Comparison of Coronary Angiography Findings in Diabetic and Non-diabetic Women with Non-ST-Segment-Elevation Acute Coronary Syndrome

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Objective

Compare hemodynamic and angiographic patterns, as well as atherosclerotic lesion morphology, in diabetic and non-diabetic females with unstable angina or non-ST-segment-elevation myocardial infarction (UA/NSTEMI).

Methods

Two interventional cardiologists, determined the presence of severe atherosclerotic lesion, defined as those ≥ 70%; plaque morphology, according to the American Heart Association classification; collateral circulation; plus ventricular and aortic pressures. Ejection fraction was calculated by angiography or echocardiography.

Results

During eight and a half years, 645 coronary angiographies were performed in women with UA/NSTEMI. In the present study, 593 female patients were assessed, (215 diabetic-36%). This group differed from the non-diabetic in the following aspects: older age (61 ± 10.6 x 58.1 ± 11.4), higher prevalence of postmenopausal women and lower prevalence of the smoking habit. Severe three-vessel disease was significantly more frequent in diabetic patients (28% x 10%), as well as totally occluded vessels: 51 (23%) x 54 (14.3%), $p < 0.005$. Additionally, ejection fraction < 50% was more common in diabetic patients.

Conclusion

These findings confirm the diffuse pattern of atherosclerotic disease in diabetic patients, as well a greater deterioration of ventricular function, which may be associated to the poorer prognosis seen in this population both in the short- and long-term.

Keywords:

diabetes mellitus, women, unstable angina, coronary angiography

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Cardiovascular diseases are the leading cause of death and morbidity in diabetic patients. This group is two or four times as likely to develop cardiovascular disease than the non-diabetic group, women and minorities being especially involved in this siuation[1].

While recent advances in the treatment of coronary heart disease (CHD) have increased the survival of these patients, mortality rate is still two times higher in diabetics than in non-diabetics, and females with diabetes have the worst prognosis. The relative risk of CHD is two or three-fold higher in this population[2].

Albeit glycemic control in diabetes is clearly related to microvascular complications, its contribution to macrovascular atherosclerosis is still controversial[3].

Most studies performed in patients with chronic angina showed that the atherosclerotic plaques are not similar in both groups, yet the disease is more diffuse and severe in diabetic patients[4].

Ambrose *et al*[5], demonstrated previously, by means of coronary angiography, a distinct lesion in patients with unstable angina compared to those with chronic stable angina. Nevertheless, coronary angiography has not been consistently evaluated in diabetic patients, especially in women with unstable angina. Therefore, this study aimed at comparing the hemodynamic pattern, the extent of atherosclerotic involvement and the plaque morphology in diabetic and non-diabetic women diagnosed with unstable angina or non-ST-segment-elevation myocardial infarction (UA/NSTEMI).

Methods

All the data of this study were prospectively collected from patients referred to coronary angiography and were included by the time this examination was done. From March/93 to August/01, 6,135 coronary angiographies were performed at a tertiary hospital in São Paulo. During this time, 645 women had earlier diagnosis of UA/NSTEMI; 593 were evaluated in this series. Fifty-two were excluded because their case report forms (CRF) were incomplete or their coronary angiography examination could not be evaluated. Before coronary angiography examination, a standard clinical history was obtained.

Angiographic data – Two interventional cardiologists, blinded to all patient data, evaluated visually the coronary angiography. Severe lesion was determined as: occlusion ≥ 50% for the left main coronary artery; and 70% or more for all other vessels. In addition, lesions ≤ 50% were also analyzed and divided as follows: plaques up to 10%; from 11 to 30%; and from 31 to 50%. These changes were considered only when at least two-thirds of the length of the studied vessel was involved. The Pearson coefficient of agreement for lesions with < 50% was 0.7 for both interventionists with $p < 0.001$. In case of disagreement, the opinion of a third interventionist was requested.

Atherosclerotic lesion morphology – Lesions ≥ 70% were classified by consensus between both cardiologists, according to the description provided by the American Heart Association/American College of Cardiology[6,7]. In the present study, only the aspects of the lesion were considered; prelesional tortuosities and angulation of the artery were not analyzed. Type A lesion: < 10 mm in length, concentric, smooth contour, little or no calcification, no thrombus; type B: 10 to 20 mm in length, eccentric, moderate to heavy calcification, some thrombus present (B1 = only one of these variables is present; B2 = two of these aspects are present); and type C: > 20 mm in length, total occlusion, saphenous bypass grafts with friable aspect. The presence of thrombus was defined as a subtraction image of intraluminal contrast.

Collateral circulation – This was classified according to the Cohen and Rentrop grading system of 0 to III[8].

Ventricular ejection fraction (EF) – This was calculated in the right anterior oblique 30-degree projection at the hemodynamic laboratory using the Stanford technique, previously described[9], by the same technician specifically trained for this procedure. When ventriculography was not performed, EF value was calculated by echocardiogram.

Hemodynamic – At the end of cardiac catheterization, aortic and left ventricle (LV) pressures were recorded on graph paper. In this study, end-diastolic and systolic LV pressures, plus mean aortic pressure, aortic systolic and diastolic pressures were measured. Aortic pulse pressure was calculated by the difference between the systolic and diastolic blood pressures, and mean blood pressure was calculated using the formula: 2 x DP/3 + SP/3, where DP is diastolic pressure and SP is systolic pressure.

Definitions – Women referred with the diagnosis of diabetes mellitus or who were on hypoglycemic therapy were considered "diabetes mellitus" patients. Hypertension, dyslipidemia, and other risk factors were considered according to the information provided by the patient.

Statistical analysis – Continuous variables with normal distribution were compared through the Student's t-test; for the categorical variables the chi-square test was used. Continuous variables without Gaussian distribution were analyzed using the Mann-Whitney test.

Results

Of the 593 women included in the study, 378 (63.7%) were non-diabetic and 215 (36%) were diabetic patients, 189 (89%) of whom had type-2 diabetes and 26 (11%) had type-1 diabetes. Unstable angina was diagnosed in 512 (86%) cases, and non-ST-elevation

myocardial infarction was diagnosed in 81 (13.7%) cases; no difference was observed between diabetic and of non-diabetic women regarding this diagnosis: 87% of the diabetic and 86% of the non-diabetic patients had unstable angina, respectively.

Diabetic patients differed from those non-diabetic in the following aspects: they were older, with higher prevalence of postmenopausal women and lower prevalence of tobacco use (table 1)

Coronary angiography – Among hospitalized patients, the procedure was performed, on average, six days after admission. Coronary angiography was normal in 14 (6.5%) diabetic and 48 (13%) in non-diabetic women $p < 0.05$. Aortic diastolic pressure was higher in non-diabetic patients, whereas pulse pressure was higher in diabetic patients (77 ± 22 mmHg versus 70 ± 19 mmHg, $p < 0.001$).

All pressure values are shown in table 2.

The number of severely involved vessels was higher among diabetic patients. Lesion equal to or higher than 70% in three vessels was statistically significant and more common in diabetic patients, whereas the involvement of one or two vessels was the same in both groups (table 3).

Intracoronary thrombus was observed in 28 patients (4.7%); 13 patients (6.0%) were diabetic and 15 (4.0%) were non-diabetic, with no statistically significant difference.

Regarding left main coronary artery disease, no differences were found between both groups; however, total occlusion was significantly more frequent in diabetic patients. 51 (23%) vs. 54 (14.3%), $p < 0.005$, as well as the presence of collateral circulation 52 (24%) vs. 53 (14%), $p = 0.002$. Besides, lesions from 31% to 50% and from 11% to 30% were more common in diabetic patients; this result was statistically significant, $p < 0.001$ (fig. 1).

Table 1 – Age, baseline characteristics and past history in both groups.

	Diabetes		
	Yes (%) (n=215)	No (%) (n=378)	p
Age (years)	61.0 ± 10.6	58.1 ± 11.4	0.001
History of hypertension	182 (84.7)	305 (80.9)	NS
Current smoking status	41 (19.1)	132 (35.1)	0.001
Use of contraceptives	13 (6.0)	30 (8.0)	NS
Physical inactivity	79 (36.9)	136 (36.2)	NS
Family history of CHD	86 (40.2)	172 (45.9)	NS
Dyslipidemia	85 (40.9)	135 (37.3)	NS
Postmenopausal women	144 (72.4)	212 (60.4)	0.001
Previous AMI	57 (26.8)	79 (21.0)	NS
Previous PTCA	7 (3.3)	13 (3.4)	NS
Previous coronary artery bypass grafting (CABG)	7 (3.3)	8 (2.1)	NS

CHD: coronary heart disease; AMI: acure myocardial infarction; PTCA: percutaneous transluminal coronary angioplasty

Table 2 – Ventricular and aortic pressures in both groups.

Pressure in mm Hg	Diabetes		p
	Yes n= 215	No n= 378	
	Mean ± (SD)	Mean ± (SD)	
LVSP	152 ± 31	149 ± 29	NS
LVEDP	16 ± 9	16 ± 8	NS
MAP	101 ± 19	102 ± 19	NS
ASP	152 ± 31	149 ± 29	NS
ADP	75 ± 17	78 ± 16	< 0.05
APP	77 ± 22	70 ± 19	0.001

LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; MAP = mean aortic pressure; ASP = aortic systolic pressure; ADP = aortic diastolic pressure; APP = aortic pulse pressure.

Table 3 – Difference between both groups with respect to the number of normal arteries and arteries with lesion equal to or higher than 70%.

Number of arteries	Diabetes		p
	Yes (%)	No (%)	
0	79 (36.7)	222 (58.7)	< 0.001
1	44 (20.5)	68 (18.7)	0.459
2	33 (15.3)	48 (12.7)	0.366
3	59 (27.4)	40 (10.6)	< 0.001

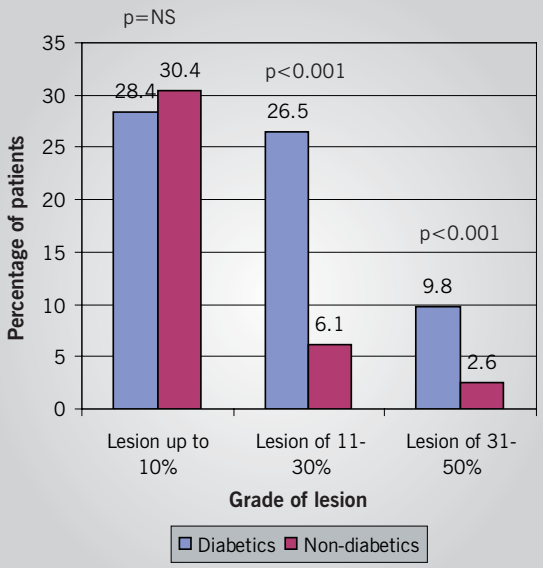

***Fig. 1** - Percentage of patients with lesions lower than 50% in both groups*

In the morphological analysis, no difference was observed between diabetic and non-diabetic patients (fig 2).

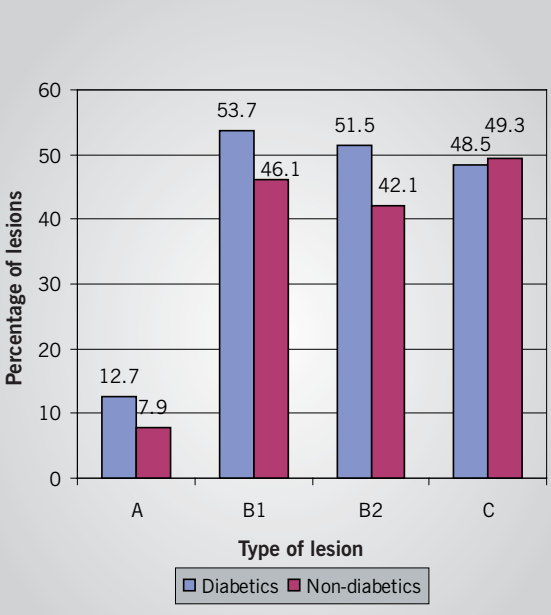

***Fig. 2** - Morphology of atherosclerotic lesion, by angiography, (according to AHA) in both groups*

Ventricular systolic function was more altered in diabetic patients: ejection fraction < 50% was significantly more frequent in this group (fig 3). Of the total number of patients, 21 had EF measured by echocardiogram.

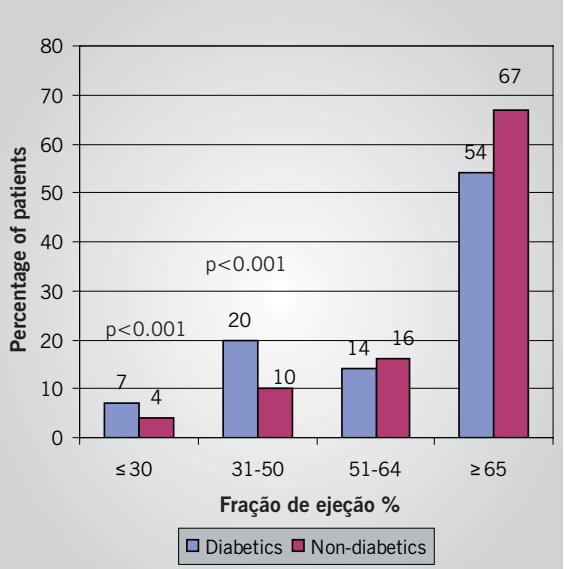

***Fig. 3** - Ejection fraction in diabetic and non-diabetic patients*

Discussion

The most relevant finding of this study was that atherosclerotic disease was more severe in diabetic women with UA/NSTEMI not only regarding the degree of obstruction of vascular lumen, but also the extent to which the vessel was affected with less severe plaques. In addition to the fact that severe lesions in three vessels have been more frequent in this group, smaller atherosclerotic plaques also were more common in this population. This finding corroborates Natali *et al*'s data[10], which showed that diabetic patients with atherosclerotic disease score higher on coronary compromise (the sum of all atherosclerotic lesions detected) than the non-diabetic: 352 ± 232 versus 211 ± 201 units, $p < 0.0001$, respectively. Also, Melidones *et al*[11] in a randomized study, distributed patients with atherosclerotic lesion detected by coronary angiography in two groups: group A with 463 diabetic patients, and group B with 210 non-diabetic patients. There were no differences in these groups concerning other risk factors, age, and sex. However, diabetic patients more frequently had more three-vessel disease and less frequently single-vessel disease; men showed the same angiographic pattern as women; yet no report was made about differences in the same sex; diabetic patient vessel involvement was 2.2 vessels versus 1.8 vessels among the non-diabetic, $p < 0.01$. Our series corroborates all these studies, showing that diabetic women with no-ST-elevation acute coronary syndrome have significantly more multivessel disease than the non-diabetic.

Another interesting finding of our study is that the angiographic morphology of atherosclerotic plaque is similar in both groups.

Diabetes mellitus is linked to a poorer prognosis in patients with coronary atherosclerotic disease, especially in women[12]. Stein *et al*[13], demonstrated that, in patients who underwent angioplasty, the presence of diabetes was related to a poorer prognosis. In our series, no difference in atherosclerotic plaque morphology was observed, meaning that the poorer prognosis in this population might be related to the number of vessels with severe and moderate plaques, rather than the type of plaque[10,11,14].

Knowing the role of small atherosclerotic plaques in triggering acute coronary syndrome, this finding might be implicated in the more severe evolution of these patients[15-19].

However, our findings differ from those observed by angioscopy in diabetic and non-diabetic patients. Silva *et al*[20] compared the angioscopic features of 55 patients with acute coronary syndrome, 31% of which were diabetic. Ulcerated plaques were found in 94% of diabetic and in 60% of non-diabetic patients ($p < 0.01$); intracoronary thrombus was observed in 94% of diabetic and only 55% of non-diabetic patients ($p < 0.004$). They concluded that diabetic patients had more complex atherosclerotic lesions regarding these aspects. Our data do not show this difference in angiographic terms, yet the angioscopic analysis is more specific and sensitive to certain characteristics of atherosclerotic plaque, especially the ones described above, and this explains this difference. In addition, due to the different prevalence of thrombus in the study of Silva *et al*[20], we can assume that their population proved to be of high risk, whereas our series was of low risk, since the prevalence of severe lesions occurred in only 50% of cases.

Concerning risk factors, the present study showed no difference at all in the prevalence of hypertension, dyslipidemia, sedentariness, family history of CHD or use of oral contraceptive, as well as history of AMI, PTCA or CABG in both groups studied. These data differ from some previous studies in which hypertension, kidney disease, and dyslipidemia are more common in diabetic patients[21,22]. With respect to age, the studies are controversial. In some of them, diabetic patients with CHD are older[21,23], whereas in others the age is similar[24,25]. This finding should be interpreted cautiously, because diabetes is associated with older age, and this, in turn, to higher prevalence of CHD, especially in women.

As in several previous studies, diabetes was associated with a more depressed systolic function[25-29]. The prevalence of ejection fraction < 50% in diabetic women was statistically significant. Several factors are implicated in this finding, including diabetic cardiomyopathy, besides the CHD itself with ischemia and silent infarctions, which are more frequent in this population.

Our study has some limitations: the data were retrospectively analyzed, in addition to the prevalence of severe CHD, which was lower in the literature even in a female population, probably reflecting a diagnosis without risk stratification of non-ST-elevation acute coronary syndrome. Also, we know now that even blood glucose levels lower than those that we have traditionally interpreted as altered are related to higher cardiovascular risk, and this was not considered in this study (fast blood glucose). Other possible diagnosis, such as esophageal disease, panic disorder, and mitral valve prolapse, were not excluded. These findings, however, confirm the diffuse aspect of CHD and the more deteriorated ventricular function in diabetic patients, which can be directly related to the poorer prognosis observed in this population.

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