

## The Risk Factors and Collateral System in Coronary Artery Disease among Patients in Bandung

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### Abstract

**Background:** The slow blood flow may cause atherosclerotic plaque, leading to an obstruction in the arterial circulation, and thus resulting in among others myocardial ischemia. There are many risk factors associated with the collateral system such as dyslipidemia, obesity, hypertension, diabetes mellitus, and smoking habit. This study aimed to determine the association between risk factors and collateral system in patients in Bandung.

**Methods:** This was an analytical cross-sectional study, using data of 186 medical records taken from Dr. Hasan Sadikin General Hospital in October 2013. The risk factors were assessed and the prevalence ratio reflected the association between the risk factors and the collateral system was analyzed.

**Results:** The study revealed no significant association between each risk factor and the collateral system, including obesity ( $p=0.690$ ), smoking ( $p=0.175$ ), dyslipidemia ( $p=0.747$ ), and diabetes mellitus ( $p=0.616$ ); however, only hypertension was associated ( $p=0.020$ ). Furthermore, no significant association was found between the number of risk factor and the collateral system ( $p=0.233$ ).

**Conclusions:** Of the risk factors published, only hypertension is a significant risk factor among patients in Bandung, while others including obesity, smoking, dyslipidemia and diabetes mellitus are not associated. Further study needs to be performed to explore other risk factors in coronary artery disease, and to prevent the disease among the population.

**Keywords:** Collateral, coronary artery disease, risk factor

### Introduction

Ischemic heart disease (IHD) is the major cause of death in the world.<sup>1</sup> According to the Ministry of Health Republic of Indonesia, cardiovascular disease, especially coronary artery disease (CAD), is the major cause of death in Indonesia and diabetes mellitus has been known as the highest co-morbidity for cardiovascular disease with 308 cases per 100.000 population.<sup>2</sup>

In more than 90% of cases, there is a lack of blood flow that causes an atherosclerotic plaque obstruction, leading to myocardial ischemia, known as an acute coronary syndrome or an acute myocardial infarct.<sup>1</sup> An adequate collateral system of coronary arteries may prevent myocardial ischemia.<sup>3,4</sup> However, the collateral system is sometimes affected by various risk factors such as dyslipidemia, obesity, hypertension, diabetes mellitus, and

smoking habit.<sup>5</sup>

The risk factors, consisting of behavioral factors and metabolic factors,<sup>6</sup> may affect the collateral systems in different ways. For example, a high level of lowdensity lipoprotein (LDL) is toxic for endothelial cells and smooth muscle cells; and inhibits the proliferation and migration of these cells. The oxidized LDL inhibits migration of vascular endothelial growth factor (VEGF) as an angiogenic agent.<sup>8</sup> Furthermore, smoking inhibits growth factor secretion that plays an important role in angiogenesis.<sup>8,9</sup> Other risk factor is hypertension which is characterized by a decrease in nitric oxide (NO) biosynthesis, and NO can disrupt the angiogenesis.<sup>10</sup>

The collateral system in diabetic patients is more pronounced compared to non-diabetic patients due to an impaired microvascular function.<sup>11</sup> Interestingly, obesity is associated with impaired coronary collateral vessel

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development, thus patients with diabetes mellitus have a more affected collateral system.<sup>12</sup> It is suggested that the more the risk factors, the more the collateral system is affected. This study aimed to determine the association between risk factors and collateral system in patients in Bandung.

### Methods

This was an analytical cross-sectional study involving data from medical records from January to December 2012, taken consecutively from the medical records archive at Dr. Hasan Sadikin General Hospital in October 2013. All patients diagnosed with CAD and had an angiographic examination were included. Clinical information, such as gender, age, and various risk factors known to influence the development of collaterals, including a history of hypertension, smoking habit, obesity, dyslipidemia, and diabetes mellitus were documented. Incomplete data on risk factors and angiographic examination were excluded. This study had been approved by the Health Research Ethics Committee.

To determine the quality of the collateral

systems in the angiograms, Rentrop Score was calculated by an experienced cardiologist interventionist. Patients were considered to have dyslipidemia when the total cholesterol level was  $\geq 200$  mg/dL, triglyceride  $\geq 200$  mg/dL, LDL  $\geq 130$  mg/dL, and High-Density Lipoprotein (HDL)  $< 40$  mg/dL.<sup>7</sup> Hypertension was defined as blood pressure  $\geq 140/90$  mmHg. Patients were considered to have diabetes mellitus when fasting blood glucose level was higher than 126 mg/dL. Obesity was designated as body mass index (BMI)  $\geq 30.00$  kg/m<sup>2</sup>.<sup>13</sup>

The statistical analysis was performed by Statistical Product and Service Solution (SPSS); bivariate analysis was used because this study involved one dependent variable and one independent variable. Hypothesis testing was determined by the chi-square method. The prevalence ratio (PR) was further calculated.

### Results

In total, there were 223 patients admitted in the Department of Cardiology, Dr. Hasan Sadikin General Hospital, consisting of 183 men and 40 women, and only 186 had complete data as

**Table 1 Baseline Characteristics**

Characteristics	Rentrop		Total n=186	
	Good n=117	Poor n=69		
Age (yr)	Mean (SD)	59.09 (9.33)	54.9 (8.51)	57.53 (9.24)
	Median	59	54	57
	Range	44	42	53
Sex; n (%)	Male	96 (82.1)	58 (84.1)	154 (82.8)
	Female	21 (17.9)	11 (15.9)	32 (17.2)
Height (m)	Mean (SD)	1.63 (0.07)	1.62 (0.07)	1.63 (0.07)
	Median	1.65	1.63	1.64
	Range	0.38	0.31	0.38
Weight (kg)	Mean (SD)	64.18 (11.24)	65.55 (10.15)	64.69 (10.84)
	Median	65	65	65
	Range	75	44	75
Risk factors; n (%)	Obesity	2 (1.7)	1 (1.4)	3 (1.6)
	Smoking	68 (58.1)	47 (68.1)	115 (61.8)
	Dyslipidemia	77 (65.8)	47 (68.1)	124 (66.7)
	Dm	31 (26.5)	16 (23.2)	47 (25.3)
	Hypertension	81 (69.2)	36 (52.2)	117 (62.9)

Note: DM=Diabetes Mellitus

**Table 2 Result of the Association between Modifiable Risk Factors and Collaterals**

Risk Factors	Rentrop		p-value	Prevalence Ratio	Confidence Interval 95%
	Poor (n=69)	Good (n=117)			
Obesity	Yes	1	0.70	0.90	n.d.
	No	68			
Smoking	Yes	47	0.18	1.32	n.d.
	No	22			
Dyslipidemia	Yes	47	0.75	1.07	n.d.
	No	22			
DM	Yes	16	0.62	0.90	n.d.
	No	53			
Hypertension	Yes	36	0.02	0.64	0.45-0.93
	No	33			

Note: DM Diabetes Mellitus; n.d.=not determined

shown in Table 1. The Rentrop score was good (n117; 62.9%) and poor (n69; 37.1%).

The result of this study revealed that there was no association between each risk factors and the collateral system, such as obesity (p=0.70), smoking (p=0.18), dyslipidemia (p=0.75) and diabetes mellitus (p=0.62), however, hypertension was associated with the collateral system (p=0.02), although the CI 95% was low 0.45-0.93 (Table 2). Furthermore, no association was found between the number of risk factors involved and the collateral system (p=0.23) as shown in Table 3.

## Discussion

This study has shown that diabetes mellitus has no association with the collateral development, conforming study performed by Zorkun et al.<sup>13</sup> The collateral flow index (CFI) has been also reported to be no difference between diabetic and non-diabetic patients.<sup>14</sup> The differentiation in cofactors that influence collaterals and the differentiation between angiogenesis and arteriogenesis may play an important role. Interestingly, our study

also shows that there is no association with other coronary risk factors, including obesity, dyslipidemia, and smoking habit. The data taken in this study did not consider any treatment used by the patients. The use of anti-hypertensive, anti-diabetic, and lipid-lowering drugs has been considered as a positive risk factor.<sup>13</sup>

The only result with a significant finding in our study is hypertension which has an association with the collateral development. Hypertension is considered to have a protective factor from poor collateral circulation, as analyzed using the prevalence ratio. The development of collateral circulation is initiated by a steep pressure gradient between high pre-occlusive and very low post-occlusive pressure regions. Subsequently, deformation of the endothelial cells might occur through the increased pulsatile Fluid Shear Stress (FSS). The process of arteriogenesis can be drastically stimulated by increases in FSS.<sup>15</sup>

Myocardial hypoxia is the main factor in stimulating collateral circulation and to dilate stenotic coronary vessels.<sup>15</sup> When the stenosis has occluded of 70% in the vessel

**Table 3 Result of the Association between the number of Risk Factors and Collaterals**

Rentrop	Category			Total	p-value
	A	B	C		
Poor (score 0-1)	17	48	4	69	0.23
Good (score 2-3)	18	93	6	117	
Total	35	141	10	186	

Note: A=<2 risk factors; B=2-3 risk factors; C=4-5 risk factors

diameter, distal coronary pressure would fall and thus increase the endothelial shear stress at the other collaterals, causing a dilation of the collateral progressively through the remodeling process.<sup>6</sup> Subsequently, the stenosis may develop into a complete occlusion and in this condition, collateral circulation may reach a maximum adaptation.<sup>15</sup>

Occlusion may cause ischemia and the development of collateral systems if the occlusions develop gradually.<sup>15</sup> The previous study showed that the development of collateral circulation is affected by ischemic symptoms and the severity of occlusion in a long-term condition. The history of angina pectoris, pre-infarction angina, and time to cardiac catheterization are associated with a higher prevalence of collateral circulation.<sup>16</sup> In this study, information about symptoms, length of the symptoms occurred, and the severity of the occlusions are lacking, therefore, as limitation of this study, the severity of the occlusion is not considered. Also, only one cardiologist interventionist has reviewed the angiograms, thus, no inter-observer data available.

To conclude, our study shows no association between various coronary risk factors and coronary collateral circulation, except for hypertension. Further study needs to be performed to explore other risk factors in coronary artery disease, and to prevent the disease among the population.

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