

Are complex coronary lesions more frequent in patients with diabetes mellitus?

Nezihi Baris MD, Bahri Akdeniz MD, Samet Uyar MD, Erdem Ozel MD, Onder Kirmli MD, Ozer Badak MD, Ozgur Aslan MD, Sema Guneri MD, FESC

N Baris, B Akdeniz, S Uyar, et al. Are complex coronary lesions more frequent in patients with diabetes mellitus? *Can J Cardiol* 2006;22(11):935-937.

BACKGROUND: Coronary atherosclerotic burden is excessive in diabetic patients. Diabetes mellitus (DM) is an independent predictor for both death and myocardial infarction. It is not known whether the prevalence of complex coronary lesions, such as bifurcation and ostial lesions, is different in diabetics from nondiabetics.

OBJECTIVE: The aim of present study was to investigate the prevalence of these lesions in patients with DM.

METHODS: One thousand fourteen consecutive patients (mean age 61.3 ± 10.7 years) were investigated. Coronary angiograms were examined for bifurcation and ostial lesions using a digital quantitative system. Patients were classified as diabetic ($n=281$) or nondiabetic ($n=733$).

RESULTS: Patient mean age, and rates of hypertension and hyperlipidemia were significantly higher in the diabetic group than in the nondiabetic group ($P < 0.0001$), although smoking was significantly lower ($P=0.001$). Reasons for coronary angiography and treatment were comparable between the two groups. The prevalence of bifurcation lesions and ostial lesions was significantly greater in the diabetic group than in the nondiabetic group (9.8% versus 4.3% [$P=0.001$] and 38.4% versus 29.2% [$P=0.003$] in the diabetic group versus the nondiabetic group). The presence of DM and greater age were found to be independent predictors for bifurcation lesions (OR=2.27 [$P=0.004$] and OR=1.03 [$P=0.01$], for DM and age, respectively) and ostial lesions (OR=1.40 [$P=0.027$] and OR=1.02 [$P=0.001$], for DM and age, respectively) in multivariate analysis.

CONCLUSIONS: Complex coronary lesions such as bifurcation and ostial lesions were significantly more common in diabetic patients than in nondiabetic patients. Greater age and the presence of DM were independent predictors for these complex lesions. These results may help to explain the poor prognosis of coronary artery disease among diabetic patients.

Key Words: *Bifurcation lesion; Coronary artery disease; Diabetes mellitus; Ostial lesion*

Among the risk factors for coronary artery disease (CAD), diabetes mellitus (DM) has a privileged position. Cardiovascular complications are the leading cause of mortality in patients with DM. DM is a strong independent predictor for both death and myocardial infarction (MI) (1). Unfortunately, the prevalence of DM in the general population is expected to increase in the coming decades (2).

As is well known, diabetic patients have more triple-vessel and less single-vessel CAD than nondiabetics (3). Autopsy studies have reported that diabetic patients had a larger extent

Les lésions coronariennes complexes sont-elles plus fréquentes chez les patients qui souffrent de diabète sucré?

HISTORIQUE : L'athérosclérose coronarienne impose un fardeau excessivement lourd aux patients diabétiques. Le diabète sucré (DS) constitue un facteur de prévisibilité indépendant de mortalité et d'infarctus du myocarde, mais on ignore si la prévalence des lésions coronariennes complexes, au niveau de la bifurcation et de l'ostium par exemple, est différente selon que les sujets sont diabétiques ou non.

OBJECTIF : Le but de la présente étude était de mesurer la prévalence de ces lésions chez les patients atteints de DS.

MÉTHODE : Mille quatorze patients consécutifs (âgés en moyenne de $61,3 \pm 10,7$ ans) ont été examinés. Leurs coronarographies ont été analysées pour dépistage de lésions au niveau de la bifurcation et de l'ostium à l'aide d'un système quantitatif numérisé. Les patients ont été classés selon qu'ils étaient diabétiques ($n = 281$) ou non-diabétiques ($n = 733$).

RÉSULTATS : L'âge moyen des patients et les taux d'hypertension et d'hyperlipidémie étaient significativement plus élevés chez les diabétiques que chez les non-diabétiques ($p < 0,0001$), tandis que le tabagisme était significativement moins répandu ($p = 0,001$). Les indications de la coronarographie et du traitement étaient comparables dans les deux groupes. La prévalence des lésions au niveau de la bifurcation et de l'ostium était significativement plus grande chez les diabétiques que chez les non-diabétiques (9,8 % contre 4,3 % [$p = 0,001$] et 38,4 % contre 29,2 % [$p = 0,003$] dans le groupe diabétique vs non-diabétique). La présence de DS et l'âge plus avancé se sont révélés être des facteurs de prévisibilité indépendants des lésions au niveau la bifurcation (RR = 2,27 [$p = 0,004$] et RR = 1,03 [$p = 0,01$] pour le DS et l'âge, respectivement) et de l'ostium (RR = 1,40 [$p = 0,027$] et RR = 1,02 [$p = 0,001$] pour le DS et l'âge, respectivement) lors de l'analyse multivariée.

CONCLUSIONS : Les lésions coronariennes complexes, par exemple au niveau de la bifurcation et de l'ostium, ont été significativement plus fréquentes chez les patients diabétiques que chez les non-diabétiques. Un âge plus avancé et la présence de DS se sont révélés être des facteurs de prévisibilité indépendants à l'égard de ces lésions complexes. Ces résultats pourraient expliquer en partie le pronostic sombre qui accompagne la coronaropathie chez les patients diabétiques.

of raised atherosclerotic lesions, greater incidence of left main coronary artery stenosis, and more extensive and diffuse disease compared with nondiabetic patients. Distal coronary involvement is also more frequent in diabetics than nondiabetics (4,5).

To our knowledge, there are currently no data concerning the prevalence of complex coronary lesions (such as bifurcation and ostial lesions) in patients with DM. The aim of the present study was to evaluate the prevalence of bifurcation and ostial coronary lesions in diabetics and to compare it with that in nondiabetics.

Department of Cardiology, Faculty of Medicine, Dokuz Eylul University, Izmir, Turkey

Correspondence: Dr Nezihi Baris, Department of Cardiology, Faculty of Medicine, Dokuz Eylul University, Izmir, Turkey.

Telephone 90-232-412-4103, fax 90-232-279-2565, e-mail nezihi.baris@deu.edu.tr

Received for publication September 22, 2005. Accepted February 6, 2006

TABLE 1
Comparison of diabetic versus nondiabetic patients for major coronary risk factors

	Diabetic (n=281)	Nondiabetic (n=733)	P
Age, years (mean ± SD)	63.4±9.4	60.5±10.9	<0.0001
Female, n (%)	121 (43.1)	213 (29.1)	<0.0001
Hypertension, n (%)	204 (72.6)	411 (56.1)	<0.0001
Hyperlipidemia, n (%)	186 (66.2)	358 (48.8)	<0.0001
Smoking, n (%)	81 (28.8)	290 (39.6)	0.001
Family history, n (%)	83 (29.5)	173 (23.6)	0.053

TABLE 2
Distribution of presenting diagnoses in diabetic versus nondiabetic patients

	Diabetic (n=281), n (%)	Nondiabetic (n=733), n (%)	P
Stable AP	142 (50.5)	398 (54.3)	NS
Unstable AP	66 (23.5)	138 (18.8)	NS
Non-ST elevation MI	33 (11.7)	73 (10.0)	NS
ST elevation MI	40 (14.2)	118 (16.1)	NS

AP Angina pectoris; MI Myocardial infarction; NS Not significant

TABLE 3
Medical treatment by group (diabetic versus nondiabetic patients)

	Diabetic (n=281), n (%)	Nondiabetic (n=733), n (%)	P
Acetylsalicylic acid	186 (66.2)	443 (60.4)	NS
Beta-blocker	164 (58.3)	387 (52.7)	NS
ACEI	208 (74.0)	497 (67.8)	NS
Statin	213 (75.8)	543 (74.0)	NS

ACEI Angiotensin-converting enzyme inhibitor; NS Not significant

PATIENTS AND METHODS

Quantitative coronary angiography (QCA) was performed on 1036 consecutive patients. Patients with previous revascularization procedures were excluded. The study was approved by the local ethics committee of Dokuz Eylul University, Izmir, Turkey. All coronary angiograms were examined for bifurcation, ostial and left main coronary artery lesions using a digital quantitative system (Philips Medical Systems, The Netherlands) by two different investigators who were unaware of the clinical status of the patients. After coronary angiographic examination, the medical records were investigated. Twenty-two patients whose medical records could not be located were excluded. If the atherosclerotic plaque included only the ostium of a side branch, it was accepted as an ostial lesion, and if the atherosclerotic plaque extended from the ostium of the side branch to the main branch, it was accepted as a bifurcation lesion. The reference segment was defined as the segment proximal to the bifurcation with no disease on QCA. Fifty per cent or greater cross-section stenosis was accepted as a significant lesion on QCA (6).

Among the 1014 patients, 540 (53.3%) had stable angina pectoris, 204 (20.1%) had unstable angina pectoris, 106 (10.5%) had non-ST elevation MI and 158 (15.6%) had ST elevation MI. The indication for angiography could not be clarified in six patients (0.8%).

Patients were divided into two groups based on the presence or absence of DM. DM was considered present if the fasting glucose

TABLE 4
Prevalence of bifurcation, ostial and left main coronary artery (LMCA) lesions in diabetic versus nondiabetic patients

	Diabetic (n=281), n (%)	Nondiabetic (n=733), n (%)	P
Bifurcation lesion	27 (9.8)	31 (4.3)	0.001
Ostial lesion	107 (38.4)	213 (29.2)	0.003
LMCA lesion	38 (13.6)	80 (11.0)	0.191

TABLE 5
Results of multivariate analysis

	OR (95% CI)	P
Bifurcation lesion		
Diabetes mellitus	2.27 (1.30–3.97)	0.004
Age	1.03 (1.00–1.06)	0.01
Ostial lesion		
Diabetes mellitus	1.40 (1.04–1.89)	0.027
Age	1.02 (1.00–1.03)	0.001

level was at least 6.9 mmol/L, or if the patient had been informed of the diagnosis and treatment had been prescribed with a special diet, oral antidiabetic drugs or insulin (7,8).

Statistical analysis

A commercially available software package (SPSS version 11.0, SPSS Inc, USA) was used to analyze the data, which are presented as mean ± SD. The statistical significance of intergroup differences was analyzed by the χ^2 test and by Student's *t* test. Correlations between two parameters were determined by the Pearson correlation coefficient. Independent variables were determined by multivariate analysis. $P < 0.05$ was considered statistically significant.

RESULTS

The mean age of the 1014 patients was 61.3±10.7 years (range 18 to 89 years). Mean age, female sex, and rates of hypertension and hyperlipidemia were all significantly greater in the diabetic group. A family history of CAD was insignificantly more frequent in diabetics. Interestingly, the percentage of smokers was significantly lower in diabetic than in nondiabetic patients (Table 1). The clinical diagnoses of those patients referred for angiography were comparable between the two groups (Table 2). There was no significant difference in medical treatment between the two groups (Table 3). Angiotensin-converting enzyme inhibitors were used more often in diabetic than in nondiabetic patients (*P* not significant).

The prevalence of bifurcation and ostial lesions was significantly higher in the diabetic group than the nondiabetic group. Unexpectedly, the prevalence of left main coronary artery lesions was comparable in the two groups (Table 4). Interobserver variability was not statistically significant for the QCA evaluation ($P=0.127$).

DM and age were independent predictors for bifurcation and ostial lesions by multivariate analysis. For DM, the OR was 2.27 (95% CI 1.30 to 3.97; adjusted $P=0.004$) for bifurcation lesions, whereas for ostial lesions, the OR was 1.40 (95% CI 1.04 to 1.89; adjusted $P=0.027$). For age, the OR was 1.03 (95% CI 1.00 to 1.06; adjusted $P=0.01$) for bifurcation lesions, whereas for ostial lesions, the OR was 1.02 (95% CI 1.00 to 1.03; adjusted $P=0.001$) (Table 5).

DISCUSSION

The present study focused on angiographic characteristics of coronary atherosclerosis, with particular attention to the prevalence of complex lesions in patients who underwent coronary angiography because of CAD. We found that the prevalence of bifurcation and ostial lesions was significantly greater in patients with DM than in those without. The two groups were not homogenous, with most of the coronary risk factors higher in the diabetic group. For this reason, multivariate analysis was used to determine the independent predictors for bifurcation and ostial lesions. Age and the presence of DM were found to be independent predictors of these lesions.

Previous studies have reported that the triple-vessel disease is more frequent in patients with DM (9-11), although other studies have demonstrated that the angiographic profiles are similar among diabetic and nondiabetic patients (12,13). However, there are no data concerning the prevalence of complex lesions such as those at bifurcations or at the ostia of branch vessels. The present study was the first to evaluate the relationship between DM and bifurcation and ostial lesions.

More frequent involvement of the left main coronary artery has been reported in diabetic patients (1). However, no significant difference was found in the prevalence of left main lesions between diabetic and nondiabetic patients in the present study.

REFERENCES

- Norhammar A, Malmberg K, Diderholm E, et al. Diabetes mellitus: The major risk factor in unstable coronary artery disease even after consideration of the extent of coronary artery disease and benefits of revascularization. *J Am Coll Cardiol* 2004;43:585-91.
- King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025. Prevalence, numerical estimates, and projections. *Diabetes Care* 1998;21:1414-31.
- Dortimer AC, Shenoy PN, Shiroff RA, et al. Diffuse coronary artery disease in diabetic patients: Fact or fiction? *Circulation* 1978;57:133-6.
- Waller BF, Palumbo PJ, Lie JT, Roberts WC. Status of the coronary arteries at necropsy in diabetes mellitus with onset after age 30 years. Analysis of 229 diabetic patients with and without clinical evidence of coronary heart disease and comparison to 183 control subjects. *Am J Med* 1980;69:498-506.
- Vigorita VJ, Moore GW, Hutchins GM. Absence of correlation between coronary arterial atherosclerosis and severity or duration of diabetes mellitus of adult onset. *Am J Cardiol* 1980;46:535-42.
- Lindvall B, Brorsson B, Herlitz J, Albertsson P, Werko L. Comparison of diabetic and non-diabetic patients referred for coronary angiography. *Int J Cardiol* 1999;70:33-42.
- Pogach LM, Brietzke SA, Cowan CL Jr, Conlin P, Walder DJ, Sawin CT; VA/DoD Diabetes Guideline Development Group. Development of evidence-based clinical practice guidelines for diabetes: The Department of Veterans Affairs/Department of Defense guidelines initiative. *Diabetes Care* 2004;27(Suppl 2):B82-9.
- Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 1997;20:1183-97.
- Ozerkan F, Ceyhan C, Baris N, Yavuzgil O, Kultursay H, Akin M. Angiographic comparison of the severity and distribution of coronary artery disease in patients with and without diabetes mellitus. *Turk J Endocrinol Metab* 2001;2:71-4.
- Uddin SN, Malik F, Bari MA, et al. Angiographic severity and extent of coronary artery disease in patients with type 2 diabetes mellitus. *Mymensingh Med J* 2005;14:32-7.
- Vigorito C, Betocchi S, Bonzani G, et al. Severity of coronary artery disease in patients with diabetes mellitus. Angiographic study of 34 diabetic and 120 nondiabetic patients. *Am Heart J* 1980;100:782-7.
- Hochman JS, Phillips WJ, Ruggieri D, Ryan SF. The distribution of atherosclerotic lesions in the coronary arterial tree: Relation to cardiac risk factors. *Am Heart J* 1988;116:1217-22.
- Pajunen P, Nieminen MS, Taskinen MR, Syvanne M. Quantitative comparison of angiographic characteristics of coronary artery disease in patients with noninsulin-dependent diabetes mellitus compared with matched nondiabetic control subjects. *Am J Cardiol* 1997;80:550-6.
- Aronson D, Bloomgarden Z, Rayfield EJ. Potential mechanisms promoting restenosis in diabetic patients. *J Am Coll Cardiol* 1996;27:528-35.
- Herlitz J, Wognsen GB, Emanuelsson H, et al. Mortality and morbidity in diabetic and nondiabetic patients during a 2-year period after coronary artery bypass grafting. *Diabetes Care* 1996;19:698-703.

Diabetic patients subjected to coronary interventions have a higher risk of complications and a worse prognosis than non-diabetic subjects (14,15). The higher prevalence of bifurcation and ostial lesions noted in the present study could be a factor contributing to this less favourable outcome.

As we expected, we found more frequent rates of hypertension, hyperlipidemia and family history of CAD in diabetic patients. Interestingly, smoking was significantly less common among diabetic than nondiabetic patients.

Limitations

In the present study, the history of DM was obtained based on information from patient histories and hospital medical records. Some patients with impaired glucose tolerance could have been accepted as nondiabetic patients. Additionally, QCA could have underestimated the plaque burden in some patients because of technical difficulties such as vessel overlap and plaque eccentricity.

CONCLUSION

DM is a major contributor to the development of CAD as well as to the outcomes following various manifestations of the disease. The higher prevalence of complex coronary lesions, such as bifurcation and ostial lesions, may help to explain the poor prognosis from CAD in diabetic patients.