Prevalence of Cognitive Impairment Among an Eastern Chinese Population At High Cardiovascular Disease Risk in 2020

Li YANG (✉ phoebe84331@hotmail.com)  
    Zhejiang Hospital

Cheng Xuan  
    Zhuji second people's hospital

Caiyan Yu  
    Zhuji second people's hospital

Pinpin Zheng  
    Fudan University

Jing Yan  
    Zhejiang Hospital

Research Article

Keywords: Cardiovascular, CVD, dementia

DOI: https://doi.org/10.21203/rs.3.rs-119002/v1

License: ☼  This work is licensed under a Creative Commons Attribution 4.0 International License.  
Read Full License
Abstract

Cardiovascular factors increased the risk of dementia. We investigated the associations between such factors, and tested that if a population with a high level of cardiovascular risk would have a higher prevalence of cognitive impairment. Participants (n=3082; ages=55+; 46.4% female) at high risk of CVD in Zhejiang province Registry for PEACE Million Persons Project, completed 3+ neuropsychological evaluations. Age-, gender- standardized prevalence rates were calculated based on the sixth population census for population of China. Adjusted logistic regression models were used to ascertain the risk factors of dementia. Trial registration number: NCT02536456. There was a high prevalence of cognitive Impairment, coupled with the fact that stroke, diabetes, hypertension and depression were significant risk factors. Cognitive impairment are highly prevalent among elderly at high risk of CVD in Zhejiang province. More population-based strategies, including preventing CVD and reducing cardiovascular risk factors would be an effective way to reduce the dementia burden.

Introduction

Dementia, a decline in memory and other cognitive functions that leads to a loss of independence, is a common and feared geriatric syndrome that affects elderly worldwide and has a large social and economic impact on patients, families, and government programs. Mild cognitive impairment (MCI) is identified as an intermediate state between normal cognitive ageing and dementia, it was showed that people with MCI are likely to progress to dementia at a rate of 12% per year, compared with about 1% for normal people at the same age.

According to the World Alzheimer's Disease (AD) report 2018, one person with dementia is born worldwide every three seconds. There are currently at least 50 million people with dementia in the world, and the number is expected to reach 152 million by 2050, with about 70% of them suffering from AD. 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. This has become a major public health problem that seriously affects the health and life quality of Chinese population.

The greater longevity has resulted in an increased population of older people at risk for cognitive impairment. China is facing substantial challenges in ageing population, of which increasing numbers will have some degree of cognitive impairment. Zhejiang province is located in eastern China, there were 10.08 million people aged 60 or above by the end of 2017, accounting for 21.8% of the total population.

Some studies suggest that key cardiovascular risk factors, such as hypertension, diabetes, and hypercholesterolemia influence the incidence of dementia. The risk of dementia was higher with increased internal carotid intimal medial thickness (IMT), and lower anklebrachial index. The prevalence of cardiovascular disease (CVD) among the participants at high-risk of CVD in Zhejiang province was about 3.9% in 2014 to 2016, and was expected to increase to 5% by 2021. But there are few
epidemiological data available on dementia in eastern China, which taking into account of cardiovascular risk factors that might influence prevalence.

Our current study is conducted to estimate the prevalence of cognitive impairment among a population at high risk of CVD, which might provide relevant information for the government, health and welfare agencies to plan adequate services, and it will be helpful to identify and evaluate specific risk factors. We also sought to test the hypothesis that the population with a high level of cardiovascular risk would have a higher prevalence of cognitive impairment than expected.

Methods

Study Design and Participants

It is a population-based closed cohort assembled in June 2020 in Zhejiang province, representative of dwellers 55 years or more at high risk of CVD (n = 3082). This project is part of the China Patient-Centered Evaluative Assessment of Cardiac Events (PEACE) Million Persons Project, a government-funded, large-scale population-based screening project in China, which has been described previously.

From April to August, 2019, we used a convenience sampling strategy to select 7 subdistricts, in which potential participants were invited to the trial by local staff via extensive publicity campaigns on television and in newspapers. Participants were enrolled if they were aged 35 years or more and registered in the selected regions, and who had lived in the selected regions for at least 6 of the previous 12 months. Of 25000 enrolled participants, 1000 (4%) were excluded because of missing data. From April to June, 2020, participants in the cohort that aged 55 years or more and at high risk of CVD were enrolled, and they were given cognitive function evaluation and diagnosis. The criteria of high risk of CVD had been described previously.

Of 3329 enrolled participants, 247 (7.4%) were excluded because of low compliance or missing data.

The central ethics committee at the China National Center for Cardiovascular Disease (NCCD) and Zhejiang hospital approved this project. We confirmed that all methods were performed in accordance with the Declaration of Helsinki. Written informed consent is obtained from all literate participants on entry into the project. And for illiterate participants, their informed consent is obtained from their literate legally authorized representatives. Trial registration number: NCT02536456.

Data Collection And Variables

For every participant, we collected information on sociodemographic characteristics, health behaviors, and medical history during the in-person interviews. We measured blood pressure (BP) two times on their right upper arm after 5 min of rest in a seated position using an electronic BP monitor (Omron HEM-7430; Omron Corporation, Kyoto, Japan). Consistent with the US Joint National Committee and Chinese definitions, hypertension was defined as an average systolic blood pressure (SBP) of at least 140 mm Hg
or an average diastolic blood pressure (DBP) of at least 90 mm Hg, or self-reported use of an antihypertensive drug in the past 2 weeks\textsuperscript{12–14}. We also took physical measurements, including height and weight, following standard protocols. Body mass index (BMI) was defined as weight (kg) divided by height\(^2\) (m\(^2\)) \textsuperscript{15}.

Participants were considered at high risk of CVD if they meet at least one of four criteria\textsuperscript{11}: 1. History of at least one of the following cardiovascular events including of MI, PCI, CABG treatment, or stroke (either ischaemic or haemorrhage); 2. SBP \(\geq\) 160 mmHg or DBP \(\geq\) 100 mmHg; 3. LDL-C \(\geq\) 4.14 mmol/L or HDL-C \(<\) 0.78 mmol/L; 4. Risk of CVD in 10 years \(\geq\) 20% based on WHO/ISH.

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 functioning, 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\textsuperscript{16}. 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\textsuperscript{17}. Participants who scored less than the MoCA cutoff points of 1.5 SDs or more below age- and education-adjusted norms were considered as MCI\textsuperscript{18}. HAD tests included two subscales of anxiety (A) and depression (D), with 7 questions for each. The sub-scale of anxiety and depression was abnormal with a score below 8, including positive for suspicious and symptomatic persons\textsuperscript{19}.

The confirmed diagnosis of dementia was conducted among the subjects with positive results of MMSE test, which included the history and personal information. The diagnostic criteria of dementia used the Chinese guidelines for the Diagnosis and treatment of dementia and Cognitive Impairment\textsuperscript{20}, but we excluded neuroimaging due to high costs\textsuperscript{21}.

**Statistical analysis**

Epidata 3.0 was used for data collection and validation, SAS 9.2 (SAS Institute Inc., Cary, NC, USA) for data management and analysis. Characteristics, cognitive function status of participants were summarized using percentages or means and standard deviations (SD), and they were compared by Student’s t tests and \(X^2\) tests, respectively. Estimates of the prevalence of dementia, MCI were calculated for the overall population and for subgroups stratified by age and gender. Age-, gender-standardized prevalence rates were calculated based on the population distribution of China in 2010 (the sixth population census for population of Zhejiang province aged 55 or more)\textsuperscript{22}. Crude univariate logistic regression models were first used to assess the risk factors associated with dementia among population at high risk of CVD, then adjusted logistic regression models were used to ascertain the risk factors considering the main effects of sociodemographic characteristics. Significance level was set at \(P < 0.05\) for all hypothesis tests.
Results

Characteristics of the populations

A total of 3329 residents were enrolled in this project, and 3082 ones completed the survey. We found no significant age or gender differences between participants and nonparticipants. The characteristics of the samples were presented in Table 1. Women accounted for 46.36% of the population, and they were older than men (69.83 vs. 68.85, P < 0.0001). Male individuals were better educated than female participants, and were more likely to smoke and drink than the female (P < 0.0001).
Table 1

**Characteristics of the study sample by gender.** BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, Total cholesterol; TG, triglycerides; HDL-C, High density lipoprotein.

Sociodemographic characteristics of participants were summarized by areas using frequencies (percentages) or means and standard deviations, and they were compared by Chi-squared tests and the Student’s t-test, respectively. *Test for differences between intensive group and standard group. Statistically significant results are presented in bold.

| Characteristic                  | Male (n = 1429) | Female (n = 1653) | Total (n = 3082) | P      |
|--------------------------------|----------------|------------------|-----------------|--------|
| Age, y                         |                |                  |                 | < 0.0001 |
| 55–64                          | 270 (18.89)    | 352 (21.29)      | 622 (20.24)     |        |
| 65–74                          | 852 (59.63)    | 1068 (64.61)     | 1920 (82.48)    |        |
| ≥ 75                           | 307 (21.48)    | 233 (14.10)      | 540 (17.52)     |        |
| Mean (SD)                      | 69.83 (5.18)   | 68.85 (4.85)     | 69.30 (5.03)    | < 0.0001 |
| Education                      |                |                  |                 | < 0.0001 |
| Illiterate (< 1 year)          | 111 (7.77)     | 375 (22.69)      | 486 (15.77)     |        |
| Primary (1–6 years)            | 814 (56.96)    | 901 (54.51)      | 1715 (55.65)    |        |
| Middle (7–12 years)            | 498 (34.85)    | 374 (22.63)      | 872 (28.29)     |        |
| High (> 13 years)              | 6 (0.42)       | 3 (0.18)         | 9 (0.29)        |        |
| State of marriage              |                |                  |                 | < 0.0001 |
| Married                        | 1313 (91.88)   | 1341 (81.13)     | 2654 (86.11)    |        |
| living alone                   | 116 (8.12)     | 312 (18.87)      | 428 (13.89)     |        |
| Cardiovascular risk factors    |                |                  |                 |        |
| Stroke                         | 67 (4.69)      | 56 (3.39)        | 123 (3.99)      | 0.066  |
| Diabetes                       | 81 (5.67)      | 121 (7.32)       | 202 (6.55)      | 0.065  |
| CHD                            | 23 (1.61)      | 14 (0.85)        | 37 (1.20)       | 0.053  |
| Hypertension                   | 779 (54.51)    | 866 (52.39)      | 1645 (53.37)    | 0.24   |
| Family history of CVD          |                |                  |                 |        |
| Hypertension                   | 270 (18.89)    | 291 (17.60)      | 561 (18.20)     | 0.354  |
| Stroke                         | 17 (1.19)      | 16 (0.97)        | 33 (1.07)       | 0.55   |
| CHD                            | 11 (0.77)      | 9 (0.54)         | 20 (0.65)       | 0.44   |
| Diabetes                       | 41 (2.87)      | 61 (3.69)        | 102 (3.31)      | 0.2    |
| Lifestyle habits               |                |                  |                 |        |
| Characteristic            | Male (n = 1429) | Female (n = 1653) | Total (n = 3082) | P     |
|--------------------------|-----------------|-------------------|------------------|-------|
| Cigarette smoking        | 418 (29.25)     | 6 (0.36)          | 424 (13.76)      | < 0.0001 |
| Heavy alcohol drinking   | 764 (53.46)     | 352 (21.29)       | 1116 (36.21)     | < 0.0001 |
| Regular exercise         | 177 (12.39)     | 246 (14.88)       | 423 (13.72)      | 0.045  |
| Anxiety                  | 9 (0.63)        | 23 (1.39)         | 32 (1.04)        | 0.038  |
| Depression               | 183 (12.81)     | 294 (17.79)       | 477 (15.48)      | 0.0001 |
| BMI                      |                 |                   |                  | 0.35   |
| <18.5                    | 307 (21.48)     | 389 (23.53)       | 696 (22.58)      |       |
| 18.5–24.9                | 544 (38.07)     | 634 (38.35)       | 1178 (38.22)     |       |
| 25.0–29.9                | 507 (35.48)     | 542 (32.79)       | 1049 (34.04)     |       |
| ≥30.0                    | 71 (4.97)       | 88 (5.32)         | 159 (5.16)       |       |
| Mean (SD)                | 24.26 (3.23)    | 24.44 (3.45)      | 25.17 (3.07)     | 0.5862 |
| Net worth (RMB)          |                 |                   |                  | 0.11   |
| ≤50000                   | 978 (86.70)     | 1136 (88.82)      | 2114 (87.83)     |       |
| >50000                   | 150 (13.30)     | 143 (11.18)       | 293 (12.17)      |       |
| SBP, mm Hg               |                 |                   |                  | 0.031  |
| <140                     | 445 (31.14)     | 586 (35.45)       | 1031 (33.45)     |       |
| 140–180                  | 810 (56.68)     | 865 (52.33)       | 1675 (54.35)     |       |
| >180                     | 174 (12.18)     | 202 (12.22)       | 376 (12.20)      |       |
| Mean (SD)                | 149.8 (19.10)   | 151.8 (19.28)     | 150.89 (19.23)   | 0.003  |
| DBP, mm Hg               |                 |                   |                  | < 0.0001 |
| <90                      | 889 (62.21)     | 1237 (74.83)      | 2126 (68.98)     |       |
| 90–110                   | 492 (34.43)     | 398 (24.08)       | 890 (28.88)      |       |
| >110                     | 48 (3.36)       | 18 (1.09)         | 66 (2.14)        |       |
| Mean (SD)                | 82.56 (10.60)   | 79.96 (10.70)     | 81.17 (10.73)    | < 0.0001 |
| TC, mmol/L               |                 |                   |                  | < 0.0001 |
| <5.7                     | 1150 (80.48)    | 1087 (65.76)      | 2237 (72.58)     |       |
| ≥5.7                     | 279 (19.52)     | 566 (34.24)       | 845 (27.42)      |       |
| Mean (SD)                | 4.99 (1.22)     | 5.62 (1.24)       | 5.33 (1.28)      | < 0.0001 |
| Characteristic       | Male (n = 1429) | Female (n = 1653) | Total (n = 3082) | P  |
|---------------------|----------------|-------------------|------------------|----|
| TG, mmol/L          |                |                   |                  |    |
| <1.7                | 928 (64.94)    | 1016 (61.46)      | 1944 (63.08)     | 0.046 |
| ≥ 1.7               | 501 (35.06)    | 637 (38.54)       | 1138 (36.92)     |    |
| Mean (SD)           | 1.91 (1.14)    | 2.03 (1.97)       | 1.97 (1.11)      | 0.015 |
| LDL-C, mmol/L       | <0.0001        |                   |                  |    |
| < 3.3               | 1188 (83.14)   | 1176 (71.14)      | 2364 (76.70)     |    |
| ≥ 3.3               | 241 (16.86)    | 477 (28.86)       | 718 (23.30)      |    |
| Mean (SD)           | 2.69 (1.06)    | 3.19 (1.14)       | 2.96 (1.13)      | <0.0001 |
| HDL-C, mmol/L       | 0.0026         |                   |                  |    |
| ≥ 1.0               | 924 (64.66)    | 1153 (69.75)      | 2077 (67.39)     |    |
| < 1.0               | 505 (35.34)    | 500 (30.25)       | 1005 (32.61)     |    |
| Mean (SD)           | 1.47 (0.47)    | 1.57 (0.43)       | 1.52 (0.45)      | <0.0001 |
| MMSE scores, Mean (SD) | 22.77 (3.07) | 21.76 (3.21) | 22.23 (3.18) | <0.0001 |
| MoCA scores, Mean (SD) | 18.71 (4.27) | 17.57 (4.36) | 18.10 (4.36) | <0.0001 |
| Had scores, Mean (SD) | 9.17 (3.39)  | 9.95 (3.60)       | 9.59 (3.52)      | <0.0001 |

**Prevalence Of Dementia And MCI**

Prevalences by age range were displayed in Table 2. Of the 3082 participants, 391 and 750 of whom were classified as having dementia and MCI respectively, giving an overall prevalence of 12.7% (95% CI 11.5 to 13.8) and 24.3 (95% CI 22.82–25.85), respectively. The prevalences of dementia and MCI standardized by age and sex with a standard population (the sixth population census of Zhejiang province) was 10.2%, 25.5% respectively. And the prevalences were associated with increased age.
Table 2

Cognitive Function by Age Range. Estimates of the prevalence of dementia, MCI were calculated for the overall population and for subgroups stratified by age and gender. Age-, gender- standardized prevalence rates were calculated based on the population distribution of China in 2010 (the sixth population census for population of Zhejiang province aged 55 or more)

| Cognitive Function | 55–64 y (n = 622) | 65–74 y (n = 1920) | 75–100 y (n = 540) | Total (Age55-100 y) (n = 3082) | Adjusted prevalences |
|--------------------|-------------------|-------------------|-------------------|-----------------------------|---------------------|
| Normal cognitive functioning | 475 (76.37) [68.75–81.23] | 1172 (61.04) [56.47–78.09] | 294 (54.44) [41.56–65.06] | 1941 (62.98) [55.46–70.06] | 64.39 (60.42–71.23) |
| Mild cognitive impairment | 86 (13.83) [11.21–15.72] | 507 (26.41) [24.54–28.16] | 157 (29.07) [27.36–31.09] | 750 (24.33) [22.82–25.85] | 25.46 (24.12–27.84) |
| Dementia | 61 (9.81) [7.56–12.33] | 241 (12.55) [10.94–14.14] | 89 (16.48) [14.06–18.72] | 391 (12.69) [11.51–13.86] | 10.15 (7.41–12.31) |

Logistic Analysis

Logistic regression models including crude and adjusted models were used to assess associated risk factors associated with dementia and MCI among the participants with high risk of CVD. Crude associations were first assessed using univariate models, then multivariate models were used for the adjusted associations, which were adjusted by age, gender and education levels. It showed that 75 years or older (AOR = 1.69, 95% CI: 1.44–2.07), having a medical history of hypertension (AOR = 1.22, 95% CI: 1.00-1.60), having a medical history of stroke (AOR = 3.10, 95% CI: 1.98–4.85) and diabetes (AOR = 1.71, 95% CI: 1.04–2.58), having the family history of hypertension (AOR = 1.82, 95% CI: 1.29–2.56), heavy drinking (AOR = 1.25, 95% CI: 1.00-1.66), depression (AOR = 4.57, 95% CI: 3.43–6.07) were associated with dementia, while female (AOR = 0.69, 95% CI: 0.50–0.95), higher education levels including middle (AOR = 0.87, 95% CI: 0.59–0.98) and high (AOR = 0.66, 95% CI: 0.07–0.93) schooling might be protective factors for dementia (Table 3).
Table 3
Odds Ratios for Presence of Dementia in 2020 Among a Population at High CVD Risk. Crude univariate logistic regression models were first used to assess the risk factors associated with dementia among population at high risk of CVD, then adjusted logistic regression models were used to ascertain the risk factors considering the main effects of sociodemographic characteristics.

| Models, OR (95% CI) |  |
|---------------------|--|
| **Variable (ref. 55–64)** | **Model1** | **Model2** |
| **Age, y** |  |
| 65–74 | 1.03 (0.83–1.29) | 0.77 (0.53–1.10) |
| ≥75 | 0.68 (0.53–0.88) | 1.69 (1.44–2.07) |
| **Gender (ref. Male)** |  |
| Female | 0.77 (0.62–0.95) | 0.69 (0.50–0.95) |
| **Education (ref. Illiterate)** |  |
| Primary (1–6 years) | 1.29 (1.04–1.60) | 1.48 (0.97–2.06) |
| Middle (7–12 years) | 1.02 (0.81–1.30) | 0.87 (0.59–0.98) |
| High (>13 years) | 1.16 (0.15–9.32) | 0.66 (0.07–0.93) |
| **State of marriage (ref. Married)** |  |
| living alone | 1.28 (0.96–1.71) | 0.88 (0.62–1.26) |
| **CVD and related risk factors** |  |
| Hypertension | 0.71 (0.58–0.88) | 1.22 (1.00–1.60) |
| Stroke | 1.28 (1.19–1.41) | 3.10 (1.98–4.85) |
| CHD | 2.56 (0.62–10.69) | 2.63 (0.60–11.55) |
| Diabetes | 0.87 (0.55–1.43) | 1.71 (1.04–2.58) |
| **Family history of CVD** |  |
| Hypertension | 1.64 (1.20–2.25) | 1.82 (1.29–2.56) |
| Stroke | 1.46 (0.44–4.79) | 1.72 (0.47–6.30) |
| CHD | 1.31 (0.30–5.66) | 0.91 (0.20–4.10) |
| Diabetes | 0.77 (0.45–1.33) | 0.76 (0.42–1.37) |
| **Lifestyle habits** |  |
| Cigarette smoking | 1.23 (0.88–1.70) | 0.92 (0.61–1.41) |
|                                    | Models, OR (95% CI) |
|------------------------------------|---------------------|
| Heavy alcohol drinking             | 1.44 (1.14–1.82)    | 1.25 (1.00–1.66) |
| Regular exercise                   | 0.345 (0.17–3.92)   | 1.36 (0.93–1.99) |
| Anxiety                            | 0.14 (0.07–0.28)    | 2.09 (0.86–5.09) |
| Depression                         | 1.20 (0.29–1.25)    | 4.57 (3.43–6.07) |
| BMI (ref. 18.5–24.9)               |                     |                   |
| <18.5                              | 1.51 (1.14–1.99)    | 0.51 (0.17–1.55)  |
| 25.0–29.9                          | 0.96 (0.77–1.20)    | 1.12 (0.86–1.46)  |
| ≥30.0                              | 0.90 (0.57–1.43)    | 1.10 (0.65–1.85)  |
| Net worth (RMB) (ref. ≤50000)      |                     |                   |
| >50000                             | 1.29 (0.88–1.89)    | 1.12 (0.74–1.69)  |
| SBP, mm Hg (ref. <140)             |                     |                   |
| 140–180                            | 0.92 (0.74–1.13)    | 1.22 (0.83–1.80)  |
| >180                               | 0.73 (0.54–1.00)    | 1.11 (0.67–1.82)  |
| DBP, mm Hg (ref. <90)              |                     |                   |
| 90–110                             | 0.97 (0.77–1.23)    | 0.83 (0.63–1.10)  |
| >110                               | 0.58 (0.32–1.08)    | 0.58 (0.29–1.17)  |
| TC, mmol/L (ref. <5.7)             |                     |                   |
| ≥5.7                               | 1.08 (0.85–1.38)    | 1.36 (0.93–1.99)  |
| TG, mmol/L (ref. <1.7)             |                     |                   |
| ≥1.7                               | 0.96 (0.77–1.19)    | 1.10 (0.85–1.42)  |
| LDL-C, mmol/L (ref. <3.3)          |                     |                   |
| ≥3.3                               | 1.00 (0.78–1.29)    | 0.95 (0.64–1.41)  |
| HDL-C, mmol/L (ref. ≥1.0)          |                     |                   |
| <1.0                               | 1.27 (1.01–1.61)    | 0.87 (0.60–1.26)  |

**Discussion**

Among a population aged 55 years or more who had high levels of cardiovascular risk, we found high dementia prevalence. Coupled with the fact that stroke, diabetes, hypertension and depression were
significant risk factors, our observations were consistent with other studies. In our sample, the age- gender adjusted prevalence of dementia was 10.15%, 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. It was also higher than that of the general population in Zhejiang province (4.9%), but lower than the nursing homes (40.6%). The age- gender adjusted prevalence of MCI was 25.46%, which was also higher than that of the general population in Zhjiang province.

Considering demographic factors, the prevalence of dementia and MCI were associated with increased age and decreased education levels, which was consistent with other studies. Our study found a higher prevalence of dementia in men than women at high risk for CVD, but other studies had shown a higher prevalence of dementia in women than men among the general population.

To our knowledge, ours was one of very few surveys of dementia prevalence in a population at high risk of CVD. The prevalence of CVD risk factors of this study population was relatively high. Hypertension was present more than half of the study population, double of the global age standardized prevalence of hypertension. The mean total cholesterol (TC) of our study was 5.33 mmol/L, which was higher than that of the general population (4.63 mmol/L). The stroke prevalence of 4.0% was higher than that of 2.88% among the general Chinese population aged 40 years or more. Furthermore, the prevalence of regular exercises of 13.7% was relatively low, compared with that of 33.9% of Chinese residents. The smoking rate of nearly 30% among men in the study was high, while it was about 0.36% for women. And the high prevalence of alcohol abuse among men (more than half) 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 was a strong risk factor for dementia in populations at high risk of CVD. Data of the survey showed that higher education including middle and high schooling were important protective factors for dementia, compared with illiteracy, which supported the view that more education could protect against the consequence of dementia. Heavy drinking was a risk factor for dementia, which was confirmed by previous studies. Prevalence of dementia had been found to be higher in women than men in some regions but not in all. In our survey, being female was a protective factor for dementia.

In addition, CVD including of diabetes, stroke and hypertension were important risk factors of dementia. Other studies showed that persons with diabetes had an increased risk for dementia. Meanwhile, some studies showed that stroke increased the risk of dementia with most of cases were preventable, and the medical history of hypertension might result in cognitive decline. 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. An association between depression and dementia had been suggested in at least 4...
independent meta-analyses, indicating close to a 2-fold higher risk of developing dementia following depression $^{36-40}$, as well as several reviews $^{41,42}$. Additionally, 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 $^{34,43}$. Further research was needed to investigate whether successful prevention and antidepressive treatment of depression decreased the risk of dementia.

Some limitations needed to be mentioned in this study. This was a cross-sectional study, which made it difficult to establish a cause-and-effect relationship for risk factors. Furthermore, due to the limited conditions, imaging and other biological indicators could not be performed for every suspected case to precisely ascertain the dementia subtypes.

Despite these limitations, the strengths included that it was one of very few surveys about dementia prevalence among a population at high risk of CVD. Meanwhile, participants were assessed by trained physicians which made results reliable. And the study was a part of the PEACE Million Persons Project, which providing regional representative data at a population level in Zhejiang province.

In conclusion, cognitive impairment are highly prevalent among elderly at high risk of CVD in Zhejiang province, and it will be increasingly so in the years to come. The existing social supports should be used adequately, focusing on modifiable risk factors of dementia, such as cardiovascular risk factors, and making patients maintain a good psychological state to better prevent CVD and dementia. Meanwhile, more population-based strategies, including raising awareness and advocate for the development of health care and primary prevention policies to address this rapidly growing dementia epidemic and the high prevalence of cardiovascular risk factors are needed. In addition, the development of standardized dementia intervention programs should also be one of the next research priorities.

**Declarations**

**Acknowledgement**

This work was funded by the National Science Foundation for Young Scientists of China (81803314), General project of Medical Science and Technology in Zhejiang province (2019KY001), General project of Medical Science and Technology in Zhejiang province (2018KY193).

**Author contributions**

Conceived and designed the experiments: Yan J., Zheng P.P.. Performed the experiments:XUAN Cheng, YU Caiyan. Analyzed the data: Yang L. Contributed materials/analysis tools: YANG L. Wrote the paper: Yang L.

**Competing interests**
The authors declare no competing interests.

References

1. Kenneth M, Eric B, Eileen M, Jessica D, Deborah A, Mohammed U, et al. A Comparison of the Prevalence of Dementia in the United States in 2000 and 2012. *JAMA Intern Med*, 2017.

2. YANG Li, YAN Jing, JING Xiaqing, et al. Prevalence of dementia, cognitive status and associated risk factors among elderly of Zhejiang province, China in 2014. *Age and Ageing*, 0: 1–5 (2016).

3. Hurd, Martorell P, Delavande A, Mullen KJ, Langa KM. Monetary costs of dementia in the United States. *N Engl J Med* 368(14):1326–1334 (2013).

4. Lewis H. Kuller, DRPH, L, Rachel H, Caterina Rosano, Daniel Edmundowicz, James T, Anne B. Subclinical Cardiovascular Disease and Death, Dementia, and Coronary Heart Disease in Patients 80þ Years. *Journal of the american college of cardiology* 9 (67): 1013–1022 (2016).

5. YANG Li, YAN Jing, JING Xiaqing, et al. Screening for dementia in older adults: Comparison of Mini-Mental State Examination, Mini-Cog, clock drawing test and AD8. *Plos one* 11(12): e0168949 (2016).

6. Larson EB, Yaffe K, Langa KM. New insights into the dementia epidemic. *N Engl J Med* 369 (24):2275–2277 (2013).

7. Wu YT, Fratiglioni L, Matthews FE, et al. Dementia in western Europe: epidemiological evidence and implications for policy making. *Lancet Neurol* 15(1):116–124 (2016).

8. Gershwin Davis, Nelleen Baboolal, Amanda Mc Rae, Robert Stewart. Dementia prevalence in a population at high vascular risk: the Trinidad national survey of ageing and cognition. *BMJ Open* 8:e018288 (2018).

9. LiYang, HaibinWu, Xiaoqing Jin, PinpinZheng, Shiyun Hu, XiaolingXu, et al. Study of cardiovascular disease prediction model based on random forest in eastern China. *Scientific Reports* 10:5245 (2020).

10. Jiapeng Lu, Yuan Lu, Xiaochen Wang, Xinyue Li, George C Linderman, Chaoqun Wu, X, et al. Prevalence, awareness, treatment, and control of hypertension in China: data from 1·7 million adults in a population-based screening study (China PEACE Million Persons Project). *Lancet* 390: 2549–58 (2017).

11. Lu J, Xuan S, Downing NS, et al. Protocol for the China PEACE (Patient-centered Evaluative Assessment of Cardiac Events) Million Persons Project pilot. *BMJ Open* 6: e010200 (2016).

12. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 311: 507–20 (2014).

13. Liu LS, Writing Group of Chinese Guidelines for the Management of H. 2010 Chinese guidelines for the management of hypertension. *Chin J Cardiol* 39: 579–615 (2011).

14. Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA* 289:
Zhou BF. Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults-study on optimal cut-off points of body mass index and waist circumference in Chinese adults. *BES* 15: 83–96 (2002).

Luis Ruano, Natalia Araujo, MScPhm, Mariana Branco, Rui Barreto, Sandra Moreira, et al. Prevalence and Causes of Cognitive Impairment and Dementia in a Population-Based Cohort From Northern Portugal. *Am J Alzheimers Dis Other Demen* 34 (1): 49–56 (2019).

YANG Li, YAN Jing, JING Xiaoping, et al. Estimation of diagnostic performance of dementia screening tests: Mini-Mental State Examination, Mini-Cog, Clock Drawing test and Ascertain Dementia 8 questionnaire. *AGING & MENTAL HEALTH* 22, 8,942–946 (2018).

JACQUELINE Dominguez, Ma. Fe de Guzman, Macario Reandelar Jr, Thien Kieu Thi Phung. Prevalence of Dementia and Associated Risk Factors: A Population-Based Study in the Philippines. *Journal of Alzheimer's Disease* 63: 1065–1073 (2018).

YANG Li, JING Xiaoping, YAN Jing, Yu Jin, Shanhu Xu, Ying Xu, Caixia Liu, Wei Yu, Pinpin Zheng. Comparison of prevalence and associated risk factors of cognitive function status among elderly between nursing homes and common communities of China: A STROBE-Compliant Observational Study. *Medicine* 11 (2019).

Chinese Dementia and cognitive Impairment Diagnosis and treatment guidelines collaboration group, Professional Committee of Cognitive Impairment diseases, Neurologist Branch, Chinese Medical Doctor Association. Chinese Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Disorders in 2018. *Natl Med J China* 98(15):1125–1129 (2018).

Sperling RA, Aisen PS, Beckett LA, et al. Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement* 7:280–92 (2011).

Jianping Jiia, Fen Wang, Cuibai Wei, Aihong Zhou, Xiangfei Jia, Fang Li, et al. The prevalence of dementia in urban and rural areas of China. *Alzheimer's & Dementia* 10:1–9 (2014).

Wayne Katon, Henrik Sondergaard Pedersen, Anette Riisgaard Ribe, Morten Fenger-Grøn, Dimitry Davydow, et al. Effect of Depression and Diabetes Mellitus on the Risk for Dementia A National Population-Based Cohort Study. *JAMA Psychiatry* 5 (2015).

Horst Bickel, Ingrid Hendlmeier, Johannes Baltasar Heßler, Magdalena Nora Junge, Sarah Leonhardt-Achilles, Joshua Weber, Martina Schäufele. The Prevalence of Dementia and Cognitive Impairment in Hospitals. *Dtsch Arztebl Int* 115: 733–40 (2018).

Kalaria RN, Maestre GE, Arizaga R, et al. Alzheimer's disease and vascular dementia in developing countries: prevalence, management, and risk factors. *Lancet Neurol* 7:812–26 (2008).

NCD Risk Factor Collaboration (NCD-RisC) Worldwide trends in blood pressure from 1975 to 2015: A pooled analysis of 1479 population-based measurement studies with 19· million participants. *Lancet* 389, 37–55 (2015).
27. Chinese Cardiovascular health and Disease Report Writing Group. Summary of China's Cardiovascular Health and Disease Report 2019. Chinese Circulation Journal 35 (9):833–854 (2020).
28. Kalaria RN, Maestre GE, Arizaga R, Friedland RP, Galasko D, Hall K, et al. Alzheimer's disease and vascular dementia in developing countries: prevalence, management, and risk factors. Lancet Neurol 7:812–26 (2008).
29. Bickel H, Kurz A. Education, occupation, and dementia: the Bavarian School Sisters Study. Dement Geriatr Cogn Disord 27:548–56 (2009).
30. Vladimir Hachinski, Karl Einhäupl, Detlev Ganten, Suvarna Alladi, Carol Brayne, Blossom C. M. Stephan, et al. Preventing dementia by preventing stroke: The Berlin Manifesto. Alzheimer's Dement 15(7): 961–984 (2019).
31. Kuzma E, Lourida I, Moore SF, Levine DA, Ukoumunne OC, Llewellyn DJ. Stroke and dementia risk: A systematic and meta-analysis. Alzheimer's Dement 14:1416–28 (2018).
32. O’Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): A case-control study. Lancet 376:112–23 (2010).
33. Feigin VL. Global burden of stroke and risk factors in 188 countries, during 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet Neurol 15:913–24 (2016).
34. Isabelle Bos, Stephanie J.B. Vos, Suzanne E. Schindler, Jason Hassenstab, Chengjie Xiong, Elizabeth Grant, et al. Vascular risk factors are associated with longitudinal changes in cerebrospinal fluid tau markers and cognition in preclinical Alzheimer disease. Alzheimer's Dementia 15(9): 1149–1159 (2019).
35. Lindsay R. Clark, Rebecca L. Koscik, Samantha L. Allison, Sara E. Berman, Derek Norton, et al. Hypertension and obesity moderate the relationship between beta-amyloid and cognitive decline in midlife. Alzheimer's Dementia 15(3): 418–428 (2019).
36. Sofie Holmquist, Anna Nordstrom, Peter Nordstrom. The association of depression with subsequent dementia diagnosis: A Swedish nationwide cohort study from 1964 to 2016. PLoS Med 17(1): e1003016 (2020).
37. Cherbuin N, Kim S, Anstey KJ. Dementia risk estimates associated with measures of depression: a systematic review and meta-analysis. BMJ Open 5(12): e008853 (2015).
38. Diniz BS, Butters MA, Albert SM, Dew MA, Reynolds CF 3rd. Late-life depression and risk of vascular dementia and Alzheimer's disease: systematic review and meta-analysis of community-based cohort studies. Br J Psychiatry 202(5):329–35 (2013).
39. Jorm AF. History of depression as a risk factor for dementia: an updated review. Aust N Z J Psychiatry 35(6):776–81 (2001).
40. Ownby RL, Crocco E, Acevedo A, John V, Loewenstein D. Depression and risk for Alzheimer disease: systematic review, meta-analysis, and metaregression analysis. Arch Gen Psychiatry 63(5):530–8 (2006).
41. Bennett S, Thomas AJ. Depression and dementia: cause, consequence or coincidence? *Maturitas* 79(2):184 – 90 (2014).

42. Da Silva J, Goncalves-Pereira M, Xavier M, Mukaetova-Ladinska EB. Affective disorders and risk of developing dementia: systematic review. *Br J Psychiatry* 202(3):177–86 (2013).

43. Forugh S. Dafsari, Frank Jessen. Depression-an underrecognized target for prevention of dementia in Alzheimer's disease. *Dafsari and Jessen Translational Psychiatry* 10:160 (2020).