Prevalence of Coronary Artery Disease in Type I Diabetic Candidates for Double Transplantation (Kidney and Pancreas)

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Objective

To assess the prevalence of coronary artery disease (CAD) in a population of type I diabetic, nephropathic patients in a dialysis program and candidates for double transplantation (kidney and pancreas).

Methods

From January 2000 to July 2002, 58 type I diabetic patients underwent coronary cineangiography as part of an assessment protocol for double transplantation. Coronary artery disease was defined as any irregularity in the coronary arteries and was classified according to the degree of luminal stenosis as mild (< 30%), moderate (≥ 30 to 70%), and severe (> 70%).

Results

The mean age of the patients was 34 ± 12 years, and 32 (55%) were men. No patient had a history of angina or acute myocardial infarction. The major risk factors for the disease were systemic arterial hypertension in 93% of the patients, dyslipidemia in 38%, familial history in 25%, and smoking in 20%. The mean duration of diabetes was 20.8 ± 9 years, and the duration of dialysis was 26 ± 9 months. Coronary angiography revealed coronary artery disease in 42 (72%) patients, which was mild in 20 (34%) patients, moderate in 9 (16%), and severe in 13 (22%).

Conclusion

Patients with type I diabetes in a dialysis program and candidates for double transplantation had an elevated prevalence of coronary artery disease. It is worth noting that those patients had no symptoms of the disease.

Key words

atherosclerosis, type I diabetes mellitus, double transplantation

It is believed that 17 million diabetic people exist in the United States of America, 90 to 95% of whom have type II diabetes and 5 to 10% have type I (TIDM) [1].

The prevalence, incidence, morbidity, and mortality of all forms of cardiovascular disease are more elevated in diabetic patients (type I or II) when compared with those of nondiabetic individuals [2-6].

The relation between coronary artery disease and diabetes mellitus in type II diabetics has been studied, and a series of factors have been identified as participating in the genesis and progression of the disease in that population. However, in regard to the type I diabetic patient, the same exuberance of information is not available [7].

Noninvasive studies have reported that type I diabetic patients have an early increase in coronary calcification and several risk factors for coronary artery disease [8].

The improvement observed in the treatment of TIDM in the past 20 years has allowed survival until adulthood for many patients, exposing the cardiovascular system to exacerbated atherogenic factors for a longer time. This has allowed a much more frequent diagnosis of coronary artery disease in clinical practice. The Stent or Surgery study [9], which compared myocardial revascularization surgery with coronary angioplasty in patients with multivessel coronary artery disease, recruited 6% of patients with TIDM.

The early or subclinical detection of cardiovascular disease has been a great challenge in the prevention and treatment of patients with TIDM [10].

The preoperative assessment protocol of candidates for double transplantation (kidney and pancreas) of the UNIFESP-EPM includes coronary cineangiography and left ventriculography. Aiming at assessing some aspects of coronary artery disease in those patients, we decided to report the initial series of this evaluation.

The primary objective of this study was to assess the prevalence of coronary artery disease in a population of TIDM patient candidates for double transplantation; the secondary objective was to assess the degree of luminal stenosis caused by coronary obstructive lesion in the population studied.

Methods

From January 2000 to July 2002, a retrospective study was carried out in the Hospital do Rim e da Hipertensão and in the Hospital São Paulo (UNIFESP-EPM) comprising patients with TIDM

and chronic renal failure in a dialysis program and candidates for double transplantation, who underwent clinical cardiological assessment followed by coronary cineangiography and left ventriculography. No patient assessed was excluded from the analysis.

Type I diabetic patients were those who initiated the use of insulin on the occasion of the diagnosis or until 6 months after being diagnosed with the disease, and who had serum levels of C peptide compatible with the diagnostic criteria of the disease.

Invasive cardiac assessment was performed by use of coronary cineangiography according to the technique of Judkins. The examinations were stored on 35-mm film or compact discs, and then analyzed by use of quantitative coronary angiography (QCA-CMS; version 3; Medis, Nuenen, The Netherlands).

Coronary artery disease is considered obstructive when the arterial luminal stenosis is ≥ 50%, and nonobstructive when the arterial luminal stenosis is < 50% [11]. Any narrowing or irregularity of the arterial lumen is considered coronary artery disease. The stenotic lesions were classified as follows: mild, luminal stenosis < 30%; moderate, luminal stenosis ≥ 30 to 70%; and severe, luminal stenosis > 70%. The left ventricular ejection fraction was determined by use of the Dodge method.

Results

According to the assessment protocol before double transplantation, 58 patients were studied at our institution. The mean age of the patients was 34 ± 12 years (median, 33.5). The mean duration of dialysis was 26 ± 9 months (median, 23), and the mean duration of diabetes mellitus was 20.8 ± 9 years (median, 21). The most common dialysis method was hemodialysis (86%).

The male sex predominated [32 men (55%) and 26 women (45%)]. The major risk factors for coronary artery disease were as follows: systemic arterial hypertension in 93%, dyslipidemia in 38%, familial history in 25%, and smoking in 20%.

Seven (12%) patients had one sign or symptom of heart failure (functional class II and III), while the others (88%) were asymptomatic. The patients had neither angina, nor ischemic equivalents, nor antecedents of myocardial infarction.

No severe complication related to coronary cineangiography occurred. The mild complications were 3 hematomas in the vascular site of access and a urticaria-like allergic reaction.

Analysis of coronary cineangiography revealed that 42 (72%) patients had coronary artery disease. Stenosis of the arterial lumen was as follows: > 70% in 13 (22%) patients; between 30 and 70% in 9 (16%) patients; and < 30% in 20 (34%) patients.

Regarding the extension of the coronary artery disease of the patients with stenosis > 30%, 7 were 2-vessel, and 2 were 3-vessel. Obstructive lesions > 30% were observed in 12 anterior descending coronary arteries, 3 circumflex arteries, and 7 right coronary arteries. The remaining lesions were located in secondary branches (diagonal or marginal).

Left ventricular ejection fraction was $54 \pm 19\%$. Left ventricular systolic dysfunction (ejection fraction < 50%) occurred in 12 patients (20%), and in 9 (75%) patients, the dysfunction was segmentary. The most common dysfunction was that of the anterior wall, which occurred in 6 (66%) patients.

Discussion

Angiographic information about coronary artery disease in patients with TIDM is scarce, unlike that in patients with TIIDM, which is abundant.

Pajune et al [12] carried out a case-control study, in which type I diabetic patients with clinical indications for coronary cineangiography were paired with nondiabetic patients for sex, age, date of catheterization, and serum level of creatinine. The following patient data were analyzed: degree of luminal stenosis, lesion length, and the atherosclerotic plaque load. The type I diabetic patients had a greater degree of luminal stenosis (49% vs 34%, P < 0.01), longer lesions (35 mm vs 18 mm, P < 0.001), and a greater plaque load (21 mm^2 vs 13 mm^2, P < 0.001) [12].

Larsen et al [13] assessed the relation between coronary artery disease (diagnosed on coronary cineangiography and intravascular ultrasound) and control of glycemia in a type I diabetic population (29 patients), which had been included in the Oslo study in the 1980s. On the occasion of the invasive study, the patients had no disease symptoms. The analysis of coronary cineangiography revealed stenosis > 50% in 34% of the patients; according to the intravascular ultrasound, however, the percentage of stenosis was > 40% in 34.5% of the patients, between 20 and 40% in 31%, and < 20% in 34.5%.

Type I diabetic patient candidates for double transplantation were studied by Jukema et al [14], who performed coronary cineangiography before and 4 years after double transplantation to assess the impact of glycemic normalization on the angiographic characteristics of coronary artery disease. The patients in this series had no severe stenoses. However, the most relevant contribution of the publication was the observation that the patients, whose renal and pancreatic grafts were functioning after 4 years, had a marked reduction in atherosclerosis. On the contrary, the 6 patients whose pancreatic grafts did not function had progression of the disease [14].

The patients in our study differed from those in the cited studies because they were candidates for double transplantation, had no symptoms of coronary artery disease, and, mainly, had an elevated rate of obstructive coronary artery disease [42 (72%) patients with stenosis > 30%, and 13 (22%) patients with stenosis > 70%].

Some studies assessed the prevalence of coronary artery disease in TIDM by using clinical, electrocardiographic, or functional test criteria. The results of the analysis of more than 5,500 patients revealed that coronary artery disease was present in a significant number of patients, reaching 35% in some age groups. The major independent risk factors were as follow: duration of TIDM, diabetic nephropathy, creatinine serum level, and presence of microalbuminuria [15-17].

In our study, the prevalence of coronary artery disease was not only high, but also revealed severe stenoses in 13 (22%) patients. However, the symptomatology of coronary artery disease was absent in all patients. One possible mechanism to explain that finding may be the presence of advanced autonomous neuropathy [18].

Our results suggest that coronary macrovascular disease in a type I diabetic candidate for double transplantation may be underdiagnosed by the noninvasive classical methods. Because that is a high-risk population for coronary artery disease [19], we believe

that the screening routines for coronary artery disease in those patients should be reviewed. This is reinforced by the knowledge that the greatest cause of death in diabetic patients is cardiovascular disease [20].

The possibility of regression of CAD with double transplantation through normalization of glycemia in TIDM has raised great expectations, which should be investigated with angiographic and serial ultrasound studies.

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