Coronary Artery Disease

Impact of Conventional Cardiovascular Risk Factors on Acute Myocardial Infarction in Young Adult Taiwanese

Yen-Chen Lin,1 Lung-An Hsu,1 Yu-Shien Ko,1 Chi-Tai Kuo,1 Wei-Jan Chen,1 Chia-Pin Lin,1 Wen-Harn Pan2* and Chi-Jen Chang1

Background: The impact of conventional cardiovascular (CV) risk factors on acute myocardial infarction (AMI) defined by the universal definition published in 2007 hasn’t been evaluated in young population in Taiwan according to the comparison of their prevalence between young AMI patients and age- and sex-matched contemporary controls.

Methods: AMI patients, aged between 18 and 44 and admitted to the First CV Division, Chang Gung Memorial Hospital, Linkou, Taiwan from Mar. 2005 to Dec. 2008, were included. Age- and sex-matched controls who had no evidence of ischemic heart disease were randomly selected with a control/patient ratio of 2:1 from the database of the Nutrition and Health Survey in Taiwan, 2005-2008. Prevalence of cigarette smoking, diabetes mellitus (DM), hypertension (HTN), dyslipidemia and obesity, as well as values of lipid profiles and body mass index (BMI) were compared between the two groups.

Results: Totally 65 male and 5 female young AMI patients were analyzed. The young AMI group had significantly higher prevalence of cigarette smoking, DM, HTN and obesity. Young AMI patients also had significantly higher mean levels of BMI, low-density lipoprotein cholesterol, total cholesterol and triglyceride, and significantly lower mean level of high-density lipoprotein cholesterol (HDL-C). Multivariate analysis showed that HTN, DM, low HDL-C and cigarette smoking were independent predictors of AMI in young people.

Conclusion: HTN, DM, low HDL-C and cigarette smoking are independent risk factors of AMI in young adult Taiwanese. Among these risk factors, cigarette smoking is the most prevalent, while HTN is the most powerful.

Key Words: Acute myocardial infarction • Premature • Risk factors • Young

INTRODUCTION

Acute myocardial infarction (AMI) in the young, defined as being less than 40-45 years of age in most studies, accounts for 3-12% of total AMI.1-5 It is reported that as many as 90-97% of young AMI patients have at least 1 conventional cardiovascular (CV) risk factor, such as cigarette smoking, diabetes mellitus (DM), hypertension (HTN), dyslipidemia or obesity.5 Although the prevalence of conventional CV risk factors varies among different age groups in the general population, most previous studies weighed the importance of those factors in young AMI by comparing their prevalence in...
young AMI cases with that in older ones, or with that in age-unmatched MI-free controls. On the other hand, two case-control studies investigated risk factors of young AMI by exactly the same very young (< 36 years of age) AMI patients and age- and sex-matched controls, but the criteria for AMI in the studies were inadequate and unacceptable at the present time. Accordingly, we designed a retrospective case-control study with age- and sex-matched contemporary controls to evaluate the impact of conventional CV risk factors on guideline-defined AMI in young adult Taiwanese.

MATERIALS AND METHODS

Young patients with guideline-defined AMI

Patients, aged between 18 and 44 and admitted with the diagnosis of acute coronary syndrome (ACS) to the First CV Division, Chang Gung Memorial Hospital, Linkou, Taiwan between Mar. 2005 and Dec. 2008 were screened initially. Patients with guideline-defined AMI were included, and those discharged with the diagnosis of acute myocarditis, apical ballooning syndrome or post-traumatic AMI were excluded. According to the universal definition published in 2007, AMI was diagnosed in the present study by detection of rise and/or fall of troponin I with at least 1 value above the 99th percentile of the upper reference limit together with evidence of myocardial ischemia with at least 1 of the following:

- Symptoms of ischemia;
- Electrocardiographic changes indicative of new ischemia (new ST-T changes or new left bundle branch block);
- Development of pathological Q waves in the electrocardiogram (ECG);
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

Controls

Age- and sex-matched contemporary controls were randomly selected with a control/patient ratio of 2:1 from the database of the Nutrition and Health Survey in Taiwan (NAHSIT) (http://nahsit.survey.sinica.edu.tw/node/1). The controls and their corresponding AMI patients had exactly the same age. The NAHSIT, conducted from July 2005 to July 2008, was sponsored by the Department of Health, Taiwan (DOH94-fs-6-4), and well demonstrated the distribution of conventional CV risk factors in different age groups of the general population in Taiwan. None of the controls had histories or ECGs suspicious for ischemic heart disease.

Cardiovascular risk factors

Conventional CV risk factors, including cigarette smoking, DM, HTN, dyslipidemia, and obesity, were the targets for evaluation. People who smoked ≥ 0.5 packs of cigarettes per day for > 1 year in the past 2 years were regarded as smokers. DM was defined as a fasting blood sugar ≥ 126 mg/dl or as using hypoglycemic agents. For AMI patients without previous history of DM, a glycohemoglobin value ≥ 6.5% was used to diagnose DM according to the clinical practical guideline of the American Diabetes Association. HTN was defined as a systolic blood pressure (BP) ≥ 140 mmHg and/or a diastolic BP ≥ 90 mmHg, or as taking antihypertensive drugs. A systolic BP ≥ 180 mmHg and/or a diastolic BP ≥ 110 mmHg on ≥ 2 occasions during the hospitalization were considered to diagnose HTN in young AMI patients. Blood samples for measuring lipid profiles were drawn after a 12-hour fast. In the young AMI group, lipid profiles obtained within the first 4 days after onset of AMI were included in the final analysis; otherwise they were treated as missing data. The levels of high-density lipoprotein cholesterol (HDL-C) considered low were serum levels of HDL-C < 40 mg/dl for men and < 50 mg/dl for women. Low-density lipoprotein cholesterol (LDL-C) levels for those with a 12-hour-fasting triglyceride (TG) < 400 mg/dl were calculated by the Friedewald equation, and for those with a 12-hour-fasting TG ≥ 400 mg/dl were treated as missing data. Body mass index (BMI) was defined as body weight in kilograms (kg) divided by squared body length in meters (m). A BMI ≥ 27 kg/m² was defined as obesity for Taiwanese by definition according to the Department of Health, Taiwan.

Statistics

Continuous data were expressed as mean ± SD for those normally distributed and as median [25th percentile, 75th percentile] for those with skewed distributions. Comparisons between groups were performed by the un-
paired t test. A chi-square test was used to examine differences among categorical data. A multivariate logistic regression analysis was used to evaluate the independent effect of investigated parameters on the risk of young AMI. Triglycerides were logarithmically transformed before statistical analysis to meet a normality assumption. A p value < 0.05 using a two-sided test was considered statistically significant.

RESULTS

General characteristics
A total of 71 patients were enrolled in the young AMI group initially. One patient in whom AMI occurred after traffic accident and angiogram showed dissection at the left anterior descending coronary was excluded since trauma was the apparent cause of AMI. Finally, 65 men and 5 women were included in the young AMI group, with a male/female ratio of 13:1. The youngest male and female AMI patients were 28 and 33 years old, respectively. The control group was composed of 140 age- and sex-matched subjects. The detailed characteristics for both the young AMI and control groups are summarized in Table 1.

Risk factor analysis
In univariate analysis (Tables 1 and 2), the young AMI group had significantly higher prevalence of cigarette smoking, DM, HTN, obesity, hypercholesterolemia (total cholesterol (TC) ≥ 240 mg/dl), hypertriglyceridemia and low HDL-C. The young AMI group also had significantly higher value of BMI, TC and TG, and significant lower value of HDL-C (Table 1). For LDL-C, while its value was significantly higher in the young AMI group, the prevalence of elevated LDL-C (≥ 130 mg/dl) was not statistically different between the two groups (Table 2).

Multivariate analysis (Table 3) revealed that the factors independently predicting AMI in young adults included HTN, DM, low HDL-C and cigarette smoking. Elevated LDL-C, hypercholesterolemia, hypertriglyceridemia, and obesity were not independent risk factors. HTN was found to be the strongest discriminator of AMI in young people.

DISCUSSION

The current study is the first study investigating the impact of conventional CV risk factors on new guideline-defined AMI in young adult Taiwanese by comparing their prevalence in a young AMI group with that in an age- and sex-matched contemporary MI-free cohort. Major conventional CV risk factors for general population including HTN, DM, low HDL-C and cigarette smoking were confirmed to be important discriminators for young AMI. However, elevated LDL-C, hypercholesterol...

Table 1. Characteristics of the young AMI patients and the age- and sex-matched contemporary controls

<table>
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<tr>
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<th>Young MI (n = 70)</th>
<th>Controls (n = 140)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Male in gender</td>
<td>65 (92.9%)</td>
<td>130 (92.9%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Age, years old</td>
<td>40 [37; 43]</td>
<td>40 [37; 43]</td>
<td>1.000</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>20 (28.6%)</td>
<td>8 (5.7%)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>34 (48.6%)</td>
<td>14 (10.0%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cigarette smoking, n (%)</td>
<td>52 (77.6%)</td>
<td>71 (50.7%)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Obesity, n (%)</td>
<td>38 (58.5%)</td>
<td>35 (25.0%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>28.1 ± 4.0</td>
<td>24.7 ± 3.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl (n)</td>
<td>207 ± 47 (68)</td>
<td>190 ± 36 (140)</td>
<td>0.010</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dl (n)</td>
<td>130 ± 47 (65)</td>
<td>114 ± 33 (135)</td>
<td>0.015</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dl (n)</td>
<td>37 ± 9 (67)</td>
<td>49 ± 14 (140)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TC/HDL-C ratio (n)</td>
<td>5.98 ± 2.03 (67)</td>
<td>4.18 ± 1.34 (140)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LDL-C/HDL-C ratio (n)</td>
<td>3.73 ± 1.70 (65)</td>
<td>2.45 ± 0.98 (135)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Triglyceride, mg/dl (n)</td>
<td>195 ± 103 (68)</td>
<td>143 ± 100 (140)</td>
<td>&lt; 0.001</td>
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Serum triglyceride values were logarithmically transformed before statistical testing to meet the assumption of normal distribution; however, the untransformed data are shown.
lesterolemia, hypertriglyceridemia or obesity didn’t significantly predict AMI in young population. This study’s design in lipid testing is unique in that we analyzed lipid profiles obtained within 4 days after an AMI attack. Since most young AMI patients did not have pre-event lipid data and received statin therapy after AMI, their baseline lipid values were usually unavailable. Earlier small studies reported that clinically significant changes in components of the lipid profile were found within hours after an AMI and persisted for around 2 months. Accordingly, the American College of Cardiology/American Heart Association guidelines of 2007 recommend that assessment of fasting lipid profile should be obtained within 24 hours after hospitalization. Recently, an analysis in 2008 from the LUNAR (Limiting UNdertreatment of lipids in ACS with Rosuvastatin) study, in which the patient number was twice as many as that of the summation of all the earlier small studies, concluded that mean lipid levels vary relatively little in the first 4 days after an ACS. Based on this finding, the European Society of Cardiology guideline published in 2008 on management of AMI suggests that fasting lipid levels checked within 4 days after an ACS can be used for clinical decisions about further therapy.

The key finding of the present study is that, in comparison to age- and sex-matched controls, low HDL-C level was not only the second most common risk factor (with prevalence of 73.1%) but also the solely significant lipid predictor for young AMI patients. In contrast, while the young AMI group had significantly higher mean level of LDL-C, prevalence of elevated LDL-C (≥130 mg/dl), although slightly higher, was not statistically different from that in the control group (41.5% vs. 31.9%, p = 0.179). Many patients with high LDL-C had multiple CV risk factors, and LDL-C didn’t predict AMI in the young after adjustment with other risk factors. In addition, although genetic or cellular diagnosis of familial hypercholesterolemia (FH) is not undertaken, there was only 1 study patient who had very high LDL-C level and could be diagnosed with FH by the clinical criteria of the Make Early Diagnosis to Prevent Early Death (MEDPED) program. Most of the previous studies dealing with

<table>
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<th>Table 2. Number and percentage of people with abnormal lipid profiles in 70 patients and 140 controls compared by ANOVA</th>
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<tr>
<td>Young MI</td>
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<tr>
<td>Total cholesterol ≥ 240 mg/dl, n (%)</td>
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<tr>
<td>Total cholesterol ≥ 200 mg/dl, n (%)</td>
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<tr>
<td>LDL cholesterol ≥ 130 mg/dl, n (%)</td>
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<tr>
<td>Low HDL cholesterol, n (%)</td>
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<tr>
<td>Triglyceride ≥ 150mg/dl, n (%)</td>
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<tr>
<td>TC/HDL-C &gt; 5, n (%)</td>
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<td>LDL-C/HDL-C &gt; 3, n (%)</td>
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Low HDL cholesterol, defined as HDL cholesterol < 40 mg/dl for men and < 50 mg/dl for women.

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<th>Table 3. Odds ratios of conventional CV risk factors on AMI among young adult Taiwanese analyzed by multivariate logistic regression</th>
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<td>Odds ratio (95% C.I.)</td>
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<tr>
<td>Hypertension, yes vs. no</td>
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<tr>
<td>Diabetes mellitus, yes vs. no</td>
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<tr>
<td>Low HDL cholesterol, yes vs. no</td>
</tr>
<tr>
<td>Cigarette smoking, yes vs. no</td>
</tr>
<tr>
<td>LDL-C/HDL-C &gt; 3, yes vs. no</td>
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<tr>
<td>Total cholesterol ≥ 240 mg/dl, yes vs. no</td>
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<tr>
<td>Body mass index ≥ 27 kg/m², yes vs. no</td>
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<tr>
<td>LDL cholesterol ≥ 130 mg/dl, yes vs. no</td>
</tr>
<tr>
<td>Triglyceride ≥ 150 mg/dl, yes vs. no</td>
</tr>
<tr>
<td>TC/HDL-C &gt; 5, yes vs. no</td>
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Similar results are obtained when patients using lipid-lowering drugs are excluded (data not shown).
risk factors of young AMI did not include detailed lipid profiles in the multivariate analysis.\textsuperscript{1-10,23} The present result manifests the importance of HDL-C in the pathogenesis of AMI in young Taiwanese population, and highlights the necessity of including complete lipid profiles in the multivariate analysis in the future studies on risk factors of young AMI. We also emphasize the value of routine complete lipid profile checkup even in the young age group.

In this study, the prevalence of cigarette smoking in the young AMI group was 77.6\%, and 50.7\% in the control group. This high percentage of smoking in young Taiwan population is further confirmed by another large survey, the Telephone Survey on the Smoking Behavior of Adults (http://olap.bhp.doh.gov.tw/), performed in 2006 by the Bureau of Health Promotion, Department of Health, Taiwan. According to this survey, the prevalence of current smoking in Taiwan is as high as 50\% in the general male population aged between 30 to 49 years. The present result that cigarette smoking was the most prevalent independent risk factor for young AMI further underscores the importance of smoking prevention and cessation in decreasing the incidence of AMI in the young population.

Although HTN and DM were less common in young AMI patients than in older ones in previous studies,\textsuperscript{1-8} they were the two most prominent independent risk factors of AMI in young Taiwanese population. Since both physicians and young patients are usually concerned about possible side effects of long-term pharmacological treatment and are unaware of the danger of HTN and DM in the young, both diseases are usually undertreated in young population. Our findings highlight the importance of early detection and control of HTN and DM even in young people.

Both the level of mean BMI and the prevalence of obesity were higher in the young AMI group compared with those in controls, but obesity defined as a BMI $\geq$ 27 kg/m$^2$ was not an independent risk factor of AMI in young adult Taiwanese. One case-control study concluded that obesity, defined as a BMI $\geq$ 25 kg/m$^2$, was a significant independent risk factor for AMI in young and middle-aged Japanese male adults; however, HDL-C is not included in the multivariate risk factor analysis.\textsuperscript{9} Some studies concluded that waist-to-hip ratio but not BMI was an independent risk factor of AMI.\textsuperscript{24,25}

The present study focused on the significance of risk factors of atherosclerosis on AMI in young people; however, pathological conditions other than atherosclerosis may also result in AMI in young population.\textsuperscript{26,27} Hypercoagulable states including antiphospholipid syndrome, factor V Leiden mutation, nephrotic syndrome and contraceptive pill use, have been reported to cause young AMI.\textsuperscript{28-34} Recreational substances such as cocaine, amphetamine, marihuana and marijuana, may also be associated with young AMI.\textsuperscript{35-37} Non-atherosclerotic coronary abnormalities like congenital coronary anomalies, spontaneous or traumatic coronary dissection, coronary aneurysm, coronary vasculitis and coronary spasm can induce AMI in young population as well.\textsuperscript{14,38-43} Correct diagnosis is based on clinical suspicion by comprehensive history-taking, detailed physical exam, and careful interpretation of lab data and coronary angiography. Management may be modified according to the different pathophysiology of the underlying etiology of AMI in a specific patient.

**Limitations**

There are two additional limitations in this study. First, this was a single-center study with a small patient number. Second, a family history of premature coronary artery disease was not included in this study. Since this data was not available in the NAHSIT database, we were unable to analyze this potential factor for young AMI.

**CONCLUSION**

Conventional CV risk factors, including HTN, DM, low HDL-C and cigarette smoking, are independent predictors of AMI in young adult Taiwanese. Among these risk factors, cigarette smoking is the most prevalent, while HTN is the most powerful. Early detection and control of these factors may be mandatory to prevent AMI in young people.

**REFERENCES**


