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Incidence of Sudden Cardiac Death in China

Analysis of 4 Regional Populations

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Sudden cardiac death (SCD) is most commonly defined as unexpected death from a cardiac cause within a limited time period, generally <1 h from symptom onset, in a person without any prior condition to explain the fatality (1–3). Often SCD is the first and only manifestation of heart disease (4). In the U.S., SCD accounts for about one-half of all coronary heart disease (CHD) deaths (5), for a total of 300,000 to 400,000 deaths annually, depending on the definition used (2,3).

China is the largest developing country in the world, with a land mass of 9.6 million km^2 and a population of 1.33 billion people. The profile of cardiovascular disease (CVD) of China is very different from Western populations: for example, compared with Western countries, the incidence of CHD is much lower in China but the incidence of stroke is higher (6,7). Consequently, the incidence of SCD in China may be lower than that of Western populations, but to our knowledge there are no currently available data on the incidence rate of SCD in China. Conversely, because of the geographic, economical, and cultural differences in different parts of China, there are significant regional variations in CHD incidence (8). Therefore, several Chinese populations would have to be assessed to obtain accurate information regarding SCD. Thus, in the present study, we explore the incidence rate of SCD in 4 regional populations.

Methods

Study population and data collection. To provide an adequate representation of socioeconomic status, geographical location, and rural versus urban environments, populations in 4 regions of mainland China were evaluated (Fig. 1). Each study region included residents of a defined geographical area, and each population studied ranged from 150,000 to 200,000 residents. In Yuxian, an undeveloped inland rural area in the Shanxi province of central China, the study population consisted of a clustered sampling of all men and women living in 158 of the 453 villages in the region. Additional study populations came from the large cities of Beijing in northern China (cluster sampled from the Xicheng district; there were 660,000 residents in the Xicheng district in Beijing in 2005) and Guangzhou in southern China (cluster sampled from the traditional Yuexiu district; there were 410,000 residents in the traditional Yuexiu district in Guangzhou in 2005). Both the Beijing and Guangzhou

Figure 1 **Geographic Locations of Study Populations**

These regions were chosen to provide representation of populations with varying socioeconomic status, geographical location, and rural versus urban environments.

study populations came from the central area of the cities and provided suitable overall representation of the citizenry in those cities. In Kelamayi, a small city in the Xinjiang Uigur autonomous region located in northwest China, all residents in the city zone were selected as the study population because of the small overall population size. Regarding socioeconomic status, Beijing and Guangzhou are the most developed areas in China, Yuxian is undeveloped and on the lower end of the socioeconomic scale, and Kelamayi falls between the socioeconomic extremes.

A 3-level case reporting and ascertainment system was established for SCD surveillance. The first level included the household administrative office and health station within the neighborhoods; the local centers, which verified data received from the administrative offices, comprised the second level; and the final evaluation of the data took place at the coordinating center. In Kelamayi and Yuxian, the local center was the central hospital in the geographic catchment area. In Beijing and Guangzhou, the local center was composed of a local hospital and the neighborhood center for disease control and prevention.

Each population was covered by the governmental household registry system, which documents births or migration into the area as well as deaths or area emigration. The household administrative office and health station were responsible for gathering information within each population center. Personnel collected the death certificate from family members of the decedent and issued the burial certificate, which is required for interment.

In China, Ministry of Health regulations insist that causes of death on death certificates be reported either by the physician who witnessed the death in a hospital or by a medical examiner when the subject dies out of hospital. Deaths are coded based on the 10th Revision of the International Classification of Diseases. Total number of subjects monitored and their age, sex, and vital status (if deceased, the cause of death) could be obtained from local administrative offices. To ensure accuracy, the household administrative worker in each station of the public safety bureau was required to collect supplemental information, such as timing from the onset of symptoms to loss of consciousness. This was obtained from family members of the decedent, hospital personnel if the decedent died in hospi-

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tal, or other witnesses to the death. In areas where data collection is difficult, we collected information on the medical history, symptoms, and circumstances surrounding each death, using multiple sources to verify the cause of death. We not only interviewed the decedent's relatives and witnesses, but also collected related medical records from the hospitals and the health station in the community. In Yuxian, such information was generally collected by an experienced cardiologist from the local center. The cardiologist would visit the home of the decedent and the hospital if the decedent had been admitted, interview witnesses, collect all relevant information, and verify each case's cause of death.

Death certificates and supplemental information were initially reported monthly to the local centers (except in Yuxian, where they were already collected by a cardiologist). At the local center, the diagnosis committee, composed of qualified physicians, verified the death certificates and supplemental information and excluded cases that were definitely not SCD (including death caused by trauma, violence, suicide, drowning, noncardiac chronic and terminal illness, and other specific noncardiac causes).

The local center diagnosis committee retained those cases that might be SCDs, including individuals who died unexpectedly and those classified under specific 10th Revision of the International Classification of Diseases codes: I00 to I09, I11, I20 to I51, Q20 to Q24, and R95 to R99. For all cases that might be SCDs, the local center sent a trained staff member to collect more detailed information (including circumstances of death, medical records, and available autopsy data) from the hospital where the death occurred, family members of the decedent, and/or witnesses. The local center diagnosis committee reviewed all data collected and issued a preliminary diagnosis. Finally, all data were dispatched to the coordinating center, where the central diagnosis committee of cardiologists and epidemiologists adjudicated the final SCD cases. The institutional review board of the Fuwai Hospital approved this study. Informed consent was obtained from the family members of all decedents.

Definition of SCD. Generally, SCD is defined as a death that occurs from cardiac causes $<$1 h after symptom onset in a person without any previous condition that would seem fatal. However, this definition is difficult to apply in a study setting because of the challenges of determining the exact cause of death and the precise timing from symptom onset to loss of consciousness. Therefore, for the purposes of this study, SCD was defined as: 1) death that occurred unexpectedly within 1 h of symptom onset without a specific noncardiac cause identified (traditional definition of SCD); 2) any unexpected death within 1 to 2 h of symptom onset and no specific noncardiac cause, which was a supplemental definition for cases in which the exact time from onset of symptoms to loss of consciousness could not always be determined; 3) death that occurred during sleep, with no symptoms before sleeping and no specific noncardiac cause; or 4) death that occurred per category 1, 2, or 3, but for which insufficient supplemental data could be obtained by the local center. In these latter instances, the death certificate and other information were collected at the household administrative office level but the local center was not able to obtain further corroborating information.

Data quality and statistical analysis. To ensure thorough and uniform data collection and verification of all possible SCD cases from the 4 study populations, a single study protocol and authorized questionnaires were used by all study staff members. Accuracy of the data collected was verified at each level by trained staff members before a final diagnosis adjudicated by the diagnosis committee at the coordinating center.

The chi-square test and Fisher exact test were used to compare proportions. A *t* test or analysis of variance was used to compare the means. The Z test was used to compare crude SCD incidence rates. To test for trends, the Cochran-Armitage trend test was performed. Test results yielding 2-tailed values of $p < 0.05$ were considered statistically significant. Age-adjusted rates were computed by the direct method with the Chinese population age 25 years and older in 2000 as the standard. The standardized rate ratios (SRRs) were calculated to compare age-standardized SCD incidence rates (9). We considered differences of the age-standardized SCD incidence rates between regions or sex to be significant if the 95% confidence interval of the SRR did not include the value of 1.0.

Results

Demographics of the study population. Between July 1, 2005, and June 30, 2006, a total of 678,718 subjects were monitored in this prospective study, and 2,983 deaths from any cause occurred in the 4 populations (Supplementary Table 1). There was a significant difference in age of the 4 study populations ($p < 0.001$ for both men and women) (Fig. 2).

Incidence of SCD. During the study period, a total of 284 SCDs (154 men, 130 women) occurred. The mean age at SCD was 66.7 ± 16.9 years (range 17.0 to 95.5

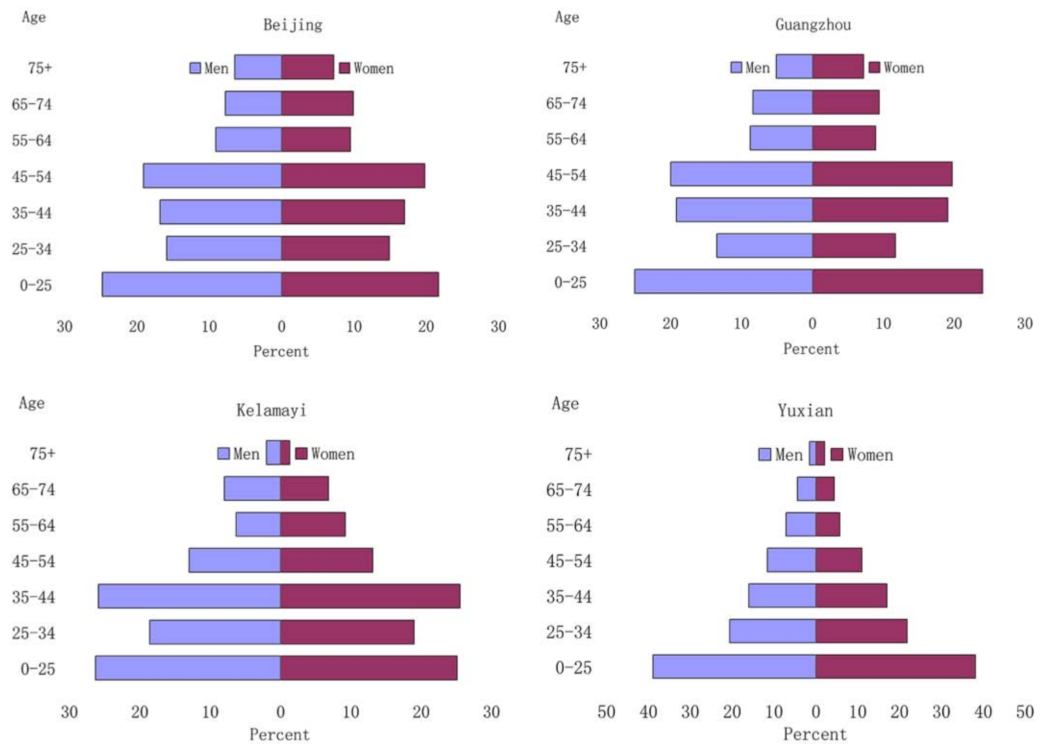

Figure 2 **Comparative Age Distributions of the 4 Regional Populations by Sex**

Note that $p < 0.001$ across the study populations.

years) for men and 73.8 ± 13.5 years (range 25.4 to 101.8 years) for women ($p < 0.001$). Of these, 174 (61.3%) occurred unexpectedly within 1 h of symptom onset, 31 (10.9%) occurred unexpectedly within 1 to 2 h, 58 (20.4%) occurred during sleep, and 21 (7.4%) had insufficient data to identify timing or cause of death

Table 1 **Characteristics of SCD Cases and Relevant Population**

	Beijing	Guangzhou	Kelamayi	Yuxian	p Value
Population size	206,046	149,222	160,460	162,990	
Number of all-cause deaths	769	821	566	827	
Number of SCD cases					
Male	54	35	29	36	
Female	49	35	18	28	
SCD category*					
1	63 (61.2%)	44 (62.9%)	29 (61.7%)	38 (59.4%)	
2	12 (11.7%)	12 (17.1%)	5 (10.6%)	2 (3.1%)	<0.001
4	19 (18.4%)	11 (15.7%)	4 (8.5%)	24 (37.5%)	
9	9 (8.7%)	3 (4.3%)	9 (19.1%)	0 (0)	
Percent of overall death	13.4%	8.5%	8.3%	7.7%	<0.001
Age of SCD cases (yrs)	75.4 ± 14.4	73.1 ± 14.0	60.6 ± 16.2	64.7 ± 15.0	<0.001

*Onset of symptoms: 1 = within 1 h, 2 = within 1 to 2 h, 4 = during sleep, 9 = insufficient data. Numbers in parentheses indicate proportion of the total cases.
SCD = sudden cardiac death.

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(Table 1). SCD accounted for 13.4%, 8.5%, 7.7%, and 8.3% of mortality in Beijing, Guangzhou, Yuxian, and Kelamayi, respectively, and accounted for 9.5% of overall mortality of the 4 populations as a whole. The overall incidence of SCD across the 4 populations was 41.8 of 100,000 per year (44.6 of 100,000 per year for men and 39.0 of 100,000 per year for women; $p = 0.26$).

The incidence of SCD increased significantly with age in all 4 populations (Fig. 3, Supplementary Table 2). Most cases occurred in populations 65 years and older, with only 2 cases in individuals <25 years of age.

Consistently, SCD incidence rates in men were higher than those for women. Significantly higher SCD incidence rates were observed in Yuxian (Tables 2 and 3, Supplementary Table 3). Among men in this undeveloped rural area, SCD incidence was nearly twice that of men in the large city of Guangzhou; for women in Yuxian, the SCD incidence rate was nearly 3 times that of women in the capital city of Beijing.

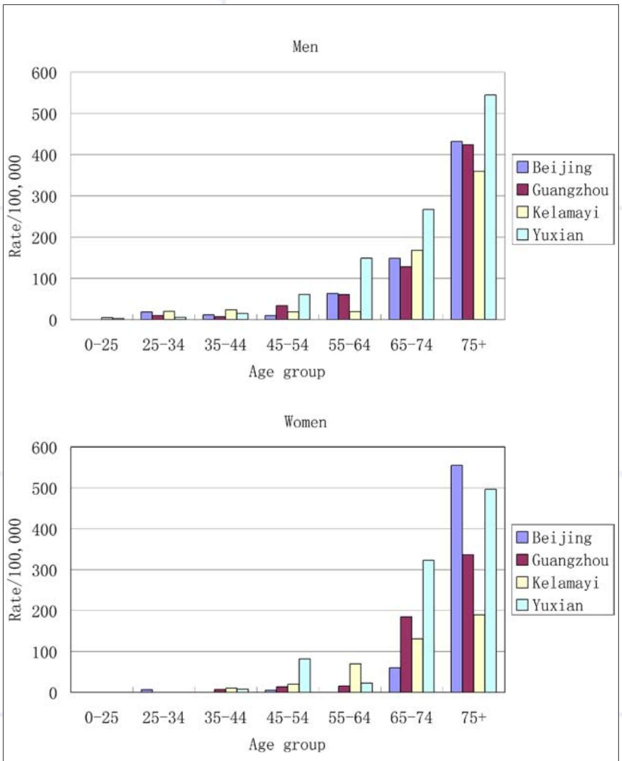

Figure 3 Age-Based Annual Incidence of Sudden Cardiac Death of 4 Regional Populations

Table 2 Age-Standardized Sudden Cardiac Death Incidence Rates of the Study Populations Ages 25 Years and Older

Study Population	Age-Standardized Rates (1/100,000)		Standardized Rate Ratios (95% Confidence Interval)*
	Men	Women	
Yuxian	66.1	56.1	1.18 (0.70–2.00)
Kelamayi	40.4	29.5	1.37 (0.73–2.57)
Beijing	37.3	19.2	1.95 (1.15–3.29)
Guangzhou	33.9	27.0	1.25 (0.71–2.23)

*Standardized rate ratio values are based on using women as the reference.

Association with CVD. Information on SCD decedents' history of CVD was assessed retrospectively (Table 4). More than one-half of the decedents had a history of CVD (56.5% of men and 57.7% of women) based on the presence of hypertension, angina pectoris, history of myocardial infarction, heart failure, and so on.

Discussion

Despite the increasing global burden of heart disease, this is the first study to explore the epidemiologic features of SCD in China. Regional variations in SCD incidence were detected, with significantly higher rates in the rural area of Yuxian, an undeveloped inland rural area, where the socioeconomic status is among the lowest in China and the residents have the poorest medical care. In Yuxian, the incidence of SCD was higher in men than in women, although the differences were not statistically significant (Table 2).

Table 3 Standardized Rate Ratios Comparing Age-Standardized Sudden Cardic Death Incidence Among Regions in the Study Population Ages 25 Years and Older

Study Population	Standardized Rate Ratio (95% Confidence Interval)*	
	Men	Women
Yuxian		
Kelamayi	1.64 (0.97–2.75)	1.90 (1.01–3.59)
Beijing	1.77 (1.08–2.91)	2.93 (1.68–5.09)
Guangzhou	1.95 (1.15–3.31)	2.08 (1.17–3.68)
Kelamayi		
Beijing	1.08 (0.64–1.84)	1.54 (0.82–2.87)
Guangzhou	1.19 (0.68–2.08)	1.09 (0.57–2.07)
Beijing		
Guangzhou	1.10 (0.64–1.88)	0.71 (0.40–1.24)

*Standardized rate ratio values are based on column 2 as the reference.

Table 4 Proportion of SCD Cases With Definite Cardiovascular History (Number of Cases)

	Population					
	Beijing	Guangzhou	Kelamayi	Yuxian	Total	p Value
Men						
n	54	35	29	36	154	
Hypertension	51.9 (28)	48.6 (17)	41.4 (12)	38.9 (14)	46.1 (71)	0.611
Angina pectoris	16.7 (9)	17.1 (6)	20.7 (6)	22.2 (8)	18.8 (29)	0.904
Myocardial infarction	16.7 (9)	11.4 (4)	6.9 (2)	8.3 (3)	11.7 (18)	0.569
Heart failure	11.1 (6)	5.7 (2)	3.5 (1)	5.6 (2)	7.1 (11)	0.670
Cor pulmonale	0 (0)	5.7 (2)	10.3 (3)	8.3 (3)	5.2 (8)	0.06
Other CVD disease*	3.7 (2)	0 (0)	0 (0)	6.9 (2)	2.6 (4)	0.026
Any one of above	59.3 (32)	51.4 (18)	58.6 (17)	55.6 (20)	56.5 (87)	0.897
Women						
n	49	35	18	28	130	
Hypertension	38.8 (19)	60.0 (21)	33.3 (6)	35.7 (10)	43.1 (56)	0.123
Angina pectoris	20.4 (10)	31.4 (11)	16.7 (3)	32.1 (9)	25.4 (33)	0.438
Myocardial infarction	22.5 (11)	28.6 (10)	0 (0)	0 (0)	16.2 (21)	<0.001
Heart failure	10.2 (5)	8.6 (3)	5.6 (1)	3.6 (1)	7.7 (10)	0.803
Cor pulmonale	4.1 (2)	2.9 (1)	0 (0)	0 (0)	2.3 (3)	0.866
Other CVD*	0 (0)	2.9 (1)	0 (0)	0 (0)	0.8 (1)	0.269
Any one of above	53.1 (26)	71.4 (25)	44.4 (8)	57.1 (16)	57.7 (75)	0.218

*Includes rheumatic heart disease, congenital heart disease, myocarditis, and cardiomyopathy.
CVD = cardiovascular disease; SCD = sudden cardiac death.

Attention to prevention of SCD in this rural area needs to become a priority.

There was no significant difference in SCD rates for the nation's capital of Beijing (in the north) and Guangzhou (to the south); both are large, well-developed cities with a high percentage of older residents. Epidemiologic studies previously suggested a higher incidence of CVD and CHD in the north than in the south of China (8,10), probably because of a greater prevalence of risk factors among those surveyed in Beijing (11) (Supplementary Table 4). However, for the last 20 years, Guangzhou has been one of the country's fastest developing areas, and this economic growth has been accompanied by a marked increase in CVD risk factors (12), which may explain in part why we found parity in SCD rates for these 2 regions.

Our study shows that among men and women, residents of Yuxian were more likely to suffer SCD. What seems to be an increasing burden of CVD combined with inferior CVD management may explain this observation. Although our previous study showed a lower incidence of CHD in Yuxian (10), more recent studies suggest that CVD risk factors have increased greatly in the rural area in China, narrowing the difference between urban and rural areas (13–15). For example, from 1992 to 2002, the prevalence of overweight and obesity increased by nearly one-half (47.4%) among urban men compared with urban women (14.1%); however, prevalence rates during this same time period increased even more among rural residents: an 83.2% increase for men and 39.9% for women (13). Similarly, a 1991 national study showed a hypertension prevalence of 16.3% in urban areas and 11.1% in rural areas (14), but by 2002 this gap largely had closed, with a 19.3% prevalence rate in urban versus 18.6% in rural areas (15). Although risk factors have increased, CVD management in Yuxian continues to be inferior to that of its urban counterparts. Even in the presence of established CVD, residents of Yuxian and similar rural areas are less likely to go to the hospital: according to the 2003 National Health Service survey, the hospitalization rate for CVD in rural areas was 4.3% versus 11.9% in urban areas (16). Moreover, knowledge regarding CVD and its risk factors is much poorer among residents in the rural area of inland China than in urban areas. For example, the proportion of residents who understood high salt intake to be a risk factor of hypertension was only 2.65% in the rural area of Shanxi (17) versus 86.6% of residents in the urban area of Beijing (18). Thus the rapid increase of CVD risk factors in rural China may create an urgency to improve the management of CVD to decrease the incidence of SCD.

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Because the present study involved only 4 regions of a country that is similar in geographic size to the U.S., it is difficult to accurately calculate the incidence of SCD in China as a whole based on these results. However, our study populations were selected after careful consideration of socioeconomic status, geography, and rural versus urban environments.

Although the size and complexity of China create barriers to obtaining nationwide data, the nature of the government household administrative system in China enhances the ability to collect complete and accurate data on specific study populations. Therefore, we think the current study permits an estimation of total incidence of SCD for the country as a whole. Based on an overall incidence rate of the 4 populations (41.8 of 100,000 per year), we estimate that the approximate annual incidence of SCD among the 1.33 billion Chinese citizens is about 500,000. This is a large number, and it helps quantify the need for prevention of SCD in the Chinese population.

Comparing China and U.S. data. In the U.S., estimates of SCD incidence vary greatly, but the most commonly used estimates range from about 300,000 to 350,000 per year (19,20). Given the current U.S. population of slightly more than 300 million, SCD incident rate estimates currently range from 100 of 100,000 to 117 of 100,000 per year, which varies greatly when analyzed by sex. A study conducted by Escobedo et al. (20), for example, suggested an SCD rate in men of 176.3 of 100,000 per year but only 85.4 of 100,000 per year among women. Even after applying a more conservative definition of SCD, the Escobedo study suggests a much higher incidence of SCD in the U.S. compared with China. Yet the only prospective U.S. study of SCD in a general population (Oregon), suggested a much lower regional annual incidence of SCD (53 of 100,000 per year) (21). Although the results of the current study are close to the Oregon analysis, our definition of SCD was broader: including patients with insufficient data and death occurring unexpectedly within 1 to 2 h of symptom onset. Also, because of the lack of autopsy data, sudden death by other causes might have been included in our study. A more narrow definition likely would have lowered the incidence rate seen in China.

Similar to the U.S., the SCD incidence in China increases sharply with increasing age. However, in our study, only 2 cases of SCD occurred in individuals younger than 25 years of age (0.7% of the 284 SCDs). Among the 4 study populations, there were a total of 55 deaths from any cause in study subjects <25 years of age (1.8% of the 2,983 deaths). Of the 55 cases, 9 died of leucocythemia and other cancers; 21 died of accidents, toxins, and suicide; 25 died of other causes (cerebral palsy, asthma, heart failure stemming from congenital heart disease, cephalitis, bedsore, uremia, systemic scleroderma, and so on) and only 3 subjects died suddenly. Of the 3 sudden death cases, 1 died of acute pancreatitis. Although the accuracy and detail of the data collected support the finding of only 2 SCDs among all deaths in subjects <25 years of age, the small number of total deaths in this younger population may have been too small to draw any conclusions and further study with a larger sample size may be needed to clarify this question.

Regarding SCD incidence by sex, the Chinese data closely follow the observations from the prospective study in Oregon (21) but sharply contrast with retrospective U.S. data suggesting a 2- to 4-fold higher incidence of SCD in men compared with women (19,22,23). (However, a prospective study conducted in the U.S. by Chugh et al. [21] did not show a sex difference.) Although our study added a more expansive definition of SCD to the more traditional definition, we do not think it explains the differences between our data and previous retrospective studies. The careful prospective case ascertainment and review in the present study is likely an important influence on the outcomes reported here.

The design and results of the current study are similar to those of Chugh et al. (21), who found that death certificate surveillance significantly overestimates SCD incidence. However, unlike Chugh et al. (21), the present study used additional measures to verify death certificate data (i.e., collecting data from relatives, witnesses, and hospitals) as well as more comprehensive evaluations of the relevant data. This may have led to the exclusion of cases that might have been classified SCD in other studies. Moreover, suspicious or abnormal deaths were confirmed via post-mortem examination by medical examiners that could provide more expert determinations of cause of death.

It is also likely that the extensive nature of this study's data collection provided more accurate information overall. Although most existing data on SCD in Chinese populations come from in-hospital studies (24,25), the present study was community based, permitting more in-depth collection of data and better analysis of demographic and regional differences. Moreover, interviews with relatives and witnesses were done on a monthly basis, which helped ensure that data would not be lost and recollections gathered would be fresher and more accurate.

Finally, because of the nature of SCD, there are often not enough clinical data available to determine an exact cause of death. Therefore, we collected retrospective patient histories of CVD to explore possible associations with SCD. Most SCD decedents had at least 1 pre-existing cardiovascular condition, such as hypertension (39% to 52%) or angina pectoris (17% to 22%). Clearly prevention of hypertension may be as important as prevention of coronary disease to curb SCD in China. Regionally, however, decedents showed differences in the prevalence of cardiovascular history among SCD cases. This may be caused by differences in access to and quality of medical care as well as variability in disease and risk factors based on environmental or lifestyle variables. In China, geography and the environment widely influence food production and dietary habits; additionally, there is a disparity in development and socioeconomic status, all of which impact disease and risk factor incidence (6,10,26).

Study limitations. Post-mortem examination is considered highly valuable in determining the etiologic basis for SCD. However, autopsies are rarely performed in China, so access to such data was negligible, which may limit the accuracy of this study. This was especially true for SCD diagnoses in Kelamayi and Yuxian, where it was difficult gathering adequate clinical data about the decedent in such remote areas because of the more primitive level of health care systems in these areas.

Additionally, inherent difficulties in determining the timing from the onset of symptoms to death created the need to expand the definition of SCD in this study. Again, the more isolated regions of Kelamayi and Yuxian, with their more limited medical facilities and residents who were less medically knowledgeable, posed particular problems in determining time of death from symptom onset. This created the need to use a more expansive, 4-pronged definition of SCD and the inclusion of certain cases for which a preliminary diagnosis of SCD was made but corroborating evidence could not be obtained. However, use of broader definitions might introduce errors that could result in an overestimation of SCD incidence in China.

Limited funding restricted the size of patient populations studied. Thus, only 4 sample populations of 150,000 to 200,000 each were included out of a country with more than 1.3 billion people. The populations were carefully chosen to reflect geographic and socioeconomic diversity, but because sample size and funding limited us to specific regions within the cities of Beijing and Guangzhou, the samples were not random from throughout the cities and the data may not consistently represent the total resident populations of those cities. Moreover, in Yuxian, clustered sampling was conducted; in Beijing and Guangzhou, clustered sampling was conducted in specific regions within the cities (the Xicheng district in Beijing and the traditional Yuexiu district in Guangzhou); and in Kelamayi, because of the small number of the city residents, all residents in the city zone were covered in our surveillance. The difference in the sampling methods in different regions and the appliance of clustered sampling in some regions may limit the accuracy of our result. Therefore, more effort is needed to obtain accurate data on the incidence of SCD in China.

Funding also limited the type of data collected. Although patient history of CVD could be determined from records and interviews, cardiovascular risk factors were not surveyed and assessed in this study. Data from a previous study (11) were considered in analyzing the potential impact of such factors on SCD in these populations.

Conclusions

This is the first study to explore the epidemiologic features of SCD in China and the findings provide a starting point for further evaluation of this problem. Although previous studies showed significant regional differences in the level of cardiovascular risk factors and incidence of CHD in China, the current study did not find similar significant variations in the incidence of SCD. The results do suggest a higher incidence of SCD in rural areas of China, especially among women. For effective prevention of SCD across China, such variations will need to be considered when developing programs to reduce this risk.

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September 15, 2009:1110–8

Acknowledgments

The study has been accomplished through the fine work of the staff at the local and national centers. The authors deeply appreciate their participation in this study.

Please note: Dr. Wu is currently at the Peking University School of Public Health, Beijing, China. This study was supported by the National 10th Five-Year Plan Science and Technology Key Projects in People's Republic of China (grant no. 2004BA714B03). Drs. Wei Hua and Lin-Feng Zhang contributed equally to this work.

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Key Words: cardiac death ▪ China ▪ populations.

APPENDIX

For supplementary tables, please see the online version of this article.

doi:10.1016/j.jacc.2009.06.016