Impact of atherosclerosis risk factors on the clinical presentation of arterial occlusive disease in Arabic patients

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BACKGROUND: Although the risk factors for atherosclerosis have been identified, their impact on the presentation of arterial occlusive disease has not been studied among Arabs.

OBJECTIVE: To determine the correlation between atherosclerotic risk factors and the extent and presentation of atherosclerotic disease in different arterial systems.

METHODS: The present case-control study was performed on a consecutive series of Arabic patients over one year. There were two groups – an atherosclerotic group, which included patients with peripheral arterial disease, extracranial cerebrovascular disease or coronary artery disease (CAD), and the control group, which included patients admitted to one of the general surgical units who were free

from atherosclerotic disease. All patients underwent evaluation of risk factors (diabetes mellitus [DM], smoking, dyslipidemia and hypertension) for atherosclerosis and systemic assessment of the vascular tree.

RESULTS: Two hundred fifteen patients in the atherosclerotic group and 191 patients in the control group were included in the study. There were positive correlations between the prevalence of DM, smoking, dyslipidemia and the severity of presentation of peripheral arterial disease, and the extent of CAD. The correlation between the incidence of DM and the severity of presentation of CAD was also significant. The correlation was also positive between the incidence of ex-smoking and hypertension, and the severity of presentation of extracranial cerebrovascular disease.

CONCLUSION: Different risk factors may interact in different ways in the clinical presentation of atherosclerotic disease in different arterial systems.

Key Words: Arabs; Atherosclerosis; Risk factors

Atherothrombosis is defined as disruption of atherosclerotic plaque with superimposed thrombosis (1). Major risk factors for atherosclerosis have been identified and include diabetes mellitus (DM), smoking, dyslipidemia and hypertension (2-5). However, the impact of these risk factors on the extent and presentation of arterial occlusive disease has not been studied among Arabs. The present study was performed to determine the correlation between atherosclerotic risk factors and the extent and presentation of atherosclerotic disease in different arterial systems.

METHODS

The present case-control study was performed on a consecutive series of Arabic patients admitted to the King Fahd University Hospital (Al-Khobar, Saudi Arabia) between May 1, 2006, and April 30, 2007. The study included two patient groups – the first group included atherosclerosis patients 40 years of age and older who were admitted to either the vascular unit, with peripheral arterial disease (PAD) or extracranial cerebrovascular disease (CVD), or to the coronary care unit with coronary artery disease (CAD). The control group included patients 40 years of age and older who were admitted to one of the general surgical units and were free of clinically documented atherosclerotic disease. All atherosclerosis patients were assessed

by vascular surgeons for PAD and CVD, and by cardiologists for CAD. King Fahd University Hospital receives patients of multiple ethnic origins; however, all non-Arabic patients were excluded from the present study.

All patients (atherosclerotic and control) underwent evaluation of the major risk factors (type 2 DM, smoking, dyslipidemia and hypertension) for atherosclerosis. Information on age, sex and nationality (Saudi or non-Saudi) was recorded.

Hypertension was defined as a mean systolic blood pressure of 140 mmHg or greater, a mean diastolic blood pressure of 90 mmHg or greater, a physician diagnosis or medication use. Mean blood pressure was composed of up to four readings on two separate occasions. Dyslipidemia was defined as a triglyceride level higher than 150 mg/dL, and/or a high-density lipoprotein cholesterol level of less than 40 mg/dL for men and less than 50 mg/dL for women, a total cholesterol level of 200 mg/dL or higher, physician diagnosis or medication use. Type 2 DM was defined by a self-reported physician diagnosis, use of antidiabetes medication, a fasting glucose level greater than 126 mg/dL, or a 2 h postprandial glucose level greater than 180 mg/dL. The duration of diabetes was also recorded.

All patients were subjected to a comprehensive physical examination in which the presence or absence of carotid bruit was recorded and the ankle-brachial index of each extremity was

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TABLE 1

ORs (adjusted for age, sex and nationality) and 95% CIs for risk factors of atherosclerosis

Risk factor	Coronary artery disease OR (95% CI)	Cerebrovascular disease OR (95% CI)	Peripheral arterial disease OR (95% CI)	Total atherosclerosis group OR (95% CI)
Diabetes mellitus	5.79 (3.7–9.4)	2.9 (1.5–5.5)	6.2 (3.7–10.4)	4.7 (3.1–7.2)
Smoking				
Current	4.1 (2.3–7.3)	8.3 (3.7–18.4)	8.1 (4.3–15.2)	10.6 (4.4–25.3)
Ex-smoker	6.1 (3.3–11.1)	18.3 (6.1–54.7)	21.5 (8.4–54.8)	15.9 (6.6–38.5)
Dyslipidemia	11.5 (6.6–18.8)	5.6 (2.8–11.2)	7.7 (4.4–13.3)	9.8 (6–16.1)
Hypertension	5.6 (3.5–8.9)	7.9 (3.7–16.9)	7.6 (4.1–14.4)	8.4 (4.8–14.8)

TABLE 2

Correlation between incidence of risk factors of atherosclerosis and presentation of peripheral arterial disease

Risk factors (%)	Category 1 (n=12)	Category 2 (n=31)	Category 3 (n=14)	Category 4 (n=6)	Category 5 (n=19)	Category 6 (n=31)	P
Age >65 years	66.7	51.6	14.3	33.3	57.9	29	0.03
Mean $\pm$ SD age, years	66.7 $\pm$ 9.9	64.03 $\pm$ 11.7	57.6 $\pm$ 5.1	61 $\pm$ 16.6	66.4 $\pm$ 11.2	62.3 $\pm$ 10.7	0.03
Male	83.3	87.1	71.4	66.7	47.4	66.7	0.06
Saudi	83.2	87.7	64.3	33	100	80.6	0.01
Diabetes mellitus	66.7	77.4	50	66.7	78.9	80.6	0.33
<5 years	0	12.9	0	0	0	12.9	
5 to 10 years	0	9.7	0	0	21	0	
>10 years	66.7	54.8	50	66.7	57.9	67.7	0.032
Smoking							
Current	50	41.9	71.4	33.3	30.8	18.5	<0.001
Ex-smoker	16.7	45.2	14.3	66.7	31.6	12.9	<0.001
Dyslipidemia	75	32.3	85.7	100	78.9	35.5	<0.001
Hypertension	66.7	32.2	57.1	33.3	47.4	35.6	0.26

Category 1 Mild claudication; Category 2 Moderate claudication; Category 3 Severe claudication; Category 4 Rest pain; Category 5 Minor tissue loss; Category 6 Major tissue loss

measured. Patients were considered to have PAD if their ankle-brachial index was less than 0.9, or if they had a history of arterial bypass, angioplasty or leg amputation for PAD. The clinical category for PAD was also reported (Rutherford classification: category 1, mild claudication; category 2, moderate claudication; category 3, severe claudication; category 4, rest pain; category 5, minor tissue loss; category 6, major tissue loss) (6). All patients underwent a carotid duplex scan and were considered to have CVD if extracranial carotid artery stenosis was present. The presentation of CVD was recorded as asymptomatic = 1, transient ischemic attack = 2 and stroke = 3. The diagnosis of CAD was based on a clinical history of angina, myocardial infarction, ischemic changes on electrocardiography or abnormal anatomy of the coronary arteries on coronary angiography. The extent of CAD was reported as one-, two- or three-vessel disease. The grading of CAD presentation was also reported as stable angina = 1, unstable angina = 2, non-ST elevation myocardial infarction = 3 or myocardial infarction with congestive heart failure = 4.

Comparison between the prevalence of risk factors in both the control and atherosclerosis groups (total and in each arterial system) was performed. Another comparison was performed between the prevalence of these factors and the presentation of atherosclerosis in different arterial systems.

Statistical analysis

Data for the groups were summarized as mean $\pm$ SD or a percentage of the risk factors. Differences between groups were tested initially for statistical significance using the χ^2 test,

Kruskal-Wallis, Fisher's exact test or ANOVA as appropriate. Significance was set at $P < 0.05$ for all comparisons. Subsequent analyses used multiple logistic regression to explore the association of risk factors with atherosclerotic disease and estimate adjusted ORs and their 95% CIs. Statistical analyses were performed using SPSS 11 software (SPSS Inc, USA).

RESULTS

During the study period, 406 patients (215 atherosclerotic and 191 controls) were included. Of these, 284 (70%) were men, 192 (47%) had type 2 DM, 205 (50%) were smokers, 166 (41%) were dyslipidemic and 118 (29%) were hypertensive. In age-, sex- and race-adjusted values, the risk of developing atherosclerosis in all arterial systems was significantly increased with all risk factors (Table 1). There were strong associations between type 2 DM and PAD (OR 6.2, 95% CI 3.7 to 10.4), ex-smoking and PAD (OR 21.5, 95% CI 8.4 to 54.8), dyslipidemia and CAD (OR 11.5, 95% CI 6.6 to 18.8), and hypertension and CVD (OR 7.9, 95% CI 3.7 to 16.9). Ex-smoking had the highest association among the risk factors in the atherosclerosis group (OR 15.9, 95% CI 6.6 to 38.5).

There were significant correlations between incidence of age older than 65 years, duration of DM, smoking, dyslipidemia and the presentation of PAD (Table 2). The correlation was also positive between the incidence of male sex, ex-smoking and hypertension, and the severity of presentation of CVD (Table 3). Significant correlation was also found between incidence of age older than 65 years, DM, smoking, dyslipidemia

TABLE 3**Correlation between the incidence of risk factors and the presentation of cerebrovascular disease**

Risk factor (%)	1 (n=27)	2 (n=2)	3 (n=19)	P
Age >65 years	37	100	52.6	0.17
Mean $\pm$ SD age, years	67.6 $\pm$ 8.8	78 $\pm$ 0.01	66.3 $\pm$ 13.4	0.35
Male	92.6	0	89.5	0.001
Saudi	77.8	100	78.9	0.76
Diabetes mellitus	55.6	100	52.6	0.43
<5 years	0	0	0	0.26
5 to 10 years	0	0	10.5	
>10 years	55.6	100	42.1	
Smoking				
Current	33.3	0	47.4	0.08
Ex-smoker	14.8	100	31.6	0.03
Dyslipidemia	48.1	100	42.1	0.29
Hypertension	40.7	0	52.6	0.032

1 = asymptomatic; 2 = transient ischemic attack; 3 = stroke

TABLE 4**Correlation between the incidence of risk factors and extent of coronary artery disease**

Risk factor (%)	1 (n=50)	2 (n=32)	3 (n=74)	P
Age >65 years	20	37.5	50	0.003
Mean $\pm$ SD age, years	55.3 $\pm$ 10.3	57.9 $\pm$ 11.4	62.5 $\pm$ 11.7	0.003
Male	16	25	16.2	0.51
Saudi	68	56.3	73	0.24
Diabetes mellitus	66	68.8	78.4	0.001
<5 years	12	6.3	13.5	0.18
5 to 10 years	12	0	6.8	
>10 years	42	62.5	58.1	
Smoking				
Current	38	45.2	24.3	0.001
Ex-smoker	16	6.5	40.5	0.001
Dyslipidemia	72	71.9	56.8	0.001
Hypertension	38	43.8	59.5	0.049

1 = one-vessel disease; 2 = two-vessel disease; 3 = three-vessel disease

and hypertension, and the extent of CAD (Table 4). The correlation between incidence of age older than 65 years and DM, and the severity of presentation of CAD was also significant (Table 5).

DISCUSSION

Atherosclerosis is considered to be the leading cause of death throughout the world (1,7). This disease is expected to constitute the primary cause of death up to the year 2020, despite ongoing efforts to extend both primary and secondary prevention to high-risk individuals (8). There are many reports in the literature about the risk factors of atherosclerosis (2-5). The present study extended our understanding by elucidating the impact of these risk factors on the clinical presentation of the disease in different arterial systems.

The strong association among traditional risk factors of atherosclerosis such as DM, smoking, dyslipidemia and hypertension

TABLE 5**Correlation between incidence of risk factors and the presentation of coronary artery disease**

Risk factor (%)	1 (n=45)	2 (n=58)	3 (n=16)	4 (n=73)	P
Age >65 years	15.6	51.7	68.8	29.7	0.001
Mean $\pm$ SD age, years	55.8 $\pm$ 8.8	61.9 $\pm$ 12	46.8 $\pm$ 12.4	56.9 $\pm$ 12.2	0.006
Male	82.2	82.8	87.5	78.4	0.87
Saudi	73.3	82.1	62.5	73	0.54
Diabetes mellitus	57.7	89.7	75	62.2	0.001
<5 years	13.3	20.7	0	0	<0.001
5 to 10 years	0	10.3	6.3	10.8	
>10 years	44.4	58.6	68.8	51.4	
Smoking					
Current	37.8	24.1	25	44.4	0.06
Ex-smoker	31.1	19	43.8	22.2	0.07
Dyslipidemia	60	63.8	81.3	64.9	0.49
Hypertension	55.6	51.7	73.8	40.5	0.53

1 = stable angina; 2 = unstable angina; 3 = non-ST elevation myocardial infarction; 4 = myocardial infarction with congestive heart failure

in the present study were consistent with previous studies (2-5,9-11). The present study, as well as other studies (12), showed that different cardiovascular risk factors have a variable influence on atherosclerosis in different arterial systems. Smoking and DM occurred more frequently in patients with PAD, in the present study and others (2,4,12-15). In contrast, another cross-sectional study reported no association with atherosclerosis in patients with type 2 DM (16). Dyslipidemia was more common in patients with CAD in the present study and others (12), and was less evident in PAD (4,17). Hypertension was more common in CVD patients in the present and other studies (18).

The major finding of the present study was that the different risk factors have a variable influence on the severity of the presentation and extent of atherosclerosis in different arterial systems. There was positive correlation between the prevalence of age older than 65 years, DM, smoking and dyslipidemia, and severity of presentation in PAD and the extent of CAD. There was also positive correlation between the prevalence of age older than 65 years and DM, and the severity of presentation of CAD. High prevalence of male sex, hypertension and smoking were correlated with the severity of presentation in CVD. Although these observations suggest different impacts of risk factors at different sites in the vascular system, the mechanism is unclear. The present study provided an opportunity for continued research on arterial pathophysiology and endothelial dysfunction. It is well known that the main risk factors for atherosclerosis – DM, smoking, dyslipidemia and hypertension – are associated with endothelial dysfunction (19). It is speculated that the risk factors have different effects on endothelial function in various arterial systems.

There are some limitations to the analysis of the present study. While it includes patients from different Arabic countries, it was a hospital-based study in which most of the patients were from Saudi Arabia. The study enrolled only inpatients with atherosclerotic disease, who may be at a higher risk than the stable outpatient population.

SUMMARY

There are positive correlations among some risk factors of atherosclerosis, and the extent and presentation of atherosclerotic disease in different arterial systems. Aggressive treatment of such risk factors can result in regression of atherosclerosis (20) and can diminish the incidence of cardiovascular events (21).

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