

Diabetes and Cardiovascular Disease. A Comprehensive Insight to the New Epidemic of the 21st Century

Xavier Bosch^a, Fernando Alfonso^b and Javier Bermejo^b

^aEditor Jefe y ^bEditores Asociados de REVISTA ESPAÑOLA DE CARDIOLOGÍA. España

Diabetes mellitus is one of the diseases with the greatest public health impact, not only because of its high rate of occurrence, but most of all because of the consequences of the chronic complications resulting from this disease, and the important role it plays as a risk factor in atherosclerosis^{1,2} and cardiovascular pathology. Taking into consideration all these factors coupled with the fact that the risk increases with the level of hyperglycemia has led to the definition of diabetes being modified in recent years, reducing it to the upper limit of a fasting glycemia level of ≥ 126 mg/dL, as well as normal glycemia becoming <110 mg/dL.³

EPIDEMIOLOGICAL DATA

Ninety percent of diabetics present with type 2 diabetes, and its prevalence has increased throughout the Western world as a consequence of the aging population and the increase in obesity and a sedentary lifestyle. In general, diabetes type 2 begins several years before clinical diagnosis, and the most important risk factors are age, obesity, and a family history of diabetes.

It is estimated that 6.6% of the population of the United States between the age of 20 years and 74 years have diabetes and that this number will increase to 10% in the coming. About 10 million Americans have diabetes and it is estimated that another 5 million have undiagnosed diabetes. In Spain, the incidence of diabetes type 2 is estimated to be 8 out of 1000 per year, with a prevalence of 6% to 10%, depending on age group and geographic area studied;^{4,5} it is notable that almost half of the patients do not know that they have the disease. Therefore, approximately 2.1 million Spaniards have diabetes although only 1.1 to 1.4 million know they have it.⁵

In the United States it is estimated that patients with diabetes make up 15% to 20% of all deaths in the population older than 25 years of age, and these numbers are double in patients older than 40 years of age. In most studies, the mortality rates are higher for women than for men. In Spain, diabetes is the third most common cause of death among women and the

seventh most common among men.

Cardiovascular repercussion

In the case of individuals genetically predisposed to the disease, obesity, and sedentary lifestyle lead to insulin resistance, which is the state that precedes diabetes type 2 and tends to be accompanied by other cardiovascular risk factors such as dyslipidemia, hypertension, and prothrombotic factors.⁶ The frequent association in the same individual of these risk factors is why the syndrome is called metabolic. The clinical evidence of insulin resistance includes abdominal obesity, slight hypertension, an increase in triglyceride levels (15 mg to 250 mg/dL), decrease in HDL (HDL-C) cholesterol, and, in some cases, slight hyperglycemia (110 mg to 126 mg/dL). Recognition of this syndrome is fundamental for the primary prevention of cardiovascular disease that it the cause of death in two-thirds of diabetic patients.

The mortality risk of patients with diabetes is the same as nondiabetic patients who have had a myocardial infarction (about 20%);⁷ this risk is tripled in those diabetic patients who have an infarct. It is not surprising, therefore, that the life expectancy of a patient who is diagnosed with diabetes type 2 is reduced by 30%. When the patient has cardiovascular pathology, mortality is much higher among patients with diabetes than those who do not have diabetes.⁷ These data are the reason several institutions such as the American Heart Association have declared diabetes a primary cardiovascular risks.⁸

On the other hand, patients with diabetes have a higher probability of presenting with an acute coronary syndrome and experiencing silent sudden death. For this reason, it is essential to detect the beginning of cardiovascular disease in these patients. One of the principal reasons for a poor prognosis of patients with diabetes and ischemic heart disease is the greater prevalence of ventricular dysfunction⁹ and cardiac insufficiency, which is now called diabetic myocardiopathy. Diabetes also increases the risk of carotid atherosclerosis—approximately 13% of

diabetic patients more than 65 years of age have had a cardiovascular accident. The mortality rate for cardiovascular accident is almost triple in patients with diabetes.

Noncardiovascular complications

The prevalence of various noncardiovascular complications varies according to the type of diabetes, the duration of the disease, and the level of metabolic control attained. It is estimated that 32% of diabetic patients present with retinopathy, 25% with neuropathy, and 23% with nephropathy.

Diabetic retinopathy affects between 15% and 50% of patients with type 2 diabetes, and approximately 10% present with proliferative retinopathy. Long term, all patients with diabetes type 1 and 60% of patients with s type 2 develop diabetic retinopathy. The risk of vision loss is 20 times higher in patients with diabetes and a quarter the cases of blindness are actually due to the presence of retinopathy.

Nephropathy is a frequent complication in these patients, especially in diabetes type 1. The risk of renal insufficiency is 25 times greater in patients with diabetes, and in Spain, diabetes is the primary reason for enrollment in hemodialysis programs.

IMPORTANCE OF SECONDARY PREVENTION

Patients with diabetes are at a high risk for contracting cardiovascular diseases, with a mortality risk similar to that already stated for cardiovascular disease. This is due to the greater prevalence of other risk factors in this population and the effect of the diabetes itself on macro- and microcirculation.^{1,2} Various consensus documents and practical clinical guidelines from scientific societies, therefore, recommend that the same coronary risk control measures be applied to patients with diabetes and applied as a secondary prevention for nondiabetic patients.¹⁰

Atherogenic dyslipidemia is characterized by the so-called lipid triad of patients with diabetes: elevation of VLDL cholesterol, small LDL particles, and low HDL cholesterol. In spite of the fact that many diabetic patients do not have an elevated LDL-C, several clinical tests, such as 4S, CARE, and LIPID, have shown that the administration of statins in these patients significantly decreases cardiovascular risk.

In spite of recent advances in the treatment of patients with cardiovascular disease, the mortality in patients with diabetes has not been reduced by the same amount as in nondiabetic patients. Among patients in Southern Germany in the MONICA study, for instance, it was observed that the 5-year mortality rate in patients who had suffered an acute coronary

syndrome was reduced from 21% to 13% among the nondiabetic patients, but remained at 37% among the patients with diabetes. This could be due to many causes, among them insufficient information of generalists and cardiologists regarding the importance of this disease and its correct treatment. In Spain, the results of the EUROASPIRE study¹¹ indicate that among patients admitted for cardiovascular problems, the prevalence of diabetes increased from 23% to 35% from 1995 to 1999. Although this difference may partially be explained by the change in the definition of diabetes, the data concur with a parallel increase in the prevalence of obesity from 28% to 34% during this period. The fact that a third of the patients admitted for cardiovascular pathology are diabetics alone indicates the need for non-endocrine physicians to train ourselves in all aspects of this illness.

Data from this same study and others¹² are particularly discouraging in that they indicate that over the years the prevalence of hypercholesterolemia has decreased, but smoking has increased and arterial hypertension has remained the same. In this respect, it is worth remembering that in the MRFIT study the risk of cardiovascular death increased in tandem with the number of cigarettes smoked per day, and it was observed that for each level of smoking the risk among diabetic patients was between 3 and 4 times greater than in the nondiabetic individuals. This same ratio has been found for systolic arterial pressure and cholesterol levels. In the case of diabetic patients who suffer an acute coronary syndrome, the aggressive treatment of risk factors is of paramount importance. Various studies such as UKPDS, HOT, and Sist-Eur, have shown a clear improvement in the prognosis when arterial pressure is reduced in patients with diabetes, and the HOPE study demonstrated a beneficial effect with the administration of ramipril.

NECESSITY OF UPDATING

The model for efficacious control of hyperglycemia changed after it was shown that strict control of glycemia decreases both the micro- and macrovascular complications of diabetes. This has caused a change in treatment strategy for diabetes and greater and better use of insulin in patients with type 2 diabetes. The treatment guidelines have also changed completely. On the other hand, a distinct group of pharmacological agents has recently been made available on the market for the treatment of diabetes type 2 (the tiazolidenediones) that reduce glycemia by decreasing insulin resistance. The new therapeutic group adds to those already available, such as the sulfonylureas, other secretagogue agents such as repaglinide and nateglinide, the biguanides, and the alpha-glucosidase inhibitors, such as acarbose and miglitol. The correct use of these medications and their combinations

requires clear knowledge of their pharmacological indications and contraindications.

All these changes that have taken place over the last years as the fundamental role of diabetes in the appearance and progression of atherosclerosis was recognized, and its role in cardiovascular mortality, together with the correct treatment of the disease, has motivated us to produce a series of monographs related to diabetes and cardiovascular illnesses. In these articles, which will begin appearing in the *REVISTA* in the next few months, recognized clinicians and scientists with broad experience in the study and treatment of diabetes from the fields of endocrinology and cardiology will discuss, in depth, the epidemiology, physiopathology, and treatment of this disease.

The fundamental role of weight reduction and increase in physical activity that in practice are difficult to achieve¹¹ will be discussed in particular. Recent therapeutic treatment, such as the importance of beta-blocker therapy in secondary prevention and angiotensin-converting enzyme inhibitors in fundamental, primary, and secondary prevention will be explored. Finally, the limitations of percutaneous treatment of coronary lesions in these patients will be discussed,^{13,14} as will the comparison of surgical results, especially the implantation of mammary arteries,¹⁵ the problem of the high incidence of post-angioplasty re-stenosis and the recent advances in solving this important problem, will also be discussed in the last chapters of this series on a disease that has already begun to be considered the new plague of the 21st century.

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