INTRODUCTION

Globally, chronic kidney disease (CKD) is a major cause of morbidity and mortality, affecting almost 700 million people, as of 2017, and with a steady increase in mortality between 1990 and 2017 [1]. The prevalence of CKD in sub-Saharan Africa (SSA) is around 14% [2]; it is estimated that SSA will contribute more than 70% of the world’s CKD burden by the year 2030. In Uganda, the prevalence is 15.2% [3].

Cardiovascular disease (CVD) is the most common cause of morbidity and premature mortality in patients on chronic haemodialysis, with CVD mortality rates up to 30 times higher than in the general population [4]. CKD is a well-established risk factor for adverse cardiac events including myocardial infarction, stroke and sudden cardiac death. The risk increases with CKD progression to end-
stage renal disease (ESRD). Left ventricular hypertrophy (LVH) and diastolic dysfunction are the two cardiac abnormalities most implicated as risk factors for cardiac death in haemodialysis patients [5,6]; echocardiography provides a non-invasive assessment for these and other abnormalities of cardiac structure and function [7].

A study from Cameroon among patients on haemodialysis found the prevalence of cardiac abnormalities to be 80%, with LVH being the most prevalent at 60% [8]. In Uganda, a previous study in Mulago Hospital found LVH in 54.4% of patients with CKD [9]; however, this study excluded patients on haemodialysis.

Over the past ten years, there have been great strides in the establishment of both public and private haemodialysis centres in Uganda but there remains a paucity of data on cardiovascular complications in these patients. We therefore sought to establish the prevalence of LVH, diastolic dysfunction and other echocardiographic abnormalities among patients on chronic haemodialysis in Mulago National Referral Hospital.

METHODS

This single-centre, cross-sectional study was carried out at Mulago National Referral Hospital in Kampala, Uganda. This has the only public dialysis unit in Uganda, and provides two subsidised, 4-hour dialysis sessions per week to each patient. In addition to serving the Ugandan population, the unit accommodates patients from the neighbouring eastern Democratic Republic of Congo and the Republic of Southern Sudan. In total, the dialysis unit has about 90–100 patients. We enrolled 80 consecutive patients aged 18 years and above from November 2017 to March 2018. Patients were eligible for inclusion if they had been on chronic haemodialysis for at least 3 months.

Baseline characteristics were collected by reviewing the patients’ charts and conducting patient interviews using a pretested questionnaire. Data included age, sex, comorbidities, date of initiation of dialysis, distance travelled to access dialysis and drug treatment history for hypertension.

Blood pressure measurements and laboratory tests

Blood pressure (BP) was measured before dialysis while the patient was lying down. Measurements were taken twice in each arm (except for patients with an arteriovenous fistula access on the arm) using a Welch Allyn DS66 Trigger Aneroid machine (Welch Allyn, USA). The higher reading was recorded. Pre-dialysis blood samples were drawn for white count, haemoglobin, serum albumin, serum creatinine, serum calcium and phosphate, and a fasting lipid profile. Blood counts were performed using a Sysmex XN 1000 CBC machine (Sysmex, USA) whereas all chemistry tests were conducted on serum using a Roche cobas® 6000 analyser (Roche Diagnostics, USA). Results for HIV, hepatitis B and C serology were abstracted from the patients’ charts. Creatinine was measured using the Jaffe method traceable to an isotope dilution mass spectrometry method [10] and estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI formula without use of the coefficient for African Americans [11]. Serum albumin was measured using capillary zone electrophoresis.

Uncontrolled hypertension was defined by systolic BP >140 mmHg or diastolic BP >90 mmHg in a patient on anti-hypertensive medication [12]. Anaemia was defined as a haemoglobin concentration < 11 g/dL. Dyslipidaemia was defined per ACC/AHA guidelines as any of: i) HDL <35 mg/dL, ii) LDL >100 mg/dL or iii) total cholesterol >190 mg/dL [13]. Hypoalbuminaemia was defined as serum albumin <35 g/L.

Echocardiography

M-mode, 2D and doppler echocardiography was performed using a Philips HD 11XE echocardiography machine (Philips, USA). For each participant, the cardiac echo was performed within 24 hours after the first dialysis session of the week. The examination was performed in the outpatient echo laboratory by a technician and all results were reviewed and reported by one cardiologist. Echo was performed according to the American Society of Echocardiography (ASE) and European Association of Cardiovascular Imaging (EACVI) guidelines for the assessment of chamber size and function, valves and pericardium [14-16]. Dimensions for left ventricular posterior wall thickness (LVPWT) and interventricular wall thickness (IVST) were measured at end diastole, while left ventricular internal diameter was measured at end systole (LVIDs) and end diastole (LVIDd). Ejection fraction was calculated using the modified Simpson’s rule. Standard four views (subcostal, four-chamber, and parasternal long and short axis) were used to evaluate patients for pericardial effusion, which was graded as mild (<10 mm), moderate (10–20 mm) and large (>20 mm) as per the European Society of Cardiology guidelines [17]. Heart valve anatomy and function were assessed and these parameters together with those of chamber function were used to grade valvular lesions.
LVH was defined as interventricular septum and/or left ventricular posterior wall diameter >11 mm [18]. Systolic dysfunction was defined by evidence of an EF <50% [19]. Left ventricular diastolic dysfunction was defined as more than two of the following: i) E/E’ >14, ii) TR velocity >2.8 m/s, iii) LA volume index > 34 mL/m² and iv) septal/medial e-velocity <7/10 m/s in a patient with an ejection fraction >50%, according to algorithm A of the 2016 ASE/EACVI guidelines [16].

**Statistical analysis**

Data were double entered into EpiData version 3.1 and exported to STATA version 14.0 (STATA Corp, Texas, USA) for analysis. Continuous variables were reported as mean ± standard deviation (SD) for normally distributed data or median with interquartile ranges (IQR) for non-normally distributed variables. Categorical variables were expressed as frequency (percent). The primary outcome was the prevalence and patterns of echo abnormalities and these are presented as frequency (percentage) or proportions. The secondary outcome, demographic and clinical factors associated with LVH and diastolic dysfunction, was evaluated by logistic regression. Those factors with P <0.2 on bivariable analysis were included in the multivariable regression model. Odds ratios and 95% confidence intervals were used to quantify associations and results were considered statistically significant when the P value was <0.05.

**Ethical approval**

The Makerere University School of Medicine Research and Ethics Committee approved the study (reference number 2017-135).

**RESULTS**

We screened 92 patients and twelve were excluded for various reasons (Figure 1). A total of 80 patients, aged 19 to 78 years, were enrolled in the study. The patient characteristics are summarized in Table 1. The mean age was 49 years, 66% were male and the median duration on dialysis was 9.5 months. One-third of the patients had to travel >50 km to access haemodialysis. All had hypertension with approximately three-quarters having uncontrolled blood pressure despite taking antihypertensive medications. Thirty-one patients (39%) had diabetes mellitus and forty-five (56%) had dyslipidaemia.

Baseline echocardiographic parameters used to define structural abnormalities (LVH, systolic and diastolic dysfunction) were similar in male and female participants (Table 2).

Seventy-four patients (93%) had at least one cardiac echo abnormality and 24 (30%) had at least three abnormalities (Table 3). We found that 68% had LVH and 64% had left ventricular diastolic dysfunction. Most patients had both LVH and diastolic dysfunction (Figure 2). Although these abnormalities were more common in older patients, there was still a high prevalence in the group <45 years (Figure 3).

Thirty-five patients (44%) had mild to moderate valvular lesions (Table 3), including 37% with mitral regurgitation, 26% with both mitral and tricuspid valve regurgitation, 17% with both mitral and aortic valve regurgitation, 17% with
Table 1. Demographic and clinical characteristics of patients (n = 80).

|                                      | Frequency (n) | Percentage (%) |
|--------------------------------------|---------------|----------------|
| Male sex                             | 53            | 66.2           |
| Age in years                         | 49 ± 16       |                |
| Distance from the hospital (km)      |               |                |
| <50                                  | 52            | 65.0           |
| >50                                  | 28            | 35.0           |
| HIV positive                         | 7             | 8.8            |
| Diabetes mellitus                    | 31            | 39.2           |
| Cardiovascular disease               | 13            | 16.3           |
| Poor BP control                      | 62            | 77.5           |
| Dyslipidaemia                        | 34            | 56.3           |
| BMI (kg/m²)                          |               |                |
| <18.5                                |               | 5.1            |
| 18.5–24.9                            | 55            | 70.5           |
| 25–29.9                              | 15.4          | 15.4           |
| ≥30                                  | 7             | 9.0            |
| Creatinine µmol/L                    | 956 ± 413     |                |
| eGFR (mL/min/1.73 m²)                | 6.4 ± 2.9     |                |
| Systolic BP (mmHg)                   | 155.0 ± 26.4  |                |
| Diastolic BP (mmHg)                  | 89.8 ± 16.3   |                |
| Antihypertensive medications         |               |                |
| ARBs/ACEIs                           | 63            | 78.8           |
| Calcium channel blockers             | 73            | 91.2           |
| Beta-blockers                        | 39            | 48.8           |
| Diuretics                            | 34            | 42.5           |
| Other                                | 4             | 36.4           |
| Duration on dialysis (months)        |               |                |
| Median (IQR)                         | 9.5 (4–24)    |                |
| <6                                   | 27            | 33.8           |
| ≥6                                   | 53            | 66.2           |
| Type of vascular access              |               |                |
| Catheter                             | 62            | 77.5           |
| Arteriovenous fistula                | 17            | 21.3           |
| Graft                                | 1             | 1.3            |
| Ca x Pi (mmol²/L²)                   |               |                |
| <4.4                                 | 70            | 87.5           |
| ≥4.4                                 | 10            | 12.5           |
| Anaemia (Hb < 11 g/dL)               | 63            | 78.8           |
| Albumin (<35 g/L)                    | 41            | 51.2           |

Abbreviations: eGFR, estimated glomerular filtration rate; HIV, human immunodeficiency virus; Hb, haemoglobin; Ca x Pi, calcium phosphate product.
only tricuspid regurgitation and 2.9% with only aortic regurgitation. All regurgitant valves were secondary to annular dilatation. None of the patients had primary valvar disease or stenosis of the valves. Only five of the 35 patients with valve lesions (14%) had mitral annular calcifications and two (5.7%) had aortic valve calcifications. Thirteen of the 80 patients (16%) had small pericardial effusions and none had moderate or large effusions, or pericardial tamponade.

The associations of potential risk factors with the occurrence of left ventricular hypertrophy are shown in Tables 4 and 5, and the associations of factors associated with diastolic dysfunction are shown in Tables 6 and 7.

**DISCUSSION**

We have found a high prevalence of echocardiographic abnormalities among Ugandan patients on haemodialysis.
This is consistent with data from the literature, particularly in studies conducted in African populations [6,8]. The reason for the high prevalence in this young population could be that our patients with CKD and ESRD present late, when they already have cardiovascular complications [20,21].

As in other studies, LVH was the most prevalent cardiac abnormality [6,8,22]. Although the pathogenesis is multifactorial, hypertension and anaemia are important determinants of increased left ventricular mass [23] and these factors were highly prevalent in our study population. The high prevalence of LVH may reflect inadequate primary health care and treatment of risk factors like hypertension, and poor access to specialized care. Many patients had to travel for more than 50 km to access dialysis, and this may have resulted in late referral and dialysis initiation. Receiving only two treatment sessions per week, as opposed to the standard three sessions, predisposes to chronic fluid overload and limits the effective removal of uraemic toxins, which are all risk factors for LVH.

Diastolic dysfunction was the second-most common cardiac abnormality in our study and its prevalence was comparable to what has been reported previously [6,20]. Hickson et al. [20] found the prevalence of diastolic dysfunction ≥grade 2 as high as 78% at the start of haemodialysis. The risk factors for diastolic dysfunction are mostly similar to those for LVH, including hypertension and volume overload [7, 24]; however, LVH itself is one of the biggest risk factors for diastolic dysfunction [25] and our study confirms data from previous literature that LVH and diastolic dysfunction often coexist.

LVH and diastolic dysfunction are independently associated with cardiovascular death among patients on haemodialysis [5]. Barberato et al. [26] studied a young cohort (52 ± 16 years) whose age was comparable to our study population and showed that diastolic dysfunction ≥grade 2 predicted cardiovascular events including heart failure, myocardial infarction and sudden cardiac death. These patients had no previous history of CVD.

The prevalence of pericardial effusion in our study is comparable to the 13% reported by Kaze et al. in Cameroon [8] among a similar group of patients on haemodialysis twice a week. This is lower than the 21.7% reported by Babua et al. among CKD patients, half of whom had ESRD, not on dialysis [9]. This study highlights the fact that dialysis improves uraemic pericarditis among patients with ESRD.

Only 10% of our patients had systolic dysfunction, comparable to the 13% reported by Kaze et al. in Cameroon [8]. As regards valvular lesions, our findings are similar to those of previous studies in terms of prevalence and type of valve lesions. Several studies have reported that these lesions are more frequent in patients with ESRD on haemodialysis and that they occur at a younger age compared to the general population [20]. Aortic valve calcification with stenosis has been found to be common in dialysis patients [27]. This was not the case in our study and may be explained by the fact that ours were young patients with a relatively short period on dialysis.

Our study has some limitations. First, it is a relatively small, single-centre study; however, it was conducted at the largest dialysis centre in Uganda and more than 90% of the available patients were included. Second, given the cross-sectional design of the study, the longer-term outcomes and complications of the observed cardiac abnormalities could not be evaluated. Third, echocardiography is not as

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**Table 3. Spectrum of echocardiographic abnormalities among patients on haemodialysis.**

| Echo abnormalities | Frequency (n) | Percentage (%) |
|--------------------|--------------|----------------|
| LVH                | 54           | 67.5           |
| Diastolic dysfunction | 51        | 63.8           |
| Systolic dysfunction | 8          | 10.0           |
| Pericardial effusion | 13         | 16.2           |
| Abnormal wall motion | 1           | 1.2            |
| Valvular lesions   | 35           | 43.8           |
| MR                 | 13           | 37.2           |
| MR and TR          | 9            | 25.7           |
| MR and AR          | 6            | 17.1           |
| TR                 | 6            | 17.1           |
| AR                 | 1            | 2.9            |
| Echo abnormalities |              |                |
| 0                  | 6            | 7.5            |
| 1                  | 21           | 26.2           |
| 2                  | 29           | 36.3           |
| ≥3                 | 24           | 30.0           |

*Abbreviations: LVH, left ventricular hypertrophy; MR, mitral valve regurgitation; TR, tricuspid valve regurgitation; AR, aortic valve regurgitation.*
### Table 4. Factors associated with left ventricular hypertrophy.

|                        | No LVH | LVH | Odds ratio (95% CI) | P value |
|------------------------|--------|-----|---------------------|---------|
| **Sex**                |        |     |                     |         |
| Male                   | 14 (26.4) | 39 (73.6) | 1                   |         |
| Female                 | 12 (44.4) | 15 (55.6) | 0.44 (0.17–1.19) | 0.107   |
| **Age (years)**        |        |     |                     |         |
| <45                    | 13 (41.9) | 18 (58.1) | 1                   |         |
| ≥45                    | 13 (26.5) | 36 (73.5) | 2.00 (0.77–5.19) | 0.155   |
| **Distance from hospital (km)** |        |     |                     |         |
| <50                    | 16 (30.8) | 36 (69.2) | 1                   |         |
| ≥50                    | 10 (35.7) | 18 (64.3) | 0.8 (0.30–2.11) | 0.653   |
| **Dialysis duration (months)** |        |     |                     |         |
| <6                     | 10 (37.0) | 17 (63.0) | 1                   |         |
| ≥6                     | 16 (30.2) | 37 (69.8) | 1.36 (0.51–3.61) | 0.537   |
| **Interdialytic weight gain (kg)** |        |     |                     |         |
| ≤2                     | 19 (35.2) | 35 (64.8) | 1                   |         |
| >2                     | 6 (25.0) | 18 (75.0) | 1.63 (0.55–4.79) | 0.376   |
| **Type of access**     |        |     |                     |         |
| Catheter              | 22 (35.5) | 40 (64.5) | 1                   |         |
| AV fistula/graft      | 4 (22.2) | 14 (77.8) | 1.93 (0.56–6.56) | 0.295   |
| **BMI (kg/m²)**       |        |     |                     |         |
| <18.5                 | 2 (50.0) | 2 (50.0) | 0.50 (0.05–4.97) | 0.554   |
| 18.5–24.9             | 18 (32.7) | 37 (67.3) | 1                   |         |
| 25–29.9               | 4 (33.3) | 8 (66.7) | 1.03 (0.27–3.86) | 0.968   |
| ≥30                   | 1 (14.3) | 6 (85.7) | 3.0 (0.26–34.20) | 0.376   |
| **BP controlled**     |        |     |                     |         |
| No                    | 5 (27.8) | 13 (72.2) | 1                   |         |
| Yes                   | 21 (33.9) | 41 (66.1) | 0.75 (0.23–2.39) | 0.628   |
| **Diabetes**          |        |     |                     |         |
| No                    | 5 (27.8) | 13 (72.2) | 1                   |         |
| Yes                   | 21 (33.9) | 41 (66.1) | 0.75 (0.23–2.39) | 0.628   |
| **Dyslipidaemia**     |        |     |                     |         |
| No                    | 10 (28.6) | 25 (71.4) | 1                   |         |
| Yes                   | 16 (35.6) | 29 (64.4) | 0.73 (0.28–1.88) | 0.509   |
| **Ca x Pi (mmol²/L²)** |        |     |                     |         |
| <4.4                  | 24 (34.3) | 46 (65.7) | 0.31 (0.04–2.81) | 0.304   |
| ≥4.4                  | 1 (14.3) | 6 (85.7) | 1                   |         |
| **Albumin (g/L)**     |        |     |                     |         |
| <35                   | 11 (26.8) | 30 (73.2) | 1                   |         |
| ≥35                   | 15 (38.5) | 24 (61.2) | 0.58 (0.22–1.51) | 0.269   |
| **Anaemia**           |        |     |                     |         |
| Yes                   | 21 (33.3) | 42 (66.7) | 0.83 (0.26–2.67) | 0.760   |
| No                    | 5 (29.4) | 12 (70.6) | 1                   |         |

Abbreviations: LVH, left ventricular hypertrophy; Ca x Pi, calcium phosphate product.
sensitive as measurements taken during cardiac catheterisation for the diagnosis of diastolic dysfunction or as sensitive as MRI for the diagnosis of asymmetric LVH. Despite these limitations, we believe that our observations are important and warrant further research into cardiac abnormalities in this young population of patients on haemodialysis.

**CONCLUSIONS**

Our study confirmed a high prevalence of cardiac abnormalities among this relatively young African population of patients with ESRD on chronic haemodialysis. Additional studies to examine risk factors associated with these abnormalities as well as their long-term outcomes are needed. We recommend that echocardiography be included in the routine evaluation of all patients on haemodialysis, to identify abnormalities that indicate high risk for cardiovascular events and to help plan early intervention and possibly improve patient outcomes.

We also recommend that the government allocate additional resources and provide the standard three haemodialysis sessions per week to contribute to better cardiac and overall outcomes for these patients.

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| Table 5. Multivariable analysis of factors associated with left ventricular hypertrophy. |
|---------------------------------|---------------------------------|-----------------|
|                                | Adjusted odds ratio | 95% confidence interval | P value |
| Sex                            | 1                          |                          |        |
| Male                           | 0.509                      | 0.17–1.48               | 0.216  |
| Female                         | 1                          |                          |        |
| Age (years)                    | 1                          |                          |        |
| <45                            | 2.142                      | 0.69–6.63               | 0.186  |
| ≥45                            | 1                          |                          |        |
| BP controlled                  | 1                          |                          |        |
| No                             | 0.763                      | 0.19–3.01               | 0.699  |
| Yes                            | 1                          |                          |        |
| Diabetes                       | 1                          |                          |        |
| No                             | 1.693                      | 0.56–5.17               | 0.353  |
| Yes                            | 1                          |                          |        |
| Anaemia                        | 1                          |                          |        |
| <6                             | 1.356                      | 0.32–5.74               | 0.679  |
| ≥6                             | 1                          |                          |        |
| Ca × Pi (mmol²/L²)             | 0.328                      | 0.03–3.41               | 0.351  |
| <4.4                           | 1                          |                          |        |
| ≥4.4                           | 1                          |                          |        |

Abbreviations: Ca × Pi, calcium phosphate product.
Table 6. Factors associated with diastolic dysfunction.

|                                | No diastolic dysfunction n (%) | Diastolic dysfunction n (%) | Odds ratio (95% CI) | P value |
|--------------------------------|--------------------------------|----------------------------|---------------------|--------|
| **Sex**                        |                                |                            |                     |        |
| Male                           | 20 (37.1)                      | 33 (62.3)                  |                     |        |
| Female                         | 9 (33.3)                       | 18 (66.7)                  | 1.21 (0.45–3.21)    | 0.699  |
| **Age (years)**                |                                |                            |                     |        |
| <45                            | 15 (48.4)                      | 16 (51.6)                  |                     |        |
| ≥45                            | 14 (28.6)                      | 35 (71.4)                  | 2.34 (0.92–5.98)    | 0.075  |
| **Distance from hospital (km)**|                                |                            |                     |        |
| <50                            | 21 (40.4)                      | 31 (59.6)                  |                     |        |
| ≥50                            | 8 (28.6)                       | 20 (71.4)                  | 1.69 (0.63–4.55)    | 0.297  |
| **Dialysis duration (months)** |                                |                            |                     |        |
| <6                             | 14 (51.9)                      | 13 (48.2)                  |                     |        |
| ≥6                             | 15 (28.3)                      | 38 (71.2)                  | 2.73 (1.04–7.14)    | 0.041  |
| **Interdialytic weight gain (kg)**|                              |                            |                     |        |
| ≤2                             | 20 (37.0)                      | 34 (63.0)                  |                     |        |
| >2                             | 7 (29.2)                       | 17 (70.8)                  | 1.43 (0.51–4.03)    | 0.501  |
| **Type of access**             |                                |                            |                     |        |
| Catheter                       | 24 (38.7)                      | 38 (61.3)                  |                     |        |
| AV fistula/graft               | 5 (27.8)                       | 13 (72.2)                  | 1.64 (0.52–5.19)    | 0.398  |
| **BP controlled**              |                                |                            |                     |        |
| No                             | 5 (27.8)                       | 13 (72.2)                  |                     |        |
| Yes                            | 24 (38.7)                      | 38 (61.3)                  | 0.61 (0.19–1.92)    | 0.398  |
| **Diabetes**                   |                                |                            |                     |        |
| No                             | 20 (41.7)                      | 28 (58.3)                  |                     |        |
| Yes                            | 9 (29.0)                       | 22 (71.0)                  | 1.74 (0.67–4.58)    | 0.258  |
| **Dyslipidaemia**              |                                |                            |                     |        |
| No                             | 16 (45.7)                      | 19 (54.3)                  |                     |        |
| Yes                            | 13 (28.9)                      | 32 (71.1)                  | 2.07 (0.82–5.23)    | 0.123  |

Abbreviations: LVH, left ventricular hypertrophy; Ca x Pi, calcium phosphate product.
Table 7. Multivariable analysis of factors associated with diastolic dysfunction.

|                        | Adjusted odds ratio | 95% confidence interval | P value |
|------------------------|---------------------|-------------------------|---------|
| Sex                    |                     |                         |         |
| Male                   | 1                   |                         |         |
| Female                 | 1.321 (0.44–3.95)   |                         | 0.618   |
| Age (years)            |                     |                         |         |
| <45                    | 1                   |                         |         |
| ≥45                    | 2.515 (0.84–7.50)   |                         | 0.098   |
| BP controlled          |                     |                         |         |
| No                     | 1                   |                         |         |
| Yes                    | 1.131 (0.30–4.26)   |                         | 0.856   |
| Diabetes               |                     |                         |         |
| No                     | 1                   |                         |         |
| Yes                    | 1.748 (0.59–5.17)   |                         | 0.313   |
| Dialysis duration (months) |                 |                         |         |
| <6                     | 1                   |                         |         |
| ≥6                     | 2.771 (0.94–8.15)   |                         | 0.064   |
| Ca × Pi (mmol²/L²)     |                     |                         |         |
| <4.4                   | 0.246 (0.02–2.67)   |                         | 0.251   |
| ≥4.4                   | 1                   |                         |         |

Abbreviations: Ca × Pi, calcium phosphate product.

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