Correlation Between Blood Glucose And Low-Density Lipoprotein Level With Pulsatility Index Of Intracranial Arteries Evaluated By Transcranial Color-Coded Duplex Ultrasonography

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ABSTRACT

Introduction : Pulsatility index (PI) measures the vascular resistence distal to the examined artery. PI of intracranial arteries may predict the future cerebrovascular event. High blood-glucose and low-density lipoprotein (LDL) level are the known risk factor for atherosclerosis. However, there were few studies which describe the correlation of the two in Indonesia. This study aimed to analyze the correlation between plasma blood-glucose and low-density lipoprotein (LDL) level and PI of intracranial arteries (right and left anterior cerebral arteries, right and left middle cerebral arteries, right and left posterior cerebral arteries, right and left vertebral arteries, and basilar artery) examined by transcranial color-coded duplex ultrasonography (TCCD)

Methods : This study is a Cross Sectional Study Design in Dr. Kariadi Hospital within Januari until December 2018. Fourty-eight patients (n = 48) who underwent a TCCD examination were tested for blood-glucose and LDL level. Normality of the data were tested using Saphirowilk, then the correlation tested using Spearman's rank correlation test.

Results : There were significant correlation between both blood-glucose or LDL level with PI of intracranial arteries (all $p < 0.05$).

Conclusions : blood glucose and LDL level is associated with PI of intracranial arteries.

Keywords : blood-glucose, low density lipoprotein, pulsatility index, vascular resistence, ischemic stroke.

Introduction

Ischaemic stroke accounts for about 80% of all stroke cases. The mortality and morbidity leaves a burden for human productivity. The prevention strategies to reduce the burden have been developed. Yet, screening modality for brain vessels have not been so popular, especially in developing country.

High blood-glucose and low-density lipoprotein (LDL) level are the known risk factor for atherosclerosis. The association of the two with cerebrovascular eventhavebeenwell-recognized.(1)Havingbloodglucose and LDL level in control have been the most popular prevention strategy, yet no one knows what have been happened with the vasculature. While MRI-and CT scan- based angiography have been a well-known methods to evaluate intracranial arteries, their high-cost and availability issue may become a challenge in developing countries. Alternatively, transcranial Doppler (TCD) ultrasonography provides cost-effective examination to evaluate physiological disorder of intracranial vasculatures.

Pulsatility index (PI) measures the vascular resistance distal to the examined artery. PI of intracranial arteries may predict the future cerebrovascular event. Lower PI may indicate lower resistance of the vascular beds with higher diastolic flow. On the opposite, higher PI may indicate higher resistance beds with lower diastolic flow. Some vascular condition, such as lipohyalinosis and atherosclerosis may narrow the lumen of distal arteries which increases the resistance of the vascular beds. Suchconditionmayuprise PI oftheexaminedarteryusingTrancranialColor-Coded Duplex Ultrasonography (TCCD).(2)

TCD examination may provide valuable screening modality for those who have uncontrolably high blood glucose and/or LDL level. However, there were few studies which describe the correlation of the blood glucose and LDL level with PI in Indonesia.This study aimed to analyze the correlation between plasma blood-glucose and low-density lipoprotein

(LDL) level and PI of intracranial arteries (right and left anterior cerebral arteries, right and left middle cerebral arteries, right and left posterior cerebral arteries, right and left vertebral arteries, and basilar artery) examined by transcranial color-coded duplex ultrasonography (TCCD).

Materials and Methods

This cross sectionalstudywasconducted in drKariadi Hospital within Januari until December 2018. Subjects of the study were patients who underwent a TCCD examination, and recruited consecutively. The inclusion criterias were (1) patient aged 40 to 80 year old, (2) patient who underwent TCCD examination, (3) the patient should be willing to participate in this study. The exclusion criterias were (1) patient who had controlled blood glucose and LDL level by medications for the last one year, (2) patient who had history of any cerebrovascular event.

Prior to examination, informed consent was obtained from all of the participants. Blood samples of patients matched with those criterias were obtained intravenously prior to the TCCD examination and tested for blood glucose and LDL level. We took TCCD examination for following arteries: (1) Anterior Cerebral Artery – right (ACA-R) and left (ACA-L); (2) Middle Cerebral Artery – right (MCA-R) and left (MCA-L); (3) Posterior Cerebral Artery – right (PCA-R) and left (PCA-L); (4) Vertebral Artery – right (VA-R) and left (VA-L); and (5) Basilar Artery (BA). All arteries were examined using each appropriate acoustic windows.

All of the data were obtained and recorded. SPSS version 21.00 was used to calculate the statistics analysis. Normality of the data were tested using Saphiro-Wilk, then the correlationswere tested using Spearman’s rank correlation test. Statistically significant was defined as $p < 0.05$.

Results

There were 48 patients who were willing to participate in the study, with 22 of them were male (45.83%) and 26 were female (54.17%).Blood glucose, LDL level,obtained from laboratory examination, and all PI of intracranial arteries, obtained by TCCD, are showed in Table I.

Tabel I. Demographic profiles of all subjects

No	**Variables**	**mean**	**±**	**SD**	**n**	**(%)**
1	Age	59.25	±	9.690		
2	Sex					
	Male				22	(45.83%)
	Female				26	(54.17%)
3	Glucose	199.4167	±	63.185		
4	LDL	177.38	±	29.152		
5	PI					
	ACA – R	1.47	±	0.453		
	ACA – L	1.24	±	0.370		
	MCA – R	1.43	±	0.520		
	MCA – L	1.27	±	0.237		
	PCA – R	1.35	±	0.302		
	PCA – L	1.22	±	0.344		
	VA – R	1.32	±	0.412		
	VA – L	1.22	±	0.391		
	BA	1.29	±	0.361		

LDL = Low Density Lipoprotein; PI = Pulsatility Index; ACA = Anterior Cerebral Artery; MCA = Middle Cerebral Artery; PCA = Posterior Cerebral Artery; VA = Vertebral Artery; BA = Basilar Artery; R annotation indicate right arteries, while L indicate left arteries.

We analysed the correlation of each PI with both blood-glucose and LDL level. There were statistically significant correlation between blood-glucose or LDL level with PI of intracranial arteries (all $p < 0.05$).The analysis results are provided in Table II. The graphs of correlation between each artery's PI and blood glucose (Fig. 1) and LDL (Fig. 2) level are also presented.

Table II. Corellation analysis of each PI with both blood-glucose and LDL level

No	Artery	Blood Glucose		LDL	
		p	r	p	r
1	ACA-R	<0.001*	0.587	0.001*	0.456
2	ACA-L	<0.001*	0.496	0.037*	0.303
3	MCA-R	0.003*	0.419	0.013*	0.355
4	MCA-L	0.004*	0.412	<0.001*	0.495
5	PCA-R	0.006*	0.390	0.042*	0.295
6	PCA-L	0.031*	0.312	0.039*	0.299
7	VA-R	0.046*	0.290	0.027*	0.319
8	VA-L	0.035*	0.305	0.003*	0.414
9	BA	0.003*	0.419	0.048*	0.287

*p value is significant
LDL = Low Density Lipoprotein; PI = Pulsatility Index; ACA = Anterior Cerebral Artery; MCA = Middle Cerebral Artery; PCA = Posterior Cerebral Artery; VA = Vertebral Artery; BA = Basilar Artery; R annotation indicate right arteries, while L indicate left arteries.

Discussion

This study show us the correlation of blood glucose and LDL level with increased resistence of intracranial arteries. Thesefindingssupportthatriskfactors, bloodglucoseand LDL, haverole in theprocessofnarrowingintracranialbloodvessel lumen, as measuredbyincreased PI, whichpredictthefuturecerebrovascularevents. TCD has demonstrated theassociation between various risk factors and small vessel disease.(3)This relationship also has beenconfirmed by MRI findings including periventricular hyperintensity, deep white matter hyperintensity, lacunardisease, andpontinehyperintensity.(2)Pathologically, thesmallvesseldiseaseisresulted from processsuch as stretching, necrosis, calcification, fibrosis, andhypertrophyofendotheliumandsmoothmusclecells.(4)Lipohyalinosisandatherosclerosismay result from increasedbloodglucoseand LDL level.

Park etaldemostratedthatPI wassignificantlyhigher in diabeticpatients ($p < 0.05$) andalso, in diabeticpatient, washigher in patientswith insulin resistancethan in patientswhostillinsulin sensitive ($p < 0.05$). Their study alsofoundassociationbetweenhigher PI andlongerdurationof diabetes ($R = 0.264$, $p = 0.025$).(5) Lee etal in 2007 alsofoundthatdiabeticpatientwithcomplication had higher PI thandiabeticpatientwithoutcomplication (p <

0.001).[6]Thesefindingsandoursconfirmthatbloodglucosemaycontribute in smallvesseldiseaseofintracranialarteries.

Jeongetalfoundthat PI wassignificantlyhigher in patientswithhyperlipidemia (total cholesterol level>220 mg/dLorlow-density lipoprotein cholesterol level >160mg/dL.) (p = 0.003).[7]However, Farhoudietalfoundthatresistence indeks ratherthanPI wassignificantlyhigher in patientswithhigherlevelsof LDL (180 mg/dL).[8]Our findingssupportthat LDL level isassociatedwith PI in thewayofhigher LDL level contribute in higher PI.

Otherthanbloodglucoseand LDL level, PI ofintracranialarteriesalsofoundtoberelatedwithage[3,7,9], hypertention[10], obesity[11], andangiopathy[9]. All ofthesefindingssuggestthat TCD maybe a valuableassessment in reassuringpeoplewithsuchriskfactorstoevaluateintracranialsmallvesseldisease.

Our study had somelimitations. Our study obtained data from crosssectionalpointofview, which limit theprogressionobservationoftheintracranialsmallvesseldisease in associatedwithincreasedbloodglucoseand LDL level. This study designmaylack in seeing long term status ofbloodglucoseand LDL level ofthe study participants. However, wepushedourbesttoselectparticipantswho had not takenmedicationforcontrollingtheirbloodglucoseand LDL level tosimulatethecondition. Our study alsomayhavesmallsizeof participants. Thismayaffectthereflectionoflargerpopulation.

Conclusions

This study show that blood glucose and LDL level is associated with PI of intracranial arteries. In the perspective of ischaemic stroke prevention, it is motivated to all patients with uncontrolled blood glucose and LDL level to be screened using TCD examination. Further study is encouraged to have larger sample size. We also need to observe in population with controlled blood glucose and LDL level to see if the preventive strategy of ischaemic stroke also affect the parameters of TCD.

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References

1. Harris S, Reyhan T, Ramli Y, Prihartono J, Kurniawan M. Middle Cerebral Artery Pulsatility Index as Predictor of Cognitive Impairment in Hypertensive Patients. Front Neurol. 2018;9:538.
2. Ghorbani A, Ahmadi MJ, Shemshaki H. The value of transcranial Doppler derived pulsatility index for diagnosing cerebral small-vessel disease. Adv Biomed Res. 2015;4:54.
3. Lee KY, Sohn YH, Baik JS, Kim GW, Kim JS. Arterial Pulsatility as an Index of Cerebral Microangiopathy in Diabetes. Stroke. 2000;31:1111-1115.
4. Kim Y, Lee H, An SA, et al. The Effect of Pulsatility Index on Infarct Volume in Acute Lacunar Stroke. Yonsei Med J. 2016;57(4):950-955.
5. Park JS, Cho MH, Lee KY, et al. Cerebral arterial pulsatility and insulin resistance in type 2 diabetic patients. Diabetes res clin pract. 2008;79:237–242

6. Lee KO, Lee KY, Lee SY, Ahn CW, Park JS. Lacunar Infarction in Type 2 Diabetes Is Associated with an Elevated Intracranial Arterial PulsatilityIndeks. Yonsei Med J. 2007;48(5):802 - 806
7. Jeong HT, Kim DS, Kang KW, Nam YT, Oh JE, Cho EK. Factors Affecting Basilar Artery Pulsatility Index on Transcranial Doppler. Korean J Clin Lab Sci. 2018;50(4):477-483.
8. Farhoudi M, Mehrvar K, Aslanabadi N, Ghabili K, Baghmishe NR, Ilkhchoei F. Doppler study of cerebral arteries in hypercholesterolemia. Vasc Health Risk Manag. 2011:7 203–207.
9. Sanahuja J, Alonso N, Diez J, etal.IncreasedBurdenofCerebralSmallVesselDisease in PatientsWithType 2 DiabetesandRetinopathy. Diabetes care. 2016;39(9):1614-20.
10. Chuang SY, Cheng HM, Bai CH, Yeh WT, Chen JR, Pan WH. Blood Pressure, Carotid Flow Pulsatility, and the Risk of Stroke: A Community-Based Study. Stroke. 2016;47:2262-2268.
11. Ozari HO, Oktenli C, Celik S, et al. Are Increased Carotid Artery Pulsatility and Resistance Indexes Early Signs of Vascular Abnormalities in Young Obese Males? J Clin Ultrasound 2012;00:000–000.

Figure Legends

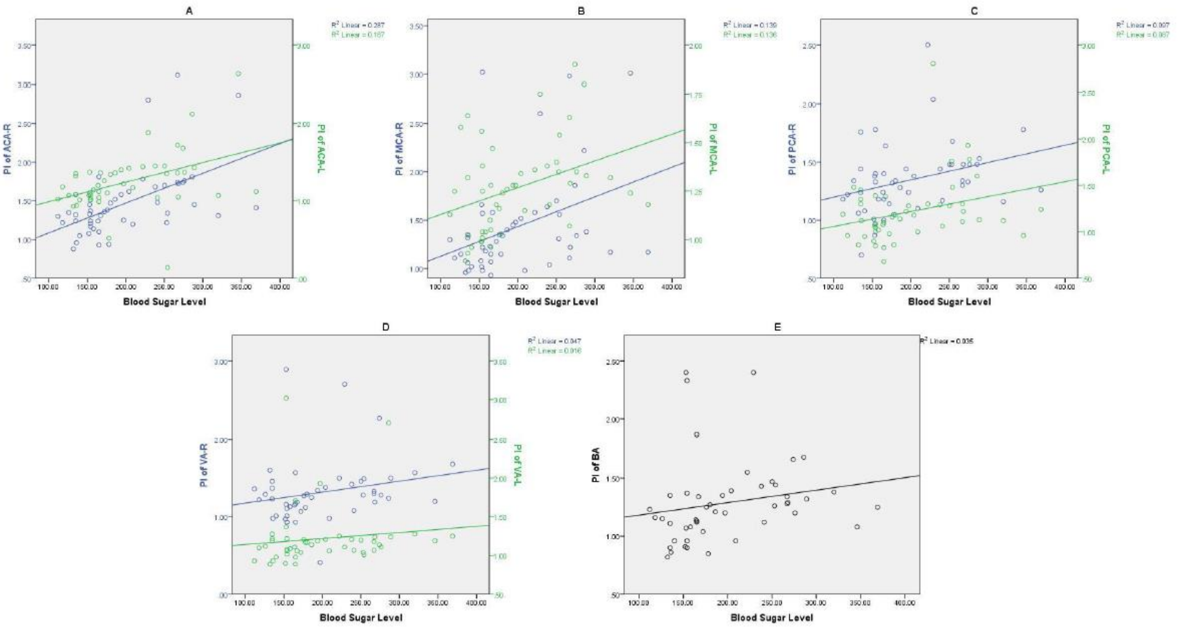

Figure 1. Correlationbetweeneachartery's PI andbloodglucose level

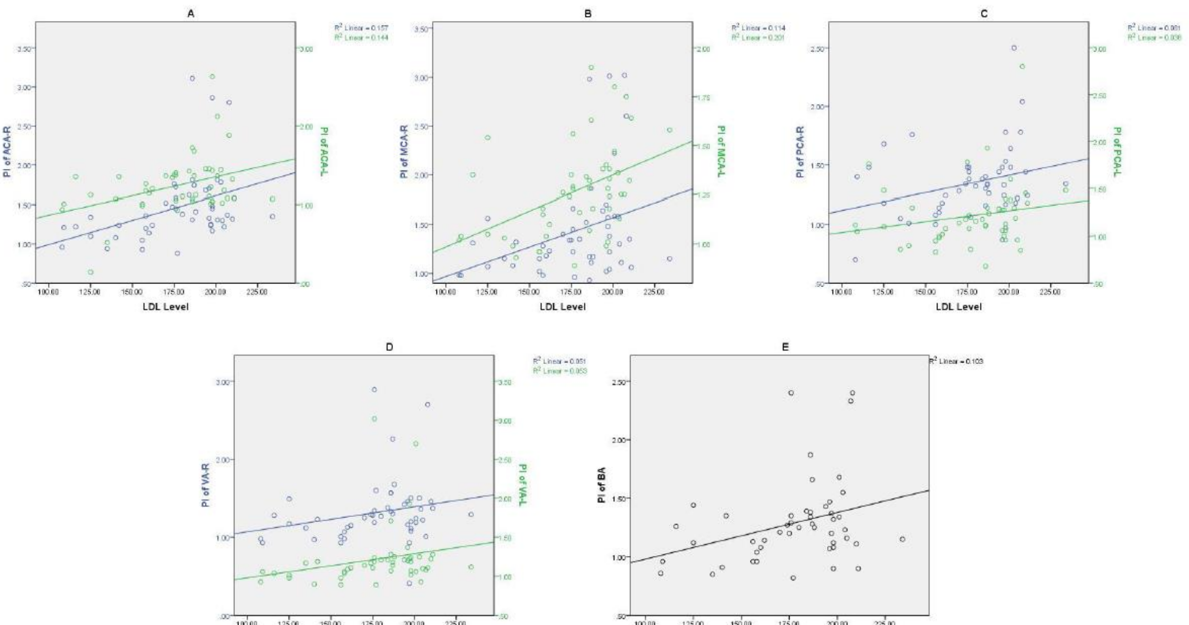

Figure 2. Correlationbetweeneachartery's PI and LDL level