

# Differences in Clinical Nature and Outcome Among Youth and Older Patients Suffering from an Acute Coronary Syndrome

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## Research Article

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# Abstract

**Objective:** Acute coronary disease (ACS) is an acute regional reduction in coronary blood flow. Pathophysiology, clinical appearance, risk factors and clinical outcomes may vary between younger and older patients. The purpose of this study was to assess these factors in patients less than 45 years of age compared to older adults admitted with a ACS diagnosis.

**Patients and methods:** Retrospective chart review study of ACS patients admitted between 2015 and 2020.

**Results:** Overall, 652 patients were enrolled. Of these, 109 patients (16.7%) were under 45, with a mean age of  $38 \pm 7$ . Younger patients showed a higher rate of palpitation (23.9% versus 13.6%;  $P = 0.019$ ). A positive smoking history and a family history of CAD were seen more often in younger patients (42.2% vs. 27.3%,  $P < 0.001$ ; 22.9% vs. 9.4%,  $P < 0.001$ , respectively). Older patients had greater renal impairment with higher creatinine (median = 1.10 mg /dl (range, 0.3-13.0) vs. 1.0 (0.3-19.0;  $p = 0.001$ ), BUN (median = 16.0 (mange, 0.9-141.0) vs 12.0 (0.9-49.0);  $P < 0.001$ )).

Younger patients had higher levels of LDL and total cholesterol (median 138c. 115;  $p < 0.001$ ) and cholesterol (median 209 vs. 178.5;  $p < 0.001$ ). Hospital mortality was 0.9% in younger patients versus 7.4% in older patients ( $P=0.004$ ).

**Conclusion:** Palpitations, smoking, family history, higher LDL levels, and total cholesterol levels were more prevalent in adults younger than 45 years old with ACS. Impaired renal function, hypertension, and diabetes were more in older patients with ACS.

## Background

Cardiovascular disease, which includes coronary heart disease and stroke, is the leading cause of death and disease burden globally.<sup>1</sup> Acute coronary syndrome (ACS) is characterized by acute local reduction in blood flow to the myocardium, also known as ischemia.<sup>2</sup> Ischemic heart disease may present with a variety of symptoms e.g. a symptom complex called acute coronary syndrome (ACS), which may lead to a diagnosis of one of unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), or ST-segment elevation myocardial infarction (STEMI). The former is a clinical diagnosis, whereas the latter two are diagnosed from the abnormalities seen on the EKG, possibly complemented by serum enzyme assays e.g. of troponin C.<sup>3</sup>

Atherosclerosis is a chronic inflammatory process of the arterial wall, and although it starts early in life, it takes years to be of serious pathological severity, so that young people do not present with ACS very often.<sup>4,5</sup> However, in recent years, coronary artery disease (CAD) has been affecting younger patients, which raises concern due to the accompanying results of premature morbidity and mortality. Patients less than 45 years of age represent 6–10% of cardiac infarctions in the United States.<sup>5–7</sup> Smoking was found to be the prevailing risk factor and was frequently found along with coronary events in young

patients.<sup>8,9</sup> ACS presents with similar clinical features irrespective of age.<sup>9</sup> The main presenting symptom is chest pain in both the young as well as in the elderly.<sup>10</sup> It is also important to note that the severity and presentation of the diseases caused by atherosclerosis seem to differ between men and women in their different stages of life.<sup>11</sup> For example, men are more likely to develop advanced coronary artery disease (CAD) in all age groups.<sup>12</sup>

The aim of this study was to assess the demographic characteristics, cardiovascular risk factors, and complications in young adults below the age of 45 years compared to older adults who were admitted with a diagnosis of ACS at King Fahd University Hospital between 2015 and 2020.

## **Material And Methods**

### **Setting**

The study was conducted at King Fahad Hospital of the University (KFHU), a tertiary care university teaching hospital with 600 beds in the Eastern Province of Saudi Arabia. It is a retrospective study that was conducted using medical records of all ACS patients admitted between 2015 and 2020.

Demographic data, presenting symptoms, risk factors, and clinical outcomes were obtained. The local institutional research body approved this study.

### **Target Population**

We recruited all patients who were diagnosed with ACS based on the international classification of diseases version 10 ICD-10, including younger adult patients (from 18–45 years old) and older patients (above 45-year-old). We excluded patients labelled DNR (do not resuscitate), and incomplete patient file.

### **Study design**

A descriptive retrospective study was conducted with the sample size determined by the number of patients in King Fahd Hospital of the University in Al-Khobar city, and this was a total of 652 patients. All methods were performed in accordance with STROBE guidelines and regulations of cohort studies.

### **Statistical analysis**

All categorical variables were represented by frequency as percentages, and were analyzed using chi-squared and Fisher's exact tests. Continuous variables were represented by median with range because the data did not follow the normal distribution. The Mann-Whitney U test was used for the comparison between the two groups. All analyses were performed using SPSS (21 version). A P value of less than 0.05 was considered significant by Kruskal–Wallis test.

## **Results**

A total of 652 patients were enrolled in this study. Of these, 109 (16.7%) patients were less than 45 years of age. The mean age was  $38 \pm 7$  vs.  $60 \pm 11$  years in the young and old groups, respectively ( $P < 0.001$ ).

Table 1 shows that younger patients had a higher frequency of palpitations (23.9% vs. 13.6%;  $P = 0.019$ ). Older patients had higher frequencies of hypertension e.g. a systolic blood pressure reading of  $> 140$  mmHg (68.7% vs. 37.6%;  $P < 0.001$ ), diabetes (61.1% vs. 37.6%,  $P < 0.001$ ), and history of CAD (52.3% vs. 30.3%;  $P < 0.001$ ), but less frequent history of smoking, and positive family history, which were higher among younger patients (42.2% vs. 27.3%,  $P < 0.001$ , 22.9% vs. 9.4%;  $P < 0.001$ ) (Table 2).

Table 1  
Clinical presentations of ACS upon admission according to age.

Presentation	Less than 45-year-old (n = 109)	More than 45-year-old (n = 543)	P value*
Chest pain	97 (89%)	444 (81.8%)	0.071**
Epigastric pain	11 (10.1%)	60 (11%)	0.929
Syncope/ Pre-Syncope	10 (9.2%)	48 (8.8%)	0.834
Dyspnea/ SOB	49 (45%)	243 (44.8%)	0.286
Palpitation	26 (23.9%)	74 (13.6%)	0.019**
Sweating	38 (34.9%)	185 (34.1%)	0.604
Nausea and vomiting	29 (26.6%)	126 (23.2%)	0.446
Cardiac arrest	3 (2.8%)	38 (7%)	0.246
<b>Abbreviations:</b> SOB, Shortness of breath; n, total number of patients.			
*Statistical significance was set at p-values $< 0.05$ .			
**Statistically significant by Kruskal–Wallis test.			

Table 2  
Risk factors of ACS patients according to age.

Risk Factor	Less than 45-year-old (n = 109)	More than 45-year-old (n = 543)	P value*
HTN	41 (37.6%)	373 (68.7%)	< 0.001**
DM	41 (37.6%)	332 (61.1%)	< 0.001**
Abnormal lipid profile	60 (55.0%)	227 (41.8%)	0.038
Smoking history	46 (42.2%)	148 (27.3%)	< 0.001**
Family history	25 (22.9%)	51 (9.4%)	< 0.001**
CAD history	33 (30.3%)	284 (52.3%)	< 0.001**
<b>Abbreviations:</b> HTN, Hypertension; DM, Diabetes Mellitus; n, total number of patients.			
*Statistical significance was set at p-values < 0.05.			
**Statistically significant by Kruskal–Wallis test.			

Table 3 shows the laboratory outcomes; older patients had significantly higher creatinine levels (median = 1.10 mg /dl (range, 0.3–13.0) vs. 1.0 (0.3–19.0; p = 0.001), BUN (Median = 16.0 (Range, 0.9–141.0) vs 12.0 (0.9–49.0); P < 0.001), but less in Hb, LDL cholesterol and total cholesterol, which were high among younger patients (14.4 g /dl (8.4–17.6) vs. 13.5 g /dl (0.11–158); P < 0.001, 138 mg /dl (43–224) vs. 115 mg /dl (25–411); p < 0.001, 209 mg /dl (59–303) vs. 178.5 mg /dl (18–485); p < 0.001) (Fig. 1).

Table 3  
Comparison of laboratory work up results in ACS patients according to age.

Lab. Result	Less than 45-year-old (n = 109) (median, average)	More than 45-year-old (n = 543) (median, average)	P value*
Creatinine (mg/dL)	1 (0.3–19)	1.1 (0.3–13.0)	0.001**
BUN (mg/dL)	12 (0.9–49.0)	16 (0.9–141.0)	< 0.001**
Hemoglobin (g/dl)	14.4 (8.4–17.6)	13.5 (0.11–158)	< 0.001**
Troponin (ng/mL)	1.63 (0.04–450)	1.08 (0.01–165.5)	0.286
LDL (mg/dL)	138 (43–224)	115 (25–411)	< 0.001**
HDL (mg/dL)	36 (10–56.0)	36 (9–172.0)	0.283
Triglyceride (mg/dL)	139 (20–1111)	126 (1.18–557.0)	0.103
Total Cholesterol (mg/dL)	209 (59–303)	178.5 (18–485)	< 0.001**
<b>Abbreviations:</b> n, total number of patients; lab., laboratory.			
*Statistical significance was set at p-values < 0.05.			
**Statistically significant by Kruskal–Wallis test.			

Table 4 shows the length of hospital admission and mortality, and there was a significant difference in mortality, that is, the in-hospital mortality was 7.4% among older patients and 0.9% among younger patients (P = 0.004).

Table 4  
In-hospital outcome for ACS patients according to age.

Outcome	Less than 45-year-old (n = 109) (median, average)	More than 45-year-old (n = 543) (median, average)	P value*
In-hospital stay (days)	5 (0–97)	5 (0–26)	0.709
Mortality	1 (0.9%)	40 (7.4%)	0.004**
<b>Abbreviations:</b> n, total number of patients.			
*Statistical significance was set at p-values < 0.05.			
**Statistically significant by Kruskal–Wallis test.			

## Discussion

Acute coronary syndrome (ACS) in young adults is a rare entity, but it does occur. It is important to assess the clinical features, risk factors, and outcomes, which may be due to the primary disease or may be secondary as complications, so that measures to prevent further episodes of ACS can be undertaken.

In this study, the cutoff point that we used to define young patients was 45 years. It was determined based on the results of similar studies in Thailand, Singapore, Israel, and California.<sup>13,14</sup> Other studies have defined the young age to be under 40 years, including studies from Japan, Poland, Germany, Australia, New Zealand, and the USA.<sup>14</sup>

Our findings are as follows: First, 109 patients who had ACS were younger than 45 years with a mean age of  $38 \pm 7$ . Second, regarding risk factors, as expected, older patients had a higher frequency of hypertension, diabetes, and a history of CAD. On the other hand, they had less frequent history of smoking and family history of ACS, which were higher among younger patients. Furthermore, a recent retrospective cohort study of two academic institutions suggests an increased likelihood of encountering ACS with a family history of hypercholesterolemia.<sup>15</sup>

In previous studies, the most crucial risk factor for the development of ACS in young adults was smoking. The literature reports that 82% of young patients who suffered from ACS were smokers. An interesting finding was reported by Huang and colleagues who found that the rate of smoking in patients aged  $\leq 35$  years and who suffered from MI was significantly higher than in patients  $> 65$  years of age who suffered from the same condition.

All of these findings suggest that a history of smoking and family history of cardiovascular disease are risk factors in young patients with ACS (Fig. 1), which is consistent with the findings of other studies.<sup>16,17,18</sup> A study in Thailand reached the same conclusion, where it was discovered that the most common risk factor of ACS in patients aged  $< 45$  years of age was smoking.<sup>13</sup> A different study found that patients whose parents developed cardiovascular disease of early onset had an increased risk of cardiovascular disease.<sup>19</sup>

Smoking is a major risk factor for ACS in young patients for multiple reasons. Both quantity and duration of smoking quicken the development of atherogenic cardiovascular disease.<sup>20,21</sup>

Furthermore, smoking also alters the defensive response of the immune system against vascular damage, which is characterized by an increase in oxidative influence on lipid peroxidation, endothelial cell dysfunction, and generation of foam cells in the tunica media.<sup>21,22</sup> It also leads to increased platelet aggregation, disrupts the metabolic activities of lipoproteins, and tends to reduce HDL cholesterol.<sup>21,22</sup> Cigarette smoking is linked to increased levels of inflammatory markers. During the acute phase of the inflammatory process, C-reactive protein is elevated, white blood cells and fibrinogen are increased, and serum albumin is decreased.<sup>20,21,22</sup> Smoking can also increase myocardial load due to stimulation by

catecholamines and reduce consumption of O<sub>2</sub> due to inhalation of carbon monoxide, which may cause tachycardia, vasoconstriction of blood vessels, and which may modify the permeability of the vessel wall.<sup>21,22</sup>

Primary and secondary prevention specifically are important in this subset of patients. In addition, one study has shown that diabetes mellitus was more prevalent in younger adults. Acute coronary syndrome is clinically similar in both young patients and the elderly, and this has been emphasized by several authors.<sup>9,23-26</sup> However, in our study, we found that palpitations occurred more frequently in younger adults.

In addition, some laboratory parameters including creatinine, and BUN, were higher in older patients, but HGB, LDL, and cholesterol levels were higher among younger patients. This result was similar to those of previous studies.

In terms of length of stay, other studies have shown that older patients with ACS had longer hospital stays.<sup>27,28</sup> on the other hand, in our study, the length of stay was not significantly different between the two age groups. In our study, in-hospital mortality was 7.4% among older patients and 0.9% among younger patients. Our findings align with those of a recent cohort of Junjie Yang et al., which have demonstrated equity among younger and older adults in terms of short- and long-term outcomes.<sup>29</sup>

Potential limitations of our study include the fact that our selected design was retrospective. However, our sample size was reasonably large (652 cases), which in our opinion reduced information bias and therefore strengthened the results.

## Conclusion

Palpitations, positive smoking history, positive family history, and higher lipid profile were more prevalent in adults younger than 45 years old with ACS than in older ones.

Impaired renal function, hypertension, and diabetes were more common in older patients with ACS. Younger patients seem to have a better outcome in terms of mortality with no difference in length of hospital stay.

## Abbreviations

ACS: Acute coronary syndrome

CAD: Coronary artery disease

NSTEMI: Non-ST-segment elevation myocardial infarction

STEMI: ST-segment elevation myocardial infarction

## **Declarations**

## **Acknowledgments:**

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## **Disclosure:**

The author reports no conflicts of interest in this work.

## **Consent for publication:**

Consent for publication of the manuscript and the related patient information has been obtained by King Fahd Hospital of the University, Imam Abdulrahman Bin Faisal University.

## **Ethics approval and consent to participate:**

Written informed consent was obtained from the patient. The Standing Committee for Research Ethics on Living Creatures (SCRELC) from the Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia approved this project by IRB number: IRB-UGS-2016-01-075. No patients were involved neither in the design, recruitment and conduct of this study, nor in the development of outcome measures.

## **Data availability:**

The datasets generated during and analysed during the current study are not publicly available due to the privacy of research participants but are available from the corresponding author on reasonable request

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## **Authors' contributions**

Conception and design: Mohammad Saeed Al-Shahrani, Faisal Ahmad Katbi, and Abdulaziz Mohammad Al-Sharydah. Acquisition, analysis and interpretation: Saad Dhafer AlShahrani, Talal Mosfer Al-Ghamdi, and Mohammad Adnan Al-Sharidah. Drafting the manuscript for important intellectual content:

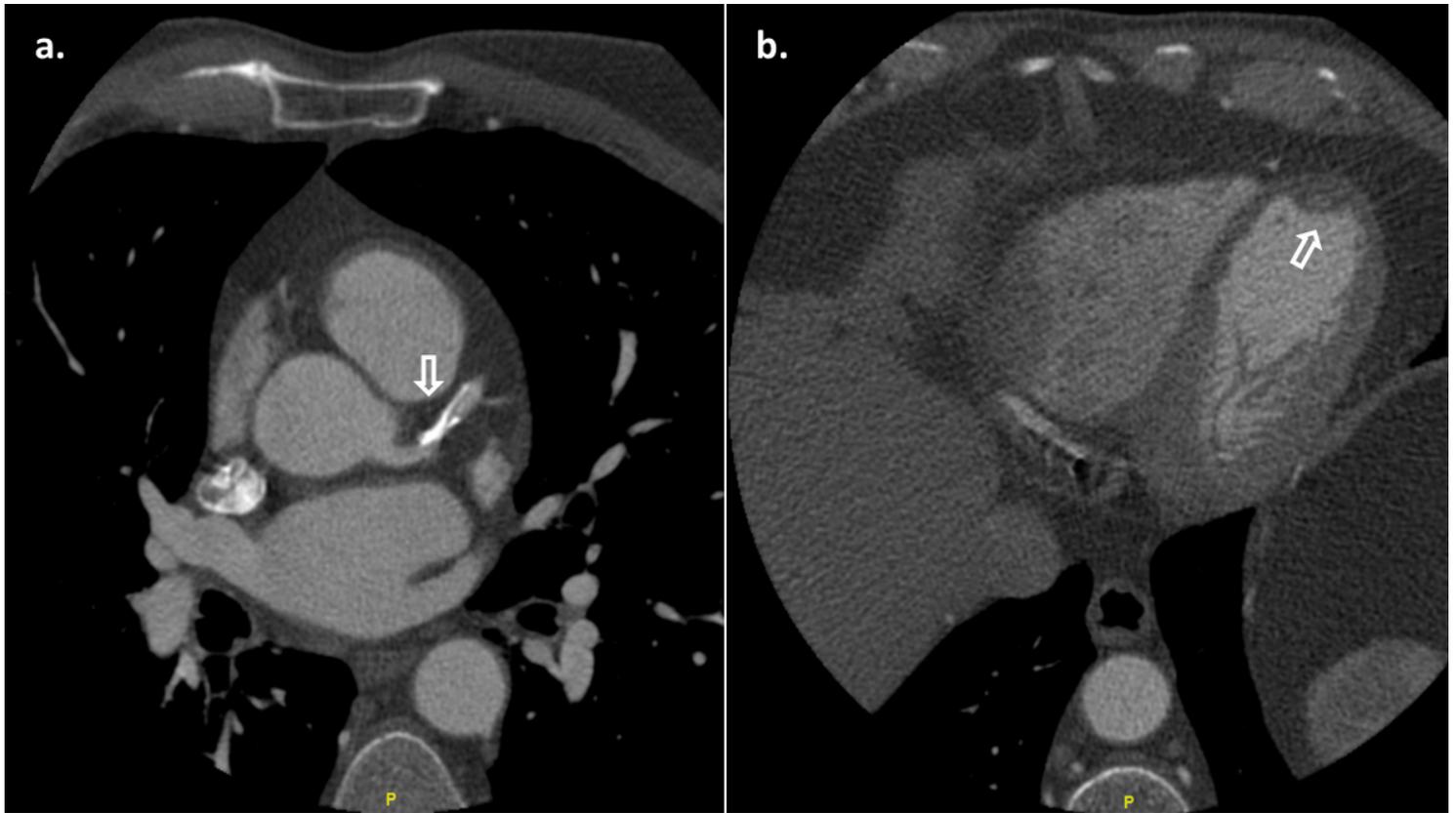
Mohammad Saeed Al-Shahrani and Faisal Ahmad Katbi. Finally, all authors reviewed and approved the final manuscript.

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## Figures



**Figure 1**

The patient is 42 years old, suffering from atypical chest pain. He's overweight, and his lab results came back positive for dyslipidemia. Cardiac CT scan performed to evaluate the presence of coronary heart disease. An ECG-gated cardiac CT acquisition was performed using an ECG-modulated radiation dose. A sublingual nitroglycerin tablet given three minutes prior to the procedure. (a) The left anterior descending artery presents a benign diffuse disease with moderate calcification and no apparent obstructive lesions (arrow). However, the presence of calcification impedes an accurate evaluation of stenosis. (b) The left ventricle is slightly dilated, the left ventricular volume at the end of diastolic is 211 ml, and the volume at the end of systole is 114 ml. The calculated ejection fraction is 46 percent. An organized small wall-mounted apical clot was displayed (arrow), which denotes an infarction of the old LAD territory with an organized old LV apical clot. There is an akinesia of the medium and distal septum and the major part of the apex (not shown).