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Age related differences in acute coronary syndrome: An observation at a central hospital in Vietnam

Dinh The Anh[1], Huynh Van Minh[2], Ho Anh Binh[3*], Tran Quang Bao[3], Nguyen Thi Thai Hai[4], Le Xuan Nam[5], Tran Duc Anh[6]

[1]Cardiac Surgical Intensive Department, Cho Ray Hospital, Vietnam;
[2]Department of Internal Medicine, Hue University of Medicine and Pharmacy, Hue University, Vietnam;
[3]Department of Emergency and Interventional Cardiology, Hue Central Hospital, Vietnam;
[4]Department of Internal Cardiology, Hue Central Hospital, Vietnam;
[5]Department of Dermatology, Hue Central Hospital, Vietnam;
[6]Stroke center, Hue Central Hospital, Vietnam

ABSTRACT

Background and Objectives: There is little data regarding the characteristics of young Vietnamese patients (<40 years old) who get acute coronary syndrome (ACS). This study aimed to compare the risk factors, clinical-subclinical characteristics, coronary lesions, and mortality prediction (based on the GRACE and TIMI scores) of young ACS patients with their older counterparts.**Methods:** A cross-sectional descriptive study was conducted amongst 69 patients with ACS at the Cardiovascular Center of Hue Central Hospital from May 2017 to December 2018. These patients were divided into two groups: 33 patients were < 40 years old (group 1), and 36 patients were ≥ 40 years old (group 2). Demographic data, risk factors profile, clinical-subclinical characteristics, coronary lesions, and mortality prediction were compared between the two groups. **Results:** Compared with group 2, group 1 had a higher proportion of severe angina (the prevalence of angina graded III-IV by CCS classification was 69.7% in group 1 *versus* 36.1% in group 2, $P = 0.0108$) and lower systolic pressure (median was 120 mmHg in group 1 *versus* 135 mmHg in group 2, $P = 0.006$). The prevalence of unstable angina and STEMI was higher in group 1 (51.5% and 36.4% in group 1 *versus* 30.6% and 11.1% in group 2, respectively), while NSTEMI was higher in group 2 (58.3% in group 2 *versus* 12.1% in group 1, $P = 0.0002$). The prevalence of single-vessel CAD, normal coronary angiography (CAG), nonobstructive CAD in group 1 was also higher and multi-vessel CAD was lower than group 2 (45.5%, 33.3%, 12.1% and 9.1% in group 1 *versus* 33.3%, 2.8%, 2.8% and 61.2% in group 2, respectively). The Gensini, GRACE, and TIMI scores were lower in group 1 (median was 5; medium was 78.55 and median was 2 in group 1 *versus* 37.5, 130.22 and 3 in group 2, respectively). Smoking was a risk factor for obstructive CAD in group 1 (OR = 7.12, 95% CI: 1.25–40.63, $P < 0.05$). **Conclusion:** Young patients with ACS tended to be males, smokers, and with positive familial history; the grade of angina was more severe, and systolic pressure was lower; the prevalence of unstable angina and STEMI was higher. Smoking was a risk factor for obstructive CAD in young patients.

Key words: Acute coronary syndrome, 40 years old, Vietnam

Address for Correspondence:
Dr. Ho Anh Binh, MD, PhD, Department of Emergency and Interventional Cardiology, Hue Central Hospital, 16 Le Loi street, Hue city, Vietnam. E-mail: drhoanhbinh@gmail.com

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INTRODUCTION

In recent years, there has been an increase in acute coronary syndrome (ACS) cases in young people. The cardiovascular risks of these patients are usually different. Data on ACS prevalence, risk factors, and clinical outcomes for young patients is limited. Young patients represent 0.4%–19% of all ACS cases, depending on the age cut-off based on the available evidence.[1] According to the Global Burden of Disease Study

2010, the average age of death from myocardial ischemia in men in low-income countries was ten years younger than in the high-income countries. This might be due to earlier onset ACS and myocardial ischemia as well as shorter survival for patients in lower-middle-income countries.[2]

ACS in young patients represents a serious health-economic problem that directly affects the main workforce of society. So far, we have only found very few similar studies in Vietnam, so we conducted this research to investigate some risk factors, clinical and subclinical characteristics, coronary lesions and prognosis of death based on the GRACE, TIMI scale of ACS in patients under 40 years of age and compared these with patients over 40 years old.

MATERIALS AND METHODS

A cross-sectional descriptive study was conducted in 69 patients who were diagnosed and treated for ACS at the Cardiovascular Center of Hue Central Hospital from May 2017 to December 2018. These patients were divided into two groups: 33 patients were < 40 years old (group 1), and 36 patients were ≥ 40 years old (group 2). The institutional review board of Hue Central Hospital approved this prospective study. Written informed consent of patients was obtained.

Diagnostic criteria: ACS was diagnosed by the 4th Universal Definition of Myocardial Infarction (MI) Consensus Document (2018),[3] in which unstable angina (UA) was diagnosed according to the standards of the European Society of Cardiology (ESC) 2019. Cardiovascular risk factors such as hypertension, diabetes, and dyslipidemia were diagnosed according to the recommendations of the ESC 2018,[4] the American Diabetes Association (ADA) 2019,[5] the National Cholesterol Education Program: Adult Treatment Panel III (NCEP: ATPIII) 2001[6] or a history of treatment or previous diagnosis. A family history of coronary artery disease (CAD) was defined when close relatives of patients had CAD before the age of 55. Overweight/ obesity was defined as BMI ≥ 23 kg/m^2. Other variables included a history of smoking, angina, angina level (according to Canadian Cardiovascular Society (CCS) grading scale[7]), other angina symptoms (sweating, shortness of breath, palpitations, vomiting, nausea, or fatigue), Killip classification, systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate. The left ventricular ejection fraction (LVEF) was measured by 2D ultrasound using the Simpson method to obtain a 55% cut-off to determine if there was an EF reduction as recommended by the American Heart Association. The severity of coronary artery stenosis was calculated based on Quantitative Analysis or visual estimation software by cardiologists who had different experiences and had the same results, from which to calculate the Gensini score. Single-vessel CAD was referred to the presence of a ≥ 50% stenosis of one of the three main coronary arteries: right coronary artery (RCA), left circumflex artery (LCx), and left anterior descending (LAD) while the two remaining arteries had 1%–49% stenosis in diameter (defined as a non-obstructive CAD) or 0% (defined as a normal coronary angiography); a ≥ 50% stenosis of Left main coronary artery (LM) was seen as two-vessel CAD (equivalent to ≥ 50% stenosis of both LAD and LCx). The GRACE and TIMI scores were calculated using software or spreadsheets using the available template.

All the data were analyzed using SPSS ver. 22. It was expressed as percentages (%) for classification variables, average ± standard deviations, or medians (25%–75% quartiles) for quantitative variables. Use T-test or Mann-Whitney to compare two averages, Chi-square or Fisher's exact test to compare two ratios.

RESULTS

The basic characteristics of the patients are presented in Table 1. In this study, men were more predominant in the younger group (84.8% compared to 55.6%; $P = 0.0177$). The prevalence of hypertension and diabetes among younger patients was lower than the older ones (30.3% compared to 69.4%, and 3% compared to 22.2%, respectively), but the family history of CAD and smoking prevalence in the younger group was higher (18.2% compared to 2.8%; $P = 0.0462$, and 57.6% compared to 33.3%; respectively, $P = 0.0443$). There was no significant difference in overweight/ obesity and dyslipidemia between the two groups.

Table 2 shows the clinical characteristics of the two age groups. Compared to the older patients, younger patients had worse angina (angina class III-IV accounted for 69.7% compared to 36.1%; $P = 0.0108$) and lower systolic blood pressure ($P < 0.05$), but there was no significant difference in the incidence of angina or other symptoms, Killip classification, diastolic blood pressure and heart rate between the 2 groups. The proportion of patients < 40 years old who were admitted to the hospital for unstable angina was the highest (51.5%), followed by ST-elevation myocardial infarction (STEMI) (36.4%) and the age group ≥ 40 years admitted to hospital for non-ST-elevation myocardial infarction (NSTEMI) was the highest (58.3%), followed by unstable angina (30.6%).

The subclinical characteristics of the two age groups are shown in Table 3. The serum glucose concentration was significantly lower, and the serum creatinine concentration was significantly higher in the younger group compared to

Table 1: The distribution of cardiovascular risk factors between two groups

Cardiovascular risk factors	< 40 years old (*n* = 33)	≥ 40 years old (*n* = 36)	*P*-value
Male	28 (84.8%)	20 (55.6%)	0.0177
Overweight/Obese	17 (51.5%)	11 (30.6%)	0.1284
Smoking	19 (57.6%)	12 (33.3%)	0.0443
Hypertension	10 (30.3%)	25 (69.4%)	0.0027
Diabetes	1 (3.0%)	8 (22.2%)	0.0445
Dyslipidemia	27 (81.8%)	33 (91.7%)	0.3886
Family history of CAD	6 (18.2%)	1 (2.8%)	0.0462

Table 2: Clinical characteristics

Clinical characteristics	< 40 years old (*n* = 33)	≥ 40 years old (*n* = 36)	*P*-value
Angina	32 (97.0)	33 (91.7)	0.6697
Non-angina and angina (class I-II)	10 (30.3)	23 (63.9)	0.0108
Angina (class III-IV)	23 (69.7)	13 (36.1)	0.0108
Other symptoms (without angina)	18 (54.5)	19 (52.8)	0.9202
STEMI	12 (36.4)	4 (11.1)	0.0277
NSTEMI	4 (12.1)	21 (58.3)	0.0002
Unstable angina	17 (51.5)	11 (30.6)	0.1284
Killip ≥II	1 (3.0)	5 (13.9)	0.2388
Systolic blood pressure (mmHg)*	120 (110–135)	135 (120–140)	0.006
Diastolic blood pressure (mmHg)*	70 (70–80)	80 (72.5–80)	0.1712
Heart rate (beats/min)*	75 (68–90)	80 (71.3–84.8)	0.4916

(*) Medians (25% - 75% quartiles)

Table 3: Subclinical characteristics

Subclinical characteristics Medians (25%–75% quartiles)	< 40 years old (*n* = 33)	≥ 40 years old (*n* = 36)	*P*-value
Glucose (mmol/L)	5.3 (4.66–6.6)	6.44 (5.51–9.23)	0.001
Total cholesterol (mmol/L)	4.83 (4.07–5.44)	4.38 (3.59–5.42)	0.256
Triglyceride (mmol/L)	1.68 (1.17–2.79)	2 (1.21–3.01)	0.657
HDL-cholesterol (mmol/L)	1.02 (0.95–1.13)	2 (1.21–3.01)	0.862
LDL-cholesterol (mmol/L)	2.9 (2.47–3.71)	2.95 (1.98–3.58)	0.759
CK (U/L)	104 (72.5–347)	2.96 (1.41–5.49)	0.552
CK-MB (ng/mL)	1.93 (1.13–4.98)	2.96 (1.41–5.49)	0.223
hs Troponin T (ng/mL)	0.01 (0.007–0.665)	0.024 (0.011–0.104)	0.234
Creatinine (μmol/L)	80 (68–94.5)	72.5 (60.5–83.75)	0.031

the older group. Levels of total cholesterol, triglycerides, LDL and HDL cholesterol, CK, CK-MB, hs Troponin T were similar between the two groups.

Compared to the age group ≥ 40 years, the proportion of patients with ST-segment elevation was significantly higher in the < 40 years group, in contrast to the significantly lower proportion of ST-segment depression or isoelectricity. There was no significant difference in the incidence of arrhythmia, as well as the reduction in EF and mean EF between the 2 age groups (Table 4).

Table 5 shows the characteristics of coronary artery lesions. Compared to the patients aged ≥ 40 years, the incidence of LAD, LCx, and RCA lesions were lower in the < 40-year-old group. The rate of single-vessel CAD, normal coronary angiography (CAG), coronary artery stenosis was insignificant in the patients < 40 years of age and the rate of muti-vessel CAD was significantly lower than the age group ≥ 40 years. There was no difference in the prevalence of LM lesions and myocardial bridging between the two age groups. The patients < 40 years of age had significantly lower Gensini, GRACE, and TIMI scores than the ≥ 40-year-old group (Table 6).

DISCUSSION

Our research showed that ACS among young people was more common in men. The proportion of smoking and family history of CAD among the younger patients was higher than the older ones, but the prevalence of

Table 4: Characteristics of ECG and LVEF

Characteristics of ECG and LVEF	< 40 years (*n* = 33)	≥ 40 years (*n* = 36)	*P*-value
Normal sinus rhythm	25 (75.8%)	32 (88.9%)	0.2641
Arrhythmia	8 (24.2%)	4 (11.1%)	0.2641
ST segment elevation	12 (36.4%)	4 (11.1%)	0.0277
ST segment depression	8 (24.2%)	10 (27.8%)	0.9476
ST-segment isoelectric	13 (39.4%)	22 (61.1%)	0.1188
Reduced EF	11 (33.3%)	16 (44.4%)	0.4858
Mean EF ± standard deviation	60.02 ± 9.97	56.22 ± 11.68	0.1526

Table 5: Characteristics of coronary artery lesions

Coronary artery lesions	< 40 years (*n*=33)	≥ 40 years (*n* = 36)	*P*-value
LM lesions	1 (3.0)	7 (19.4)	0.0798
LAD lesions	17 (51.5)	32 (88.9)	0.0016
LCx lesions	3 (9.1)	17 (47.2)	0.0013
RCA lesions	6 (18.2)	22 (61.1)	0.0007
Normal CAG	11 (33.3)	1 (2.8)	0.0025
Nonobstructive CAD	4 (12.1)	1 (2.8)	0.3060
Single-vessel CAD	15 (45.5)	12 (33.3)	0.4293
Two-vessels CAD	1 (3.0)	11 (30.6)	0.0069
Three-vessels CAD	2 (6.1)	11 (30.6)	0.0220
Myocardial bridging	7 (21.2)	2 (5.6)	0.1180

Table 6: Gensini, GRACE and TIMI score

Gensini, GRACE, and TIMI score	< 40 years (*n* = 33)	≥ 40 years (*n* = 36)	*P*-value
Gensini score (median, range)	5 (0–32)	37.5 (13.25–75.5)	0.001
GRACE score (Mean ± standard deviation)	78.55 ± 26.23	130.22 ± 31.6	0.001
TIMI score (median, range)	2 (1–3)	3 (2–4)	0.003

hypertension and diabetes in this group was less common; this was consistent with the majority of previous domestic and foreign studies.[8–11] Smoking and dyslipidemia had been reported as the most important cardiovascular risk factors for young patients with myocardial infarction.[11] Our research also showed the same thing in young ACS patients. In addition, the predominance of a family history of CAD in young ACS patients had also been recorded through many studies.[11–13] This highlighted the role of genetic factors in the cause of ACS among young individuals.

In our study, the distribution of ACS types was markedly different when the rates of unstable angina and STEMI were significantly higher in the younger patients compared to the older ones. According to Klein *et al.* (1987), most young CAD patients had no previous history of angina until being hospitalized for acute myocardial infarction.[14] Data on STEMI prevalence in young ACS patients varied widely in different studies-ranging from 6%–73%, but all of them had in common that the proportion of STEMI in young patients was higher when compared with the group of elderly patients.[12,13,15,16]

In this study, younger patients had worse angina and lowered systolic blood pressure. In the literature, there is little available comparative data related to angina in young ACS patients. Most previous studies reporting data on angina have just focused on young patients with MI or ACS in general.[11,17]

Younger ACS patients had lower plasma glucose concentrations and higher plasma creatinine concentrations than older individuals. This can be explained by the fact that younger people are less likely to suffer from diabetes, and they often have a larger lean mass as well as a higher meat diet than older people. However, comparative data relating to subclinical characteristics in young ACS patients is still limited; some previous studies have shown different results, possibly due to differences in sample selection and anthropometry characteristics of research subjects.[16,18,19]

Younger patients with ACS had a higher incidence of normal CAG and non-obstructive CAD than the older ones. The pathogenesis of ACS in young patients without obstructive CAD may be related to coronary artery spasm, spontaneous coronary artery dissection, endothelial

dysfunction, myocardial bridging, or non-coronary causes (*e.g.*, anemia, respiratory failure, hypovolemic shock, tachycardia/slow arrhythmia). Similar to other studies, the majority of single-vessel CAD was in younger patients, while most multi-vessel CAD was more common in older patients.[17,20]

Compared to the older patients, the younger ACS ones had lower coronary artery lesions on the Gensini score and a lower prognosis of death on the GRACE, TIMI scores. In other words, the younger patients have a better prognosis than the older ones. This has also been noted in previous studies.[21,22]

CONCLUSION

ACS patients in young adults had a higher incidence in males accompanied with smoking and family medical history of CAD; the grade of angina was more severe and systolic blood pressure was lower; the prevalence of Unstable angina and STEMI was also higher compared to the elderly patients. Elderly patients had higher blood glucose levels and lower creatinine levels; the rate of CAD with multi-vessel disease was higher in the young patients. Additionally, in the young patients, the Gensini, GRACE, and TIMI scores were lower, and smoking was the risk factor for obstructive CAD.

Further efforts are needed to prevent smoking among adolescents to avoid and overcome smoking addiction. Clinicians should carefully assess the suspicion of ACS in young people to avoid missing the diagnosis of ACS.

Author's contribution

All the authors participated in the study design, data collection, and literature search. Data was analyzed by DTA. HAB wrote the paper. All the authors read and approved the final manuscript.

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Conflicts of Interest

The authors declare no conflict of interest

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