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RESEARCH ARTICLE

Correlation Abnormal Ankle-Brachial Index and Multivessel Coronary Artery Disease in Acute Coronary Syndrome Patients

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Abstract

BACKGROUND: Many studies showed the association between peripheral artery disease (PAD) and coronary artery disease (CAD). The ankle-brachial index (ABI) was a simple, noninvasive, and not expensive test that showed high sensitivity and specificity in the diagnosis of PAD. Previous studies showed PAD correlation with the number of coronary artery lesions and higher complexity of the lesions. These correlations might contribute to worse cardiovascular outcomes, especially acute coronary syndrome (ACS) cases. Aim of this study is to evaluate the correlation abnormal ABI with the risk of ACS patients to have multivessel coronary artery lesions.

METHODS: This was a retrospective analytical case control study. The data were taken from Dr. Wahidin Sudirohusodo Hospital medical records from November 2015 to February 2016. The inclusion criteria were (>18 years old) patients with ACS who had underwent ABI examination and coronary angiography.

RESULTS: The prevalence of patients with ST-elevation myocardial infarction (STEMI) was lower than non-ST elevation ACS (NSTE-ACS). The prevalence of patients with abnormal ABI was 43.3% and patients with multivessel CAD was 65%. Male patients dominated the ACS population with 73.3%, about half of patients were smoking, and 86.7% had dyslipidemia. Patients with abnormal ABI and multivessel disease had greater number than patients with normal ABI (p=0.025). Analysis with binary logistic regression model showed abnormal ABI (odd ratio [OR] 4.83; p=0.021) and male sex (OR 19.35; p=0.010) were associated with greater risk of multivessel CAD.

CONCLUSION: An abnormal ABI is associated with greater risk of multivessel CAD in ACS patients.

KEYWORDS: ankle-brachial index, multivessel, coronary, acute coronary syndrome

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Introduction

Atherosclerosis had become one of the leading cause of death in the world.(1) It has three main manifestations which involve coronary, cerebrovascular and peripheral arteries. Many studies had shown the association between these artery diseases, including the peripheral artery disease (PAD) and coronary artery disease (CAD).(2) The association between the PAD, high risk cardiovascular events and death also have been proven.(3) However, most patients with PAD were underdiagnosed because the asymptomatic clinical presentation and the physician's awareness of the disease are relatively low.(4)

The ankle-brachial index (ABI), as a noninvasive and simple modality, have high sensitivity and specificity for PAD diagnosis. ABI is not only useful as a diagnostic tool, but also is a powerful indicator of atherosclerotic disease

in other vascular bed and prognostic modality (increased cardiovascular morbidity/mortality with low ABI).(5,6)

The previous studies have shown PAD correlation with the number of coronary artery lesions and the higher complexity of the lesions.(7,8,9) These correlations might contribute to worse cardiovascular outcomes, especially the acute coronary syndrome (ACS) cases. The aim of this study is to evaluate the correlation abnormal ABI with the risk of ACS patients to have multivessel coronary artery lesions.

Methods

This was a retrospective analytical case control study. The data were taken from Dr. Wahidin Sudirohusodo Hospital medical records since November 2015 until February 2016. In Dr. Wahidin Sudirohusodo Hospital, we performed ABI examination in patients with CAD.

ACS patients (>18 years old) who underwent coronary angiography and had the ABI examined previously were included. The exclusion criteria were patients with non-atherosclerotic ACS, clinically suspected or history of congenital vascular abnormalities (*e.g.,* coarctation aorta) and ABI value >1.4. The Health Research Ethics Board of the Hasanuddin University approved the research protocol (Number: 676/H04.8.4.5.31/PP36-KOMETIK/2016).

Patients were categorized as abnormal ABI if the ABI ≤0.9. Significant coronary stenosis was defined as the presence of coronary artery stenosis ≥50% of epicardial coronary artery, and we classified the patient into group with multivessel CAD if there were involvement of at least two main vessels and/or the left main coronary artery.

The differences characteristic data between two dependent (multivessel diseases) groups, nominal and numerical data were examined using Chi-Square and Independent Sample T-Test, respectively. A binary logistic regression model was used to determine the relationship between independent variable and multivessel CAD. Significance was set at $p<0.05$. All calculations were performed using SPSS version 18.0 software for Windows.

Results

The baseline characteristics of the study population are listed in Table 1 and Table 2. Sixty patients who were hospitalized due to ACS at Dr. Wahidin Sudirohusodo Hospital, underwent coronary angiography. The prevalence

Table 1. Baseline characteristics of categorical variables (n=60).

Characteristic	Category	n	%
ACS Diagnosis	STEMI	27	45
	NSTEMI	27	45
	UAP	6	10
Abnormal ABI	Yes	26	43.3
	No	34	56.7
Multivessel CAD	Yes	39	65
	No	21	35
Sex	Male	44	73.3
	Female	16	26.7
Smoking	Yes	32	53.3
	No	28	46.7
Family History	Yes	4	6.7
	No	56	93.3
History of Stroke	Yes	2	3.3
	No	58	96.7
History of CAD	Yes	25	41.7
	No	35	58.3
Hypertension	Yes	29	48.3
	No	31	51.7
Dyslipidemia	Yes	52	86.7
	No	8	13.3
Diabetes Mellitus	Yes	19	31.7
	No	41	68.3
Number of Lesion	Non-significant	5	8.3
	1 Vessel Disease	16	26.7
	2 Vessel Disease	15	25
	3 Vessel Disease	24	40
Coronary Lesion	Left Main	9	15
	LAD	46	76.7
	LCX	29	48.3
	RCA	36	60

ACS: acute coronary syndrome; STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; UAP: unstable angina; ABI: ankle-brachial index; CAD: coronary artery disease; LAD: left anterior descending; LCX: left circumflex atery; RCA: right coronary artery.

of patients with ST-elevation myocardial infarction (STEMI) (45%) was lower than non-ST elevation ACS (NSTE-ACS) (55%). ACS patients with abnormal ABI (43.3%) had lower numbers than the normal ones. Meanwhile patients with multivessel CAD had higher prevalence (65%). Male patients dominated the ACS population with 73.3% and about half of patients were smoker. The majority of the sample had dyslipidemia (86.7%). Left Anterior Descending (LAD) coronary artery was the most frequent coronary stenosis involved (76.7%).

The mean age was 54.13 years old and mean blood pressure was 137.00/84.16 mmHg. The highest random blood glucose level was 433mg/dL. We found that high total cholesterol (mean=204.16mg/dL), low HDL (mean=39.76mg/dL), and high triglyceride (mean=154.13mg/dL) were consistent with high number of dyslipidemia prevalence.

Among several variables that had been evaluated, only abnormal ABI value showed significances. The prevalence of patients with multivessel CAD was found higher in patients with abnormal ABI than patients with normal ABI (p=0.025) (Table 3). Analysis with binary logistic regression model showed that abnormal ABI (odds ratio [OR] 4.83; p=0.021) and male sex (OR 19.35; p=0.010) were associated with a greater risk of multivessel CAD (Table 4).

Discussion

Total ACS patients that had been hospitalized since November 2015 until February 2016 were 159 patients, but only 37.7% (60 patients) underwent coronary angiography due to financial problem/insurance and/or patient refused the procedure. The prevalence of STEMI in this study was quite high (45%), whereas in the US approximately 30% of ACS patients had STE-ACS (10), but the result was consistent with several previous studies in Makassar, Indonesia. Even in Brazil, the prevalence of patients with STEMI was higher (57%) than patients with NSTE-ACS (11).

The prevalence of multivessel CAD in ACS patients was higher than one vessel disease or non-significant stenosis as have been reported in many studies. Similar finding is also proved in our study that patients with abnormal ABI had higher prevalence of multivessel CAD than those with normal index (p=0.025).

In high risk CAD patients (and also already known CAD), the prevalence of abnormal ABI is higher than those in general population, which is up to 42% (12,13), in our study the prevalence was 43.3%. The data in sub-analysis of The Global Registry of Acute Coronary Events (GRACE) study, the prevalence of PAD was only 9.7% out of 41,108 patients admitted with ACS.(14) It was likely that PAD was underdiagnosed in the study because the PAD patients included were only those in whom diagnosis had already been made, whereas about half of patients with PAD are asymptomatic. Another study analyzed the presence of PAD by measuring the ABI in patient with ACS, the study only identified 26% patients.(15) This finding almost 50% lower than ours, this is probably because our study had no upper limit of ages. As other study reported, PAD or abnormal ABI was more frequent in older group patients.(16) Another reason that made our prevalence of abnormal ABI relatively high was the measurement of ABI. We used lower ABI (more patients would be identified), because it has better sensitivity and it was a good predictor for PAD.(17)

Sex (male) had been established in another study to be associated with the presence of multivessel CAD (18), but in our study its statistically significances showed only with another variable in binary logistic regression. This might be

Table 2. Baseline characteristics of categorical variables (n=60).

Characteristic	Mean±SD	Min	Max
Age (years old)	54.13±9.07	32	73
Systolic Blood Pressure (mmHg)	137±28.48	80	240
Diastolic Blood Pressure (mmHg)	84.16±12.79	60	120
Random Blood Glucose (g/dL)	171.71±93.32	67	433
Total Choleserol (mg/dl)	204.16±52.34	99	401
HDL (mg/dl)	39.76±10.63	18	69
LDL (mg/dl)	139.9±51.37	45	368
Tryglyseride (mg/dl)	154.13±77.26	60	548

Table 3. Association between independent and control variable to dependent variable (n=6).

Variable	Category	Multivessel		*p*
		Yes	No	
Sex	Male	31	13	0.14
	Female	8	8	
Smoking	Yes	21	11	0.91
	No	18	10	
Hypertension	Yes	20	9	0.53
	No	19	12	
Dyslipidemia	Yes	33	19	0.52
	No	6	2	
Diabetes Mellitus	Yes	13	6	0.71
	No	26	15	
History of Hypertension	Yes	24	12	0.74
	No	15	9	
History of Diabetes Mellitus	Yes	12	5	0.57
	No	27	16	
Family History	Yes	3	1	0.66
	No	36	20	
History of Stroke	Yes	2	0	0.29
	No	37	21	
History of Dyslipidemia	Yes	3	1	0.66
	No	36	20	
History of CAD	Yes	17	8	0.68
	No	22	13	
Abnormal ABI	Yes	21	5	0.02
	No	18	16	

*Pearson chi-square test, significant if $p<0.05$

Table 4. Analysis comparison of abnormal ABI and control variable with multivessel CAD.

Variable	OR	*p*
Abnormal ABI	4.83	0.02
Hypertension	1.59	0.48
Smoking	0.30	0.20
Dyslipidemia	0.58	0.59
Diabetes Mellitus	0.94	0.93
Age	0.93	0.10
Sex	19.35	0.01

*Binary logistic regression test, significant if $p<0.10$

due to the population of the present study were not stable CAD and including myocardial infarct (MI) patients. The similar result from Chiha J, *et al.,* said that women had less severe CAD than men significantly, but not in MI patients.(18)

Our hypothesis had been proven in present study that abnormal ABI was an independent risk factor for multivessel CAD and it was associated with more prevalent multivessel CAD in ACS patients (OR 4.83; p=0.021).

The abnormal ABI represented stenosis of lower peripheral artery. The coexistence of PAD and CAD had been established by many previous studies, it caused the patient had higher inflammatory status, especially in circulation system. Brevetti G, *et al.,* evaluated PAD (ankle/brachial pressure index <0.9) and also measured plasma levels of C-reactive protein (CRP), interleukin-6 (IL-6), the soluble forms of intercellular adhesion molecule-1 (sICAM-1) and vascular cell adhesion molecule-1 (sVCAM-1) in 234 patients who underwent coronary angiography. After the adjustment for confounding factors, only PAD was independently associated with three-vessel CAD (p<0.001). This association was maintained after adjustment for IL-6, the only inflammatory parameter significantly associated with three-vessel CAD at univariate analysis (p<0.01).(19) Another study showed that the transfemoral gradients of neutrophil MPOx content and IL-6 were higher (p<0.01, for both) than in the healthy leg of CAD-only patients. At multivariate analysis, CAD+PAD patients with transfemoral gradients of MPOx and IL-6 higher than median value had a more compromised coronary artery endothelial function (p<0.05, for both).(20) This high inflammatory status would make the development of coronary atherosclerosis more progressive (21) and the coronary artery plaque will be more prone and become such vulnerable plaque, thus the risk of acute coronary events (*e.g.,* myocardial infarction) would be higher (20).

Conclusion

An abnormal ABI is associated with greater risk of multivessel CAD in ACS patients. An abnormal ABI should raise the suspicion of advanced disease, alerting the physicians and the patients of the need for more aggressive diagnostic, precise therapeutic and even earlier strategies for another high risk atherosclerotic disease cases or stable CAD/PAD, so the acute event can be prevented. Future studies are needed for further evaluation, whether the presence of peripheral inflammation plays a mechanistic role in CAD evolution.

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