Clinical Characteristics and Cardiometabolic Control of Persons with Diabetes in the Cardiology Office in Argentina

Caracteristicas clínicas y control cardiometabólico de personas con diabetes en el consultorio de cardiología en la República Argentina

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ABSTRACT

Background: Cardiology has a leading role in the control and treatment of persons with type 2 diabetes mellitus (DM2). We do not have local epidemiological data about patients with DM2 treated by cardiologists.
Objectives: The aim of this study was to evaluate the clinical characteristics, cardiovascular disease (CVD) and treatment of patients with DM2 attending a cardiology office.
Methods: We conducted and observational study in 17 provinces of Argentina during three months.
Results: A total of 694 patients were included in the study. Mean age was 64.7 ± 10.5 years, time of disease progression 10.7 ± 9.3 years, body mass index 32 ± 5.9 kg/m2, HbA1c $7.3\%\pm1.6$, and blood pressure 135/80 mm Hg. Seventy percent of the patients presented two or more risk factors, 48.1% had CVD and microvascular disease was present in 40.9% of cases (kidney disease in 31.4%, retinopathy in 10.5%, neuropathy in 8.3% and diabetic foot in 3.3%). Patients were receiving antiplatelet agents in 57.3% of cases, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (ACEIs/ARBs) in 84.3% and 79.5% were treated with statins. Hypoglycemic agents included metformin in 85.9% of patients, dipeptidyl peptidase 4 (DPP4) inhibitors in 24.1%, sulfonylureas (SU) in 14.3%, sodium-glucose co-transporter 2 (SGLT2) inhibitors in 9.8%, glucagon-like peptide 1 receptor agonists (GLP-1 RAs) in 3% and glitazones in 1.3%. HbA1C levels ≤7% were achieved by 55.9% of patients, BP <140/90 mm Hg by 61.7%, and LDL-C <100 mg/dL by 58.5% and <70 mg/dL by 28.5%.
Conclusions: Most patients with DM2 presented two or more cardiovascular risk factors and a high prevalence of associated complications. Treatment goals were achieved by a low number of patients and the use of medications with demonstrated cardiovascular benefit was low.

Key words: Diabetes Mellitus, Type 2 – Cardiovascular Diseases – Risk Factors - Argentina

RESUMEN

Introducción: La cardiología tiene un rol protagónico en el control y el tratamiento de las personas con diabetes mellitus tipo 2 (DM2). No contamos con datos epidemiológicos locales acerca de los pacientes con DM2 asistidos por la especialidad.
Objetivos: Evaluar las características clínicas, enfermedad cardiovascular (ECV) y tratamiento de personas con DM2 en el consultorio de cardiología.
Material y métodos: Se realizó un estudio observacional en 17 provincias de la Argentina durante 3 meses.
Resultados: Se incluyeron 694 pacientes. La edad media fue de 64.7 ± 10.5 años, con un tiempo de evolución de la DM2 de 10.7 ± 9.3 años, índice de masa corporal de $32\pm5,9$ kg/m2, HbA1c de $7,3\pm1,6$ % y tensión arterial 135/80 mmHg. El 70% de los pacientes presentaba 2 o más factores de riesgo. El 48,1% presentaba ECV y el 40,9% enfermedad microvascular (31,4% nefropatía, 10,5% retinopatía, 8,3% neuropatía, 3,3% pie diabético). El 57,3% se encontraban con antiagregantes, 84,3% con inhibidores del sistema renina/angiotensina/aldosterona (iECAS/ARAII), 79,5% con estatinas. Asimismo, el 85,9% recibía metformina, seguido de inhibidores de la dipeptidil peptidasa-4 (iDDP4) (24,1%), insulina (22,2%), sulfonilureas (SU) (14,3%), inhibidores del cotransportador sodio-glucosa tipo 2 (iSGLT2) (9,8%), agonistas del receptor glucagón like (arGLP1) (3%) y glitazonas (1,3%). El 55,9% tenía HbA1c <=7%, 61,7% TA <140/90 mmHg, 58,5% LDL <100 mg/dl y 28,5% LDL <70 mg/dl.
Conclusiones: La mayoría de los pacientes con DM2 presentaba dos o más factores de riesgo cardiovasculares y una elevada prevalencia de complicaciones asociadas. Observamos un bajo alcance de los objetivos terapéuticos, así como también un bajo uso de fármacos con beneficio cardiovascular.

Palabras clave: Diabetes mellitus Tipo 2 - Enfermedad cardiovascular - Factores de riesgo – Argentina

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INTRODUCTION

The prevalence of type 2 diabetes mellitus (DM2) is significantly increasing worldwide. (1) According to data of the last National Survey of Risk Factors (NSRF), the prevalence of self-reported DM2 in Argentina increased from 8.4% in 2005 to 12.7% in 2018. (2) Diabetes has always attracted interest in the cardiology community, but it was not until recent years that the introduction of new drugs with impact on cardiovascular mortality has granted cardiology a leading role in the therapeutic approach of people with DM2. (3) Clinical practice guidelines recommend a multifactorial intervention and a transdisciplinary approach, focusing both on glycemic control and on the other risk factors (RF) to obtain the greatest benefit in reducing mortality and complications, as observed in the Steno-2 study. (4)

The aim of this study was to learn the clinical characteristics, the presence of cardiovascular disease (CVD) and the treatment of patients with DM attending a cardiology office.

METHODS

We conducted an observational, cross-sectional study between May and July 2019. The first two patients with DM2 who visited a cardiology office each day were included. Each investigator had to include at least 20 patients. Hospitalized patients, those with type 1 diabetes, secondary diabetes, pregnancy, mental disorders and those who refused to be included in the protocol were excluded from the study. Clinical characteristics and laboratory findings were evaluated. The definitions used in this registry can be accessed in the supplementary material. The information was submitted online using Google Forms. Each investigator received the instructions, definitions, protocol and a single password to enter patients' information.

The therapeutic targets were blood pressure (BP) <140/90 mm Hg, HbA1c ≤7%, LDL-C <100 mg/dL (without CVD) and LDL-C <70 mg/dL (with CVD).

Statistical analysis

Descriptive statistics were used to describe quantitative and qualitative data according to their distribution (frequency, mean, standard deviation). The chi square test, Student's t test or the Mann-Withney test were used depending on the characteristics of the variables. Multivariate logistic regression analysis was performed to identify the relative influence of the qualitative factors associated with CVD using those variables with significant association on simple regression analysis. A P value <0.05 was considered statistically significant. All calculations were performed using Epi-Info 7.0 software package.

Ethical considerations

The study was conducted following the recommendations of the Declaration of Helsinki revised in 2003. The participation was voluntary, and all the patients signed an informed consent form to be included in the study.

RESULTS

The registry was completed by 44 investigators from 17 provinces in Argentina (Figure 1). During the study period, 8,405 patients attended the cardiology offices; 1,189 (14.1%) presented DM2 and 58% (n = 694) were included in the registry.

Mean age was 64.7±10.5 years and 58.5% were men. Time of DM2 progression was 10.7±9.3 years, body mass index (BMI) 32±5.9 kg/m2, HbA1c 7.3%±1.6, systolic blood pressure (SBP) 135±16.1 mmHg and diastolic blood pressure (DBP) 80±9.2 mmHg. Chronic complications reported were CVD in 48.1% of the patients and microvascular disease in 40.9% (kidney disease in 31.4%, retinopathy in 10,5%, neuropathy in 8.3% and diabetic foot in 3.3%). Most patients (90.8%) had medical coverage (prepaid medical insurance or social security system). Table 1 summarizes the general characteristics of the population and subgroups according to the presence or absence of CVD.
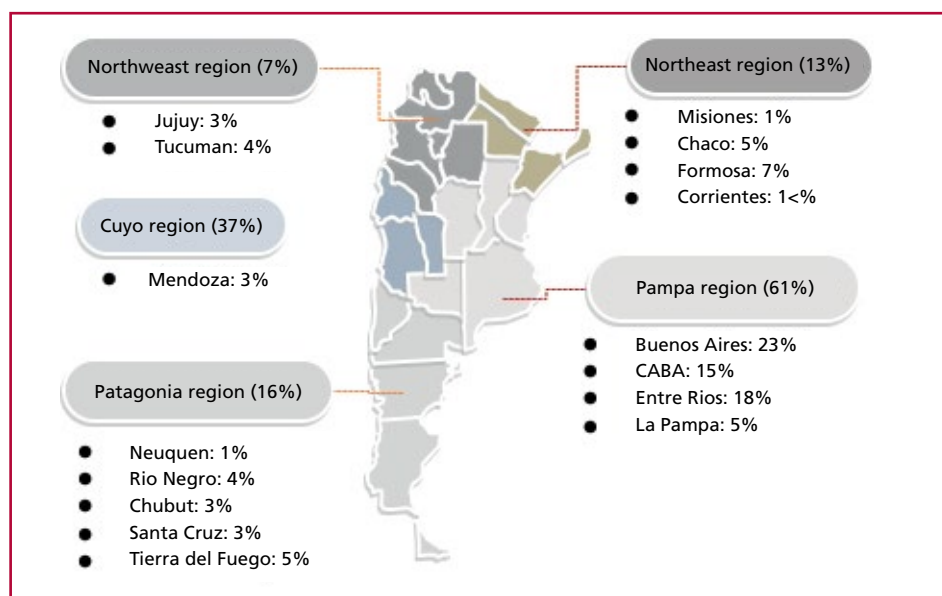

Fig. 1. Distribution of patients by province and by region

Seventy percent of the patients had two or more RF (hypertension, dyslipidemia, current/former smoker), independently of the presence of CVD (Figure 2).

Diabetes was followed-up by specialists in endocrinology or diabetes in 63.7% of cases, by clinicians or primary care physicians in 23% and by cardiologists in 12.2%. History of ischemic heart disease was present in 34% of the patients and was the most prevalent cardiovascular condition, followed by heart failure (HF) in 27%, peripheral vascular disease (PVD) in 7%, stroke in 4% and atrial fibrillation in 2.7%. On the multivariate analysis, the variables with independent association with CVD were age (OR, 1.04; 95% CI, 1.02 - 1.06; P = 0.001), male sex (OR, 2.2; 95% CI, 1.4 - 2.8; P=0.001) and microvascular disease (OR, 2.5; 95% CI, 1.6 - 3.1; P=0.001).

Among patients with CVD, 71%, 23% and 6% had involvement of one, two and three vascular territories, respectively.

Figure 3 illustrates the pharmacologic treatment in the entire population and by subgroups with or without CVD. Forty-five percent of the patients received monotherapy (41% with metformin) and 22% were at least treated with two oral hypoglycemic drugs.

Figure 4 describes the treatment goals according to the presence or absence of CVD. The triple goal of BP <140/90 + HbA1c ≤7% + LDL-C <70 mg/dL was achieved by 14.2% of the patients with CVD, and 18.8% of those without CVD reached the triple goal of BP <140/90 + HbA1c ≤7% + LDL-C <100 mg/dL.

DISCUSSION

Type 2 DM increases 2 to 4 times the risk of cardiovascular events, and it is one of the major RF for atherosclerotic disease. (5) Our study is the first to obtain epidemiological data from patients with DM2 in the cardiology office in Argentina. The prevalence of DM2 in the patients evaluated was 14.1%, lower than the 19.3% reported by the Fourth National Survey of Risk Factors (NSRF) for the age group of our study, (2) considering that half of the population presented CVD, a condition which is associated with greater prevalence of DM2. This could be due to the fact that few patients with DM2 were referred to the cardiologist or to low screening for DM2 in patients with CVD.

In our study, only 1 out of 10 cardiologists had an active role in glycemic control. This finding could be explained by the availability of specialists, although

Table 1. General characteristics; CVD + 335 p CVD – 359. Part 1

General	Total	With CVD	Without CVD	p
Men	406 (58.5%)	230 (68.7%)	176 (49%)	0.001
Age >60 years	460 (66%)	253 (76.9%)	207 (56.7%)	0.001
Time of DM2 progression (years)	10.7	12	8.9	0.001
Time of DM2 progression >10 years	257 (37.1%)	142 (43.3%)	115 (31.6%)	0.0001
HTN	631 (90.9%)	311 (92.8%)	320 (89.1%)	0.03
Dyslipidemia	549 (79.1%)	285 (85.3%)	264 (73.3%)	0.001
BMI 25-29.9	218 (31.4%)	119 (35.5%)	99 (27.6%)	0.003
BMI >30	417 (60.1%)	182 (54.6%)	235 (65.1%)	0.002
Abdominal obesity	543 (78.5%)	253 (75.5%)	290 (80.8%)	0.2
Sedentary lifestyle	400 (57.6%)	188 (56.1%)	212 (59%)	0.2
Smoking habits	61 (8.8%)	23 (6.8%)	38 (10.5%)	0.004
Former smoker	226 (32.5 %)	136 (40.6%)	90 (25%)	0.001

General	Total	With CVD	Without CVD	p
<5 servings of fruits and vegetables	348 (50.1%)	168 (50.1%)	180 (50%)	0.4
SBP mm Hg, mean (SD)	135.1 (16.1)	133 (16.9)	136.4 (15.3)	0.02
DBP mm Hg, mean (SD)	80 (9.2)	79.2 (9.2)	80.6 (9.2)	0.04
BP <140/90	428 (61.6%)	215 (65.3%)	213 (58.3%)	0.02
HbA1c, mean (SD)	7.2 (1.6)	7.17 (1.4)	7.27 (1.7)	0.3
HbA1c <7%	388 (55.9%)	187 (56.8%)	201 (55.1%)	0.3
LDL-C, mean (SD)	97.3 (40.3)	88.6 (37)	105.4 (41)	0.001
LDL-C <100 mg/dL	406 (58.5%)	226 (68.7%)	180 (49.3%)	0.001
LDL-C <70 mg/dL	198 (28.5%)	130 (39.5%)	68 (18.6%)	0.001
Creatinine clearance, mean (SD)	82.5 (34)	76.3 (32)	89.6 (37)	0.001
Microvascular damage	282 (40.6%)	179 (54.4%)	103 (28.2%)	0.001
Renal disease	2.8 (31.4%)	144 (43.7%)	74 (20.3%)	0.001
Retinopathy	73p (10.5%)	49 p (14.6%)	24 p (6.6%)	0.001
Neuropathy	58p (8.3%)	38 p (11.5%)	20 p (5.5%)	0.002
Diabetic foot	23p (3.3%)	15 p (4.4%)	8 p (2.2%)	0.4

SD: Standard deviation. LDL-C: Low density lipoprotein-cholesterol. CVD: Cardiovascular disease

we cannot rule out that many cardiologists form part of multidisciplinary treatment teams.

The prevalence of RF was obviously high; in fact, more than half of the sample presented two or more associated RF. Hypertension and overweight were present in 9 out of 10 patients with DM2, a percentage similar to the one reported by the FRADYC registry. (6) Smoking habits deserve special attention, not only by the well-known association with CVD, but also by the high prevalence found in our population: one out of every two patients with CVD and one third of those without CVD had a history of smoking habits.

Cardiovascular disease is common in subjects with DM2 and is the main cause of mortality. (7) The presence of CVD was high in our registry compared with the mean estimated in other studies. (8) This difference could be attributed to the population evaluated. Patients with CVD had higher prevalence of male sex, hypertension, dyslipidemia, abdominal obesity and

sedentary life, and higher presence of microvascular complications. The high prevalence of CVD could also be explained by the time of DM2 progression, which was longer than the one reported by other registries as DISCOVER (9) and IDMPS. (10)

In a review by Einarson et al., coronary artery disease was the most prevalent CVD, followed by HF and cerebrovascular disease. (8) We found similar results in our population, as coronary artery disease was the most prevalent CVD, followed by HF and PVD. Conversely, the incidence of stroke was low, probably linked to the low prevalence of atrial fibrillation and adequate blood pressure control.

Most of the patients had involvement of only one vascular territory, mainly the coronary arteries, and this finding was also reported by other epidemiological studies. (11) We should mention that we did not conduct a systematic screening for subclinical atheromatosis, which could explain the high involvement of
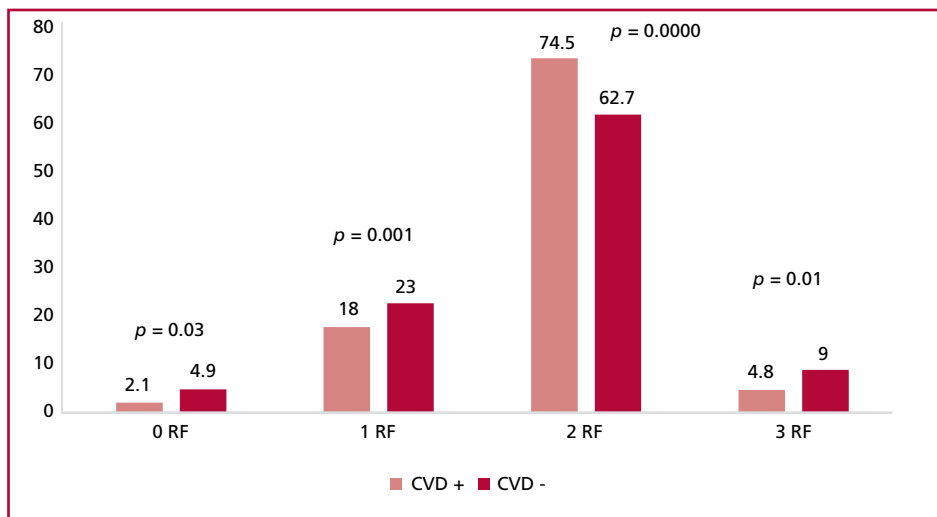

Fig. 2. Distribution of risk factors by presence of cardiovascular disease (CVD)

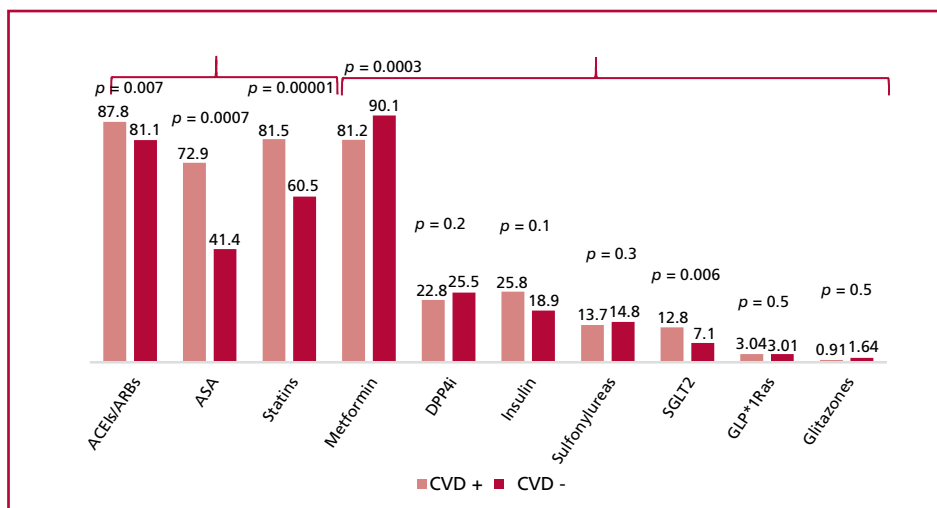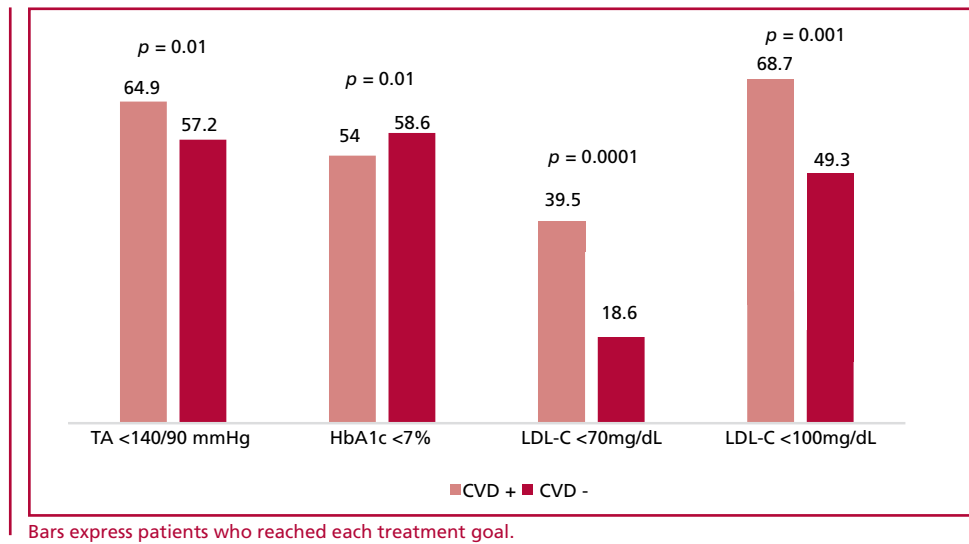Bars express the proportion of patients with 0 - 3 risk factors.

Fig. 3. Treatment of patients with and without cardiovascular disease (CVD)

Bars express the proportion of patients treated with each drug.

Fig. 4. Treatment goals in patients with and without cardiovascular disease (CVD)

Bars express patients who reached each treatment goal.

a single vascular territory.

Microvascular complications and CVD share mechanistic denominators as endothelial dysfunction, low-grade inflammation and rheological abnormalities, which worsen the prognosis of patients with DM2. (12) In this sense, we found a close association between the presence of CVD and microvascular complications; in fact, more than half of the patients with CVD had microvascular damage and kidney disease was the most prevalent microvascular complication. This association could be greater as many of these complications were self-reported.

Mean HbA1c was 7%, a value similar to the one reported by other Latin American registries. (13) The percentage of patients with HbA1c <7% was similar to that of the FRADYC registry and lower than the IMDPS registry despite our population had a time of disease progression >10 years with high prevalence of complications. Probably, the metabolic characteristics and the high percentage of patients followed-up by specialists could justify these observations. The absence of HbA1c standardization in Argentina could be another explanation.

When the use of cardiovascular drugs was evaluated, we found that ACEIs and ARBs were the agents most commonly used due to the high prevalence of hypertension, with results similar to the DECLARE and the REWIND studies. (14, 15) The use of antiplatelet agents was low in the subgroup of patients without CVD, probably as a result of recent studies questioning the benefit in these patients. (16) The use of statins in 80% of the population is adequate, but in patients without CVD the prescription is lower than expected according to the recommendations of international guidelines. (17) When the hypoglycemic treatment is analyzed, the percentage of monotherapy was high and metformin was the drug most used, in line with current recommendations. (18) Dipeptidyl peptidase 4 (DPP4) inhibitors were the second drugs most used, similar to the DISCOVER registry (region

of the Americas), (19) though use of insulin was higher, probably due to the longer time of disease progression, higher percentage of patients with CVD, as well as of follow-up by specialists, type of medical coverage and access to treatment.

The use of drugs with demonstrated cardiovascular benefits, such as sodium-glucose co-transporter 2 (SGLT2) inhibitors and glucagon-like peptide 1 receptor agonists (GLP-1 RAs), was low, despite almost half of the population had CVD. This could have many explanations, as difficult access, costs of medications, professional inertia and persistent glucocentric approach.

Reaching the treatment goals has prognostic implications in patients with DM2. (20) In our registry, only 14% of the patients with CVD reached the triple treatment goals for HBA1c, BP y LDL-C, which is 21% lower than the one observed in the Diabetes Collaboratory Registry. (21) In addition, in the subgroup of patients without CVD, the triple treatment goal was achieved by only 18.8%, which could represent 60% excess risk of cardiovascular events. (22) The low percentages observed emphasize the need of implementing strategies for a multifactorial approach to reduce cardiovascular risk.

CONCLUSIONS

Most patients with DM2 presented two or more cardiovascular RF and a high percentage of associated complications. Despite the very high risk of this population, treatment goals were achieved by a low number of patients and the use of medications with demonstrated cardiovascular benefit was low. We believe it is important to have cardiologists more actively involved in the comprehensive management of this group of patients.

Conflicts of interest
None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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DEFINITIONS

- Diabetes: Pre-study diagnosis in patients receiving treatment with hypoglycemic agents or insulin. Or else, disease diagnosed in the physician's office according to the Argentine Diabetes Society (SAD), of at least 3 months evolution.
- Dyslipidemia: In patients without treatment: total cholesterol ≥200 mg/dl, LDL-C ≥130 mg/dl, HDL-C ≤40 mg/dl in men and ≤50 mg/dl in women and ≥TG 150 mg/dl, or else, active treatment.
- HTN: SBP ≥140 mmHg and/or DBP ≥90 mmHg in two successive measurements with an interval of 15 days and/or under anti-hypertensive treatment.
- Obesity: Based on body mass index (BMI) ≥30.
- Overweight: Based on body mass index (BMI) between 25 and 29.
- Smoking: Smoker is every person who until the time of the survey smoked at least one cigarette in the last 6 months and former smoker is every person who has smoked for more than 10 years and has quitted smoking for at least 6 months.
- Sedentarism: It is self-reported, and is considered as less than 150 minutes of physical activity per week.
- Left ventricular hypertrophy (LVH): The Sokolov electrocardiographic criteria will be adopted, or else LVH in the echocardiogram (if one has been taken in the last 12 months).
- Kidney disease: Creatinine clearance <60 ml/min/1.73 m2 (CKD-EPI) and/or urine albumin >30 mg/g.
- Abdominal obesity: Waist circumference >88 cm for women and >102 cm for men. To obtain the waist index, the abdominal circumference will be measured at the level of the umbilicus.
- Brain damage: Previous stroke, cognitive impairment, or else CT/MRI leukoarariosis, subcortical atherosclerotic encephalopathy or else lacunar infarctions.
- Cardiovascular disease: Coronary artery disease (AMI, ACS, ischemia or coronary plaques in an imaging study), peripheral vascular disease (imaging studies, ankle-brachial index or presence of intermittent claudication), carotid artery disease (presence of atherosclerotic plaques in imaging study), or cerebrovascular disease (previous stroke with sequelae or imaging study). Active treatment of atherosclerotic vascular disease (angioplasty in any territory or bypass surgery).
- Chronic microvascular complications: Nephropathy or retinopathy (ocular fundus study performed by a specialist) or neuropathy (clinic, reflexes and monofilament and/or conduction velocity).
- Heart failure: History of clinical heart failure considered by the cardiology specialist or ventricular dysfunction in the echocardiogram.

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