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Original Study

A U-shaped Association Between Blood Pressure and Cognitive Impairment in Chinese Elderly

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A B S T R A C T

Objectives: Higher or lower blood pressure may relate to cognitive impairment, whereas the relationship between blood pressure and cognitive impairment among the elderly is not well-studied. The study objective was to determine whether blood pressure is associated with cognitive impairment in the elderly, and, if so, to accurately describe the association.
Design: Cross-sectional data from the sixth wave of the Chinese Longitudinal Healthy Longevity Survey (CLHLS) conducted in 2011.
Setting: Community-based setting in longevity areas in China.
Participants: A total of 7144 Chinese elderly aged 65 years and older were included in the sample.
Measures: Systolic blood pressures (SBP) and diastolic blood pressures (DBP) were measured, pulse pressure (PP) was calculated as (SBP) − (DBP) and mean arterial pressures (MAP) was calculated as 1/3(SBP) + 2/3(DBP). Cognitive function was assessed via a validated Mini-Mental State Examination (MMSE).
Results: Based on the results of generalized additive models (GAMs), U-shaped associations were identified between cognitive impairment and SBP, DBP, PP, and MAP. The cutpoints at which risk for cognitive impairment (MMSE <24) was minimized were determined by quadratic models as 141 mm Hg, 85 mm Hg, 62 mm Hg, and 103 mm Hg, respectively. In the logistic models, U-shaped associations remained for SBP, DBP, and MAP but not PP. Below the identified cutpoints, each 1-mm Hg decrease in blood pressure corresponded to 0.7%, 1.1%, and 1.1% greater risk in the risk of cognitive impairment, respectively. Above the cutpoints, each 1-mm Hg increase in blood pressure corresponded to 1.2%, 1.8%, and 2.1% greater risk of cognitive impairment for SBP, DBP, and MAP, respectively.
Conclusion: A U-shaped association between blood pressure and cognitive function in an elderly Chinese population was found. Recognition of these instances is important in identifying the high-risk population

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for cognitive impairment and to individualize blood pressure management for cognitive impairment prevention.

Hypertension and hypotension are important risk factors for vascular diseases, which may lead to cognitive impairment due to stroke or chronic cerebral hypoperfusion in the elderly.[1] This suggests that hypertension and hypotension may both be associated with cognitive impairment, a common neurological disorder in the elderly.

In recent years, the link between blood pressure, including systolic blood pressures (SBP) and diastolic blood pressures (DBP), to cognitive function has attracted much attention, but the role of blood pressure in cognitive impairment is still unclear.[2–14] Several studies reported a linear association between elevated blood pressure and increased risk of cognitive impairment or dementia,[2,3] and low blood pressure was related to higher risk of dementia in the elderly.[4,5] Additionally, antihypertensive medicines have a valuable role in the prevention of dementia or cognitive impairment,[6,7] whereas some studies failed to confirm this association.[8,9]

One proposed explanation for inconsistencies among these studies is that the relationship between blood pressure and cognitive function is nonlinear. Several investigators have demonstrated a U-shaped relationship[10–14] or a J-shaped association between cognitive function and blood pressure.[4] Most related research uses a linear model including multivariate regression model,[12,15] hierarchical linear model,[14,16] or mixed-effects regression analyses[11] to examine the possible relations. Few studies use splines to determine presence and type of the curvilinear relationships.[17] None of the curvilinear associations were demonstrated using generalized additive models (GAMs) and quadratic models, whose strengths include the ability to determine the natural shape of the relationship, sensitivity to detect nonlinear relationships and identifying the optimal cutpoints between dependent and predictor variable(s).

Combined measures, such as pulse pressure (PP) or mean arterial pressure (MAP), may be a salient blood pressure index in the elderly,[18] as SBP continuously increases and DBP continuously decreases after age 60.[19] Notably, PP and cognitive function have not been extensively studied, with positive associations with cognitive impairment being reported in some[20–23] but not all[24] studies. Some studies suggest that MAP may be a more accurate predictor than other blood pressure indices.[25,26]

It is important to clarify whether blood pressure is associated with cognitive impairment in the elderly, and, if so, to accurately describe the association. In the present study, we investigated the relationship between blood pressure (as measured by SBP, DBP, PP, and MAP) and cognitive impairment among Chinese elderly, and the possibility of a linear or curvilinear relationship using GAMs and quadratic models.

Methods

Study Population

A sample of 7144 elderly aged 65 years and older was included in the sixth wave of the Chinese Longitudinal Healthy Longevity Survey (CLHLS) conducted in 2011. The details of the CLHLS and sample design have been described elsewhere.[27,28] Informed consent was obtained from all participants and/or their relatives, and the study was approved by the Ethics Committee of Peking University.

Assessment of Cognitive Function

Cognitive function was assessed by the Mini-Mental State Examination (MMSE),[29] which has been widely applied in epidemiological studies. Five domains of cognitive function were included, namely orientation, registration, attention, memory, language. and visual construction skills.[30] The scores ranged from 0 to 30 points, and cognitive impairment was identified if the MMSE score was less than 24.[31]

Assessment of Blood Pressure

After having rested for 5 minutes under supervision of trained research assistants, arterial blood pressure was measured with a mercury sphygmomanometer on the right arm at heart level of the seated subject. In our analysis, the mean value of 2 blood pressure measurements was calculated and used for further analyses. PP was calculated as (SBP) − (DBP) and MAP was calculated as 1/3(SBP) + 2/3(DBP). Hypertension was defined as SBP ≥140 mm Hg and/or DBP ≥90 mm Hg.

Assessment of Covariates

Covariates were collected by a structured questionnaire; one part is sociodemographic characteristics, including age, sex, educational background, and residence; the other part is health characteristics, including physical activity, measured waist circumference, and self-reported diabetes mellitus, cardiovascular diseases, and stroke and other cerebrovascular diseases. Age and education were 2 of the most important confounders in the analysis of association between cognitive impairment and blood pressure, and were modeled as continuous variables in years. Residence was categorized as urban or rural. Physical activity was classified into "yes" or "no" by the question "Do you often participate in physical activities, including walking, playing ball, running, and Qigong?" Nonstretchable tape was used to measure waist circumference at a level between the lowest rib and iliac crest. Central obesity was identified if the participant's waist circumference was ≥85 cm in men or ≥80 cm in women.

Statistical Analyses

GAMs were performed to explore the linear or curvilinear association between SBP, DBP, PP, MAP and odds of having cognitive impairment. GAMs establish a relationship between the mean of a dependent variable and a smoothed (nonparametric) function of the predictor variable(s) via a link function. As GAM analysis suggested U-shaped associations between SBP, DBP, PP, MAP and risk of cognitive impairment on the basis of smoothed curve (Figure 1), quadratic regression was performed predicting risk of cognitive impairment: $\Pr(\text{Cognitive impairment} \mid \text{Blood pressure}) = \{1 + \exp[-(\alpha + \beta_1(\text{Blood pressure}) + \beta_2(\text{Blood pressure}^2))]\}^{-1}$, with model parameters α, β_1, and β_2 estimated using maximum likelihood methods. If β_1 and β_2 are both nonzero and statistically significant, then the estimated level of blood pressure at which risk of cognitive impairment is minimized is $-(\beta_1/2\beta_2)$. These values are used as cutpoints of blood pressure for further analysis. For SBP,

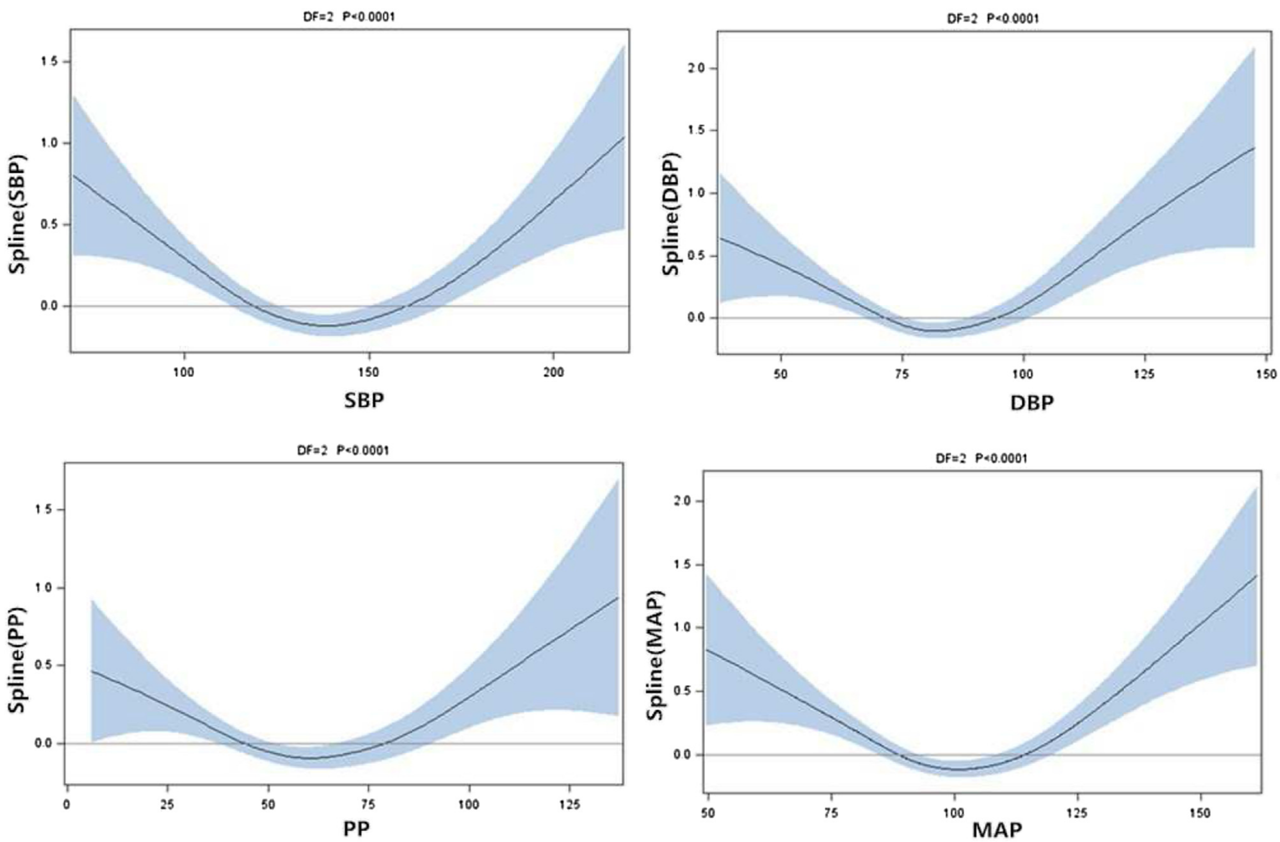

Fig. 1. Smoothing component for cognitive impairment. Associations of SBP, DBP, PP, and MAP with cognitive impairment for the elderly, Chinese Longitudinal Healthy Longevity Survey, China, 2011. The lines depict the estimated function of SBP, DBP, PP, and MAP, respectively, for risk of cognitive impairment among the elderly, and the shaded area indicates the 95% CIs.

DBP, PP, and MAP, the β_1 were estimated as −0.07908, −0.10114, −0.03585, and −0.13279, respectively, and the β_2 were estimated as 0.00028, 0.00059, 0.00029, and 0.00064, respectively; all *P* values were less than 0.01. The blood pressure values associated with lowest risk were identified as 141 mm Hg, 85 mm Hg, 62 mm Hg, and 103 mm Hg for SBP, DBP, PP, and MAP, respectively. For each blood pressure measure, individuals were divided into 4 groups, first based on whether they were above or below the cutpoint for that measure, and within these 2 groups whether they were above or below the mean value of that measure. Thus, individuals were first stratified into 2 groups by cutpoints of each blood pressure index (values noted previously); individuals in the low group were then divided into 2 subgroups (denoted low and medium-low) using medians of each index (127 mm Hg, 77 mm Hg, 49 mm Hg, and 93 mm Hg for SBP, DBP, PP, and MAP, respectively) and subjects in the high group were divided into 2 subgroups (denoted high and medium-high) using the medians of each index (155 mm Hg, 90 mm Hg, 73 mm Hg, and 110 mm Hg for SBP, DBP, PP, and MAP, respectively).

Then logistic regression models were performed to assess the risk of cognitive impairment with SBP, DBP, PP, and MAP as continuous or binary predictor variables below and above the cutpoints. In a basic model, we adjusted for demographic variables, including age, gender, years of education, and residence, and further adjusted for physical activity, central obesity, diabetes mellitus, cardiovascular diseases, stroke, and cerebrovascular diseases in the final model. Odds ratios (ORs) with 95% confidence intervals (CIs) in logistic regression models were presented. SAS 9.2 (SAS Institute Inc., Cary, NC) was used for all analyses.

Results

Description of Population

The age of 7144 participants ranged from 65 to 115 years, with an average of 87 years; 55% of participants were women. The mean SBP, DBP, PP, and MAP were 135.5, 80.1, 55.4, and 98.6 mm Hg, respectively; 42.3% of participants had hypertension (Table 1). The average MMSE score was 21.1, and prevalence of cognitive impairment was 38.5% (27.8% for men and 47.3% for women). The participants who were men, living in urban areas, participating in physical activity, and with cardiovascular diseases were less likely to be cognitively impaired. The participants with type 2 diabetes or stroke and cerebrovascular diseases were more likely to be cognitively impaired (Table 1). The prevalence of hypertension or blood pressure measures was not significantly different in those with and without cognitive impairment.

Associations Between Blood Pressure and Cognitive Impairment

The results of GAMs and quadratic models suggested a U-shaped association between SBP, DBP, PP, and MAP and cognitive impairment. Logistic models were consistent with the U-shaped associations between cognitive impairment and SBP, DBP, and MAP; however, such an association was not apparent for PP, regardless of considering PP as a continuous or categorical variable.

SBP and Cognitive Impairment

Among the participants whose SBP levels were below the cutpoint (141 mm Hg), there was a trend toward significantly decreasing

Table 1
Characteristics of 7144 Chinese Elderly by Cognitive Status, 2011

Factors*	Normal Cognition n = 4393	Cognitive Impairment n = 2751	Total n = 144	*P*
MMSE	26.8 (2.3)	9.2 (6.7)	21.1 (10.9)	<.0001
Age, y	83.3 (9.7)	93.2 (9.7)	87.1 (10.9)	<.0001
Gender				
Male	2335 (46.9)	900 (32.7)	3235 (45.3)	<.0001
Female	2058 (53.1)	1851 (67.3)	3909 (54.7)	
Residence				
Urban	2226 (59.8)	1464 (53.2)	4430 (57.2)	<.0001
Rural	1787 (40.2)	1287 (46.8)	3054 (42.8)	
Education, y	3.2 (3.0)	1.1 (2.5)	2.4 (3.6)	<.0001
Physically active	2100 (48.0)	671 (24.5)	2771 (39.0)	<.0001
Good visual function	3749 (85.3)	1577 (57.3)	5326 (74.6)	<.0001
Central obesity	2198 (50.0)	1102 (40.1)	3300 (46.2)	<.0001
Diabetes mellitus	248 (5.9)	92 (3.7)	340 (5.1)	<.0001
Cardiovascular diseases	653 (15.5)	324 (12.8)	977 (14.5)	.0024
Stroke and cerebrovascular diseases	332 (7.9)	265 (10.4)	597 (8.8)	.0004
SBP, mm Hg	135.7 (19.4)	135.2 (22.0)	135.5 (20.4)	.3055
DBP, mm Hg	80.3 (11.2)	79.8 (12.9)	80.1 (11.9)	.1302
PP, mm Hg	55.4 (15.9)	55.4 (17.5)	55.4 (16.6)	.8600
MAP, mm Hg	98.8 (12.3)	98.3 (14.3)	98.6 (13.1)	.1494
Hypertension	1859 (42.3)	1162 (42.2)	3021 (42.3)	.9481

*Dichotomous variables listed as n (%), including gender, current smoking practice, alcohol drinking habits, central obesity, diabetes, cardiovascular diseases, stroke and cerebrovascular diseases, and hypertension, were compared between 2 cognitive status groups using χ^2 tests; continuous variables listed as mean (SD), including age, education, SBP, DBP, PP, MAP, were comparted between 2 groups using Student *t* tests or Cochran-Cox tests.

risk of cognitive impairment with increasing levels of SBP; each 1 mm Hg lower SBP corresponded to a 1.4% higher risk of cognitive impairment before adjustment (OR 1.014; 95% CI 1.009–1.019). The risk attenuation remained significant after adjusting for covariates in the basic and final models, which decreased to 0.8% (OR 1.008; 95% CI 1.003–1.014) and 0.7% (OR 1.007; 95% CI 1.002–1.013), respectively (Table 2). Participants whose SBP levels were below the cutpoint were stratified into 2 equal-sized groups, the univariate analysis showed that the low SBP group had higher risk of cognitive impairment compared with the medium-low SBP group (OR 1.25; 95% CI 1.12–1.41). The multivariate OR (95% CI) reported in the basic model was 1.15 (1.00–1.32) and in the final model was 1.18 (1.02–1.35) (Table 3).

In contrast with findings below the cutpoints, the risk of cognitive impairment was greater with each higher unit of SBP among the participants whose SBP levels were above the cutpoints. Each 1 mm Hg higher SBP corresponded to a 1.2% greater risk of cognitive impairment in the univariate and multivariate models (Table 2). Compared with the medium-high SBP group, participants with high SBP level had a 23% higher risk of cognitive impairment in the final model (OR 1.23; 95% CI 1.02–1.49) (Table 3).

DBP and Cognitive Impairment

Similar to the relationship seen for SBP, for DBP below the cutpoints of 85 mm Hg the increased risk of cognitive impairment was also found with lower DBP, there was a 1.1% greater risk of cognitive impairment with each 1 mm Hg lower DBP after full adjustment (OR 1.011; 95% CI 1.003–1.020). Compared with the medium-low DBP group, participants with low DBP levels had a 33% higher risk of cognitive impairment before adjustment (OR 1.33; 95% CI 1.19–1.49), and the association remained after the adjustment.

Above the cutpoint of 85 mm Hg, when DBP was taken as a continuous variable, there was a 1.8% greater risk of cognitive impairment with each 1 mm Hg increment of DBP before adjustment and full adjustment (Table 2). When higher DBP was stratified into 2 equal groups, participants with high DBP levels had a 24% higher risk of cognitive impairment compared with the medium-high DBP group in the final model (OR 1.24; 95% CI 1.02–1.52).

PP and Cognitive Impairment

Although we found a U-shaped association between cognitive impairment and PP in the GAMs models (Figure 1), quadratic models, and as a continuous variable in the univariate logistic model, it was nonsignificant based on multivariate logistic regression (Tables 2 and 3).

MAP and Cognitive Impairment

As shown in GAMs and in quadratic models, the U-shaped association was confirmed in the logistic regression model; that is, each 1 mm Hg lower MAP corresponded to a 1.1% greater risk in cognitive impairment below the cutpoints of 103 mm Hg, and each 1 mm Hg higher MAP corresponded to a 2.1% greater risk in cognitive impairment above the cutpoints of 103 mm Hg (Table 2). Poorer cognitive performance was found in those with low MAP level compared with those with medium-low MAP level, and in those with high MAP level compared with those with medium-high MAP level (Table 3)

Discussion

U-shaped Association Between Blood Pressure and Cognitive Impairment

In this cross-sectional study of 7144 Chinese elderly aged 65 years and older, we observed U-shaped associations between blood pressure (SBP, DBP, and MAP) and cognitive impairment, with extremes of

Table 2
Logistic OR (95% CIs) for Cognitive Impairment and Continuous Measures of Blood Pressure Among Chinese Elderly

Variables	Unadjusted	Basic Model*	Final model†
Each 1 mm Hg lower in participants with SBP <141 mm Hg (n = 4733)	1.014 (1.009–1.019)‡	1.008 (1.003–1.014)‡	1.007 (1.002–1.013‡
Each 1 mm Hg higher in participants with SBP ≥141 mm Hg (n = 2411)	1.012 (1.006–1.017)‡	1.010 (1.004–1.017)‡	1.012 (1.005–1.019)‡
Each 1 mm Hg lower in participants with DBP <85 mm Hg (n = 5180)	1.023 (1.015–1.030)‡	1.011 (1.003–1.019)‡	1.011 (1.003–1.020)§
Each 1 mm Hg higher in participants with DBP ≥85 mmHg (n = 1964)	1.018 (1.007–1.028)‡	1.021 (1.009–1.033)‡	1.018 (1.006–1.030)‡
Each 1 mm Hg lower in participants with PP <62 mm Hg (n = 5111)	1.013 (1.007–1.20)‡	1.008 (1.001–1.015)§	1.008 (1.000–1.015)§
Each 1 mm Hg higher in participants with PP ≥62 mm Hg (n = 2033)	1.009 (1.002–1.017)§	1.002 (0.994–1.011)	1.005 (0.996–1.013)
Each 1 mm Hg lower in participants with MAP <103 mm Hg (n = 4792)	1.022 (1.014–1.029)‡	1.012 (1.004–1.021)‡	1.011 (1.003–1.020)§
Each 1 mm Hg higher in participants with MAP ≥103 mm Hg (n = 2352)	1.021 (1.012–1.030)‡	1.022 (1.012–1.033)‡	1.021 (1.011–1.032)‡

*Adjusted for demographic variables including age (year), gender, education level (year), residence in basic model.
†Further adjusted physical activity, vision, waist circumference, type 2 diabetes mellitus, cardiovascular diseases and stroke, and cerebrovascular diseases in final model.
‡$P < .01$.
§$P < .05$.

Table 3
Logistic OR (95% CIs) for Cognitive Impairment and Blood Pressure Categories Among Chinese Elderly

Variables	Unadjusted	Basic Model*	Final Model†
SBP			
Low (SBP <127 mm Hg, n = 2324)	1.25 (1.12–1.41)‡	1.15 (1.00–1.32)§	1.18 (1.02–1.35)§
Medium-low (127 ≤ SBP <141 mm Hg, n = 2409)	1.00 reference	1.00 reference	1.00 reference
Medium-high (141 ≤ SBP <155 mm Hg, n = 1284)	1.00 reference	1.00 reference	1.00 reference
High (SBP ≥155 mm Hg, n = 1127)	1.21 (1.02–1.42)‡	1.18 (0.99–1.42)	1.23 (1.02–1.49)§
DBP			
Low (DBP <77 mm Hg, n = 2536)	1.33 (1.19–1.49)‡	1.20 (1.05–1.36)‡	1.20 (1.05–1.37)‡
Medium-low (77 ≤ DBP <85 mm Hg, n = 2644)	1.00 reference	1.00 reference	1.00 reference
Medium-High (85 ≤ DBP <90 mm Hg, n = 989)	1.00 reference	1.00 reference	1.00 reference
High (DBP ≥90 mm Hg, n = 975)	1.26 (1.07–1.50)‡	1.26 (1.04–1.52)§	1.24 (1.02–1.52)§
PP			
Low (PP <49 mm Hg, n = 2523)	1.18 (1.05–1.32)‡	1.08 (0.95–1.23)	1.09 (0.95–1.25)
Medium-low (49 ≤ PP <62 mm Hg, n = 2588)	1.00 reference	1.00 reference	1.00 reference
Medium-high (62 ≤ PP <73 mm Hg, n = 1035)	1.00 reference	1.00 reference	1.00 reference
High (PP ≥73 mm Hg, n = 998)	1.04 (0.87–1.24)	0.90 (0.74–1.10)	1.04 (0.84–1.28)
MAP			
Low (MAP <93 mm Hg, n = 2560)	1.31 (1.17–1.48)‡	1.15 (1.00–1.33)	1.15 (1.00–1.34)§
Medium-low (93 ≤ MAP <103 mm Hg, n = 2232)	1.00 reference	1.00 reference	1.00 reference
Medium-high (103 ≤ MAP <110 mm Hg, n = 1186)	1.00 reference	1.00 reference	1.00 reference
High (MAP ≥110 mm Hg, n = 1166)	1.21 (0.99–1.33)	1.20 (0.99–1.44)	1.22 (1.01–1.48)§

*Adjusted for demographic variables including age (year), gender, education level (year), residence in basic model.
†Further adjusted physical activity, vision, waist circumference, type 2 diabetes mellitus, cardiovascular diseases and stroke, and cerebrovascular diseases in final model.
‡$P < .01$.
§$P < .05$.

blood pressures associated with poorer cognitive performance after controlling for demographic, lifestyle, and biological confounding factors. This association was less evident for PP, as the U-shaped relationship identified in the GAMs, quadratic models, and univariate logistic models disappeared in the multivariate logistic regression.

Previous studies have provided inconsistent results, indicating linear, J-shaped, or no association.[2–9] Notably, one proposed explanation was that linear function based on experience rather than the natural shape between blood pressure and cognitive impairment may not adequately describe the association.

Several previous reports are consistent with our finding of a U-shaped association of blood pressure with cognitive impairment or dementia.[10–14] In a cross-sectional study conducted in a biracial community, the highest cognitive function scores were found in the elderly aged 65 and older whose SBP was at the mean of 140 mm Hg, or in the persons whose DBP was at the mean of 77 mm Hg.[10] Similarly, this phenomenon was also confirmed in a 9-year longitudinal study in which a U-shaped association with higher risk of cognitive impairment among individuals with higher (≥160 mm Hg) and lower SBP (<130 mm Hg), as well as higher DBP (≥80 mm Hg) and lower DBP (<70 mm Hg).[12] This was somewhat consistent for the very elderly, aged 75 and older, where SBP was significantly associated with MMSE in a U-shaped fashion and there was also a linear relationship with PP but no association with DBP.[13] What is distinctive in the current study is that it includes a large sample of the very elderly, and applies GAMs, and the quadratic models identify cutpoints that more naturally describe the shape of the relationship between blood pressure and cognitive impairment.

High PP in older adults is recognized as a marker of increased artery stiffness and widespread atherosclerosis,[32] and may lead to decreased perfusion of the cerebral white matter and ultimately increase the risk for cognitive impairment as seen in some previous studies.[21–23] A U-shaped association between PP and cognitive impairment, found in a previous study,[20] was also found in GAMs, quadratic models, and univariate logistic models, but not confirmed when logistic models were further performed in our study.

It has been speculated that low or high blood pressure may be an early manifestation of the same pathological changes that lead to cognitive impairment; that is, damage to the brain regions that regulate blood pressure.[33] The association between blood pressure and cognitive impairment is problematic, and may be an effect of intermediate confounding factors affecting both blood pressure and cognitive performance, such as weight loss and dietary change,[34,35] or an effect of shared risk factors, such as psychological stress and oxidative stress.[36–38] Another hypothesis is the healthy survivor bias. It is possible that some people whose blood pressure was too low or too high had died before aged 65 years due to a window of susceptibility to related diseases (such as hemorrhagic or ischemic stroke) in middle age; thus, the elderly in our study were a selected middle blood pressure population whose health status was better, including a better cognitive performance.

Notably, the explanations and mechanisms of how both higher blood pressure and lower blood pressure impairs cognitive function are likely to be different.

High Blood Pressure was Associated With Cognitive Impairment

The association between hypertension and cognitive performance may be atherosclerosis, cerebral hypoperfusion, and white matter lesions.[39–43] Hypertension is a powerful risk factor for atherosclerosis throughout the arterial tree,[40] which leads to redistribution of blood flow and further decrease in cerebral perfusion.[41] This phenomenon has been shown to be exceedingly important for cerebral metabolism and cognition.[42] Additionally, studies have indicated relationships between abnormalities of the white matter and hypertension,[43] and such white matter lesions are frequently associated with cognitive impairment.[42]

Abnormalities of the renin-angiotensin system also have been involved in the pathogenesis of both hypertension and cognitive impairment. Also, in recent years, antihypertensive drugs have been used in the treatment and prevention of Alzheimer disease via the renin-angiotensin system.[44] It is also hypothesized that hypoperfusion-hypoxia might accelerate cognitive impairment through inducing expression of vasoactive mediators, such as nitric oxide, hypoxia-inducible-factor-1α, and vascular endothelial growth factor.[45]

Low Blood Pressure was Associated With Cognitive Impairment

For obvious reasons, low blood pressure can cause cerebral hypoperfusion.[46] It had also been argued that decline in blood pressure may reduce the velocity of cerebral blood flow, which can further cause damage to neural tissue and add to the pathological mechanisms of cognitive impairment. Reduced cerebral blood flow has been found both in individuals with dementia and in those showing early signs of dementia.[46,47] Furthermore, it has been proposed that severe atherosclerosis resulting from long-standing low blood pressure in midlife and later-life may lead to cerebral hypoperfusion, which may be 2 biological pathways.[48] The review by Duschek and colleagues[49] suggested the mechanisms of hypotension for reducing cognitive performance include diminished cortical activity, deficient regulation of cerebral blood flow in persons with low blood pressure, and insufficient adjustment of blood flow to cognitive requirements. However, most studies focus on possible mechanisms of cognitive impairment caused by low blood pressure; we have not found related research on the mechanism of lower blood pressure within the normotensive range.

Limitations

Our study has several limitations. First, it is not possible to assess the direction of the association because both exposure and outcome are assessed simultaneously. Second, the blood pressure measurement took place at a single visit and missing data on use of antihypertensive medications may diminish the data accuracy. Third, our findings may not be applicable to younger populations because CLHLS oversampled the oldest-old and dynamics of blood pressure changes with age. Finally, weight loss and dietary change, psychological stress, and oxidative stress may be confounding factors, but they were not measured and controlled in this study.

Conclusions

Our results suggest a U-shaped association between blood pressure (including SBP, DBP, MAP) and cognitive functions; that is, both higher and lower levels of blood pressure were associated with higher risk of cognitive impairment, which may have several implications for clinical practice and cognitive impairment prevention. First, both lower and higher blood pressure may be used to identify the high-risk population for cognitive impairment. Furthermore, it may point to the need to individualize blood pressure management for cognitive impairment prevention; that is, we should not only address blood pressure–lowering therapy in elderly with hypertension, but may also focus on raising blood pressure in elderly with relatively lower blood pressure. Future prospective longitudinal studies with blood pressure monitoring and extensive cognitive testing are needed to confirm the association we found in this study.

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