In-Hospital Mortality Among Black Patients Admitted for Hypertension-Related Disorders in Mbuji Mayi, Congo

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BACKGROUND
As a consequence of hypertension, sub-Saharan Africa faces an epidemic of cardiovascular disease.

METHODS
We assessed in-hospital mortality among patients admitted for hypertension-related diseases to two city hospitals in Mbuji Mayi, Congo. On admission, we obtained anthropometric measurements, blood pressure, information on cardiovascular risk factors, and on the awareness and treatment of hypertension. We modeled the probability of death, using stepwise logistic regression.

RESULTS
Of 401 consecutive patients (mean age, 54.3 years; 129 women), 118 (29.4%) were unaware of their hypertension. Among 283 aware patients (70.6%), 126 (44.5%) were untreated. Systolic/diastolic blood pressure on admission averaged 178/106 mm Hg. In addition to hypertension, 390 patients (97.3%) had other cardiovascular risk factors, including a creatinine clearance below 60 ml/min/1.73 m² in 47 subjects (11.7%). Over 15 days (median) of hospitalization, 89 deaths (22.2%) occurred. The multivariable-adjusted probability of death increased with systolic blood pressure (odds ratio (95% confidence interval) for +10 mm Hg, 1.43 (1.15–1.77); P < 0.01), body mass index (+5 kg/m², 2.40 (1.39–4.17); P < 0.01), being aware vs. unaware of hypertension (3.17 (1.52–6.61); P < 0.01), and being untreated (2.33 (1.12–4.76); P < 0.05), but it decreased with age (+10 years, 0.65 (0.46–0.92); P < 0.05) and higher creatinine clearance (+10 ml/min/1.73 m², 0.71 (0.61–0.82); P < 0.001).

CONCLUSIONS
The in-hospital mortality among African patients hospitalized for hypertension-related disorders in a Congolese provincial capital city is over 20%. These findings underscore that screening and treatment for hypertension and the prevention of cardiovascular disease should be placed much higher on the political agenda in sub-Saharan Africa.


Poverty, famine, and infectious diseases, such as malaria and AIDS, are well-known and long-standing causes of premature death and disability in sub-Saharan Africa. However, this region of the world also faces an emerging epidemic of cardiovascular disease. Indeed, already in 2001, cardiovascular disease was the leading cause of mortality in both low- and high-mortality developing countries, causing over 10 million deaths. Global trade and urbanization expose developing populations to an unhealthy lifestyle, which leads to hypertension, obesity, diabetes mellitus, and dyslipidemia. Together with smoking, these risk factors explain at least 75% to 85% of the modifiable cardiovascular risk. Moreover, in low-income nations, the social gradient in the risk of cardiovascular disease is reversing from the scarce affluent layers of society, initially at the highest risk, to the much larger group of poor people.

Although hypertension did not virtually exist in black Africa in the first half of the 20th century, currently, by 65 years of age and over, hypertension affects 30–60% of African blacks. This proportion is approaching the 60–70% range for American blacks of similar age. Most sub-Saharan countries have scarce resources to keep reliable nationwide health statistics. Few previous studies investigated the prevalence of hypertension-related admissions to hospitals and the associated mortality in black African patients. To improve our understanding of the implications of hypertension in the Democratic Republic of Congo, we undertook a study on the frequency and determinants of in-hospital mortality among consecutive patients admitted for hypertension-related disorders to two hospitals in Mbuji Mayi, Congo.
Methods
Study population. From 2001 until 2003, 6,567 patients were admitted to the Dipumba and Bonzola city hospitals (Minière de Bakwanga, “MIBA”), Mbuji Mayi, Democratic Republic of Congo. We assessed the in-hospital mortality in 401 consecutive patients (6.1% of all admissions), who were specifically hospitalized for hypertension-related disorders. Mbuji Mayi is the capital of the Kasai-Oriental province in the south-central part of the Democratic Republic of Congo and has an estimated population of 3.8 million. The immediate reasons for admission were life-threatening cerebrovascular, cardiovascular, renal or peripheral vascular diseases; symptoms of uncontrolled or malignant hypertension; comorbid conditions, such as diabetes mellitus; or adverse reactions to antihypertensive drugs. Of the 401 patients, 374 (93.3%) took themselves the initiative to seek medical care for an acute condition. Of the remaining 27 patients (6.7%), three were referred by an ophthalmologist of the study hospitals and 24 by primary care health centers in the neighborhood. The Ethics Committee of the University of Mbuji Mayi approved the study and the patients or their relatives gave informed consent.

Clinical and biochemical measurements on admission. On admission to the emergency department or the in-patient ward, we obtained from each patient information on the medical history, current smoking and drinking habits, awareness of hypertension, and the use of antihypertensive drugs. With the patient resting in the supine position on a bed with the headrest tilted 30° upward, one of the two doctors involved in admitting the patient measured blood pressure two times consecutively with a standard mercury sphygmomanometer. Body mass index was calculated as weight in kilograms divided by the square of height in meters. Overweight was a body mass index of 25 kg/m² or higher. Abdominal obesity was a waist circumference recorded to the nearest centimeter of at least 88 cm or 102 cm in women and men, respectively. Diabetes mellitus was a self-reported diagnosis, use of antidiabetic medication, or a plasma glucose level above 126 mg/dl. We computed the creatinine clearance standardized to a body surface area of 1.73 m² from serum creatinine, according to the Modification of Diet for Renal Disease formula, with the correction factor for subjects of black African ancestry applied. Chronic renal dysfunction was a creatinine clearance below 60 ml/min/1.73 m². Left ventricular hypertrophy was an R-wave in unipolar lead aVL of 1.3 mV or higher in a standard 12-lead electrocardiogram. The primary outcome measure of our study was all-cause mortality. We evaluated the cardiovascular risk factors on admission according to the 1999 WHO/ISH guideline.

Statistical methods. For database management and statistical analysis, we used SAS software, version 9.1.3 (SAS Institute, Cary, NC). We compared means and proportions by Student’s t-test and the χ²-statistic, respectively, and survival curves by Kaplan–Meier survival function estimates and the log-rank test. For the survival analysis, we subdivided patients according to the awareness and treatment of hypertension on admission or the presence of chronic renal dysfunction, as defined above. In multivariable analyses, we modeled the probability of in-hospital death, using stepwise logistic regression with the P value for independent variables to enter and stay in the model set at 0.10. The independent predictors considered for entry into the model were sex, age, body mass index, waist circumference, systolic and diastolic blood pressures, creatinine clearance, electrocardiographic left ventricular hypertrophy, and classification variables coded 0 or 1 for current smoking (≥1 cigarette per day), current alcohol use, treated for hypertension, and diabetes mellitus.

Table 1 | Characteristics of patients on admission by vital status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Death</th>
<th>Alive</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>89</td>
<td>312</td>
<td></td>
</tr>
<tr>
<td>Mean (s.d.) of characteristic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>53.3 ± 9.9</td>
<td>54.3 ± 9.2</td>
<td>0.38</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.4 ± 10.6</td>
<td>67.6 ± 6.4</td>
<td>0.0017</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168 ± 5</td>
<td>168 ± 5</td>
<td>0.27</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.3 ± 3.2</td>
<td>23.8 ± 2.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>96 ± 10</td>
<td>93 ± 8</td>
<td>0.012</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>189 ± 16</td>
<td>175 ± 15</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>111 ± 8</td>
<td>104 ± 10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pulse rate (beats/min)</td>
<td>80 ± 8</td>
<td>75 ± 9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>11.2 ± 1.3</td>
<td>11.7 ± 1.1</td>
<td>0.0023</td>
</tr>
<tr>
<td>Plasma glucose (mg/dl)</td>
<td>133 ± 50</td>
<td>106 ± 24</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>1.55 ± 0.69</td>
<td>1.09 ± 0.25</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min/1.73 m²)</td>
<td>66.9 ± 28.3</td>
<td>86.5 ± 17.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Number of subjects (%) with characteristic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>31 (34.8)</td>
<td>98 (31.4)</td>
<td>0.54</td>
</tr>
<tr>
<td>Smokers</td>
<td>16 (18.0)</td>
<td>47 (15.1)</td>
<td>0.50</td>
</tr>
<tr>
<td>Drinking alcohol</td>
<td>57 (64.0)</td>
<td>186 (59.6)</td>
<td>0.45</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>36 (40.4)</td>
<td>49 (15.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body mass index ≥ 25 kg/m²</td>
<td>39 (43.8)</td>
<td>64 (20.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Central obesity</td>
<td>39 (43.8)</td>
<td>87 (27.9)</td>
<td>0.0043</td>
</tr>
<tr>
<td>R-wave in aVL ≥ 1.3 mV</td>
<td>23 (25.8)</td>
<td>168 (53.8)</td>
<td>0.0006</td>
</tr>
<tr>
<td>Creatinine clearance (&lt;60 ml/min/1.73 m²)</td>
<td>36 (40.4)</td>
<td>11 (3.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Aware of hypertension</td>
<td>69 (77.5)</td>
<td>214 (68.6)</td>
<td>0.11</td>
</tr>
<tr>
<td>Treated for hypertension</td>
<td>24 (27.0)</td>
<td>133 (42.6)</td>
<td>0.0076</td>
</tr>
</tbody>
</table>

P values are for the differences between patients leaving the hospital death vs. alive.

Abdominal obesity was a waist circumference of at least 88 cm or 102 cm in women and men, respectively.
intake (≥1 beverage per day), a history of previous cardiovascular disease, diabetes mellitus, and the awareness and treatment of hypertension. To assess the independent correlates of creatinine clearance, we applied a stepwise linear regression procedure. Statistical significance was a $P$ value of 0.05 or less on two-sided tests.

RESULTS

Patient characteristics

The study series (Table 1) comprised 401 hypertensive patients, of whom 129 were female (32.2%). On admission, 283 patients (70.6%) were aware of their hypertension (Figure 1). Of those aware, 157 (55.5%) were on antihypertensive drug treatment. The prevalence of awareness was similar among patients who died or survived ($P = 0.11$), but being treated on admission was more prevalent among survivors ($P = 0.008$). No patient had an admission blood pressure below 140 mm Hg systolic and below 90 mm Hg diastolic. With the exception of 11 women, all other patients had in addition to hypertension at least one other cardiovascular risk factor. In these 390 patients, the number of additional risk factors amounted to 1 in 9.0%, 2 in 22.0%, 3 in 28.5%, 4 in 20.8%, and from 5–8 risk factors in 19.7% of these patients. Supplementary Table S1 online, provides the clinical diagnosis on admission by vital status on discharge.

Determinants of creatinine clearance on admission

Using stepwise linear regression analysis, 34.0% of the variability in creatinine clearance was explained by waist circumference (partial regression coefficient (95% CI) per cm, 0.44 (0.21 to 0.66) ml/min/m²; $P < 0.001$), systolic blood pressure (per mm Hg, −0.62 (−0.73 to −0.50) ml/min/m²; $P < 0.001$), alcohol intake (drinkers vs. nondrinkers, 8.12 (4.32 to 11.9) ml/min/m²; $P < 0.001$), diabetes mellitus (present vs. absent, −15.2 (−19.8 to −10.6) ml/min/m²; $P < 0.001$), and antihypertensive treatment (present vs. absent, −6.58 (−10.6 to −2.60) ml/min/m²; $P < 0.01$). The variables not entering the regression model were smoking ($P = 0.32$), awareness of hypertension ($P = 0.86$), and electrocardiographic left ventricular hypertrophy ($P = 0.20$).

In-hospital blood pressure lowering treatment

Of 401 patients, six (1.5%) did not receive blood-pressure lowering agents during their hospitalization and the nature of antihypertensive treatment was not recorded in 13 patients (3.2%). The proportion of all patients prescribed specific drug classes during hospitalization amounted to 81.8% for diuretics, 65.1% for calcium channel blockers, 40.9% for inhibitors of the renin system (angiotensin-converting enzyme inhibitors or angiotensin receptor blockers), 36.4% for β-blockers, and 15.0% for centrally acting drugs. There was no difference in the in-hospital use of antihypertensive drugs between patients who died and those who left the hospital alive ($P ≥ 0.41$). The blood pressure lowering drug classes used for specific hypertension-related disorders appears in Supplementary Table S2 online.

Seven days after admission, 41 patients had left the hospital (20 alive and 21 dead). Among the remaining 360 patients, blood pressure averaged 142 ± 12 mm Hg systolic and 94 ± 8 mm Hg diastolic. In no patient blood pressure normalized without medication.

Predictors of in-hospital mortality

Among 401 patients, the median duration of the hospitalization was 15 days (range, 1–64 days). During this period, 89 deaths (22.2%) occurred among the 401 hypertensive patients; 547 deaths occurred among 6,166 patients admitted for reasons other than hypertension (8.9%; $P < 0.001$ for comparison with hypertensive patients).

Figure 1 | Flow chart showing awareness of hypertension and treatment status by vital status at discharge from the hospital. The prevalence of awareness was similar among patients who died or survived ($P = 0.11$). Being treated on admission was more prevalent among survivors ($P = 0.008$). Percentages of specific drug classes taken on admission do not add up to 100% because of combination therapy.
In unadjusted analyses (Figure 2a), aware and untreated patients had a significantly higher mortality than those aware and treated ($P < 0.01$) and than those who were unaware and therefore untreated ($P < 0.01$). If patients were dichotomized in only two groups by treatment status on admission, the difference in survival between untreated and treated patients was only borderline significant ($P = 0.082$; see Supplementary Figure S1 online). All-cause mortality was also significantly higher ($P < 0.001$) in patients with chronic renal dysfunction than in those with normal renal function (Figure 2b).

Table 2 shows the multivariable-adjusted odds ratios for all-cause mortality. The probability of death increased with systolic blood pressure (odds ratio for $+10$ mm Hg, 1.43; $P < 0.01$), body mass index ($+5$ kg/m$^2$, 2.40; $P < 0.01$), being untreated (2.33; $P < 0.05$), and being aware vs. unaware of hypertension (3.17; $P < 0.01$), but it decreased with age ($+10$ years, 0.65; $P < 0.05$) and higher creatinine clearance ($+10$ ml/min/1.73 m$^2$, 0.71; $P < 0.001$). Sensitivity analyses in women ($n = 129$) and men ($n = 272$) and in younger ($<55$ years; $n = 225$) and older ($≥55$ years; $n = 176$) patients were confirmatory with regard to the predictors of mortality, although in the smaller subgroups not all predictors reached statistical significance. In particular, age was a consistent predictor of death in younger as well as in older patients (odds ratio (95% confidence interval), 0.46 (0.22 to 0.96) vs. 0.62 (0.28 to 1.10); $P$ value for heterogeneity 0.40). Our results did also not materially change if we applied Cockcroft–Gault's formula$^{23}$ instead of the Modification of Diet for Renal Disease formula$^{19}$ to estimate creatinine clearance.

**DISCUSSION**

The key finding of our study was that among patients hospitalized for hypertension-related disorders in two city hospitals in Mbuji Mayi, the mortality within a median of 15 days of admission was as high as 22.2%. Mortality also increased with higher systolic blood pressure on admission. Young age, being untreated, having renal dysfunction, or being obese, especially among women, were the major predictors of death. Symptoms for which patients had previously sought medical assistance or a more long-standing history of hypertension probably contributed to awareness and explained why the aware patients had a threefold higher risk of dying than unaware subjects.

Because of referral bias and the location of our study in Mbuji Mayi, the capital city of the East-Kasai province, our cohort does not constitute a representative sample of all Congolese citizens. In addition, our patients were selected in the sense that they could access health care. Our current findings might therefore not be representative for the whole Democratic Republic of Congo. Reports from the Ministry of Public Health (http://www.minisanterdc.cd) state that <30% of the 515 health districts are currently operational in the Democratic Republic of Congo, leaving the majority of Congolese citizen deprived of any health care, while 70% of patients do not have access to modern health care. Moreover, the rate of health service utilization per year is about 0.15 visits (range, 0.07–0.42) per inhabitant, corresponding to one visit per inhabitant every 6 years (http://www.minisanterdc.cd). Because there is no functioning health insurance system, patients themselves or their relatives have to carry all costs of health care. As a consequence, health care is mainly provided outside the regular governmental system, through self-medication and healers.$^{22}$ What is functioning of the Congolese health care system remains donor-dependent, either from development or humanitarian funds.$^{22}$

Overall, on admission, 283 of our patients (70.6%) were aware of their hypertension, and among those aware 55.5% were on antihypertensive drug treatment. These proportions are comparable with other studies in Africa.$^{23,24}$ In a health survey in South Africa, among women with hypertension,$^{23}$ awareness and treatment had a prevalence of 67% and 55%; among hypertensive men, these proportions were 41% and 39%, respectively. In a systematic review of five African studies covering the 1980–1998 interval,$^{24}$ the frequencies of awareness and treatment of hypertension ranged from 33–73% and from 4–59%, respectively.

Studies in the South African black population highlighted that hypertension typically behaves in an explosive manner with death occurring frequently from cerebral hemorrhage, uremia, or congestive heart failure.$^9$ We hypothesize that our younger patients with an aggressive course of hypertension
were more likely to be hospitalized than older patients with long-standing less fulminating hypertension. This might explain why in our selected hospitalized patients younger rather than older age was associated with higher mortality and why this inverse association was consistent after we had dichotomized our patients according to median age. Along these lines, many reports presenting crude rather than age-specific mortality rates underestimate the importance of cardiovascular disease in sub-Saharan Africa. Age-specific mortality rates are essential for policy makers for reaching well informed decisions.

The in-hospital death rate in our series was almost twice as high as in a previous report by Diallo and colleagues. These investigators observed among 7,491 patients admitted from 1991–1992 to the emergency department of a university hospital in Abidjan, Ivory Coast, that hypertension was the reason for hospitalization in 620 cases. The death rate of 13.0% was higher than in the patients admitted for other reasons (7.2%). However, the Abidjan study is difficult to interpret because the investigators did not state the duration of follow-up and lost 320 cases (51.6%) to follow-up. Of 3,317 acute medical admissions to a teaching hospital in Ghana, 593 (17.9%) were ascribable to cardiovascular disease, mainly hypertension, heart failure, or stroke. Of these patients, 171 died (28.8%). A further 146 patients (5.0%) had renal dysfunction, of whom 45 (27.1%) died. In a series of 22,791 Nigerian patients admitted over a 3 year period, cardiovascular disease explained 25.2% of the 18,187 nontraumatic deaths. Of 139 patients admitted in our series for stroke, 58 (41.7%) died. In a study conducted in Dakar, Senegal, the 1-month death rate of ischemic stroke was 38% and that of hemorrhagic stroke was 56%.

The appalling death rate in our study mirrors the mortality of hypertension in the United States in the 1960s before antihypertensive drugs became available. In the untreated patients randomized in the Veterans Administration Study, as reviewed by Moser, the death rates from cerebrovascular and coronary heart disease were 10.3% and 6.7%, respectively. The 20-year mortality from stroke, coronary heart disease, and other cardiovascular diseases, which amounted respectively to 2.9%, 6.9%, and 5.7% in women, and to 3.4%, 16.1%, and 7.1%, in men in the 1950 cohort, fell to 1.8%, 3.4%, and 0.9% in women, and to 2.2%, 9.0%, and 0.9% in men. From 1950–1970, the rate of use of antihypertensive medications increased from 5.7% to 27.7% in women and from 2.3 to 24.6% in men.

In almost all our patients, hypertension clustered with other cardiovascular risk factors, such as obesity and increased waist circumference. Severe obesity was not a major problem in our series, but on a continuous scale, the risk of death increased more than twofold for each 5 kg/m² increase in body mass index. In line with other reports in black patients, the risk of death was significantly higher in patients with chronic renal dysfunction. In a meta-analysis of four community-based studies in the United States, chronic kidney disease defined as a creatinine clearance ranging from 15–60 ml/min/1.73 m² had a prevalence of 7.4%. It was an independent predictor of the composite outcome of myocardial infarction, fatal coronary heart disease, stroke, and death, with a hazard ratio of 1.19 (95% confidence interval, 1.07–1.32). Moreover, the risk was significantly greater in blacks than in whites (hazard ratios, 1.76 (1.35–2.31) vs. 1.13 (1.02–1.26)). The mean value of the creatinine clearance in our patients suggested that uremia by itself was not the major cause of mortality. Instead, the cardiovascular complications resulting from mild renal dysfunction might be incriminated. Dyslipidemia, diabetes mellitus, low hemoglobin concentration, and disturbance in serum electrolytes might also have played a role. The lower blood hemoglobin among our patients who died, compared with survivors, might be regarded as a consequence of renal dysfunction, although in the African setting other causes of anemia should always be considered. Nevertheless, in the current study, mortality was not associated with the blood hemoglobin concentration, but as expected creatinine clearance was inversely correlated with systolic blood pressure and lower in diabetic patients.

Our results must be interpreted within the limitations of the present study. We obtained information on the previous history of our patients, including awareness and treatment of hypertension. However, given the low level of education of our patients, this information cannot always be viewed as completely reliable. In addition to the history and the use of antihypertensive drugs, the diagnosis of hypertension on admission rested on the average of only two measurements of blood pressure. However, subsequent measurements of blood pressure during hospitalization confirmed the diagnosis of hypertension in all patients. A major limitation of our study was that we had to rely mainly on a clinical diagnosis. This was the best that we could achieve under present-day hospital conditions in Congo, where imaging of the brain and the heart by computerized tomography or ultrasound is unavailable. Three patients, of whom two died, fulfilled the electrocardiographic criteria of acute myocardial infarction, but the diagnosis could not be confirmed by measurement of cardiac enzymes. Because there is no functioning health insurance system, patients themselves or their relatives had to carry the costs of biochemical analyses and drugs. This explains why we could not systematically measure cholesterol as a risk factor. For the same reason, there might have been undocumented differences between the drugs prescribed during hospitalization and those actually taken by the patients. Finally, in this highly selected series of patients, unlikely to reflect the status of hypertension in the general population, we only assessed all-cause mortality. On the other hand, vital status at discharge is an objective measurement not subject to diagnostic misclassification.

In conclusion, the present findings support a radical change in the policies toward the impoverished countries of sub-Saharan Africa. Policy makers in Congo and donor countries should urgently address issues, such as educating patients; giving training to nurses, nonphysician clinicians, and doctors; providing cheap but life-saving medications to patients who cannot afford them; and making simple laboratory and imaging techniques available at regional hospitals. Investing...
in basic health care in a country experiencing severe deprivation would save many lives, avert poverty, and support sustainable development.

Supplementary material is linked to the online version of the paper at http://www.nature.com/ajh

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