

Short Trends and Associated Factors of Cognitive Impairment in a Population at High Cardiovascular Risk

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Abstract

Background: It has been proposed that some risk factors of cardiovascular disease

(CVD) are associated with and contribute to the development of all cause of dementia. Our aim was to examine the short trends and associated factors of cognitive impairment among a eastern Chinese population at high risk of CVD.

Methods: We used a convenience sampling strategy to select 7 subdistricts in Zhejiang province, which was a part of China Patient-Centered Evaluative Assessment of Cardiac Events (PEACE) project. Participants in 2018 (n=3089) and in 2020 (n=3082) at high risk of CVD in Zhejiang province with registry for the PEACE Project. Participants completed 3+ neuropsychological evaluations including of Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Hospital Anxiety and Depression Scale (HAD) tests. Age-, gender- standardized prevalence rates were calculated based on the sixth population census for population of China. Cox proportional hazards regression models to estimate hazard ratios (HR) for the associations between the risk for all-cause dementia. Trial registration number was NCT02536456.

Results: There was an increase prevalence of dementia and MCI among the individuals at high risk of CVD between 2018 and 2020. It showed that older age, lower education levels, having a medical history of hypertension, stroke and diabetes, having the family history of hypertension, heavy drinking, depression, and obesity were associated with dementia, while female might be a protective factor for dementia.

Conclusion: More population-based strategies should be focusing on modifiable risk factors of dementia, such as CVD risk factors.

Background

Dementia has been considered as a public health priority as it commonly leads to increase in terms of disability, mortality, and cost [1, 2]. The number is expected to reach 152 million by 2050, with about 60 to 70% of them suffering from Alzheimer's disease (AD). Mild cognitive impairment (MCI) is identified as an intermediate state that cognitive impairment does not reach the threshold for dementia diagnosis, which is associated with increased risk of dementia [3, 4]. Some studies suggest that key cardiovascular risk factors, such as hypertension, diabetes, and hypercholesterolemia influence the incidence of dementia [5–7].

As the country with the world's largest population, China is facing substantial challenges in ageing population, of which increasing numbers will have some degree of dementia and cardiovascular disease (CVD). At present, there are about 10 million AD patients in China, and it is estimated that by 2050, the number of patients will exceed 40 million. Zhejiang province is located in eastern China, people that aged 60 or above accounted for 21.77% of the total population by the end of 2017 [4, 8]. And the incidence of CVD among the participants with high risk of CVD is about 3.9% in 2014 to 2016, and is expected to increase to 5% by 2021 [9]. But there are few epidemiological data available on dementia in eastern China, which taking into account of CVD risk factors.

Our study explores the short trends and associated factors of dementia prevalence among population at high CVD risk in eastern China for the years 2018 and 2020.

Methods

Population

It is a population-based closed cohort assembled in April 2018 and June 2020 in Zhejiang province, representative of dwellers 55 years or more at high risk of CVD. This project is part of the China Patient-Centered Evaluative Assessment of Cardiac Events (PEACE) Million Persons Project, which has been described previously [10].

Then participants were given cognitive function evaluation and diagnosis. The criteria of high risk of CVD had been described previously [10, 11]. The baseline sample was initially interviewed in 2018 (N = 3500), and the replenishment sample was interviewed in 2020, with 1724 of whom were continuing and the others interviewed for the first time. The central ethics committee at the China National Center for Cardiovascular Disease (NCCD) and Zhejiang hospital approved this project. Written informed consent is obtained from all literate participants without cognitive decline on entry into the project. And for illiterate participants or ones with cognitive decline, their informed consent is obtained from their literate legally authorized representatives. Trial registration number: NCT02536456.

Assessments

The cognitive function evaluation was carried out by a multidisciplinary team comprised of a nurse and a neurologist. Participants were classified into three categories: normal cognitive function, MCI and dementia. Screening was performed using the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), the Hospital Anxiety and Depression Scale (HAD) tests [12]. Participants who scored below the MMSE cutoff points of 20 for 0–2 years, 23 for 3–6 years and 27 for 7 years or more of schooling were considered as positive results, which had the tendency of dementia [13]. Participants who scored less than the MoCA cutoff points of 1.5 standard deviations (SD) or more below age- and education-adjusted norms were considered as MCI [14]. HAD tests included two sub-scales of anxiety (A) and depression (D), the sub-scale of anxiety and depression was abnormal with a score below 8 [15].

The confirmed diagnosis of dementia was conducted among the subjects with positive results of MMSE test. The diagnostic criteria of dementia used the Chinese guidelines for the diagnosis and treatment of dementia and cognitive impairment [16]. There were no questionnaires or measures used in our study require a license in order to administer them.

Statistical analysis

Characteristics, cognitive function status of participants were summarized using percentages or means and SD, and they were compared by Student's t tests and χ^2 tests, respectively. Age-, gender- standardized prevalence rates were calculated based on the population distribution of China in 2010 (the sixth population census for population of China) [17].

We used Cox proportional hazards regression models to estimate hazard ratios (HR) and 95% CIs for the associations between the risk for all-cause dementia. Crude regression models were first used to assess the risk factors associated with dementia among population at high risk of CVD, then adjusted regression models were used to ascertain the risk factors considering the main effects of sociodemographic characteristics. 2-sided significance tests were used for all analyses, with statistical significance set at $P < 0.05$. SAS 9.2 (SAS Institute Inc., Cary, NC, USA) for data management and analysis.

Result

Characteristics of the population

The characteristics of the population matched cohort were displayed in Table 1. A total of 3500 residents were enrolled in this project in 2018, and 3089 ones completed the survey. The replenishment sample was interviewed in

2020, with 1724 ones were continuing and 1358 interviewed for the first time in 2020.

Table 1
 Characteristics of the 2018 and 2020 Cohorts

Characteristic	2018 (n = 3089)	2020 (n = 3082)	X ² / t	P
Age, y			269.13	< 0.0001
55–64	986 (31.94)	622 (20.24)		
65–74	1759 (56.98)	1920 (82.48)		
≥ 75	342 (11.08)	540 (17.52)		
Mean (SD)	67.07 (12.45)	69.30 (5.03)	-40.27	< 0.0001
Gender			1.03	0.3112
Male	1472 (47.65)	1429 (46.37)		
Female	1617 (52.35)	1653 (53.63)		
Education			32.36	< 0.0001
Illiterate (< 1 year)	584 (18.91)	486 (15.77)		
Primary (1–6 years)	1569 (50.79)	1715 (55.65)		
Middle (7–12 years)	901 (29.17)	872 (28.29)		
High (> 13 years)	35 (1.13)	9 (0.29)		
Cardiovascular risk factors				
Stroke	145 (4.69)	123 (3.99)	1.8382	0.1752
Diabetes	228 (7.38)	202 (6.55)	1.628	0.202
CHD	50 (1.62)	37 (1.20)	1.9478	0.1628
Hypertension	1411 (45.68)	1437 (46.63)	0.5571	0.4554
Lifestyle habits				
Cigarette smoking	422 (16.99)	424 (13.76)	1619.32	< 0.0001
Heavy alcohol drinking	724 (29.15)	1116 (36.21)	639.06	< 0.0001
Regular exercise	281 (11.29)	423 (13.72)	3110.85	< 0.0001
Anxiety	89 (2.88)	32 (1.04)	5696.49	< 0.0001
Depression	468 (15.15)	477 (15.48)	2969.85	< 0.0001
BMI, Mean (SD)	25.22 (3.11)	25.17 (3.07)	0.54	0.5862
SBP, mm Hg, Mean (SD)	160.95 (20.09)	162.18 (19.97)	-2.16	0.0309
DBP, mm Hg, Mean (SD)	86.56 (11.32)	86.83 (11.30)	-0.83	0.408
TC, mmol/L, Mean (SD)	5.28 (1.31)	5.33 (1.28)	-1.42	0.1552
TG, mmol/L, Mean (SD)	2.04 (1.16)	1.97 (1.11)	1.92	0.0549
LDL-C, mmol/L, Mean (SD)	2.95 (1.15)	2.96 (1.13)	-0.28	0.7828

Characteristic	2018 (n = 3089)	2020 (n = 3082)	X2 / t	P
HDL-C, mmol/L, Mean (SD)	1.48 (0.45)	1.52 (0.45)	-3.57	0.0004
MMSE scores, Mean (SD)	23.33 (7.13)	22.23 (3.18)	7.87	< 0.0001
MoCA scores, Mean (SD)	18.17 (5.60)	18.10 (4.36)	0.5	0.6146
Had scores, Mean (SD)	7.56 (5.22)	9.59 (3.52)	-17.87	< 0.0001

Prevalence trend of dementia and MCI

Table 2 displayed the prevalence and adjusted prevalence of individuals in each cognitive function category stratified by age groups (55–64 years, 65–74 years, and ≥ 75 years) in 2018 and 2020. The data showed an increase prevalence of dementia among the individuals aged 55 years or older at high risk of CVD between 2018 and 2020 (8.68% in 2018 compared with 10.15% in 2020, $P < 0.05$). The prevalence of MCI also increased significantly across the 2 cohorts from 22.04–25.46% ($P < 0.05$). And the data showed an increase trend of dementia and MCI prevalence with the increase of age ($P < 0.05$).

Table 2
Cognitive Function, by Age Range, 2018 and 2020 Cohorts

Cognitive Function	55–64 y		65–74 y		75- y		Total (Age ≥ 35 y)		Adjusted prevalence	
	2019 (n = 988)	2020 (n = 622)	2019 (n = 1759)	2020 (n = 1920)	2019 (n = 342)	2020 (n = 540)	2019 (n = 3089)	2020 (n = 3082)	2019 (n = 3089)	2020 (n = 3082)
Normal cognitive function	836 (84.6) [82.0–90.2]	475 (76.4) [68.7–81.2]	1082 (61.5) [56.2–71.3]	1172 (61.0) [56.5–78.1]	191 (55.9) [77.5–81.2]	294 (54.4) [41.6–65.1]	2109 (68.3) [56.9–73.5]	1941 (63.0) [55.5–70.1]	2109 (69.3) [58.9–78.5]	64.39 [60.4–71.2]
Mild cognitive impairment	90 (9.1) [7.8–12.0]	86 (13.8) [11.2–15.7]	462 (26.26) [24.7–28.9]	507 (26.41) [24.5–28.2]	98 (28.60) [37.7–41.3]	157 (29.07) [27.4–31.1]	650 (21.0) [18.8–23.7]	750 (24.33) [22.8–25.8]	650 (22.04) [18.8–23.7]	25.46 [24.1–27.8]
Dementia	62 (6.3) [4.8–7.9]	61 (9.8) [7.6–12.3]	215 (12.22) [10.7–13.7]	241 (12.55) [10.9–14.1]	53 (15.47) [18.8–21.7]	89 (16.48) [14.1–18.7]	330 (10.7) [8.1–12.4]	391 (12.69) [11.5–13.9]	330 (8.68) [7.1–12.4]	10.15 [7.4–12.3]

Associated risk factors

Table 3 reported the results of 2 Cox proportional hazards regression models with the presence of dementia as the outcome variable, using pooled 2018 and 2020 data. Model 1 showed the unadjusted univariate models, and Model 2 showed the multivariate models adjusted by age, gender and education levels. It showed that older age including the age range of 65–75 (adjusted hazard ratio [AHR] = 1.77, 95% CI: 1.24–2.52) and 75 or more (AHR = 3.19, 95% CI: 2.00–5.05) compared with the age range of 55–64, lower education levels including primary (AHR = 1.44, 95% CI: 1.05–1.97) and middle or more (AHR = 1.43, 95% CI: 1.00–2.14) compared with illiterate, having a medical history of hypertension (AHR = 1.37, 95% CI: 1.03–1.83), stroke (AHR = 2.31, 95% CI: 1.47–3.63) and diabetes (AHR = 1.76, 95% CI: 1.42–2.37), having the family history of hypertension (AHR = 1.61, 95% CI: 1.14–2.28), heavy drinking (AHR = 1.56, 95% CI: 1.00–2.17), depression (AHR = 1.59, 95% CI: 1.04–3.00), and obesity (BMI ≥ 30.0 kg/ m²) compared with normal

(BMI = 18.5–24.9 kg/ m²) were associated with dementia, while female (AHR = 0.57, 95% CI: 0.41–0.78) might be a protective factor for dementia.

Table 3
Relative Risks for Presence of Dementia

Models, RR (95% CI)		
Variable (ref. 55–64)	Model1 ^a	Model2 ^b
Age, y		
65–74	0.79 (0.63–1.00)	1.77 (1.24–2.52)
≥75	2.34 (1.76–3.12)	3.19 (2.00–5.05)
Gender (ref. Male)		
Female	0.58 (0.46–0.74)	0.57 (0.41–0.78)
Education (ref. Illiterate)		
Primary (1–6 years)	1.19 (0.95–1.49)	1.44 (1.05–1.97)
Middle or more (≥ 7 years)	1.48 (1.13–1.93)	1.43 (1.00–2.14)
State of marriage (ref. Married)		
living alone	1.10 (0.75–1.63)	0.73 (0.49–1.10)
CVD and related risk factors		
Hypertension	1.38 (1.10–1.72)	1.37 (1.03–1.83)
Stroke	2.58 (1.72–3.85)	2.31 (1.47–3.63)
CHD	0.77 (0.35–1.73)	0.82 (0.34–1.99)
Diabetes	0.77 (0.45–1.33)	1.76 (1.42–2.37)
Family history of CVD		
Hypertension	1.72 (1.25–2.37)	1.61 (1.14–2.28)
Stroke	0.65 (0.29–1.46)	0.68 (0.28–1.64)
CHD	0.57 (0.19–1.68)	0.37 (0.12–1.19)
Diabetes	1.42 (0.71–2.84)	1.21 (0.59–2.46)
Lifestyle habits		
Cigarette smoking	1.33 (0.98–1.90)	0.96 (0.71–1.54)
Heavy alcohol drinking	1.32 (0.99–1.77)	1.56 (1.00–2.17)
Regular exercise	0.83 (0.57–1.21)	0.73 (0.49–1.08)
Anxiety	2.70 (1.65–4.44)	1.59 (0.84–3.00)
Depression	1.72 (1.30–2.26)	1.59 (1.04–3.00)

Abbreviation: RR, hazard ratio.

a Model 1 showed the unadjusted univariate models.

b Model 2 showed the multivariate models adjusted by age, gender and education levels.

Models, RR (95% CI)		
BMI (ref. 18.5–24.9)		
<18.5	0.88 (0.67–1.16)	0.40 (0.15–1.07)
25.0–29.9	1.14 (0.90–1.45)	1.18 (0.89–1.55)
≥30.0	1.38 (0.82–2.34)	1.66 (1.00–2.92)
Net worth (RMB) (ref. ≤50000)		
>50000	1.71 (1.17–2.51)	1.39 (0.92–2.10)
SBP, mm Hg (ref. <140)		
140–180	1.06 (0.84–1.32)	1.10 (0.74–1.64)
>180	0.94 (0.67–1.32)	1.16 (0.69–1.97)
DBP, mm Hg (ref. <90)		
90–110	1.17 (0.91–1.50)	0.83 (0.61–1.14)
>110	1.04 (0.41–2.64)	0.64 (0.23–1.74)
TC, mmol/L (ref. <5.7)		
≥5.7	0.97 (0.76–1.25)	1.03 (0.69–1.53)
TG, mmol/L (ref. <1.7)		
≥1.7	1.03 (0.82–1.29)	0.94 (0.72–1.24)
LDL-C, mmol/L (ref. <3.3)		
≥3.3	0.96 (0.74–1.25)	0.99 (0.66–1.50)
HDL-C, mmol/L (ref. ≥1.0)		
<1.0	1.07 (0.84–1.36)	0.97 (0.65–1.44)
Abbreviation: RR, hazard ratio.		
a Model 1 showed the unadjusted univariate models.		
b Model 2 showed the multivariate models adjusted by age, gender and education levels.		

Discussion

Among eastern Chinese population aged 55 years or more at high risk of CVD, we found high dementia prevalence, and the prevalence of dementia and MCI increased over the short period of 2018 to 2020. Coupled with the fact that

older age, low education levels, stroke, diabetes, hypertension and depression were significant risk factors, which were consistent with other studies [18, 19].

Compared with the 2018 cohort, the 2020 cohort had a higher prevalence of dementia and MCI at every age range. The age- gender adjusted prevalence of dementia was 10.15% in 2020, which was about twice as high compared to the general population aged 65 or older in China (5.14%), according to the national epidemiological survey [4]. It was also higher than that of the general population in Zhejiang province (4.9%), but lower than the nursing homes (40.6%) [15]. The age- gender adjusted prevalence of MCI was 25.46%, which was also higher than that of the general population in Zhjiang province [4, 15].

To our knowledge, ours was one of very few surveys of dementia prevalence and trend in a population at high risk of CVD. The prevalence of CVD risk factors of this study population was relatively high. Hypertension was present almost half of the study population in 2018 and 2020, double of the global age standardized prevalence of hypertension [20, 21]. The mean total cholesterol (TC) of our study was 5.33 mmol/L in 2020, which was higher than that of the general population (4.63 mmol/L). The stroke prevalence of 4.7% in 2018 and 4.0% in 2020 was higher than that of 2.8% among the general Chinese population aged 40 years or more [22]. Furthermore, the prevalence of regular exercises of 11.3% in 2018 and 13.7% in 2020 was relatively low, compared with that of 33.9% of Chinese residents [22]. The smoking rate of nearly 30% in 2020 among men in the study was high, while it was about 0.36% for women. And the high prevalence of alcohol abuse of more than half among men in 2020 was also of great concern and needed to be addressed.

Many factors had been associated with a risk for dementia. Consistent with previous investigations in China and other countries, our study confirmed that older age, lower education levels, heavy drinking were a strong risk factor for dementia in populations at high risk of CVD [4, 23, 24]. Prevalence of dementia had been found to be higher in women than men in some regions but not in all [14]. In our survey, being female was a protective factor for dementia. Obesity was associated with an increased risk of dementia, consistent with the hypothesis that obesity triggering vascular dementia decreased not only blood supply to the brain, but also increased fat cells that damaged the brain white matter leading to loss of cognitive and intellectual behaviors [25].

In addition, CVD including of diabetes, stroke and hypertension were important risk factors of dementia showed in this study. Other studies found that persons with diabetes had an increased risk for all cause dementia [14]. Meanwhile, some studies showed that stroke doubled the chances of developing dementia [26, 27]. Preventing diabetes, stroke, hypertension and reducing cardiovascular risk factors would be an effective way to reduce the dementia burden.

It should be mentioned that depression was a strong risk factor for dementia among this survey population. Evidence suggested that cerebrovascular changes might constitute a link between depression and dementia, it was not only epidemiologically but also biologically plausible that depression increased dementia risk [28]. Further research was needed to investigate whether successful prevention and antidepressive treatment of depression decreased the risk of dementia.

Strengths And Weaknesses

Some limitations needed to be mentioned in this study. The intervals between the two surveys were relatively short. Additional cohort survey data should be required in the future. Furthermore, the sample size was relatively small, a larger scale, larger sample size and longer period of study which including of more collected information are needed in the further.

Despite these limitations, the strengths included that it was one of very few surveys about dementia prevalence and prevalence trend among a population at high risk of CVD in eastern China. And the study was a part of the PEACE Million Persons Project, which providing regional representative data at a population level in eastern China.

Conclusion

In conclusion, cognitive impairment is highly prevalent among elderly at high risk of CVD in eastern China, and the prevalence of dementia and MCI increases over the short period of 2018 to 2020. More population-based strategies should be focusing on modifiable risk factors of dementia, such as cardiovascular risk factors including of heavy drinking, obesity, depression and else. And longer studies enrolling larger populations are needed in the future.

Abbreviations

AD

Alzheimer's disease; MCI:Mild cognitive impairment; CVD:cardiovascular disease; PEACE:Patient-Centered Evaluative Assessment of Cardiac Events; NCCD:National Center for Cardiovascular Disease; MMSE:Mini-Mental State Examination; MoCA:Montreal Cognitive Assessment; HAD:Hospital Anxiety and Depression Scale; SD:standard deviations; HR:hazard ratios; AHR:adjusted hazard ratio; TC:total cholesterol.

Declarations

Ethics approval and consent to participate

The central ethics committee at the China National Center for Cardiovascular Disease (NCCD) and Zhejiang hospital approved this project. Written informed consent is obtained from all literate participants without cognitive decline on entry into the project. And for illiterate participants or ones with cognitive decline, their informed consent is obtained from their literate legally authorized representatives. Trial registration number: NCT02536456.

Consent for publication

Not applicable.

Availability of data and material

The data sets used or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors have no conflict of interest to report.

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Authors' contributions

Substantial contributions to the conception or design of the work: Z P, Y J; Acquisition, analysis, or interpretation of data for the work: Y L;

Drafting the work for important intellectual content: H S, X X, H Y, X C, Y C.

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