

# Comparison of Coronary Angiography Characteristics among Acute Coronary Syndrome Patients in Young and Old Age Patients at Cipto Mangunkusumo Hospital Jakarta

*Rahmad Isnanta, Marulam M. Panggabean, Idrus Alwi*

Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia – Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

## **Correspondence mail:**

Division of Cardiology, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia – Cipto Mangunkusumo Hospital. Jl. Diponegoro no. 71, Jakarta 10430, Indonesia. email: rahmadisnantadr@gmail.com.

## **ABSTRAK**

**Tujuan:** mengetahui perbedaan karakteristik angiografi koroner pada pasien sindrom koroner akut (SKA) usia  $\leq 45$  tahun dengan pasien SKA usia  $> 45$  tahun. **Metode:** diteliti sebanyak 322 pasien SKA yang telah menjalani angiografi koroner di ICCU RS Cipto Mangunkusumo Jakarta mulai Januari 2008 sampai Desember 2012. Beratnya stenosis pembuluh darah diukur dengan skor vessel (jumlah pembuluh darah koroner yang sakit dengan stenosis  $\geq 70\%$ ) dan skor stenosis. Pasien dibagi ke dalam dua kelompok, yaitu usia  $\leq 45$  tahun (72 kasus) dan usia  $> 45$  tahun (250 kasus). Analisis statistik menggunakan Chi-square untuk data kategorik yang tidak berpasangan dan t-tes untuk data numerik atau Mann-Whitney. **Hasil:** distribusi jumlah pembuluh darah yang sakit (skor vessel) 1 VD (single vessel diseases) terbanyak pada usia  $\leq 45$  tahun (43,1% vs 26,0%), sedangkan 3 VD (triple vessel diseases) terbanyak pada usia  $> 45$  tahun (31,6% vs 18,1%). Hasil skor stenosis menunjukkan lebih rendah pada usia  $\leq 45$  tahun dibandingkan usia  $> 45$  tahun (median skor stenosis 4 vs 8) dengan perbedaan yang bermakna ( $p < 0,001$ ). Pembuluh darah yang mengalami aterosklerosis terbanyak adalah left anterior descending baik kelompok usia  $\leq 45$  tahun dan usia  $> 45$  tahun (65,3% dan 74,0%). Pembuluh darah left circumflex dan right coronary artery lebih sedikit pada usia  $\leq 45$  tahun dan bermakna secara statistik (26,4% dan 31,9% vs 46,4% dan 57,2%,  $p = 0,002$  dan  $0,001$ ). **Kesimpulan:** jumlah pembuluh darah koroner yang sakit (vessel score) dan skor stenosis (stenosis score) lebih kecil pada usia  $\leq 45$  tahun dibanding usia  $> 45$  tahun.

**Kata kunci:** sindrom koroner akut, angiografi koroner, usia muda.

## **ABSTRACT**

**Aim:** to identify the difference between coronary angiography in patients with acute coronary syndrome (ACS) aged  $\leq 45$  years and those aged  $> 45$  years. **Methods:** a total of 322 ACS patients who underwent coronary angiography in ICCU of Cipto Mangunkusumo Hospital, Jakarta between January 2008 and December 2012 were included in this study. The severity of coronary stenosis was determined by vessel score and coronary score. A significant vessel score was defined as a stenosis of coronary vessel of  $\geq 70\%$ . Patients were divided into two groups: those aged  $\leq 45$  years (72 cases) and those aged  $> 45$  years (250 cases). The statistical analysis was performed with Chi-square test for categorical data with two-unpaired groups and the t-test or Mann-Whitney for numerical data. **Results:** the highest distribution of 1-VD (single-vessel disease) patients was found the group of patients aged  $\leq 45$  years (43.1% vs 26.0%); while for 3-VD (triple-vessel disease) patients, the highest distribution was noticed in the group of patients aged  $> 45$  years (31.6% vs 18.1%). The stenosis score was lower in patients aged  $\leq 45$  years compared those aged  $> 45$  years (median stenosis score 4 vs 8),  $p < 0.001$ . Atherosclerosis was found most common for the left anterior descending artery in both age groups (65.3% and

74.0%). However, there was less significant stenosis lesion for the Left Circumflex and Right Coronary Arteries in patients aged  $\leq 45$ . The result was statistically significant (26.4% and 31.9% vs 46.4% and 57.2%,  $p=0.002$  and  $0.001$ ). **Conclusion:** the number of coronary artery diseases (vessel score) and stenosis score is lower in patients aged  $\leq 45$  years compared to patients aged  $>45$  years.

**Key words:** acute coronary syndrome, coronary angiography, young age.

## INTRODUCTION

Acute coronary syndrome (ACS) is a manifestation of coronary heart disease and it may lead to sudden death. ACS mostly occurs at the age of more than 45 years, while the incidence in patients less than 45 years old is about 5-10%.<sup>1,2</sup> The age limit for ACS in young patient is different in various studies, which vary between  $<35$  years and  $<60$  years, and approximately ranges between 40-45 years.<sup>1,2</sup> Tungsubutra W (Thailand) and Pong Wong (Singapore) defined in their studies that the young age patients were those aged  $\leq 45$  years; while Yildirim who conducted a study in Turkey defined young age as those with age of  $<40$  years.<sup>2,3</sup>

The main causes of ACS in young patients are atheromatosis, heart disease and non-atheromatotic hypercoagulable state.<sup>4-6</sup> Coronary angiography is an accurate examination to identify variations and anatomical abnormalities of the coronary arteries, the degree of obstruction in the lumen, as well as the length, diameter, and contours of coronary arteries. This examination can also assess the characteristics of lumen obstruction may include the presence of atheroma, thrombus, dissection, spasm, or myocardial bridging, and the presence and extent of collateral vessels.<sup>6</sup>

In the last few years, the incidence of myocardial infarction has been increasing at young age ( $\leq 45$  years). There are many of Indonesian people who do not believe that heart attack can occur at the young age. Heart attack will cause great impacts on morbidity, psychology, and financial condition to the patients and their family, especially when it occurs at the young age. Therefore, it is necessary to conduct a study to observe the characteristics of angiography in young patients with ACS.

## METHODS

This was a cross-sectional study using secondary data from patients with acute coronary syndrome who had undergone angiography examination during their hospitalization at the Intensive Cardiac Care Unit (ICCU) of Cipto Mangunkusumo Hospital Jakarta, between January 2008 and December 2012.

The patients were categorized into two groups for comparison. The first group (the young-age group) consisted of patients aged less than and equal to 45 years; while the second group (the old-age group) included those patients aged more than 45 years. Sample size was calculated and 64 patients were needed in each group.

Vessel score was defined as the number of vessel with coronary artery lesion of  $\geq 70\%$  stenosis. The range of score was: 0-3 points depending on the number of coronary artery involved. The score of 0 VD (normal angiogram/non-significant CAD) showed that there was no coronary artery with  $>70\%$  stenosis; 1-VD (single vessel disease) indicated that there was 1 vessel with  $>70\%$  stenosis; 2-VD (double-vessel disease) showed that there were two vessels with  $>70\%$  stenosis and 3-VD (triple-vessel disease) indicated that there were three vessels with  $>70\%$  stenosis.<sup>7</sup>

Stenosis score was categorized into the following four levels according to stenosis severity: grade 0 (no stenosis), grade 1 (stenosis with 1-49% reduction of lumen diameter), grade 2 (50-74% reduction of lumen diameter), grade 3 (75-99% reduction of lumen diameter), and grade 4 (total occlusion).<sup>7</sup>

All of obtained data was analyzed using SPSS 16.0 statistical analysis computer software. The statistical analysis included Chi-square test for categorical data with two-unpaired groups and the t-test for numerical data. When

the distribution of data was not normal, Mann-Whitney analysis was carried out. P value <0.05 was considered statistically significant.

## RESULTS

There were 322 patients who fulfilled study criteria, i.e. those who underwent angiography and had a complete laboratory data. The patients were categorized into two groups for comparison. The first group consisted of 72 cases (22.4%) of patients aged less than and equal to 45 years; while the second group included 250 cases (77.6%) of those patients aged more than 45 years. There were 56 male patients (77.8%) and 16 female (22.2%) in the first group (age ≤ 45 years). In contrast, there were 171 male patients (68.4%) and 79 female patients (31.6%) in the second group.

The dominant risk factors in the age group ≤45 years were smoking, dyslipidemia and hypertension, which included 48 cases (66.7%), 35 cases (48.6%) and 33 cases (45.8%), respectively. Meanwhile, the risk factors frequently found in the age group of > 45 years were hypertension, dyslipidemia and smoking with 178 cases (84.4%), 133 (53.2%) and 124 cases (49.6%) respectively.

There were significant differences regarding the distribution of risk factors in both groups. There was a higher number of some risk factors, including smoking (p=0.011), family history (p=0.002) and psychological stress (p=0.023) in the age group of ≤45 years compared to the age group of >45 years.

Based on the diagnosis, the patients aged ≤45 years had been mostly diagnosed with UAP (Unstable angina pectoris), i.e. 31 cases (43.1%); while patients aged >45 years mostly had STEMI (ST elevation myocardial infarction), i.e. 96 cases (38.4%). The youngest patient was 28 years old; while the age of most patients ranged between 41 and 45 years (62.5%). (Table 1)

### Proportion on Angiographic Characteristics in Patients Aged ≤45 Years and >45 Years

The characteristics of blood vessel on angiography were demonstrated by the number of coronary vessel disease (vessel score) and obstruction (stenosis score). The distribution

of blood vessel disease showed that the highest number of 1-VD (single vessel disease) was found in the group of ≤ 45 years (43.1%); while 3-VD (triple vessel diseases) was found mostly in the group of age > 45 years (31.6%). (Table 2)

**Table 1.** Baseline characteristics in the ACS patients whose age ≤45 years and age >45 years

Variables	Group of ACS patients	
	Age ≤45 years	Age >45 years
Sex		
- Men	56 (77.8)	171 (68.4)
- Women	16 (22.2)	79 (31.6)
Risk factors		
- DM	11 (15.3)	83 (33.2)
- Dyslipidemia	35 (48.6)	133 (53.2)
- Smoking	48 (66.7)	124 (49.6)
- Obesity	18 (25.0)	64 (25.8)
- Hypertension	33 (45.8)	178 (65.5)
- Family history	18 (24.0)	27 (10.8)
- Psychological stress	14 (19.4)	24 (11.8)
Diagnosis		
- UAP	31 (43.1)	90 (36.0)
- NSTEMI	12 (16.7)	64 (25.6)
- STEMI	29 (40.3)	96 (38.4)

**Table 2.** Vessel diseases involved in patients age ≤45 years and age >45 years

Number of vessel diseases involved	Group of ACS patients		p
	Age ≤45 years (n=72)	Age >45 years (n=250)	
Normal angiogram/non significant CAD	18 (25.0)	32 (12.8)	0.012
Single vessel disease	31 (43.1)	65 (26.0)	0.005
Double vessel disease	10 (13.9)	74 (29.6)	0.007
Triple vessel disease	13 (18.1)	79 (31.6)	0.025

Chi-square test

### Comparison of Stenosis Score between the Age Group of ≤45 Years and >45 Years

Lower stenosis score was also found in patients of ≤45 years age group, i.e. 4 (0-18) compared to and 8 (0-25) in patients aged >45 years with a significant difference (p<0.001).

Blood vessel that mostly had advanced atherosclerosis was the LAD (left anterior descending), which was observed in both groups of patients aged  $\leq 45$  years and  $>45$  years.

#### Differences on the Number of Coronary Artery Disease Involved between the Group of Patients Aged $\leq 45$ Years and $>45$ Years with Various Risk Factors

In the group with one risk factor, the angiogram showed that most patients had normal angiogram/non-significant CAD in the group of patients aged  $\leq 45$  years (40.9%); while in the patients aged  $>45$  years, the angiogram showed that double-vessel disease (2-VD) were the most frequently found.

In the group with two risk factors, it was demonstrated that the majority of patients had single-vessel disease (1-VD) in the group of patients aged  $\leq 45$  years (40%); while in group of patients aged  $>45$  years, most findings were triple-vessel disease (31.3%).

In the group with three risk factors, the study demonstrated that single-vessel disease was also found mostly in patients aged  $\leq 45$  years (50%); while in patients aged  $>45$  years, most findings were triple-vessel disease (35.2%). (Table 4)

**Table 3.** Coronary artery involved in patient age  $\leq 45$  years and age  $>45$  years

Coronary Artery involved	ACS Patients Group		P
	Age $\leq 45$ years	Age $>45$ years	
LM disease	3 (4.2)	25 (10.0)	0.089
LAD disease	47 (65.3)	185 (74.0)	0.278
LCX disease	19 (26.4)	116 (46.4)	0.002
RCA disease	23 (31.9)	143 (57.2)	0.001

Chi-square test

#### DISCUSSION

There were 72 cases (22.4%) aged  $\leq 45$  years and 250 cases (77.6%) aged  $>45$  years of patients. 77.8% of patients were male and 22.2% were female; while in the group of patients aged  $>45$  years, there were 68.4% male patients and 31.6% female patients.

In this study, the cut-off point for young patient age of  $\leq 45$  years was determined based on results of some studies in Thailand, Singapore and other studies such as in Israel and California.<sup>2,9</sup> Other studies had determined the young age of 40 years, including studies from Japan, Poland, Germany, Australia, New Zealand and USA.<sup>9</sup> The youngest patient was 28 years old and most

**Table 4.** Proportion of coronary artery involved between patients age  $\leq 45$  years and patients age  $>45$  years in various groups of risk factor

Number of vessel disease	Groups of ACS patients	
	Age $\leq 45$ years	Age $>45$ years
<b>One risk factor</b>	n=22	n=57
Normal angiogram/non significant CAD	9 (40.9)	9 (15.8)
Single vessel disease	8 (36.4)	15 (26.3)
Double vessel disease	3 (13.6)	19 (33.3)
Triple vessel disease	2 (9.1)	14 (24.6)
<b>Two risk factors</b>	n=20	n=77
Normal angiogram/non significant CAD	3 (15.0)	11 (16.4)
Single vessel disease	8 (40.0)	17 (25.4)
Double vessel disease	3 (15.0)	18 (26.9)
Triple vessel disease	6 (30.0)	21 (31.3)
<b>Three risk factors</b>	n=30	n=125
Normal angiogram/non significant CAD	6 (20.0)	12 (9.6)
Single vessel disease	15 (50.0)	32 (25.6)
Double vessel disease	4 (13.3)	37 (29.6)
Triple vessel disease	5 (16.7)	44 (35.2)

Chi-square test

patients were at the age between 41 years and 45 years (62.5%).

The most major risk factor in patients aged  $\leq 45$  years was smoking (66.7%) followed by dyslipidemia and hypertension, with the percentage of 48.6% and 45.8%, respectively; while the major risk factors in patients aged  $>45$  years were hypertension (84.4%) followed by dyslipidemia and smoking, with the percentage of 53.2% and 49.6%, respectively.

However, some risk factors were significantly more common in patients aged  $\leq 45$  years compared to patients aged  $>45$  years, i.e. smoking ( $p=0.011$ ), family history ( $p=0.002$ ) and psychological stress ( $p=0.023$ ). These results were similar to the results of a study in Thailand, which found that most common risk factor of ACS in patients aged  $<45$  years was smoking.<sup>2</sup> Another study conducted by Yildirim N from Turkey and a study from Bangladesh also found that smoking is a major risk factor for ACS in young patients.<sup>3,10</sup> Another study indicated that patients whose parents experienced early cardiovascular disease would have increased risk of cardiovascular disease.<sup>11</sup>

Smoking is a major risk factor for ACS in young patients because cigarettes will accelerate the process of atherogenic cardiovascular disease depending on both dose and duration of smoking.<sup>12,13</sup> In addition, smoking also affects immunological response against vascular injury, which is described as an increase of oxidative stress on lipid peroxidation, endothelial cell dysfunction and proliferation of foam cells in tunica media.<sup>13,14</sup>

Smoking also increases platelet aggregation, interfere with the metabolism of lipoproteins, suppresses HDL cholesterol and lowers pressing distension of vessel wall.<sup>13,14</sup> Cigarette smoking is associated with elevated levels of inflammatory markers. During the acute phase of the inflammatory state, there is an increase in C - reactive protein, white blood cells, fibrinogen, and also decreased albumin serum.<sup>12-14</sup> Effect of smoking also causes increased myocardial load due to stimulation by catecholamines and decreasing consumption of  $O_2$  due to inhalation of CO that may lead to tachycardia, vasoconstriction of blood vessels and also altered

permeability of the vessel wall.<sup>13-14</sup> In elderly age, LDL level tends to be increased; while in young age, most patients have low HDL level and high triglyceride level. However, some studies demonstrated that high LDL level may be found due to familial LDL disorders.<sup>11,15</sup>

This study showed that the diagnosis of acute coronary syndromes in patients aged  $\leq 45$  years mostly was UAP (43.1%); while patients aged  $>45$  years mostly had STEMI (38.4%). In contrast, a study in Thailand showed that patients aged  $\leq 45$  years mostly had STEMI (67.3 %).<sup>2</sup>

This study also found that based on the number of coronary artery diseases, most patients aged  $\leq 45$  years mostly had single-vessel disease (43.1%), while in the group of patients aged  $>45$  years, triple-vessel disease was the most common finding (31.6%).

Several studies have also found similar results with our study, i.e. studies conducted by Rajesh SK,<sup>16</sup> Goornavar,<sup>17</sup> Badran,<sup>18</sup> Trzos E et al.<sup>19</sup> which also found a single-vessel disease in angiogram of young patients. In contrast, a study conducted by Alizadehasl et al from Iran found that the result of angiography in young patients was normal angiogram (43.8%), which was more common than the single-vessel disease (30.1%).<sup>20</sup>

In ACS patients aged  $\leq 45$  years, the angiogram showed abnormalities that relatively more minimal than patients with older age. The incidence of normal coronary arteries in group of patients aged  $\leq 45$  years ranged between 11% and 22.5%.<sup>2</sup>

In this study, the incidence of myocardial infarction in young patients with normal angiographic feature/non-significant CAD (no blood vessels with  $>70\%$  stenosis) was 25%; while a study in Iran showed higher incidence, which was 43.8%.<sup>2</sup>

Although most cases of acute myocardial infarction are caused by coronary atherosclerosis, but it may occur in patients with normal coronary angiogram. The mechanism of pathogenesis for myocardial infarction in patients with normal arteries remains unclear, but it may be due to the presence of coronary vasospasm, thrombosis, hypercoagulable state, embolism and coronary trauma.<sup>21</sup> Coronary artery spasm causes vascular injury and increases platelet

aggregation and activation of the coagulation system, which eventually may lead to thrombosis and myocardial infarction.<sup>2</sup>

The type of blood vessels that mostly had atherosclerosis in our study was LAD (Left Anterior Descending) arteries, which was found similar in both groups of patients aged  $\leq 45$  years and  $>45$  years. In the similar studies conducted by Yildirim N,<sup>3</sup> Badran et al,<sup>18</sup> and Alizadehasl et al, they also found that LAD arteries were the most common vessel involved in young and old patients. However, there was a significant difference, i.e. LCX (Left Circumflex) and RCA (Right Coronary Artery) were less commonly affected at the age of  $\leq 45$  years. The reason of why LAD is more commonly involved in ACS is still unknown.

After the patients were grouped as patients with one risk factor, two risk factors and three risk factors, an analysis of vessel score (number of vessels diseases) was performed against the different age groups. As a result, the study found that the group of patients with one risk factor mostly had normal angiogram/non-significant CAD result in patients aged  $\leq 45$  years (40.9%); while in patients aged  $>45$  years, the result was double-vessel disease.

In the group of patients with two risk factors, single-vessel disease (1VD) was mostly found in age group of  $\leq 45$  years (40%); while in age group  $>45$  years, the patients mostly had triple-vessel disease (31.3%).

In the group of patients with three risk factors, single-vessel disease (1VD) was also mostly found in age group of  $\leq 45$  years (50%); while in age group  $>45$  years, the patients mostly had triple-vessel disease (35.2%).

A study conducted by Saghir T e al from Pakistan found that in the group of young patients with one risk factor, most of angiographic features were single vessel disease (39 %),<sup>22</sup> as well as in those patients who had two factors and three risk factors, the single vessel disease was found in 43% and 41% of patients respectively.<sup>22</sup> Therefore, we can see that at the age of less than 45 years, regardless of the number of risk factors (one, two and three risk factors), coronary arteries disease still remains to be the single-vessel disease (1VD).

There is a possibility that in younger age, there are other risk factors that play a role in addition to the traditional risk factors, such as hypercoagulability factors and coronary artery spasm. Meanwhile, patients aged  $>45$  years with two or more risk factors will have more coronary arteries vessels involved. Hence, the greater number of risk factors, the more severe and greater number of blood vessels diseases involved.

## CONCLUSION

The number of coronary arteries diseases (Vessel score) and Stenosis score are lower in ACS patients aged  $\leq 45$  years compared to those aged  $>45$  years.

Further studies should be conducted, particularly on other risk factors considering that young patients with only one risk factor and normal/non-significant CAD angiogram may have heart attack of acute coronary syndrome.

The risk factor of high psychological (psychosocial) stress in patients aged  $\leq 45$  years compared to those aged  $>45$  years should be studied further, especially on the correlation between psychosocial stress and acute coronary syndrome in young patients.

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