ORIGINAL ARTICLE

Cognitive impairment and hypertension among Chinese nonagenarians and centenarians

Chang-Quan Huang^{1,2}, Bi-Rong Dong¹, Yan-Ling Zhang¹, Hong-Mei Wu¹, Qing-Xiu Liu² and Joseph H Flaherty³

In this study, we explore the association between hypertension and cognitive impairment in the very elderly, using a sample ranging in age from 90 to 108 years. This work was conducted as a cross-sectional study. Our population included 782 unrelated Chinese nonagenarians and centenarians (67.5% women, mean age 93.62 years). The mean cognitive function score for the sample was 14.95 (s.d.: 5.99 , range: 0 – 28). There were no significant differences between individuals with and without hypertension with regard to cognitive function scores (14.95 ± 6.01 vs. 14.95 ± 5.82 , $P=0.997$) or cognitive impairment prevalence (59.52 vs. 59.42 , $P=0.976$). There were also no significant differences in the prevalence of hypertension (56.99 vs. 57.10 , $P=0.976$) or in the levels of arterial blood pressure (including systolic blood pressure (SBP) and diastolic blood pressure (DBP)) (139.86 ± 22.69 vs. 140.28 ± 23.51 , $P=0.799$ and 73.05 ± 12.07 vs. 72.11 ± 12.06 , $P=0.678$, for SBP and DBP, respectively) between individuals with and without cognitive impairment. Multiple logistic regression showed that cognitive impairment and hypertension were not risk factors for each other (odds ratio (OR) of cognitive impairment as a function of increased hypertension: 0.938 (0.655 , 1.341); OR of hypertension as a function of increased cognitive impairment: 0.920 (0.643 , 1.317)). In summary, we found that cognitive impairment was not directly correlated with hypertension among Chinese nonagenarians and centenarians. *Hypertension Research* (2009) **32**, 554–558; doi:10.1038/hr.2009.72; published online 29 May 2009

Keywords: Chinese; cognitive impairment; hypertensive; nonagenarians and centenarians

INTRODUCTION

About 10% of people older than 65 years have cognitive impairment, ranging from mild deficits to dementia.¹ Hypertension has been viewed as a common risk factor for cognitive disorders.^{2–4} Many prospective and cross-sectional observational studies have shown that hypertension is associated with cognitive decline in older persons.^{5–14} Common to each of these studies, however, has been the relatively young age of the participants. The average age of these populations has been under 85 years; only a few studies have included individuals aged 90 years or above, and no studies have focused only on individuals aged 90 years or older. Cognitive impairment and hypertension are both major components of age-related deterioration.^{15,16} As the population of older persons increases, the number of cognitively impaired older individuals is expected to rise.^{17,18} To the best of our knowledge, no studies have explored whether cognitive impairment is associated with hypertension among very old people, that is, those aged 90 years and above. In this study, we sought to observe the association of cognitive impairment with hypertension among very old people using a cohort of Chinese men and women aged 90–108 years.

METHODS

Study participants

The methods of this study have been reported previously.¹⁹ In brief, as part of the Project of Longevity and Aging in Dujiangyan, a cross-sectional study of

age-related diseases was conducted in 870 long-living individuals (>90 years) on the basis of the Dujiangyan (located in Sichuan province, southwest China) 2005 census. The aims of the Project of Longevity and Aging in Dujiangyan were to investigate the relationship between environment, lifestyle, genetics, longevity and age-related diseases. Participants were examined by trained professional physicians using basic health criteria, and age-related diseases were recorded, including cancer, type 2 diabetes, hypertension, heart failure, chronic obstructive pulmonary disease, Alzheimer's and Parkinson's diseases and so on. In this analysis, long-living individuals with cancer, secondary hypertension, severe heart failure and terminal stage of chronic obstructive pulmonary disease were excluded. Our study population ultimately consisted of 782 long-living individuals. Informed consent was obtained from all participants (or their legal proxies). The Research Ethics Committee of the Sichuan University approved the study.

Data collection and measurements

Measurement of blood pressure. Right-arm blood pressure (BP) was measured with participants in the sitting or recumbent position by trained nurses or physicians. BP was taken twice, to the nearest 2 mm Hg, using a standard mercury sphygmomanometer (phases I and V of Korotkoff). The mean value of the two measurements was used to calculate systolic BP (SBP) and diastolic BP (DBP), and the SBP and DBP were calculated as the mean of the right- and left-arm values in exceptional cases (upper-extremity vascular disease). The mean of the two readings was used for the classification of BP according to the Joint National Committee VII criteria into normal (SBP < 120 mm Hg and DBP < 80 mm Hg), pre-hypertension (SBP 120–139 mm Hg and/or DBP

¹Department of Geriatrics, West China Hospital, Sichuan University, Sichuan province, China; ²Department of Geriatrics, The Third Hospital of Mianyang, Mianyang, Sichuan, China and ³Geriatric Research, Education and Clinical Center, St Louis Veteran's Affairs Medical Center, St Louis, MO, USA

Correspondence: Professor B-R Dong, Department of Geriatrics, West China Hospital, Sichuan University, Guoxuexiang 37, Chengdu, Sichuan province 610041, China.

E-mail: birong_d@yahoo.cn

Received 24 September 2008; revised 15 March 2009; accepted 23 March 2009; published online 29 May 2009

80–89 mm Hg), stage 1 hypertension (SBP 140–159 mm Hg and/or DBP 90–99 mm Hg) or stage 2 hypertension (SBP > 160 mm Hg and/or DBP > 100 mm Hg). Isolated systolic hypertension was defined as SBP > 140 mm Hg and DBP < 90 mm Hg, and isolated diastolic hypertension was defined as SBP < 140 mm Hg and DBP > 90 mm Hg. Hypertension was defined as SBP > 140 mm Hg and/or DBP > 90 mm Hg and/or receiving antihypertensive treatment. Participants with confirmed hypertension and no identified cause of secondary hypertension were diagnosed with essential hypertension.

Assessment of cognitive function. Cognitive function was measured using the 30-item Mini-Mental State Examination (MMSE), which is a global test with components of orientation, attention, calculation, language and recall. Cognitive impairment was defined as a score below 24 in the MMSE. This score has been shown to be 80–90% sensitive and 80–100% specific for a diagnosis of dementia.^{20,21} To decrease methodological errors and assure methodological reliability, the administrator reviewed the MMSE procedure and grading system outlined in a short booklet and video, observed a geriatrician conducting the MMSE on residents not part of the study and was supervised when conducting the MMSE on residents not part of the study. The MMSE was administered on individuals who gave consent for study participation. The individuals were categorized as follows: cognitive impairment (scores between 0 and 18), mild cognitive impairment (scores between 19 and 24) and normal (scores between 25 and 30). A diagnosis of vascular dementia was considered for individuals with dementia combined with a history or clinical evidence of stroke, and a diagnosis of non-vascular dementia was considered for individuals with dementia without a history or clinical evidence of stroke.

Assessment of covariates. Trained study personnel conducted face-to-face interviews, including standardized inquiries for self-reported medical history, medication and anthropometric measurements, as well as a standardized physical examination and a 12-lead electrocardiogram. On the basis of the prepared questionnaire for the medical record, we obtained information on age (years), gender (female/male), educational levels (illiteracy, primary school, secondary school, college or post-graduate), sleep time per day, satisfaction of sleep (very satisfied, generally satisfied or not satisfied), sleep at noon (every day, usually, occasionally or never), religion (yes or no), temperament (introversion, general or extroversion), smoking habits, alcohol consumption, tea consumption, exercise and activities of daily living (ADL). Body mass index (kg m^{-2}) was calculated as body weight (kilograms) divided by height (meters squared). Habits of smoking, alcohol consumption, tea consumption and exercise (including former and current) were collected using a general questionnaire in which every item had two options (yes or no). ADL was measured using the MDS-ADL scale, which is composed of seven ADL items (scores ranging from 0 to 7).²² Other variables were collected using a general questionnaire.

Statistical analysis

All statistical analyses for this study were performed with the SPSS for Windows software package, version 11.5 (SPSS Inc., Chicago, IL, USA). In the oldest-old sample, that is, the centenarians, the prevalence rate of cognitive impairment was 86.6% (including mild cognitive impairment (27.1%) and dementia (59.5%)); therefore, we combined mild cognitive impairment and normal cognitive function in this analysis. We compared baseline characteristics between those with and without prevalent cognitive impairment and hypertension using the χ^2 or Fisher's exact test (in which an expected cell count was < 5) for categorical variables and unpaired Student's *t*-test for continuous variables. We used analysis of variance to test for differences in cognitive function scores among the four arterial BP groups. Multiple logistic regressions were used to estimate odds ratios (ORs) and 95% confidence intervals for hypertension as a function of increased cognitive impairment and for cognitive impairment as a function of increased hypertension. To assess the association between hypertension and cognitive impairment beyond that explained by demographic and clinical covariates, we calculated multivariate-adjusted ORs for each hypertension and cognitive impairment index. Two-sided *P*-values were considered to be statistically significant at < 0.05.

RESULTS

Baseline characteristics and prevalence of cognitive impairment and hypertension

Among the 782 participants, mean age was 93.62 years, 76 were centenarians and 527 were women. Ninety percent of participants lived in the countryside. The mean cognitive function score for the population was 14.95 (s.d.: 5.99, range: 0–28). Only 105 volunteers had scores higher than 24, so we defined cognitive impairment as a score lower than 19. In the oldest-old sample, the prevalence of cognitive impairment was 59.5%. Of the participants with cognitive impairment, 14 had vascular dementia (3.01%). The prevalence rate of hypertension was 57.1%, including stage 1 (32.9%) and stage 2 (24.2%) hypertension. Of those with hypertension, 43.9% had isolated systolic hypertension and 1.9% had isolated diastolic hypertension, and only 35 (7.88%) were receiving antihypertensive medication. There were 229 participants (43.0%) who were classified as pre-hypertensive.

Participants with hypertension had a higher body mass index than those without hypertension (mean difference: 0.77, $P=0.004$), but did not differ significantly on other covariates, including age, gender, educational levels, ADL problems, temperament, or sleeping, smoking, alcoholic, tea, exercise or religious habits (Table 1). The prevalence of cognitive impairment in women was higher than that in men ($P<0.001$). Participants with and without cognitive impairment also showed significant differences in sleeping habits, temperament and educational levels (Table 1).

Comparison of cognitive impairment prevalence and cognitive function scores between participants with and without hypertension

There were no significant differences between participants with and without hypertension with regard to cognitive function scores (14.95 ± 6.01 vs. 14.95 ± 5.82 , $P=0.997$) or with regard to the prevalence of cognitive impairment (59.42 vs. 59.52 , $P=0.976$). Cognitive function scores are shown by BP classifications (Figure 1), and analysis of variance was used to test for differences in cognitive function scores among arterial BP groups ($F=0$, $P=0.997$).

Comparison of hypertension prevalence between participants with and without cognitive impairment

There were no significant differences between participants with and without cognitive impairment with regard to the prevalence of hypertension (56.99 vs. 57.10 , $P=0.976$) or levels of arterial BP (including SBP and DBP) (139.86 ± 22.69 vs. 140.28 ± 23.51 , $P=0.799$; 73.05 ± 12.07 vs. 72.11 ± 12.06 , $P=0.678$; for SBP and DBP, respectively) (Figure 2). Moreover, there were no significant differences in the prevalence of hypertension between participants with and without vascular dementia or between participants with and without non-vascular dementia (Table 1). We further compared levels of arterial BP between participants with vascular and non-vascular dementia (140.04 ± 27.32 vs. 139.78 ± 43.51 , $P=0.846$; 73.11 ± 10.13 vs. 71.68 ± 9.19 , $P=0.479$; for SBP and DBP, respectively).

Multivariate-adjusted associations between cognitive impairment and hypertension

We further assessed whether cognitive impairment was associated with increased risk of hypertension and vice versa (Table 2). After adjustment for age, gender, ADL problems, temperament, educational levels, and sleeping, smoking, alcoholic, tea, exercise and religious habits, the OR of cognitive impairment as a function of increased hypertension was 0.938 (0.655, 1.341) and the OR of hypertension as a function of increased cognitive impairment was 0.920 (0.643, 1.317) (Table 2).

Table 1 Baseline characteristics according to arterial blood pressure and cognitive function (*n*=782)

Characteristics	Hypertension (<i>n</i> =446)	Normotension (<i>n</i> =336)	P-value	Cognitive impairment (<i>n</i> =465)	Non-cognitive impairment (<i>n</i> =317)	P-value
Age (years)	93.60 ± 3.41	93.69 ± 3.38	0.852	93.85 ± 3.48	94.28 ± 3.25	0.020
Gender (female/male)	307/139	221/115	0.350	360/105	168/149	<0.001
BMI (kg m ⁻²)	19.41 ± 3.72	18.64 ± 3.29	0.004	19.15 ± 3.43	18.98 ± 3.74	0.505
Systolic BP (mm Hg)	154.86 ± 17.40	120.34 ± 12.27	<0.001	139.86 ± 22.69	140.28 ± 23.51	0.799
Diastolic BP (mm Hg)	77.02 ± 12.11	66.89 ± 9.35	<0.001	73.05 ± 12.07	72.11 ± 12.06	0.678
Hypertension (%)	—	—	—	56.99	57.10	0.976
With antihypertensive medication	7.88	—	—	4.52	4.41	0.947
Without antihypertensive medication	92.12	—	—	95.48	95.59	0.982
Cognitive function score	14.95 ± 6.01	14.95 ± 5.82	0.997	11.63 ± 4.38	21.03 ± 2.49	<0.001
<i>Cognitive impairment (%)</i>	59.42	59.52	0.976	—	—	—
Vascular dementia (%)	3.13	1.78	0.312	3.01	—	—
Non-vascular dementia (%)	57.62	57.74	0.961	96.99	—	—
Sleep time per day	10.38 ± 1.49	10.27 ± 1.64	0.301	10.38 ± 1.63	10.27 ± 1.59	0.206
<i>Satisfaction of sleep</i>						
High satisfaction	261	191		255	197	
General satisfaction	75	60		81	54	
No satisfaction	94	72	0.808	118	48	0.009
<i>Sleep at noon</i>						
Everyday	135	84		133	86	
Usually	66	53		74	45	
Occasionally	45	47		57	35	
Never	190	146	0.210	194	142	0.769
<i>Smoking habits</i>						
Former (%)	56.52	64.42	0.066	59.52	60.46	0.698
Current (%)	42.44	44.48	0.570	43.41	43.17	0.948
<i>Alcoholic habits</i>						
Former (%)	42.92	40.43	0.488	39.65	45.13	0.132
Current (%)	28.73	24.55	0.193	26.03	28.25	0.493
<i>Tea habits</i>						
Former (%)	44.01	46.60	0.477	38.73	54.82	<0.001
Current (%)	40.54	44.61	0.255	40.10	51.91	<0.001
<i>Exercise habits</i>						
Former (%)	32.71	32.18	0.882	31.94	33.33	0.690
Current (%)	41.04	37.31	0.295	37.61	42.21	0.201
<i>Educational levels</i>						
Illiteracy	329	239		397	171	
Primary school	73	58		48	83	
Secondary school	25	31		16	40	
College and post-graduate	16	6	0.191	4	18	<0.001
Religion (%)	22.52	24.17	0.601	25.92	19.23	0.066
<i>Temperament</i>						
Introversion	52	38		62	28	
General	303	222		318	201	
Extroversion	73	58	0.821	67	64	0.032
ADL problems	1.41 ± 1.19	1.07 ± 2.23	0.477	1.34 ± 1.89	1.15 ± 2.21	0.639

Abbreviations: ADL, activities of daily living; BMI, body mass index; BP, blood pressure.

Baseline characteristics were compared between those with and without prevalent hypertension or between those with and without prevalent depression using χ^2 or Fisher's exact test (where an expected cell count was <5) for categorical variables and unpaired Student's *t*-test for continuous variables. In the testing, a *P*-value <0.05 was considered to be statistically significant.

DISCUSSION

In this cross-sectional sample of community-dwelling Chinese nonagenarians and centenarians, we observed a high prevalence of both cognitive impairment (59.5%) and hypertension (57.1%). There were no significant differences in either cognitive function scores or in the prevalence of cognitive impairment between participants with and without hypertension, nor were there significant differences in either levels of arterial BP or in the prevalence of hypertension between

participants with and without cognitive impairment. Furthermore, cognitive impairment and hypertension were not risk factors for each other.

To the best of our knowledge, this was the first research that focused on the association between cognitive impairment and hypertension in nonagenarians and centenarians. This study provides useful new information in that cognitive impairment and hypertension are independent of each other among nonagenarians and centenarians. It is generally thought that hypertension and cognitive impairment are significantly and highly correlated in both younger adults and the elderly.^{23–25} Many earlier studies have inferred causality between hypertension and cognitive impairment in old age. Some studies have found that hypertension is a risk factor for the development of cognitive decline; on the other hand, others report that hypertension in old age is a concomitant phenomenon of already-existing cognitive impairment, rather than an independent risk factor.^{23–25} Our findings in this very elderly population are not consistent with studies based on people aged 65 years or older. However, participants in these earlier studies were younger and had better cognitive function and lower prevalence of hypertension than the participants in this study. Cognitive impairment and hypertension are both components of age-related deterioration. Imhof *et al.*²⁶ reported that, in nonagenarians and centenarians, brain aging is characterized by the formation of neurofibrillary tangles and senile plaques, which are generally viewed as pathological changes in patients with Alzheimer's disease and dementia. This study showed that individuals with cognitive impairment were older than those without cognitive impairment; therefore, age-related deterioration was the main reason for the higher prevalence of cognitive impairment among the very elderly.²⁶ Therefore, it is a reasonable inference that the differences between individuals with regard to cognitive function, in this study and in earlier studies, were mainly because of the different age structures of the studied groups. Further, within the nonagenarian and centenarian populations, cognitive impairment from age-related deterioration may attenuate the contribution of general risk factors for cognitive impairment, such as hypertension. On the other hand, it has been confirmed that hypertension in the elderly differs from that in younger individuals in terms of etiology, presentation, treatment and outcome. This study shows that hypertension in the oldest-old population may exhibit a different association with cognitive impairment than the association seen in the general population. Hypertension in this population was also mainly a function of age-related deterioration. Therefore, although our results did not show an association between cognitive impairment and hypertension among nonagenarians/centenarians, this is not necessarily contradictory with earlier studies; in fact, this study extends the findings of earlier studies.

This study not only provided evidence that women were more likely than men to exhibit cognitive impairment, but our findings also support those of earlier studies showing a higher risk of cognitive

Figure 1 The analysis of variance was used to test for differences owing to depression scores among the different arterial BP groups ($F=0.000$, $P=0.997$).

Figure 2 Unpaired Student's *t*-test was used to test for differences owing to arterial BP between participants with and without cognitive impairment. (139.86 ± 22.69 vs. 140.28 ± 23.51 , $P=0.799$ and 73.05 ± 12.07 vs. 72.11 ± 12.06 , $P=0.678$, for SBP and DBP, respectively.)

Table 2 Multiple logistic regression was used to estimate the OR and 95% CI of cognitive impairment as a function of increased hypertension or hypertension as a function of increased cognitive impairment

	Depression		Hypertension	
	Hypertension	Normotension	Cognitive impairment	Non-cognitive impairment
Unadjusted OR (CI)	0.996 (0.746, 1.328)	1.00 (reference)	0.996 (0.746, 1.328)	1.00 (reference)
Multiple adjusted OR (CI)	0.920 (0.643, 1.317)	1.00 (reference)	0.938 (0.655, 1.341)	1.00 (reference)

Abbreviations: ADL, activities of daily living; CI, confidence interval; OR, odds ratio.

Adjusted for age, gender, sleep habits, smoking habits, alcoholic habits, tea habits, exercise habits, educational levels, religion habits, ADL problems and temperament.

impairment among the very elderly. Furthermore, tea-drinking habits (former and current), satisfaction of sleep, educational level and temperament were all associated with cognitive impairment among the very elderly. This finding has implications for the prevention of cognitive impairment in the elderly; such prevention strategies may include advocating for tea use and extroverted behavior, and improving satisfaction of sleep.

Our study also has several limitations that deserve mention. First, there was a gender imbalance in our population, a common characteristic of very old populations. Of the 870 long-living individuals (≥ 90 years) in the Dujiangyan district (2005), 527 women and 255 men were included in this study. Second, we assessed cognitive function using MMSE scores, although the Diagnostic and Statistical Manual of Mental Disorders-IV is considered to be the gold standard for the diagnosis of dementia. When this cross-sectional study was conducted in 2005, assessments using the Diagnostic and Statistical Manual of Mental Disorders-IV had not been carried out; therefore, this criterion was not available for use. However, compared with the Diagnostic and Statistical Manual of Mental Disorders-IV, diagnosis of dementia by MMSE has been shown to be 80–90% sensitive and 80–100% specific. Therefore, the diagnosis of cognitive impairment in this study was also considered to be reliable. Third, the participants in this study with both dementia and a history or clinical evidence of stroke were classified as having vascular dementia. Therefore, even individuals for whom dementia was independent of stroke may have been given a diagnosis of vascular dementia. As the prevalence of supreme cognitive impairment was high, and we did not identify the onset of cognitive impairment, we were unable to confirm the temporal relationship between stroke and dementia. As stroke is a definite risk factor for cognitive impairment, it was reasonable to assume that stroke was a cause of dementia in individuals with dementia and a history or clinical evidence of stroke. Fourth, although there may be differences in BP measurements between the sitting and recumbent positions, we did not differentiate the two. In general, the BP measurements in the sitting and recumbent positions were different, especially in the older- and oldest-aged population. Therefore, body position may be a potential confounder in BP measurements. BP in the recumbent position may be higher than that in the sitting position, and individuals with dementia were more likely to be measured in the recumbent position. Therefore, body position may increase the association of cognitive impairment with hypertension, but may not remove it. Finally, we were unable to adjust for other potential confounders, such as socioeconomic status and family history of cognitive impairment. Most (90%) participants lived in the countryside in this study, and some had been working on a farm everyday, making physical activity a potential confounder. Therefore, this population might not be representative of the urban aged population.

In conclusion, we found no significant correlation between cognitive impairment and hypertension among nonagenarians and centenarians.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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