Epidemiological Features and Clinical Presentations of Acute Coronary Syndrome in Young Patients

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Abstract:
Objective Although acute coronary syndrome (ACS) is an uncommon entity in young patients, it constitutes an important problem due to the devastating effects of the disease on the more active lifestyle of young patients. At present, there are no guidelines regarding the prevention of ACS in young patients.
Methods We performed a retrospective study of ACS patients between 2014 and 2017. Epidemiological data, clinical findings, and short-term outcomes were evaluated between young ACS patients (≤50 years old) and elderly ACS patients (>50 years old).
Results Of a total of 361 consecutive ACS patients, 37 were young ACS patients (10.2%). Compared with elderly ACS patients, young ACS patients showed a higher prevalence of males (94.6% vs. 73.8%, p<0.001), current smoking (70.3% vs. 29.9%; p<0.001), and overweight persons (67.6% vs. 27.8%, p<0.001). The eicosapentaenoic acid (EPA)/arachidonic acid (AA) ratio was significantly lower in young ACS patients than in elderly ACS patients (0.17 [0.12-0.25] vs. 0.25 [0.18-0.37], p=0.002). The prevalence of cardio-pulmonary arrest and percutaneous cardiopulmonary support use was higher in young ACS patients than in elderly ACS patients (24.3% vs. 8.6%, p=0.003, 16.2% vs. 3.1%, p<0.001).
Conclusion The features were markedly different between young ACS patients and elderly ACS patients. In young ACS patients, smoking, being overweight, and a low EPA/AA ratio were distinctive risk factors, and more serious clinical presentations were observed at the onset of ACS than in older patients.

Key words: acute coronary syndrome, young patients, smoking, EPA/AA, Cardiac arrest

Introduction

Coronary heart disease remains a major cause of death and disability in all regions of the world (1). Although acute coronary syndrome (ACS) primarily occurs in the older age group, younger people can also be affected, and the number of ACS in younger people has been gradually increasing (2). Furthermore, it constitutes an important problem for patients and treating physicians due to the devastating effects of the disease on the more active lifestyle of younger patients. However, there are currently no guidelines or consensus regarding the prevention and treatment of ACS in young patients.

In the present study, we compared the clinical pictures of ACS in young patients with those of elderly patients to help determine the optimal prevention and treatment strategies.

Materials and Methods

Study population
This study was designed as a single-center retrospective study to evaluate the predictive factors and clinical characteristics of ACS in young patients. We analyzed the data of consecutive patients with ACS who underwent percutaneous coronary intervention (PCI) for de novo native coronary artery lesions between January 2014 and December 2017 at Aichi Medical University. ACS included ST segment elevation myocardial infarction, non-ST segment elevation myoe-
cardiac infarction, or unstable angina. Patients <50 years old were classified as young ACS patients, while those ≥50 years old were classified as elderly ACS patients.

**Procedures and coronary risk factors**

PCI was performed according to the standard techniques. Stenting strategy (stent type, stent size, direct stenting, or non-stent strategy), thrombus aspiration or distal protection, and post-dilatation were left to the operator’s discretion. Before or during PCI, all patients were administered 200 mg of aspirin and a loading dose of a P2Y12 inhibitor (300 mg of clopidogrel or 20 mg of prasugrel). On the day after the loading dose, a maintenance dose of dual antiplatelet therapy (aspirin 100 mg and a P2Y12 inhibitor [75 mg of clopidogrel or 3.75 mg of prasugrel]) was administered. Hypertension was defined as a medical history of systemic hypertension or the use of antihypertensive treatment. Dyslipidemia was defined as a previous diagnosis of dyslipidemia or the use of a lipid-lowering treatment. Overweight was defined as having a body mass index (BMI) ≥25 kg/m² based on the proposed classification by the WHO (3). For the short-term outcome, the all-cause mortality within 30 days after the index PCI was evaluated.

**Statistical analyses**

All statistical analyses were performed with the SPSS software program (version 22.0; IBM, Armonk, NY, USA). Data are expressed as the mean ± standard deviations or as medians and interquartile ranges with differences (95% confidence intervals). Categorical variables are expressed as frequencies (%). The normality of distribution was tested by the Kolmogorov-Smirnov test. Continuous variables were compared using the unpaired Student’s t-test, and categorical variables were compared using the chi-squared or Fisher’s exact tests where appropriate. Mann-Whitney U tests were performed for non-parametric data. Statistical significance was assumed at a probability (P) value of <0.05.

**Results**

**Patient characteristics**

A total of 361 consecutive ACS patients were evaluated in the present study. Of these, 37 were young ACS patients, accounting for 10.2% of total ACS patients, and the remaining 324 (89.8%) were elderly ACS patients (Supplementary Fig. 1). The proportion of men was predominantly higher among the young ACS patients than among the elderly ACS patients (94.6% vs. 73.8%, p<0.001). In terms of conventional risk factors, there were no significant differences in the prevalence of hypertension, diabetes, and dyslipidemia between the two groups (Table 1). The prevalence of current smoking was significantly higher among young ACS patients than among elderly ACS patients (Fig. 1). Regarding anthropometric measurements, in young ACS patients, the BMI was significantly higher (27.8±4.7 kg/m² vs. 23.0±3.8 kg/m², p<0.001) as was the prevalence of overweight than in elderly ACS patients (Fig. 1). Regarding the medications administered before admission, angiotensin receptor blockers, Ca-channel antagonists, and antiplatelet agents were more commonly used in elderly ACS patients than in young ACS patients (Supplementary Table 1).

![Figure 1. Distinctive risk factors associated with ACS in young patients. (A) Prevalence of current smoking between young ACS patients and elderly ACS patients. (B) Prevalence of overweight between young ACS patients and elderly ACS patients. (C) Prevalence of EPA/AA ≤0.3 between young ACS patients and elderly ACS patients. ACS: acute coronary syndrome, EPA: eicosapentaenoic acid, AA: arachidonic acid](image-url)
Lab 


ter findings

Low-density lipoprotein cholesterol levels were similar between the two groups. High-density lipoprotein cholesterol levels were significantly lower and triglycerides significantly higher in young ACS patients than in elderly ACS patients (Table 1; 38.4±7.1 mg/dL vs. 42.7±12.4 mg/dL, p=0.02; 156 [114-198] mg/dL vs. 102 [73-138] mg/dL, p<0.001, respectively). The HbA1c values were similar between the two groups. Serum eicosapentaenoic acid (EPA) and serum docosahexaenoic acid were significantly lower and serum arachidonic acid (AA) significantly higher in young ACS patients than in elderly ACS patients. Consequently, the EPA/AA ratio was significantly lower in young ACS patients than in elderly ACS patients (0.17 [0.12-0.25] vs. 0.25 [0.18-0.37], p=0.002). The prevalence of patients with an EPA/AA ratio ≤0.3 was significantly higher in young ACS patients than in elderly ACS patients (Fig. 1).

Clinical presentations

Angiographic findings and clinical presentations are shown in Table 2. There was no significant difference in the classification of ACS (ST segment elevation myocardial infarction, non-ST segment elevation myocardial infarction, or unstable angina) between the two groups. Single-vessel disease predominated in young ACS patients (83.8%), whereas it was found in approximately half of the elderly ACS patients (51.5%). Regarding the clinical presentations, more serious conditions were observed in young ACS patients than in elderly ACS patients. Patients with a higher Killip class were more frequently observed among young ACS patients than among elderly ACS patients. The prevalence of patients with cardio-pulmonary arrest (CPA) on arrival as well as those requiring percutaneous cardiopulmonary support (PCPS) was significantly higher among young ACS patients than among elderly ACS patients (Fig. 2). Even after PCI, patients with a lower TIMI flow grade were more frequently observed among young ACS patients than among elderly ACS patients. While the difference was not statistically significant, the 30-day mortality was numerically higher in young ACS patients than in elderly ACS patients.

Discussion

The present study highlighted the differing features between young and elderly ACS patients. The main findings were as follows: 1) a higher prevalence of men, current smokers, and overweight individuals was observed among young ACS patients; 2) the EPA/AA ratio was lower in young ACS patients than in older ones; and 3) despite multi-vessel diseases being uncommon, serious conditions were more frequently observed in young ACS patients than in older ones.

Although ACS has a tragic impact on the daily life of younger patients, there are currently no guidelines or consensus regarding the prevention and treatment of ACS in this population. Furthermore, there have been almost no large-scale trials recently focusing on young ACS patients. Under
Table 2. Clinical Presentations.

|                      | Young ACS (n=37) | Elderly ACS (n=324) | p    |
|----------------------|------------------|---------------------|------|
| Clinical presentation|                  |                     |      |
| STEMI                | 30 (81.1)        | 211 (65.1)          | 0.47 |
| NSTEMI               | 2 (5.4)          | 25 (7.7)            |      |
| UAP                  | 5 (13.5)         | 88 (27.2)           |      |
| Systolic blood pressure, mmHg | 139.6±27.8     | 147.0±29.6          | 0.24 |
| Killip classification|                  |                     | <0.001|
| Class I              | 23 (62.2)        | 269 (83.0)          |      |
| Class II             | 1 (2.7)          | 10 (3.1)            |      |
| Class III            | 1 (2.7)          | 16 (4.9)            |      |
| Class IV             | 12 (32.4)        | 29 (9.0)            |      |
| Vessel related to the ACS|              |                     | 0.22 |
| Left anterior descending artery | 22 (59.5) | 137 (42.3) |      |
| Left circumflex artery | 2 (5.4)       | 45 (13.9)           |      |
| Right coronary artery | 13 (35.1)      | 129 (39.8)          |      |
| Left main artery     | 0 (0)            | 12 (3.7)            |      |
| Bypass graft         | 0 (0)            | 1 (0.3)             |      |
| No. of affected vessels|                |                     | 0.01 |
| 1                    | 31 (83.8)        | 167 (51.5)          |      |
| 2                    | 6 (16.2)         | 103 (31.8)          |      |
| 3                    | 0 (0)            | 54 (16.7)           |      |
| TIMI flow grade before PCI |            |                     | 0.07 |
| 0                    | 23 (62.2)        | 146 (45.1)          |      |
| I                    | 0 (0)            | 39 (12.0)           |      |
| II                   | 6 (16.2)         | 48 (14.8)           |      |
| III                  | 8 (21.6)         | 91 (28.1)           |      |
| TIMI flow grade after PCI |            |                     | <0.001|
| 0                    | 1 (2.7)          | 0 (0)               |      |
| I                    | 3 (8.1)          | 0 (0)               |      |
| II                   | 3 (8.1)          | 16 (4.9)            |      |
| III                  | 30 (81.1)        | 308 (95.1)          |      |
| Maximum CK, IU/L     | 2,135 (792-5,383)| 1,154 (307-2,762)   | <0.001|
| 30-day mortality     | 5 (13.5)         | 22 (6.8)            | 0.14 |

Values are means±SD or n (%).

STEMI: ST segment elevation myocardial infarction, NSTEMI: Non-ST segment elevation myocardial infarction, UAP: Unstable angina, ACS: Acute coronary syndrome, TIMI: Thrombolysis in myocardial infarction, PCI: Percutaneous coronary intervention, IABP: intra-aortic balloon pump counterpulsation, PCPS: Percutaneous cardiopulmonary support

these circumstances, the present study might therefore provide a roadmap for the more effective prevention and management of young ACS patients.

ACS is generally known to occur more often in men than in women (4). In the present study as well, an overwhelming majority of young ACS patients were men (94.6%), which is consistent with the high prevalence of men reported in the Framingham Heart Study (5). It has also been well established that cigarette smoking is a powerful risk factor for coronary artery disease (6, 7). Cigarette smoking promotes vascular endothelial dysfunction and inflammation, resulting in atherosclerosis progression and changes in plaque composition (8, 9). In public settings, the smoking rate is higher among younger people than older people, and Japan Tobacco Inc. reported that the smoking rate of Japanese men in their 30s and 40s was around 35% (10). The smoking rate in young ACS patients (70.3%) in the present study is still higher than in the general population. Being overweight was also found to be characteristic of young ACS patients (67.6%) in this study and is widely recognized as a risk factor for coronary heart disease in the elderly. An autopsy study demonstrated that a high BMI was associated with both fatty streaks and raised coronary atherosclerotic lesions in young men (11).

Of note, however: hypertension, diabetes, and dyslipidemia were not distinctive features in this population when compared with elderly ACS patients. Laboratory findings showed that young ACS patients had lower HDL cholesterol levels and higher triglyceride levels than elderly ACS patients, which was consistent with the results of a previous study (12). The EPA/AA ratio was also a contributor to ACS in young patients, and almost all young ACS patients (96.8%) showed an EPA/AA ratio ≤0.3. Several epidemiologic studies have shown that a lower EPA/AA ratio was
associated with unstable plaque composition (13-15), cardiovascular events (including ACS) (16-18) and fatal arrhythmic events in the early phase of AMI (19). EPA has beneficial effects on multiple atherosclerotic processes, from protecting against endothelial dysfunction to reducing plaque formation, inflammation, and vulnerability (20-23). In the present study, elderly ACS patients also showed low EPA/AA ratios (0.25 [0.18-0.37]), while young ACS patients showed still lower EPA/AA ratios (0.17 [0.12-0.25]), representing an even higher risk of ACS in young patients. The EPA/AA ratio generally increases with age (24) due to differences in the consumption of dietary fish and age-related changes in serum fatty acid metabolism (25). Therefore, we cannot rule out the possibility that a lower EPA/AA ratio in young ACS patients represents the general findings in young people. This result is in line with the findings of a previous study that showed a reduced EPA/AA ratio as a contributor to the early onset of ACS (26).

Ultimately, the present study extracted three modifiable risk factors (current smoking, being overweight and a low EPA/AA ratio) as distinctive features of young ACS patients. The prevalence of these three cumulative risk factors is indicated in Fig. 3. It is noteworthy that about 90% of young ACS patients had multiple risk factors, while only 40% of elderly ACS patients had multiple risk factors. From a practical point of view, our results suggest that the modification of these risk factors can be expected to prevent the onset of ACS in younger populations. This hypothesis needs to be investigated through prospective interventional trials in the future.

Despite the number of coronary lesions being fewer, a higher Killip class and a higher prevalence of CPA and PCPS use were observed in young ACS patients than in older patients. Previous studies have shown a younger age to be significantly associated with the occurrence of life-

![Figure 2. Prevalence of CPA on arrival and PCPS use. (A) Prevalence of CPA on arrival between young ACS patients and elderly ACS patients. (B) Prevalence of PCPS use between young ACS patients and elderly ACS patients. CPA: cardiopulmonary arrest, PCPS: percutaneous cardiopulmonary support, ACS: acute coronary syndrome](image)

![Figure 3. Prevalence of cumulative three risk factors (current smoking, overweight and EPA/AA ≤0.3). The prevalence of three cumulative risk factors (current smoking, overweight and EPA/AA ≤0.3) in both young ACS patients and elderly ACS patients is shown. Patients with two or more risk factors accounted for 90.3% of young ACS patients and 36.4% of elderly ACS patients. Conversely, patients with no risk factors accounted for only 3.2% of young ACS patients. ACS: acute coronary syndrome, EPA: eicosapentaenoic acid, AA: arachidonic acid](image)
threatening arrhythmia in the setting of acute myocardial infarction (27, 28). The absence of angina before the onset of ACS, which is a characteristic finding in young ACS patients (29), is also associated with life-threatening arrhythmia (27).

**Study limitations**

Several limitations associated with the present study warrant mention. This was a single-center study with a relatively small population, which might have resulted in the lack of statistical power. Consequently, the present study might have missed important features of young ACS patients. In addition, this was a post-hoc analysis; the results are therefore hypothesis-generating. Larger prospective studies are warranted to validate our results.

**Conclusions**

Young ACS patients present with markedly different features from those seen in elderly ACS patients. In young ACS patients, smoking, being overweight, and a low EPA/AA ratio were distinctive risk factors, and more serious clinical presentations were observed at the onset of ACS.

**Acknowledgement**

We thank the patients who participated in the present study.

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