of HF took place according to the 2021 European Society of Cardiology (ESC) Guidelines for the diagnosis and treatment of acute and chronic HF (4). To determine the severity of HF, an objective measure, the LVEF, and a subjective

measure, the NYHA score were used (3,7). The severity grade was associated with the presence or absence of DM to investigate whether patients with DM have a worse HF disease severity than those without. The LVEF was measured by the cardiologist via a TTE. An LVEF < 30 % was considered a severe dysfunction. An LVEF between 30 and 39 % and 40 and 49 % indicated respectively moderate and mild dysfunction. A heart with a normal function has an LVEF ≥ 50 % (table 2) (7). The NYHA score was ascertained by asking the patient. NYHA score I indicates that the patients have no limitation of physical activity and ordinary physical activity does not cause undue fatigue, palpitation or dyspnoea. NYHA score II means the patient has a light limitation of physical activity, is comfortable at rest and ordinary physical activity results in fatigue, palpitation or dyspnoea. NYHA score III implies that the patient has marked limitation of physical activity, is comfortable at rest and less than ordinary activity causes fatigue, palpitation or dyspnoea. Finally, having an NYHA score of IV requires the inability to carry on any physical activity without discomfort, symptoms of HF at rest and if any physical activity is undertaken, discomfort (table 3) (3). To evaluate health literacy and dietary habits, respectively the Atlanta Heart Failure Knowledge Test (A-HFKT) and an epidemiological questionnaire were used. The English version of the A-HFKT was validated in 2019 by Butts *et al*. who stated that it can be applied to HF patients and family members. Though, we translated it to French to ensure a good understanding by the local French-speaking population. Since Swahili is also a primary language in the eastern part of the DRC, a translator was often brought in to administer the surveys. Originally, the A-HFKT consisted of 30 questions related to HF pathophysiology, nutrition, behaviour, medications and symptoms and is

Table 2: Objective classification of heart failure severity using the left ventricular ejection fraction.

Classification	Description
LVEF < 30 %	Severe dysfunction
30 % ≤ LVEF ≤ 39 %	Moderate dysfunction
40 % ≤ LVEF ≤ 49 %	Mild dysfunction
LVEF ≥ 50 %	Normal function

Table 3: Subjective classification of heart failure severity using the left ventricular ejection fraction.

Classification	Description
NYHA I	- No limitation of physical activity - Ordinary physical activity does not cause undue fatigue, palpitation or dyspnoea
NYHA II	- Slight limitation of physical activity - Comfortable at rest but ordinary physical activity results in fatigue, palpitation or dyspnoea
NYHA III	- Marked limitation of physical activity. - Comfortable at rest but less than ordinary activity results in fatigue, palpitation or dyspnoea
NYHA IV	- Unable to carry out any physical activity without discomfort - Symptoms at rest - If any physical activity is undertaken, discomfort is increased

scored by adding up the amount of rightly answered questions and dividing this by the total amount of questions (i.e. 30) (39). Yet, we eliminated three questions since they were not applicable on a Congolese population, leaving us with 27 questions. The epidemiological questionnaire to investigate dietary habits was validated on a Congolese population. This questionnaire consists of nine parts about the identification of the patient, arterial hypertension, DM, tabagism and alcoholism, physical activity, nutritional habits, HF and two parts concerning medical examinations. All of the questions were evaluated individually without an overall score being assigned to them. The questionnaires were completed in writing, after which the results were immediately transferred to the eCRF. Then, the completed questionnaires were stored in folders in an enclosed space at Clinique Universitaire to which only study employees had access.

Data analysis and statistics – All analyses were performed using IBM SPSS v.28.0 for Windows (IBM, New York, NY, USA). Data were shown as mean ± SD, median (IQR) or n (%) as appropriate. Data were analysed and interpreted at a significance level of 0,95 %. Thus, statistical significance was determined as a p-value < 0,05. A p-value between 0,05 and 0,10 was considered as a tendency toward significance. Descriptive statistics were used to demonstrate the prevalence of DM among HF patients. For continuous variables, differences between two groups were evaluated using a t-test or its non-parametrical alternative (i.e. Mann-Whitney U test) as appropriate. For categorical variables, the chi-square test was used for this purpose. Associations between continuous variables were analysed using Pearson's or Spearman's correlation coefficient as appropriate.

RESULTS

Demographics and description of the patient population – In total, 40 patients were enrolled in the analysis, of which 36 (90.0 %) suffered from HF and four (10.0 %) were diagnosed with both HF and DM. Most were diagnosed with HF during a hospitalisation (n = 35, 87.5 %) and only five (12.5 %) during an outpatient visit. The mean age and BMI of the included patients were respectively 50.1 ± 20.0 years and 27.0 ± 7.55 kg/m^2. With 62.5 % of all the enrolled patients, there was a preponderance of females over males in our study. The most commonly reported symptoms were fatigue and weakness (92.5 %), decreased exercise capacity (85.0 %), dyspnoea (80.0 %), orthopnoea (80.0 %), oedema of lower extremities (75.0 %), paroxysmal nocturnal dyspnoea (65.0 %), palpitations (60.0 %), bloated feeling (57.5 %), persistent cough (57.5 %) and sudden weight gain or loss (55.0 %). The leading cause of HF was dilated cardiomyopathy (DCM), from which 22 (55.0 %) patients suffered, followed by pulmonary hypertension (PAH; n = 13, 32.5 %) and peripartum cardiomyopathy (PPCM; n = 11, 27.5 %). Six (15.0 %) patients were alcohol abusers, no patients smoked actively and six (15.0 %) had smoked in the past. Only 14 (35.0 %) patients had a history of CVD. Lastly, the median hospital LOS was 8.0 (11.0) days and four (10.0 %) patients suffered from all-cause in-hospital mortality (table 4).

Primary outcome – The prevalence of DM in this sample of HF patients was 10.0 %. Mean LVEF was 37.6 ± 16.9 % and six (15.0 %) patients had an NYHA score of one, 11 (27.5 %) had one of two, 18 (45.0 %) of three and five (12.5 %) patients had a score of four. Classified based on LVEF, eight (20.0 %) patients suffered from severe cardiac dysfunction, five (12.5 %) from moderate dysfunction, and respectively five (12.5 %) and four (10.0 %) patients had mild or no dysfunction (table 4). Using the Mann-Whitney U test, no significant difference in median LVEF between the groups of patients with and without DM has been found (p = 0.651) (figure 1).

Health literacy results – The mean score on the A-HFKT was 41.6 ± 11.0 %. Moreover, with Pearson's correlation coefficient, a significantly unexpected negative association was found between the A-HFKT score and LVEF (R = -0.555, p = 0.021). Out of four answering options, only 20 (50.0 %) patients knew that HF is a condition in which usually the heart is unable to pump enough blood throughout the body. In addition, only six (15.0 %) knew that it cannot be cured, but only controlled. Merely 12 (30.0 %) patients could link a weight gain of two to three kilograms in a few days to fluid excess in the body. Also regarding oedema, only 10 (25.0 %) patients thought it to be important to weigh themselves daily. Moreover, only 15 (37.5 %) patients seemed to believe it is useful to do exercise every day being an HF patient.

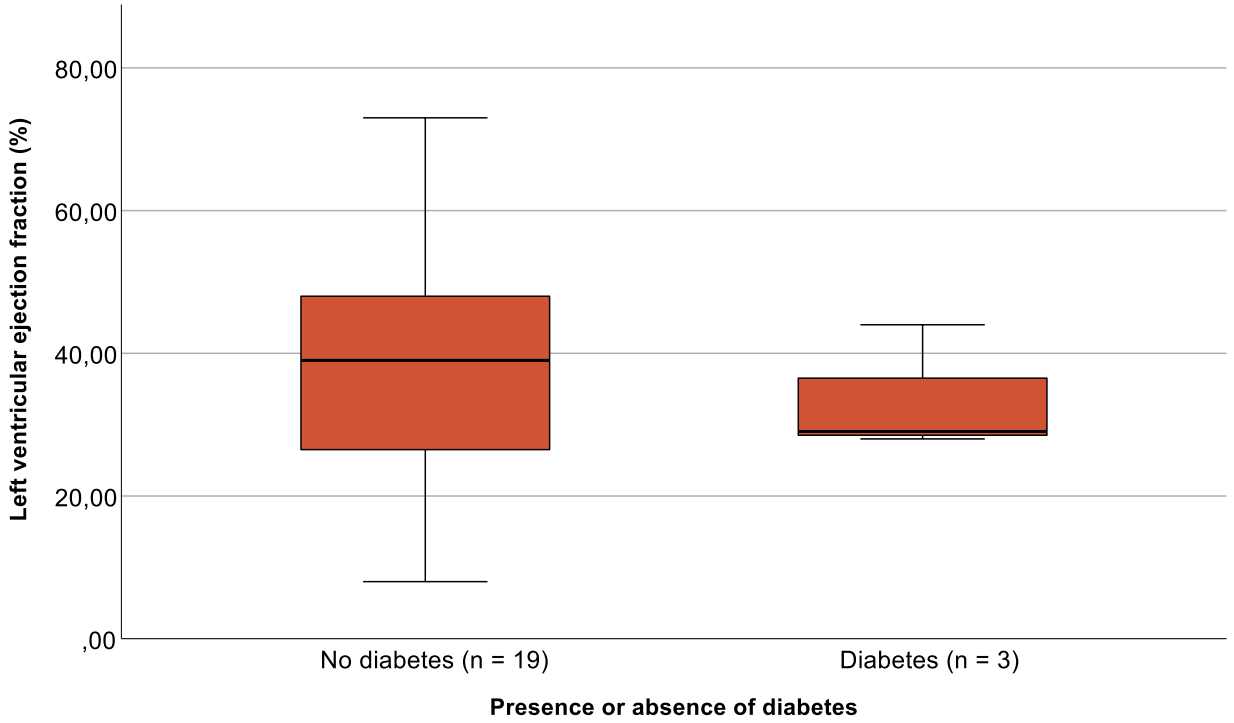

Figure 1: Difference in median LVEF, a measure of HF severity, between HF patients with and without DM in Lubumbashi, DR Congo. The Mann-Whitney U test has shown no significant difference in median LVEF between HF patients with and without DM (p = 0.651).

On the salt content in the diet, respectively six (15.0 %), 14 (35.0 %) and 10 (25.0 %) patients could point out the foodstuffs with the highest or lowest amount of salt in it in three different questions with four answering options. Besides, merely six (15.0 %) patients appeared to know that it is essential to take your HF medication once you remember it if you forgot to take them. Finally, two (5.0 %) patients confessed that they were not informed by their physician that they were suffering from HF.

Dietary habits results – The standard diet in Lubumbashi comprises fruit, leafy vegetables, rice, manioc, corn, fish and meat. In this study, 34 (85.0 %) patients indicated that they eat at least once a week fruit, 34 (85.0 %) vegetables, 33 (82.5 %) fish, 33 (82.5 %) meat, 28 (70.0 %) corn, 25 (62.5 %) manioc and 24 (60.0 %) rice. Although 85.0 % of patients claimed to eat fruit at least once a week, as many as 21 (52.5 %) of them only ate it three times or less weekly. No relevant, nor statistically significant differences in median LVEF were found between the groups that consumed a low (0 to 3 times a week) versus a high (4 to 7 times a week) amount of fruit (p = 0.672), vegetables (p = 0.500), rice (p = 0.064), manioc (p = 0.391), corn (p = 0.157), fish (p = 0.353) or meat (p = 0.095) (figure 2). Similarly, no visible differences in median LVEF are observed in milk (p = 0.397), yoghurt (p = 0.200), cheese (p = 0.749), bread (p = 1.00), potatoes (p = 0.316), eggs (p = 0.933) or legumes (p = 0.200) consumption (figure 2). Ultimately, 33 (82.5 %) patients had access to drinking water. For 21 (63.6 %) patients the water source was tap water, for two (6.06 %) patients rainwater, for four (12.1 %) well water and for four (12.1 %) patients borehole water.

Other social determinants of health – The median number of children of patients was 4.0 (7.0). In this population, 25 (62.5 %) patients were married, three (7.50 %) divorced, five (12.5 %) widowed and two (5.0 %) single. The median monthly salary was 100 (358) USD, while patients had a mean number of dependants in the household of 6.10 ± 3.34. In total, three (7.50 %) patients had health insurance and 32 (80.0 %) family support, which we defined as the presence of financial and emotional support of family members in the course of the hospitalisation.

DISCUSSION

Demographics and description of the patient population – Patients included in this study were relatively young and presented late during their disease course accompanied by many symptoms, which corresponds to previously conducted studies in the Sub-Saharan African region (13,20). The majority of the patients, and more than reported in the past (13,20), were female, most likely related to the high amount of PPCMs. The most common cause, however, was DCM. This was expected, as a previous study has reported a percentage of 47.6 % of this type of cardiomyopathy in Lubumbashi (13). Possible risk factors for DCM and PPCM might be black race, alcohol abuse, overweight, overconsumption of salty food and clay, nutritional deficiencies, psychological stress and environmental pollution (13). Finally, 10.0 % of patients suffered from all-cause in-hospital mortality, which is substantially higher than previously reported in Europe (6.7 %) and China (4.1 %) (40). This could be because patients were admitted to the hospital in an advanced stadium of HF. In our study, 20 % came to the hospital with a severely dysfunctional heart (i.e. LVEF < 30 %), probably due to a combination of factors (e.g. low salaries, absence of health insurance and social security, high hospitalisation costs, inadequate hospital equipment, etc.) that make for poor physical and economic accessibility to health care services. Besides, many patients had to leave the hospital prematurely and forcibly due to financial hardship that impeded them from paying the hospital bills. As a result, patients often had to go home without the necessary examinations done or proper treatment given. Finally, a genetic component most likely also plays a role in the HF outcomes in the Sub-Saharan African population. Studies have shown that the black population has a lot of genetic heterogeneity, which predisposes them to worse HF outcomes and treatment responses (41). This genetic component is possible also the key to why DCM is the major cause of HF in our patient population, given that it has been previously demonstrated that 35 % of DCM patients seem to have genetic alterations that could contribute to its development (42). Another contributing factor could be excessive exposure to HMs that are present in the food chain and air in Lubumbashi. Indeed, a recent case-control study executed in the Katangese Copperbelt mining region has demonstrated that increased urinary concentrations of several HMs were significantly associated with a higher DCM probability (43). In conclusion, given these regional differences in risk factors and mortality, public health policies related to HF management must be targeted to local conditions.

Prevalence of DM in HF – Having an estimation of the prevalence of DM in HF is crucial, as it provides a specific epidemiological profile of patients in particular regions. It allows local physicians to have a better picture of the profile of HF patients and it can guide a more evidence-based, integrated and targeted care of patients with said comorbidity. In our study, the prevalence of DM in HF patients was 10 %. This corresponds to some extent with what has been earlier reported in literature. It seems that this prevalence strongly depends on the region of research. Indeed, multiple clinical trials in the developed world have established prevalence rates up to 50 % (19,44). Various other multinational, observational trials have demonstrated a wide range of prevalence rates of DM in HF. The global congestive heart failure (G-CHF) registry has shown an overall worldwide prevalence of 30.9 %, with a marginally higher proportion in acutely hospitalized (34.5 %) than in ambulatory (29.2 %) patients (45). The REPORT-HF cohort study has demonstrated a global prevalence of 37 %, with compelling disparities between different regions from 31 % in Central- and South America to 47 % Eastern Mediterranean region and Africa (46). The international Congestive Heart Failure (INTER-CHF) study on its turn discovered a DM prevalence in HF of 17.1 %, 21.9 % and 27.9 % in respectively Africa, South America and Asia, and a remarkably high percentage of 56 % in the Middle East (47). In conclusion, in the Sub-Saharan Africa Survey of Heart Failure (THESUS-HF) study, a prevalence of 11.4 % in 9 African countries was shown (20). Nevertheless, no study regarding this topic has yet been performed in the Democratic Republic of Congo. The observed DM prevalence in HF in this study does comply with data from other studies carried out in Sub-Saharan Africa, aside from the high percentage shown in the REPORT-HF study. This difference can be justified by the fact that, in this particular study, the prevalence in Africa was taken together with that in the Eastern

Table 4: Patient demographics

Variable	Values (n = 40)
Age (years), mean ± SD	50.1 ± 20.0
Gender (male), n (%)	15 (37.5)
BMI (kg/m^2), mean ± SD	27.0 ± 7.55
NYHA score	
I, n (%)	6 (15.0)
II, n (%)	11 (27.5)
III, n (%)	18 (45.0)
IV, n(%)	5 (12.5)
LV function	
Severe dysfunction: LVEF < 30 %, n (%)	8 (20.0)
Moderate dysfunction: LVEF 30 – 39 %, n (%)	5 (12.5)
Mild dysfunction: LVEF 40 – 49 %, n (%)	5 (12.5)
Normal function: LVEF > 50 %, n (%)	4 (10.0)
Family support, n (%)	32 (80.0)
Health insurance, n (%)	3 (7.50)
Patient characteristics	
Smoker, n (%)	0 (0)
Ex-smoker, n (%)	6 (15.0)
Diabetes mellitus, n (%)	31 (77.5)
Arterial hypertension, n (%)	17 (42.5)
Dyslipidaemia, n (%)	0 (0)
Family cardiac history, n (%)	3 (7.50)
Medical history	
CVA, n (%)	1 (2.50)
MI, n (%)	0 (0)
CAD, n (%)	0 (0)
CMP, n (%)	3 (7.50)
Atrial fibrillation, n (%)	0 (0)
Chronic renal disease, n (%)	0 (0)
COPD, n (%)	2 (5.0)
HF aetiology	
DCM, n (%)	22 (55.0)
Cor pulmonale, n (%)	1 (2.50)
PPCM, n (%)	11 (27.5)
HTN-CM, n (%)	6 (15.0)
PAH, n (%)	13 (32.5)
Medication	
ACE-I, n (%)	28 (70.0)
ARB, n (%)	0 (0)
β-blocker, n (%)	7 (17.5)
Digoxin, n (%)	6 (15.0)
Nitrates, n (%)	3 (7.50)
Loop diuretics, n (%)	31 (77.5)
Aspirin, n (%)	10 (25.0)
Antiarrhythmics, n (%)	0 (0)
Anticoagulants, n (%)	12 (30.0)

Abbreviations: BMI, body mass index; NYHA, New York Heart Association; LV, left ventricle; LVEF, left ventricular ejection fraction; CVA, cerebrovascular accident; MI, myocardial infarction; CAD, coronary artery disease; CMP, cardiomyopathy; COPD, chronic obstructive pulmonary disease; DCM, dilated cardiomyopathy, PPCM, peripartum cardiomyopathy; HTN-CM, hypertensive cardiomyopathy; PAH, pulmonary arterial hypertension; ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Mediterranean region, where the diabetes prevalence has been proven to be exceptionally high. Thus, these results strengthen what has previously been found. HF and DM are ever more emerging together, which emphasises the need for targeted therapies to address this comorbidity. There are well-established distinct guidelines to manage DM and HF in isolated circumstances, yet,

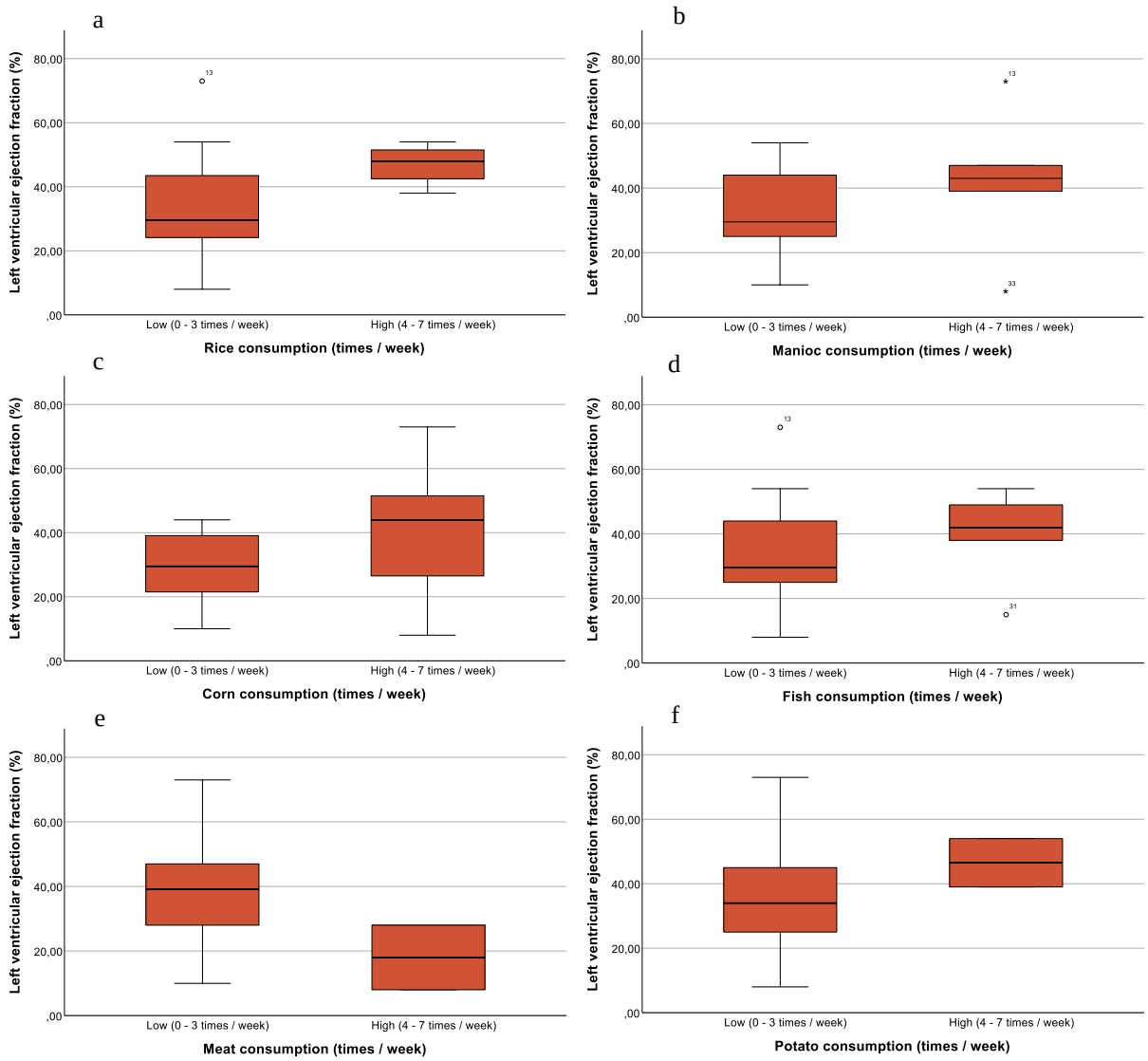

Figure 2: Differences in median LVEF between HF patients with low or high consumption of locally grown and caught foodstuffs in Lubumbashi, DR Congo. The Mann-Whitney U test has shown no significant differences in median LVEF between HF patients with low or high a) rice (n = 20, p = 0.064), b) manioc (n = 19, p = 0.391), c) corn (n = 20, p = 0.157), d) fish (n = 20, p = 0.353), e) meat (n = 20, p = 0.095) or f) potato (n = 20, p = 0.316) consumption.

guidance for the management of patients who suffer from both conditions simultaneously is absent. Future clinical trials should focus on investigating the disease outcomes of patients with concomitant HF and DM (16,17). Hence, given these high prevalence percentages and the almost 50 % increase in the global burden of CVD between 1990 and 2017 (14), the magnitude of the growing epidemic of non-communicable diseases in Sub-Saharan Africa must be taken seriously.

DM presence and HF severity – Even though we could not show a lower LVEF in HF patients with DM than those without, countless other studies have already ascertained that DM patients have a higher risk of developing HF and are significantly more prone to a worse disease progression. First of all, DM has been proven to have a serious impact on the structure and function of the heart. Adjusted for covariates, patients with DM seem to have a higher left ventricular mass (LVM), thicker left ventricular wall (LVW) (48,49), lower left ventricular fractional shortening (LVFS) (48), higher left ventricular end-diastolic diameter (LVEDD) (49), higher stroke volume to pulse

pressure ratio (SV/PP) and worse left ventricular and myocardial function (48) than non-diabetics. All these harmful dynamics are detrimental to the heart and could increase the risk of HF. Furthermore, various studies, among which The Framingham Heart study have demonstrated a two- to fourfold increase in HF incidence in diabetic patients compared to those without DM (6). Not to mention that concomitant HF and DM has also been associated with a significantly worse quality of life than HF alone (50). Yet, most notably, in HF patients, those with concurrent diabetes have a 30 to 50 % increased hospitalisation risk (51) and in the MAGGIC meta-analysis of 30 cohort studies comprising 39 372 HF patients performed by Pocock *et al.*, DM was even identified as an independent predictor of HF mortality (52). Hence, given this undeniable evidence, the major reasons explaining the lack of significant results in our study are most probably the small sample size combined with a lack of echocardiographic data due to the absence of study financing.

Health literacy results – As already mentioned, low health literacy has been associated with low health knowledge (25), low medication knowledge (26), high health care costs (27), low self-reported health status (28), and most importantly higher risk of hospitalisation (29) and mortality (30). Given these data, it seems rather plausible that insufficient HF health literacy is also associated with a worse HF disease severity. We did indeed find exceedingly low health literacy results with a mean score of 41.6 ± 11.0 %. This could be explained by the fact that the A-HFKT is a fairly difficult questionnaire with specific questions and that it has never been validated in our patient population, which could contribute to detection bias. It is a survey containing questions about HF pathophysiology, nutrition, behaviour, medications and symptoms. Its internal consistency, reliability and validity have already been established. However, higher levels of knowledge were shown to be associated with a higher education level in this validation study (39). Given the clear positive association between educational attainment and health literacy and the still existing problems in education accessibility in DR Congo, this could be an explanation for the extremely low scores. Nonetheless, even on the more important questions about self-care behaviour (i.e. symptom recognition, salt content of edibles and medication intake), many patients were not able to provide a correct answer. Approximately a third of the patients realised that a sudden weight gain in a few days in HF patients is probably due to a failing heart which causes fluid to build up in the extracellular tissue. This is worrying since symptom recognition in HF patients is associated with better self-care behaviours (53). Moreover, patients with good symptom response behaviour are less likely to develop HF decompensation or to decease (54). The same applies to exercise and medication intake. Exercise training and adequate medication adherence in HF patients both significantly reduce the risk of cardiovascular mortality and HF hospitalisation (55,56). Yet, less than 50 % of our patient population seemed to grasp the importance of exercise and appropriate daily medication intake for their health. On top of this, the majority of patients could not point out the foodstuffs with the highest or lowest sodium content out of four answering options. This denotes insufficient knowledge on salt intake, despite its known numerous detrimental effects on the cardiovascular system. In spite of this, unlike literature reporting a clear correlation between HF severity and health literacy, we could not find such correlation in our study. One possible reason could be the low sample size. Moreover, because of the language barrier and limited access to one Swahili-speaking person, the questionnaires were conducted by 11 different individuals, with one French-speaking researcher who was always present. Most probably, this has contributed considerably to detection bias. Yet, these data point out a severe lack of knowledge concerning HF pathophysiology, nutrition, behaviour, medications and symptoms. Even if widely accepted, whether this lack of knowledge is also associated with the severity of HF remains to be determined in Lubumbashi. Future health interventions should focus on these aspects to reduce the hospitalisation and mortality rate of HF patients in Lubumbashi.

Dietary habits results – The best diet to reduce the risk of developing CVD includes fruit and vegetables, whole grains, nuts, fish, poultry and vegetables; moderate to no consumption of alcohol, red or processed meat, refined carbohydrates, foods and beverages with added sugar, sodium and foods with trans-fats. In a 32-year prospective cohort study, it was indeed shown that greater adherence to such healthy eating patterns was consistently

associated with a significantly lower risk of CVD (57). In our study, we observed that the previously mentioned shift from the traditional African diet to the unhealthier Western diet has not yet taken place, despite reports from the literature. It is clear that, in this particular patient population, everyone still eats locally grown foodstuffs, most likely due to the high prices of Western food in Sub-Saharan Africa combined with the exceedingly low salaries (ca. 100 USD per month for a family counting six persons on average). Nonetheless, despite everyone's own choice of diet, unfavourable eating patterns are also driven by a combination of biological, social, economic, psychological and environmental factors. Numerous studies have already uncovered severe environmental HM pollution in the Katangese Copperbelt Area, a region in which Lubumbashi is embedded. Due to intensive and uncontrolled, artisanal and industrial metal mining, soil (58), rivers and lakes (59) in this region have been severely contaminated with HMs. Inevitably, this has led to contamination of the food chain, since many foodstuffs are locally grown or caught in Lubumbashi. Multiple studies have shown unusually high HM concentrations, well beyond reference values, in drinking water (35,37), locally grown leafy vegetables (e.g. cassava, sweet potato, pumpkin and tomato leaves) (35,37), fruits (35,37), beans (35) and fish caught in nearby lakes (37). As a result, residents of this region are chronically and from low age exposed extensively to these metals through their diet, which has been proven in a few case-control studies that measured urinary and blood HM concentrations in the inhabitants of Lubumbashi and a control area. Urinary cobalt (Co), arsenic (As), cadmium (Cd), copper (Cu) and lead (Pb) concentrations were shown to be substantially higher in the CMA compared to reference areas without industrial or mining activities (38). Given the detrimental health effects of HMs on multiple organ systems, among which the cardiovascular system (60), the abundant presence of these elements in the food chain could contribute to the development and progression of NCDs. However, oddly enough, no significant differences in LVEF were found between patients with high or low consumption of local edibles in this study. The main reason for this could be, as already mentioned, the small sample size of 40 patients, which did not allow us to do statistically relevant analyses and the lack of more advanced data sampling and analyses, being a major limitation of our study.

Other social determinants of health – The social determinants of health (SDH) are defined by the World Health Organisation (WHO) as the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life. It is estimated that these factors, such as income, health insurance, social security, housing, employment and education, account for up to 55 % of health outcomes (61). Previous research has already shown that HF patients of low-income groups have a significantly higher in-hospital mortality rate, higher risk of post-discharge HF readmission and higher all-cause mortality than those of high-income groups (62). The median income of patients in this study was 100 (358) USD, but no significant association between income and HF severity was found. Furthermore, merely three (7.50 %) patients had health insurance, which means the majority of the patients had to pay themselves for their health services without governmental reimbursement. This can lead to so-called catastrophic health expenditures, which is classified as being catastrophic if a household's financial contributions to the health system exceed 40 % of the income remaining after subsistence needs have been met. This situation arises if out-of-pocket payments are required to pay for health services, households have a low capacity to pay for health services and there is a lack of health funds, collected through taxes or insurance, for risk pooling (63). This may push patients even further into poverty, especially in low-income countries with a defectively organised health care system. For this purpose, the WHO has developed a framework, universal health coverage (UHC), so that all people have access to the health services they need, when and where they need them, without financial hardship (64). It has been shown that public funds for health services and out-of-pocket spending, two UHC indicators, are respectively positively and negatively associated with life expectancy at birth (65). However, yet again, no significant association with HF severity was observed in this study, which corresponds with previous research in which the correlation between health insurance and HF outcomes was assessed (66).

Improvements to be made – In this paragraph, a summary of improvements that could be made to

enhance public health in the DRC is given. First of all, inadequate road infrastructure, public transport and ambulance services should be improved to increase the physical accessibility of health centres (67). The availability of affordable nutritious foodstuffs should be improved as well and campaigns to promote a healthy diet should be done to stimulate healthy and varied dietary habits (68). Structured waste management and car inspection systems have to be initiated to decrease exposure to toxic gases, due to uncontrolled waste incineration and car exhaust, given their detrimental health effects (69). Campaigns to enhance the credibility of modern medicine could also be done to eradicate the often harmful effects of herbal remedies and beliefs such as witchcraft and sorcery (70). Moreover, the organisation of the Congolese healthcare system should be turned upside down to increase the economic accessibility of healthcare services. A structured system of interconnected general practices with less corruption at decision-maker's level, private clinics and public and university hospitals should be established. Medical equipment should be distributed to the hospitals that need it the most. Medical specialists need to be encouraged by the government to stay in the DRC instead of moving abroad. Lastly, a social safety net, including social security and health insurance using public funds collected through taxation, has to be built as urgently as possible in order to promote ill people to seek hospital treatment without delay as a result of financial problems (71). Finally, specifically in the Katangese Copperbelt mining area, measures to eliminate corruption, improve export controls, increase returns from the DRC's minerals to the state and improve labour conditions and safety for artisanal miners should be established by a multidisciplinary team of the Congolese government, trading and mining companies, financing institutions and the governments of countries to which the minerals are exported. This is important to increase overall regulation of the mining industry and decrease its harmful effects on public health (72).

Limitations – This study has numerous limitations. First and foremost, the envisaged sample size of 137 was not attained, but only 40 patients were included. This could be because patients wait a long time before they go to the hospital. They know the costs, their salaries are low and there is no social security network or health insurance. They do not want to be pushed further into poverty, which withholds a lot of patients to go to the hospital. Yet, this aggravates their condition even more, which in turn leads to even longer hospitalisations and higher mortality rates. This is seen in this study by the severe symptomatology, high NYHA and LVEF scores and the rather long hospital LOS. Besides, as mentioned earlier, probably a proportion of the patients first seek traditional or herbal medicine or smaller and less equipped local hospitals, before being referenced to a larger hospital, despite the often mild to severe adverse effects of these herbal remedies (70). Yet, this is a consequence of the failing health care system in the DRC. Furthermore, it is likely that patients, possibly due to poverty, still do not trust modern medicine and consider witchcraft, sorcery, poisoning or punishment by ancestors as primary causes of illness (73). Secondly, we were strongly dependent on the ability of patients to pay for the medical examinations, since there was no financing. This has led to many missing data, due to many reasons, which were partly mentioned previously (i.e. low wages, absence of a social security network and well organised health insurance, high overall hospitalisation costs). This is not the only barrier to doing clinical research in a developing context we encountered. Patient records were handwritten and often not complete. There was no structured communication system to know whether and where there were patients with a certain disease. Next, patients often had difficulties understanding what a clinical study entails, despite an extensive explanation. Furthermore, French was not spoken by everyone, so a local doctor was needed to translate the questionnaires in Swahili. In Swahili, not every word has a translation. For example, there exists no specific interpretation for "heart failure", but only for "heart problem" in general (i.e. "malali ya coeur", "malali ya moyo" or "magonjwa ya moyo"). As a result, it was rather tough to explain specifically what heart failure means since heart disease for these patients is always the same thing. In reality, however, there is a large difference between different heart diseases (coronary heart disease, myocardial infarction, aortic stenosis, heart failure, etc.). Besides, since the questionnaires were conducted by 11 different doctors, a large amount of bias was probably introduced in the data collection. The fact that the echocardiograms were performed by multiple

cardiologists with different devices most likely enhanced this effect even more. Thus, the measurements of the several study outcomes (i.e. health literacy, dietary habits and LVEF) were not consistent for all participants in our study. This substantial amount of detection bias could be a major factor in the unexpected results of our study. To conclude, all the limitations discussed in this section largely comply with the barriers to conducting clinical trials in developing countries described in a systematic review of 15 articles by Alemayehu *et al*., which urgently prompts governmental interventions to ameliorate research circumstances in these regions (74). All these abovementioned limitations considerably reduced the quality of this clinical study, so our results should be interpreted with great caution and a critical mind.

Current issues and future directions – Health care is not just about medical care. To improve it, a multidisciplinary approach is essential. To reduce the risk of developing HF or other CVDs, multiple issues need to be addressed. In general, it can be said that tailored policies to population-specific risks and underlying aetiologies are essential to assess and manage the risk of developing HF and other NCDs around the world. To do this, epidemiological studies should be done to increase knowledge on region-specific public health issues, after which larger randomised trials could be initiated to investigate the problems that arose. However, given the unfavourable clinical research circumstances in the developing world, it is extremely difficult to realise such projects. Governments, research institutions and independent researchers should be encouraged to do clinical research in developing Sub-Saharan Africa, since this is where it makes the biggest difference, given the many still existing knowledge gaps regarding public health and disease mechanisms in this region.

CONCLUSION

Detailed epidemiological data of HF aetiologies are lacking in Sub-Saharan Africa. In our study, we determined the prevalence of DM in an HF population in Lubumbashi, DRC. Additionally, we analysed whether patients with DM had a worse HF severity than those without. We found a prevalence of 10 %, which corresponds to previous literature on Sub-Saharan Africa. However, no significant difference in LVEF was found between the patients with and without DM, despite the detrimental effects of DM on HF outcomes previously reported. Secondly, we also evaluated the health literacy and dietary habits of inhabitants of Lubumbashi. We have shown that HF patients in Lubumbashi have exceedingly little knowledge of their condition, which could be detrimental to their disease progression. Yet, an unexpected significant negative association was found between health literacy scores and LVEF, likely due to low sample size and detection bias. Besides, we discovered that the shift from the local African to the unhealthier Western diet, rich in saturated fats and sugar, has not yet taken place, even if previous epidemiological studies in Sub-Saharan Africa have shown otherwise. We did not find differences in LVEF between patients with high or low consumption of local foodstuffs either, despite the substantial pollution of the food chain by HMs derived from the poorly regulated Katangese mining industry. In conclusion, our study provides preliminary epidemiological data on HF patients in Lubumbashi, DRC. Future studies should be initiated upon the results found in this and other studies. More accurate epidemiological studies in Lubumbashi are necessary to determine the profile of HF patients, given its increasing incidence in this region. This is important for decision-makers to organise better health care and in this way improve HF outcomes.

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Author contributions – Mr. Stef Thonissen, Prof. Dr. Didier Malamba-Lez and Prof. Dr. Virginie Bito proposed and initiated this study. Prof. Dr. Didier Malamba-Lez performed the echocardiograms. Mr. Stef Thonissen enrolled the patients in the study, interrogated them and performed the data analysis. Mr. Stef wrote the dissertation with the assistance of Prof. Dr. Virginie Bito.

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