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Comparison of Demographical Properties, Biochemical Parameters, Flow-mediated Dilatation Values and Carotis Intima Media Thickness of Patients with Coronary Artery Disease

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Abstract

Objectives: To compare demographic characteristics, biochemical parameters, flow-mediated dilatation (FMD) values and carotid intima-media thickness (CIMT) between older (>45 years) and younger (<45 years) patients with coronary artery disease (CAD).

Materials and Methods: The present study comprised a total of 114 patients divided into four groups. For the study groups, group 1 had 30 patients with CAD <45 years of age, and group 2 had 32 patients with CAD >45 years of age. Group 3 and group 4 were used as controls, comprising 28 (<45 years) and 24 (>45 years) healthy participants, respectively. Demographic characteristics, biochemical parameters, FMD values and CIMT were recorded and compared statistically among patients.

Results: The median age of patients was 47.81±14.50 years. Hereditary risk factors and hyperlipidemia were statistically significant in group 1 than those in group 3. Likewise, fasting blood glucose levels and CIMT values were statistically higher in group 1 than those in group 3. Gender distribution and hyperlipidemia were statistically significant in group 2, in contrast to those in group 4. The values of FMD was lower in group 2 than those in group 4, which seemed to be statistically significant. The values of CIMT were higher whereas platelet counts were lower

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Abstract

in group 2 than those in group 1, both findings of which were also statistically significant. The values of CIMT and Neutrophil/Lymphocyte (N/L) ratios increased whereas the values of FMD decreased significantly as the ages of participants increased.

Conclusion: The factors where CAD was more common in subjects were as follows: being over 45 years of age (2.36 times), the presence of hyperlipidemia (3.58 times), increased N/L ratios (1.6 times), a combination of increased CIMT values and age (12 times), and decreased FMD values (2 times).

Keywords: Carotid intima-media thickness, coronary artery disease, endothelial dysfunction, flow-mediated dilatation values

Introduction

Cardiovascular disease is the most common cause of death worldwide and its prevalence is increasing in every last decade[1,2]. The incidence of coronary artery disease (CAD) is 1.2% under the age of 45 years and 7.1% over the age of 45 years and the incidence increases to 19% over the age of 65 years[3]. Namely, the incidence of CAD increases as the age gets older.

In this study, demographic, biochemical and endothelial functions of patients older than 45 years and patients younger than 45 years were compared. We investigated the relationship between atherosclerosis and endothelial functions and carotid intima-media thickness (CIMT) with age.

We thought that it would be important to diagnose CAD early with a noninvasive test and to start treatment quickly. Especially, these noninvasive tests may be useful for selected patients who have CAD risk factors such as diabetes, genetic history, familial hypercholesterolemia, etc.

Materials and Methods

The present study comprised a total of 114 patients divided into four groups. For the study groups, group 1 had 30 patients with CAD <45 years of age, and group 2 had 32 patients with CAD >45 years of age. Group 3 and group 4 were used as controls, comprising 28 (<45 years) and 24 (>45 years) healthy participants, respectively. Ethics committee approval for the study was obtained from Zeynep Kamil Hospital, with June 2015 protocol number 78, İstanbul, Turkey. Informed consent for the study and the investigation was received from each patient in accordance with the principles outlined in the Declaration of Helsinki.

Demographic characteristics, biochemical parameters, FMD values and CIMT were recorded and compared statistically among patients.

The patients who had their coronary artery stenosis at least 30% after performing coronary angiography were included in the study. Participants with normal coronary angiography were also included in the control group. The FMD test was performed after 8-12 hours of fasting for all participants. Alcohol, caffeine and vasodilator medication were not provided 12 hours before the FMD test. Brachial artery (BA) was found in antecubital fossa with Philips IE33 X MATRIX echo device and L11-3 probe at room temperature (21-25 °C). The anterior-posterior wall and lumen of the BA were imaged. Three different measurements were made in the diastole according to electrocardiography (ECG) for BA diameter (intima to intima). Averages of these three measurements were taken for basal BA diameter. The blood pressure device was inflated over 50 mmHg of systolic blood pressure and waited for 5 minutes so the flow was cut off and the ischemia occurred. Then, the blood pressure device was deflated. One minute later, three different measurements were made in the diastole according to ECG for ischemic

BA diameter. FMD was calculated using this formula; FMD: Ischemic BA diameter - basal BA diameter/ basal BA diameter x 100[4,5]. Then, the right common carotid artery was visualized. Intima-media thickness measurement was performed from the posterior wall. Three measurements were made and averaged[6,7]. In healthy population, normal CIMT was accepted as 0.25-1.0 mm. CIMT increased by 0.01-0.02 mm per year associated with age.

Exclusion Criteria

1. Individuals under the age of 18 years
2. Carotid revascularization that was previously performed
3. Those with a history of previous cerebrovascular events (CVO)
4. Those with collagen tissue disease
5. Patients whose carotid or brachial arteries were not well visualized

Statistical Analysis

Statistical analyses were performed using the IBM-SPSS Statistics version 20 software (SPSS Inc., Chicago, Illinois). In the comparison of quantitative data, the Mann-Whitney U test was used to determine the difference between the two groups. For the comparison of categorical variables, the chi-square test was used. Pearson correlation coefficient was employed to determine relationships. P values less than 0.05 were accepted to be statistically significant.

Results

The median age of patients was 47.81±14.50 years. Hereditary risk factors and hyperlipidemia were statistically significant in group 1 than those in group 3 (Table 1). Likewise, fasting blood glucose levels and CIMT values were statistically higher in group 1 than those in group 3. But, FMD values were not statistically significant between group 1 and group 3 (Table 2). Gender distribution and hyperlipidemia were statistically significant in group 2, in contrast to those in group 4 (Table 3). The values of FMD were lower in group 2 than those in group 4, which seemed to be statistically significant (Table 4). The values of CIMT were higher whereas platelet counts were lower in group 2 than those in group 1, both findings of which were also statistically significant (Table 5). N/L ratio and CIMT values were higher in group 4, compared to group 3 (Table 6). The values of CIMT and neutrophil/ lymphocyte (N/L) ratios increased whereas the values of FMD decreased significantly as the ages of participants increased (Table 7).

Discussion

In patients under 45 years of age, when compared to the control group under the age of 45 years, the value of CIMT was found to be statistically significantly higher. Similar to our findings, Limbu et al.[8] found that ultrasonographic measurement of CIMT was valuable in young individuals with CAD risk factors. On the other hand, CIMT values were similar between patients older than 45 years and its control group. These results suggest that CIMT measurements may be more useful in predicting CAD especially in young patients with risk

Table 1. Controllable risk factors in individuals younger than 45 years

		Patients, under 45 years of age group 1	Control group, under 45 years of age group 3	p
Sex	Male	21 (91.3%)	23 (82.14%)	0.44
	Female	2 (8.7%)	5 (17.86%)	
Smoking	No	14 (60.87%)	19 (67.86%)	0.6
	Yes	9 (39.13%)	9 (32.14%)	
HT	No	17 (73.91%)	25 (89.29%)	0.27
	Yes	6 (26.09%)	3 (10.71%)	
HL	No	11 (47.83%)	26 (92.86%)	**0.0001***
	Yes	12 (52.17%)	2 (7.14%)	
DM	No	19 (82.61%)	26 (92.86%)	0.39
	Yes	4 (17.39%)	2 (7.14%)	
Heredity	No	6 (26.09%)	15 (53.57%)	0.047*
	Yes	17 (73.91%)	13 (46.43%)	

DM: Diabetes mellitus, HL: Hyperlipidemia, HT: Hypertension
**: Important p values*

Table 2. Comparison of FMD, CIMT and biochemical parameters between group 1 and group 3

	Patients under the age of 45 years Group 1		Control group under the age of 45 years Group 3		p
	Mean	SD	Mean	SD	
Basal BA diameter (cm)	0.39	0.05	0.37	0.05	0.072
Ischemic BA diameter (cm)	0.44	0.06	0.43	0.05	0.145
FMD (%)	12.93	6.81	16.17	6.69	0.127
CIMT (cm)	0.051	0.006	0.045	0.007	**0.019***
Glucose (mg/dL)	107.47	47.77	89.81	6.74	**0.009***
Neutrophil (%)	56.35	4.87	54.41	7.14	0.303
Lymphocytes (%)	33.27	5.31	35.50	7.01	0.233
Neut/Lymp	1.75	0.40	1.64	0.57	0.218
Hgb (mg/dL)	14.45	1.01	14.43	1.47	0.714
PLT	283.21	59.77	254.29	42.12	0.203
MPV (fL)	7.66	0.80	7.55	0.75	0.588
HDL-C (mg/dL)	46.65	10.07	44.33	8.28	0.627
TRIG (mg/dL)	186.28	124.58	125.29	64.19	0.111
Total-C (mg/dL)	197.28	53.53	176.00	39.98	0.254
LDL-C (mg/dL)	112.34	35.14	106.50	32.10	0.714
BMI (kg/m²)	28.03	3.43	27.31	5.74	0.216

BA: Brachial artery, BMI: Body mass index, HDL-C: High density lipoprotein cholesterol, Hgb: Hemoglobin, LDL-C: Low density lipoprotein cholesterol, MPV: Mean platelet volume, PLT: Platelet, TRIG: Triglyceride, CIMT: Carotid intima-media thickness test, Neut: Neutrophil, FMD: Fibromuscular dysplasia, Total-C: Total cholesterol, SD: Standard deviation
**: Important p values*

Table 3. Controllable risk factors in individuals older than 45 years

		Patients over the age of 45 years Group 2	Control group over the age of 45 years Group 4	p
Sex	Male	22 (88%)	9 (37.5%)	**0.0001***
	Female	3 (12%)	15 (62.5%)	
Smoking	No	15 (60%)	18 (75%)	0.26
	Yes	10 (40%)	6 (25%)	
HT	No	6 (24%)	12 (50%)	0.059
	Yes	19 (76%)	12 (50%)	
HL	No	2 (8%)	17 (70.83%)	**0.0001***
	Yes	23 (92%)	7 (29.17%)	
DM	No	17 (68%)	21 (87.5%)	0.102
	Yes	8 (32%)	3 (12.5%)	
Heredity	No	16 (64%)	16 (66.67%)	0.84
	Yes	9 (36%)	8 (33.33%)	

DM: Diabetes mellitus, HL: Hyperlipidemia, HT: Hypertension
**: Important p values*

factors such as hyperlipidemia, diabetes and heredity. Thus, these patients may be treated more aggressively in advance. On the other hand, the value of FMD was found to be higher in patients older than 45 years than its control group. Similarly, in the study of Ono et al.[9], there were 292 patients with diabetes (mean age, 65±12 years; 59% men) and statistically significant correlation was found between coronary artery calcification and FMD values. In addition, ultrasonographic measurement of CIMT and FMD is an easy and inexpensive method. Our study showed that the measurement of FMD could also provide more valuable information in patients over 45 years of age.

Table 4. Comparison of FMD, CIMT and biochemical parameters between group 2 and group 4

	Patients over the age of 45 years Group 2		Control group over the age of 45 years Group 4		p
	Mean	SD	Mean	SD	
Basal BA diameter (cm)	0.42	0.06	0.37	0.05	0.006*
Ischemic BA diameter (cm)	0.47	0.05	0.43	0.06	0.010*
FMD (%)	11.67	8.06	14.70	6.25	0.075
CIMT (cm)	0.065	0.01	0.062	0.01	0.357
Glucose (mg/dL)	115.16	48.90	100.96	41.45	0.269
Neut (%)	59.34	8.02	57.66	6.56	0.457
Lym (%)	29.89	7.24	31.57	6.08	0.436
Neut/Lym	2.17	0.85	1.94	0.59	0.624
Hgb (mg/dL)	14.39	1.57	13.74	1.44	0.092
PLT	213.31	69.33	241.39	64.75	0.154
MPV (fL)	8.26	1.35	7.85	0.91	0.483
HDL-C (mg/dL)	45.80	9.84	58.52	19.83	0.035*
TRIG (mg/dL)	152.08	82.58	144.57	111.13	0.434
Total-C (mg/dL)	187.44	29.30	222.57	59.43	0.037*
LDL-C (mg/dL)	111.92	28.72	138.02	45.02	0.028*
BMI	27.12	4.73	27.69	4.49	0.764

BA: Brachial artery, BMI: Body mass index, HDL-C: High density lipoprotein cholesterol, Hgb: Hemoglobin, LDL-C: Low density lipoprotein cholesterol, MPV: Mean platelet volume, PLT: Platelet, TRIG: Triglyceride, CIMT: Carotid intima-media thickness test, Neut: Neutrophil, Lym: Lymphocyte, FMD: Fibromuscular dysplasia, Total-C: Total cholesterol, SD: Standard deviation
**: Important p values*

In our study, FMD values were not statistically significant between group 1 and group 3. Unlike, in the study of Kaźmierski et al.[10], FMD values were found to be significantly lower in patients younger than 45 years compared to the control group.

A significant positive correlation was found between CIMT value and N/L ratio in our study. Similar to our findings, Demirkol et al.[11] found a significant positive correlation between the CIMT value and the plasma N/L ratio. We found a negative correlation between FMD and CIMT. Likewise, Chequer et al.[12] showed a statistically significant relationship between CIMT and FMD in their study. We found that the FMD value decreased significantly with age. Similarly, in a study on 2,511 Chinese adults, there was a negative correlation between age and FMD[13]. Again, there was also an inverse relationship between age and FMD in the study of Kirma et al.[14] In this study, carotid plaques were not evaluated, only CIMT measurements were performed. However, in previous studies, carotid plaques were more important than CIMT for prognosis especially in cardiac events. Yuk et al.[15] showed that carotid plaques were more important than CIMT in determining the prognosis of cardiac events in patients with CAD.

Table 5. Comparison of FMD, CIMT and biochemical parameters between group 1 and group 2

	Patients under the age of 45 years	Patients over the age of 45 years	p
	Group 1	Group 2	
FMD (%)	12.93±6.81	11.67±8.06	0.42
CIMT (cm)	0.051±0.006	0.065±0.01	0.001*
Glu (mg/dL)	107.47±47.77	115.16±48.9	0.80
Neut/Lym ratio	1.75±0.4	2.17±0.85	0.17
Hgb (mg/dL)	14.45±1.01	14.39±1.57	0.81
Platelet	283.21±59.77	213.31±69.33	0.001*
MPV (fL)	7.66±0.8	8.26±1.35	0.21
HDL-C (mg/dL)	46.65±10.07	45.8±9.84	0.93
TG (mg/dL)	186.28±124.58	152.08±82.58	0.48

CIMT: Carotid intima media thickness, FMD: Flow mediated dilatation, Glu: Glucose, HDL-C: High density lipoprotein cholesterol, Hgb: Hemoglobin, Lym: Lymphocyte, MPV: Mean platelet volume, Neut: Neutrophil, TG: Triglyceride
**: Important p values*

According to our results, the factors where CAD was more common in subjects were as follows: being over 45 years of age (2.36 times), the presence of hyperlipidemia (3.58 times), increased N/L ratios (1.6 times), a combination of increased CIMT values and age (12 times), and decreased FMD values (2 times).

Study Limitations

The present study has a small population size. One of the limitations of our study was that the relationship between FMD and CIMT values and future coronary events was not evaluated. The other limitation is that we did not evaluate the carotid plaques, we only measured the CIMT. So, it would be more useful for researchers to evaluate both in their studies. Future studies are needed to confirm our finding and evaluate the usefulness of CIMT and FMD as a surrogate marker of CAD and future cardiovascular events.

Table 6. Comparison of FMD, CIMT and biochemical parameters between group 3 and group 4

	Group 3	Group 4	p
FMD (%)	16.17±6.69	14.7±6.25	0.53
CIMT (cm)	0.045±0.007	0.062±0.01	0.001*
Glu (mg/dL)	89.81±6.74	100.96±41.45	0.64
Neu/Lym ratio	1.64±0.57	1.94±0.59	0.05
Hgb (mg/dL)	14.43±1.47	13.74±1.44	0.13
Platelet count	254.29±42.12	241.39±64.75	0.42
MPV (fL)	7.55±0.75	7.85±0.91	0.24
HDL (mg/dL)	44.33±8.28	58.52±19.83	0.02*
TG (mg/dL)	125.29±64.19	144.57±111.13	0.89

CIMT: Carotid intima media thickness, FMD: Flow mediated dilatation, Glu: Glucose, HDL: High density lipoprotein, Hgb: Hemoglobin, Lym: Lymphocyte, MPV: Mean platelet volume, Neu: Neutrophil, TG: Triglyceride
**: Important p values*

Table 7. Relationship between age and other variables: As age increases, FMD values and PLT counts decrease. CIMT and MPV values increase. These are all statistically significant

Age	r	p
FMD	-0.230	0.022
CIMT	0.707	0.0001
PLT	-0.292	0.006
MPV	0.212	0.048

CIMT: Carotid intima media thickness, FMD: Flow mediated dilatation, MPV: Mean platelet volume, PLT: Platelet

Conclusion

In conclusion, it may be meaningful to evaluate the CIMT value for primer protection in younger individuals, especially those with risk factors, and these patients may be treated more aggressively.

Ethics

Ethics Committee Approval: There is ethics committee approval from Zeynep Kamil Hospital, June 2015 protocol number 78, İstanbul, Turkey for the study.

Informed Consent: Informed consent for the study and the investigation was received from each patient in accordance with the principles outlined in the Declaration of Helsinki.

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Authorship Contributions

Surgical and Medical Practices: E.E., M.G., M.İ., N.Ö., Concept: E.E., M.G., M.İ., N.Ö., Design: E.E., M.G., M.İ., N.Ö., Data Collection or Processing: E.E., Analysis or Interpretation: E.E., M.İ., Literature Search: E.E., Writing: E.E.

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