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Coronary Artery Disease

Clinical Characteristics of Patients Less than Forty Years Old with Coronary Artery Disease in Taiwan: A Cross-Sectional Study

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Background: Coronary artery disease (CAD) rarely occurs in young adults. Our objective was to investigate the baseline characteristics and outcomes of young patients with CAD.

Methods: We retrospectively enrolled patients aged < 40 years of age who underwent coronary angiography in a tertiary hospital in Taiwan between 2002 and 2015. The baseline characteristics and in-hospital outcomes of patients with acute coronary syndrome (ACS) and occlusive CAD (stenotic lesions > 50%) were compared with those of patients without ACS and non-occlusive CAD, respectively.

Results: We enrolled 245 young patients including 131 (53.5%) with ACS and 178 with occlusive CAD. The median age of the patients was 36.08 years and the mean follow-up period was 4.84 years. Of all study subjects, 220 (89.8%) were men and 140 (57.1%) were current smokers; there was an overall in-hospital mortality rate of 3.3%. Furthermore, age, body mass index, smoking, total leukocyte count, neutrophil-to-lymphocyte ratio, total cholesterol, and low-density lipoprotein were higher in patients with ACS and significant CAD than in those without ACS and nonstenotic CAD. Interestingly, triglyceride (TG) levels and the TG to high-density lipoprotein ratio were significantly higher in patients with ACS and occlusive CAD than in those without ACS and non-occlusive CAD. Logistic regression analysis revealed that smoking is an independent predictor of ACS and occlusive CAD.

Conclusions: Our findings suggest that classical risk factors, obesity, and inflammation remain potent contributors to occlusive CAD and ACS in young adults in Taiwan. Efforts to prevent or minimize these risk factors, such as smoking cessation and aggressive lipid control, are necessary in young adults.

Key Words: Acute coronary syndrome • Coronary artery disease • Young adults

INTRODUCTION

Coronary artery disease (CAD) is a major cause of morbidity and mortality in the general population worldwide. Although atherosclerosis, the main cause of CAD, develops in the early stage of life,[1] symptomatic CAD and acute coronary syndrome (ACS) rarely occur in young adults less than 40 years of age. The incidence of ACS in such young adults has been reported to account for 0.4-19% of all ACS cases.[2-12] Studies have suggested that the early incidence of CAD is increasing in young people because of their preference for high-fat diets and unhealthy lifestyles, in addition to their increased

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incidence of metabolic syndrome, hypertension, and dysglycemia.[13-15] Moreover, studies have suggested that conventional vascular risk factors encountered in the middle-aged population in the Framingham study are present in the young population.[18] Smoking, hypercholesterolemia, and low high-density lipoprotein (HDL) levels are associated with CAD in young patients. In addition, obesity, insulin resistance, and hypertriglycemia are risk factors for CAD in the young population.[19] In addition, nonatherosclerotic factors such as cocaine use, high homocysteine levels, connective tissue diseases, and hypercoagulopathy, including antiphospholipid syndrome and nephrotic syndrome, may precipitate CAD.[20-24]

An earlier study from Chu et al. involving 31 young Chinese patients with catheterization-documented CAD pointed out the most important risk factors of CAD are male gender and smoking among.[25] However, data regarding the analysis of baseline characteristics and clinical outcomes in young adults in Taiwan are lacking. Therefore, in the current study, we investigated the baseline characteristics and in-hospital outcomes of Taiwanese patients aged < 40 years of age, who were suspected of having CAD and thus underwent coronary angiography.

METHODS

Study population and data collection

We included patients aged < 40 years of age who underwent coronary angiography at Tri-Service General Hospital between January 1, 2002 and March 31, 2015. Indications for coronary angiography included ischemic electrocardiographic changes in a treadmill exercise test, perfusion defect results in a thallium scan, and ACS presentation. Occlusive CAD defines as ≥ 50% stenosis in coronary lumen in coronary angiography. Non-occlusive CAD is defined as angiographic stenotic severity less than 50%. Exclusion criteria are patient age younger than 18 years or older than 40 years.

On the basis of the European Society of Cardiology/American College of Cardiology/American Heart Association/World Heart Federation taskforce, ACS diagnosis was defined as the presentation of both ST- and non-ST-segment elevation myocardial infarction (STEMI and NSTEMI, respectively) and unstable angina.[26] Hypertension was defined as a resting blood pressure of > 140/90 mmHg or the use of antihypertensive medications. Diabetes mellitus was defined as a fasting glucose level of > 126 mg/dL, random glucose level of > 200 mg/dL, or hemoglobin A1c level of > 6.5% or the use of oral hypoglycemic agents. In accordance with the reports of the National Cholesterol Education Program (Adult Treatment Panels II and III), dyslipidemia was defined as a total cholesterol level of > 200 mg/dL, low-density lipoprotein (LDL) level of > 100 mg/dL, HDL level of < 40 mg/dL, and triglyceride (TG) level of > 200 mg/dL.[27-28] Body mass index (BMI) was defined as the body weight (kg) divided by the height (m) squared. Obesity was defined as a BMI of ≥ 27 kg/m^2. Warning symptoms included chest discomfort or dyspnea requiring medical assistance. The study complied with the Declaration of Helsinki regarding investigations in humans, and was approved by the hospital's Institutional Ethics Committee.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences software (Version 22.0) for Windows (SPSS Inc., Chicago, IL, USA). Quantitative data are presented as mean ± standard deviation for continuous variables and as number of patients (percentage) for categorical variables. The baseline characteristics and in-hospital outcomes of patients with ACS and CAD were compared with those of patients without ACS or CAD. The Kolmogorov-Smirnov coefficient was evaluated for continuous variables. The continuous variables were compared using the Mann-Whitney *U* test and *t* test. Categorical variables were compared using the chi-squared test and logistic regression. The odds ratios (ORs) and 95% confidence intervals were calculated. A p value < 0.05 was considered significant.

RESULTS

Baseline characteristics of the young patients with or without CAD

We enrolled 245 young patients including 131 (53.5%) with ACS and 178 with occlusive CAD (Table 1, Table 2). The median age of the patients was 36.08 years (minimum: 18.25 years, maximum: 40.75 years). Of all the patients, 220 (89.8%) were men. Among the classi-

cal risk factors, current smoking (n = 140, 57.1%) was the most prevalent, followed by hypertension (n = 73, 29.8%) and dyslipidemia (n = 71, 29%). Of all the patients, 5 had a history of cerebrovascular accident (CVA) or transient ischemic accident (TIA), which was no statistically different between the ACS and non-ACS groups.

Coronary angiographic characteristics

Of all the patients, 67 (27.3%) had non-occlusive CAD and 91 (37.1%) had single-vessel disease; the remaining patients had > 2-vessel disease. The left anterior descending artery (LAD) was the most frequently occluded vessel (n = 141, 79.2%), followed by the right coronary artery (n = 95, 53.4%) and left circumflex artery (n = 79, 44.4%). Only 3 (1.7%) patients had left main CAD (Table 2). Among the patients with non-occlusive CAD, the most common etiology was myocardial bridging (n = 67, 27.3%). In addition to myocardial bridging, possible causes of young patients presenting with ACS who had non-occlusive CAD include coronary spasm and pericarditis/myocarditis.

Baseline characteristics of the young patients with ACS or occlusive CAD

STEMI was the most common presentation (n = 56, 42.7%), followed by NSTEMI (n = 48, 36.6%) and unstable angina (n = 27, 20.6%; Table 2). More than half of the patients (n = 86, 65.6%) experienced no warning symptoms or signs. Current smoking (n = 90, 68.7%, p = 0.000), followed by dyslipidemia (n = 40, 30.5%, p = 0.565) and hypertension (n = 37, 28.2%, p = 0.569) were the most common classical risk factors for ACS (Table 1).

Table 1. Clinical characteristics and lab findings of young patients

	All	ACS	Non-ACS	p
Number	245	131	114	
Age (years)	33.5 ± 6.1	35.0 ± 4.9	31.8 ± 7.0	0.036
Male, n (%)	220 (89.8)	121 (92.9)	99 (86.8)	0.154
BMI (kg/m^2)	26.7 ± 4.2	27.4 ± 4.2	26.0 ± 4.2	0.011
Previously known risk factors				
Hypertension, n (%)	73 (29.8)	37 (28.2)	36 (31.6)	0.569
Dyslipidemia, n (%)	71 (29)	40 (30.5)	31 (27.2)	0.565
Diabetes, n (%)	35 (14.3)	17 (13)	18 (15.8)	0.53
Smoking, n (%)	140 (57.1)	90 (68.7)	50 (43.9)	< 0.001
Family history, n (%)	37 (15.1)	22 (16.8)	14 (12.3)	0.384
Stroke/TIA, n (%)	5 (2)	2 (1.5)	3 (2.6)	0.542
Warning sign/symptom, n (%)	148 (60.4)	45 (34.4)	103 (90.4)	< 0.001
Expired, n (%)	8 (3.3)	6 (4.6)	2 (1.8)	
Lab findings				
WBC (cells/μL)	9203.5 ± 3346.9	10508.9 ± 3531.9	7703.3 ± 22364.7	< 0.001
Hb (gram/dL)	14.9 ± 1.7	15.1 ± 1.7	14.6 ± 1.7	0.019
Platelet (billion/L)	255.4 ± 73.6	263.2 ± 87.7	246.3 ± 51.8	0.064
N/L	3.0 ± 2.9	3.6 ± 3.7	2.2 ± 1.2	0.004
PLR	128.1 ± 136.4	138.6 ± 181.2	115.7 ± 40.8	1.000
eGFR (mL/min/1.73 m^2)	103 ± 27.5	100.4 ± 27.9	106.1 ± 26.8	0.474
Uric acid (mg)	6.6 ± 2.1	6.4 ± 2.2	6.8 ± 2.0	0.220
Total cholesterol (mg/dL)	187.4 ± 51.9	195.6 ± 51.7	177.3 ± 50.5	0.008
LDL (mg/dL)	119.2 ± 41.9	127.1 ± 43.2	109.1 ± 38.0	0.003
HDL (mg/dL)	37.7 ± 13.0	35.0 ± 12.7	41.2 ± 12.6	0.001
TG (mg/dL)	192.9 ± 247.7	219.4 ± 274.0	160.3 ± 207.9	< 0.001
TG/HDL	6.3 ± 10.5	8.0 ± 13.1	4.1 ± 4.6	0.003

ACS, acute coronary syndrome; BMI, body mass index; Hb, hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; N/L, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; TG, triglyceride; TG/HDL, triglyceride to high density lipoprotein ratio; TIA, transient ischemic attack; warning sign/symptom, chest discomfort causing caution for medical aids; WBC, white blood cell count.

Table 2. Angiography characteristics in ACS and Non-ACS

	All	ACS	Non-ACS
Number	245	131	114
STEMI	-	56 (42.7)	-
NSTEMI	-	48 (36.6)	-
Unstable angina	-	27 (20.6)	-
Non-occlusive CAD	67 (27.3)	13 (9.9)	54 (47.3)
Bridge	61 (61/67, 91)	13 (13/13, 100)	48 (48/54, 88.9)
Coronary spasm	3 (3/67, 4.5)	3 (3/13, 23.1)	0 (0)
Autoimmune diseases	3 (3/67, 4.5)	0 (0)	3 (3/54, 5.6)
Pericarditis/myocarditis	2 (2/67, 3.0)	2 (2/13, 15.4)	0 (0)
Unknown/undifferentiated	6 (6/67, 9.0)	2 (2/13, 15.4)	4 (4/54, 7.4)
Occlusive CAD	178 (72.7)	118 (9)	60 (52.6)
Single vessel disease	91 (37.1)	55 (42.0)	36 (31.6)
Double vessel disease	43 (17.6)	32 (24.4)	11 (9.6)
Triple vessel disease	41 (16.7)	29 (22.1)	12 (10.5)
Left main	3 (3/178, 1.7)	2 (2/118, 1.7)	1 (1/60, 1.7)
LAD	141 (141/178, 79.2)	89 (89/118, 75.4)	52 (52/60, 86.7)
LCX	79 (79/178, 44.4)	53 (53/118, 44.9)	26 (26/60, 43.3)
RCA	95 (95/178, 53.4)	71 (71/118, 60.2)	24 (24/60, 40)

Non-occlusive CAD is defined as angiographic stenotic severity less than 50%; occlusive CAD is defined as ≥ 50% stenosis in coronary lumen in coronary angiography; LAD, left anterior descending artery; LCX, left circumflex artery; NSTEMI, non-ST elevation myocardial infarction; RCA, right coronary artery; STEMI, ST elevation myocardial infarction; autoimmune diseases include lupus related vasculitis, Kawasaki disease, and Takayasu's disease.

Furthermore, age, BMI, total leukocyte count, neutrophil-to-lymphocyte ratio, total cholesterol, LDL, TG levels; and TG-to-HDL ratio were higher in young adult patients with ACS and occlusive CAD than in those patients without ACS or non-occlusive CAD (Table 1, Table 3). Finally, by logistic regression analysis, smoking is suggested to be an independent predictor of ACS and occlusive CAD (Table 4).

Clinical outcomes

In total, 22 (9%) patients underwent coronary artery bypass grafting (CABG) in the same hospital, and 42 (17.1%) patients underwent revascularization either through repeated percutaneous coronary intervention, CABG, or heart transplantation during the follow-up period (data not shown). The overall mortality rate was 3.3%.

DISCUSSION

In this study, we evaluated the clinical presentation, classical risk factors, and angiographic characteristics of CAD and possible contributing variables to ACS in young patients in Taiwan. Most of the enrolled 245 patients were men, and smoking was the leading risk factor. More than half of the patients presented with ACS, particularly STEMI. Moreover, most of the patients had single-vessel occlusion, particularly in the LAD, and did not experience warning signs or symptoms before a heart attack. In addition, age, smoking, and metabolic syndrome components such as BMI and high non-HDL and low HDL levels differed between the ACS and non-ACS groups. By logistic regression analysis, this study suggests that smoking is an independent predictor in young patients with ACS and occlusive CAD.

Because of the differing lifestyles and dietary patterns between young and elderly people, specific consideration for CAD in young people is required.[16,17] Moreover, a combination of infrequent health checkups and ignorance about CAD prevented the young population from seeking medical assistance.[29] Therefore, early diagnosis and risk factor modification are critical in this patient population. Although classical risk factors such as hypertension, diabetes, smoking, and dyslipidemia contributed to CAD in the elderly patients, these factors

Table 3. Clinical characteristics between occlusive and non-occlusive CAD in young patients

	All	Occlusive	Non-occlusive	p value
Number	245	178	67	
Age (years)	33.5 ± 6.1	35.0 ± 4.8	29.6 ± 7.4	< 0.001
Male, n (%)	220 (89.8)	163 (91.6)	57 (85.1)	0.134
BMI (kg/m^2)	26.7 ± 4.2	27.4 ± 4.2	25.0 ± 3.9	< 0.001
Known risk factors before heart attack				
Hypertension, n (%)	73 (29.8)	63 (35.4)	10 (14.9)	0.002
Dyslipidemia, n (%)	71 (29)	59 (33.1)	12 (17.9)	0.019
Diabetes, n (%)	35 (14.3)	31 (17.4)	4 (6.0)	0.022
Smoking, n (%)	140 (57.1)	114 (64.0)	26 (38.8)	< 0.001
Family history, n (%)	37 (15.1)	31 (17.4)	6 (9.0)	0.042
Stroke/TIA, n (%)	5 (2)	3 (1.7)	2 (3.0)	0.52
Warning sign/symptom, n (%)	148 (60.4)	95 (53.4)	53 (79.1)	< 0.001
Lab findings				
Platelet (billion/L)	255.4 ± 73.6	259.5 ± 79.4	244.3 ± 54.3	0.090
N/L	3.0 ± 2.9	3.2 ± 3.2	2.3 ± 1.7	0.041
PLR	128.1 ± 136.4	134.3 ± 157.1	111.4 ± 45.6	0.082
eGFR (mL/min/1.73 m^2)	103 ± 27.5	101.0 ± 28.2	108.1 ± 25.2	0.062
Uric acid (mg)	6.6 ± 2.1	6.6 ± 2.2	6.5 ± 2.0	0.871
Total cholesterol (mg/dL)	187.4 ± 51.9	196.2 ± 54.2	161.0 ± 32.3	< 0.001
LDL (mg/dL)	119.2 ± 41.9	125.6 ± 44.0	99.5 ± 26.2	0.001
HDL (mg/dL)	37.7 ± 13.0	36.9 ± 13.1	40.1 ± 12.5	0.146
TG (mg/dL)	192.9 ± 247.7	217.3 ± 278.6	119.1 ± 73.6	0.010
TG/HDL	6.3 ± 10.5	7.1 ± 11.8	3.9 ± 3.7	0.005

Table 4. Risk factors of occlusive CAD and ACS in logistic regression analysis

Risk factors	ACS (95% CI)	p value	Occlusive CAD (95% CI)	p value
Age	1.109 (1.042-1.181)	0.001	1.121 (1.061-1.184)	< 0.001
Male	0.999 (0.297-3.365)	0.999	0.668 (0.231-1.937)	0.458
Hypertension	0.635 (0.284-1.421)	0.269	2.120 (0.859-5.228)	0.103
Dyslipidemia	1.088 (0.504-2.349)	0.829	1.094 (0.473-2.529)	0.834
Diabetes	0.715 (0.278-1.844)	0.488	1.947 (0.589-6.438)	0.275
Smoking	3.780 (1.726-8.279)	0.001	2.208 (1.094-4.459)	0.027
Family history	1.231 (0.488-3.104)	0.660	1.846 (0.625-5.456)	0.268
Stroke/TIA	0.441 (0.038-5.057)	0.510	0.276 (0.037-2.089)	0.213

also caused the occlusion of the coronary artery in the young patients (Tables 1 and 3), indicating the universal and vital role of these risk factors in CAD, regardless of age.

Consistent with the suggestions of previous studies, our study suggests that smoking is the leading risk factor for occlusive CAD and ACS in young patients.[1,29-34] The relationship between smoking and myocardial infarction has been reported, with an OR ranging from 1.89 to 3.5,[1,29-36] and persistent smoking increased the rate of major adverse cardiac events by 4.8 times in young Chinese patients.[37] All of these studies have emphasized the importance of smoking cessation to help prevent CAD.

One study from the Taiwanese Secondary Prevention for patients with AtheRosCLErotic disease (T-SPARCLE) Registry enrolled 2568 Taiwanese CAD patients with a mean age of 65.9 years. Of them, 1911 (74.4%) were male with a mean BMI of 26.2 kg/m^2.[38,39] Our study indicated that in Taiwanese CAD patients less than 40 years of age, 220 (89.9%) were male with a mean BMI of 27.4 kg/m^2 (Table 3). Such evidence supports the gender difference in young patients with CAD. Moreover, although the most prevalent risk factors in CAD pa-

tients in Taiwan are hypertension (n = 1856, 72.3%), followed by diabetes (n = 1088, 42.4%) and smoking (n = 1015, 40.9%),[39] our study indicated that current smoking (n = 140, 57.1%) is the most prevalent factor, followed by hypertension (n = 73, 29.8%) and dyslipidemia (n = 71, 29%) in CAD patients less than 40 years old (Table 3). These results highlight the critical role of smoking in young patients with CAD.

Regarding the risk factor of dyslipidemia for CAD, we observed significantly higher non-HDL and lower HDL levels in the ACS group than in the non-ACS group; these results are consistent with those reported from China[30,36] and Japan.[40] Moreover, hypertriglycemia, which was previously neglected, was significantly higher in both the occlusive CAD and ACS groups than in the nonocclusive CAD and non-ACS groups. Consistent with our results, studies from several groups indicated hypertriglycemia is associated with premature CAD and young patients with ACS.[40-42] These findings indicate that the role of intensive lipid control exceeds that expected in young patients and that hypertriglycemia, in addition to LDL, is a critical risk factor for CAD in young patients.

Studies have reported an established relationship among inflammation, atherosclerotic processes, and prothrombotic states.[43,44] Several studies have focused on biomarkers for risk estimation. Jayesh et al. reported that the platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte (N/L) ratio were significantly higher in patients with ACS compared with other patients.[45] Moreover, the N/L ratio was higher in young patients with non-ST elevation ACS, including NSTEMI and unstable angina.[46] We observed that the N/L ratio was higher in the ACS group than in the non-ACS group (Table 1). However, no significant difference was observed in PLR between these groups. This difference in results may be attributed to racial difference, indicating that the N/L ratio is an easily accessible inflammation biomarker for the presentation of ACS in the general young population. In addition, histological studies have reported that atherosclerotic plaques in young patients have a high number of lipid-containing foam cells and relatively less acellular scar tissue.[47,48] These plaques are presented more rapidly and can rupture easily compared with those observed in elderly patients, which partly explains the absence of warning signs before a heart attack in young patients.

We included few patients who had a history of CVA or TIA. However, we did not observe a significant association of CVA or TIA with either coronary artery occlusion or ACS. This suggests that the pathophysiology of stroke and CAD may differ in the young population. Additional studies are necessary to confirm this hypothesis.

Study limitations

Our study had several limitations that should be addressed. First, our study involved a single-center, retrospective design; therefore, selection bias may be present. Second, only conventional CAD risk factors and laboratory findings were identified in our study without a sequential follow-up. Widely used atherosclerosis markers such as high-sensitivity C-reactive protein and genetic factors were not evaluated.[49] Third, the inclusion of few female patients with missing data such as menopause may have caused a deviation in the analysis. Fourth, certain lipid profile values were calculated using the following formula: total cholesterol = HDL + LDL + TG/5; hence, bias may be present associated with extreme hypertriglycemia. Moreover, because it is a retrospective study evaluating clinical characteristics of young patients with coronary artery disease, the detailed cardiovascular outcome and survival analysis were not performed in the current study. Finally, adequate information regarding psychosocial stress, marriage status, and physical activity was unavailable. Therefore, a prospective study with a larger population is required to confirm our findings.

CONCLUSIONS

CAD diagnosed in young patients is an uncommon condition. Age (particularly > 35 years), BMI, and smoking in combination with dyslipidemia (high non-HDL and low HDL levels and hypertriglycemia) and inflammation contribute to ACS in young patients. Among these risk factors, smoking effectively predicted the occurrence of occlusive CAD and ACS in the young patients. Our study indicated that weight reduction, smoking cessation, and intensive lipid control, particularly of both LDL and TG levels, are crucial for preventing ACS and occlusive CAD in the young population.

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CONFLICT OF INTEREST

None.

REFERENCES

1. Puricel S, Lehner C, Oberhänsli M, et al. Acute coronary syndrome in patients younger than 30 years - aetiologies, baseline characteristics and long-term clinical outcome. *Swiss Med Wkly* 2013;143:w13816.
2. Wolfe MW, Vacek JL. Myocardial infarction in the young. Angiographic features and risk factor analysis of patients with myocardial infarction at or before the age of 35 years. *Chest* 1988; 94:926-30.
3. Gotsman I, Lotan C, Mosseri M. Clinical manifestations and outcome of acute myocardial infarction in very young patients. *Isr Med Assoc J* 2003;5:633-6.
4. Morillas P, Bertomeu V, Pabon P, et al. Characteristics and outcome of acute myocardial infarction in young patients. The PRIAMHO II study. *Cardiology* 2007;107:217-25.
5. Hoit BD, Gilpin EA, Henning H, et al. Myocardial infarction in young patients: an analysis by age subsets. *Circulation* 1986; 74:712-21.
6. Doughty M, Mehta R, Bruckman D, et al. Acute myocardial infarction in the young - the University of Michigan experience. *Am Heart J* 2002;143:56-62.
7. Rumboldt Z, Rumboldt M, Pesenti S, et al. Peculiarities of myocardial infarction at young age in Southern Croatia. *Cardiologia* 1995;40:407-11.
8. Teixeira M, Sa I, Mendes JS, Martins L. Acute coronary syndrome in young adults. *Rev Port Cardiol* 2010;29:947-55.
9. Hamsten A, Norberg R, Bjorkholm M, et al. Antibodies to cardiolipin in young survivors of myocardial infarction: an association with recurrent cardiovascular events. *Lancet* 1986;1:113-6.
10. Kanitz MG, Giovannucci SJ, Jones JS, Mott M. Myocardial infarction in young adults: risk factors and clinical features. *J Emerg Med* 1996;14:139-45.
11. Siwach SB, Singh H, Sharma D, Katyal VK. Profile of young acute myocardial infarction in Harayana. *J Assoc Physicians India* 1998; 46:424-6.
12. Ueda Y, Okada K, Ogasawara N, et al. Acute myocardial infarction without disrupted yellow plaque in young patients below 50 years old. *J Interv Cardiol* 2007;20:177-81.
13. Zhong XY, Qin Ying, Wang ZH, et al. Risk factors and coronary lesions characteristics of coronary heart disease in youth. *Zhongguo Wuzhen Xue Za Zhi* 2004;4:649-51.
14. Zhao XW, Wu N, Wang SD, et al. Coronary characters and analysis of correlative dangerous factors in young patients with coronary artery disease (CAD). *Chin J Cardiovasc Med* 2004;9:222-4.
15. Aggarwal A, Aggarwal S, Sharma V. Cardiovascular risk factors in young patients of coronary artery disease: differences over a decade. *J Cardiovasc Thorac Res* 2014;6:169-73.
16. Kawabata T, Hirota S, Hirayama T, et al. Age-related changes of dietary intake and blood eicosapentaenoic acid, docosahexaenoic acid, and arachidonic acid levels in Japanese men and women. *Prostaglandins Leukot Essent Fatty Acids* 2011;84: 131-7.
17. Kuriki K, Nagaya T, Imaeda N, et al. Discrepancies in dietary intakes and plasma concentrations of fatty acids according to age among Japanese female dietitians. *Eur J Clin Nutr* 2002;56: 524-31.
18. Trzos E, Uznańska B, Rechciński T, et al. Myocardial infarction in young people. *Singapore Med J* 2006;47:27-30.
19. Alkhawam H, Zaiem F, Sogomonian R, et al. Coronary artery disease in young adults. *Am J Med Sci* 2015;350:479-83.
20. Qureshi AI, Suri MF, Guterman LR, Hopkins LN. Cocaine use and the likelihood of nonfatal myocardial infarction and stroke: data from the Third National Health and Nutrition Examination Survey. *Circulation* 2001;103:502-6.
21. Jouhikainen T, Pohjola-Sintonen S, Stephansson E. Lupus anticoagulant and cardiac manifestations in systemic lupus erythematosus. *Lupus* 1994;3:167-72.
22. Tanis BC, Bloemenkamp DG, van den Bosch MA, et al. Prothrombotic coagulation defects and cardiovascular risk factors in young women with acute myocardial infarction. *Br J Haematol* 2003;122:471-8.
23. Takahashi K, Oharaseki T, Yokouchi Y. Pathogenesis of Kawasaki disease. *Clin Exp Immunol* 2011;164:20-2.
24. Foody JM, Milberg JA, Robinson K, et al. Homocysteine and lipoprotein(a) interact to increase CAD risk in young men and women. *Arterioscler Thromb Vasc Biol* 2000;20:493-9.
25. Chu PH, Chiang CW, Ko YL. Catheterization-documented coronary artery disease in young Chinese adults. *Int J Cardiol* 1998; 64:301-3.
26. Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. *J Am Coll Cardiol* 2007;50:2173-95.
27. National Cholesterol Education Program. Second report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel II). *Circulation* 1994;89:1333-445.
28. Third Report of the National Cholesterol Education Program (NCEP). Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. *Circulation* 2002;106:3143-421.
29. Jamil G, Jamil M, Alkhazraji H, et al. Risk factor assessment of young patients with ST-segment elevation myocardial infarction. *Am J Cardiovasc Dis* 2013;3:170-4.

30. Yang WX, Yang Z, Wu YJ, et al. Factors associated with coronary artery disease in young population (age ≤ 40): analysis with 217 cases. *Chin Med Sci J* 2014;29:38-42.
31. Tungsubutra W, Tresukosol D, Buddhari W, et al. Acute coronary syndrome in young adults: the Thai ACS Registry. *J Med Assoc Thai* 2007;90 Suppl 1:81-90.
32. Bhardwaj R, Kandoria A, Sharma R. Myocardial infarction in young adults-risk factors and pattern of coronary artery involvement. *Niger Med J* 2014;55:44-7.
33. Sarr M, Ba DM, Ndiaye MB, et al. Acute coronary syndrome in young Sub-Saharan Africans: a prospective study of 21 cases. *BMC Cardiovasc Disord* 2013;13:118.
34. Shiraishi J, Kohno Y, Sawada T, et al. Pathogenesis of acute myocardial infarction in young male adults with or without obesity. *J Cardiol* 2007;49:13-21.
35. Shiraishi J, Kohno Y, Yamaguchi S, et al. Acute myocardial infarction in young Japanese adults. *Circ J* 2005;69:1454-8.
36. Yunyun W, Tong L, Yingwu L, et al. Analysis of risk factors of ST-segment elevation myocardial infarction in young patients. *BMC Cardiovasc Disord* 2014;14:179-83.
37. Qian G, Zhou Y, Liu HB, Chen YD. Clinical profile and long-term prognostic factors of a young Chinese Han population (≤ 40 years) having ST-segment elevation myocardial infarction. *Acta Cardiol Sin* 2015;31:390-7.
38. Yin WH, Wu CC, Chen JW. Registry of lipid control and the use of lipid-lowering drugs for secondary prevention of cardiovascular events in patients with established atherosclerotic disease in Taiwan: rotionality and methods. *Int J Gerontol* 2012;241-6.
39. Jeng JS, Yin WH, Huang CC, et al. Guideline-adherent therapy in patients with cardiovascular diseases in Taiwan. *J Formos Med Assoc* 2015;114:1000-7.
40. Jinnouchi H, Sakakura K, Wada H, et al. Clinical features of myocardial infarction in young Japanese patients. *Int Heart J* 2013; 54:123-8.
41. Chen L, Chester M, Kaski JC. Clinical factors and angiographic features associated with premature coronary artery disease. *Chest* 1995;108:364-9.
42. Bhardwaj R, Kandoria A, Sharma R. Myocardial infarction in young adults-risk factors and pattern of coronary aretery involvement. *Niger Med J* 2014;55:44-7.
43. Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. *Circulation* 2002;105:1135-43.
44. Kaya MG, Akpek M, Elcik D, et al. Relation of left atrial spontaneous echocardiographic contrast in patients with mitral stenosis to inflammatory markers. *Am J Cardiol* 2012;109:851-5.
45. Prajapati JH, Sahoo S, Nikam T, et al. Association of high density lipoprotein with platelet to lymphocyte and neutrophil to lymphocyte ratios in coronary artery disease patients. *J Lipids* 2014;2014:686791.
46. Oztürk S, Erdem A, Ozlü MF, et al. Assessment of the neutrophil to lymphocyte ratio in young patients with acute coronary syndromes. *Turk Kardiyol Dern Ars* 2013;41:284-9.
47. Dollar AL, Kragel AH, Fernicola DJ, et al. Composition of atherosclerotic plaques in coronary arteries in women less than 40 years of age with fatal coronary artery disease and implications for plaque reversibility. *Am J Cardiol* 1991;67:1223-7.
48. Gertz SD, Malekzadeh S, Dollar AL, et al. Composition of atherosclerotic plaques in the four major epicardial coronary arteries in patients greater than or equal to 90 years of age. *Am J Cardiol* 1991;67:1228-33.
49. Liu PY, Chen JH, Li YH, et al. Synergistic effect of stromelysin-1 (matrix metallo-proteinase-3) promoter 5A/6A polymorphism with smoking on the onset of young acute myocardial infarction. *Thromb Haemost* 2003;90:132-9.