Healthy Tadulako Journal (Jurnal Kesehatan Tadulako)
Vol. 12 No. 3, July 2026
P-ISSN : 2407-8441/e-ISSN : 2502-0749

Original Research Paper

Association Between Age and Fazekas Defined White Matter Hyperintensity on Brain MRI at Royal Taruma Hospital

Yenny Defi Halim[1], Inge Friska Widjaya[2]*

[1]*Faculty of Medicine, Tarumanagara University, Jakarta, Indonesia*
[2]*Department of Radiology, Faculty of Medicine, Tarumanagara University, Jakarta, Indonesia*

Access this article online
Quick Response Code :

DOI : 10.22487/htj.v12i3.2012

Email Corresponding:
ingew@fk.untar.ac.id

Page : 386 - 394

Article History:
Received: 2025-10-09
Revised: 2026-06-28
Accepted: 2026-07-31

Published by:
Tadulako University,
Managed by Faculty of Medicine.

Website :
https://jurnal.fk.untad.ac.id/index.php/htj/index

Abstract

Background: White matter hyperintensities (WMH) on T2 weighted and FLAIR brain MRI are common neuroimaging markers of cerebral small vessel disease (CSVD), but Indonesian hospital based data on their age related distribution remain limited. **Objective:** To examine the association between age and Fazekas defined WMH among adults undergoing brain MRI. **Methods:** This retrospective analytical cross sectional study included 143 consecutive eligible MRI records from Royal Taruma Hospital, Jakarta, collected from August to December 2024. WMH was graded using the Fazekas scale; grade ≥1 was operationally classified as a WMH marker of CSVD. Age groups (<60 and ≥60 years) were compared using the chi square test, and an unadjusted prevalence ratio (PR) with 95% confidence interval (CI) was calculated. **Results:** Fazekas grade ≥1 was present in 95 of 143 records (66.4%). Prevalence was 87.9% among patients aged ≥60 years and 48.1% among those aged <60 years. Older patients had 1.8-fold higher prevalence (PR 1.8; 95% CI 1.43-2.34; p<0.001). **Conclusion:** Age was significantly associated with Fazekas defined WMH prevalence. The retrospective, cross sectional design and absence of vascular comorbidity adjustment preclude causal inference and do not establish a basis for routine MRI screening.

Keywords: White matter hyperintensity; cerebral small vessel disease; aging; brain MRI; Fazekas scale.

Introduction

Cerebral small vessel disease (CSVD) encompasses a group of pathological processes affecting the brain's small arteries, arterioles, capillaries, and venules[1,2]. It is clinically important because the cumulative burden of small vessel injury is associated with lacunar stroke, cognitive impairment, gait disturbance, mood symptoms, and vascular dementia. Neuroimaging manifestations are heterogeneous and include recent small subcortical infarcts, lacunes, cerebral microbleeds, enlarged perivascular spaces, brain atrophy, and white matter hyperintensities (WMH)[3]. Among these markers, WMH are frequently encountered on T2 weighted and fluid attenuated inversion recovery (FLAIR) MRI and represent areas of altered white matter signal related to chronic microvascular and tissue injury[4,5,6]. Because WMH are common with increasing age, accurate terminology is essential: the presence of WMH can support assessment of CSVD burden, but WMH alone does not capture the complete radiological spectrum of CSVD.

Aging is consistently associated with a greater burden of WMH and other cerebral small vessel abnormalities. Age related vascular stiffening, endothelial dysfunction, impaired autoregulation, and changes in cerebral perfusion provide biologically

plausible pathways through which WMH may become more prevalent in older adults[7]. Nevertheless, vascular comorbidities such as hypertension and diabetes mellitus may also contribute to cerebral microvascular injury and can coexist with older age[8,9]. This is particularly relevant in hospital based studies because referral patterns and comorbidity profiles may differ from those of the general population. Therefore, a cross sectional association between age and WMH should not be interpreted as proof that age independently causes the lesions, predicts their future occurrence, or determines disease progression.

Indonesian data describing age related WMH in routine clinical MRI populations remain limited. Many published investigations focus on stroke cohorts, cognitive impairment, or selected community samples, whereas patients referred for MRI in clinical practice represent a broader mixture of indications. Royal Taruma Hospital provides an urban hospital setting in which such data can be examined. The present study therefore focuses specifically on Fazekas graded WMH as the measured MRI outcome and uses it as an operational marker of CSVD. This narrower definition responds to the available study data and avoids equating a single imaging marker with a comprehensive diagnosis that would ordinarily consider other CSVD features such as lacunes, microbleeds, enlarged perivascular spaces, and atrophy.

The primary research question was whether age group was associated with the prevalence and severity distribution of Fazekas defined WMH among adults who underwent brain MRI at Royal Taruma Hospital. The study objectives were to describe the demographic and Fazekas grade distribution of the sample, compare WMH prevalence between patients aged <60 years and those aged ≥60 years, and quantify the crude prevalence association between age group and WMH presence. The prespecified hypothesis was that the older group would show a higher prevalence of Fazekas defined WMH, while recognizing that a cross sectional comparison cannot establish temporal sequence or causal direction.

The expected contribution is local descriptive and analytical evidence that may help clinicians contextualize WMH findings in older adults who already undergo MRI for clinical indications. The results may also inform the design of future studies that include vascular comorbidities, standardized imaging parameters, longitudinal follow up, and population based sampling. They should not, however, be taken as evidence for population MRI screening because the present study did not evaluate screening accuracy, feasibility, cost effectiveness, harms, or improvement in clinical outcomes. At a public health level, established vascular risk assessment and control remain central within the broader prevention of noncommunicable and cerebrovascular disease[10].

Materials and Methods

Research Design

This research used a retrospective analytical cross sectional design to evaluate the association between age and Fazekas defined WMH at a single observation period[11,12]. Existing MRI examinations and electronic medical records were analyzed without prospective follow up or direct participant contact. The design is appropriate for estimating the prevalence of an imaging finding and comparing prevalence between age groups within the hospital referred population. Because exposure and outcome information were evaluated from existing records, the analysis cannot determine whether age preceded the development of individual WMH lesions, estimate incidence, or measure lesion progression over time. Accordingly, the

observed association should be interpreted as an age related difference in WMH burden rather than evidence of a temporal or causal relationship.

Sample

The source population comprised all adults who underwent brain MRI at Royal Taruma Hospital, Jakarta, Indonesia, from August through December 2024. Consecutive sampling was implemented as consecutive inclusion of all eligible MRI records identified during the study period; patients were not prospectively invited or recruited[13]. Inclusion criteria were age ≥18 years, completion of a brain MRI protocol containing T2-weighted and FLAIR sequences, and availability of a medical record containing the required demographic information. Exclusion criteria were congenital brain malformation, intracranial tumor, and a documented history of traumatic brain injury or neurosurgical procedures because these conditions could complicate interpretation of white matter signal abnormalities. The minimum sample size was estimated using the Fleiss approach for comparison of two independent proportions, assuming WMH/CSVD marker prevalences of 50% in the <60 year group and 80% in the ≥60 year group, 80% statistical power, and $\alpha=0.05$[14]. This yielded a minimum of 62 records per group. The final analytic sample comprised 143 eligible records and therefore exceeded the calculated minimum overall requirement.

Data Collection Technique

Data were collected retrospectively in January 2025 from the hospital Picture Archiving and Communication System (PACS) and electronic health record (EHR). The variables extracted were age, sex, and MRI findings. Age was analyzed both descriptively and categorically as <60 years or ≥60 years. WMH were assessed on the available T2-weighted and FLAIR images using the Fazekas visual rating scale, which classifies white matter abnormalities from grade 0 to grade 3[15]. Grade 0 represented no WMH, while grade ≥1 was operationally classified as WMH present and used in this study as an MRI marker of CSVD. This operational definition does not include other recognized CSVD markers such as lacunes, cerebral microbleeds, enlarged perivascular spaces, recent small subcortical infarcts, or atrophy. Two radiologists independently applied the same prespecified Fazekas criteria; when their interpretations differed, the final grade was established through joint consensus. The retrospective archive did not document a formal reader blinding procedure, so blinding cannot be claimed. Individual reader level grades before consensus were not retained, which prevented calculation of weighted kappa or another inter observer agreement coefficient. The analytic dataset also did not retain scanner manufacturer, magnetic field strength, or sequence-specific acquisition parameters such as TR, TE, TI, and slice thickness. These technical parameters therefore cannot be reconstructed or reported reliably. All extracted data were anonymized before analysis.

Data Analysis Technique

Descriptive statistics were used to summarize the study sample. Categorical variables were presented as frequencies and percentages, while continuous variables were summarized using mean, standard deviation (SD), median, minimum, and maximum where available. The primary inferential analysis used the chi-square (χ^2) test to evaluate the association between age group (<60 versus ≥60 years) and Fazekas defined WMH status (present versus absent)[16]. The magnitude of the prevalence association was expressed as a prevalence ratio (PR) with a 95% confidence interval (CI). The reported PR is crude and unadjusted. A two sided p value <0.05 was considered statistically significant,

with very small values reported as p<0.001 rather than p=0.000. Analyses were performed using SPSS version 25.0 for Windows (IBM Corp., Armonk, NY, USA). Information on hypertension, diabetes mellitus, dyslipidemia, smoking, and other vascular comorbidities was not available in the analytic dataset. Consequently, an adjusted multivariable model could not be constructed, and residual confounding is explicitly considered in the interpretation.

Ethical Clearance

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was granted by the Ethics Committee of the Faculty of Medicine, Tarumanagara University (No. 426/KEPK/FK UNTAR/X/2024), and administrative permission was obtained from Royal Taruma Hospital (No. 355/Dir/RSRT/XII2024). Because the study used anonymized retrospective secondary data and involved no direct participant contact, the requirement for individual informed consent was waived by the ethics committee. Access to PACS and medical record information was limited to study purposes, identifiers were removed from the analytic file, and no personally identifiable information was included in the analysis or manuscript.

Results

A total of 143 eligible MRI records were included in the analysis. The sample contained 76 female patients (53.1%) and 67 male patients (46.9%), showing a relatively balanced sex distribution. Patient age ranged from 22 to 93 years. The mean age was 56.03 years (SD 16.9), and the median was 58 years. Seventy-seven patients (53.8%) were aged <60 years and 66 patients (46.2%) were aged ≥60 years. Table 1 summarizes these demographic characteristics together with the Fazekas-grade distribution.

Fazekas grade 0 was recorded in 48 patients (33.6%), grade 1 in 52 (36.4%), grade 2 in 31 (21.7%), and grade 3 in 12 (8.4%). Thus, the most frequent category was grade 1, followed by grade 0 and grade 2; grade 3 represented the smallest group. These data describe the severity distribution of WMH within this clinically referred MRI sample and should not be interpreted as a population distribution for Jakarta or Indonesia.

Table 1. Characteristics of the Study Sample

Variable	Category	Frequency (n)	Percentage (%)
Age			
	< 60 years	77	53.8%
	≥ 60 years	66	46.2%
Sex			
	Male	67	46.9%
	Female	76	53.1%
Fazekas Scale			
	Grade 0	48	33.6%
	Grade 1	52	36.4%
	Grade 2	31	21.7%
	Grade 3	12	8.4%

Source: Secondary data, Royal Taruma Hospital PACS/EHR, 2024

Table 2. Descriptive Statistics of Fazekas Score

Variable	Mean ± SD	Min-Max
Fazekas Score	1.05 ± 0.9	0 - 3

Source: Secondary data, Royal Taruma Hospital PACS/EHR, 2024

The mean Fazekas score for the entire sample was 1.05±0.9, with an observed range of 0-3. Under the prespecified operational definition, grade 0 represented WMH absent, while Fazekas grade ≥1 represented WMH present as an MRI marker of CSVD. On this basis, 95 of 143 patients (66.4%) had the operational WMH/CSVD marker and 48 (33.6%) did not. Because the study outcome was based on WMH alone, the 66.4% value

describes the prevalence of Fazekas-defined WMH in the sample rather than the prevalence of every possible imaging manifestation of CSVD.

Age-group analysis demonstrated a clear difference in WMH prevalence. Among patients aged ≥60 years, 58 of 66 (87.9%) had Fazekas grade ≥1, whereas 8 (12.1%) had grade 0. Among those aged <60 years, 37 of 77 (48.1%) had grade ≥1 and 40 (51.9%) had grade 0. The chi-square test showed a statistically significant association between age group and WMH status (p<0.001). The crude PR was 1.8 (95% CI 1.43-2.34), indicating that the prevalence of Fazekas defined WMH was 1.8-fold higher in the ≥60-year group than in the younger group. This measure describes a prevalence difference at the time of observation and is not a prospective risk estimate.

Table 3. Association Between Age Group and Fazekas Defined White Matter Hyperintensity

Age	WMH Present n (%)	WMH Absent n (%)	Total	PR	95% CI		p-value
					Lower	Upper	
≥ 60 years	58 (87.9%)	8 (12.1%)	66	1.8	1.43	2.34	<0.001
< 60 years	37 (48.1%)	40 (51.9%)	77				
Total	**95 (66.4%)**	**48 (33.6%)**	**143**				

**Note: WMH present = Fazekas grade ≥1; PR is unadjusted; p<0.05 indicates statistical significance.*

The results therefore support the study hypothesis that older patients in this hospital referred sample had a higher prevalence of Fazekas defined WMH. However, the association is unadjusted. Because vascular comorbidity data were unavailable, age cannot be described from these data as an independent or dominant determinant of WMH, and the possibility of residual confounding should be retained throughout the interpretation.

Discussion

This study identified a statistically significant cross sectional association between age and Fazekas defined WMH on brain MRI. WMH prevalence was 87.9% among patients aged ≥60 years and 48.1% among those aged <60 years. The corresponding unadjusted PR of 1.8 (95% CI 1.43–2.34) indicates that WMH prevalence was approximately 1.8 fold higher in the older group. This is an important distinction from the wording of prospective risk: all data were obtained from a retrospective cross-sectional hospital sample, so the analysis shows a difference in observed prevalence and does not demonstrate that age caused the lesions, independently determined CSVD, or predicted future progression. The findings therefore support age as a marker associated with a greater WMH burden in this clinical population, rather than as an independently established causal risk factor. Because the estimate was unadjusted, residual confounding by vascular, metabolic, and other clinical characteristics should also be considered when interpreting the magnitude of the observed association.

The direction of the association is consistent with established biological and neuroimaging knowledge. Aging is accompanied by changes in the structure and function of cerebral small vessels, including increased arterial stiffness, endothelial dysfunction, altered autoregulation, and impaired microvascular integrity. These processes can contribute to chronic white matter injury and WMH formation[17]. At the same time, older adults are more likely to have hypertension, diabetes, dyslipidemia, smoking exposure, and other vascular conditions that may independently influence cerebral small vessel injury. Because those variables were not

available in the present dataset, biological plausibility should not be confused with proof of an age specific causal mechanism in this sample.

The present results are broadly compatible with previous empirical research. Fatmawati et al. reported an association between increasing age and greater white matter lesion severity in an Indonesian ischemic stroke cohort[18]. Longitudinal research has also shown relationships between blood pressure history and cerebral white-matter lesions, indicating that vascular exposures remain important when age-related WMH is interpreted[19]. Studies of older adults without stroke and broader work on brain aging similarly demonstrate that WMH burden becomes more common with advancing age, although prevalence estimates differ by population, clinical selection, MRI acquisition, and the thresholds used to define abnormality[20,21,22]. The 66.4% overall prevalence and 87.9% prevalence in the older group in the current study should therefore be viewed as hospital sample estimates, not as representative prevalence estimates for the general Indonesian population.

The operational definition used in this study also affects interpretation. Fazekas grade ≥1 was used to indicate WMH presence and was treated as an MRI marker of CSVD. This approach is practical because the Fazekas scale is well established for visual grading of white matter signal abnormalities, but CSVD is a broader radiological construct. Contemporary neuroimaging frameworks consider multiple markers, including lacunes, cerebral microbleeds, enlarged perivascular spaces, recent small subcortical infarcts, and atrophy, in addition to WMH[3]. Accordingly, the current findings are most accurately described as an age association with Fazekas defined WMH/CSVD marker burden, rather than as proof that all patients with grade ≥1 have a complete CSVD phenotype.

From a clinical perspective, the data support careful attention to WMH when interpreting brain MRI in older adults who have a clinical indication for imaging. WMH and other manifestations of small vessel disease are relevant to cognitive and cerebrovascular outcomes, and their presence may prompt clinicians to consider the patient's broader neurological and vascular context[23,24]. Nevertheless, this study did not enroll an asymptomatic screening population and did not compare screening strategies, diagnostic pathways, costs, harms, or clinical outcomes. It therefore cannot establish that routine MRI screening of older adults is necessary, effective, feasible, or cost effective. Any imaging decision should remain clinically indicated and individualized rather than being inferred from this cross sectional association alone.

Several methodological strengths support the internal clarity of the study. Eligible records were included consecutively within the defined period, the outcome was graded with a standardized Fazekas scale, and two radiologists independently reviewed the MRI examinations before resolving disagreements by consensus. The revised reporting also distinguishes the imaging outcome from the broader CSVD construct and identifies the PR as unadjusted. Important limitations remain. The retrospective cross sectional design prevents temporal and causal inference; the single private-hospital setting creates referral and selection considerations; and the absence of hypertension, diabetes mellitus, dyslipidemia, smoking, and other vascular covariates means residual confounding cannot be quantified. In addition, pre consensus reader scores were not retained, so inter observer agreement could not be calculated, and detailed scanner or sequence parameters were unavailable for retrospective reporting.

Future research should retain complete vascular-risk information and imaging

metadata so that age can be evaluated in multivariable models rather than as an isolated crude exposure. Prospective and longitudinal designs would permit assessment of incident or progressive WMH, while multicenter or population-based sampling would improve generalizability across Indonesian settings[25,26]. Formal inter reader reliability should be reported when reader level scores are available, and standardized acquisition parameters should be documented prospectively[27]. Local HTJ literature also provides relevant context: previous studies have examined cognitive function in geriatric populations, blood pressure in older adults, and vascular factors such as hypertension, diabetes mellitus, and dyslipidemia in ischemic stroke outcomes[28,29,30,]. These findings reinforce the clinical relevance of aging, cognition, and vascular health while underscoring why the age WMH association observed here should be interpreted within a wider risk profile.

Conclusion

In this retrospective hospital based cross sectional sample, age ≥60 years was significantly associated with a higher prevalence of Fazekas-defined WMH, an MRI marker of CSVD. WMH prevalence was 87.9% in the older group and 48.1% in patients aged <60 years, corresponding to an unadjusted PR of 1.8 (95% CI 1.43-2.34; p<0.001). These findings support careful consideration of age when interpreting WMH on clinically indicated brain MRI, but they do not demonstrate a causal or independent effect of age and do not provide evidence for routine population MRI screening. Prospective multicenter studies incorporating vascular comorbidities, standardized MRI acquisition information, and formal inter reader agreement are needed to clarify independent associations and longitudinal change.

Acknowledgment

The authors thank the management of Royal Taruma Hospital for permission and support in accessing the study data and the Faculty of Medicine, Tarumanagara University, for institutional and academic guidance. Appreciation is also extended to the radiologists and staff who supported image review, record access, and data management.

References

1. De Silva TM, Faraci FM. Contributions of Aging to Cerebral Small Vessel Disease. *Annu Rev Physiol*. 2020;82:275-295. doi:10.1146/ANNUREV-PHYSIOL-021119-034338/CITE/REFWORKS
2. Pantoni L. Cerebral small vessel disease: from pathogenesis and clinical characteristics to therapeutic challenges. *Lancet Neurol*. 2010;9(7):689-701. doi:10.1016/S1474-4422(10)70104-6
3. Wardlaw JM, Smith EE, Biessels GJ, et al. Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration. *Lancet Neurol*. 2013;12(8):822-838. doi:10.1016/S1474-4422(13)70124-8
4. Ghaznawi R, Geerlings MI, Jaarsma-Coes M, Hendrikse J, De Bresser J. Association of White Matter Hyperintensity Markers on MRI and Long-term Risk of Mortality and Ischemic Stroke: The SMART-MR Study. *Neurology*. 2021;96(17):E2172-E2183. doi:10.1212/WNL.0000000000011827;REQUESTEDJOURNAL:JOURNAL:WNL;JOURNAL:JOURNAL:WNL;WGROUP:STRING:PUBLICATION
5. Inoue Y, Shue F, Bu G, Kanekiyo T. Pathophysiology and probable etiology of cerebral small vessel disease in vascular dementia and Alzheimer's disease. *Mol Neurodegener 2023 181*. 2023;18(1):46-. doi:10.1186/S13024-023-00640-5
6. Singh A, Bonnell G, De Prey J, et al. Small-vessel disease in the brain. *Am Hear J plus Cardiol Res Pract*. 2023;27(3).

doi:10.1016/J.AHJO.2023.100277

7. Shi Y, Thrippleton MJ, Makin SD, et al. Cerebral blood flow in small vessel disease: A systematic review and meta-analysis. *J Cereb Blood Flow Metab*. 2016;36(10):1653-1667. doi:10.1177/0271678X16662891
8. Hachinski V, Iadecola C, Petersen RC, et al. National Institute of Neurological Disorders and Stroke-Canadian Stroke Network vascular cognitive impairment harmonization standards. *Stroke*. 2006;37(9):2220-2241. doi:10.1161/01.STR.0000237236.88823.47;ISSUE:ISSUE:DOI
9. Pasi M, Cordonnier C. Clinical Relevance of Cerebral Small Vessel Diseases. *Stroke*. 2020;51(1):47-53. doi:10.1161/STROKEAHA.119.024148;WGROUP:STRING:PUBLICATION
10. World Health Organization. Noncommunicable diseases. 2025. https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases
11. Hulley S, Cummings S, Browner W, Grady D, Hearst N, Newman T. Estimating sample size and power. *Des Clin Res*. 2001;2:85.
12. Mann CJ. Observational research methods. Research design II: cohort, cross sectional, and case-control studies. *Emerg Med J*. 2003;20(1):54-60. doi:10.1136/EMJ.20.1.54
13. Etikan I, Musa SA, Alkassim RS. Comparison of Convenience Sampling and Purposive Sampling. *Am J Theor Appl Stat 2016, Vol 5, Page 1*. 2015;5(1):1-4. doi:10.11648/J.AJTAS.20160501.11
14. Fleiss JL, Tytun A, Ury HK. A Simple Approximation for Calculating Sample Sizes for Comparing Independent Proportions. *Biometrics*. 1980;36(2):343. doi:10.2307/2529990
15. Fazekas F, Chawluk J, Alavi A, et al. MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. *Am J Roentgenol*. 2012;149(2):351-356. doi:10.2214/AJR.149.2.351
16. McHugh ML. The Chi-square test of independence. *Biochem Medica*. 2013;23(2):143-149. doi:10.11613/BM.2013.018/FULLARTICLE
17. Lahna D, Schwartz DL, Woltjer R, et al. Venous Collagenosis as Pathogenesis of White Matter Hyperintensity. *Ann Neurol*. 2022;92(6):992. doi:10.1002/ANA.26487
18. Fatmawati H, Pramono CA, Jauhani MA, Purwandhono A, Santosa A. Correlation of White Matter Lesions Severity and Age in Ischemic Stroke at Siloam Jember Hospital. *Jember Med J*. 2023;2(1):20-25. doi:10.19184/JMJ.V2I1.291
19. De Leeuw FE, De Groot JC, Oudkerk M, et al. A follow-up study of blood pressure and cerebral white matter lesions. *Ann Neurol*. 1999;46(6):827-833. doi:10.1002/1531-8249(199912)46:6
20. Zheng K, Wang Z, Chen X, Chen J, Fu Y, Chen Q. Analysis of Risk Factors for White Matter Hyperintensity in Older Adults without Stroke. *Brain Sci 2023, Vol 13, Page 835*. 2023;13(5):835. doi:10.3390/BRAINSCI13050835
21. Blinkouskaya Y, Caçoilo A, Gollamudi T, Jalalian S, Weickenmeier J. Brain aging mechanisms with mechanical manifestations. *Mech Ageing Dev*. 2021;200. doi:10.1016/j.mad.2021.111575
22. Ter Telgte A, Van Leijsen EMC, Wiegertjes K, Klijn CJM, Tuladhar AM, De Leeuw FE. Cerebral small vessel disease: from a focal to a global perspective. *Nat Rev Neurol*. 2018;14(7):387-398. doi:10.1038/s41582-018-0014-y
23. O'Brien JT, Thomas A. Vascular dementia. *Lancet*. 2015;386(10004):1698-1706. doi:10.1016/S0140-6736(15)00463-8
24. Gorelick PB, Scuteri A, Black SE, et al. Vascular contributions to cognitive impairment and dementia: A statement for healthcare professionals from the

American Heart Association/American Stroke Association. *Stroke*. 2011;42(9):2672-2713. doi:10.1161/STR.0B013E3182299496;PAGE:STRING:ARTICLE/CHAPTER

25. Szklo M, Nieto FJ. *Measuring Associations Between Exposures and Outcomes*.; 2014.
26. Kalaria RN, Maestre GE, Arizaga R, et al. Alzheimer's disease and vascular dementia in developing countries: prevalence, management, and risk factors. *Lancet Neurol*. 2008;7(9):812-826. doi:10.1016/S1474-4422(08)70169-8
27. Halim YD, Widjaya IF. Hubungan Usia Dengan Cerebral Small Vessel Disease Pada Mri Kepala Di Rs Royal Taruma. *J Muara Sains, Teknol Kedokt dan Ilmu Kesehat*. 2025;9(2):1-6. doi:10.24912/5S5W1457
28. Handayani F. Hubungan Durasi Tidur Dengan Fungsi Kognitif Geriatri. *Heal Tadulako J (Jurnal Kesehat Tadulako)*. 2019;5(3):75. doi:10.22487/j25020749.2019.v5.i3.14060
29. Setiawati D, Nuraeni I, Karimah I, Agus HR, Poltekkes B, Tasikmalaya K. Hubungan Indeks Massa Tubuh dengan Tekanan Darah Lansia di Puskesmas Kahuripan Kota Tasikmalaya. *Heal Tadulako J (Jurnal Kesehat Tadulako)*. 2022;8(2):114-119. doi:10.22487/HTJ.V8I2.511
30. Handayani F, Bintang AK, Kaelan C. Hubungan Hipertensi, Diabetes Mellitus Dan Dislipidemia Dengan Luaran Klinis Pasien Iskemik Stroke Dengan Hipersomnia. *Heal Tadulako*. 2018;4(1):1-6. Accessed September 8, 2019. http://jurnal.untad.ac.id/jurnal/index.php/HealthyTadulako/article/view/10192