

#### ORIGINAL

# Socioeconomic factors and cardiovascular risk associated with cognitive decline in older adults with Alzheimer's disease: a crosssectional study\*

Fatores socioeconômicos e risco cardiovascular associados ao declínio cognitivo em idosos com Alzheimer: estudo transversal

#### Factores socioeconómicos y riesgo cardiovascular asociados al deterioro cognitivo en ancianos con enfermedad de Alzheimer: un estudio transversal

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**Objective:** To verify the association between cognitive decline, socioeconomic factors, and cardiovascular risk in older adults with Alzheimer's disease. **Method:** A cross-sectional study was carried out with 75 older adults with Alzheimer's disease. Pulse pressure, cardiovascular risk, Mini-Mental State Examination, Mini-Nutritional Assessment, and biochemical tests were performed. **Results:** Ninety-two percent of patients had cognitive decline, with an average of three years of schooling. There was a predominance of women (62.3%) and older adults with two or more comorbidities (62.3%). Most participants had arterial hypertension (65.2%), had elevated pulse pressure during the examination (85%), were overweight (49%), and were at nutritional risk (78%). The daily average of antihypertensive drugs was 2, and angiotensin receptor blockers were the most used drugs. **Conclusion:** The population studied had an increased cardiovascular risk. The nursing consultation was important for recognizing clinical data, such as cognitive decline, cardiovascular risk, nutritional risk, and altered biochemical results.

**Descriptors:** Alzheimer Disease; Nursing Assessment; Hypertension.

#### RESUMO

ABSTRACT

**Objetivo:** verificar associação do declínio cognitivo e dos fatores socioeconômicos com o risco cardiovascular em idosos com Alzheimer. **Método:** estudo transversal, em que se incluíram 75 idosos com Alzheimer. Verificaram-se pressão de pulso, risco cardiovascular, Miniexame do Estado Mental, Miniavaliação Nutricional e exames bioquímicos. **Resultados:** 92% dos pacientes apresentaram declínio cognitivo, com média de três anos de escolaridade. Houve prevalência entre as mulheres (62,3%) e idosos com duas ou mais comorbidades (62,3%). Eram hipertensos (65,2%), estavam com a pressão de pulso elevada (85%), com sobrepeso (49%) e em risco nutricional (78%). Média diária de dois anti-hipertensivos, e a classe medicamentosa mais utilizada foi bloqueador do receptor da angiotensina. **Conclusão:** a população estudada apresentou risco cardiovascular aumentado. A consulta de enfermagem foi importante para o reconhecimento dos dados clínicos, como declínio cognitivo, risco cardiovascular, risco nutricional e análise bioquímica.

Descritores: Doença de Alzheimer; Avaliação em Enfermagem; Hipertensão.

#### RESUMEN

**Objetivo:** Verificar la asociación entre deterioro cognitivo, factores socioeconómicos y riesgo cardiovascular en ancianos con enfermedad de Alzheimer. **Método:** Se realizó un estudio transversal con 75 ancianos con enfermedad de Alzheimer. Se realizaron pruebas de presión de pulso, riesgo cardiovascular, Mini-Examen del Estado Mental, Mini-Evaluación Nutricional y pruebas bioquímicas. **Resultados:** El 92% de los pacientes presentó deterioro cognitivo, con un promedio de tres años de escolaridad. Hubo predominio de mujeres (62,3%) y ancianos con dos o más comorbilidades (62,3%). La mayoría de los participantes tenía hipertensión arterial (65,2%), presión de pulso elevada durante el examen (85%), sobrepeso (49%) y riesgo nutricional (78%). El promedio diario de fármacos antihipertensivos fue de 2, siendo los bloqueadores de los receptores de angiotensina los más utilizados. **Conclusión:** La población estudiada presentaba riesgo cardiovascular aumentado. La consulta de enfermería fue importante para el reconocimiento de datos clínicos, como deterioro cognitivo, riesgo nutricional y análisis bioquímico.

**Descriptores:** Enfermedad de Alzheimer; Evaluación de Enfermería; Hipertensión.

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### INTRODUCTION

Increasingly, researchers associate Systemic Arterial Hypertension (SAH) with increased cardiovascular risk in patients with cognitive decline and dementia syndromes. One of them is Alzheimer's Disease (AD)<sup>(1)</sup>, progressive and irreversible disease with an insidious onset and leads to spatial disorientation and gradual loss of memory, initially, of recent events. These particularities, associated with other factors, potentiate AD<sup>(2)</sup>. As a result of this process, damage to neurons and synapses involved in memory, learning, visuospatial skills, and other cognitive functions leads to cognitive decline<sup>(2)</sup>.

The female sex is an important risk factor for AD, and there is a growing interest in investigating the onset of the disease in women in the Menopause Transition (MT), regardless of the longer life expectancy. MT can manifest some neurological symptoms, including estrogen disruption, such as thermoregulation, sleep and circadian rhythms, depression, and impairment in various cognitive domains. Alteration of brain energy metabolism, due to the absence of estrogen, induces a hypometabolic state associated with neurological and cardiac symptoms<sup>(3,4)</sup>.

Of the non-communicable chronic diseases, SAH is the main modifiable, linear, and continuous risk factor for cardiovascular diseases (CVD) and potentiates the risk of damage to target organs<sup>(5)</sup>. High levels of systemic blood pressure (SBP) can be identified during nursing consultations and through the indirect measurement technique using a cuff attached to the upper limb is considered an independent factor for cardiovascular risk<sup>(5)</sup>.

It is unclear how SAH contributes to AD development, although it is a risk factor for late-onset dementia in older adults<sup>(1,2)</sup>. Uncertainty makes it difficult to construct parameters to control SBP in patients with AD. The scarcity of studies to understand these factors in a longitudinal way can contribute to the diseases.

The components of SBP change and progressively increase with aging. Thus, Systolic Blood Pressure (SP) and Pulse Pressure (PP) are early and independent markers of cardiovascular risk<sup>(4)</sup>. Researchers describe PP as a new biomarker of CVD, resulting from the subtraction of SP and Diastolic Blood Pressure (DBP)<sup>(4,6)</sup>.

In this sense, the variability of pressure components, such as PP, has predictive value alone in patients with cerebrovascular accidents (CVA) and AD progression<sup>(1)</sup>. Efforts are not only focused on reducing PP<sup>(4)</sup> but also on stabilizing blood pressure and controlling cognitive decline<sup>(1,7)</sup>.

Studies investigating the variability of blood pressure levels with AD are limited. However, recent evidence has shown that high variability is associated with cerebrovascular injuries, accelerated cognitive decline, and CVD incidence, aided by the Mini-Mental State Examination (MMSE)<sup>(7,8)</sup>. In other words, the measurement of SBP components, especially PP, using the MMSE to estimate the cognitive decline in older adults with AD, can be implemented during the nursing consultation<sup>(9)</sup>.

Thus, the nursing consultation, based on the systematization of nursing care, emphasizing older adult care in different contexts, is one of the nurse's duties. During nurses' theoretical/ practical training, clinical reasoning in aging is improved, and the students are instructed to respect the National Health Policy for older adults. In addition, the constant qualification of health professionals is valued for encouraging the development of teaching, research, and extension of the aging process<sup>(10)</sup>.

Population aging is increasing worldwide and nationally, which favors an increase in life expectancy, with AD being one of the most frequent dementias. Therefore, although there are national policies aimed at care for the elderly, in practice, nursing students and professionals generally do not relate PP parameters such as cardiovascular risk, MMSE to estimate the cognitive decline in AD, Mini Nutritional Assessment® (MNA) for nutritional risk assessment (11), and laboratory analysis.

This evidence motivated the search for understanding the following question: is there a relationship between cognitive decline, socioeconomic factors, and cardiovascular risk in older adults with AD?

Thus, the present study aimed to verify the association between cognitive decline, socioeconomic factors, and cardiovascular risk in older adults with Alzheimer's disease.

## METHOD

A quantitative, descriptive, cross-sectional study was carried out with older adults  $\geq$  60 years of age with a diagnosis of AD and, due to the COVID-19 pandemic, recruited at home and selected from the scheduled demand of the Association for Research Studies and Support for Alzheimer's Patients (AEPAPA in Portuguese) of Guarapuava-PR, Brazil, from January to August 2021.

The international guidelines of the Enhancing the Quality and Transparency of Health Research (EQUATOR) network, developed specifically for reports of scientific articles, were followed. The guideline above helped write the manuscript with the necessary information that must be included in a cross-sectional study report (STROBE checklist: cross-sectional studies).

Inclusion criteria were applied to the 75 older adults with mild or moderate AD, registered in the Unified Health System (SUS in Portuguese) and the Municipal Health System of Guarapuava-PR, followed up for approximately 12 months at AEPAPA. Patients were active and stable. Among the exclusion criteria, 19 had COVID-19 restrictions, died during the research, or had visual, auditory, and psychiatric dysfunctions that prevented performing the evaluative tests.

Data collection followed the biosafety protocol against COVID-19 of the municipality's Health Department, and participants should have received at least 2 doses of the COVID-19 vaccine. Subsequently, an individualized nursing consultation was carried out, in which vital signs, socioeconomic factors, cardiovascular risk, the daily number of antihypertensive drugs with the respective doses, and lifestyle factors were verified. In addition, the MNA and MMSE instruments were applied, and laboratory/biochemical tests were analyzed.

SBP was measured using the oscillometric technique and followed the current norms of the 2020 Brazilian Guidelines on Hypertension<sup>(5)</sup>. SAH was defined as SBP  $\geq$  140x90 mmHg or < 140x90 mmHg using one or more antihypertensive drugs to control blood pressure.

The MMSE was applied, one of the most used and most studied tests in the world for the assessment of cognitive function, whose score ranges from a minimum of zero, which indicates the highest degree of cognitive impairment, to a maximum of 30, which, in turn, corresponds to the best cognitive ability. According to *Cadernos de Atenção Básica* series - nº 19, this score varies according to the individual's level of education and the presence or absence of dementia, defined by the following cut-off points for screening cognitive deficits: illiterate = 19; 1 to 3 years of schooling = 23; 4 to 7 years of schooling = 24, and > 7 years of schooling =  $28^{(8)}$ .

The classification of the nutritional status was based on the gross value of the Body Mass Index

(BMI). However, for the stage of life investigated, two different cut-off points are defined based on the BMI (BMI values 22.0 and 27.0). The BMI was calculated from the total body weight ratio in kilograms and height squared in meters. People with BMI less than or equal to 22 kg/m<sup>2</sup>, were classified as low, with BMI greater than 22 kg/m<sup>2</sup> and less than 27 kg/m<sup>2</sup> as eutrophic, and with BMI above or equal to 27 kg/m<sup>2</sup> as overweight<sup>(11)</sup>.

The MNA instrument was used to assess the nutritional status of the elderly with AD, a validated method that is considered the gold standard for this assessment, as it is easy, non-invasive, painless, quick, and simple to apply if performed by a trained professional. This instrument can also estimate BMI and other anthropometric criteria to assess nutritional status<sup>(11, 12)</sup>.

The variables age, sex, and MMSE were considered sociodemographic characteristics. The latter evaluated the level of education in complete years of formal education. In addition, the MNA scale was included, which assessment covers mobility, if the patient lives in his own house, how many meals the person eats a day, and what kind of meals the person eats.

Blood collection for laboratory/biochemical tests was performed at the patient's home by qualified researchers, following the Brazilian Society of Clinical Pathology/Laboratory Medicine recommendations, using kits provided by Gold Analyzes Diagnostic. The analyses described were performed in semi-automated biochemistry equipment CA 2006, manufactured by SHEL - B4B Group, in the laboratory of the Midwest State University (UNICENTRO).

Two groups of patients were divided: I – patients with cognitive decline:  $78 \pm 6.2$  years of age, n = 68, and; II – patients with no cognitive decline:  $78 \pm 6.9$  years of age, n = 7.

Data were collected, summarized, and categorized by the program Microsoft Excel® 2021 version (Microsoft Corporation, Redmond, United States). Correlation with cognitive decline stratified by sex was performed, considering the variable cognitive decline as the outcome (dependent variable) and the others as independent variables. Poisson Regression was applied for processing the absolute and relative analysis, calculating the prevalence ratio and respective confidence intervals. A p-value <.05 was considered statistically significant in all analyses. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 22.0 (International Business Machines Corporation, New York, United States - IBM®). This article composes the postdoctoral thesis entitled "Creation of a calculator for pulse pressure and its correlation with the cognition scale in elderly people with Alzheimer's disease", from the Postgraduate Program in Intellectual Property and Technology Transfer for Innovation (PROFNIT in Portuguese), at UNICENTRO, in partnership with the Technological Incubator of Guarapuava (INTEG in Portuguese). The present study complied with the ethical precepts of Resolution 466/12 and was approved by the Research Ethics Committee of UNICENTRO, according to opinion no. 3,261,976/2019.

### RESULTS

Among the 75 respondents, the mean age was  $78\pm6$  years. There was a higher percentage of females (62.7%). As for chronic diseases, the most prevalent were SAH (65%), diabetes mellitus (DM) (36%), and 48% had two or more comorbidities. The overall prevalence of cognitive decline was 92%. The highest prevalence of cognitive decline was observed among women (62%); 85% had high PP, 49% were overweight, and 78% were at nutritional risk, according to the MNA instrument. In this population, the average daily use of antihypertensives was two tablets, and the most used drug class was angiotensin receptor blockers (24%), as shown in Table 1.

**Table 1 -** Clinical and sociodemographic characteristics of the groups from the Association for Research Studies and Support for Alzheimer's Patients. Guarapuava, PR, Brazil, 2021 (N=75)

Parameters	With cognitive decline (N=69) N% 78 ± 6		With no cognitive decline (N=6) N% 78 ± 7		Total population (N=75) N% 78 ± 6								
							Female	43	62.3	4	66.7	47	62.7
							Male	26	37.7	2	33.3	28	37.3
HAS													
Yes	45	65.2	4	66.7	49	65.3							
No	24	34.8	2	33.3	26	34.6							
Comorbidities													
One	26	37.7	1	16.7	27	36							
Two or more	43	62.3	5	83.3	48	64							
Pulse pressure													
High	59	85.5	5	83.3	64	85.3							
Normal	10	14.5	1	16.7	11	14.7							
BMI													
Low or adequate	35	50.7	3	50.0	38	50.6							
Overweight	34	49.3	3	50.0	37	49.3							
MNA													
At risk	54	78.3	4	66.7	58	77.3							
Nourished	15	21.7	2	33.3	17	22.7							
Antihypertensive (d)	$2 \pm 1$		$1 \pm 1$		2 ± 1								
BB	7	10.1	-	-	7	9.3							
ARB	17	24.6	1	16.6	18	24							
ACEI	4	5.8	2	33.3	6	8							
Diuretics	13	18.4	1	16.6	14	18.6							
Education (years)	3 ± 2		4 ± 2		3 ± 2								
MMSE	$15 \pm 4$		24 ± 2		$16 \pm 5$								

SAH = systemic arterial hypertension; BMI = body mass index; MNA = Mini Nutritional Assessment; N = number of participants; % = percentage; d = daily; BB = beta adrenergic blocker; ARB = angiotensin receptor blocker; ACEI = angiotensin-converting enzyme inhibitor; MMSE = Mini-Mental State Examination. Results for continuous variables were expressed as mean  $\pm$  standard deviation, as a proportion or percentage. Source: Elaborated by the authors, 2021. A statistically significant association was identified between cognitive decline and being well-nourished in the female group (p<0.05). Therefore, being well-nourished, according to the MNA classification, was a protective factor for cognitive decline, both in the crude analysis [PR 0.90 (95%CI 0.83 -0.98)] and in the adjusted analysis [PR 0.91 (PR 0.91) 95%CI 0.84 - 0.99)], according to Table 2. Table 3 shows the assessment of biochemical indicators. The altered variables, such as parathyroid hormone (PTH) and creatinine, were associated with cognitive decline in women (p<0.05). Among men, the probability of experiencing cognitive decline was higher among those with altered High-Density Lipoprotein (HDL) [PR 2.98 (95%CI 1.18 – 7.54)].

## DISCUSSION

For years, women consistently comprise two-thirds of people living with AD, regardless of age and ethnicity. Thus, the prevalence of women with advanced age in society is higher than that of men, and consequently, they may develop AD more frequently<sup>(3)</sup>. In addition, the highest mortality rate is also among women. This is because men have higher rates of associated comorbidities and early mortality from CVD, while women have a longer life expectancy, with a greater functional and hormonal decline in later stages of life. These data corroborate this research, in which most women (62%) had advanced age, with a mean age of 78 years.

**Table 2 -** Correlation between cognitive decline and sex in the patients from the Association for Research Studies and Support for Alzheimer's Patients. Guarapuava, PR, Brazil, 2021 (N=75)

	Ma	ale	Female		
Parameters	Gross RP (95%CI)	Adjusted RP (95%CI)	Gross RP (95%CI)	Adjusted RP (95%CI)	
HAS					
No	1.00	1.00	1.00	1.00	
Yes	0.89	1.07	1.06	1.06	
	(0.78 - 1.02)	(0.96 - 1.21)	(0.89 - 1.26)	(0.87 - 1.30)	
Comorbidities					
One	1.00	1.00	1.00	1.00	
Two or more	1.11	1.13	1.03	1.07	
	(0.97 - 1.26)	(0.97 - 1.33)	(0.90 - 1.20)	(0.92 - 1.24)	
Pulse pressure					
High	1.00	1.00	1.00	1.00	
Normal	0.92	0.95	1.06	1.06	
	(0.83 - 1.02)	(0.83 - 1.08)	(0.83 - 1.35)	(0.79 - 1.41)	
ВМІ					
Low or adequate	1.00	1.00	1.00	1.00	
Overweight	1.10	1.01	0.96	0.97	
	(0.97 - 1.24)	(0.94 - 1.08)	(0.83 - 1.11)	(0.83 - 1.13)	
MNA					
At risk	1.00	1.00	1.00	1.00	
Nourished	1.22	1.24	0.90	0.91	
	(0.97 - 1.52)	(0.99 - 1.57)	(0.83 - 0.98*)	(0.84 - 0.99*)	

SAH = Systemic Arterial Hypertension; BMI = Body Mass Index; MNA = Mini Nutritional Assessment; PR = Prevalence Ratio; CI = Confidence Interval; \* = statistically significant value (p<0.05). Source: Elaborated by the authors, 2021.

**Table 3** - Prevalence of cognitive decline, according to the biochemical variables of the patients from the Association for Research Studies and Support for Alzheimer's Patients. Guarapuava, PR, Brazil, 2021 (N=75) (continued)

Parameters	Male		Female		
	Gross RP (95%CI)	Adjusted RP (95%CI)	Gross RP (95%CI)	Adjusted RP (95%CI)	
Albumin					
Normal	1.00	1.00	1.00	1.00	
Altered	-	-	0.90	1.72	
			(0.73 - 1.10)	(0.96 - 3.07)	
Cortisol					
Normal	1.00	1.00	1.00	1.00	
Altered	0.81	0.56	0.90	0.38	
	(0.61 - 1.08)	(0.15 - 2.13)	(0.75 - 1.09)	(0.12 - 1.19)	
Parathyroid hormone					
Normal	1.00	1.00	1.00	1.00	
Altered	0.80	0.19	0.90	0.41	
	(0.58 - 1.09)	(0.01 - 2.85)	(0.75 - 1.09)	(0.19 - 0.89*)	
Calcium					
Normal	1.00	1.00	1.00	1.00	
Altered	1.16	3.27	0.90	0.50	
	(0.62 - 2.17)	(0.37 - 28.61)	(0.75 - 1.09)	(0.23 - 1.10)	
Vitamin D	. ,				
Normal	1.00	1.00	1.00	1.00	
Altered	0.93	1.43	1.14	1.29	
	(0.54 - 1.59)	(0.32)	(0.88 - 1.48)	(0.86 - 1.95)	
Insulin	(0.01 1.00)	(0102)	(0.00 1110)	(0.00 1.90)	
Normal	1.00	1.00	1.00	1.00	
Altered	-	-	0.90	-	
Altered			(0.75 - 1.09)		
Cholesterol			(0.75 - 1.09)		
Normal	1.00	1.00	1.00	1.00	
Altered	1.00	0.64	0.85	0.81	
Cusatinina	(0.60 - 1.65)	(0.21 - 1.95)	(0.63 - 1.16)	(0.54 - 1.22)	
Creatinine	1.00	1.00	1.00	1.00	
Normal	1.00	1.00	1.00	1.00	
Altered	0.71	0.70	1.16	1.92	
	(0.44 - 1.14)	(0.20 - 2.42)	(0.86 - 1.57)	(1.06 - 3.48*)	
Urea					
Normal	1.00	1.00	1.00	1.00	
Altered	0.80	0.88	-	-	
	(0.58 - 1.09)	(0.27 - 2.85)	-	-	
HDL					
Normal	1.00	1.00	1.00	1.00	
Altered	1.25	2.98	0.83	-	
	(0.91 - 1.70)	(1.18 - 7.54*)	(0.58 - 1.19)		
LDL					
Normal	1.00	1.00	1.00	1.00	
Altered	0.93	-	1.12	-	
	(0.54 - 1.59)		(0.89 - 1.41)		
Triglycerides					
Normal	1.00	1.00	1.00	1.00	
Altered	1.07	-	0.80	-	
	(0.62 - 1.82)		(0.51 - 1.21)		
TSH	. ,				
Normal	1.00	1.00	1.00	1.00	
Altered	1.80	-	-	-	
	(0.44 - 7.30)				

HDL = High-Density Lipoprotein; LDL = Low-Density Lipoprotein; TSH = Thyroid Stimulating Hormone; VDRL = Venereal Disease Research Laboratory; AST = Aspartate Transaminase; ALT = Alanine Aminotransferase; PR = Prevalence Ratio; CI = Confidence Interval; \* = statistically significant value (p<0.05). Source: Elaborated by the authors, 2021.

Parameters	N	lale	Female		
	Gross RP (95%CI)	Adjusted RP (95%CI)	Gross RP (95%CI)	Adjusted RP (95%CI)	
VDRL		-			
Normal	1.00	1.00	1.00	1.00	
Altered	1.50	-	0.83	-	
	(0.85 - 2.62)		(0.58 - 1.19)		
Vitamin B12					
Normal	1.00	1.00	1.00	1.00	
Altered	1.07	-	1.50	2.02	
	(0.62 - 1.82)		(0.67 - 3.33)	(0.91 - 4.50)	
Iron					
Normal	1.00	1.00	1.00	1.00	
Altered	1.80	-	0.90	-	
	(0.44 - 7.30)		(0.73 - 1.10)		
Blood glucose					
Normal	1.00	1.00	1.00	1.00	
Altered	1.33	-	0.90	-	
	(0.58 - 3.06)		(0.73 - 1.10)		
Leptin					
Normal	1.00	1.00	1.00	1.00	
Altered	2.00	-	0.80	-	
	(0.75 - 5.32)		(0.51 - 1.24)		
AST					
Normal	1.00	1.00	1.00	1.00	
Altered	0.90		0.94		
	(0.59 - 1.10)		(0.78 - 1.19)		
ALT			, , , , , , , , , , , , , , , , , , ,		
Normal	1.00	1.00	1.00	1.00	
Altered	0.80		0.90		
	(0.58 - 1.09)		(0.75 - 1.09)		
Potassium					
Normal	1.00	1.00	1.00	1.00	
Altered	0.81	-	-	-	
	(0.61 - 1.08)				
Sodium					
Normal	1.00	1.00	1.00	1.00	
Altered	0.81		0.88		
	(0.61 - 1.08)		(0.70 - 1.12)		

**Table 3** - Prevalence of cognitive decline, according to the biochemical variables of the patients from the Association for Research Studies and Support for Alzheimer's Patients. Guarapuava, PR, Brazil, 2021 (N=75) (conclusion)

HDL = High-Density Lipoprotein; LDL = Low-Density Lipoprotein; TSH = Thyroid Stimulating Hormone; VDRL = Venereal Disease Research Laboratory; AST = Aspartate Transaminase; ALT = Alanine Aminotransferase; PR = Prevalence Ratio; CI = Confidence Interval; \* = statistically significant value (p<0.05).

Source: Elaborated by the authors, 2021.

Although the symptoms of late-onset AD generally appear up to 70 years of age, AD appears during the prodromal (preclinical) phase, close to menopause, at approximately 50 years of age<sup>(3)</sup>. Due to the complexity of MT, clinical trials that examine the effectiveness of estrogen-based interventions, pharmacological interventions, and lifestyle interventions would benefit from stratification by sex rather than investigating a heterogeneous female population. Scholars describe that approximately 70% of AD cases can be attributed to genetics. However, factors associated with cerebrovascular diseases and cardiovascular risk (SAH, DM, obesity, and dyslipidemia) increase the risk of developing AD<sup>(2)</sup>. Important scientific evidence from a systematic review and meta-analysis suggested that at least 10 risk factors are associated with AD, including SAH, DM, hyperhomocysteinemia, inadequate BMI control, reduced education, orthostatic hypotension,

head trauma, lower activity, cognitive impairment, stress and depression<sup>(13)</sup>. The population of this study presented similar risk factors that may be associated with cognitive decline in elderly people with AD, corroborating the study above.

The progression and lack of control of SAH can develop a cognitive decline in people with advanced age. This pathology causes changes in vascular walls, hypoperfusion, ischemia, and, consequently, cerebral hypoxia. Cerebral ischemia causes an excessive concentration of Amyloid Precursor Protein (APP) and Beta-amyloid (A $\beta$ ), which physiologically play important roles in brain homeostasis, which can cause dysfunction in the blood-brain barrier, an event associated with the genesis of AD<sup>(2)</sup>.

Of the AD patients in this study, 65% had hypertension, and when PP levels were checked, 85% had increased values. A study showed that men and women with PP  $\geq$  50 mmHg had a double increase in future cardiovascular risk/events, even when other CVD factors were ruled out<sup>(4,14)</sup>, the 59 patients in group I with cognitive decline and five in group II without cognitive decline had high PP. Of the 75 patients with AD evaluated, 64 had cardiovascular risk factors. Antihypertensive therapy reduces cardiovascular morbidity and mortality in patients with hypertension. However, groups I and II used one or more antihypertensive drugs, which was insufficient to control their blood pressure levels<sup>(4)</sup>.

Epidemiological studies describe DM as a high cardiovascular risk factor in the development of AD. Some mechanisms for this association are suggested, including insulin resistance and insulin deficiency, impaired insulin receptors, hyperglycemia toxicity, adverse effects due to advanced glycation end products, cerebrovascular damage, vascular inflammation, and others<sup>(15)</sup>. AD may be even higher than estimated as the worldwide prevalence of DM continues to rise. Diabetic patients in this study represented 35% of the entire sample, which may characterize an increased risk of developing AD. In addition, conditions related to DM, including obesity, sedentary lifestyle, SAH, dyslipidemia, hyperinsulinemia, and Metabolic Syndrome (MS), may also be cardiovascular risk factors for AD<sup>(2.14)</sup>.

MS is a disease of the modern population, associated with obesity due to inadequate diet and a sedentary lifestyle. Having three or more cardiovascular risk factors (SAH, high triglycerides, and low HDL) is a sign of insulin resistance. Of the patients in this research, 65% had arterial hypertension, with mean triglycerides higher than 154 mg/dL and HDL below 40 mg/dL, and a significant association between males with cognitive decline and altered HDL [PR 2.98 (95%CI 1.18 – 7.54)]. Most people with MS feel fine and have no symptoms. However, they are at risk for developing serious diseases, such as CVD and  $DM^{(2,15,16)}$ .

Controversy persists about the associations between BMI and risk of cognitive impairment and dementia. According to a meta-analysis<sup>(16)</sup>, obesity (BMI  $\geq$  30 kg/m<sup>2</sup>) is a significant and independent risk factor for AD. Almost half of the patients in group I (49.3%) had a BMI close to 30 kg/m<sup>2</sup>. The progression from overweight to obesity increases the risk of dementia. In addition, being overweight is not related to being well-nourished as 78% of patients in group I were at nutritional risk, according to the MNA instrument, and, without distinguishing between sex, 77% of the population surveyed also had a risk or adequate diet.

However, low weight for the elderly (BMI < 20 kg/ $m^2$ ) is also associated with an increased risk of dementia and sarcopenia. Weight loss occurs concurrently with other comorbidities at older ages and may even precede the onset of dementia by 10 years<sup>(2,17)</sup>. Of the 50.7% of patients with cognitive decline in group I, low or adequate weight was found, and 62% had two or more comorbidities indicative of health problems.

As a result of this research, there was a significant association between cognitive decline and being well nourished for females. That is, being well nourished, according to the MNA classification, was a protective factor for cognitive decline. During the nursing consultation, both the nursing student and the professional nurse, in addition to measuring vital signs, performing physical examinations, applying scales, and collecting information from laboratory tests, can advise on the use of some components of the diet that are essential for neurocognitive protection, such as fatty acids (fish oil), antioxidants (vitamins E and C), fruits and vegetables, vitamins B6, B12 (cobalamin) and folate, in addition to caloric restriction<sup>(18)</sup>.

Evidence found an association between PTH and cognitive decline in women, and this association was discussed in a prospective cohort study<sup>(19)</sup>. In a prospective cohort of 988 Swedish men, altered PTH concentrations were significant when associated with the risk of vascular dementia

(41% increase in risk). However, there were no associations involving the risk of AD or other dementias<sup>(19)</sup>. However, another more recent study indicates that higher concentrations of PTH are not associated with  $AD^{(20)}$ . Thus, our research findings are exclusively from patients diagnosed with AD, with PTH being a protective factor for females [PR 0.41 (95%CI 0.19 – 0.89)].

The association of creatinine with cognitive decline found in this study may corroborate another finding<sup>(21)</sup> [PR 1.92 (95%CI 1.06 – 3.48)], which adjusted apolipoproteins with creatinine and identified significantly higher values in the group with AD compared to the control group. In this way, there is a greater risk of CVD by potentiating the metabolism of triglycerides through atherogenic effects.

The limitations of this study may be specific to the 75 elderly people from AEPAPA in the Midwest Region of Paraná, Brazil. Therefore, expansion in other territories is suggested. Another limitation may be related to the cross-sectional research design with the inherent restrictions of this method. Furthermore, it is mentioned that some patients examined had acute elevations in blood pressure levels due to stress during the measurement. Therefore, study participants used several classes of antihypertensive drugs, which did not effectively lower blood pressure levels.

## CONCLUSION

Elevated PP is considered an independent marker of cardiovascular mortality. Thus, 85% of the population studied had increased cardiovascular

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risk factors. In addition, the results demonstrated in this study constitute the best evidence available in the Brazilian scenario when relating the parameters of PP with cardiovascular risk, application of the MMSE to estimate the cognitive decline in the population with AD, application of the MNA instrument for nutritional risk assessment, and biochemical analysis during nursing consultation.

New studies that verify the differences between the sexes can advance rapidly in the detection, treatment, and care of AD in clinical aspects. The collection of prospective data may be used to describe the impact of these variables on cognitive decline.

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#### **CONFLICT OF INTEREST**

The authors have declared that there is no conflict of interest.

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