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Original article

Time-dependent depressive symptoms and risk of cardiovascular and all-cause mortality among the Chinese elderly: The Beijing Longitudinal Study of Aging

Haibin Li (PhD)[a,b], Nicholas Van Halm-Lutterodt (MD, PhD)[c], Deqiang Zheng (PhD)[a,b], Yue Liu (MD)[a,b], Jin Guo (PhD)[d], Wei Feng (MD)[a,b], Xia Li (PhD)[e], Anxin Wang (PhD)[a,b], Xiangtong Liu (PhD)[a,b], Lixin Tao (PhD)[a,b], Chengbei Hou (PhD)[a,b], Yanxia Luo (PhD)[a,b], Feng Zhang (PhD)[a,b], Xinghua Yang (PhD)[a,b], Qi Gao (PhD)[a,b], Wei Wang (PhD)[f], Zhe Tang (PhD)[g,*], Xiuhua Guo (PhD)[a,b,**]

[a] Department of Epidemiology and Health Statistics, School of Public Health, Capital Medical University, Beijing, China
[b] Beijing Municipal Key Laboratory of Clinical Epidemiology, Capital Medical University, Beijing, China
[c] Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[d] Greenwood Medical Company, Melbourne, Victoria, Australia
[e] Department of Mathematics and Statistics, La Trobe University, Melbourne, Victoria, Australia
[f] Global Health and Genomics, School of Medical Sciences and Health, Edith Cowan University, Perth, Western Australia, Australia
[g] Beijing Geriatric Healthcare Center, Xuan Wu Hospital, Capital Medical University, Beijing, China

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ABSTRACT

Background: Depressive symptoms tend to fluctuate over time. Data on the relationship between time-dependent depressive symptoms and the risk of cardiovascular and all-cause mortality among the elderly in China are lacking.

Methods and results: A prospective cohort of 1999 subjects aged ≥55 years were enrolled in the Beijing Longitudinal Study of Aging since 1992. Depressive symptoms were assessed at baseline (0 years) and after 2, 5, 8, and 12 years, defined as a score of ≥16 on the 20-item Center for Epidemiological Studies Depression Scale. Mortality status was obtained from the local death registry until December 31st, 2012. Hazard ratio (HR) for all-cause mortality and sub-distribution HR (SHR) for cardiovascular mortality were respectively deduced from time-dependent Cox and competing risk models. During 19,658 person-years of follow-up, 1127 (55.65%) deaths were recorded, of which 483 (23.85%) were attributable to cardiovascular inclinations. Baseline depressive symptoms were neither associated with all-cause mortality (adjusted HR: 1.12, 95% confident interval, CI: 0.94–1.33) nor cardiovascular mortality (adjusted SHR: 1.10, 95% CI: 0.82–1.46) after adjustment of potential cardiac-risk factors. When depressive symptoms were used as time-dependent variable updated from 1992 to 2004, the associations were significant for both all-cause mortality (adjusted HR: 1.48, 95% CI: 1.26–1.73) and cardiovascular mortality (adjusted SHR: 1.40, 95% CI: 1.08–1.82) in the full adjusted model.

Conclusions: Time-dependent depressive symptoms increased the risk of all-cause and cardiovascular mortality among the elderly in China.

Introduction

Depressive symptoms are mundanely encountered in the elderly population globally [1]. Several systematic reviews [2,3] and epidemiological studies show that depressive symptoms are strongly associated with cardiovascular death in the general population [4–10]; however, the conclusions are still inconsistent

* Corresponding author at: Beijing Geriatric Healthcare Center, Xuan Wu Hospital, Capital Medical University, 45 Changchun Street, Beijing 100053, China.
** Corresponding author at: School of Public Health, Capital Medical University, No. 10 Xitoutiao, You'anmen Wai, Fengtai District, Beijing 100069, China.
E-mail addresses: tangzhe@medmail.com.cn (Z. Tang), statguo@ccmu.edu.cn (X. Guo).

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[11,12]. Several reasons may explain this outcome of inconsistency. Primarily, the residual confounding and mediating factors such as disability, antidepressants [2], and physical activity [10–12] have been observed to play a role. Secondarily, depressive symptoms tend to fluctuate over time with age advancement in the elderly population [13].

However, in most studies depressive symptoms are exclusively measured at a single time point [6,8,12], which may not entail the periodic long-term episodes and cumulative effect on mortality risk [14]. Only a few studies have investigated the relationship between repeated measurements of depressive symptoms and the risk of cardiovascular outcomes and all-cause mortality [15,16]. For instance, in the Italian Longitudinal Study of Aging cohort, depressive symptoms were only measured at baseline and the second survey at 3 years after the baseline [16] clearly demonstrating the lack of interval-reproducible depressive episodic outcomes within the given long-term time frame. Most reported studies conducted in Western populations also demonstrate similar limiting patterns of periodic depressive symptom assessments of enrolled subjects [5,6,8], even though the association between cardiovascular mortality and depressive symptoms may vary geographically [17]. The association between time-dependent depressive symptoms and the risk of all-cause and cardiovascular mortality in Chinese elderly adults is enormously understudied and remains unclear.

Therefore, we aimed to investigate the relationship between time-dependent depressive symptoms and cardiovascular and all-cause mortality. We hypothesized that time-dependent association is stronger than baseline-only association of depressive symptoms impact on cardiovascular and all-cause mortality in this prospective cohort study.

Methods

Study population

Data for this analysis were acquired from the Beijing Longitudinal Study of Aging (BLSA), a community-based prospective cohort of Chinese people aged 55 and older, conducted by the Beijing Xuanwu Hospital affiliated Capital Medical University [18]. A full description of sampling and data collection has been previously published elsewhere [19,20]. In brief, a random sample of 3257 community residents aged at least 55 years were recruited in August 1992 [21] based on a three-stage stratification random clustering procedure from three districts of Beijing (Xuanwu district, Daxing district, and Huairou district). Approximately 1156 subjects declined the completion of blood examination while 99 subjects who had incomplete data on depressive symptoms status at baseline were excluded. A total of 1999 participants were included in the final analysis. All participants provided written informed consent and the study protocol was approved by the ethics committee of Beijing Xuanwu Hospital and Capital Medical University.

Assessment of depressive symptoms

Depressive symptoms were repeatedly evaluated using a 20-item of the Center for Epidemiological Studies Depressive symptoms scale (CES-D) [19] at baseline (1992), and years 1994, 1997, 2000, and 2004. Utilizing CES-D has been demonstrated to have high sensitivity and specificity for major depressive symptoms among adults and the elderly [22–24]. CES-D score represents the sum of the 20 questions with a possible range of 0–60, with higher scores indicating severity of symptoms. In accordance with previously published studies [25], a total CES-D score of $\geq$16 was classified as the presence of depressive symptoms in this study. In the current analysis, we examined baseline and time-dependent depressive symptoms over a 12-year period to evaluate the associated risk of cardiovascular and all-cause mortality among the elderly in Beijing, China. Fig. 1 shows the study design and the time line of analysis.

Confounding factors

In each visit (years 1992, 1994, 1997, 2000, and 2004), data on demographics, health conditions, behavior lifestyles, medical history, and medication use were collected using a *vis-à-vis* standardized questionnaire administered by trained researchers. In this analysis, we included the following demographic characteristics as potential confounding variables: age, sex (male or female), residence (rural, suburban, or urban), marital status (married or single), and education level (<high school or $\geq$ high school). Smoking status (never, ever, and current) and alcohol consumption (never, ever, and current) were ascertained from self-administered questionnaires. Body mass index (BMI) of participants was calculated as weight in kilograms (kg) divided by height in meters squared (m^2). Blood pressures were measured twice in the seated position at least 5 min apart by the trained physicians or nurses. Overnight fasting venous blood samples were collected for the testing of fasting blood glucose levels and serum lipid profiles included total cholesterol (TC), high-density lipoprotein (HDL-C), and low-density lipoprotein (LDL-C) cholesterols. Details on the procedure and quality control have been previously published [26]. Hypertension was defined as self-reported use of anti-hypertensive medication and/or history of hypertension or measured systolic blood pressure $\geq$140 mmHg or diastolic blood pressure $\geq$90 mmHg. Diabetes mellitus was defined as a fasting

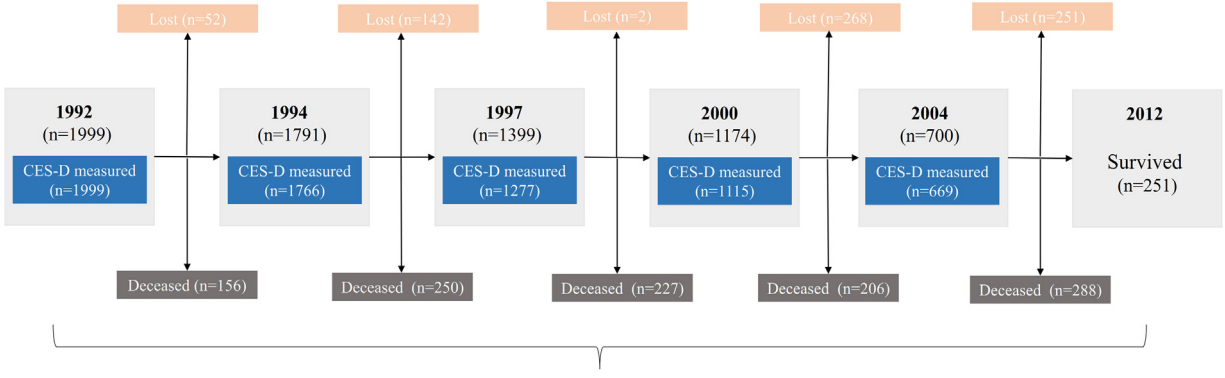

Fig. 1. Study design showing the time line of analysis. CES-D, Center for Epidemiological Studies Depressive symptoms scale.

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