Classical cardiovascular risk factors and all-cause mortality in rural Cameroon

A.P. KENGNE1,2 and P.K. AWAH1

From the 1 The Health of Population in Transition (HOPIT) Research Group, Yaounde, Cameroon, and 2 The George Institute for International Health, The University of Sydney, Australia

Received 9 October 2008 and in revised form 11 December 2008

Summary

Background: High levels of cardiovascular risk factors have been reported in rural Africa. How these translate into major outcomes remain unknown.

Aim: To assess the association between selected risk factors and all-cause mortality in rural Cameroon.


Methods: The 9-year’s vital status was ascertained for 350 participants screened for cardiovascular risk factors in Bafut, Cameroon in 1998. Cox models were used to compute the hazard ratio (HR) and 95% confidence interval (CI) for selected risk factors.

Results: Vital status was available for all participants, except 22 (6.3%) who were excluded from analyses. At baseline, compared with women, men had significantly higher waist-to-hip ratio, were more likely to be ex- or current smokers and alcohol consumers (all \( P < 0.008 \)). The total duration of follow-up was 2771 person-years. This duration was longer for women (\( P = 0.04 \)). During follow-up 47 deaths were recorded, 31 (66%) in men (\( P = 0.023 \)). In multivariate Cox analyses, age, male gender, current smoking, systolic blood pressure and fasting capillary glucose were significant predictors of total mortality during follow-up.

Conclusions: Gender, smoking, fasting capillary glucose, blood pressures and age are potential determinants of overall death in rural Cameroon. More elaborated cohort studies are needed to refine these conclusions and monitor the progression of these populations through epidemiological transition stages.

Introduction

In developing countries and particularly those of sub-Saharan Africa (SSA), the registration of vital statistics is minimal or non-existent. In the absence of such strategic information, alternative approaches including verbal autopsy and time-to-event studies have been advocated.1 Time-to-event studies have the advantage of providing for the assessment of predictors at baseline, and relate them to the outcome of interest, death in this case. Interest for such studies has been very limited in SSA. This in part results from the fact that acute infectious diseases have been the dominant causes of death in this region, and assessing infection as cause of death if needed does not necessarily require long-term follow-up horizon.2 However, SSA is undergoing epidemiologic transitions, with a shift toward co-occurrence of acute infectious and chronic conditions as major causes of mortality and morbidity.1 Determinants of chronic diseases and particularly cardiovascular diseases are well known and have been reported at high prevalence in SSA.4–6 Their relationship with diseases and death has been

Address correspondence to Dr A.P. Kengne, The George Institute for International Health, Level 10, KGV Building, Missenden Road, Camperdown 2050 NSW, Australia. email: apkengne@yahoo.com; akengne@george.org.au

© The Author 2009. Published by Oxford University Press on behalf of the Association of Physicians. All rights reserved. For Permissions, please email: journals.permissions@oxfordjournals.org
established in most parts of the world, but not in SSA. Although the relationship between predictors and cardiovascular outcomes has been found to be similar across populations, demonstrating such relationship for SSA population has relevance for informing local policy and monitoring of the burden of cardiovascular disease in this region. This task requires good quality cohort studies with assessment of key predictors at baseline, and ascertainment of causes of diseases and deaths during follow-up. In the absence of such studies, alternative designs could be used to approach the same problem.

In this study, we took advantage of a cardiovascular risk factors screening survey conducted in the rural health area of Bafut in Cameroon in 1998, to explore the association between selected cardiovascular risk factor and total death, assuming that total death was a surrogate of cardiovascular death (CVD).

**Methods**

**Study setting and population**

Details on the purpose, design and organization of the Cameroon Essential Non-Communicable Diseases Health Intervention Project (CENHIP) are available elsewhere. Results of the baseline evaluation relating to cardiovascular risk factors screening have also been published. In brief, the rural health district of Bafut is a local kingdom situated ~285 miles to the Northwest of Yaounde, the capital city of Cameroon. In February 1998, a randomly selected sample of adult individuals (age >15 years) was screened for hypertension, diabetes, asthma and epilepsy. Records were kept for the 350 participants detected during the screening.

**Baseline measurements**

During the screening survey in 1998, participants underwent a physical examination, anthropometric measurements, blood pressure determination and tip finger pricking for fasting glucose measurement. Blood pressure measurements were made on the left arm of the seated participants with a mercury-column sphygmomanometer, and appropriate sized cuff. Two physician-obtained measures were averaged and used as examination blood pressure. Hypertension was considered as a prior physician-diagnosed hypertension treated or not, or a blood pressure $\geq 140/90$ mmHg. Diabetes mellitus was defined as fasting capillary glucose $\geq 6.1$ mmol/l or use of oral hypoglycemic agents or insulin. Status for smoking was ascertained by a self-report as never-smokers, ex-smoker and current smokers. Weight was measured at the nearest kilogram in light dressing, and height measured to the nearest centimeter. Body mass index (BMI) was derived as weight (kg) divided by height squared (m$^2$). Waist circumference was measured at mid-point between the lowest rib margin and iliac crest, and hip circumference at the level of the greater trochanters. The waist-to-hip ratio was derived. Alcohol consumption was based on self-reported history and participants classified as drinkers and non drinkers. A validated questionnaire was used to assess leisure time physical activity and participants ranked for their level of physical activity as: none, light, moderate and intense.

**Outcomes ascertainment**

The outcome of interest in this study is total death. Vital status ascertainment was conducted in February 2007 by a trained state-registered nurse who was also involved in baseline survey 9 years earlier. Participants’ codes recorded during baseline survey were used to trace them in the community. These codes were designed to localize participants to their neighborhood and at times to the households. Proxies, neighbors and community leaders were interviewed to obtain information on deceased participants. Date of death was ascertained to the nearest month. No verbal autopsy was conducted. Participants with missing code, or wrongly assigned code were systematically traced in all settings where baseline survey was conducted. Despite these efforts, 6.3% of participants could not be traced.

**Statistical methods**

Statistical analyses were conducted using SPSS® software and stratified by sex where relevant. Comparison of baseline characteristics between the groups of participants was performed using Student $t$-tests and Chi-squared tests and equivalents as appropriate. The normal distribution assumption for continuous variables was assessed with the use of Kolmogorov–Smirnov test, after stratification by sex. Where this assumption is violated, results are presented as median and 25th to 75th percentiles, and groups compared using non-parametric tests. Death rate was standardized using the Cameroon 2004 Demographic and Health survey. Kaplan–Meier curves were used to summarize incident deaths separately for men and women during follow-up, and the log rank test to compare the curves by sex. We used Cox proportional-hazards regressions models to relate cardiovascular risk factors to death incidence during a maximum
follow-up period of 9 years. Predictors considered for inclusion in the models were age, sex, systolic and diastolic blood pressure, status for hypertension, fasting glucose, status for diabetes, smoking, body mass index, status for obesity and waist circumference. Exploratory sex and aged adjusted analyses were conducted to select significant predictors who were then mutually assessed using a backward approach to select the final predictors. Secondary analyses were also conducted for significant predictors selected in univariate analyses, and their interaction with sex using similar backward approach with a $P$-value of $\leq 0.05$ for entry and $\geq 0.10$ for removal. The validity of the proportional hazard assumption was checked graphically with the log-cumulative hazard plots against survival time.

Ethics
The study protocol was approved by the National Ethical Committee for Ethical Review. Participants in the 1998 population survey of risk factors had accepted to be contacted in subsequent evaluations relating to their conditions. They were handed information sheets relating to the study and then consented for their participation.

Results
Data available and baseline characteristics
Vital status was available for 328 (93.7%) participants. Those excluded were likely to be women (15 vs. 7, $P=0.082$), to be older (58.86 vs. 50.88 years, $P=0.02$) (19 aged 50+ years), to have low BMI (20.51 vs. 22.62; $P=0.01$). At baseline, compared with women, men were more likely to be taller, heavier, drinkers, current or ex-smokers, to display a lower hip girth and a higher waist-to-hip ratio (Table 1). Otherwise, hypertension and diabetes mellitus was equally distributed between men and women.

Outcomes
The average duration (95% CI) of follow-up was 8.63 (8.43–8.84) and 8.27 (7.99–8.55) years among women and men respectively ($P=0.04$). During the 2771 person-years of follow-up 47 deaths were recorded (66% in men). The survival probability was higher in women than men (Figure 1). The overall crude event rate per 10 000 person-years (95% CI) overall and among men and women was, respectively, 169.6 (124.6–221.6), 221.7 (150.6–315.1) and 116.6 (69.5–189.7). The equivalents figures for the age-group 15–49 years were: Overall 57.4 (22.7–118.9); men 68.9 (17.9–178.2) and women 46.9 (8.84–138.8). Overall and across age strata, there was a trend toward higher event rate among men than women (Figure 2). Compared with the $\geq 65$ years, the event rate was lower in other age strata, although not always significantly. This was observed for the overall cohort and among men and women (Figure 3). The age standardized event rate was Overall: 95.64/10 000; Men: 142.883/10 000, Women: 81.936/10 000. Compared with the national death rate, the age standardized mortality ratio (SMR) among the 15–49 years age group was 1.036 for men and 0.75 for women, with a nonsignificant lower ratio for women; SMR ratio women/men 0.72 (0.11–4.76).

Predictors of death during follow-up
In Cox analysis adjusted for age and stratified by sex (except when age and sex were the variables of interest), age, male sex, current smoking, systolic and diastolic blood pressures, history of hypertension and fasting blood glucose were significant predictors of death during follow-up. There was a positive correlation ($r=0.71$, $P<0.001$) between systolic (SBP) and diastolic (DBP) blood pressures and hazard ratio (HR) in univariate analysis was higher for SBP, therefore, DBP was not included in multivariate analyses. Status for hypertension was also dropped because its definition used categorical levels of SBP and DBP. In multivariate model using a stepwise approach that included all other variables, significant predictors of death during follow up were age (HR: 95% CI) 1.29 (1.03–1.60) per 10 years, sex (men vs. women) 1.91 (1.02–3.57), systolic blood pressure 1.23 (1.10–1.38) per 10 mmHg, fasting capillary glucose 1.19 (1.04–1.35), and smoking (current/not current) 2.14 (1.17–3.91). Replacing SBP with DBP (for each 5 mmHg) knocked out sex from the model as predictor. However, no major change was observed for the association with other significant predictors. The HR (95% CI) for each 5 mmHg greater DBP was 1.34 (1.12–1.61), $P=0.0012$. When all sex interactions were included in the variables selection step, age and fasting glucose were no longer retained in the final model. But their interaction term with sex was significant (Table 2). This indicated that age and fasting glycaemia were significant predictors in men, but not in women. This, however, has to be interpreted in the context of the small number of events in women. Together in same model, age, fasting glucose and their interaction
Table 1  Baseline characteristics by gender

<table>
<thead>
<tr>
<th>Variables</th>
<th>Women (n = 159)</th>
<th>Men (n = 169)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.42 ± 16.59</td>
<td>51.33 ± 14.54</td>
<td>0.597</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>56.87 ± 11.32</td>
<td>61.68 ± 10.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>157.15 ± 6.72</td>
<td>166.19 ± 7.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.4 (20–25)</td>
<td>22.1 (20–24)</td>
<td>0.114</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>81.72 ± 9.29</td>
<td>81.14 ± 12.02</td>
<td>0.631</td>
</tr>
<tr>
<td>Hip (cm)</td>
<td>94 (88–100)</td>
<td>92 (87–97)</td>
<td>0.003</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.86 ± 0.07</td>
<td>0.88 ± 0.06</td>
<td>0.002</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>139.65 ± 22.01</td>
<td>141.57 ± 23.43</td>
<td>0.474</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>88.17 ± 14.12</td>
<td>91.33 ± 16.53</td>
<td>0.065</td>
</tr>
<tr>
<td>FCG (mmol/l)</td>
<td>4.9 (4.3–5.7)</td>
<td>4.9 (4.2–5.7)</td>
<td>0.332</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>14 (8.8)</td>
<td>22 (13)</td>
<td>0.29</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>113 (71.1)</td>
<td>123 (72.8)</td>
<td>0.806</td>
</tr>
<tr>
<td>Drinkers, n (%)</td>
<td>129 (81.1)</td>
<td>158 (93.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

 Smoking

<table>
<thead>
<tr>
<th></th>
<th>Women (n = 159)</th>
<th>Men (n = 169)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non smokers, n (%)</td>
<td>132 (83)</td>
<td>115 (68)</td>
<td>0.008</td>
</tr>
<tr>
<td>Ex-smokers, n (%)</td>
<td>5 (3.1)</td>
<td>8 (4.7)</td>
<td></td>
</tr>
<tr>
<td>Smokers, n (%)</td>
<td>22 (13.8)</td>
<td>45 (26.6)</td>
<td></td>
</tr>
</tbody>
</table>

 Physical activity

<table>
<thead>
<tr>
<th></th>
<th>Women (n = 159)</th>
<th>Men (n = 169)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>None, n (%)</td>
<td>5 (3.1)</td>
<td>10 (5.9)</td>
<td></td>
</tr>
<tr>
<td>Light, n (%)</td>
<td>24 (15.1)</td>
<td>35 (20.7)</td>
<td></td>
</tr>
<tr>
<td>Moderate, n (%)</td>
<td>90 (56.6)</td>
<td>77 (45.6)</td>
<td></td>
</tr>
<tr>
<td>Intense, n (%)</td>
<td>37 (23.3)</td>
<td>47 (27.8)</td>
<td></td>
</tr>
</tbody>
</table>

Continuous variables are mean and standard deviation, except where indicated by (asterisk) where median and 25–75th percentiles are used to account for the skewed distribution. FCG: fasting capillary glucose.

Figure 1. Kaplan–Meier curves describing the 9-year’s event rates for men (lower line) and women (upper line); Log rank statistics 4.6; P=0.032. The horizontal line is shifted downward purposefully to all better visualization of the curves.

Figure 2. Mortality rate ratio (women/men), overall and by age groups. Boxes are for the effect estimates (rate ratios) and are proportional to the inverse of the variance. The horizontal axes are for the 95% confidence interval (95% CI).

Discussion

Analyses conducted in this paper indicate that in a rural population with high profile for cardiovascular diseases, age, male sex, systolic blood pressure and
fasting capillary glucose were significantly related to
the risk of total death during an average 9 years of
follow-up. In this relatively young adult population
at baseline, the 9-year death rate was high, and
more in men than women. This significant associa-
tion with known CVD risk factors indicates that
considerable part of the recorded death must have
occurred through chronic cardiovascular
complications.

The magnitude of the association between blood
pressure variables, fasting capillary glucose and
9-year’s death in our study, was within sampling
variation of the effect estimates from meta-analyses
of observational studies and clinical trials on the
association between these variables and cardiovas-
cular diseases.\textsuperscript{12,13} The exact magnitude of these
associations is likely underestimated by the use of
the combined outcome of all-cause death, through
dilution of a real association with CVD deaths with
the non-association with non-CVD deaths. The
assessment of the associations with blood pressures
and fasting glucose without accounting for

\begin{table}
\centering
\begin{tabular}{lcc}
\hline
Age group & Rate Ratio & 95\% CI \\
\hline
Women & & \\
15–49 & 0.29 (0.08 to 1.05) & \\
15–24 & 0.26 (0.01 to 4.35) & \\
25–34 & 0.59 (0.08 to 4.58) & \\
35–44 & 0.37 (0.05 to 2.88) & \\
45–54 & 0.37 (0.08 to 1.71) & \\
55–64 & 0.73 (0.20 to 2.67) & \\
65+ & 1.00 (0.40 to 2.50) & \\
Overall & 0.71 (0.32 to 1.60) & \\
\hline
Men & & \\
15–49 & 0.26 (0.09 to 0.77) & \\
15–24 & 0.22 (0.01 to 3.69) & \\
25–34 & 0.59 (0.08 to 4.41) & \\
35–44 & 0.42 (0.10 to 1.82) & \\
45–54 & 0.12 (0.02 to 0.93) & \\
55–64 & 1.41 (0.66 to 2.99) & \\
65+ & 1.00 (0.50 to 1.98) & \\
Overall & 0.84 (0.46 to 1.52) & \\
\hline
Total & & \\
15–49 & 0.26 (0.11 to 0.61) & \\
15–24 & 0.12 (0.01 to 1.90) & \\
25–34 & 0.55 (0.13 to 2.31) & \\
35–44 & 0.40 (0.12 to 1.32) & \\
45–54 & 0.22 (0.07 to 0.72) & \\
55–64 & 1.18 (0.62 to 2.25) & \\
65+ & 1.00 (0.58 to 1.73) & \\
Overall & 0.78 (0.48 to 1.27) & \\
\hline
\end{tabular}
\caption{Mortality rate ratio by age groups (relative to the $\geq 65$ years), for men, women and total participants. For each age
group, the box represents the effect estimate (rate ratio), and the horizontal lines about are for the 95\% CI. The sizes of
the boxes are proportional to the inverse of the variance.}
\end{table}
regression dilution bias would have furthermore altered the precision about our estimates. Vital status was missing for 22 participants who were excluded from the analyses. The advanced age of those excluded suggests that more events would have accumulated if these participants were successfully traced. This in some way would have affected the precision about our estimates, without necessarily altering the conclusions of this study. We feel that these participants were non-residents of the study area who temporarily migrated to the area to take advantage of the baseline survey. Therefore, with unreliable information provided by such participants relating to their residence at baseline, all efforts to subsequently trace them would be unfruitful.

There have been limited attempts to prospectively relate cardiovascular risk factors to hard fatal and non fatal cardiovascular outcomes or total mortality in SSA. In a verbal autopsy study in Nigeria, age and smoking were identified as predictors of death in Adults. During the 5-year follow-up into this study, cardiovascular disease was the most common known cause of death, accounting for 18% of total death recorded. In agreement with our study, most death in the Nigerian cohort occurred among the 50 years and above, and death rate among men was higher than that among women. Elsewhere, there are a number of areas in SSA on which demographic events are prospectively monitored, with causes of death assigned using verbal autopsy methods. Reports from these centers suggest that cardiovascular diseases are major causes of death in some age segments (≥45 years) of the population in SSA. In general, available longitudinal studies of adult mortality in SSA are either outdated or have focused on children or acute conditions.

Our study has some limitations that worth been mentioned. This was a post-hoc analysis, without prior determination of the sample size required to detect significant association between risk factors and the outcome of interest. The small size of our population and the limited number of events could affect the precision about our estimates, but were unlikely to reveal any spurious association. Although death registration in the study country is a legal requirement, in practice such activity is very limited and not centralized. For the few registered cases, the cause of death is usually not assigned; including for those who died in hospitals. This precluded the use of death registries to assign the causes of death in this study. Similarly, the long-time interval between baseline evaluation and vital status ascertainment made the use of verbal autopsy method unreliable.

This study has provided some evidences in support of the harmful effects of some cardiovascular risk factors in this relatively young rural SSA population. These findings need to be refined in the context of well-designed longitudinal studies. For such studies to be useful, they must collect information about known and putative cardiovascular risk factors at baseline, and provide for future assessment of unknown predictors through biorepositories. They must also provide for the evaluation of the burden of CVD within the context of overall burden of diseases through prospective data collection on causes-specific mortality and other major outcomes. Already, the current knowledge pertaining to prevention of CVD must be translated into concrete actions to limit the devastating effects of CVD in rural SSA.

### Acknowledgements

We are grateful to the ENHIP investigators for the baseline data collection.

Conflict of interest: None declared.
References