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RESEARCH ARTICLE

THE RELATIONSHIP BETWEEN PULSE PRESSURE AND DEMENTIA IN OLDER ADULTS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Purpose: As a risk factor for cardiovascular disease, wide pulse pressure may be related to cognitive impairment across the lifespan.

Methods: A total of 313 patients with dementia and 1117 cognitively healthy individuals were included in this study. Blood pressure measurements, demographic data, comorbid conditions, laboratory findings, and parameters from a comprehensive geriatric assessment were evaluated.

Results: While the mean age of the patients and the number of drugs were higher; the frequency of female sex and years of education were lower in the dementia group than in the control group ($p<0.001$ for each). Also, the Mini Nutritional Assessment scores, estimated Glomerular Filtration Rate, folate, and 25 hydroxy vitamin D levels were lower in the dementia group than in the control group ($p<0.001$; $p<0.001$; $p<0.001$ and $p=0.001$, respectively). While the dementia group had wider pulse pressure than controls($p=0.006$); there were no differences between the groups in systolic, diastolic, and mean arterial blood pressure values. When confounding factors were adjusted, the pulse pressure and dementia was related($p=0.032$). In addition, pulse pressure was positively correlated with dementia($p<0.01$).

Conclusion: This study showed that dementia seems to be related to wider pulse pressure in older adults. Healthcare professionals should be aware of the importance of pulse pressure in geriatric practice.

Keywords: Dementia; Pulse Pressure; Mean Arterial Blood Pressure, Older Adults

INTRODUCTION

Hypertension (HT), one of the most common comorbidities, is highly prevalent in older adults (1). Dementia, a geriatric syndrome, is also one of the common comorbidities in older adults. It causes mental and physical disabilities in individuals and poses a significant limitation for their families and caregivers (2). Studies have shown that high blood pressure (BP) that is not treated at an early age is associated with an elevated risk of cognitive decline in older adults (3). Given that there is no definitive cure for many types of dementia, which becomes more common with advancing age, the management of the risk factors such as HT becomes even more important (4). Although the relationship between HT and dementia has been rather well-established over

decades, the association between BP and cognition is complex across the lifespan.

With advancing age, systolic BP tends to increase, while diastolic BP decreases (5,6). This phenomenon attributed to age-related aortic stiffening, which reduce the elastic reservoir capacity of vessel, leading to increased stroke volume during systole and a diminished aortic blood volume at the onset of diastole (7). Also, a drop in diastolic pressure occurs with advancing age due to decreased elastic rebound and increased pressure drop velocity in the arterial system (8). Such changes in older people lead to wide pulse pressure (PP), which may play a role as a cardiovascular risk factor (5). PP, in addition to being a cardiovascular risk factor, may also be associated with cognitive health (9), particularly given that wide PP may accelerate parenchymal aging and adversely affect cognitive functions by leading to cerebral hypoperfusion, micro bleeding, and neuroinflammation (10). Besides, wide PP is closely associated with orthostatic hypotension, which is associated with falls, sarcopenia, frailty, and dementia in the elderly (11–13) and increases mortality from all causes (5). Current guidelines have no recommendation for PP control, and there is no widely accepted value for normal PP (14–16). Moreover, and the relationship between wide PP and dementia has only been evaluated in a few conflicting studies thus far (17, 18). Therefore, this study sought to examine the potential association between PP and dementia in older adults.

MATERIALS AND METHODS

Participants

For this study, 5940 patients who applied to the geriatric outpatient clinic between January 2013 and February 2022 were screened. The patients with a diagnosis of infection, acute cerebrovascular disease, those with missing Comprehensive Geriatric Assessment (CGA) parameters and drug information in their files, and those whose BP was taken by a device other than Biolight1 BIOM69 (Australia) or by manual sphygmomanometer were excluded from the study. After applying the exclusion criteria, a total of 1,430 participants aged 60 years and above who provided informed consent were enrolled in the study.

Ethical Statement

Permission for our study was granted from Dokuz Eylul Non-Interventional Research Ethics Committee (Date: 2 March 2022, Decision no: 2022/08-21), and informed consent for the procedure was obtained from the participants or a proxy on behalf of the patient. The investigation conformed to the Declaration of Helsinki of 1975.

Comprehensive geriatric assessment (CGA)

Demographic characteristics of the patients and comorbid conditions including HT, diabetes mellitus (DM), peripheral vascular disease, coronary artery disease (CAD), cerebrovascular events, congestive heart failure, as well as the number of drugs, antihypertensive drugs, and other drug usage were recorded. Additionally, the Yesevage Geriatric Depression Scale, Lawton-Brody Instrumental Daily Living Activity Scale (IADL), and Barthel Index (BI), Mini Nutritional Assessment (MNA), FRAIL and FRIED scales were collected from patients' files. Dementia, also referred to as major neurocognitive disorder, was diagnosed using The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria (19). Additionally, brain imaging was carried out in all the demented patients, and with the consent of the patients, cerebrospinal fluid (CSF) analysis was performed.

Evaluation of pulse pressure and mean arterial blood pressure

The Biolight1 BIOM69 (Australia) measured BP after the patient rested for at least 5 minutes in a quiet room, avoiding smoking or drinking tea or coffee for 30 minutes prior to measurement. While the PP was obtained by subtracting the diastolic BP from the systolic BP, mean arterial BP was calculated as, mean BP = PP x (1/3) + diastolic BP.

Laboratory evaluation

In the study, the estimated glomerular filtration rate (eGFR) level; 25-Hydroxy (OH) vitamin D, vitamin B12, low-density lipoprotein (LDL), folic acid, and thyroid stimulating hormone (TSH) results, which may be related to cardiovascular and cognitive health, were evaluated from the laboratory data of the patients. The tests were conducted with the auto-analyzer diagnostic modular system (Roche E170 and P-800), and Serum 25-OH Vitamin D was measured with the radioimmunoassay.

Statistical analysis

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 24.0 (SPSS Inc). Participants were divided into two

groups: those diagnosed with dementia and cognitively healthy individuals. Continuous variables were presented as mean ± standard deviation and categorical data were expressed as percentages (%). The distribution of continuous variables was evaluated using the Kolmogorov–Smirnov test and Skewness and Kurtosis values. Normally distributed continuous variables were compared using Student's t-test, whereas non-normally distributed continuous variables were analyzed with the Kruskal Wallis and Mann-Whitney U tests. Categorical variables were compared using Pearson's chi-squared or Fisher's exact test. To examine associations among non-normally distributed and/or ordinal variables, Spearman's rank correlation coefficients and their corresponding significance levels were computed. A 5% type I error rate was adopted to determine statistical significance. Binary Logistic Regression analysis was performed to reveal the relationship between dementia and PP, considering other related factors, and $p<0.05$ was considered statistically significant.

RESULTS

A total of 313 patients with dementia and 1117 cognitively healthy individuals were included in the study. The frequency of female sex was lower (54.3%) in the demented individuals who were older and less educated than in the controls ($p<0.001$). While the prevalence of HT was lower in the dementia group than in the control group (66.7% vs 60.3%; $p=0.036$); the use of anti-hypertensive medications usage was not significantly different. The eGFR, folate, and 25 OH vitamin D levels were lower in the

Table 1. Characteristics of Participants

	Control n=1117	Dementia n=313	p**
Demographic characteristics (*,%)			
Age (year)*	73.18 ± 7.33	76.78 ± 7.68	**<0.001**
Sex (female) %	67.1	54.3	**<0.001**
Education year*	8.01 ± 4.65	6.58 ± 4.61	**<0.001**
Number of drugs*	4.87 ± 3.21	6.23 ± 3.05	**<0.001**
Anti - hypertensive medications %	59.8	52.7	0.052
Comorbidities (%)			
Hypertension	66.7	60.3	**0.036**
Diabetes Mellitus	29.3	27.6	0.550
Congestive heart failure	5.5	6.7	0.409
Cerebrovascular events	5.7	7.1	0.355
Coronary artery disease	17.1	21.1	0.109
Peripheral vascular disease	5.1	5.4	0.818
Laboratory Results (*)			
eGFR mL/min 1.73 m2	75.86 ± 18.57	71.11 ± 18.98	**<0.001**
Vitamin B12 pg/mL	418.83 ± 301.33	428.36 ± 343	0.503
Folate ng/mL	9.34 ± 4.57	8.11 ± 5.01	**<0.001**
25 OH vitamin D ng/mL	22.58 ±11.84	20.26 ± 11.58	**0.001**
TSH m(IU)/L	1.89 ± 3.01	1.65 ± 1.41	0.212
LDL mg/dL	133.47 ± 29.24	134.68 ± 39.51	0.648
Comprehensive Geriatric Assessment (*, %)			
YGDS	3.24 ± 3.48	3.46 ± 3.5	0.272
BADL	92.22 ± 11.5	83.22 ± 18.19	**<0.001**
IADL	20.266 ± 7.69	11.17 ± 8.67	**<0.001**
MNA	12.63 ± 1.96	11.26 ± 2.33	**<0.001**
Frailty (%)	26.1	49.5	**<0.001**
Blood Pressure Measurements (mmHg) (*)			
Pulse Pressure	60.57 ± 15.03	63.22 ± 14.56	**0.006**
Systolic BP	134.12 ± 18.73	136.02 ± 16.84	0.087
Diastolic BP	73.55 ± 12.04	72.80 ± 10.22	0.272
Mean arterial BP	93.74 ± 12.78	93.87 ±10.82	0.854

BADL: Barthel Basic Activity of Daily Living; BP: Blood Pressure; eGFR: estimated Glomerular Filtration Rate; IADL: Lawton-Brody Instrumental Activity of Daily Living; LDL: Low Density Lipoprotein; MNA: Mini Nutritional Assessment; OH: Hydroxy; PP: Pulse Pressure; TSH: Thyroid Stimulating Hormone; YGDS: Yesevage Depression Scale . * Mean ± SD **Statistically significant p values ($p < 0.05$) are shown in bold characters

dementia group (p<0.001, p<0.001 and p=0.001, respectively).

The demographic characteristics, comorbidities, and laboratory findings of the study participants are summarized in Table 1. While the dementia group had a wider pulse pressure than controls (p=0.006); there was no difference between the groups in systolic, diastolic and mean arterial blood pressure values. When the regression analysis was performed according to age, sex, education year, HT, frailty, MNA score, eGFR, folate, and 25 OH vitamin D, the significance of the relationship between PP and dementia remained (OR:1.011, 95% CI 1.001-1.022, p= 0.032) (Table 2). A positive correlation was observed between PP and dementia (r = 0.080, p <0.01), whereas no significant associations were found with mean arterial BP, systolic BP, or diastolic BP. Table 3 shows the correlation analysis between the variables.

DISCUSSION

This retrospective and cross-sectional study demonstrated that wider PP was associated with dementia in older adults.

The lack of a curative treatment option for demented individuals has made it even more significant to take preventive interventions by regulating the accompanying risk factors such as HT in these patients (20, 21). With advancing age, PP increases due to the aforementioned changes in BP and the arterial system (5,22). Furthermore, recent evidence has suggested that PP may be related to cognitive impairment. The relationship between cognitive function and PP may be linked to the “biomechanical brain injury hypothesis”, which includes microvascular and neuronal damage (10). Accordingly, it has been shown that wide PP targets brain microvascular endothelial cells, leads to leaks in the blood-brain barrier and creates microvascular damage (22–24). Consequently, wide PP caused by age-related increased peripheral arterial stiffness may increase penetration into cerebral micro vessels and cause functional, structural, metabolic, and hemodynamic changes that may lead to neuronal dysfunction and cognitive decline (25). Additionally, microvascular damage in the brain impairs the function of the blood-brain barrier and increases its permeability, which increases the accumulation of β-amyloid in the cerebral cortex, the basis of the neurodegeneration process (26). Accordingly, the present study found that wider PP was associated with dementia in older adults.

On the other hand, there is no consensus on the relationship between PP and dementia in the available studies. In a meta-analysis, no relationship was found between PP and dementia (17). However, Qiu et al reported that both higher and lower tertiles of PP were associated with an increased risk of dementia especially among women in the categorical analysis (27). Accordingly, lower PP was associated with probable dementia in a recent study which defined probable dementia with Mini Mental State Examination Score ≤23 and that was conducted with 432 patients (28). Furthermore, Jung Y et al found a higher risk of dementia in older females with a wider PP but not in males (18), and suggested that this may be related to the lower education level, the stronger effect of apolipoprotein E and the increased frequency of depression in females, nevertheless, the underlying mechanism has not been fully accounted

Table 2. The Relationship Between Pulse Pressure and Dementia After Regression Analysis

	Dementia		
	OR	95% CI	**p***
Pulse Pressure	1.011	1.001-1.022	**0.032**

Model: Adjusted for age, sex, years of education, number of drugs, HT, Frailty, MNA, eGFR, folate, and 25 hydroxy vitamin D levels. CI: Confidence Interval; eGFR: estimated Glomerular Filtration Rate; HT: Hypertension; MNA: Mini Nutritional Assessment; OR: Odds Ratio. *Statistically significant p values (p < 0 0.05) are shown in bold characters.

Table 3. Correlation between blood pressure parameters and dementia

	Pulse Pressure	**Mean arterial BP**	**Systolic BP**	**Diastolic BP**
Dementia	**0.080****	-0.005	0.041	-0.040

BP: Blood Pressure. ** Correlation is significant at the 0.01 level (2-tailed).

for. The other research extracted from Hypertension in the Very Elderly Trial (HYVET) demonstrated that wider achieved PP, which was calculated as a mean of PPs from multiple visits during the trial, was associated with an increased risk of dementia in treatment groups (placebo and active) (9). Furthermore, in the study by Peters et al. (9), it was observed that achieved diastolic blood pressure did not predict subsequent dementia in the placebo group; however, a U-shaped association was identified in the active treatment group. In contrast, systolic blood pressure was not found to be associated with dementia. In our study, although the frequency of HT was different between the groups, there was no difference between the groups in systolic, diastolic and mean arterial BP values, probably due to proper anti-hypertensive treatment. These results support the notion that PP rather than mean arterial BP, systolic or diastolic BP may be associated with dementia. Within this context, as far as we are concerned, this is one of the first studies to thoroughly evaluate such a relationship in older adults naturalistically and in real-life conditions. However, prospective, cohort and follow-up studies that evaluate this relationship in subtypes of dementias, especially in AD and vascular dementia, are needed to elucidate this relationship in detail.

The study's strengths are the high number of patients and the measurement of BP of all patients with the same model and brand BP monitor. All the patients underwent CGA, and antihypertensive drug use was evaluated in detail. On the other hand, the retrospective and cross-sectional design are the limitations of the study. Another limitation of the study is the lack of differentiation between dementia subtypes, which may involve distinct pathophysiological pathways in relation to pulse pressure. Additionally, despite being under optimal conditions, all the measurements were based on single BP readings in the study.

CONCLUSION

This study demonstrated that wider pulse pressure may be related to dementia in older adults. Therefore, healthcare professionals dealing with geriatric patients should be aware of the importance of pulse pressure in the management of dementia and hypertension.

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REFERENCES

1. Altunkalem Seydi K, Ates Bulut E, Yavuz I, et al. E-mail-based health care in patients with dementia during the pandemic. Front Psychiatry 2022;13:863923.
2. Harada CN, Natelson Love MC, Triebel K. Normal Cognitive Aging. Clinics in Geiatric Medicine 2013;29:737-752.
3. Walker KA, Sharrett AR, Wu A, et al. Association of Midlife to Late-Life Blood Pressure Patterns With Incident Dementia. JAMA 2019;322:535–545.
4. Williamson JD, Pajewski NM, Auchus AP, et al. Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia: A Randomized Clinical Trial. JAMA 2019;321:553–561.
5. Tang KS, Medeiros ED, Shah AD. Wide pulse pressure: A clinical review. J Clin Hypertens 2020;22:1960–1967.
6. Nichols WW, Nicolini FA, Pepine CJ (1992) Determinants of isolated systolic hypertension in the elderly. J Hypertens Suppl 10:S73-7.
7. Stone J, Johnstone DM, Mitrofanis J, O'Rourke M. The mechanical cause of age-related dementia (Alzheimer's Disease): The brain is destroyed by the pulse. Journal of Alzheimer's Disease 2015;44:355–373.
8. Folkow B. Structure and function of the arteries in hypertension. Am Heart J 1987;114:938–948.
9. Peters R, Beckett N, Fagard R, et al. Increased pulse pressure linked to dementia: Further results from the Hypertension in the Very Elderly Trial - HYVET. J Hypertens 2013;31:1868–1875.
10. Maillard P, Mitchell GF, Himali JJ, et al. Aortic Stiffness, Increased White Matter Free Water, and Altered Microstructural Integrity: A Continuum of Injury. Stroke. 2017;48(6):1567-1573.
11. Kocyigit SE, Ates Bulut E, Aydin AE, et al. The relationship between cognitive frailty, physical

frailty and malnutrition in Turkish older adults. Nutrition 2024;126:112504.
12. Isik AT, Kocyigit SE, Kaya D, et al. The Relationship between the Most Common Subtypes of Dementia and Orthostatic Hypotension in Older Adults. Dement Geriatr Cogn Disord 2021;49:628–635.
13. Canaslan K, Ates Bulut E, Kocyigit SE, Aydin AE, Isik AT. Predictivity of the comorbidity indices for geriatric syndromes. BMC Geriatr 2022;22:440.
14. Pareek M, Vaduganathan M, Biering-Sørensen T, et al. Pulse Pressure, Cardiovascular Events, and Intensive Blood-Pressure Lowering in the Systolic Blood Pressure Intervention Trial (SPRINT). Am J Med 2019;132:733–739.
15. Fyhrquist F, Dahlöf B, Devereux RB, et al. Pulse pressure and effects of losartan or atenolol in patients with hypertension and left ventricular hypertrophy. Hypertension 2005;45:580–585.
16. Melgarejo JD, Thijs L, Wei D-M, et al. Relative and Absolute Risk to Guide the Management of Pulse Pressure, an Age-Related Cardiovascular Risk Factor. Am J Hypertens 2021;34:929–938.
17. Ou YN, Tan CC, Shen XN, et al. Blood Pressure and Risks of Cognitive Impairment and Dementia: A Systematic Review and Meta-Analysis of 209 Prospective Studies. Hypertension 2020;76:217–225.
18. Jung Y, Choi DW, Park S, Jang SI, Park EC. Association between pulse pressure and onset of dementia in an elderly Korean population: A cohort study. Int J Environ Res Public Health 2020;17(5):1657.
19. American Psychiatric Association. (2022). Diagnostic and statistical manual of mental disorders (5th ed., text rev.).
20. Ates Bulut E, Soysal P, Isik AT. Frequency and coincidence of geriatric syndromes according to age groups: single-center experience in Turkey between 2013 and 2017. Clin Interv Aging 2018;13:1899–1905.
21. De Heus RAA, Tzourio C, Lee EJL, et al. Association between Blood Pressure Variability with Dementia and Cognitive Impairment: A Systematic Review and Meta-Analysis. Hypertension 2021;1478–1489.
22. O'Rourke MF, Safar ME. Relationship between aortic stiffening and microvascular disease in brain and kidney: cause and logic of therapy. Hypertension 2005;46:200–204.
23. Thorin-Trescases N, de Montgolfier O, Pinçon A, et al. Impact of pulse pressure on cerebrovascular events leading to age-related cognitive decline. Am J Physiol Heart Circ Physiol 2018;314:H1214–H1224.
24. Chuang SY, Liu WL, Cheng HM, et al. Pulse pressure is associated with decline in physical function in older adults. Maturitas 2024;185:108000.
25. Hanon O, Haulon S, Lenoir H, et al. Relationship between arterial stiffness and cognitive function in elderly subjects with complaints of memory loss. Stroke 2005;36:2193–2197.
26. Liu Y, Braidy N, Poljak A, Chan DKY, Sachdev P. Cerebral small vessel disease and the risk of Alzheimer's disease: A systematic review. Ageing Res Rev 2018;47:41–48.
27. Qiu C, Winblad B, Viitanen M, Fratiglioni L.Pulse pressure and risk of alzheimer disease in persons aged 75 years and older: A community-based, longitudinal study. Stroke 2003;34:594–599.
28. Ishikawa J, Toba A, Futami S, et al. Association of pulse pressure and mean blood pressure to frailty, sarcopenia, and cognitive dysfunction in elderly outpatients with history of hypertension. Hypertension Research 2024;47:2029–2040.