Gender disparities in pulmonary hypertension at a tertiary centre in Cameroon

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Background. Pulmonary hypertension (PH) is a potent cause of heart failure and has been little investigated in the African setting.

Objective. To investigate the effects of gender on the clinical presentation, echocardiographic features and outcomes of patients with PH in Douala, Cameroon.

Methods. A prospective cohort study was conducted from March 2012 to December 2013 as part of the Pan African Pulmonary Hypertension Cohort study. PH was diagnosed by echocardiography and defined as a right ventricular systolic pressure >35 mmHg in the absence of acute right heart failure. Patients were followed up for a maximum of 12 months for primary endpoint mortality.

Results. In total, 130 patients with PH were recruited; 71 (54.6%) were women. The median age was 59.2 years for men and 58.3 years for women (p=0.76). Active smoking and alcohol use were more frequent in men than women (both p<0.001), but women had greater exposure to indoor cooking fumes than men (p<0.001). Previous tuberculosis infection (11.3% v. 1.7%) and S3 gallop rhythm (30.9% v. 11.9%) were more common in women (both p<0.03). Women had a significantly higher mean systolic blood pressure (134 mmHg v. 125 mmHg; p=0.04) and pulse pressure (53.8 mmHg v. 44.9 mmHg; p=0.01) and a lower mean haemoglobin concentration (10.4 g/dL v. 12.4 g/dL; p=0.05) compared with men. Echocardiographic left ventricular (LV) systolic dysfunction was more frequent in men: mean LV ejection fraction 51.3% (p=0.01) and mean fractional shortening 21.4% v. 28.6% (p=0.01). The overall mortality rate was 20.3%, and rates were similar in the two groups (Kaplan-Meier log rank 1.1; p=0.30).

Conclusions. Despite differences in baseline characteristics including cardiovascular risk factors, mortality rates on follow-up were similar in men and women in this study. However, these different baseline characteristics probably suggest differences in the pathogenesis of PH in men and women in our setting that need further investigation.

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Pulmonary hypertension (PH) describes a group of disorders resulting from an increase in pulmonary vascular resistance, pulmonary blood flow, pulmonary venous pressure, or a combination of these.1 PH is defined as an increase in mean pulmonary arterial pressure of ≥25 mmHg at rest, assessed by right heart catheterisation (RHC).2 Based on shared pathological and haemodynamic characteristics and therapeutic approaches, PH is currently classified into five subtypes, namely PH groups 1 - 5.3 Epidemiological studies from Western countries suggest that the prevalence of PH among African Americans is higher than that among Caucasians,4 while in a community-based echocardiographic cohort study in Armadale, Australia, a prevalence of 9.1% and high mortality were observed.5

In sub-Saharan Africa (SSA) however, there is some evidence that, based on the high prevalence of risk factors such as hypertension and other endemic communicable diseases such as schistosomiasis and HIV infection, the prevalence of PH may be higher than in Western countries.6 Moreover, it has been suggested that left heart disease is the most frequent cause of PH worldwide.7,8

PH is a disease with devastating effects on quality of life and life expectancy, and is a potent cause of heart failure (HF) in general.9,10 Indeed, one autopsy study from South Africa identified PH as one of the commonest causes of death, accounting for...
31% of all cardiovascular deaths.\textsuperscript{[13]} The Pan African Pulmonary Hypertension Cohort (PAPUCO) study was established to investigate the epidemiology, causes and natural history of PH in Africa.\textsuperscript{[14,15]} While the epidemiology of PH in Africa remains largely unknown, it is important to highlight the fact that clinical features of PH are often subtle and nonspecific, especially in the early stages, and may mimic other diseases, so that PH remains undiagnosed. Risk factors, epidemiology, clinical characteristics and outcomes of HF have gender variations that have been described among Caucasians.\textsuperscript{[16-18]} Recent data from the largest HF registry in SSA suggest that HF was more likely to have been caused by rheumatic heart disease in women and conventional modifiable cardiovascular risk factors in men, although outcomes appeared to be similar.\textsuperscript{[19]} The PAPUCO study presents a broad picture of PH in Africa,\textsuperscript{[11]} but country-specific data on gender differences in the characteristics and outcomes of PH in Africa are still lacking.

**Objective**

To investigate gender differences in clinical characteristics, echocardiographic findings and outcomes in a cohort of patients with PH in Douala, Cameroon.

**Methods**

**Study design and setting**

The PAPUCO study design has been described in detail,\textsuperscript{[14]} and was registered on ClinicalTrials.gov (NCT02265887). In short, PAPUCO was a prospective pan-African multicentre cohort study of patients newly diagnosed with PH involving 12 specialist centres in SSA including Cameroon. The registry adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational outcomes.

**Eligibility**

Through convenient sampling, all adult patients (≥18 years of age) who presented to the PAPUCO centre in Douala, Cameroon, with newly diagnosed PH were invited to take part in the study.

**Diagnosis of PH**

Diagnosis of PH was based on echocardiographic measurement of the right ventricular systolic pressure (RVSP) in the absence of acute right HF, reflecting pulmonary artery systolic pressure in the absence of pulmonary artery stenosis. The RVSP was obtained by measuring the tricuspid regurgitant jet velocity via a pulsed Doppler study of the tricuspid valve. The gradient between right atrium (RA) and right ventricle (RV) was obtained using the simplified Bernoulli equation \((4 \times \text{tricuspid jet velocity}^2)\). This value was then added to the RA pressure (fixed value from 5 to 20 mmHg estimated by measuring the inferior vena cava size and its change with spontaneous respiration during echocardiography) for RVSP. A value of >35 mmHg was considered PH. Details of the echocardiographic assessment have been described previously.\textsuperscript{[14]}

**Data collection and study procedures**

Patients were interviewed and examined and data were entered on an electronic case report form.\textsuperscript{[14]} General and clinical characteristics included age, sex and risk factors for cardiovascular disease (CVD). A family history of CVD was defined as a documented family history of CVD; hypertension as a systolic (diastolic) blood pressure of ≥140 (90) mmHg, a documented history of hypertension or prescribed antihypertensive medication; presence of diabetes as a fasting blood glucose level of ≥7 mmol/L, a documented history of diabetes or prescribed blood sugar-lowering agents; smoking as never having smoked, being an ex-smoker (if the patient had smoked for at least 3 years in the past, but had stopped at time of presentation) or being a current smoker (patients who smoked at least one cigarette per day at the time of presentation); and alcohol abuse as intake of either more than three (two for women) standard glasses of wine per day or more than ten (five for women) local beers (one local beer contains 28 g of alcohol) per week. The presence of symptoms (dyspnoea, fatigue, cough, palpitation) and signs on physical examination (distended jugular vein, pedal oedema, ascites, S3 gallop, P2 sound) was ascertained. The 6-minute walk test was also performed and the distance covered recorded in patients who had no contraindications. Patients underwent 12-lead electrocardiography, and standard blood results were obtained.

**Follow-up and outcome assessment**

From the time of recruitment, patients were followed up for 12 months. During the follow-up visit or interview, conducted either in person or via telephone calls, patients and their relatives were questioned about the number of hospitalisations since recruitment (if patients were alive); if they were dead, the time lapse from recruitment to death was recorded.

**Data and statistical analysis**

Data were analysed using the Statistical Package for the Social Sciences IBM statistical software version 20 for Windows (SPSS Inc., USA). Categorical variables were summarised using frequencies and proportions, while continuous variables were summarised using means and standard deviations or medians with 25th and 75th percentiles. Group comparisons used \(\chi^2\) and Fisher's exact (where applicable) tests for categorical variables and the independent-samples \(t\)-test for continuous variables. The Kaplan-Meier estimator was used to assess the risk of death during follow-up, with group comparisons based on the log-rank test. The Cox proportional hazard model was used to further investigate the differential effect of gender on mortality. Statistical significance was set at \(p<0.05\).

**Ethical considerations**

Approval was obtained from the Institutional Review Board of the Faculty of Health Sciences, University of Buea (ref. no. 2013/0080/UB/FHS/IRB) and Douala General Hospital, Cameroon (ref. no. 179 AR/MINSANTE/HGD/DM/12/12) as well as from the National Ethics Committee (ref. no. 2013/11/363/L/CNERSH/SP). The PAPUCO study was approved by the University of Cape Town's Human Research Ethics Committee (ref. no. 241/2011). The study adhered to the Declaration of Helsinki and all participants provided informed written consent prior to participation.

**Results**

**Sociodemographic characteristics, risk factor profile and clinical findings**

During the study period, 1 855 patients underwent echocardiographic examination. Of these, 130 (7.0%) had an RVSP >35 mmHg and were included in the study. All were of black African descent, and 71 (54.6%) were women. Table 1 summarises the baseline sociodemographic characteristics, risk factor profile and clinical findings of the cohort on a gender-specific basis. The mean age of the patients was 59 years, with no difference between men and women \((p=0.76)\). Men were more likely to be in the age group 55 - 64 years, while the majority of women were aged ≥75 years. Fig. 1 depicts the age distribution of the study population according to gender. Cardiovascular risk factors...
were prevalent in our cohort, hypertension (55.9% v. 52.1%), diabetes (15.3% v. 14.1%) and hypercholesterolaemia (16.9% v. 14.1%) being similarly distributed between men and women. Alcohol abuse (44.1% v. 14.1%) and current or previous smoking (32.2% v. 11.2%) were significantly more common in men (both \( p < 0.01 \)), while exposure to indoor cooking fumes (36.6% v. 3.4%) and previous tuberculosis (TB) infection (11.3% v. 1.7%) were more common in women (both \( p < 0.03 \)).

At presentation, similar proportions of men and women were in New York Heart Association (NYHA) classes III and IV (74.6% v. 70.4%), although S3 gallop (30.9% v. 11.9%; \( p = 0.011 \)) was more common in women. Mean systolic blood pressure (134 mmHg v. 125 mmHg; \( p = 0.041 \)) and mean pulse pressure (53.9 mmHg v. 44.9 mmHg; \( p = 0.01 \)) were also significantly higher in women than in men.

### Electrocardiographic, laboratory and echocardiographic findings

Table 2 summarises electrocardiographic and laboratory findings at presentation. No gender-specific differences were identified on
electrocardiography. The mean haemoglobin concentration was lower in women than in men (10.4 g/dL v. 12.4 g/dL; \( p = 0.042 \)), while apparent differences in other biological characteristics did not reach statistical significance. Table 3 summarises the echocardiographic findings. Compared with women, men had significant left ventricular (LV) systolic dysfunction: mean LV end-systolic diameter 47.3 mm v. 38.6 mm, \( (p < 0.01) \), mean LV ejection fraction 42.6 v. 51.5 \( (p = 0.01) \), and mean fractional shortening 21.4 mm v. 28.6 mm \( (p = 0.01) \). Overall the mean RVSP was 55.6 mmHg without gender difference. A borderline difference in the severity of mitral regurgitation was apparent between men and women \( (p = 0.070) \).

Aetiology of pulmonary hypertension, severity grading and outcome

Table 4 summarises subgroup classification of PH, severity at presentation and outcome in a subset of patients. Overall, 78.5% \( (n=102) \) of the cohort had PH caused by left heart disease, which was similar in men and women (81.3% v. 76.0%; \( p=0.05 \)). Chronic thromboembolic PH was the least observed cause of PH in this study population (one patient). The majority (76.9%) of patients had moderate or severe PH (RVSP ≥45 mmHg). No difference was found between men and women.

We recorded 29 deaths (20.3%) and 15 readmissions (11.5%) after a median follow-up of 60 days (interquartile range 30 - 150). The in-hospital mortality rate was 18.5%. Kaplan-Meier estimator (log rank 1.1; \( p=0.30 \)) as well as age-adjusted Cox regression models did not show a significant difference in survival between men and women (hazard ratio 0.82 (95% confidence interval 0.38 - 1.74); \( p=0.601 \)) (Table 5).

**Table 2. Baseline electrocardiographic and laboratory characteristics of patients with pulmonary hypertension in Douala, Cameroon, 2014**

| Variables                      | Males (N=59) | Females (N=71) | Total (N=130) | \( p\)-value* |
|--------------------------------|--------------|----------------|---------------|--------------|
| Electrocardiographic findings, \( n \)(%) |              |                |               |              |
| Atrial fibrillation            | 16 (27.1)    | 19 (26.8)      | 35 (26.9)     | 0.848        |
| Normal sinus rhythm            | 15 (25.4)    | 22 (30.9)      | 37 (28.5)     | 0.320        |
| AV block type I                | 8 (13.5)     | 9 (12.7)       | 17 (13.1)     | 1            |
| AV block type III              | 1 (1.7)      | 2 (2.8)        | 3 (2.3)       | 1            |
| Sinus tachycardia              | 21 (35.6)    | 16 (22.5)      | 37 (28.5)     | 0.231        |
| RV hypertrophy                 | 6 (10.2)     | 6 (8.4)        | 12 (9.2)      | 1            |
| LV hypertrophy                 | 13 (22.0)    | 11 (15.5)      | 24 (18.5)     | 0.645        |
| Laboratory findings, mean (SD) |              |                |               |              |
| Haemoglobin (g/dL)             | 12.4 (2.3)   | 10.4 (2.0)     | 11.4 (2.2)    | 0.042\(\dagger\) |
| Haematocrit (%)                | 37.0 (7.5)   | 33.7 (6.1)     | 35.9 (6.8)    | 0.220        |
| Platelet count (10\(^9\)/L)   | 192.6 (84.4) | 258.4 (255.8)  | 225.1 (191.2) | 0.123        |
| Sodium (mmol/L)                | 138.0 (9.7)  | 137.3 (5.1)    | 137.7 (7.9)   | 0.708        |
| Potassium (mmol/L)             | 4.1 (0.9)    | 4.1 (0.8)      | 4.0 (0.8)     | 0.911        |
| Urea (mmol/L)                  | 7.5 (12.0)   | 11.1 (22.0)    | 9.9 (35.1)    | 0.416        |
| Creatinine (µmol/L)            | 93.6 (160.6) | 56.4 (63.2)    | 75.9 (124.9)  | 0.180        |
| Total cholesterol (mmol/L)     | 2.4 (1.3)    | 4.1 (2.8)      | 3.3 (2.0)     | 0.181        |
| HDL cholesterol (mmol/L)       | 0.5 (0.2)    | 0.6 (0.3)      | 0.5 (0.2)     | 0.667        |
| LDL cholesterol (mmol/L)       | 1.7 (1.1)    | 1.4 (0.9)      | 1.6 (1.0)     | 0.590        |
| Triglycerides (mmol/L)         | 1.2 (0.7)    | 1.1 (0.5)      | 1.2 (0.6)     | 0.779        |
| Fasting blood glucose (mmol/L) | 9.4 (9.4)    | 10.6 (7.8)     | 10 (8.3)      | 0.643        |
| C-reactive protein (nmol/L)    | 4 647.6 (4 247.6) | 3 695.2 (4 504.8) | 4 133.3 (4 323.8) | 0.601        |

AV = atrioventricular; RV = right ventricular; LV = left ventricular; SD = standard deviation; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

* \( p\)-values based on \( t\)-test, \( \chi^2 \) test or Fisher’s exact test, where appropriate.

\( \dagger\) Significant at \( p<0.05 \).

**Discussion**

In this prospective cohort of patients with PH from specialised centres in Douala, Cameroon, a number of gender-related differences were observed. At baseline, men had smoking as a modifiable risk factor for CVD, while women had greater exposure to indoor cooking fumes. Both presented at advanced stages of the disease, men seeming more affected. Anaemia was more common in women, while...
echocardiographic LV systolic dysfunction was frequent in men. Left heart disease was the main cause of PH in the two groups, and survival rates were similar.

The overall mean age in our study was 58 years, which is two decades younger than in reports from most industrialised countries,

Table 3. Baseline echocardiographic parameters of patients with pulmonary hypertension in Douala, Cameroon, 2014

| Variables                                      | Males (N=59) | Females (N=71) | Total (N=130) | p-value* |
|------------------------------------------------|--------------|----------------|--------------|----------|
| Echocardiographic measurement, mean (SD)       |              |                |              |          |
| Left atrial size (mm)                          | 47.4 (8.0)   | 46.9 (11.7)    | 47.1 (10.2)  | 0.701    |
| Left ventricular end-systolic diameter (mm)    | 47.3 (16.1)  | 38.6 (14.5)    | 42.5 (15.8)  | <0.01†   |
| Left ventricular end-diastolic diameter (mm)   | 56.2 (14.8)  | 51.7 (12.9)    | 53.7 (13.9)  | 0.072    |
| Left ventricular ejection fraction (%)         | 42.6 (19.9)  | 51.5 (18.9)    | 47.4 (19.8)  | 0.01†    |
| Fractional shortening (mm)                     | 21.4 (11.3)  | 28.6 (12.0)    | 22.8 (10.8)  | 0.01†    |
| Interventricular septal diastolic diameter (mm)| 12.1 (2.9)   | 10.6 (2.6)     | 11.3 (2.8)   | <0.001†  |
| Interventricular septal systolic diameter (mm) | 14.3 (3.6)   | 14.2 (4.7)     | 14.3 (4.2)   | 0.988    |
| Posterior wall diastolic diameter (mm)         | 12.1 (4.5)   | 10.7 (2.9)     | 11.3 (3.8)   | 0.030†   |
| Posterior wall systolic diameter (mm)          | 14.7 (4.0)   | 14.2 (3.3)     | 14.5 (3.6)   | 0.521    |
| RVSP (mmHg)                                    | 53.6 (14.9)  | 57.3 (16.5)    | 55.6 (15.8)  | 0.168    |
| TAPSE (mm)                                     | 18.1 (6.2)   | 19.3 (6.4)     | 18.7 (6.3)   | 0.541    |
| Cardiac chamber and valvular evaluations, n (%)|              |                |              |          |
| Right atrial dilatation                        |              |                |              | 0.478    |
| Mild                                           | 11 (18.6)    | 14 (19.7)      | 25 (19.2)    |          |
| Moderate                                       | 33 (55.9)    | 33 (46.5)      | 66 (50.8)    |          |
| Severe                                         | 8 (13.6)     | 16 (22.5)      | 24 (18.5)    |          |
| Right ventricular dilatation                   |              |                |              | 0.551    |
| Mild                                           | 18 (30.5)    | 21 (29.6)      | 39 (30.0)    |          |
| Moderate                                       | 21 (35.6)    | 21 (29.6)      | 42 (32.3)    |          |
| Severe                                         | 6 (10.2)     | 8 (11.3)       | 14 (10.8)    |          |
| Mitral regurgitation                           |              |                |              | 0.070    |
| Mild                                           | 20 (33.8)    | 25 (35.2)      | 45 (34.6)    |          |
| Moderate                                       | 19 (32.2)    | 12 (16.9)      | 31 (23.8)    |          |
| Severe                                         | 0            | 4 (5.6)        | 4 (3.1)      |          |
| Mitral stenosis                                |              |                |              | 0.302    |
| Mild                                           | 0            | 0              | 0            |          |
| Moderate                                       | 1 (1.7)      | 2 (2.8)        | 3 (2.3)      |          |
| Severe                                         | 1 (1.7)      | 5 (7.0)        | 6 (4.6)      |          |
| Aortic regurgitation                           |              |                |              | 0.389    |
| Mild                                           | 13 (22.0)    | 12 (16.9)      | 25 (19.2)    |          |
| Moderate                                       | 3 (5.1)      | 8 (11.3)       | 11 (8.5)     |          |
| Severe                                         | 0            | 0              | 0            |          |
| Aortic stenosis                                |              |                |              | 0.651    |
| Mild                                           | 0            | 0              | 0            |          |
| Moderate                                       | 0            | 1 (1.4)        | 1 (0.8)      |          |
| Severe                                         | 1 (1.7)      | 1 (1.4)        | 2 (1.5)      |          |
| Tricuspid regurgitation                        |              |                |              | 0.376    |
| Mild                                           | 13 (22.0)    | 15 (25.4)      | 28 (21.5)    |          |
| Moderate                                       | 39 (66.1)    | 39 (54.9)      | 78 (60.0)    |          |
| Severe                                         | 6 (10.2)     | 15 (21.1)      | 21 (16.2)    |          |

SD = standard deviation; RVSP = right ventricular systolic pressure; TAPSE = tricuspid annular plane systolic excursion.

*p-values based on t-test, χ2 test or Fisher's exact test, where appropriate.

†Significant at p<0.05.

The most frequent risk factors/comorbidities in the overall cohort were hypertension, diabetes, alcohol abuse and smoking. Alcohol abuse and active smoking were more common among men. This is similar to findings from the Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL) registry on pulmonary arterial hypertension in the USA,
and lung function testing. Among the risk factors for chronic lung disease, more intensively investigated. However, this requires additional equipment such as high-resolution computed tomography and lung function testing. Among the risk factors for chronic lung disease, a history of previous TB infection was also significantly more common in women than in men in our cohort. Unfortunately, the relationship to HIV infection (with a higher incidence of TB in HIV-infected individuals) could not be investigated, because HIV testing is not performed as a standard test in cardiac patients in the case in our cohort, probably owing to the high prevalence of TB in our setting, although obesity has been independently associated with PH, this finding could simply reflect the high prevalence of female obesity in our population. The reasons for some of our findings are unclear, but it remains possible that exposure of women to PH risk factors in our setting may be more complex and multifactorial than that of men, owing to a combination of the above risk factors (chronic lung disease and HIV) in varying degrees.

Table 4. Pulmonary hypertension subgroup classification, severity grading and outcome of patients with PH in Douala, Cameroon, 2014

| Variables | Males (N=59) | Females (N=71) | Total (N=130) | p-value* |
|-----------|--------------|---------------|---------------|----------|
| Subgroup classification of PH, n (%) | | | | 0.828 |
| PAH (group 1) | 5 (8.5) | 6 (8.4) | 11 (8.4) | |
| PHLHD (group 2) | 48 (81.3) | 54 (76.0) | 102 (78.5) | |
| PHLD (group 3) | 3 (5.1) | 4 (5.6) | 7 (5.4) | |
| CTEPH (group 4) | 0 | 1 (1.4) | 1 (0.8) | |
| Multifactorial (group 5) | 3 (5.1) | 6 (8.4) | 9 (6.9) | |
| Severity grading of PH, n (%) | | | | 0.241 |
| Mild PH (RVSP 36 - 44 mmHg) | 17 (28.8) | 13 (18.3) | 30 (23.1) | |
| Moderate PH (RVSP 45 - 59 mmHg) | 27 (45.8) | 32 (45.1) | 59 (45.4) | |
| Severe PH (RVSP ≥ 60 mmHg) | 15 (25.4) | 26 (36.6) | 41 (31.5) | |
| Outcome of PH | | | | |
| Overall mortality, n (%) | 15 (25.4) | 14 (19.7) | 29 (20.3) | 0.348 |
| In-hospital mortality, n (%) | 14 (23.7) | 10 (14.1) | 24 (18.5) | 0.211 |
| Overall time from presentation to death (days), mean (SD, range) | 78.0 (77.2, 10 - 270) | 121.5 (91.7, 7 - 270) | 99.0 (85.9, 7 - 270) | 0.170 |
| Overall time from presentation to death (days), median (IQR)† | 30 (20 - 150) | 90 (30 - 240) | 60 (30 - 150) | 0.303 |
| Overall re-hospitalisation rate through 360 days, n (%) | 6 (10.2) | 9 (12.6) | 15 (11.5) | 0.670 |
| All-cause 90-day mortality, n (%)† | 10 (16.9) | 7 (9.9) | 17 (13.1) | 0.122 |
| All-cause 180-day mortality, n (%)† | 14 (23.7) | 10 (14.1) | 24 (18.5) | 0.901 |
| All-cause 270-day mortality, n (%)† | 15 (25.4) | 14 (19.7) | 29 (22.3) | 0.303 |
| All-cause 360-day mortality, n (%)† | 15 (25.4) | 14 (19.7) | 29 (22.3) | 0.303 |

PH = pulmonary hypertension; PAH = pulmonary arterial hypertension; PHLHD = pulmonary hypertension due to left heart disease; PHLD = pulmonary hypertension due to lung disease or hypoxia; CTEPH = chronic thromboembolic pulmonary hypertension; RVSP = right ventricular systolic pressure; IQR = interquartile range; SD = standard deviation.

*Compared using the Kaplan-Meier log-rank test.
†p-values based on t-test, χ2 test or Fisher’s exact test, where appropriate.

Table 5. Age-adjusted Cox regression analysis of the influence of age and gender on mortality among patients with pulmonary hypertension in Douala, Cameroon, 2014

| Variables | Univariate analysis | Multivariate analysis |
|-----------|---------------------|----------------------|
|           | HR (95% CI)         | p-value   | HR (95% CI) | p-value   |
| Age       | 0.98 (0.95 - 1.00)  | 0.061     | 0.98 (0.96 - 1.00) | 0.081     |
| Gender    | 0.72 (0.34 - 1.51)  | 0.385     | 0.82 (0.38 - 1.74) | 0.601     |

HR = hazard ratio; CI = confidence interval.

where hypertension was a frequent comorbidity. Similarly, a cross-sectional survey in Tanzania recently highlighted the fact that women had a 50% lower odds of hypertension compared with men. The slight predominance of conventional modifiable risk factors for CVD among men in this cohort is similar to findings among patients with HF in Africa, but is contrary to reports from the EuroHeart Failure Survey. The finding of hypertension as the most frequent comorbidity is unsurprising, as over three-quarters of the patients had group 2 PH caused by left heart disease, which in our setting is frequently hypertensive heart disease with a final progression to left HF. Exposure to indoor cooking fumes, especially from burning wood, was significantly more frequent among women. It is common for women in Africa to cook over an open fireplace, particularly in rural settings. However, this is not the case in middle- and high-income countries. The contribution of this exposure to the occurrence, severity and outcome of PH in African women still needs to be explored, and group 3 PH, caused by chronic lung disease, more intensively investigated. However, this requires additional equipment such as high-resolution computed tomography and lung function testing. Among the risk factors for chronic lung disease, a history of previous TB infection was also significantly more common in women than in men in our cohort. Unfortunately, the relationship to HIV infection (with a higher incidence of TB in HIV-infected individuals) could not be investigated, because HIV testing is not performed as a standard test in cardiac patients in Cameroon. Also, women were generally more obese than men, although obesity has been independently associated with PH, this finding could simply reflect the high prevalence of female obesity in our population. The reasons for some of our findings are unclear, but it remains possible that exposure of women to PH risk factors in our setting may be more complex and multifactorial than that of men, owing to a combination of the above risk factors (chronic lung disease and HIV) in varying degrees.

The majority of our patients, particularly men, presented at advanced stage of the disease (NYHA III/IV). This is similar to reports from Nigeria, Australia and Portugal, where most patients present with features of advanced HF. This late presentation is probably due to nonspecific symptoms of PH in the early stages, as well as limited availability of diagnostic tools. Anaemia was observed more often in women than in men. Similar observations were made in The sub-Saharan Africa Survey of Heart Failure (THESUS-HF) registry, probably related to menstruation.

Atrial fibrillation, sinus tachycardia and LV hypertrophy were the main electrocardiographic abnormalities in our cohort. Although previous reports and clinical guidelines suggest that patients with PH have RV hypertrophy on electrocardiograms, this was not the case in our cohort, probably owing to the high prevalence of hypertension, LV dysfunction leading to LV hypertrophy; this consequently increases the left atrial pressure and may predispose to arrhythmias such as atrial fibrillation. Supraventricular
arrhythmias such as atrial fibrillation are, however, said to occur in advanced stages of PH and are associated with clinical deterioration, potentialy reveal different pathogeneses of PH in men and women in our setting, which need further investigation.

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