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Risk Factors and Angiographic Characteristics of Coronary Artery Disease Requiring Revascularisation In Young Adults: A Single Centre Experience

Gençlerde Revaskülarizasyon Gerektiren Koroner Arter Hastalığı Risk Faktörleri ve Anjiyografik Özellikleri: Tek Merkez Deneyimi

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Öz

Kardivovasküler hastalık (KVH) en sık ölüm ve morbidite nedenlerindendir. İleri yaş aterosklerozun ilerlemesinde en önemli risk faktörlerinden biridir. Koroner arter hastalığı (KAH) genellikle erkeklerde 45 yaşın ve kadın popülasyonda 55 yaş üstünde görülür. Bununla birlikte, genç popülasyonda miyokard enfarktüsünün (MI) prevalansında önemli bir artış vardır. Bu çalışmanın amacı, kalp şikayetleri ile başvuran ve koroner anjiyografi (KAG) yapılan genç popülasyonda KAH için en yaygın risk faktörlerini tanımlamak ve tedavi stratejileri ile birlikte birincil ve ikincil önleme stratejilerini belirlemektir. Metod: Son 10 yıl içinde kardiyak şikayetlerle gelerek KAG yapılmış genç hastalar geriye dönük olarak tarandı. Çalışmaya toplam 113 olgu alındı. Revaskülarizasyon ihtiyaçlarına göre iki ana gruba ayrıldı. KAG sonrası koroner revaskülarizasyon gerektirmeyen olgular kontrol, (Grup 1); Koroner revaskülarizasyon ihtiyacı olanlar ise hasta grubu (Grup 2) şeklinde sınıflandırıldı. İstatistiksel analiz için SPSS 15.0 for Windows programı kullanıldı. Kategorik değişkenler için tanımlayıcı istatistikler; sayı ve yüzde olarak ifade edildi. Sayısal değişkenler için tanımlayıcı istatistikler; ortalama, standart sapma, minimum, maksimum, medyan şeklinde ifade edildi. İki değişkenli bağımsız değişkenlerin sayısal dağılımları normal dağılım koşulu sağladığında, Student t testi, normal dağılım koşulu sağlanamadığında Mann-Whitney U testi yapıldı. Bağımsız gruplardaki oranlar Ki kare testi ile karşılaştırıldı. Alfa'nın istatistiksel anlamlılık düzeyi p<0,05 olarak kabul edildi. Sonuç: Erkek cinsiyet prevalansı, gruplar arasında kadın cinsiyetten anlamlı olarak daha yüksekti (p=0.002). BKİ'nin ortalama değerinde gruplar arasında istatistiksel olarak anlamlı bir fark yoktu (p=0.105). Sigara ve ortalama sigara sayısı Grup 2'de anlamlı derecede yüksekti (p<0.001; p=0.002). İlave komorbiditeler açısından gruplar arasında istatistiksel olarak anlamlı bir fark yoktu.

Anahtar kelimeler: genç erişkinde koroner arter hastalığı, aterosklerotik risk faktörleri

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Abstract

Cardiovascular disease (CVD) is one of the most frequent cause of mortality and morbidity world-wide. Advanced age is one of the most important risk factor for progression of atherosclerosis and coronary artery disease (CAD) is often seen over 45-years in male and 55 years in female population. However, there is a significant increase in the prevalence of myocardial infarction (MI) in young population recently. The aim of this study is to identify the most prevalent risk factors for CAD in the young population who presented with cardiac complaints and underwent coronary angiography (CAG) and to determine the primary and secondary prevention strategies along with the treatment strategies. Method: Young patients who have had cardiac complaints and received CAG during the last 10 years were screened retrospectively. Patient demographics, clinical characteristics and medications were collected retrospectively from the review of the medical records and cardiac catheterization database. A total of 113 cases were enrolled to the study. In all patients CAG was performed. Subjects were then classified in to two main groups according to their needs for revascularisation. Those subjects who didn't require coronary revascularisation after CAG were enrolled to the control group (Group 1); and those who needed coronary revascularisation were enrolled to the patient group (Group 2). SPSS 15.0 for Windows program was used for statistical analysis. For categorical variables descriptive statistics were; number and percentage. For numerical variables descriptive statistics were; mean, standard deviation, minimum, maximum, median. When the independent two-group comparisons of numerical variables provided normal distribution condition the Student's t test was performed, while Mann-Whitney U test was performed when the normal distribution condition was not met. Rates in independent groups were compared with Chi square test. Statistical significance level of alpha was accepted as p<0,05. Results: The prevalence of male gender was significantly higher than female gender among the groups (p=0.002). There was no statistically significant difference between groups in respect to mean value of BMI (p=0.105). Smoking and average number of cigarettes smoked was significantly higher in Group 2 patients (p<0.001; p=0.002). There were no statistically significant difference between the groups regarding to their additional co-morbidities.

Key words: coronary artery disease in young, risk factors for atherosclerosis

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Introduction

Cardiovascular disease (CVD) is one of the most frequent cause of mortality and morbidity world-wide (1). There have been many trials on cardiovascular disease pathogenesis, and several variables were identified as risk factors. Advanced age is one of the most important risk factor for progression of atherosclerosis and coronary artery disease (CAD) is often seen over 45-years in male and 55-years in female population (2). However, there is a significant increase in the prevalence of myocardial infarction (MI) in young population. Although there have been various studies to investigate the factors that determine the risk of CAD in the young population there hasn't been a consensus yet. Recent trials focused on the presentation, risk factors and prognosis of myocardial infarction in young population (3-5). Male gender, hyperlipidaemia, cigarette smoking, cocaine and other illegal drug use (4, 5), sedentary lifestyle, urban lifestyle (3), oral contraceptive use and family history of MI was found to be related with coronary syndromes in young. Moreover, coagulation disorders may cause MI in young population with normal coronary arteries (6).

The aim of this study is to identify the most prevalent risk factors for CAD in the young population who presented with cardiac complaints and underwent coronary angiography (CAG) and to determine the primary and secondary prevention strategies along with the treatment strategies.

Method

Young patients who have had cardiac complaints and received CAG during the last 10 years were screened retrospectively. Patient demographics, clinical characteristics and medications were collected retrospectively from the review of the medical records and cardiac catheterization database.

Those patients under the age of 18 years or patients over the age of 45 years in men and 55 years in women were excluded. Chronic renal failure of stage 4-5 or acute renal failure was not included. A total of 113 cases were enrolled to the study. In all patients CAG was performed. Regarding CAG data, number of vessels involved and treatment variables were also recorded. 56 patients underwent revascularisation whereas 57 had no need for revascularisation. Subjects were then classified in to two main groups according to their needs for revascularisation. Those subjects who didn't require coronary revascularisation after CAG were enrolled to the control group (Group 1) and those who needed coronary revascularisation were enrolled to the patient group (Group 2).

The following risk factors were recorded: family history of heart disease (defined as atherosclerosis diagnosed in parents or siblings <55 years for men and <65 years for women), smoking (defined as active smoker or quit within 1 year), hyperlipidaemia (HL) (defined as low density lipoprotein-cholesterol (LDL-C) ≥ 160 mg/dL, triglyceride (TG) ≥ 200 mg or treatment with any hypolipidemic medication), hypertension (HT) (defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg or treatment with any antihypertensive medications), diabetes mellitus (DM) (defined as two fasting plasma glucose levels ≥ 126 mg/dL or history of treatment with any oral hypoglycaemic drugs and/or insulin), presence of obesity (defined as body mass index ≥ 30 kg/m²). In addition, prior manifestation of atherosclerotic disease (previous CAD proven with any imaging technique or coronary stent story), laboratory results and blood pressure at the time of admission were recorded from the patients' files. Local ethic committee approved the study with ethical file KA (18/41).

According to their presentation to hospital, subjects were defined as follows: elective coronary angiography (CAG), myocardial infarction without ST elevation (NSTEMI), and myocardial infarction with ST elevation (STEMI), unstable coronary artery disease (USAP). USAP was defined as angina within 2 weeks, ST segment changes on ECG, negative enzyme;

STEMI was defined as ST-segment elevation at least two contiguous leads and positive troponin level; NSTEMI was defined as positive troponin level and ST-segment depression or T wave changes. 50% stenosis in left main coronary artery (LMCA) and more than 70% stenosis in left anterior descending coronary artery (LAD), circumflex coronary artery (CX) or right coronary artery (RCA) was defined as indication for coronary revascularisation. Side branch disease was also recorded according to the same definitions as main vessels. The interventional procedures were performed through femoral or radial artery sheaths, with weight-adjusted heparin administered at the outset. PCI was considered successful if the final percentage diameter of stenosis was less than 20% with TIMI III flow in the absence of death, recurrent ischemia, acute myocardial infarction, or urgent coronary bypass graft surgery during hospitalization.

Statistical Analysis

SPSS 15.0 for Windows program was used for statistical analysis. For categorical variables descriptive statistics were; number and percentage. For numerical variables descriptive statistics were; mean, standard deviation, minimum, maximum, median. When the independent two-group comparisons of numerical variables provided normal distribution condition the Student's t test was performed, while Mann-Whitney U test was performed when the normal distribution condition was not met. Rates in independent groups were compared with Chi square test. Statistical significance level of alpha was accepted as p<0,05.

Age, years	45.2 ± 5.9	
Gender, n (%)	Female	56 (49.6)
	Male	57 (50.4)
Smoking, n (%)		55 (53.4)
Obesity, n (%)	BMI $\geq 30 \text{kg/m}^2$ 27 (37.0)	
Comorbidities, n (%)		
	Diabetes	27 (24.1)
	Hypertension	43 (38.4)
	Hyperlipidemia	25 (22.3)
	Previous history of CAD	10 (9.8)
	Family history	38 (58.5)

Table1. Baseline characteristics

BMI: Body mass index; CAD: coronary artery disease

Results

From March 2007 to December 2017, patients who admitted to our hospital and underwent CAG under 55 years in female and 45 years in male were screened retrospectively. A total of 113 patients (45.2±5.9 years, 50.4% male) were recorded. Of these patients, 53.4% were smokers and 37.0% had a higher BMI of 30kg/m². In their past medical history 24.1% of the patients had DM, 38.4% had HT, 22.3% had HL, 9.8% had previous history of CAD, and 58.5% had family history of CAD (Table 1).

The male gender was significantly higher than female gender among the groups (p=0.002). There was no statistically significant difference between groups in the mean value of BMI (p=0.105). Smoking and average number of cigarettes smoked was significantly higher in Group 2 patients (p<0.001; p=0.002). There were no statistically significant difference between the groups regarding to their additional co-morbidities; such as DM, HT, HL (p=0.381; p=0.501; p=0.377; respectively). Although, those patients with a prior story of

CAD required intervention more frequent than those who didn't have a prior history of CAD (p<0.001), no significant difference were seen between the groups regarding to family history of CAD (p=1.000). All these findings are summarized in Table 2.

		Need for revascularisation				
		Group 1		Group 2		
		Mean.±SD	Min-Max	Mean±SD	Min- Max	Р
Age (years)		47.9 ± 7.2	32-55	42.9±5.1	32-55	< 0.001
BMI (kg/m ²)		32.6 ± 8.7	22.7-53.3	28.5±3.9	18-39.1	0.093
Smoked cigarette count (n)		5.8±12.1	0-60	15.2±17.7	0-80	0.002
Gender, n (%)	Female	37 (63.8)		19 (34.5)		0.002
	Male	21 (36.2)		36 (65.5)		
Obesity, n (%)	$BMI \geq \!\! 30 kg/m^2$	14 (48.3)		13 (29.5)		0.105
Smoking, n (%)		18 (32.7)		37 (77.1)		< 0.001
Comorbidities, n (%)	Diabetes mellitus	12 (20.7)		15 (27.8)		0.381
	Hypertension	24 (41.4)		19 (35.2)		0.501
	Hyperlipidemia	11 (19.0)		14 (25.9)		0.377
Medical story, n (%)	Prior CAD	0 (0.0)		10 (21.7)		< 0.001
	Family history	19 (57.6)		19 (59.4)		1.000
	Prior PCI	0 (0.0)		7 (13.2)		0.005
	CABG	0 (0.0)		1 (1.9)		0.482
Admission, n (%)	Elective	53 (92.9)		17 (30.3)		< 0.001
	USAP	4 (7.1)		10 (17.8)		
	NSTEMI	0 (0.0)		12 (21.4)		
	STEMI	0 (0.0)		15 (26.7)		
	Not mentioned			2 (3,5)		

 Table 2: Demographic variables according to the need for revascularization

BMI: body mass index; CAD: coronary artery disease; PCI: percutaneous coronary intervention; CABG: coronary bypass greft; USAP: unstable angina pectoris; NSTEMI: non-ST segment elevation myocardial infarction; STEMI: ST segment elevation infarction

Overall symptoms typical angina pectoris was the most frequent symptom in Group 2 whereas atypical angina was the most seen presentation in Group 1 (p<0.001 for both). There were no differences among the symptoms and/or indications for CAG at admission between the groups (Table 3).

	Group 1	Group 2	р
Angina, n (%)	16 (40.0)	46 (95.8)	<0,001
Atypical angina, n (%)	15 (37.5)	1 (2.1)	<0,001
Palpitation, n (%)	0 (0.0)	2 (4.2)	0,498
Dyspnea, n (%)	0 (0.0)	2 (4.2)	0,498
MSCT-coronary, n (%)	1 (2.5)	0 (0.0)	0,455
Low ejection fraction, n (%)	1 (2.5)	0 (0.0)	0,455
Weakness, n (%)	0 (0.0)	1 (2.1)	1,000
Syncope, n (%)	1 (2.5)	0 (0.0)	0,455

Table 3: Symptoms and/or Indications for CAG at admission

CAG: coronary angiography; USAP: unstable angina pectoris; MSCT: multi-slice computed tomography

Table 4 shows the laboratory characteristics of the groups. Leukocyte count, glycated hemoglobin A1c (HbA1c), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and TG levels were significantly higher, high density lipoprotein (HDL) levels were significantly lower in Group 2 when compared to Group 1 (p<0.00, p=0.008, p=0.002, p<0.001, p=0.003, p<0.00; respectively). However, there was no significant difference between the low density lipoprotein (LDL) levels between the groups (p=0,761). Considering overall patients, some subjects were already on statin therapy so we performed a sub-group analysis according to statin use. Our results showed that statin naïve Group 2 patients had statistically higher LDL and TG levels, and statistically significant lower HDL levels (p=0.049; p=0.001; p<0.001, respectively), whereas no differences were found those who were already on statin therapy (p<0.005 for both TG, LDL, HDL levels). There were also no difference between total cholesterol neither in statin naïve nor on statin receiving group (p<0.005) (Table 5).

At the admission, 70 (62.5%) patients underwent elective CAG. Fourteen (12.5%) of patients diagnosed as USAP, 12 (10.7%) patients diagnosed as NSTEMI, and 16 (14.3%) of patients were diagnosed as STEMI. After CAG 50.4% patients had normal coronary arteries, whereas

40.6% patients had coronary artery disease. 30 (26.5%) patients had single, 8 (7.1%) patients had two, 5 (4.4%) patients had 3, 2 (1.8%) had side branch disease, and 11 (9.7%) patients had both main coronary and side branch disease. Of these patients, 48.7% underwent revascularization. LAD was affected more than the other coronary arteries. Overall intervention those patients implanted stent only to LAD was 26 (24.1%), only CX was 9 (8.3%), only RCA was 13 (12.0%), 1 patient was given to CABG operation (Table 6).

	Group 1	Group 2	р
BUN (mg/dL)	13,8±4,2	13,0±4,4	0,151
Creatinine(mg/dl)	0,78±0,13	$0,87{\pm}0,41$	0,126
Na(mmol/l)	138,8±2,0	138,5±2,6	0,620
K(mmol/l)	4,3±0,4	4,1±0,4	0,061
Uric acid(mg/dl)	5,6±1,3	5,6±1,7	0,995
HB(gr/dL)	13,6±1,5	14,0±1,7	0,191
WBC(/µL)	7375,6±1925,3	9796,9±2805,0	<0,001
PLT(/µL)	8731,5±43488,9	258,9±60,3	0,791
MPV(fl)	$7,1{\pm}0,8$	7,6±1,4	0,104
Fasting glucose(mg/dL)	135,5±172,2	134,8±72,6	0,404
HbA ₁ c (%)	5,9±1,3	9,8±2,4	0,008
Clearance(ml/dk)	91,6±22,6	105,2±10,0	0,119
ALT(U/L)	22,9±12,1	39,3±28,0	0,002
AST(U/L)	20,6±11,1	40,0±26,9	<0,001
GGT(U/L)	25,2±13,2	23,4±14,6	0,781
LDL(mg/dl)	134,1±41,1	136,6±42,9	0,761
HDL(mg/dl)	49,7±13,1	39,2±18,5	<0,001
TC(mg/dl)	213,3±52,9	219,2±68,5	0,291
TG(mg/dl)	155,1±94,9	273,6±458,0	0,003

Table 4: Laboratory findings

BUN: Blood urine nitrogen; Na: plasma sodium; K: Potasium; Hb: Haemoglobin; WBC: White blood cell; PLT: Platelet; MVP: Mean platelet volume; HbA1C: Haemoglobin A1C; ALT: Alanine amino transferase; AST: Aspartate aminotransferase; GGT: Gama glutmyl transferase; LDL: Low density lipoprotein; HDL: High density lipoprotein; TC: Total cholesterol; TG: Triglyceride
 Tablo 5: Relationship between intervention and lipid profile

		Group 1	Group 2	р
Statin naive patients	LDL(mg/dl)	133,3±38,1	145,6±39,1	0,049
	HDL(mg/dl)	49,4±13,4	39,0±19,9	<0,001
	TC(mg/dl)	209,9±47,1	227,3±68,7	0,098
	TG(mg/dl)	151,6±97,6	297,2±501,3	0,001
Patients on statin therapy	LDL(mg/dl)	151,6±64,8	95,8±36,5	0,109
	HDL(mg/dl)	54,7±12,1	40,0±9,7	0,138
	TC(mg/dl)	257,3±82,2	169,0±46,5	0,248
	TG(mg/dl)	210,3±41,9	161,6±54,4	0,126

LDL: low density lipoprotein; HDL: High density lipoprotein, TC: Total cholesterol; TG: Triglyceride

Discussion

Cardiovascular disease is one of the major causes of mortality and morbidity among young adults (1). Conventional risk factors (2) may not be useful to assess the cardiovascular risk of young patients. In a study performed by Matsis K et al.(7) showed that MI in young patients were more likely to occur in male gender, smokers and those with increased BMI.

According to some investigators considering the genetic variation between ethnic groups it was hypothesed that the risk factors for each ethnic group might differ. In a study by Xie CB et al.(8) the Chinese, Malay and Indian women who presented with AMI were compared. It was reported that HL was more frequent among Indian patients, while DM was more prevalent among Malay patients. (8) Our study population was only consisting of Caucasians admitted to a tertiary hospital and the results of this study reflect a single centre data.

Compatible with our data most of the studies have shown smoking as the major risk factor in young MI, with a prevalence of 65% to 95% (7-17). It is known that smoking causes hypercoagulability state and endothelial dysfunction predisposing intracoronary thrombi (18). Moreover, smoking plays an important role in the progression and destabilization of

atherosclerotic plaques. In a study by Konishi et al. (19) they found that current smoking is a significant independent predictor of death and recurrence of acute coronary syndromes (ACS) in young.

Indication for intervention, n (%)	Elective	70	62.5
	Usap	14	12.5
	Nstemi	12	10.7
	Stemi	16	14.3
Number of diseased vessels, n (%)	Normal	57	50.4
	One vessel	30	26.5
	Two vessel	8	7.1
	Three vessel	5	4.4
	Side branch	2	1.8
	Side branch+ coronary artery	11	9.7
РТСА			
LMCA		0	0.0
LAD		21	19.3
CX		6	5 5
RCA		10	9.2
Side branch		0	0.0
IMA		1	1.0
Stent			
LMCA		0	0.0
LAD		26	24.1
CX		9	8.3
RCA		13	12.0
Side branch		2	1.9
IMA		0	0.0
CABC on			
Three vessel		1	0.78
11100 105501		1	0.70

Tablo 6:	Angiographic and	revascularization	characteristics

USAP: Unstable angina pectoris; NSTEMI: NON-ST elevation myocardial infarction; STEMI: ST elevation myocardial infarction; LMCA: Left main coronary artery; LAD: Left anterior descending artery; RCA: Right coronary artery; Cx: Circumflex artery; IMA: Intermediary coronary artery.

In our study, male gender had a higher frequency of revascularization. In one study comparing the basal variables between old and young patients who experienced MI, it was demonstrated that 92.5% of the patients under 45 years old were male whereas this ratio was 76% in older population (20).

There is conflicting data about the relationship between family history of CAD and coronary events. Most of the studies showed a strong relation between family history and coronary events (9, 11, 13, 16, 17, 21-26), whereas some other studies did not show a relation likewise our study (15, 27, 28). Still, considering genetic tendency is a strong predictor for several pathologies, family history is indicative for early coronary atherosclerosis. Our conflicting results with literature might be explained by the inadequate knowledge of our patients about their family history of CAD.

Dyslipidaemia is found to be another cause of cardiovascular events among young population (9, 10, 16, 29-32). In one study it was demonstrated that familial combined hyperlipidemia was associated with a 24-fold increased in acute coronary syndromes (8). Increased TG levels were also found to be associated with early onset of cardiovascular disease (3, 24, 33). Moreover, low HDL levels were shown to be associated with MI in young patients (34). In our study, we found no relation in regards to HL history and none of our subjects had a history of familial combined hyperlipidaemia. However, patients requiring revascularization had lower HDL and higher TG levels, but had no statistically significant difference between LDL levels which was compatible with the majority of the studies (9, 10, 29-31). Considering some patients were already on statin therapy we found that statin naïve patients had higher LDL and TG levels, and lower HDL levels in patients requiring revascularization.

In the present study, we found no relation with prior DM, HT histories between two groups. Our results were concordant with most studies which found that co-morbidities like HT, DM were likely to be seen in elder population (12, 17, 21). Beyond being primary risk factors these co-morbidities might affect the mortality and morbidity of these patients in the follow-up period. One study showed that in addition to smoking and low ejection fraction, DM was a predictor of increased mortality in young patients in long term prognosis (35). Because atherosclerosis is a multifactorial process that involves multiple risk factors, we may hypothesize that risk factors like DM and HT needs time to cause vasculopathy, endothelial dysfunction to develop CAD and cardiovascular event.

In Thai ACS registry, young patients comprised of 5.8% of all ACS patients. Among these patients, the prevalence of STEMI was 67%; NSTEMI was 20% and USAP 14%, respectively (17). Moreover, majority of the studies have demonstrated that among young patients presented with ACS is frequently seen in male gender, STEMI is the main presentation type (9, 11, 32) However, our results were discordant with the data in which we found less frequency of STEMI. Comparing the demographic variables in young patients requiring revascularization or not and having an elective CAG group might cause this difference. Compatible with our findings, the most involved coronary is LAD in majority of young patients (10, 21, 32, 36).

Study Limitations

There are some limitations to our study. This was a retrospective study and follow-up of the patients for re-vascularization, morbidity and mortality of the study population did not done. Moreover, the medical history was based on the patients' declaration. We did not compare the demographic variables between the old and young people. Also, the population size was relatively small. For this reason, long-term and large-scale prospective studies are needed to determine the predictive value of demographic variables in this population.

Conclusion

In young population the most prevalent risk factors for CAD in overall patients were; male gender, high TG and LDL and low HDL levels (in statin naive patients) and smoking. There for, life style changes are essential to prevent coronary artery disease in young adults.

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