# Risk factors of CVD mortality among the elderly in Beijing, 19922009: An 18-year cohort study 

Tao Zhou
Xia Li
Zhe Tang
Changchun Xie
Lixin Tao

See next page for additional authors

Follow this and additional works at: https://ro.ecu.edu.au/ecuworkspost2013
Part of the Cardiovascular Diseases Commons

[^0]
## Authors

Tao Zhou, Xia Li, Zhe Tang, Changchun Xie, Lixin Tao, Lei Pan, Da Huo, Fei Sun, Yanxia Luo, Wei Wang, Aoshuang Yan, and Xiuhua Guo

International Journal of Environmental Research and

Public Health
ISSN 1660-4601
www.mdpi.com/journal/ijerph

## Article

# Risk Factors of CVD Mortality among the Elderly in Beijing, 1992 - 2009: An 18-year Cohort Study 

Tao Zhou ${ }^{1,2, \dagger}$, Xia Li ${ }^{1,2,3, \dagger}$, Zhe Tang ${ }^{4, \dagger}$, Changchun Xie ${ }^{5}$, Lixin Tao ${ }^{1,2}$, Lei Pan ${ }^{1,2}$, Da Huo ${ }^{6}$, Fei Sun ${ }^{4}$, Yanxia Luo ${ }^{1,2}$, Wei Wang ${ }^{7}$, Aoshuang Yan ${ }^{8, *}$ and Xiuhua Guo ${ }^{1,2, *}$

${ }^{1}$ School of Public Health, Capital Medical University, 10 Xitoutiao, Youanmen, Beijing 100069, China; E-Mails: zhoutaosmile@126.com (T.Z.); lixia_new@163.com (X.L.); taolixin.2008@163.com (L.T.); panlei_helen@163.com (L.P.); lyx100@ccmu.edu.cn (Y.L.);
2 Beijing Municipal Key Laboratory of Clinical Epidemiology, 10 Xitoutiao, Youanmen, Beijing 100069, China
3 Epidemiology and Public Health, University College Cork, Western Road, Cork 78746, Ireland
4 Xuan Wu Hospital, Capital Medical University, 45 Changchun Street, Beijing 100069, China; E-Mails: tangzhe@medmail.com.cn (Z.T.); sf69@163.com (F.S.)
5 Division of Epidemiology and Biostatistics, Department of Environmental Health, University of Cincinnati, Ohio, OH 45267, USA; E-Mail: xiecn@ucmail.uc.edu
${ }^{6}$ Institute for Infectious Disease and Endemic Disease Control, Beijing Center for Disease Prevention and Control, No. 16 Hepingli Middle Street, Dongcheng District, Beijing 100013, China; E-Mail: howardhuo@139.com
7 School of Medical Science, Edith Cowan University, 2 Bradford Street, Mount Lawley, Massachusetts, WA 6050, Australia; E-Mail: wei6014@yahoo.com
${ }^{8}$ Beijing Municipal Science and Technology Commission, Sijiqing Street, Beijing 100195, China
$\dagger$ These authors contributed equally to this work.

* Authors to whom correspondence should be addressed; E-Mails: statguo@ccmu.edu.cn (X.G.); hnlg0771@hotmail.com (A.Y.); Tel.: +86-108-391-1508 (X.G.); Fax: +86-108-391-1508 (X.G.).

Received: 11 November 2013; in revised form: 14 January 2014 / Accepted: 21 January 2014 / Published: 21 February 2014


#### Abstract

Few researchers have examined the effects of multiple risk factors of cardiovascular disease (CVD) mortality simultaneously. This study was to determine the associations of combined lifestyle and other factors with CVD mortality among the elderly ( $\mathrm{n}=3,257$ ), in Beijing, China, through data mining of the Beijing Longitudinal Study of


Aging (BLSA). BLSA is a representative cohort study from 1992 to 2009, hosted by Xuan Wu Hospital. Competing risk survival analysis was conducted to explore the association between risk factors and CVD mortality. The factors focused mainly on lifestyle, physical condition, and the model was adjusted for age and gender. There were 273 of the 1,068 recorded deaths caused by CVD among the 2010 participants. Living in a suburban area ( $\mathrm{HR}=0.614,95 \% \mathrm{CI}: 0.410-0.921$ ) was associated with lower CVD mortality. Increasing age (66-75: $\mathrm{HR}=1.511,95 \% \mathrm{CI}: 1.111-2.055 ; \geq 76: \mathrm{HR}=1.847,95 \% \mathrm{CI}: 1.256-2.717$ ), high blood pressure ( $\mathrm{HR}=1.407,95 \% \mathrm{CI}: 1.031-1.920$ ), frequent consumption of meat ( $\mathrm{HR}=1.559,95 \% \mathrm{CI}: 1.079-2.254$ ) and physical inactivity ( $p=0.046$ ) were associated with higher CVD mortality. The study provides an instructional foundation for the control and prevention of CVD in Beijing, China.

Keywords: cardiovascular disease; competing risk model; Fine and Gray's test; risk factors

## 1. Introduction

Cardiovascular disease (CVD) is an important worldwide public-health challenge because of its high prevalence and mortality [1-3]. It accounted for $30 \%$ of all global deaths in 2011, according to the World Health Organization [4,5] and CVD has also become the top cause of diseases and deaths among the Chinese [6]. As the greater likelihood of early death and huge disability-adjusted life-years caused by CVD, the discussion of the risk factors for CVD would allow public-health policy-makers to assign effective priority and resources to its management and prevention [7].

The increasing prevalence of CVD results from the aging population, and Beijing has already entered the aged society status in 1990 [8,9]. Many epidemiologic studies have examined the association of individual lifestyle practices, such as smoking, physical activities, etc. [10,11], but few studies have addressed the effects of simultaneous multiple risks factors as well as considering the competing risk events.

Survival techniques are well developed and implemented in major statistical software to the time-to-event analysis. Yet, there are some situations where it may not be appropriate to apply the usual survival methods. Such as analysis of the data when competing risk are present requires specific methods, the Kaplan-Meier method has been shown to overestimate the probability of death in comparison with the more specific competing risk model [12,13]. Individuals are generally observed from the study entry until the occurrence of the event of interest, a competing risk event, or censoring [14-16]. In general, a competing risks situation arises when an individual can experience more than one type of event and the occurrence of one type of event hinders the occurrence of other types of events. [17,18]. The aims of the present study were to determine the major predictors of CVD mortality by a comprehensive model, while incorporating the competing events of the alternate outcomes into the analysis.

## 2. Methods

### 2.1. Study Design and Population

Data were derived from the BLSA, a community-based prospective cohort study hosted by Xuan Wu Hospital in Beijing, which began in August 1992. A random sample of 3,257 community dwellers aged 55 years or above was recruited from three districts: Xuanwu (urban), Daxing (suburban), Huairou (rural). All participants completed a questionnaire regarding lifestyle and health behaviors, ets., and 2,101 subjects who had undergone routine blood biochemical examination at baseline were selected from the 3,257 participants. Because of missing data, 2,010 subjects were finally included in the analysis.

### 2.2. Assessment of Risk Factors

The study was mainly focused on lifestyle, physical condition and dietary habits. Several conditions (high blood pressure, high blood glucose, and blood fat) which could be consequences of an unhealthy lifestyle or dietary habits were also included. Activities of Daily Living (ADL) scale and Center for Epidemiological Studies Depression (CES-D) scale were detailed measured. All risk factors were assessed by self-reporting on the questionnaires with a high degree of reliability and accuracy. The follow-up studies were conducted every two or three years. Baseline values were used in this analysis to minimize the potential of clinical or subclinical diseases affecting the risk factor status.

Age was divided into several groups according to the initial age. Height, BMI (Body Mass Index) [19], blood pressure (BP), smoking status, drinking status, and the frequency of physical activities were measured and assessed at the beginning of the study. Blood samples were collected after an overnight fasting of at least 12 h . Glucose, high density lipoprotein (HDL), and triglycerides (TG) were subsequently measured. BP was measured on the right arm of seated subjects and at rest at least 10 min by a trained nurse. Then the subjects were divided into normal or abnormal groups according to the standard of diabetes mellitus [20] and dyslipidemia [21]. Dietary factors were assessed by a food frequency questionnaire. The average consumption of fish, meat, vegetables, fruit, and quantity of salt were reported by the subjects. According to the results of Latent Class Model [22], the subjects were divided into three groups. The first group represented sufficient nutrients, the second group comprised the intermediate-type diets, and the third group consumed meat-based diets. Generally, the intake of milk, fruits, bean products, and eggs were lower in the second and the third group. Physical limitation was assessed using the 12 items of ADL, which consists of two categories: Instrumental Activities of Daily Living (IADL) and Basic Activities of Daily living (BADL) [23]. The elderly were divided into self-care ability and self-care disability. In this study, CESD was used to assess depression symptoms. The total score was 60 and the standard cut-off value was 16 [24].

### 2.3. Ascertainment of Mortality

The main outcome was death from all causes, occurring after the return of 1992 questionnaire but before 31 December 2009. Years of follow-up were accrued from the return data of the questionnaire until either of the following first occurs: death, loss to follow-up or the end of follow-up. Causes of
death were grouped into four broad categories indicated by the International Classification of Disease, ninth revision (ICD-9) or ICD-10: Cardiovascular disease, cerebrovascular disease (CBVD), cancer and other diseases. The primary interested endpoint was death from CVD. Other causes of death comprised the competing risk events.

### 2.4. Statistical Analysis

Multiple Imputation (MI) was performed to fill in a few missing serum biochemical data. The Markov chain Monte Carlo method was chosen to avoid the loss of generality, which have considered the distribution of data. The MI procedure of SAS software package (version 9.2; SAS Institute, Chicago, IL, USA) was used [25].

The competing risk model was extended from Cox's proportional hazards model to competing-risks data and it has considered the sub-distribution hazard [26,27]. Contrary to a cause-specific analysis that censor competing event(s), the Fine-Gray approach "carries forward" the competing event(s) in the risk set with appropriate weighting [28-39]. In addition, the cumulative incidence functions (CIF) between different groups were compared, such as gender, status of self-health assessment, and so on. Univariate and multivariate analysis were used to identify the association between covariates and CVD mortality. Statistical significance was considered as a 2 -sided p -value of less than 0.05 . The results of univariate analysis ( $p$ value $<0.3$ ) were the criteria for inclusion of risk factors in the final multivariate model. Basic statistical analysis was performed by SAS version 9.2. Competing risk analysis was implemented in R (version 3.0.2) [30,31].

## 3. Results

### 3.1. Basic Characteristics and the CIF of Death

A total of 2,010 participants were included in the analysis. The number of participants who were excluded and the reasons for their exclusion are shown in Figure 1. The enrolled and the missed subjects were compared to assess enrolment bias, the differences of characteristics between these two groups were not statistical significant ( $p<0.05$ ). By the end of follow-up in 2009, there were 356 surviving subjects, 585 missing subjects, and 1,068 deaths. Among the 1,068 deaths, 273 were caused by CVD ( $25.54 \%$ ), 246 by cerebrovascular disease ( $23.01 \%$ ), 140 by cancer ( $13.10 \%$ ), and 409 were caused by "other causes" ( $38.35 \%$ ), shown in Table 1. At the end of follow-up, considering the competing risks, the CIF of CVD death was 0.19 , CBVD was 0.17 , and cancer was 0.10 . Additionally, the age of death was used as the abscissa to adjust the different distribution of age in different groups. The CIF of death due to CVD at age 85 was 0.20 , cerebrovascular disease was 0.16 , and cancer was 0.11 (Figure 2).

Table 1. Characteristics of subjects in Beijing between 1992 and 2009.

| Characteristic |  | Total Subjects (\%) | Total Deaths (\%) | CVD Deaths (\%) |
| :---: | :---: | :---: | :---: | :---: |
| Total |  | 2,010 (100) | 1,068 (100) | 273 (100) |
| Gender | male | 987 (49.104) | 545 (51.030) | 133 (48.718) |
|  | female | 1,023 (50.509) | 523 (48.970) | 140 (51.282) |
| Age group | 55-65 | 705 (35.075) | 246(23.034) | 67 (24.542) |
|  | 66-75 | 728 (36.219) | 408(38.202) | 106 (38.828) |
|  | $\geq 76$ | 577 (28.706) | 414 (38.764) | 100 (36.630) |
| Smoke | no | 593 (29.502) | 738 (69.101) | 83 (30.403) |
|  | yes | 1,417 (70.498) | 330 ( 30.899) | 190 (69.597) |
| Drink | no | 1,569 (78.060) | 832 (42.24) | 222 (81.319) |
|  | yes | 441 (21.940) | 236 (22.097) | 51 (18.681) |
| Depression | no | 1,649 (82.040) | 849 (79.494) | 215 (78.755) |
|  | yes | 361 (17.960) | 219 (20.506) | 58 (21.245) |
| Sad event | no | 1,364 (67.861) | 724 (67.790) | 177 (64.835) |
|  | yes | 646 (32.139) | 344 (32.210) | 96 (35.165) |
| Exercise | no | 806 (40.100) | 419 (39.232) | 111 (40.659) |
|  | yes | 1,204 (59.900) | 649 (60.768) | 162 (59.341) |
| BADL | normal | 1,936 (74.378) | 1,010 (94.570) | 264 (96.703) |
|  | disability | 74 (25.622) | 58 (5.431) | 9 (3.297) |
| IADL | normal | 1,495 (74.378) | 696 (65.169) | 183 (67.033) |
|  | disability | 515 (25.622) | 372 (34.831) | 90 (32.967) |
| Marital | have a spouse | 1,354 (67.363) | 645 (60.393) | 135 (49.451) |
|  | mateless | 656 (32.637) | 423 (39.607) | 90 (32.967) |
| Self-report | health | 1,639 (81.542) | 826 (77.341) | 211 (77.289) |
|  | not health | 371 (18.458) | 242 (22.659) | 62 (22.711) |
| Diabetes | abnormal | 1,698 (84.478) | 876 (82.022) | 222 (80.889) |
|  | normal | 312 (15.522) | 192 (17.978) | 51 (19.111) |
| Blood lipid | abnormal | 500 (24.876) | 251 (23.502) | 65 (24.4) |
|  | normal | 1,510 (75.124) | 817 (76.498) | 208 (75.6) |
| BP | $\begin{gathered} \mathrm{Sbp} \leq 120 \text { or } \\ \mathrm{dbp} \leq 80 \end{gathered}$ | 551 (27.413) | 245 (22.940) | 60 (21.978) |
|  | $\begin{gathered} \mathrm{Sbp}>120 \text { or } \\ \mathrm{dbp}>80 \end{gathered}$ | 255 (12.687) | 106 (9.925) | 22 (8.059) |
|  | $\begin{gathered} \mathrm{Sbp} \geq 140 \text { or } \\ \mathrm{dbp} \geq 90 \end{gathered}$ | 1,240 (61.692) | 717 (67.135) | 191 (69.963) |
| Education | college or above | 137 (6.816) | 48 (4.494) | 13 (4.762) |
|  | high school | 96 (4.776) | 34 (3.184) | 14 (5.128) |
|  | junior diploma | 165 (8.209) | 73 (6.835) | 18 (6.593) |
|  | primary school | 579 (28.806) | 283 (26.498) | 64 (23.443) |
|  | illiterate | 1,033 (51.393) | 630 (58.989) | 164 (64.073) |
| BMI | normal | 1,102 (54.826) | 579 (54.213) | 155 (56.777) |
|  | thin | 376 (18.706) | 239 (22.378) | 58 (21.245) |
|  | overweight | 276 (13.731) | 118 (11.049) | 26 (9.524) |
|  | obesity | 256 (12.736) | 132 (12.360) | 34 (12.454) |

Table 1. Cont.

| Characteristic |  | Total Subjects (\%) | Total Deaths (\%) | CVD Deaths (\%) |
| :---: | :---: | :---: | :---: | :---: |
| Residence | rural | $283(14.080)$ | $168(15.730)$ | $50(18.315)$ |
|  | suburban | $508(25.274)$ | $338(31.648)$ | $58(21.245)$ |
|  | urban | $1,219(60.647)$ | $562(52.622)$ | $165(60.440)$ |
|  | intermediate- <br> type diet | $1,016(50.547)$ | $569(53.277)$ | $131(47.985)$ |
|  | sufficient <br> nutrients | $693(34.478)$ | $300(28.090)$ | $85(31.136)$ |
|  | meat based diet | $301(14.975)$ | $199(18.633)$ | $57(20.879)$ |

Figure 1. The population flow chart.


Figure 2. CIFs for three main outcomes: CVD, CBVD and cancer.


Note: Abbreviations: $\mathrm{CVD}=$ cardiovascular disease; $\mathrm{CBVD}=$ cerebral vascular disease.

### 3.2. Competing Risk Model

Table 2 shows the association of each risk factor with CVD mortality. After considering competing risks of death, the mortality rates of the elderly without spouse, disabilities assessed by IADL, and poor self-assessed health were respectively at a higher risk than those who had a spouse, able-bodied, and with a healthy self-assessment. Additionally, subjects aged above 76, with high blood pressure, consuming more meat and illiterate were also associated with higher CVD mortality risk. Overweight, living in suburban, consuming sufficient nutrient were associated with a lower CVD mortality. In the final model, after all of the adjustments, the risk of CVD mortality increased sharply with age ( $66 \leq$ age $\leq 75: ~ \mathrm{HR}=1.511,95 \%$ CI: 1.111-2.055, age $\geq 76: \mathrm{HR}=1.847,95 \%$ CI: $1.256-2.717$ ). Subjects with hypertension were at a higher risk of CVD death (HR $=1.407,95 \%$ CI: 1.031-1.920). And the CVD mortality of the elderly in suburban was significantly lower than that of the elderly in the rural area ( $\mathrm{HR}=0.614,95 \% \mathrm{CI}: 0.410-0.921$ ). In addition, frequent consumption of meat was associated with increased risk of CVD mortality ( $\mathrm{HR}=1.518,95 \% \mathrm{CI}$ : 1.044-2.207) (Table 2).

Besides, the same analysis was subsequently repeated after further stratification according to gender. Univariate analysis for male showed height was inversely related to mortality of CVD. Disability assessed by IADL, excessive drinking, without spouse, poor self-health rated, age above 76, with hypertension, illiterate and consuming more meat were positively associated with increased risk of CVD mortality. Multivariate analysis showed age, BMI and diet were associated with CVD mortality (Table 3). Univariate analysis for female showed age and hypertension were associated with rising CVD mortality, multivariate analysis also showed consuming more meat significantly increased CVD mortality (Table 4). Additionally, no significant interactions were demonstrated.

Table 2. Predictors of CVD mortality, using competing risks models.

| Variables | Univariate Analysis |  |  | Multivariate Analysis |  |  |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HR | $95 \% \mathrm{CI}$ | $p$ value | HR | $95 \% \mathrm{CI}$ | $p$ value |
| Gender (male) | 0.530 | $0.732-1.171$ | 0.530 | - | - | - |
| Height | 0.989 | $0.976-1.011$ | 0.120 | 1.006 | $0.989-1.023$ | 0.491 |
| Depression (normal) | 0.977 | $0.756-1.262$ | 0.150 | 1.102 | $0.800-1.518$ | 0.546 |
| Smoking (no-smoke) | 0.908 | $0.966-1.887$ | 0.861 | - | - | - |
| Drink (no-drink) | 1.270 | $0.942-1.723$ | 0.122 | 1.215 | $0.876-1.686$ | 0.238 |
| Sad-event (experienced) | 0.887 | $0.693-1.141$ | 0.341 | - | - | - |
| Exercise (always) | 0.996 | $0.783-1.274$ | 0.983 | - | - | - |
| BADL (can take care) | 0.915 | $0.465-1.798$ | 0.824 | - | - | - |
| IADL (can take care) | 1.540 | $1.231-1.990$ | $<0.001$ | 1.172 | $0.860-1.596$ | 0.320 |
| Marital status ( have a spouse) | 1.370 | $1.073-1.754$ | 0.011 | 0.998 | $0.730-1.336$ | 0.939 |
| Assessment of health (normal) | 1.340 | $1.011-1.790$ | 0.043 | 1.141 | $0.831-1.568$ | 0.410 |
| Blood lipid (normal) | 0.932 | $0.707-1.232$ | 0.621 | - | - | - |
| Diabetes (normal) | 1.290 | $0.954-1.741$ | 0.100 | 1.332 | $0.972-1.823$ | 0.074 |

Table 2. Cont.

| Variables | Univariate Analysis |  |  | Multivariate Analysis |  |  |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HR | $95 \% \mathrm{CI}$ | $p$ value | HR | $95 \% \mathrm{CI}$ | $p$ value |
| Age-group (55-65) |  |  |  |  |  |  |
| 66-75 | 1.122 | $0.883-1.431$ | 0.341 | 1.511 | $1.111-2.055$ | 0.008 |
| $\geq 76$ | 1.692 | $1.321-2.164$ | $<0.001$ | 1.847 | $1.256-2.717$ | 0.002 |
| Blood-pressure (normal) |  |  |  |  |  |  |
| Sbp $>120$ or dbp $>80$ | 0.577 | $0.374-0.889$ | 0.013 | 0.799 | $0.488-1.308$ | 0.370 |
| Sbp $\geq 140$ or dbp $\geq 90$ | 1.620 | $1.260-2.133$ | $<0.001$ | 1.407 | $1.031-1.920$ | 0.032 |
| Education level (graduate) |  |  |  |  |  |  |
| high school diploma | 1.150 | $0.675-1.960$ | 0.610 | 1.519 | $0.715-3.228$ | 0.280 |
| Junior diploma | 0.748 | $0.468-1.191$ | 0.220 | 1.102 | $0.535-2.267$ | 0.769 |
| primary school | 0.745 | $0.564-0.984$ | 0.038 | 1.129 | $0.603-2.113$ | 0.701 |
| Illiterate | 1.450 | $1.141-1.840$ | $<0.001$ | 1.525 | $0.815-2.853$ | 0.189 |
| Body-mass-index (normal) |  |  |  |  |  |  |
| thin | 1.180 | $0.888-1.580$ | 0.250 | 1.074 | $0.783-1.471$ | 0.660 |
| overweight | 0.630 | $0.421-0.942$ | 0.025 | 0.673 | $0.439-1.031$ | 0.069 |
| obesity | 0.969 | $0.678-1.390$ | 0.870 | 0.965 | $0.652-1.428$ | 0.861 |
| Area (rural) |  |  |  |  |  |  |
| suburban | 0.728 | $0.544-0.974$ | 0.033 | 0.614 | $0.410-0.921$ | 0.018 |
| urban | 1.080 | $0.851-1.379$ | 0.520 | 1.080 | $0.707-1.651$ | 0.720 |
| Diet (intermediate-type diets) |  |  |  |  |  |  |
| sufficient nutrients | 0.852 | $0.662-1.104$ | 0.210 | 0.954 | $0.694-1.312$ | 0.768 |
| meat based diets | 1.460 | $1.093-1.949$ | 0.012 | 1.559 | $1.079-2.254$ | 0.018 |

Table 3. Predictors of CVD mortality in male, using competing risks models.

| Variables | Univariate analysis |  |  | Multivariate analysis |  |  |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HR | $95 \%$ CI | $p$ value | HR | $95 \% \mathrm{CI}$ | $p$ value |
| Height | 0.968 | $0.945-0.991$ | 0.008 | 0.984 | $0.954-1.012$ | 0.281 |
| Depression (normal) | 1.129 | $0.715-1.812$ | 0.590 | - | - | - |
| Smoking (no smoke) | 1.110 | $0.795-1.560$ | 0.544 | - | - | - |
| Drink (no drink) | 1.431 | $1.100-2.041$ | 0.0480 | 1.375 | $0.955-1.980$ | 0.087 |
| Sad event (experienced) | 1.051 | $0.734-1.532$ | 0.794 | - | - | - |
| Exercise (always) | 1.157 | $0.824-1.689$ | 0.413 | - | - | - |
| BADL (can take care) | 0.773 | $0.243-2.445$ | 0.662 | - | - | - |
| IADL (can take care) | 1.909 | $1.320-2.769$ | $<0.001$ | 1.462 | $0.955-2.238$ | 0.081 |
| Marital status (have a spouse) | 1.469 | $1.020-2.131$ | 0.044 | 1.125 | $0.729-1.741$ | 0.586 |
| Assessment of health (normal) | 1.550 | $1.020-2.351$ | 0.041 | 1.076 | $0.679-1.714$ | 0.746 |
| Blood lipid (normal) | 1.211 | $0.795-1.801$ | 0.386 | - | - | - |
| Diabetes (normal) | 1.220 | $0.789-1.889$ | 0.371 | - | - | - |
| Age-group (55-65) |  |  |  |  |  |  |
| $66-75$ | 1.120 | $0.794-1.567$ | 0.535 | 1.622 | $1.021-2.582$ | 0.041 |
| $\geq 76$ | 1.671 | $1.189-2.345$ | 0.003 | 1.681 | $0.965-2.930$ | 0.046 |
| Blood pressure(normal) |  |  |  |  |  |  |
| Sbp $>120$ or dbp $>80$ | 0.536 | $0.289-0.992$ | 0.047 | 0.817 | $0.406-1.64$ | 0.570 |
| Sbp $\geq 140$ or dbp $\geq 90$ | 1.751 | $1.220-2.510$ | 0.002 | 1.362 | $0.880-2.101$ | 0.168 |

Table 3. Cont.

| Variables | Univariate analysis |  |  | Multivariate analysis |  |  |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HR | $95 \% \mathrm{CI}$ | $p$ value | HR | $95 \% \mathrm{CI}$ | $p$ value |
| Body mass index (normal) |  |  |  |  |  |  |
| thin | 1.110 | $0.721-1.697$ | 0.641 | 1.237 | $0.763-2.013$ | 0.389 |
| overweight | 0.604 | $0.336-1.089$ | 0.092 | 0.769 | $0.404-1.459$ | 0.418 |
| obesity | 1.712 | $1.121-2.620$ | 0.013 | 1.889 | $1.159-3.078$ | 0.011 |
| Area (rural) |  |  |  |  |  |  |
| suburban | 0.696 | $0.457-1.058$ | 0.092 | 0.631 | $0.342-1.164$ | 0.140 |
| urban | 1.093 | $0.774-1.529$ | 0.630 | 1.154 | $0.599-2.220$ | 0.671 |
| Diet (intermediate-type diets) |  |  |  |  |  |  |
| sufficient nutrients | 0.768 | $0.536-1.089$ | 0.150 | 0.806 | $0.513-1.272$ | 0.350 |
| meat based diets | $1.881-$ | $1.280-2.778$ | 0.001 | 2.158 | $1.245-3.741$ | 0.006 |

Table 4. Predictors of CVD mortality in female, using competing risks models.

| Variables | Univariate analysis |  |  | Multivariate analysis |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | HR | 95\%CI | $p$ value | HR | 95\%CI | $p$ value |
| Height | 0.981 | 0.951-1.011 | 0.202 | 0.995 | 0.959-1.031 | 0.810 |
| Depression (normal) | 1.340 | 0.922-1.945 | 0.131 | 1.256 | 0.827-1.910 | 0.289 |
| Smoking (no smoke) | 0.827 | 0.534-1.278 | 0.390 | - | - | - |
| Drink (no drink) | 1.133 | 0.561-2.256 | 0.739 | - | - | - |
| Sad event (experienced) | 0.744 | 0.528-1.050 | 0.092 | 0.732 | 0.510-1.052 | 0.091 |
| Exercise (always) | 0.876 | 0.624-1.230 | 0.441 | - | - | - |
| BADL (can take care) | 1.020 | 0.442-2.371 | 0.962 | - | - | - |
| IADL (can take care) | 1.343 | 0.948-1.900 | 0.097 | 0.995 | 0.643-1.544 | 0.981 |
| Marital status (have a spouse ) | 1.376 | 0.981-1.910 | 0.066 | 0.935 | 0.613-1.436 | 0.745 |
| Assessment of health (normal) | 1.211 | 0.821-1.823 | 0.331 | - | - | - |
| Blood lipid (normal) | 0.785 | 0.544-1.144 | 0.212 | 0.734 | 0.499-1.081 | 0.123 |
| Diabetes (normal) | 0.771 | 0.501-1.191 | 0.243 | 1.608 | 1.028-2.509 | 0.037 |
| Age group (55-65) |  |  |  |  |  |  |
| 66-75 | 1.128 | 0.811-1.589 | 0.491 | 1.583 | 1.012-2.473 | 0.044 |
| $\geq 76$ | 1.712 | 1.210-2.430 | 0.003 | 2.109 | 1.116-3.982 | 0.021 |
| Blood-pressure(normal) |  |  |  |  |  |  |
| Sbp $>120$ or dbp $>80$ | 0.616 | 0.335-1.133 | 0.120 | 0.962 | 0.477-1.941 | 0.911 |
| Sbp $\geq 140$ or dbp $\geq 90$ | 1.520 | 1.051-2.190 | 0.027 | 1.739 | 1.102-2.740 | 0.018 |
| Body mass index(normal) |  |  |  |  |  |  |
| thin | 1.273 | 0.859-1.871 | 0.230 | 1.072 | 0.697-1.652 | 0.750 |
| overweight | 0.651 | 0.373-1.132 | 0.130 | 0.704 | 0.392-1.263 | 0.241 |
| obesity | 0.668 | 0.379-1.181 | 0.161 | 0.674 | 0.371-1.219 | 0.189 |
| Area(rural) |  |  |  |  |  |  |
| suburban | 0.761 | 0.509-1.140 | 0.193 | 0.636 | 0.366-1.115 | 0.112 |
| urban | 1.070 | 0.761-1.521 | 0.681 | 0.930 | 0.517-1.674 | 0.810 |
| Diet(intermediate-type diets) |  |  |  |  |  |  |
| sufficient nutrients | 0.938 | 0.659-1.330 | 0.718 | 1.155 | 0.751-1.786 | 0.510 |
| meat based diets | 1.003 | 0.854-1.971 | 0.219 | 1.786 | 1.041-3.062 | 0.035 |

### 3.3. Fine and Gray Test

In order to determine the tendency of CVD mortality in different age groups, Gray's test was used to compare the CIFs for the six age groups (Figure 3). After five years from the beginning of the follow-up, the CIF of CVD mortality increased with the increasing age, and the elderly aged between 75 and 79 had the highest ( $p<0.001$ ). Gray's test was also used to compare the CIFs of other groups, including gender, marital status, self-assessed health, depression, etc. Age of death was the abscissa to adjust the effect of age distribution in different groups. Several results are listed in Figure 4. As shown in Figure 4a, the mortality of the elderly who exercise infrequently was significantly higher than that of those who exercise frequently and regularly ( $p=0.047$ ), and that of subjects with poor self-assessed health were higher than that of those with good self-assessed health ( $p=0.065$ ) (Figure 4b). As shown in Figure 4 c , the CVD mortalities among the different places of residence were statistically significant ( $p=0.012$ ). It was the highest for the elderly living in a rural area, the CIF at aged 85 of the rural area reached 0.23 , the elderly in the suburban area came second and urban inhabitants had the lowest (CIF $\leq 0.15$ ). For dietary intake, the mortality of subjects of meat-based diets was the highest, and that of the intermediate-type diets with balanced diet was the lowest ( $p=0.012$ ) (Figure 4d).

Figure 3. CIFs for death due to CVD: Compare the different age-groups.


Figure 4. CIFs for death due to CVD: Comparing the different groups after adjusting age.


Figure 4. Cont.


Notes: Abbreviations: (a) CIFs for the exercise group and exercise infrequently group; (b) CIFs for the results of self-health assessment; (c) CIFs for the different places of residence; (d) CIFs for the different diet habits groups.

## 4. Discussion

Previous studies [32-34] have focused primarily on examining the effect of a single risk factor on mortality, rather than developing a more comprehensive model that incorporates the effects of multiple risk factors. Our findings confirm those in other studies, showing strong and significant associations of gender, age, blood pressure, residence place, and diet with the risk of CVD mortality in elderly people. Advanced age, high blood pressure, rural residence, and consuming more meat were associated with higher CVD mortality. Previous researches have confirmed that clinical manifestations and prognosis of CVD are likely altered in older people, because interactions that occur between age-associated cardiovascular changes in health and specific pathophysiologic mechanisms underlie a disease [35,36]. Our study also showed age was an independent risk factor associated with CVD morality after considering the competing risk events.

Age is by far the strongest determinant of CVD risk in the given multiple risk factors [37], and the prevalence of hypertension rises rapidly and steadily with aging. Hypertension might even lead to the further increases of CVD morbidity and mortality [38].

In addition, a healthier diet is associated with a lower risk of recurrent CVD events among people aged over 55 years with CVD [39]. A healthier diet indicates more frequent consumption vegetables and fruits as well as a higher consumption of fish relative to meat, poultry, and eggs [40]. In a multicenter trial in Spain, a Mediterranean diet supplemented with extra-virgin olive oil or nuts was confirmed to reduce the incidence of major cardiovascular events [41-43]. This research likewise showed more frequent intake of meat (the third group: Meat-based diets) increased the risk of death from CVD ( $\mathrm{HR}=1.578$ ). The participants in this group consumed less of soy foods, fruits, vegetables, and fish, as well as more frequently consumed grains ( $\geq 350$ grams per person per day), meat ( $>$ twice a week). Furthermore, the percentage of animal oils intake in this group was higher than in the other diet groups. According to our previous study [22], the elderly in the sufficient nutrients group primarily lived in the urban area and they always took breakfast and less meat, had more frequent consumption of soy foods, fruits, vegetables, and fish, whereas, the elderly in meat-based diet group primarily lived
in the rural area. This study showed that the CVD mortality of residents in rural areas was significantly higher than those in urban and suburban ones $(p=0.012)$. Besides the dietary factor, it may be also related with the health systems in rural areas are not well equipped and medical resources are sparse.

Aside from that, evidence from the Framingham heart study has confirmed that cumulative long-term physical activity has a protective effect on the incidence of CVD-attributable mortality compared with the long-term physical inactivity [44]. This was consisted with our results. The result of Gray's test showed that the cumulative CVD mortality of the elderly who exercised regularly were significantly lower than those without a long-term physical activity ( $p=0.047$ ), and a recent study in Canadians also confirms that the risk of CVD death decreases with the frequency of physical activity [45].

Additionally, our study confirmed that taller height may contribute to deceased CVD mortality risk (Table 3), which was consisted with a study in Chinese people in 2011 [46]. By Gray's test, poor self-assessed health was markedly associated with higher CVD mortality ( $p=0.065$ ).

At a methodological standpoint, several advantages exist in using competing risks survival analysis to analyze the composite endpoint of mortality. Unlike the Cox proportional hazards regression model, in which risk factors are constrained to have common associations with all components of the outcome and ignoring the competing risks, this competing risk model allows for several risk factors to have different associations with single causes of death [47,48]. This study also has several limitations. Risk factors in the competing risk model were not updated year by year. The risk factor status at the beginning of the follow-up was used in order to avoid the possibility of any clinical or subclinical disease affecting the risk factor status.

## 5. Conclusions

At the end of follow-up, considering the competing risks, the CIF of CVD death was 0.19 , CBVD was 0.17 , and cancer was 0.10 . A competing risk model was developed for a specific cause (CVD) of mortality in this study. Increasing age, raised blood pressure, living in a rural area and frequent consumption of meat was associated with higher CVD mortality of the elderly in Beijing, China. The study provided foundation of decision-making and instruction for the controlling and prevention of CVD. In the future, competing risk model could be used to identify individuals who are at higher risk of specific mortality.

## Acknowledgments

We would like to thank the staff in Xuan Wu Hospital for collecting the epidemiologic data and maintaining the database.

## Author Contributions

Conceived and designed the experiments: Zhe Tang; Xiuhua Guo; Aoshuang Yan Performed the experiments: Xia Li; Wei Wang; Fei Sun Analyzed the data: Tao Zhou; Lixin Tao; Lei Pan; Changchun Xie Wrote the paper: Tao Zhou; Zhe Tang; Contributed to discussions and interpretation of the data: Xia Li; Yanxia Luo; Da Huo.

## Conflicts of Interest

The authors declare no conflict of interest.

## References

1. Lopez, A.D.; Mathers, C.D.; Ezzati, M.; Jamison, D.T.; Murray, C.J. Global and regional burden of disease and risk factors, 2001: Systematic analysis of population health data. Lancet. 2006, 367, 1747-1757.
2. Ngian, G.S.; Sahhar, J.; Proudman, S.M.; Stevens, W.; Wicks, I.P.; van Doornum, S. Prevalence of coronary heart disease and cardiovascular risk factors in a national cross-sectional cohort study of systemic sclerosis. Clin. Epidemiol. Res. 2012, 71, 1980-1983.
3. Hu, F.B.; Willett, W.C.; Li, T.; Stampfer, M.J.; Colditz, G.A.; Manson, J.E. Adiposity as compared with physical activity in predicting mortality among women. N. Engl. J. Med. 2004, 351, 2694-2703.
4. The Top 10 Causes of Death. Available online: http://who.int/mediacentre/factsheets/fs $310 / \mathrm{en} /$ (accessed on 11 November 2013).
5. Heart Disease and Stroke Statistics-2009 Update: A Report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Available online: http://circ.ahajournals.org/content/119/3/e21\# (accessed on 11 November 2013).
6. Yang, Z.; Xing, X.; Xiao, J.; Lu, J.; Weng, J.; Jia, W.; Ji, L.; Shan, Z.; Liu, J.; Tian, H.; et al. Prevalence of cardiovascular disease and risk factors in the Chinese population with impaired glucose regulation: The 2007-2008 China national diabetes and metabolic disorders study. Exp. Clin. Endocrinol. Diabet. 2013, 121, 372-374.
7. Smith, S.C., Jr.; Chen, D.; Collins, A.; Harold, J.G.; Jessup, M.; Josephson, S.; Logstrup, S.; Jur, C.; Sacco, R.L; Vardas, P.E.; et al. Moving from political declaration to action on reducing the global burden of cardiovascular diseases: A statement from the global cardiovascular disease taskforce. Circulation 2013, 62, 2151-2153.
8. Chen, Z.; Yu, J.; Song, Y.; Chui, D. Aging Beijing: Challenges and strategies of health care for the elderly. Ageing Res. Rev. 2010, 9, s2-s5.
9. Cheng, Y.; Rosenberg, M.W.; Wang, W.; Yang, L.; Li, H. Aging, health and place in residential care facilities in Beijing, China. Soc. Sci. Med. 2011, 72, 365-372.
10. Rockhill, B.; Willett, W.C.; Manson, J.E.; Leitzmann, M.F.; Stampfer, M.J.; Hunter, D.J.; Colditz, G.A. Physical activity and mortality: A prospective study among women. Am. J. Public Health 2001, 91, 578-583.
11. Kenfield, S.A.; Stampfer, M.J.; Rosner, B.A.; Colditz, G.A. Smoking and smoking cessation in relation to mortality in women. JAMA 2008, 299, 2037-2047.
12. Beuscart, J.B.; Pagniez, D.; Boulanger, E.; Celia Sainte Foy, C.L.; Salleron, J.; Frimat, L.; Duhamel, A. Overestimation of the probability of death on peritoneal dialysis by the Kaplan-Meier method: Advantages of a competing risks approach. BMC Nephrol. 2012, 13, doi:10.1186/ 1471-2369-13-31.
13. Syrjanen, K.; Shabalova, I.; Sarian, L.; Naud, P.; Longatto-Filho, A.; Derchain, S.; Kozachenko, V.; Zakharchenko, S.; Roteli, C.M.; Nerovjna, R. Longitudinal outcomes of high-risk human papillomavirus (HPV) infections as competing-risks events following cervical HPV test at baseline visit in the NIS-LAMS cohort. Eur. J. Gynaecol. Oncol. 2012, 33, 341-352.
14. Varadhan, R.; Weiss, C.O.; Segal, J.B.; Wu, A.W.; Scharfstein, D.; Boyd, C. Evaluating health outcomes in the presence of competing risks. Med. Care 2010, 48, 96-105.
15. Bryan, L.; Stephen, R.C.; Stephen, J.G. Competing risk regression models for epidemiologic data. Am. J. Epidemiol. 2009, 170, 244-256.
16. Bachmann, J.M.; Willis, B.L.; Ayers, C.R.; Khera, A.; Berry, J.D. Association between family history and coronary heart disease death across long-term follow-up in men: The Cooper Center Longitudinal Study. Circulation 2012, 125, 3092-3098.
17. Austin, P.C.; Anderson, G.M.; Cigsar, C.; Gruneir, A. Compared the cohort design and the nested case-control design in the presence of both time-invariant and time-dependent treatment and competing risks: Bias and precision. Pharmacoepidem. Dr. S. 2012, 21, 714-724.
18. Scheike, T.H.; Maiers, M.J.; Rocha, V.; Zhang, M.J. Competing risks with missing covariates: Effect of haplotypematch on hematopoietic cell transplant patients. Lifetime Data Anal. 2013, 19, 19-32.
19. Chen, C.; Lu, F.C.; Department of Disease Control Ministry of Health, PR China. The guidelines for prevention and control of overweight and obesity in Chinese adults. Biomed. Environ. Sci. 2004, 17, 1-36.
20. World Health Organization (WHO). Definition, Diagnose and Classification of Diabetes Mellitus and Its Complications: Report of A WHO Consultation. Part 1: Diagnoses and Classification of Diabetes Mellitus; World Health Organization: Geneva, Switzerland, 1999.
21. Catapano, A.L.; Chapman, J.; Wiklund, O.; Taskinen, M.R. The new joint EAS/ESC guidelines for the management of dyslipidemias. Atherosclerosis 2011, 1 , doi:10.1016/j.atherosclerosis.
22. Wang, W.; Tang, Z.; Li, X.; Gao, Q.; Sun, F.; Diao, L.J.; Guo, X. Eight-year change in dietary pattern and metabolic status among the elderly people in Beijing. J. Cap. Med. Univ. 2012, 33, 218-222.
23. Jefferson, A.L.; Byerly, L.K.; Vanderhill, S.; Lambe, S.; Wong, S.; Ozonoff, A.; Karlawish, J.H. Characterization of activities of daily living in individuals with mild cognitive impairment. Am. J. Geriat. Psychiat. 2008, 16, 375-383.
24. Radloff, L.S. The CES-D scale: A self-report depression scale for research in the general population. Appl. Psychol. Meas.1977, 1, 385-401.
25. Schafer, J.L. Multiple imputation: A primer. Stat. Methods Med. Res. 1999, 8, 3-15.
26. Nicolaie, M.A.; van Houwelingen, J.C.; de Witte, T.M.; Putter, H. Dynamic prediction by landmarking in competing risks. Stat. Med. 2012, 32, 2031-2047.
27. Pintilie, M. Competing Risks: A Practical Perspective; Wiley: Chichester, UK, 2006.
28. Baer, H.J.; Glynn, R.J.; Hu, F.B.; Hankinson, S.E.; Willett, W.C.; Colditz, G.A.; Stampfer, M.; Rosner, B. Risk factors for mortality in the nurses' health study: A competing risks analysis. Am. J. Epidemiol. 2010, 173, 319-329.
29. Beyersmann, J.; Schumacher, M. Time-dependent covariates in the proportional sub-distribution hazards model for competing risks. Biostatistics 2008, 9, 765-776.
30. Latouche, A.; Porcher, R.; Chevret, S. A note on including time-dependent covariate in regression model for competing risks data. Biom. J. 2005, 47, 807-814.
31. Thomas, H.S.; Me, J.Z. Analyzing competing risk data using the R timereg package. J. Stat. Softw. 2011, 38, 1-9.
32. Masic, I.; Alajbegovic, J. The significance of the psychosocial factors influence in pathogenesis of cardiovascular disease. Int. J. Prev. Med. 2013, 4, 1323-1330.
33. Ahmed, H.M.; Blaha, M.J.; Blumenthal, R.S. Modifiable lifestyle risks, cardiovascular disease, and all-cause mortality. Int. J. Cardiol. 2013, 13, doi: 10.1016/j.ijcard.2013.12.073.
34. Dhaliwal, S.S.; Welborn, T.A.; Howat, P.A. Recreational physical activity as an independent predictor of multivariable cardiovascular disease risk. PLoS One 2013, 8, doi:10.1371/ journal.pone. 0083435.
35. Wald, N.J.; Simmonds, M.; Morris, J.K. Screening for future cardiovascular disease using age alone compared with multiple risk factors and age. PLoS One 2011, 6, 1-7.
36. Rhoades, D.A.; Welty, T.K.; Wang, W.; Yeh, F.; Devereux, R.B.; Fabsitz, R.R.; Lee, E.T.; Howard, B.V. Aging and the prevalence of cardiovascular disease risk factors in older American Indians: The strong heart study. J. Am. Geriatr. Soc. 2007, 55, 87-94.
37. Lakatta, E.G. Age-associated cardiovascular changes in health: Impact on cardiovascular disease in older persons. Heart Fail. Rev. 2002, 7, 29-49.
38. Gu, Q.; Burt, V.L.; Paulose-Ram, R.; Yoon, S.; Gillum, R.F. High blood pressure and cardiovascular disease mortality risk among U.S. adults: The third National Health and Nutrition Examination Survey mortality follow-up study. Ann. Epidemiol. 2008, 18, 302-309.
39. Estruch, R.; Ros, E.; Salas-Salvado, J.; Covas, M.I.; Corella, D.; Aros, F. Primary prevention of cardiovascular disease with a Mediterranean diet. N. Engl. J. Med. 2013, 368, 1279-1290.
40. Dehghan, M.; Mente, A.; Teo, K.K.; Gao, P.; Sleight, P.; Dagenais, G.; Avezum ,A.; Probstfield, J.L.; Dans, T.; Yusuf, S. Relationship between healthy diet and risk of cardiovascular disease among patients on drug therapies for secondary prevention-A prospective cohort study of 31,546 high-risk individuals from 40 countries. Circulation 2012, 126, 2705-2712.
41. Verschuren, W.M. Diet and cardiovascular disease. Curr. Cardiol. Rep. 2012, 14, 701-708.
42. Tresserra-Rimbau, A.; Medina-Remon, A.; Perez-Jimenez, J.; Martinez-Gonzalez, M.A.; Covas, M.I.; Corella, D.; Salas-Salvado, J.; Gomez-Gracia, E.; Lapetra, J.; Aros, F. Dietary intake and major food sources of polyphenols in a Spanish population at high cardiovascular risk: The PREDIMED study. Nutr. Metab. Cardiovas. 2013, 23, 953-959.
43. Tognon, G.; Lissner, L.; Sabye, D.; Walker, K.Z.; Heitmann, B.L. The Mediterranean diet in relation to mortality and CVD: A Danish cohort study. Br. J. Nutr. 2013, 3, 1-9.
44. Shortreed, S.M.; Peeters, A.; Forbes, A.B. Estimating the effect of long-term physical activity on cardiovascular disease and mortality: Evidence from the Framingham Heart Study. Heart 2013, 99, 649-654.
45. Gaesser, G.A. Exercise for prevention and treatment of cardiovascular disease, type 2 diabetes, and metabolic syndrome. Curr. Diab. Rep. 2007, 7, 14-19.
46. Wang, N.; Zhang, X.; Xiang, Y.B.; Yang, G.; Li, H.L.; Gao, J.; Cai, H.; Gao, Y.T.; Zheng, W.; Shu, X.O. Associations of adult height and its components with mortality: A report from cohort studies of 135,000 Chinese women and men. Int. J. Epidemiol. 2011, 40, 1715-1726.
47. Wolbers, M.; Koller, M.T.; Witteman, J.C.; Steyerberg, E.W. Prognostic models with competing risks: Methods and application to coronary risk prediction. Epidemiology 2009, 20, 551-561.
48. Glynn, R.J.; Rosner, B. Comparison of risk factors for the competing risks of coronary heart disease, stroke, and venous thromboembolism. Am. J. Epidemiol. 2005, 162, 975-982.
© 2014 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (http://creativecommons.org/licenses/by/3.0/).

[^0]:    10.3390/ijerph110202193

    Zhou T., Li X., Tang Z., Xie C., Tao L., Pan L., Huo D., Sun F., Luo Y., Wang W., Yan A., Guo X. (2014). Risk factors of CVD mortality among the elderly in Beijing, 1992-2009: An 18-year cohort study. International Journal of Environmental Research and Public Health, 11(2), 2193-2208. Available here
    This Journal Article is posted at Research Online.
    https://ro.ecu.edu.au/ecuworkspost2013/219

