Epidemiology of sudden cardiac death in Cameroon: Rationale and design of the Douala-SUD survey

Épidémiologie de la mort subite cardiaque au Cameroun : protocole de l’enquête Douala-SUD

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Abbreviations: CAD, coronary artery disease; COSA, comité de santé (Community Healthcare Committee); Douala-SUD, Douala sudden unexplained death; NCD, non-communicable disease; SCA, sudden cardiac arrest; SCD, sudden cardiac death.

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Background

The overwhelming proportion of sudden death is of cardiac origin [1,2]. Sudden cardiac death (SCD) is an unexpected death from cardiac causes occurring within a short time period in a person without any prior condition that would appear fatal [3–10]. Studies assessing risk predictors of SCD have been performed in community-based cohorts [11–18] and have shown that definitions can be standardized and systematic circumstantial and clinical evidence can be obtained and used to maximize accuracy in identifying the SCD phenotype [19]. Therefore, Fishman et al. developed a unified definition for SCD that can be used to ascertain the SCD phenotype in community-based cohort studies as well as in investigations conducted in the general population. An “established SCD” is an unexpected death without obvious extracardiac cause, occurring with a rapid witnessed collapse or, if unwitnessed, occurring within 1 hour after the onset of symptoms. A “probable SCD” is an unexpected death without obvious extracardiac cause, which occurred within the previous 24 hours. In any situation, the death should not occur in the setting of a prior terminal condition, such as a malignancy that is not in remission or end-stage chronic obstructive lung disease. The term “sudden cardiac arrest”
Sudden unexplained death in Cameroon 435

Up to half of all cases of cardiac death are attributable to SCD [7–9,11,16]. It is estimated that more than 3.7 million lives per year are lost to SCD worldwide, including 250,000 to 300,000 in the USA [15,20]. In the USA and Europe, the annual incidence of SCD ranges from 50 to 100 per 100,000 in the general population [11,19–21]. In Asia, the incidence of SCD has been reported to range from 37 to 43 per 100,000 person-years [13,14,17,18]. SCD is mainly caused by coronary artery disease (CAD) [22–25]. Although cases of SCA due to CAD and other causes have been reported in the black African population [26–33], these studies had mainly a cross-sectional, retrospective design (Table 1). The lack of diagnostic tools to rule out inherited arrhythmogenic aetiologies leads to miss diagnosis as well as to misdiagnosis [29].

To be eligible, subjects must be a resident of the administrative area (district) included in the study registry and the Department of Public Health Services. The estimated population of each of the eight health districts of Douala is ≥ 30,000 inhabitants. The sampling is based on the selection of areas with ≥ 30,000 inhabitants as the first step and random sampling among them as the second step.

Main study period
Two health areas were excluded for inaccurate data collection and two others were randomly disqualified as we had previously decided to conduct the survey in fewer than four areas. The mode of randomization aimed to include no more than one health area per health district. Finally, investigators retained four health areas representing four of the six health districts of Douala (Table 2). Thus, the sampling of 240,384 inhabitants will be monitored prospectively. All administrative staff and the community healthcare committee — the so-called ‘comité de santé’ (COSA; Table 2) — of each health area will be a key component of the research team, helping to identify each case of death in the area of concern.

Every case of death will be recorded by the COSA staff on a specific questionnaire form (Table 3). A nurse will collect the circumstances of death, to rule out non-natural deaths, such as those caused by road accidents, intoxication and other factors. A postgraduate medical fellow will collect sociodemographic and clinical data for every victim of natural death. A senior physician will study every case of suspected SCD, using all medical files available as well as information from relatives. The final diagnosis of SCD will be made by at least two cardiologists; in case of disagreement between both experts, a third opinion will be sought.

Population monitoring
Given the known 2012 population size of each health area and the population growth rate of 2.5% in Cameroon [40], the estimated population size of the areas of interest is about 240,384 inhabitants. As 57% of people are aged > 15 years in Cameroon [40], the study sample consists of 137,018 residents. Given the overall mortality rate of 14.1 deaths per 1000 inhabitants, the expected annual all-death rate in the sample is 1423 cases. Akimwusu et al. found a prevalence of sudden death of 4% in a Nigerian registry [26]. Therefore, investigators expect to observe 41 sudden deaths per 100,000 inhabitants/year. This incidence is similar to incidences found in several Asian populations [13,14,17,18]. Hence, during the 3-year follow-up period, investigators expect to detect 120 cases of sudden death. Over this period, eligible residents of all four health areas of interest will be monitored regarding death occurrence. Monthly, each health district’s administrative staff and the COSA will organize a meeting together with the study medical staff.

Methods
Study design
Study population
This is a prospective, multiple-source, community-based, cohort surveillance of all cases of sudden and unexpected death in the city of Douala.

Objectives
The specific objectives of the registry are as follows:
• to estimate the incidence of SCD in the city of Douala;
• to characterize all unexplained premature deaths;
• to evaluate the extent of the use of cardiopulmonary resuscitation efforts in this remote community area;
• to evaluate outcomes of survivors of SCA.

Study eligibility
To be eligible, subjects must be a resident of the administrative area (district) included in the study registry and the district must have an updated population census. Subjects can be included if they are a person who has experienced an unexpected sudden natural death or a victim of cardiac arrest who has been resuscitated. Subjects will be excluded if they are aged ≤ 15 years or if consent has been refused by the subject (if resuscitated) or by the family.

Data collection
Run-In period
In eight of 57 health areas constituting all six Health Districts of the city of Douala, investigators conducted a pilot survey to determine the trend of sudden death and evaluate the adherence of each health area team to the effective collection of data during a 6-month run-in period. The choice of these eight health areas was based on the selection of areas with > 30,000 inhabitants as the first step and random sampling among them as the second step.
Table 1  Reported cases of syncope or sudden death in black Africans living in Africa.

<table>
<thead>
<tr>
<th>Case</th>
<th>Main disease</th>
<th>Authors</th>
<th>Title</th>
<th>Country</th>
<th>Type of publication</th>
<th>Journal, year</th>
<th>Size (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BrS</td>
<td>Bonny et al.</td>
<td>Brugada syndrome in pure black Africans</td>
<td>Ivory Coast, Benin, DR of Congo</td>
<td>Article</td>
<td>Journal of Cardiovascular Electrophysiology, 2008</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>IHD</td>
<td>Rotimi et al.</td>
<td>Sudden unexpected death from cardiac causes in Nigerians: a review of 50 autopsied cases</td>
<td>Nigeria</td>
<td>Article</td>
<td>International Journal of Cardiology, 1998</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>Paediatric sample</td>
<td>Arthur et al.</td>
<td>Sudden deaths: cardiac and non-cardiac in children in Accra Ababa, Ethiopia</td>
<td>Ghana</td>
<td>Article</td>
<td>West African Journal of Medicine, 1995</td>
<td>16</td>
</tr>
<tr>
<td>8</td>
<td>Multiple causes (CAD, DCM, LQTS, RHD)</td>
<td>Talle et al.</td>
<td>SCD in sub-Saharan Africa: a 12-month review in the University of Maiduguri Teaching Hospital, Nigeria</td>
<td>Nigeria</td>
<td>Abstract</td>
<td>PASCAR Conference, Dakar; 15–20 May, 2013</td>
<td>17</td>
</tr>
<tr>
<td>9</td>
<td>Multiple causes (DCM, CAD, RHD)</td>
<td>Thiam et al.</td>
<td>La mort subite cardio-vasculaire au Sénégal : étude rétrospective sur 7 ans</td>
<td>Senegal</td>
<td>Abstract</td>
<td>PASCAR Conference, Dakar; 15–20 May, 2013</td>
<td>235</td>
</tr>
<tr>
<td>10</td>
<td>LQTS</td>
<td>Leye et al.</td>
<td>QT long congenital syncopal évocateur de syndrome de Jervell Lange Nielsen</td>
<td>Senegal</td>
<td>Abstract</td>
<td>PASCAR Conference, Dakar; 15–20 May, 2013</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>ARVD/C</td>
<td>Kouakam</td>
<td>Syncope in a black African with arrhythmogenic right ventricular dysplasia</td>
<td>Cameroon</td>
<td>Unpublished data</td>
<td>Unpublished data</td>
<td>1</td>
</tr>
</tbody>
</table>
Table 1 (Continued)

<table>
<thead>
<tr>
<th>Case</th>
<th>Main disease</th>
<th>Authors</th>
<th>Title</th>
<th>Country</th>
<th>Type of publication</th>
<th>Journal, year</th>
<th>Size (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>Hypertensive CM (mainly)</td>
<td>Akinwusi et al.</td>
<td>Pattern of sudden death at Ladoke Akintola University of Technology Teaching Hospital, Osogbo, South West Nigeria</td>
<td>Nigeria</td>
<td>Article</td>
<td>Vascular Health and Risk Management, 2013</td>
<td>~16</td>
</tr>
</tbody>
</table>

ARVC: arrhythmogenic right ventricular cardiomyopathy; ARVD: arrhythmogenic right ventricular dysplasia; BrS: Brugada syndrome; CAD: coronary artery disease; CM: cardiomyopathy; DCM: dilated cardiomyopathy; DR: Democratic Republic; HCM: hypertrophic cardiomyopathy; IHD: ischaemic heart disease; LQTS: long QT syndrome; NCCM: non-compaction cardiomyopathy; PASCAR: Pan-African Society of Cardiology; RHD: rheumatic heart disease; SCD: sudden cardiac death.

Table 2 Demographic and ethnic characteristics of Health Districts included in the Douala-SCD survey.

<table>
<thead>
<tr>
<th>HD</th>
<th>Total population in 2013 (n)</th>
<th>HAs (n)</th>
<th>Mean population†; range, smallest HA—largest HA (n)</th>
<th>HA of the study; population‡ (n)</th>
<th>Main ethnic groups of the study population§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logbaba</td>
<td>308,230</td>
<td>7</td>
<td>44,032; 18,817—86,803</td>
<td>None</td>
<td>Ewondo-Bulu-Eton, Bamiléké, Bassa, Bamoun, from Benin, Nigeria and Niger Bamoun, Sawa</td>
</tr>
<tr>
<td>Nylon</td>
<td>468,298</td>
<td>9</td>
<td>52,033; 4859—109,323</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>New-Bell</td>
<td>259,948</td>
<td>10</td>
<td>25,994; 16,795—37,751</td>
<td>Mbam Ewondo; 35,726</td>
<td>Ewondo-Bulu-Eton, Bamiléké, Bassa, Bamoun, from Benin, Nigeria and Niger Bamoun, Sawa</td>
</tr>
<tr>
<td>Deido</td>
<td>608,965</td>
<td>12</td>
<td>50,747; 19,190—122,995</td>
<td>Bessengue; 38,878</td>
<td>Sawa, Bassa, Bamiléké, Bamoun, Toupouri-Aoussa-Foulbé, from Nigeria and Senegal Bassa, Sawa, Ewondo-Bulu</td>
</tr>
<tr>
<td>Bonassama</td>
<td>309,619</td>
<td>11</td>
<td>28,147; 675—48,753</td>
<td>Bonamikano; 48,753</td>
<td></td>
</tr>
<tr>
<td>Cité des Palmiers</td>
<td>423,584</td>
<td>8</td>
<td>52,948; 17,460—117,027</td>
<td>Cité des Palmiers 1; 117,027</td>
<td>Sawa, Bassa, Bamiléké, Bamoun, Toupouri-Aoussa-Foulbé, from Nigeria and Senegal Bassa, Sawa, Ewondo-Bulu</td>
</tr>
<tr>
<td>Total</td>
<td>2,378,644</td>
<td>57</td>
<td>41,730; 675—122,995</td>
<td>Four HAs; 240,384</td>
<td></td>
</tr>
</tbody>
</table>

HA: health area; HD: health district.

a Given the health sectoral policy in Cameroon aiming at decentralize healthcare, HDs were created, following the demarcation of administrative territories (districts). The HD is an operative geographic unit offering basic healthcare for a given population. Douala is a city divided into six HDs and 57 HAs. An HA is a subdivision of an HD consisting of at least one village or some neighbourhoods. HAs have dialogue structures, which are a kind of operative ‘link’ between healthcare institutions and the general population. The community healthcare committee (COSA) is one of these dialogue structures; its members are non-medical residents of the HA.

b Growth rate 2.5%.
c As the 2013 population census is pending, we calculated the projection of population size using the growth rate of 2.5%.
d Cameroon is divided into provinces. The distribution of ethnic groups per province is as follows: North provinces = Toupouri, Aoussa and Foulbé; West provinces = Bamiléké and Bamoun; Central and South provinces = Ewondo, Bulu, Eton, Bassa and Bafia; Province of Littoral = Sawa (Douala, Bakoko, Aboh, Pongo, etc.) and Bassa.

the major coronary arteries [41]) will be tracked and the revised definition of myocardial infarction will be used [42]. In addition to the deaths noted by members of each COSA, investigators will pay attention to all notices of deaths in local newspapers and on the radio, questioning of health area residents and death certificates from local medical centres. Data on the medical history of victims will be gathered by collecting information from general practitioners and examining the records of each medical centre where the victim was being followed.

Study management

The research team in each health area will record data for victims on the questionnaire form. The research team comprises: one postgraduate fellow with the thesis topic
'Epidemiology of SCD in sub-Saharan Africa' (apart from when required to check an index case, this student must visit the mortuary and the staff of the COSA bimonthly, collect all data files for the victim that can help to rule out causes of death and have a monthly brainstorming meeting with the research team); qualified nurses, who will be the first line for evaluation of natural deaths and will work in collaboration with district administrators and community health committees; the District’s administrator and the COSA will provide information about all deaths among inhabitants of each health area; and physicians will be leading coordinators in all health areas where the survey is being conducted (together with all members of the research team, they will analyse all deaths and resolve all uncertainties in suspected cases).

Ethical issues
Approval from National Ethical Committees and local institutions will be obtained before starting the survey. Before sampling, informed consent will be obtained from the victim (for survivors of SCA) or their legal representatives and family members (for SCD) prior to inclusion in this study. Confidentiality will be ensured in accordance with the Declaration of Helsinki.

Statistical analysis
The yearly incidence of SCD will be assessed by dividing the number of cases registered each year by the total number of inhabitants in the same age range, standardized for 10,000 inhabitants. Standard errors and 95% confidence intervals around the point estimates will be calculated assuming a Poisson error distribution. Missing data related to the undetermined causes of death after investigation may affect the exhaustiveness of incidence rate estimates; this will be managed through simple imputation based on the rate of SCD in sub-Saharan countries [26], using the hypothesis that the causes of death are missing at random. Sensitivity analyses will be performed to assess the robustness of our incidence rate estimates by assuming, on the one hand, that missing data are linked to SCD and, on the other hand, that missing data are not related to SCD and will not be considered in incidence rate calculations. Characteristics of patients experiencing SCD will be presented as frequencies or mean values with standard deviations. Differences between men and women will be tested by Chi² tests for categorical variables and t tests for continuous variables. Furthermore, the temporal trends in the incidence and the association between sudden death and sociodemographic/clinical factors will be assessed through Poisson regression and logistic regression models, respectively.

Discussion
The Douala-SCD study is an attempt to characterize comprehensively the burden of sudden death in a sub-Saharan African country. The structure and functioning of health districts (Table 2) allow communities to manage their own health care. This optimal organization will facilitate collection of data on sociodemographics and clinical characteristics of victims, and will minimize loss of cases. Thus, the results of this survey will provide contemporary data on the incidence, aetiology, patient characteristics and outcomes of SCD in the city of Douala, which has all the sociodemographic characteristics of the population of the country.

Study strengths and limitations
The Douala-SCD study is a community-based, prospective registry aimed at determining the incidence and prevalence of SCD in the biggest town in Cameroon. Although this study follows recommendations that favour a multiple-source approach rather than a retrospective death certificate-based review [43—45], several weaknesses will limit the pertinence of the collected data. Firstly, the lack of complex and expensive cardiovascular diagnostic tools, such as exercise electrocardiogram testing, stress echocardiography, radionuclide imaging, coronary computed tomography scanning and coronary angiography, may underestimate the CAD burden, which is the leading cause of sudden death in developed Western countries. Secondly, the underuse of drug challenges and electrophysiological studies limits investigation of inherited arrhythmogenic disorders, which are the first cause of SCD in young people aged <40 years [37—39]. Lastly, a centralized medical records database with software tools facilitating extraction of useful information about underlying diseases is unavailable. Hence, our results will address a global view of SCD burden rather than show the real phenotype/genotype characteristics of each case.
Difficulties and perspectives

The results of this survey should help us to understand if SCD is a public health problem in Africa. As preliminary reports tend to indicate, and in the light of what is being done in Western and Asian countries [46], this maiden survey in the field of SCD in Africa will create the platform for advocating preventive public health policies in the fight against SCA, as well as for primary cardiovascular prevention in general. However, to achieve this goal, investigators will face some barriers. Indeed, the run-in period allowed investigators to identify factors limiting optimal data collection. The first difficulty is low population adherence to sharing information about their private life with unknown people (investigators). In fact, some people are not willing to give information about the circumstances of death, particularly when the first-line investigator is a non-medical person. The second difficulty is the cultural resistance to signing any consent form. Convincing people is time-consuming and requires the accurate explanation of why it is important for relatives to exclude an inherited disorder as the cause of death of their family member. The third difficulty is the problem with performing autopsies, because of cultural and religious beliefs. The fourth difficulty is the lack of data regarding past medical history (including imaging records). Therefore, the phenotype characteristics of deaths will be based more on clinical description rather than on detailed physical, imaging and anatomopathological features. This justifies the use of the term ‘sudden unexplained death’ for cases when cardiac causes of death are difficult to establish. Finally, local fundraising is a great challenge.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Acknowledgments

The investigators acknowledge all people who will help with data collection and other issues necessary to obtain robust study results. The run-in period was funded by SANOFI corporation, France, via the French medical organization Association pour la Recherche Cardio Vasculaire (ARCV), France. SANOFI corporation donated 15,000 euros to ARCV for the activities of this organization. ARCV who sponsored the run-in period of the study used a part of this grant. Based on the run-in period expenses, the main study needs about 25,000 Euros per year for data collection and sample analyses (genetic and autopsy). Funding of the main study is pending. To facilitate international fundraising, collaboration with leading laboratories and researchers in Western countries has already been established.
# Appendix A. Electronic case report form (Douala Sudden Cardiac Death Survey).

<table>
<thead>
<tr>
<th>Country</th>
<th>[choose one]</th>
<th>State</th>
<th>[choose one]</th>
<th>Ethnicity</th>
<th>[choose one]</th>
<th>Completed by</th>
<th>[choose one]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identity</td>
<td>[male] [female]</td>
<td>Sex</td>
<td>[male] [female]</td>
<td>Date of birth</td>
<td>Select Date</td>
<td>Age</td>
<td>[choose one]</td>
</tr>
</tbody>
</table>

## Epidemiology of SCD and Initial Clinical Presentation - Criteria for Eligibility
- Abnormal death defined as death, sudden, unexplained, unexpected, or occurring within 1 h of the onset of acute symptoms.
- Presence of heart disease may have been known to be present, but the time and mode of death are unexpected.

- In hospital SCD
- Out of hospital SCD
- Home
- Work
- Public place
- Others, precise:
- Unwitnessed SCD
- Witnessed SCD
- Family
- Friends
- Colleagues
- Others, precise:

### Resuscitation attempts
- No
- Yes
- Defibrillation

### Documented ECG
- No
- Yes
- VT
- VF

### Activity at the time of SCD
- Sleeping
- Resting
- Physical activity
- Sport activity
- Others, precise:

### Hour of occurrence
- Night time
- Day time
- Hour (if available)

### Time interval between cardiac arrest and first CPR (if available)
- (min)
- Survive
- Yes
- No

### Post-resuscitation syndrome
- Cardiac death
- Neurological death
- Motor and/or cognitive deficits

### Previous history of structural cardiac disease
- No
- Yes, precise
- LV ejection fraction:
- NYHA

### Classification:

#### Previous cardiac evaluation
- Ambulatory
- Yes
- No
- In-hospital
- Yes
- No

### Medical history

#### Cardiologic?
- Yes
- No
- HF
- Congenital
- Family history of SCD
- RAA
- Coronary artery diseases
- Idiopathic Dilated Cardiomyopathy
- Hypertrophic Cardiomyopathy
- Other Cardiomyopathy
- Pacemaker or ICD
- Hypertension

#### Neurological?
- Yes
- No
- Core pulmonary
- Epilepsy
- Cerebro-vascular disease
- Other, precise

### Tropical Diseases
- No
- Yes, precise
- Other, precise

#### Others?
- Yes
- No
- Diabetes
- Alcoholism
- Smoking
- Other addiction
- Depression/Anxiety disorders
- HIV/AIDS
- Other, precise
All information of interest for establishing causes of death will be recorded in the e-CRF. These data include socio-demographic (identity, age, gender, nationality, employment status, monthly incomes), past medical history focusing on cardiovascular conditions, the etiology of death and the associated medical conditions. In-hospital/out-of-hospital, unwitnessed/witnessed deaths, activity of the time of SCD, time of occurrence (day/night) and post-resuscitation outcome will be noticed. Medical history reports heart diseases (as HF, MI, CM, CAD, RHD), neurological, tropical, infectious and other. Clinical evaluation and diagnostic tests refer to physical examination, 12-lead ECG, blood biochemistry, non-invasive cardiac tests (TTE, Holter ECG, stress imaging, signal-averaged ECG, cardiac MRI), invasive tests (coronarography, electrophysiological study, autopsy) and genetic screening. e-CRF: electronic case report form; SCD: sudden cardiac death; HF: heart failure; MI: myocardial infarction; CM: cardiomyopathy; CAD: congenital heart disease; RHD: rheumatic heart disease; ECG: electrocardiogram; TTE: transthoracic echocardiography; MRI: magnetic resonance imaging.

References

[34] Uniting against NCDs: the time to act is now. The Brazzaville declaration on noncommunicable diseases prevention and control in the WHO African region. Available at: http://www.who.int/en/.