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The relationship between LDL-c and platelet count with lacunar stroke findings on brain MRI

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ABSTRACT

Objectives. Lacunar stroke or cerebral small vessel disease accounts for 15-30% of all ischemic stroke. The golden standard to identify lacunar stroke is by using MR imaging with diffusion-weighted imaging (DWI) sequence. In prior studies LDL-c and platelet count were described as contributing factors in lacunar stroke event. The aim of this study is to examine whether LDL-c and platelet value may have a contribution in lacunar stroke finding.

Methods. In cross-sectional study, we consecutively collected patients older than 18 years old who had undergone brain MRI and had their LDL-c and platelet count laboratory results and we also took their history of diabetes mellitus and hypertension to evaluate risk factor association.

Outcomes. We collected 93 patients who underwent brain MRI obtained lacunar stroke in 20 patients (21.5%) and non-lacunar stroke findings in 78.5%. We found no significant association between LDL-c and platelets with lacunar stroke findings in brain MRI. However we found that lacunar stroke findings had significant association with hypertension with $P < 0.05$.

Conclusion. LDL-c and platelets were not statistically significant in lacunar stroke findings in brain MRI, while hypertension was the risk factor associated with lacunar stroke event.

Keywords: lacunar stroke, LDL-c, platelets, hypertension, diabetes mellitus

INTRODUCTION

Stroke is a terminology to describe a sudden onset of a neurological event. Stroke can be classified into 3 main categories: atherosclerotic, cardioembolic and small vessel disease or lacunar stroke. Atherosclerotic stroke is often embolic originated from a thrombus. The most common place is in carotid bifurcation in which middle cerebral artery (MCA), posterior cerebral artery (PCA) and vertebrobasilar circulation are the most affected places, respectively [1].

Lacunar stroke or cerebral small vessel disease accounted 15-30% of all ischemic stroke. This subtype is a subcortical infarct due to single perforating artery occlusion with the lesion measured approximately 3-9 mm or 20 mm in numerous literature from axial reformatted images [1–3].

The golden standard to identify acute lacunar stroke is by using Magnetic Resonance (MR) imaging, especially with diffusion-weighted imaging (DWI) sequence. Lacunar stroke may be shown as having different pictures, depends on the pathogenesis including recent small subcortical infarcts, lacunes/cavities, white matter hyperintensities (WMH), enlarged perivascular space and microbleeds [3,4]. The lacunes may be shown as a round or oval subcortical lesion measured approximately 3-15 mm, consistent with one of the perforating arteriole [3].

Low density lipoprotein cholesterol (LDL-c) may have a role in lacunar stroke pathogenesis, as the main atherogenic lipoprotein. According to the study conducted by Matz et al, LDL value is higher in patients with nocturnal stroke [5] In other studies, significantly increasing LDL-c may be a risk factor on patients with atherothrombotic stroke, associated with the location of the lacunar stroke in cortical areas or internal capsule [5–8].

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Besides LDL, platelet may also contribute in lacunar stroke event. Platelet is the key mediator in plaque rupture and atherothrombosis. [9] According to Kim et al, stroke could be caused by several process in which one of them was thromboembolic event by platelet aggregation or activation [10].

Lacunar stroke may be treated the same as another ischemic stroke. The primary prevention is to avoid developing risk factors like hypertension, diabetes mellitus, dyslipidemia, and smoking. If a hyperacute condition occurs, airway, hemodynamic, intracranial pressure should be monitored accordingly. Thrombolysis may be the treatment of choice if the onset is within 4.5-6 hours, not including wake up stroke. If the onset is more than 6 hours, routine anticoagulant and antiplatelets are recommended, and statins as lipid lowering agents are given if LDL-c is above 150 mg/dL [11].

The aim of this study is to examine whether LDL-c and platelet value may have a contribution in lacunar stroke finding.

METHODS

In this cross-sectional study, we consecutively collected patients in Radiology Department Prof. Dr. IGNG Ngoerah Hospital, Denpasar Bali between January to June 2022. We enrolled patients with older than 18 years old who had undergone brain MRI and had their LDL-c and platelet count within the sampling time period. The exclusion criterion was incomplete medical record. The following variables were recorded from each patient: age, gender, history of diabetes mellitus, hypertension, lipid-lowering agent and anti-platelet consumption.

Lacunar stroke findings in MRI including recent small subcortical infarct, lacunes/cavities, white matter hyperintensities (WMH), enlarged perivascular space and microbleeds with <20 mm in size [3]. LDL-c was classified into normal and high value based on a guideline by Indonesian Association of Endocrinology. Less than 160 mg/dL was normal, and more than 160 mg/dL was high [12]. Platelet count was grouped based on our center's standard, in which >440.000/uL were high and otherwise were normal. The statistical analysis was done by using IBM SPSS 25.0.

This study was approved by the ethics committee of Universitas Udayana – RSUP Prof. Dr. IGNG Ngoerah. All study procedures were performed in accordance with the ethical standards.

The data was obtained from the medical record. Distribution of patient characteristics and risk factors among patients with brain MRI results were compared. Numerical variables were described as mean ± standard deviation (SD). Categorical variables were described as percentage and analyzed based on the Fisher's exact test. Sociodemographic, clinical characteristics and risk factors of patients with brain MRI results, were also analyzed by logistic regression.

RESULTS

TABLE 1. Demographic and clinical characteristics

Variable	N=93
Age (years) mean ± SD	51.3±14.4
Gender	
Male	48 (51.6%)
Female	45 (48.4%)
Lipid-lowering agent therapy	
Yes	25 (26.9%)
No	68 (73.1%)
Anti-platelet therapy	
Yes	21 (22.6%)
No	72 (77.4%)
History of Diabetes mellitus	
Yes	14 (15.1%)
No	79 (84.9%)
History of Hypertension	
Yes	25 (26.9%)
No	68 (73.1%)

Demographic and clinical characteristics of this study were shown in table 1. We acquired mean age ± SD was 51.3±14.4 years old with 48 male (51.6%) and 45 female (48.4%). Patients on lipid-lowering agents, anti-platelet therapy, had history of diabetes mellitus and had history of hypertension were 14 (15.1%), 21 (22.6%), 14 (15.1%) and 25 (26.9%) respectively.

TABLE 2. Lacunar stroke findings proportion

Variable	N=93
Lacunar stroke findings	20 (21.5%)
Non lacunar stroke findings	73 (78.5%)

Lacunar stroke findings may be seen in table 2. Based on the results of brain MRI, we obtained lacunar stroke in 20 patients (21.5%) and non-lacunar stroke findings in 78.5%.

TABLE 3. LDL-c dan Platelets laboratory findings

Variable (n=93)	Mean ± SD
LDL-c (mg/dL)	126.9 ± 35.0
Platelets (10^3/µL)	311.6 ± 98.7

LDL-c and platelets laboratory results have shown that the average of LDL was 126.9 ± 35.0 mg/dL and platelets were 311.6 ± 98.7 10^3/μL.

TABLE 4. Lacunar stroke findings and LDL-c relationship

Variable (n=93)		Lacunar Stroke		p
		Yes	No	
LDL-c	High	2 (10%)	18 (90%)	0.224
	Normal	18 (24.7%)	55 (75.3%)	

Table 4 categorized LDL-c results into high (>160 mg/dL) and normal (<160 mg/dL). We obtained patients with lacunar stroke findings and high LDL in 2 patients (10%), but there was no association between lacunar stroke findings and LDL-c results with P value > 0.05 (0.224).

TABLE 5. Lacunar stroke findings and platelet relationship

Variable (n=93)		Lacunar Stroke		p
		Yes	No	
Platelet	High	3 (20%)	12 (80%)	1.000
	Normal	17 (21.8%)	61 (78.2%)	

TABLE 6. Lacunar stroke findings and gender relationship

Variable (n=93)		Lacunar Stroke		p
		Yes	No	
Gender	Male	11 (22.9%)	37 (77.1%)	0.804
	Female	9 (20%)	36 (80%)	

TABLE 7. Lacunar stroke findings and age relationship

Variable (n=93)		Lacunar Stroke		p
		Yes	No	
Age	Adult	16 (23.2%)	53 (76.8%)	0.578
	Older adult	4 (16.7%)	20 (83.3%)	

TABLE 8. Lacunar stroke findings and lipid-lowering agent relationship

Variable (n=93)		Lacunar Stroke		p
		Yes	No	
Lipid lowering agent	Yes	8 (32%)	17 (68%)	0.159
	No	12 (17.6%)	56 (82.4%)	

TABLE 9. Lacunar stroke findings and anti-platelet relationship

Variable (n=93)		Lacunar Stroke		p
		Yes	No	
Anti-platelet	Yes	11 (52.4%)	10 (47.6%)	0.000
	No	9 (12.5%)	63 (87.5%)	

TABLE 10. Lacunar stroke findings and diabetes mellitus relationship

Variable (n=93)		Lacunar Stroke		p
		Yes	No	
Diabetes Mellitus	Yes	3 (21.4%)	11 (78.6%)	1.000
	No	17 (21.5%)	62 (78.5%)	

TABLE 11. Lacunar stroke findings and hypertension relationship

Variable (n=93)		Lacunar Stroke		p
		Yes	No	
Hypertension	Yes	9 (36%)	16 (64%)	0.041
	No	11 (16.2%)	57 (83.8%)	

This study was analyzed comparatively by using Fisher exact test in patients with lacunar stroke findings and platelets, gender, antiplatelet and lipid-lowering agent consumption, diabetes mellitus and hypertension. According to our comparative study, there was significant association between lacunar stroke findings and patients with anti-platelet consumption P < 0.05 (0.000). We also found that lacunar stroke findings had significant association with hypertension with P < 0.05 (0.041). On the other hand, there was no significant association with the other variables (platelet, age, gender, lipid-lowering agent and diabetes mellitus).

TABLE 12. Multiple logistic regression of risk factors associated with lacunar stroke findings

		CI 95%		
	OR	Min	Max	P value
Gender	1.143	0.378	3.460	0.813
Age	1.630	0.435	6.110	0.469
Diabetes mellitus	0.438	0.078	2.456	0.348
Hypertension	4.629	1.331	16.098	0.016
LDL-c	0.251	0.049	1.290	0.098
Platelet	1.072	0.238	4.829	0.928

Multiple logistic regression showed the factor that independently associated with the lacunar stroke findings was hypertension. The other variables such as gender, diabetes mellitus, age, LDL-c and platelet showed no association.

DISCUSSION

Subjects of this study have average age of 51.3±14.4 years old. While our subjects were mostly under 60 years old, this was consistent with prior study by Cai et al, in which they stated that lacunar stroke prevalence increase before 60 years old and decline after more than 69 years old. This is proba-

bly due to the evolution of lacunar lesion to be a cavity, in which they will be absorbed gradually as the time goes by. It is also mentioned that people under 60 years old are more prone to get lacunar stroke [13].

Gender proportion in this study was male predomination (51.6% vs 48.4%), but no statistical significance was found between gender and lacunar stroke. This was not consistent with the prior study by Harris et al in Indonesia, in which they found male was associated with lacunar stroke (P<0.05). Male has higher risk to get lacunar stroke because of the risk factors such as hypertension and atherosclerotic disease are more common in male, but the proportion would be the same after menopause in female [7].

The main variables of this study were LDL-c and platelets in patients with lacunar stroke. LDL-c was one of the main contributors (besides HDL and triglycerides) in dyslipidemia [14]. Our study found that there are no association between LDL-c with lacunar stroke (P>0.05). Role of dyslipidemia in accordance with lacunar stroke were not consistent, in one study it is stated that LDL-c may contribute in atherosclerosis and have a very important role in ischemic stroke. However Mok et al stated that high LDL-c may have a protective role in incidental lacunar stroke findings (3-10 mm) [15,16]. We also did not found significant association between platelets and lacunar stroke findings, knowing the platelet role in focal cerebral ischemia and thromboembolic events [17]. Sadeghi et al, stated that high Mean Platelet Volume (MPV) that had significant association with ischemic stroke event, and low platelet count associated with acute stroke and hemorrhagic stroke event [18].

Meanwhile, in our study hypertension was associated with lacunar stroke event, in accordance with the study by Pu et al, which stated hypertension as risk factor had higher correlation with lacunar infarct compared with large artery atherosclerosis [19]. However in contrast with hypertension, the association of diabetes mellitus and lacunar stroke was not statistically significant. This was not consistent with prior studies, probably due to small subject samples and successful medical intervention was done to control blood glucose, because Tali et al. stated that low capillary perfusion and direct brain damage occurred in hyperglycemic state, with blood glucose level more than 190 mg/dL. This may also be seen in people with high A1C level [20]. Besides, in our center CT scan was the first-line diagnostic procedure in acute stroke setting, while brain MRI were done afterwards, therefore the patients were already on medication for their risk factors as the lacunar stroke diagnosis made by brain MRI [7].

Compared to patients receiving antiplatelet agents, the association between lipid-lowering agent medication and lacunar stroke findings was not statistically significant. This was probably because we did not trace the initial and therapy duration after the lacunar stroke onset. In prior study, The Cardiovascular Risk Factors and the Aging and Incidence of Dementia MRI substudy showed that the consumption of lipid-lowering agent was associated with lower WMH-type lacunar stroke incidence, while in the study by The Stroke Prevention by Aggressive Reduction of Cholesterol Level Stroke (SPARCL) which compared 80 mg Atorvastatin and placebo in patients with stroke or TIA with LDL-c >100 mg/dL, resulted in 80 mg per day Atorvastatin may reduce recurrent stroke risk, but in small vessel disease patients, no significant lowering of recurrent stroke incidence [4,11].

This study had data limitation in patients with lipid-lowering agent medications, so that in the next study, baseline LDL-c laboratory result must be taken before the therapy, also the dose and duration of the treatment must also be recorded. It is also encouraged for the next research samples should be taken from patients with brain MRI as the first line diagnostic imaging for acute stroke and larger sample size.

CONCLUSION

In conclusion, lacunar stroke proportion in this study was 21.5%, LDL-c and platelets were not statistically significant in lacunar stroke findings in brain MRI, while hypertension was the risk factor associated with lacunar stroke event.

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