Postprint of a Study on the Association of Hypertension and Its Comorbidities with Dementia Among Chinese Community-Dwelling Elderly

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Abstract

Background: China' s aging process is accelerating, with an increasing number of elderly patients with chronic diseases. The association between hypertension and its comorbidities with dementia in the elderly population requires further investigation.

Objective: To understand the prevalence of hypertension and its comorbidities among community-dwelling elderly and their association with dementia, providing a reference basis for dementia prevention.

Methods: Based on cross-sectional data from 14,732 elderly individuals aged $ $65 years regarding sociodemographic characteristics, chronic disease profiles, and cognitive function assessments from the China Multi-center Dementia Survey (CMDS) conducted from 2018 to 2023, multivariate Logistic regression models were used to analyze the association between hypertension and its comorbidities with dementia in the total population and across different age and gender groups.

Results: Among the 14,732 elderly individuals aged $ $65 years, 8,293 (56.3%) had two or more comorbidities, 7,786 (52.9%) had hypertension and its comorbidities, of which hypertension with 1-4 comorbidities accounted for 2,569 (17.4%), 2,064 (14.0%), 1,018 (6.9%), and 443 (3.0%) cases, respectively; 1,111 (7.5%) had dementia. After adjusting for covariates, multivariate Logistic regression results showed that compared with elderly individuals without any diseases, the risk of dementia in the hypertension-only group was 1.516 times higher (95% CI=1.014-2.267, P=0.042), and the risks of dementia for hypertension with 1-4 comorbidities were 1.879 times (95% CI=1.312-2.692, P=0.001), 2.071 times (95% CI=1.428-3.004, P<0.001), 2.338 times (95% CI=1.612-3.392, P<0.001), and 2.591 times (95% CI=1.634-4.108, P<0.001), respectively. Hypertension

with cerebrovascular disease had the highest dementia risk at 2.550 times (95% CI=1.384-4.700, P=0.003). Stratified by gender and age, the risk of dementia prevalence increased with the number of hypertension comorbidities, and all were statistically significant (P<0.05). Hypertension with cerebrovascular disease carried the highest dementia risk for males and females at 2.842 times (95% CI=1.095-7.375, P=0.032) and 2.348 times (95% CI=1.060-5.203, P=0.036), respectively. In the <75 years group, hypertension with diabetes had the highest risk (OR=2.833, 95% CI=1.046-7.675, P=0.041), while in the $ $75 years group, hypertension with cerebrovascular disease had the highest risk (OR=2.707, 95% CI=1.168-6.273, P=0.020). Among hypertension with two comorbidities, the combination of hypertension with heart disease and cerebrovascular disease had the highest dementia prevalence (OR=3.559, 95% CI=1.338-9.468, P=0.011); among hypertension with three comorbidities, the combination of hypertension with heart disease, cerebrovascular disease, and autonomic nervous dysfunction had the highest dementia prevalence (OR=3.881, 95% CI=1.736-8.677, P=0.001).

Conclusion: The prevalence of hypertension and its comorbidities is high among Chinese elderly, and patients with hypertension and its comorbidities have a significantly increased risk of dementia with age and gender differences, suggesting that clinical practice should emphasize chronic disease management in this population and adopt targeted prevention and treatment strategies based on individual characteristics, providing a reference for reducing the risk of dementia.

Full Text

Study on the Relationship between Hypertension and its Comorbidity and Dementia in Chinese Community-dwelling Older Adults

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Abstract

Background: China' s aging process is accelerating, and the number of older adults with chronic diseases is increasing. The association between hypertension, along with its comorbidities, and dementia in older adults requires further

investigation.

Objective: To investigate the association between hypertension, its comorbidities, and dementia in community-dwelling older adults, and to provide evidence for dementia prevention.

Methods: This study utilized cross-sectional data from 14,732 individuals aged $ $65 years from the China Multicenter Dementia Survey (CMDS, 2018-2023). Data on sociodemographic characteristics, chronic diseases, and cognitive function were collected. We employed a multivariate Logistic regression model to analyze the association between hypertension and its comorbidities and dementia in the total population and different age and sex groups.

Results: Among the 14,732 older adults ($ $65 years), 8,293 (56.3%) had two or more comorbidities, and 7,786 (52.9%) had hypertension along with other comorbidities. Of these hypertensive individuals, the numbers with 1, 2, 3, and 4 comorbidities were 2,569 (17.4%), 2,064 (14.0%), 1,018 (6.9%), and 443 (3.0%), respectively. Dementia was identified in 1,111 participants (7.5%). After adjusting for covariates, multivariate Logistic regression results showed that the risk of dementia in the hypertension-only group was 1.516 times (95%CI=1.014-2.267, P=0.042), and the risk of dementia among those with hypertension and 1 to 4 comorbidities was 1.879 times (95%CI=1.312-2.692, P=0.001), 2.071 times (95%CI=1.428-3.004, P<0.001), 2.338 times (95%CI=1.612-3.392, P<0.001), and 2.591 times (95%CI=1.634-4.108, P<0.001). The highest risk of dementia was observed in individuals with hypertension coexisting with cerebrovascular disease (OR=2.550, 95%CI=1.384-4.700, P=0.003). In analyses stratified by sex and age, the risk of dementia increased significantly with the number of hypertension comorbidities (P<0.05). The strongest association was observed for hypertension coexisting with cerebrovascular disease, with adjusted odds ratios of 2.842 (95%CI=1.095-7.375, P=0.032) in men and 2.348 (95%CI=1.060-5.203, P=0.036) in women. In the group aged <75 years, the highest risk was observed for hypertension coexisting with diabetes (OR=2.833, 95%CI=1.046-7.675, P=0.041), while in the group aged $ $75 years, the highest risk was observed for hypertension coexisting with cerebrovascular disease (OR=2.707, 95%CI=1.168-6.273, P=0.020). Among participants with hypertension and two comorbidities, the highest dementia risk was observed in those with coexisting heart disease and cerebrovascular disease (OR=3.559, 95%CI=1.338-9.468, P=0.011). Similarly, among those with hypertension and three comorbidities, the highest prevalence of dementia was observed in individuals with coexisting heart disease, cerebrovascular disease, and autonomic dysfunction (OR=3.881, 95%CI=1.736-8.677, P=0.001).

Conclusion: The prevalence of hypertension and its comorbidities is high among Chinese older adults. Patients with hypertension and its comorbidities have a significantly elevated risk of dementia, which varies by age and sex. These findings underscore the importance of optimized management of chronic diseases in this population. Implementing tailored prevention and treatment strategies based on individual characteristics could contribute to reducing the

risk of dementia.

Keywords: Hypertension; Dementia; Aged; Comorbidities; Correlational study

Introduction

Dementia is a collective term for acquired severe cognitive decline across multiple domains that significantly impairs patients' functional abilities [1]. Global dementia cases are projected to increase from approximately 57 million in 2019 to 153 million by 2050 [2]. Recent data indicate that among Chinese individuals aged 60 and above, there are already 15.07 million dementia patients, accounting for one-quarter of global cases [3], imposing enormous economic and caregiving burdens on families and society. The etiology of dementia is complex, its pathogenesis remains unclear, and there are still no drugs that can cure or delay its progression [4]. Moreover, the prodromal phase of dementia can last for decades, shifting the focus of prevention from pharmacological intervention to non-pharmacological interventions during the preclinical stage.

Both domestic and international studies have shown that genetic susceptibility and exposure to risk factors, particularly chronic diseases such as hypertension, cardiovascular and cerebrovascular diseases, and metabolic disorders, produce a series of molecular changes and alterations in brain structure that constitute the primary causes of cognitive impairment [5]. Consequently, preventing chronic diseases in older adults is widely recognized as an effective strategy for reducing dementia risk [6,7]. A recent study published in *The Lancet* indicated that targeting modifiable risk factors (primarily chronic diseases in older adults) could prevent up to 45% of dementia cases [8].

As China's population ages, the coexistence of multiple diseases in older adults is becoming increasingly common. A 2020 analysis of data from the China Health and Retirement Longitudinal Study (CHARLS) found that the prevalence of chronic diseases among middle-aged and older Chinese adults was 80.9%, with comorbidity at 34.4%, and hypertension had the highest prevalence (40.2%) [9]. Current research on the association between multimorbidity and all-cause dementia remains inconclusive and has primarily focused on metabolic and cardiovascular comorbidities, neglecting the impact of insomnia and autonomic dysfunction on cognition. Therefore, it is necessary to explore the effect of hypertension comorbidity burden with a broader range of diseases on dementia. This study investigated the comorbidity patterns of hypertension with five other chronic diseases reported in the literature to be associated with cognitive impairment (diabetes, heart disease, cerebrovascular disease, insomnia, and autonomic dysfunction) among urban and rural residents aged 65 and above across eight Chinese community-based dementia research centers, and analyzed the association between hypertension and its comorbidity combinations and dementia risk to provide evidence for dementia prevention and healthy aging promotion in

China.

Methods

1.1 Study Participants The China Multicenter Dementia Survey (CMDS) [10] was conducted from 2018 to 2023. The sampling process accounted for dietary differences between northern and southern China. Following China' s administrative regional divisions, we selected eight survey centers in Northeast (Jilin Province), North (Tianjin), East (Fujian Province), Central-South (Hubei and Hainan Provinces), Southwest (Chongqing and Guizhou), and Northwest (Xinjiang Uygur Autonomous Region) China. Each center chose 1-2 urban communities (under the jurisdiction of secondary or higher-level hospitals) and 1-2 rural communities (under the jurisdiction of county-level hospitals) as bases for face-to-face interviews, neuropsychological testing, physical examinations, and clinical assessments.

Inclusion criteria: (1) Long-term residents of the target communities; (2) Aged $ $65 years; (3) Available electronic health records at the jurisdiction hospital.

Exclusion criteria: (1) Bedridden or too frail to stand or walk; (2) Major psychiatric disorders (e.g., major depression, bipolar disorder, schizophrenia) or life-threatening diseases; (3) Severe hearing or visual loss preventing survey completion.

The sample size was calculated using the formula: $n = (Z^2_{1\ \alpha/2} \times pq)/d^2$, where $Z\alpha/_2$ is the test statistic for significance ($Z_{1\ \alpha/2} = 1.96$ when $\alpha = 0.05$); p is the expected prevalence of the target disease; q = 1-p; and d is the allowable error (set at 0.1p). Based on the latest 2024 report by GAN et al. [11] on dementia prevalence and risk factors among Chinese older adults, p was estimated at 8.8%, yielding n = 3,981. To account for potential sampling errors and low response rates during actual sampling, we increased the theoretically required sample size by an additional 30% to ensure statistical power, resulting in a final required sample size of approximately 5,175 cases. According to the inclusion/exclusion flowchart (Figure 1 [Figure 1: see original paper]), the actual number of participants included in this study was 14,732, meeting the requirements for observational study sample size. After fully explaining the purpose and procedures to participants, written informed consent was obtained. This study was approved by the Ethics Committee of Tianjin Huanhu Hospital (Ethics Approval No. 201940) and the Medical Ethics Committee of Wuhan University of Science and Technology (Ethics Approval No. 201945).

1.2 Research Methods The survey was conducted face-to-face at the investigation site. Participants, either alone or accompanied by an informant, completed a 30-40 minute assessment in a relatively private space, comprising three parts: sociodemographic information, chronic disease status, and cognitive function screening.

1.2.1 Sociodemographic Information Trained and certified investigators (qualified clinicians and medical graduate students) collected data through face-to-face interviews or measurements, including: residence location, sex, age, education level, marital status (married with spouse alive or remarried defined as currently having a spouse; divorced, widowed, or never married defined as currently without a spouse), BMI [calculated as weight (kg)/height $(m)^2$], smoking status (defined as smoking at least one cigarette daily for more than 6 months continuously or cumulatively), alcohol consumption (defined as drinking white liquor at least once per week with >25g each time), and social activity frequency (options: less than once per week, 1-2 times per week, and $ $3 times per week, defined as basically none, occasional, and frequent, respectively).

1.2.2 Chronic Disease Status The presence of hypertension, diabetes, heart disease, cerebrovascular disease, insomnia, and autonomic dysfunction was based on self-reported diagnoses confirmed by secondary or higher-level medical institutions or recorded in hospital electronic health archives. Specifically: hypertension was diagnosed based on previous medical history or on-site measurement of systolic blood pressure $ $140 mmHg (1 mmHg = 0.133 kPa) and/or diastolic blood pressure $ $90 mmHg (using Omron HBP1300 electronic blood pressure monitor); diabetes was diagnosed when fasting blood glucose (measured using Beckman LX-20 automatic biochemical analyzer with hexokinase method after centrifugation with DT5-2 medical centrifuge) $ $7.0 mmol/L; heart disease was diagnosed based on clinically confirmed history of coronary heart disease, vascular heart disease, arrhythmia, heart failure, cardiomyopathy, or other clinically diagnosed cardiac diseases; cerebrovascular disease was diagnosed based on clinically diagnosed history of hemorrhagic or ischemic cerebrovascular disease; insomnia was assessed using the Athens Insomnia Scale (AIS) [12], with a total score >6 defined as insomnia; autonomic dysfunction was assessed using the Composite Autonomic Symptom Score (COMPASS-31) [13,14], which evaluates 31 items across 6 domains (orthostatic intolerance, vasomotor, secretomotor, gastrointestinal, bladder, and pupillomotor function) to assess severity of autonomic symptoms over the past year, with higher scores indicating more severe dysfunction, using >19.5 points as the cutoff for autonomic dysfunction. Multimorbidity was defined as having $ $2 chronic diseases simultaneously.

1.2.3 Cognitive Function Screening A series of standardized neuropsychological assessment scales [15] were used to evaluate participants' cognitive function and daily living abilities. The Mini-Mental State Examination (MMSE) [16] assessed overall cognitive function, comprising 30 items covering orientation, memory, calculation, language, attention, and executive function, with total score of 30 points (lower scores indicating worse cognitive function). The Activities of Daily Living (ADL) scale [17] assessed daily living abilities across 20 items, including physical self-maintenance and instrumental activities, with total scores of 20-80 points (higher scores indicating greater impairment). The

Neuropsychiatric Inventory (NPI) assessed 12 neuropsychiatric symptoms including affective symptoms, psychotic symptoms, disinhibition, and hyperactivity. Dementia diagnosis followed PETERSEN' s criteria [18] combined with the "2018 Chinese Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Impairment"[19,20]: (1) Informant (family member or physician) reported cognitive impairment; (2) Objective cognitive impairment (MMSE: $ $17 points for illiterate group, $ $20 points for primary school group, $ $24 points for middle school and above group); (3) Abnormal daily living abilities (ADL>23 points for <75 years, ADL>25 points for $ $75 years); (4) Presence of neuropsychiatric symptoms that cannot be explained by delirium or other psychiatric disorders. Based on these criteria, participants were classified into non-dementia and dementia groups.

1.3 Quality Control Before the formal survey launch, a pilot study was conducted to ensure standardization of survey procedures and oral instructions for scale administration across all centers. All investigators had clinical medical backgrounds and received systematic training (including three rounds of centralized training and two assessments one week after training completion). During implementation, investigators first explained the study purpose and procedures in detail to each participant, obtained informed consent, then conducted one-on-one interviews, accurately recording responses and completing corresponding tests while patiently addressing participants' questions. Each center established a quality control team to daily review survey quality, checking for missing items and logical errors in scales; if problems were identified, telephone follow-up was conducted for verification and timely correction or supplementation. Dementia diagnoses were jointly determined by two neurologists based on scale scores and clinical presentations; disagreements were arbitrated by a third expert. Data were independently double-entered on the day of collection using EpiData 3.0 software by two personnel, with accuracy ensured through comparison.

1.4 Statistical Analysis Data analysis was performed using SPSS 26.0 and R 4.1.3 software. Categorical data were described using relative frequencies, with inter-group comparisons using ^{2} tests. Normally distributed continuous data were described as ($\bar{x}\pm s$), with independent samples t-tests for two-group comparisons. Covariates including residence location, sex, age, education level, marital status, BMI, smoking, alcohol consumption, and social activity frequency were included in multivariate Logistic regression analysis to explore the association between hypertension comorbidity count and hypertension with a single specific disease and dementia, with stratified analyses by age and sex. The same covariates were included in multivariate Logistic regression analysis to examine associations between hypertension with multiple specific diseases and dementia. Considering that sample size decreases with more comorbidities, we used a 5-fold sample size of independent variables to ensure adequate statistical power and model accuracy [21], including comorbidity combinations with >50 cases in the analysis. The significance level was set at α=0.05.

Results

2.1 Basic Characteristics, Chronic Disease Prevalence, and Dementia Prevalence of Study Population Among the 14,732 older adults included in this study, 7,108 (48.2%) were from rural areas, 8,161 (55.4%) were female, 4,593 (31.2%) were aged $ $75 years, 8,001 (54.3%) had $ $6 years of education, and 3,724 (25.3%) were without a spouse. The prevalence of chronic diseases was: hypertension 52.9% (7,786/14,732), diabetes 16.1% (2,376/14,732), heart disease 16.3% (2,407/14,732), cerebrovascular disease 16.7% (2,462/14,732), insomnia 37.7% (5,557/14,732), and autonomic dysfunction 42.5% (6,256/14,732). The prevalence of multimorbidity was 56.3% (8,293/14,732), with hypertension comorbidity prevalence at 41.4% (6,094/14,732). Among those with hypertension, 2,569 (17.4%) had 1 comorbidity, 2,064 (14.0%) had 2 comorbidities, 1,018 (6.9%) had 3 comorbidities, and 443 (3.0%) had $ $4 comorbidities (Table 1 ~2).

Dementia was present in 1,111 (7.5%) of the 14,732 older adults. Comparisons between dementia and non-dementia groups showed statistically significant differences in residence location, sex, age, education level, marital status, BMI, smoking status, social activity frequency, hypertension, heart disease, cerebrovascular disease, autonomic dysfunction, and multimorbidity status ($P<0.05$) (Table 1).

2.2 Multivariate Logistic Regression Analysis of Hypertension Comorbidity Count and Hypertension with a Single Specific Disease and Dementia Using dementia as the dependent variable, hypertension comorbidity count and hypertension with a single specific disease as independent variables, and residence location, sex, age, education level, marital status, BMI, smoking, alcohol consumption, and social activity frequency as covariates, multivariate Logistic regression analysis (variable assignments in Table 2) showed that compared with older adults without any of the six diseases, those with hypertension only had 1.516 times higher dementia risk ($P=0.042$). Among the five diseases (diabetes, heart disease, cerebrovascular disease, insomnia, and autonomic dysfunction), individuals with hypertension plus 1, 2, 3, and $ $4 comorbidities had dementia risk ratios of 1.879, 2.071, 2.338, and 2.591 times, respectively ($P<0.05$). Analysis of hypertension with a specific disease revealed that hypertension coexisting with diabetes, heart disease, cerebrovascular disease, and autonomic dysfunction was associated with dementia risks of 2.128, 2.248, 2.550, and 1.792 times higher than those without these baseline diseases ($P<0.05$) (Table 3).

2.3 Stratified Multivariate Logistic Regression Analysis by Sex and Age of Hypertension Comorbidity Count and Hypertension with a Single Specific Disease and Dementia Further stratified analysis by sex and age examined dementia risk associated with hypertension comorbidity count and hypertension with a single specific disease. Results showed that dementia risk increased significantly with the number of hypertension comor-

bidities (P<0.05). Compared with older adults without any of the six diseases, men with hypertension coexisting with cerebrovascular disease had increased dementia risk (OR=2.842, P=0.032); women with hypertension coexisting with cerebrovascular disease (OR=2.348, P=0.036) and autonomic dysfunction (OR=2.104, P=0.015) had increased dementia risk. In the <75 years group, hypertension coexisting with diabetes increased dementia risk (OR=2.833, P=0.041), while in the $ $75 years group, hypertension coexisting with heart disease (OR=2.571, P=0.022) and cerebrovascular disease (OR=2.707, P=0.020) increased dementia risk (Figure 2 [Figure 2: see original paper]).

2.4 Multivariate Logistic Regression Analysis of Hypertension with $ $2 Specific Diseases and Dementia Using dementia as the dependent variable, hypertension with $ $2 specific diseases as independent variables (22 combination groups, Table 4), and residence location, sex, age, education level, marital status, BMI, smoking, alcohol consumption, and social activity frequency as covariates, multivariate Logistic regression analysis (variable assignments in Table 2) showed that compared with community-dwelling older adults without any of the six specific diseases, those with hypertension coexisting with heart disease and cerebrovascular disease had the highest dementia prevalence (OR=3.559, P=0.011), followed by hypertension coexisting with diabetes and cerebrovascular disease (OR=3.159, P=0.026). Among those with hypertension and three comorbidities, the highest dementia prevalence was observed in individuals with coexisting heart disease, cerebrovascular disease, and autonomic dysfunction (OR=3.881, P=0.001), followed by hypertension coexisting with diabetes, cerebrovascular disease, and autonomic dysfunction (OR=3.024, P=0.041). Among those with hypertension and four comorbidities, the highest dementia prevalence was observed in individuals with coexisting heart disease, cerebrovascular disease, insomnia, and autonomic dysfunction (OR=2.850, P=0.002). When all six diseases coexisted, dementia risk increased significantly (OR=3.266, P=0.010) (Table 4).

Discussion

This study surveyed 65 years and older residents across multiple rural and urban communities in eight Chinese centers, finding that the self-reported prevalence of chronic diseases among older adults was: hypertension 52.9% (7,786/14,732), autonomic dysfunction 42.5% (6,256/14,732), insomnia 37.7% (5,557/14,732), cerebrovascular disease 16.7% (2,462/14,732), heart disease 16.3% (2,407/14,732), and diabetes 16.1% (2,376/14,732). The multimorbidity prevalence was 56.3% (8,293/14,732), with hypertension comorbidity prevalence at 41.4% (6,094/14,732). Dementia prevalence was 7.5% (1,111/14,732). These results are similar to other recent Chinese cohort studies. The CHARLS cohort survey of residents $ $60 years found hypertension prevalence of 46.46 $45 years) showed a prevalence of 41% [95%CI (35%-46%)] [23]. Chronic disease and multimorbidity are particularly prominent among hospitalized patients, with heart disease combined with hypertension ranking first [24]. Dementia

prevalence aligns with other cohort studies [25-27], with differences in chronic disease and dementia prevalence likely due to survey methods, participant age, and urban-rural composition.

Multiple lines of evidence indicate that hypertension is a risk factor for all-cause dementia. Meta-analyses by TULLY et al. [28] and DING et al. [29] found that controlling hypertension reduced the risk of Alzheimer' s disease and all-cause dementia compared with uncontrolled hypertension. The association between hypertension and dementia risk relates to age of onset, duration, and severity of hypertension, as well as blood pressure changes in late life. MCGRATH et al. [30] found in a 26-year follow-up study of 1,440 individuals that late-life blood pressure decline was associated with higher all-cause dementia risk compared with those with persistent hypertension or normalized blood pressure from midlife. Thus, the association between late-life hypertension and dementia is more complex and uncertain. This study found that compared with those without chronic diseases, older adults with hypertension only had 1.516 times higher dementia risk, with higher risk in women (1.778 times), though prevalence increased in men and different age groups without reaching statistical significance.

Currently, the association between chronic multimorbidity as a risk factor and dementia has been extensively studied, but results show considerable heterogeneity, with limited and complex interpretation. Cerebral small vessel disease (CSVD) is thought to cause 25% of vascular stroke events and 30% of lacunar events. While lesions may lack acute clinical progression, they can aggravate brain pathological damage and white matter changes over time, leading to approximately 45% of dementia cases, with age, chronic disease, infection, and genetics as risk factors [31]. Although pathogenic mechanisms are not fully understood, they are generally believed to involve chronic hypoperfusion, chronic brain inflammation, and altered oxidative stress responses, inducing endothelial activation and subsequent tissue remodeling [32]. ZHAO et al. [33] analyzed 14 longitudinal cohorts showing that cardiometabolic multimorbidity ($ $2 of hypertension, hyperlipidemia, diabetes, stroke, and heart disease) was associated with lower cognitive function and faster cognitive decline. AKUSHEVICH et al. [34] analyzed Health and Retirement Study (HRS) cohort data showing that chronic disease multimorbidity (hypertension, traumatic brain injury, cerebrovascular disease) and genetic factors (APOE4) had the strongest association with dementia risk, emphasizing that multimorbidity has predictive ability equivalent to genetic susceptibility. HAINSWORTH et al. [35] confirmed CSVD lesions through the Religious Orders Study and Rush Memory and Aging Project (ROSMAP) cohort of over 1,700 donated brains, finding CSVD closely related to age and hypertension, with neuropathological sequelae manifesting as diffuse white matter lesions, small ischemic foci, and subcortical microhemorrhages in over 50% of individuals $ $65 years.

This study found that among the five diseases of hypertension coexisting with diabetes, heart disease, cerebrovascular disease, insomnia, and autonomic dys-

function, the risk ratios for dementia were 1.879, 2.071, 2.338, and 2.591 times higher for those with 1, 2, 3, and $ $4 comorbidities, respectively (P<0.05). The comorbidities in this study all relate to vascular structure and function regulation, likely producing additive effects on hypertensive CSVD and thereby causing greater dementia risk. However, this study did not find increased dementia risk from hypertension coexisting with insomnia, possibly due to the bidirectional relationship between insomnia and dementia, with dementia patients less likely to report insomnia, as noted in other studies [36].

This study further found that comorbidities showed sex and age differences in dementia impact. Both men and women with hypertension coexisting with cerebrovascular disease had higher dementia risk, while women with hypertension coexisting with autonomic dysfunction also showed increased risk. In the <75 years group, hypertension coexisting with diabetes increased dementia risk, while in the $ $75 years group, hypertension coexisting with heart disease and cerebrovascular disease increased dementia risk. Current research on sex and age differences in the association between chronic diseases and dementia is limited, but related studies can partially explain these findings. The ROSMAP cohort study found that arteriolosclerosis was significantly associated with hypertension severity and age, and was more common in women [37]. LEVINE [38] found that increased dementia risk in older age was associated with midlife onset of comorbidities such as hypertension. CSVD-induced brain parenchymal changes are heterogeneous and depend on comorbidity severity (hypertension, diabetes, etc.), CSVD type, and location [39], with lesions in "critical" locations more likely to cause cognitive impairment [31]. Whether CSVD induces cognitive impairment also depends on individual brain resilience and reserve, with brain resilience related to pre-existing brain disease, cognitive reserve, age, and persistent inflammation triggered by comorbidity-induced immune responses. This study' s results reflect these complex relationships: among hypertension with 2 comorbidities, hypertension coexisting with heart disease and cerebrovascular disease showed higher dementia prevalence (OR=3.559); among hypertension with 3 comorbidities, hypertension coexisting with heart disease, cerebrovascular disease, and autonomic dysfunction showed higher dementia prevalence (OR=3.881). Other combinations had OR>1.000 but did not reach significance due to limited sample size.

This study' s innovation lies in adding insomnia and autonomic dysfunction—highly prevalent among older adults and causing small vessel dysregulation—to traditional cardiovascular chronic disease impacts on dementia. Autonomic dysfunction is often overlooked in multimorbidity research among older adults, primarily due to limited objective measurement methods, multiple complex mechanisms, and potential bidirectional causality with diseases, hindering clinical application. However, high prevalence of autonomic dysfunction has been found in all-cause dementia patients, making symptom identification beneficial for understanding its association with dementia and for patient treatment and care.

This study found that hypertension and its comorbidities significantly increase

dementia risk among Chinese community-dwelling older adults, with age and sex differences in these associations, but has several limitations: (1) As a cross-sectional study, it cannot establish causality between risk factors and dementia; (2) Self-reported variables may introduce bias; (3) Only six diseases were considered, ignoring potential effects of other conditions, which will be explored in follow-up data. With China' s aging process, the association between hypertension and related chronic diseases with dementia risk warrants attention. Addressing these risk factors represents an effective approach to dementia prevention and control. Given the close association between multimorbidity and dementia, regular health examinations and chronic disease screening are particularly important for older adults. Community health education facilitates access to correct medical knowledge and self-management, while standardized chronic disease treatment can reverse or delay disease progression, and promoting healthy lifestyles (diet, physical exercise, and intellectual leisure activities) benefits older adults' health.

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