TITLE: Prevalence, impact and management of hypertension-mediated organ damage in patients with type 2 diabetes in Spain. Data from the IBERICAN study.

SHORT TITLE: hypertension-mediated organ damage in patients with type 2 diabetes in Spain.

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Conflict of interest

All the authors declare that they have no type of conflict of interest that may affect the contents of this article.

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TITLE: Prevalence, impact and management of hypertension-mediated organ damage in patients with type 2 diabetes in Spain. Data from the IBERICAN study.

SHORT TITLE: Hypertension-mediated organ damage in patients with type 2 diabetes in Spain.

TÍTULO: Prevalencia, impacto y manejo del daño orgánico mediado por la hipertensión arterial en pacientes con diabetes tipo 2 en España. Datos del estudio IBERICAN.

Título breve: Daño orgánico mediado por la hipertensión arterial en pacientes con diabetes tipo 2 en España.

Abstract.

Objective: To determine the prevalence, impact and management of hypertension-mediated organ damage (HMOD) according to the presence of type 2 diabetes (T2DM).

Methods: IBERICAN is an ongoing multicenter, observational and prospective study, including outpatients aged 18 to 85 years who attended the Primary Care setting in Spain. In this study, the prevalence, impact and management of HMOD according to the presence of T2DM at baseline were analyzed.

Results: At baseline, 8,066 patients (20.2% T2DM, 28.6% HMOD.) were analyzed. Among patients with T2DM, 31.7% had hypertension, 29.8% dyslipidemia and 29.4% obesity and 49.3% had ≥1 HMOD, mainly high pulse pressure (29.6%), microalbuminuria (16.2%) and moderate renal impairment (13.6%). The presence of T2DM significantly increased the risk of having CV risk factors and HMOD. Among T2DM population, patients with HMOD had more dyslipidemia (78.2% vs 70.5%; P=0.001), hypertension (75.4% vs 66.4%; P=0.001), any CV disease (39.6% vs 16.1%; P=0.001) and received more drugs. Despite the majority of types of glucose-lowering agents were more frequently taken by those patients with HMOD, compared to the total T2DM population, the use of SGLT2 inhibitors and GLP-1 receptor agonists was marginal.

Conclusions: In patients daily attended in primary care setting in Spain, one in five patients had T2DM and nearly half of these patients had HMOD. In patients with T2DM, the presence of HMOD was associated with a higher risk of CV risk factors and CV disease. Despite the very high CV risk, the use of glucose-lowering agents with proven CV benefit was markedly low.

Key words: cardiovascular; diabetes; GLP-1 receptor agonists; SGLT2 inhibitors; hypertension-mediated organ damage.

RESUMEN

Objetivo: Determinar la prevalencia, impacto y manejo del daño orgánico mediado (LOD) por hipertensión arterial (HTA) según la presencia de diabetes tipo 2 (DM2).

Método: IBERICAN es un estudio multicéntrico, observacional y prospectivo en curso, que incluye pacientes ambulatorios de 18 a 85 años que acuden a consultas de Atención Primaria en España. En este estudio se analizó la prevalencia, el impacto y el manejo del LOD por HTA según la presencia de DM2 al inicio del estudio.

Resultados: Se 8.066 pacientes (20,2% DM2, 28,6% daño orgásnico mediado por HTA). Entre los pacientes con DM2, el 31,7% tenía HTA, el 29,8% dislipidemia y el 29,4% obesidad y el 49,3% tenía ≥1 lesión de daño de órgano diana, principalmente presión de pulso alta (29,6%), microalbuminuria (16,2%) e insuficiencia renal moderada (13,6%). La presencia de DM2 aumentó significativamente el riesgo de tener factores de riesgo CV y LOD. Entre la población con DM2, los pacientes con LOD tenían más dislipidemia (78,2% frente a 70,5%; P = 0,001), hipertensión (75,4% frente a 66,4%; P = 0,001), cualquier enfermedad CV (39,6% frente a 16,1%; P = 0,001) y recibió más medicamentos. A pesar de que los pacientes con LOD tomaban con mayor frecuencia la mayoría de los tipos de agentes hipoglucemiantes, en comparación con la población total de DM2, el uso de inhibidores de SGLT2 y agonistas del receptor de GLP-1 fue marginal.

Conclusiones: En los pacientes atendidos diariamente en atención primaria en España, uno de cada cinco pacientes tenía DM2 y casi la mitad de estos

pacientes tenían LOD. En pacientes con DM2, la presencia de LOD se asoció con un mayor riesgo de factores de riesgo CV y enfermedad CV. A pesar del riesgo CV muy alto, el uso de agentes hipoglucemiantes con beneficio CV demostrado fue notablemente bajo.

Palabras clave: Cardiovascular; diabetes; agonistas del receptor del GLP1; inhibidores SGLT2; Daño orgánico mediado por hipertensión arterial.

Introduction.

Type 2 diabetes (T2DM) is a main health care problem in Spain [1,2]. The Di@bet.es study showed a decade ago that the overall prevalence of DM adjusted for age and sex was around 14%, of which 6% had unknown DM [1]. However, data from the IDF 2021 Diabetes Atlas showed that the number of people with DM in Spain had increased from 2.8 million in 2011 to 5.1 million in 2021 [2]. In addition, total diabetes-related health expenditure in 2021 in Spain was huge, accounting for $15.5 billion, $3,000 per person with DM [2].

The presence of DM doubles the risk of developing CV disease [3]. The recent 2023 European guidelines for the management of CV disease in patients with T2DM consider that patients with clinically established atherosclerotic CV disease, or severe hypertension-mediated organ damage (HMOD), or 10-year CV disease risk ≥20% using SCORE2-Diabetes have a very high CV risk [4]. In other words, having severe HMOD could be considered an equivalent of CV disease. As a result, it is mandatory to improve the prevention and early detection of complications of patients with T2D, such as HMOD, through and holistic management to reduce the CV burden of this population [4,5]. European guidelines define severe HMOD as the presence of any of the following conditions: estimated glomerular filtration rate (eGFR) <45 mL/min/1.73 m^2 irrespective of albuminuria, eGFR 45–59 mL/min/1.73 m^2 and microalbuminuria (urinary albumin-to-creatinine ratio [UACR] 30–300 mg/g), proteinuria (UACR >300 mg/g), or presence of microvascular disease in at least three different sites, such as microalbuminuria plus retinopathy plus neuropathy [4,6-8]. Therefore, the search and identification of HMOD in patients with T2DM should be strengthened in clinical practice. In this context, it is important to ascertain the prevalence and impact of HMOD in real-life population with T2DM.

IBERICAN (Identificación de la poBlación Española de RIesgo CV y reNal -Identification of the Spanish population at risk of CV and renal disease-) is currently determining in more than 8,000 subjects attended in primary care in Spain, the prevalence of CV risk factors and the incidence of CV events, after 10 years of follow-up [9-13]. In this study, the prevalence, impact and management of HMOD according to the presence of T2DM at baseline were analyzed.

Methods.

IBERICAN [9-13] is an ongoing epidemiological, multicenter, observational and prospective study, which has included outpatients aged 18 to 85 years who attended the Primary Care setting of the National Health System in Spain, regardless of the presence of CV risk factors or CV disease, and who agreed to participate in the study by giving their written informed consent, with a follow-up for at least 10 years. Patients that changed the habitual residence to another city or country within the first six years after inclusion, with terminal disease, a life expectancy less than five years, or manifest difficulties to be followed-up were excluded from the study. The study was approved by the Independent Ethics Committee of the University Hospital Clínico San Carlos (Madrid, Spain) and was registered at https://clinicaltrials.gov under the number NCT02261441.

The data were analyzed from the period of patient inclusion, period from April 2014 to October 15, 2021. Data were collected from the electronic medical history of patients, direct interview and medical examination and were entered into an electronic Case Report Form (CRF) specifically created for the study. Sociodemographic data, CV risk factors (hypertension, dyslipidemia, smoking, obesity, sedentary lifestyle), HMOD (pulse pressure ≥60 mmHg in subjects >65 years of age, ankle brachial index <0.9, microalbuminuria: UACR between 30-299 mg/g, eGFR [CDK-EPI] 30-59 ml/min, left ventricular hypertrophy), and vascular disease (ischemic heart disease, heart failure, stroke, peripheral arterial disease and chronic kidney disease) were recorded. All variables were defined according to the 2013 European Society of Hypertension/European Society of Cardiology guidelines [14]. Physical examination included blood pressure, heart rate, and body mass index. Data from a 12-lead electrocardiogram and blood and urine tests (glycaemia, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, creatinine, uric acid and UACR) performed according to clinical practice in the previous 6 months before inclusion were considered valid for the study. Total number of drugs, as well as the type of glucose-lowering agents (metformin, sulphonylureas, glinides, glitazones, dipeptidyl peptidase 4 [DPP-4] inhibitors, glucagon-like peptide 1 receptor agonists [GLP-1 RA], sodium-glucose cotransporter 2 [SGLT2] inhibitors, insulin and others) were also recorded. A good glycemic control was considered as HbA1c ≤7% [15]. Obesity was defined

as a body mass index >30 Kg/m^2, and sedentarism as doing physical less than 30 min of physical activity or absence of activity.

Statistical analysis

Qualitative variables were defined by their absolute and relative frequencies, and continuous variables as mean and standard deviation. Statistical tests were performed according to the nature of the variables. To study the relationship between the categorical variables, the chi-squared test was used (where more than 20% of the cells had an expected frequency of less than five, Fisher's exact test was performed). Student's t-test was used to compare continuous variables between groups. Multivariate analyses were performed to determine those factors associated with an increased risk of CV risk factors and HMOD according to the presence of T2DM and among patients with T2DM, those factors associated with an increased risk of CV risk factors and CV disease according to the presence of HMOD. All those variables that showed a p-value <0.05 in the bivariate analysis were included as independent variables in the initial model. From the initial model, the non-significant variables were manually eliminated, until the final model was reached. All comparisons rejected the null hypothesis with an alpha error <0.05. IBM SPSS version 22.0 was used for data analyses.

Results.

Of the total of 8,066 patients included in the IBERICAN study at baseline, 8,056 (99.9%) were valid for the analysis. Of these, 20.2% had T2DM and 28.6% HMOD.

Among patients with T2DM, 35.6% had a sedentary lifestyle, 31.7% hypertension, 29.8% dyslipidemia, and 29.4% were obese. In addition, 49.3% had at least one HMOD, mainly high pulse pressure (29.6%), microalbuminuria (16.2%) and moderate renal impairment (13.6%) (table 1). The prevalence of any HMOD was similar between men and women, but microalbuminuria was more common in men (20.6% vs 10.8%; P<0.001) and moderate renal impairment in women (11.7% vs 16.1%; P=0.01) (table 2). Control of DM was numerically higher in patients with HMOD, but without significant statistical differences (74.4% vs 66.2%; P=0.81), and time of evolution of DM was significantly greater in those

patients with HMOD (≥10 years: 47.3% vs 34.7%, ≥15 years: 21.8% vs 14.7%; P<0.001).

With regard to the biochemical parameters in patients with T2DM, mean glycemia was 137.6±43.0 mg/dL, mean LDL cholesterol 100.9±36.9 mg/dL, mean creatinine 0.9±0.5 mg/dL and mean UACR 1.2±0.5 mg/g (table 1). Compared to patients without T2DM, patients with T2DM had more CV risk factors and HMOD (table 1). The presence of T2DM significantly increased the risk of having CV risk factors (hypertension, dyslipidemia and obesity) and HMOD (any HMOD, including high pulse pressure, microalbuminuria, moderate renal disease, left ventricular hypertrophy and ankle brachial index <0.9) (table 3). Except in very elderly patients, the prevalence of HMOD increased with age, in both patients with and without T2DM (supplementary figure 1).

Among patients with T2DM, with regard to CV risk factors, patients with HMOD (vs no HMOD) had more dyslipidemia (78.2% vs 70.5%; P=0.001), hypertension (75.4% vs 66.4%; P=0.001), and sedentarism (38.6% vs 32.6%; P=0.012). The risk was particularly high for hypertension (OR 2.78; 95% CI 2.18-3.54). Regarding CV disease, the presence of any CV disease, ischemic heart disease, peripheral artery disease, atrial fibrillation, heart failure, and stroke was more frequent in those patients with HMOD compared to those without HMOD, particularly peripheral artery disease (OR 4.77; 95% CI 3.12-7.31) and heart failure (OR 3.50; 95% CI 2.21-5.55) (table 4).

The number of drugs taken by patients with T2DM according to the presence of HMOD was presented in figure 1. Those patients with HMOD received more drugs than those without HMOD (bitherapy: 32.8% vs 30.4%; 3 drugs 14.8% vs 12.4%; P<0.001). In the overall population with T2DM, the most common glucose-lowering agents prescribed were metformin (35%), dipeptidyl peptidase IV inhibitors (15%) and insulin (9%). Only 3% of patients were taking SGLT2 inhibitors and 2% GLP-1 RA. The majority of types of glucose-lowering agents were more frequently taken by those patients with HMOD, compared to the total T2DM population (figure 2).

Discussion.

Our study showed in a wide sample of patients daily attended in primary care setting in Spain that one in five patients had T2DM and that nearly half of

these patients had HMOD, being high pulse pressure and microalbuminuria the most common ones. In patients with T2DM, the presence of HMOD was associated with a higher risk of CV risk factors and CV disease. Despite this high CV risk, the use of glucose-lowering agents with proven CV benefit was markedly low.

Different studies, such as ENRICA, DARIOS, ESCARVAL, or FRESCO, among others, have analyzed CV risk factors or CV disease in Spain. Unfortunately, these studies are outdated, not reflecting the current epidemiology of T2DM, have focused on particular populations or some risk factors in isolation, or have analyzed only specific regions of Spain [16-20]. By contrast, IBERICAN is currently analyzing the distribution of CV risk factors and the incidence of CV disease in adult population attended in primary care throughout Spain. Therefore, IERICAN is a large nationwide study, in which more than 500 investigators have included more than 8,000 patients, making this study representative of the Spanish population attended in primary care setting [21].

In our study, 20% of patients had T2DM. In these patients, around one third had hypertension, and 30% dyslipidemia and obesity. As expected, the presence of CV risk factors and HMOD was more common in this population, compared to patients without T2DM. This is in line with previous studies that have shown that the management of patients with T2DM is challenging, as these patients have many comorbidities, particularly CV risk factors and HMOD [22,23].

The presence of T2DM significantly increased the risk of having CV risk factors, particularly hypertension (OR 4.4) and dyslipidemia (OR 3.6). Of note, these diabetes-associated conditions share bidirectional pathogenic relationships [24]. Thus, the incidence of hypertension increases markedly in patients with T2DM through different mechanisms, including the hyperactivation of the renin-angiotensin-aldosterone system and the sympathetic nervous system, oxidative stress, inflammation, endothelial dysfunction or abnormal sodium processing in the kidneys [25]. Hypertension in patients with T2DM markedly increases the risk of CV events and appropriate control with combined therapy, on the top of renin angiotensin system inhibition is mandatory [25,26]. On the other hand, patients with T2DM exhibit high plasma triglycerides and small dense LDL cholesterol levels, as well as a low HDL cholesterol concentration, leading to a more proatherogenic lipid profile [24]. Therefore, attaining LDL

cholesterol recommended targets through intensive lipid lowering therapy seems essential to reduce CV burden in diabetic population [4].

T2DM also increased the risk of having HMOD. In fact, the prevalence of HMOD raised from 23.5% in patients without T2DM (28.6% in the general population) to 49.3% among patients with T2DM (OR 2.42). The most common HMOD found in T2DM population were high pulse pressure (29.6%), followed by microalbuminuria (16.2%) and moderate renal dysfunction (13.6%). High pulse pressure, defined as the difference between systolic and diastolic blood pressure, is the clinical manifestation of arterial stiffness and is more frequent in patients with T2DM. In fact, high pulse pressure has been associated with a higher risk of mortality in patients with T2DM [27,28]. Microalbuminuria and renal impairment are two common early complications in the evolution of T2DM. According to the last European guidelines, the concomitance of both conditions in patients with T2DM are considered as very high CV risk, regardless of SCORE2-Diabetes [4,29]. As guidelines recommend, patients with T2DM should be routinely screened for kidney disease by assessing eGFR and UACR [4,30]. Although less than 10% of patients with T2DM exhibited left ventricular hypertrophy and low ankle brachial index, both conditions markedly increase the risk of MACE, and should be routinely ruled out in all patients with T2DM, particularly in those patients with other CV risk factors, such as hypertension [31-33]. A recent study has shown in a Mediterranean region of Spain, that the majority of patients with T2DM have other CV risk factors, and that half of them have a very high CV risk and 40% a high CV risk (less than 10% have moderate CV risk) [34]. Therefore, as guidelines recommend, the presence of severe HMOD should be screened in every patient with T2DM [4]. Moreover, our study showed that among patients with T2DM, those patients with HMOD exhibited more CV risk factors (except smoking), and any CV disease, regardless of the vascular bed (i.e., ischemic heart disease, stroke or peripheral artery disease). As a result, it is obligatory the clinical assessment of atherosclerotic vascular disease in patients with T2DM on a regular basis, particularly when HMOD are present. Of note, stricter goals and intensification of treatment are required in these patients [4]. On the other hand, although some studies have suggested a different CV risk in patients with T2DM according to sex, mainly due to hormonal factors or different artery diameter, the fact is that more than a half of patients with T2DM have a very high CV risk,

regardless of sex [34,35]. Moreover, our study showed that although microalbuminuria was more common in men and moderate renal impairment in women, the prevalence of any HMOD was similar regardless of gender and a similar approach should be performed in men and women.

Guidelines recommend an optimal and holistic management of patients with T2DM with the control of all comorbidities, including CV risk factors and CV disease [4,5]. With regard to the antihyperglycemic treatment, in the light of evidence, the therapeutic management has been moved from a glucocentric approach, to a CV and renal protection approach in addition to metabolic control [4,36]. Thus, different meta-analyses have shown that both SGLT2 inhibitors and GLP-1 receptor agonists provide CV benefits in patients with T2DM, particularly in those with a high or very high CV risk, regardless of glycemic control or metformin use [37-39]. In this context, international guidelines recommend tight glycemic control (HbA1c <7%) to reduce microvascular complications and also the use of glucose-lowering agents with proven CV benefits (i.e., SGLT2 inhibitors and GLP-1 receptor agonists), mainly in patients at high/very high CV risk, such as those with HMOD [4,36]. Unfortunately, our study showed that despite control of DM was numerically higher in patients with HMOD (74.4% vs 66.2%; P=0.81), the use of SGLT2 inhibitors and GLP-1 receptor agonists was marginal in patients with T2DM and HMOD (6.5% and 3.7%, respectively).

This study has some limitations. First, the lack of randomization of investigators, with the participation of the most motivated physicians in CV care, could have overestimated the control of CV risk factors. Second, this was an observational study, without a control group and this may difficult to ascertain the impact of changes in the management of patients on the incidence of CV complications. Finally, patients were selected from primary care setting in Spain and this could limit the generalizability of the results to the overall Spanish population.

In conclusion, the presence of HMOD is common in patients with T2DM and is associated with a higher risk of having CV risk factors and CV disease. Despite these patients have a very high CV risk, the use of glucose-lowering agents with proven CV benefits was markedly low. Therefore, the search for HMOD in patients with T2DM should be strengthened in clinical practice. It is necessary to increase the awareness and knowledge of primary care physicians

about the importance of the early identification of HMOD in this high risk population and the implementation of the more appropriate therapeutic approach in this population.

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Tabla (si formato es distinto al doc)

Table 1. Baseline clinical characteristics according to the presence of T2DM.

	T2DM (20.2%)	No T2DM (79.8%)	P
Cardiovascular risk factors			
Hypertension, %	31.7	9.6	0.001
Dyslipidemia, %	29.8	10.4	0.001
Obesity, %	29.4	15.3	0.001
Smoking, %	15.2	21.3	0.001
HMOD			
Any	49.3	23.5	<0.001
PP*, mmHg	29.6	13.5	<0.001
Microalbuminuria, %	16.2	5.5	<0.001
eGFR 30-60 ml/min/1.73 m^2, %	13.6	5.7	<0.001
LVH, %	7.3	3.1	<0.001
ABI <0.9, %	2.8	1.4	<0.001
Physical examination			
Waist circumference, cm	103.3± 15.0	94.7± 14.52	<0.001
BMI (kg/m^2)	30.5 ±5.2	28.0±5.4	<0.001
SBP (mmHg)	134.4±15.8	127.63±15.7	<0.001
DBP (mmHg)	76.9±10.1	76.59±10.3	0.271
HR (lpm)	74.7±11.1	73.0±10.8	<0.001
Biochemical parameters			
Glycemia (mg/dL)	137.6±43.0	93.4±13.2	<0.001
Total cholesterol (mg/dL)	177.2±39.6	199.4±38.4	<0.001
HDL cholesterol (mg/dL)	49.0±14.1	56.5±15.3	<0.001
LDL cholesterol (mg/dL)	100.9±36.9	121.2±34.1	<0.001
Triglycerides (mg/dL)	147.9±87.8	118.8±76.2	<0.001
Creatinine (mg/dl)	0.93±0.5	0.85±0.5	<0.001
UACR (mg/g)	1.2±0.5	1.1±0.3	<0.001
Uric acid	5.5±1.5	5.2±1.5	<0.001

ABI: Ankle Brachial Index; BMI: body mass index; HR: heart rate; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; LVH: left ventricular hypertrophy; PP: pulse pressure; SBP: systolic blood pressure; T2DM: type 2 diabetes mellitus; HMOD: hypertension-mediated organ damage; UACR: urinary albumin-to-creatinine ratio. *PP: >60 mmHg in subjects >65 years.

Table 2. Prevalence of HMOD in patients with T2DM according to sex.

	Total	Men (55.7%)	Women (44.3%)	P
Any	49.3	48.8	49.9	0.688
PP*, mmHg	29.6	28.7	30.8	0.35
Microalbuminuria, %	16.2	20.6	10.8	<0.001
eGFR 30-60 ml/min/1.73 m^2, %	13.6	11.7	16.1	0.01
LVH, %	7.3	7.4	7.1	0.77
ABI <0.9, %	2.8	2.2	3.6	0.10

ABI: Ankle Brachial Index; eGFR: estimated glomerular filtration rate; LVH: left ventricular hypertrophy; PP: pulse pressure; T2DM: type 2 diabetes mellitus; HMOD: hypertension-mediated organ damage. *PP: >60 mmHg in subjects >65 years.

Table 3. Risk of cardiovascular risk factors and HMOD in patients with T2DM (vs no T2DM).

	OR	95% CI
Cardiovascular risk factors		
Hypertension, %	4.36	3.86-4.94
Dyslipidemia, %	3.64	3.22-4.11
Obesity, %	2.31	2.07-2.58
Smoking, %	0.67	0.57-0.78
HMOD		
Any	2.42	2.22-2.63
PP*, mmHg	2.69	2.37-3.06
Microalbuminuria, %	3.34	2.81-3.95
eGFR 30-60 ml/min/1.73 m^2, %	2.62	2.19-3.13
LVH, %	2.45	1.94-3.10
ABI <0.9, %	2.08	1.45-2.98

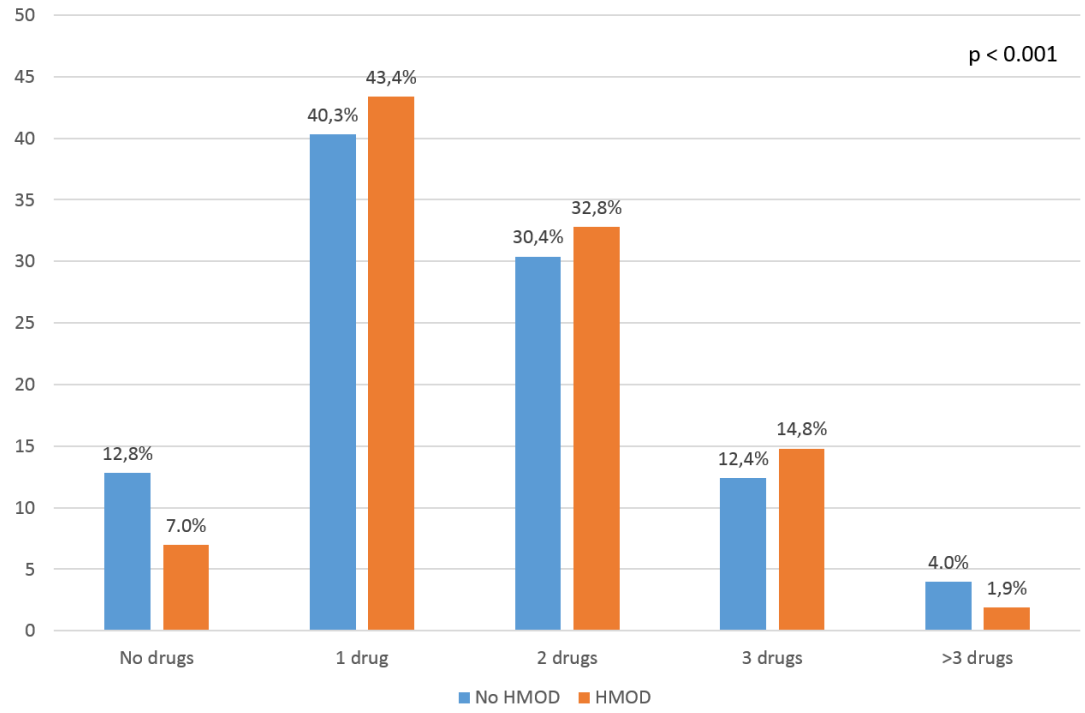
ABI: Ankle Brachial Index; CI: confidence interval; eGFR: estimated glomerular filtration rate; LVH: left ventricular hypertrophy; PP: pulse pressure; OR: Odds Ratio; T2DM: type 2 diabetes mellitus; HMOD: hypertension-mediated organ damage. *PP: >60 mmHg in subjects >65 years.

Table 4. Prevalence and risk of cardiovascular risk factors and HMOD in patients with T2DM according to the presence of HMOD.

	HMOD	NO HMOD	OR	95% CI	p
Cardiovascular risk factors					
Dyslipidemia, %	78.2	70.5	1.5	1.20-1.88	0.001
Hypertension, %	75.4	66.4	2.78	2.18-3.54	0.001
Obesity, %	52.5	49.8	1.11	0.91-1.35	0.289
Sedentarism, %	38.6	32.6	1.3	1.06-1.60	0.012
Smoking, %	11.2	15.2	0.7	0.53-0.94	0.018
Cardiovascular disease					
Any cardiovascular disease, %	39.6	16.1	3.43	2.71-4.34	0.001
Ischemic heart disease, %	17.2	7.8	2.43	1.78-3.33	0.001
Peripheral artery disease, %	14.5	3.4	4.77	3.12-7.31	0.001
Atrial fibrillation, %	13.9	5.4	2.83	1.96-4.07	0.001
Heart failure, %	10.0	3.1	3.50	2.21-5.55	0.001
Stroke, %	9.1	3.1	3.16	1.98-5.04	0.001

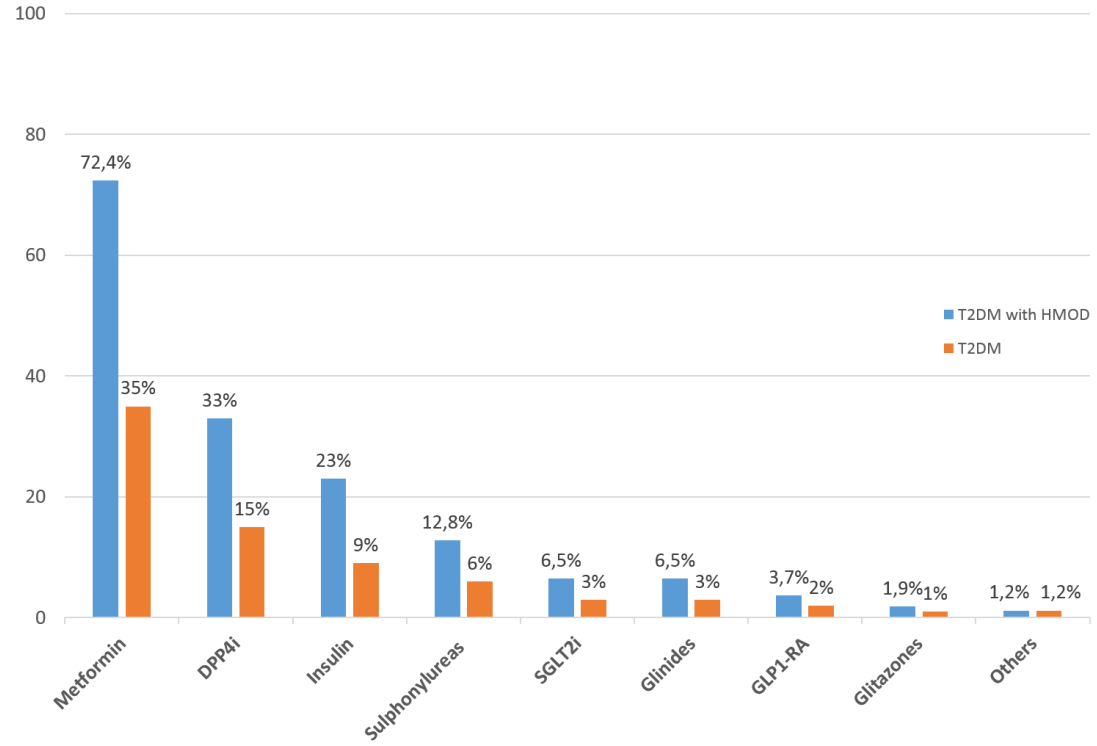
CI: confidence interval; OR: Odds Ratio; T2DM: type 2 diabetes mellitus; HMOD: hypertension-mediated organ damage.

Figure 1. Number of drugs taken by patients with T2DM according to the presence of HMOD.



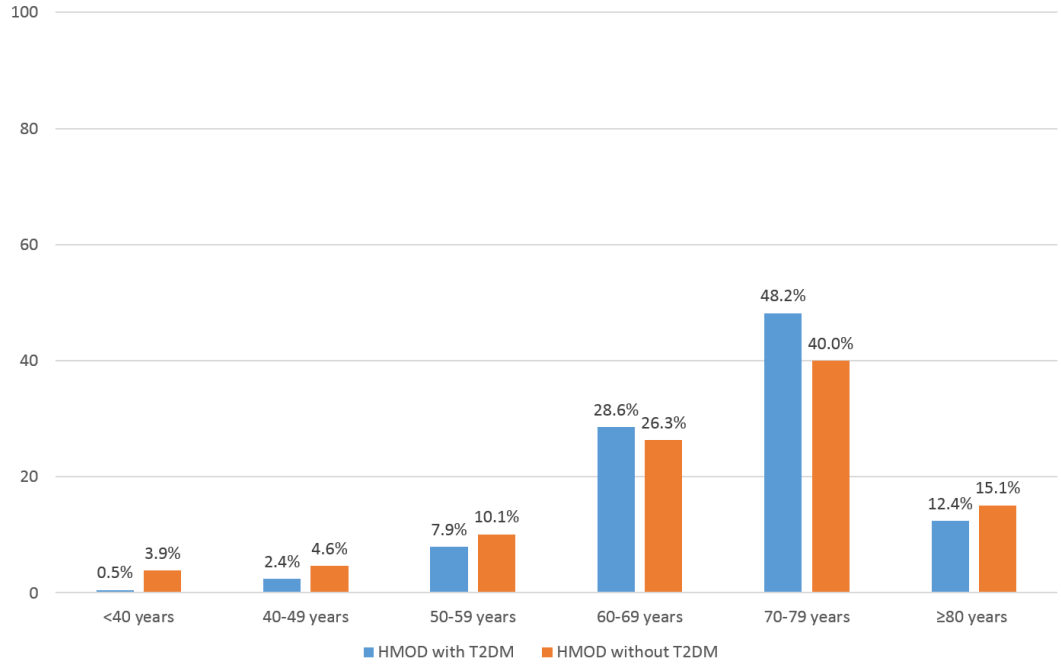
T2DM: type 2 diabetes mellitus; HMOD: hypertension-mediated organ damage.

Figure 2. Glucose-lowering agents in patients with T2DM and HMOD (vs total T2DM population).



DPP4i: dipeptidyl peptidase IV inhibitors; GLP1-RA: glucagon-like peptide-1 receptor agonists; SGLT2i: sodium-glucose cotransporter-2 inhibitors; T2DM: type 2 diabetes mellitus; HMOD: hypertension-mediated organ damage.

Supplementary figure 1. Prevalence of HMOD according to the presence of T2DM, according to age.



p < 0.001

T2DM: type 2 diabetes mellitus; HMOD: hypertension-mediated organ damage.