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Population-based cross-sectional study of 11 645 Spanish nonagenarians with type 2 diabetes mellitus: cardiovascular profile, cardiovascular preventive therapies, achievement goals and sex differences

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ABSTRACT

Objectives To evaluate the risk profile, achievement of cardiometabolic goals, and frequency and optimal use of cardiovascular preventive therapies among nonagenarians with type 2 diabetes mellitus (T2DM). To investigate possible sex differences.

Design and setting A cross-sectional population study of 11 645 persons aged ≥90 years with T2DM living in Madrid (Spain). Sociodemographic, clinical and therapy profiles were collected through electronic records in primary care. We considered antihypertensive therapy and lipid-lowering therapy to be optimal when known patients with hypertension with albuminuria received renin–angiotensin system blockers and statins had been prescribed for overt cardiovascular disease.

Results The prevalence of coronary artery disease was higher in males than in females (21.5% vs 12.6%, p<0.01), as was that of peripheral artery disease (8.5% vs 2.3%, p<0.01). However, the prevalence of cerebrovascular disease was similar in both sexes (16.5% vs 16%; p=0.44). Haemoglobin A1c was lower than 7% in 64.4% of cases, with female predominance in patients with known dementia (67.1% female vs 59.9% male; p<0.01). Antiplatelet therapy was significantly more frequent in males than in females (48.1% vs 44.3%; p<0.01), as were statins (43.2% vs 40.2%; p<0.01). Both in primary and in secondary prevention, rates for simultaneous achievement of the HbA1c, blood pressure, LDL-C goals were significantly lower among females (p<0.01). For each criterion of optimal use of cardiovascular preventive therapies, adherence was significantly better in males than in females.

Conclusion Our study showed that the risk of cerebrovascular disease was similar in both male and female Spanish nonagenarians. Adherence was poorer in females for all criteria of optimal use of cardiovascular preventive therapies. Our findings indicate that the known sex differences in younger patients with T2DM persist in patients aged ≥90 years. There is considerable room for improvement in standards of preventive care in nonagenarians with T2DM, especially in females.

Strengths and limitations of this study

- ► The strength of the study is based on the inclusion of all diabetic people of our region that avoids selection bias.
- ► The use of data on real-life clinical practice at the primary care level increases knowledge of different health workers and health political makers and confers the possibility of improving the clinical management of patients and reorienting the clinical practice.
- ► The limitation of this study is that it is not possible to establish causal relationships between variables given its cross-sectional design.
- ► The study has an excessive number of missing data for some variables such as blood pressure, body mass index, estimated glomerular filtration rate, albumin, haemoglobin A1c, density lipoprotein cholesterol, low-density lipoprotein cholesterol and fasting plasma glucose.

INTRODUCTION

Between 2000 and 2015, global life expectancy experienced its fastest growth since the 1990s, increasing by 5 years, according to WHO.[1] Older people have a high risk of developing coronary artery disease, cerebrovascular disease and peripheral artery disease, and cardiovascular disease is the leading cause of death in this age group.[2] In addition, the prevalence of type 2 diabetes mellitus (T2DM) increases with age,[3] and poor glycaemic control may worsen cardiovascular risk and accelerate the cognitive ageing process.[4]

However, evidence remains limited regarding the use of drugs for primary prevention in persons with diabetes aged >75 years. This group is not included in the

American College of Cardiology/American Heart Association guidelines.[5] Suboptimal use of drugs such as statins has been reported in elderly patients with symptomatic atherosclerosis.[6] Furthermore, the Screening Tool of Older Persons' potentially inappropiate Prescriptions (STOPP) criteria do not recommend that elderly patients discontinue statins.[7]

The multiple factors that have to be considered when prescribing for elderly patients include frailty, comorbidities, the patient's own wishes regarding the goals of therapy, pharmacodynamic and pharmacokinetic changes associated with ageing (eg, decreased gastrointestinal absorption, reduced renal and hepatic clearance, lower lean muscle mass), polypharmacy, cost of therapy and the risk for drug–drug interactions. Other variables such as sex may also affect prescription, as previously reported in patients with diabetes.[8 9]

Data on the management of very aged patients with T2DM are scarce.[10] This is particularly true for cardiovascular preventive therapies such as statins and antithrombotic drugs.

In the present study, we evaluated risk profile, achievement of cardiometabolic goals, and frequency and pattern of use of evidence-based cardiovascular preventive therapies in persons with T2DM aged ≥90 years in the Community of Madrid (Spain). We also studied sex differences in the prevalence of cardiovascular diseases and cardiovascular risk factors.

PATIENTS AND METHODS

Study design

We performed a population-based, cross-sectional study of all residents aged ≥90 years living in the Community of Madrid (Spain). The Community of Madrid is a public entity providing healthcare coverage to 100% of the population. It provides primary care through 3881 general practitioners working in 265 health centres. All residents have an electronic clinical record in primary care. The record constitutes a clinical database of anonymised data. As at 31 December 2015, it contained data for 61 059 persons aged ≥90 years. Data were available for 59 423 subjects, of whom 11 645 were diagnosed with T2DM. In order to avoid selection bias, we analysed all subjects with T2DM.

Variables and definitions

Data for all participants (n=11 645) were collected through electronic clinical records in primary care. We included age, sex, cardiovascular risk factors, comorbidities and medication prescriptions as at 31 December 2015. Comorbidities were recorded according to the International Classification of Primary Care-Second Edition (ICPC-2).

The most recent blood analysis was recorded only if it was performed during 2014 or 2015. Data on low-density lipoprotein cholesterol (LDL-C) were available for 8167 subjects. Similarly, anthropometric measurements, smoking history, basic and instrumental activities of daily life, and blood pressure were only collected if obtained during the 2 years before data collection. Smoking status was available for 7512 subjects, basic and instrumental activities of daily life for 5631 and 5,582, respectively, and blood pressure for 8455.

Basic and instrumental activities of daily life were measured using the Barthel Index[11] and Lawton and Brody Index,[12] respectively. The Charlson Index,[13] which predicts 10-year mortality according to a wide range of comorbid conditions (eg, age, diabetes with or without organ damage, liver disease, chronic kidney disease, AIDS, malignancy, congestive heart failure, previous acute myocardial infarction, chronic obstructive pulmonary disease (COPD), peripheral vascular disease, transient ischaemic attack or stroke, dementia, haemiplegia, connective tissue disease and peptic ulcer disease), was calculated for all participants.

We recorded the percentage of patients with the following analytical values: haemoglobin A1c (HbA1c) <7.0% and <8.0%; blood pressure <130/80 mm Hg,[14] <140/85 mm Hg[15] and <140/90 mm Hg[16]; LDL-C <130mg/dL (3.4 mmol/L) <100 mg/dL (2.6 mmol/L) and <70 mg/dL (1.81 mmol/L); and the composite endpoint of HbA1c <7.0%, blood pressure <140/85 mm Hg and LDL-C <100 mg/dL (2.6 mmol/L).

Cardiovascular disease was defined as a previous diagnosis of angina pectoris, myocardial infarction, stroke or peripheral artery disease in the electronic clinical record (ICPC-2 codes K74, K75, K76, K90 and K92). Dementia was identified by the P70 code of ICPC-2.

We considered antihypertensive therapy to be optimal when known hypertensive patients with albuminuria received ACE inhibitors or angiotensin II receptor blockers (ARBs).[17] We considered lipid-lowering therapy to be optimal when statins had been prescribed for overt cardiovascular disease. We considered the use of statins for primary prevention not clearly indicated, as this practice derives mainly from subgroup analyses and post hoc data of studies that do not include nonagenarians.[18–25] Antithrombotic therapy was labelled as optimal when antiplatelet drugs or anticoagulants had been prescribed for pre-existing cardiovascular disease or chronic atrial fibrillation in the absence of contraindications.[26] The use of antiplatelet medication for primary prevention was, therefore, not considered optimal treatment.[27–29]

The quality of the primary care electronic clinical record for research use has previously been validated,[30] and the database has been widely used to study the epidemiology of cardiovascular risk factors in the study population.[31]

Statistical analysis

Continuous variables are presented as mean (SD), and categorical variables as percentages. Continuous variables were compared using the t-test, and categorical variables were compared using the χ^2 test. Effect sizes were calculated using Cohen's d for continuous measures and Cramer's V for categorical variables. The magnitude of

difference was classified as small if the value of Cohen's d ranged from 0.2 to 0.5, as moderate if it ranged from 0.5 to 0.8 or, as large if Cohen's d value was greater than 0.8. Logistic regression analyses were performed in order to evaluate the independent contribution of different variables to the adequacy of prescription of statins.

Data were processed using SPSS for Windows, V.19.0 (IBM).

Patient and public involvement

No patient involved.

RESULTS

Of a total population of 59 423 individuals aged ≥90 years and resident in Madrid as at 31 December 2015, 11 645 people were diagnosed with T2DM, that is, a prevalence of 19.6% (20.4% in males and 19.3% in females; p<0.01). All of these patients were included in the study. Mean age was 92.9 (2.5) years, 73.1% were females and 13.6% were living in a nursing home. There were 175 subjects (1.5%) aged ≥100 years.

Cardiovascular disease was present in 3602 subjects (30.9%); only 1 vascular territory was involved in 27% and ≥2 in 3.9%. The global prevalence of cardiovascular disease was higher in males than in females (39.5% vs 27.8%, p<0.01), as was the prevalence of coronary artery disease and peripheral artery disease (21.5% vs 12.6% (p<0.01) and 8.5% vs 2.3% (p<0.01); respectively). However, the prevalence of cerebrovascular disease was similar in both sexes (16.5% vs 16%; p=0.44)

The clinical characteristics of the population are shown in table 1. Male subjects had a higher prevalence of chronic atrial fibrillation, current smoking, chronic kidney disease, albuminuria and other comorbidities (ie, solid organ cancer, COPD). They also had a lower prevalence of dependence and dementia, and, consequently, a lower proportion were living in a nursing home than female subjects (9.1% vs 15.3%; p<0.01).

Females had a significantly higher prevalence of cardiovascular risk factors such as hypertension, dyslipidaemia and obesity. They also had significantly higher values of systolic blood pressure, diastolic blood pressure and body mass index than males, irrespective of whether they lived in nursing homes or in their own homes.

As for laboratory parameters, females had significantly worse values in total cholesterol, LDL-C, triglycerides, albumin and estimated glomerular filtration rate.

With respect to cardiovascular preventive therapies, nearly half of the patients were taking antiplatelet agents, which were significantly more common in males (48.1% vs 44.3%; p<0.01), as were statins (43.2% vs 40.2%; p<0.01). Of 8043 people free of cardiovascular events (primary prevention), 2795 (34.8%) were taking statins and 22.4% (n=627) had no previous known LDL-C value (figure 1). Of the 3602 patients in secondary prevention, 1981 (55%) were taking statins, and 23.8% (n=472) had no known LDL-C value (figure 2). Therefore, regardless of the type of prevention, approximately a quarter of the diabetic nonagenarians who received statins had no follow-up of their lipid level.

T2DM was managed exclusively with dietary and lifestyle changes in 24.7% of patients; the finding was significantly higher in females than in males (25.2% vs 23.4%; p<0.01). Use of insulin alone was more common in females, and insulin combined with oral glucose-lowering drugs was more frequent in males. Oral glucose-lowering drugs alone were more common in males (54.7% vs 51.4%; p<0.01).

The achievement goals are summarised in table 2. Briefly, approximately one-third of the patients (31.6%) had no HbA1c value recorded in their electronic clinical record during the previous year. This figure was higher in patients with known dementia (36.4%). Of 7961 patients with recorded HbA1c values, a total of 5129 (64.4%) achieved HbA1c <7%. Sex differences were observed in patients with known dementia, namely, achievement was higher in females than in males (67.1% vs 59.9%; p<0.01). HbA1c <8% was observed in 6860 subjects (86.2%), with no sex differences. LDL-C values were available for 8167 patients (70.1%), of whom 4828 (59.1%) achieved LDL-C <100 mg/dL. Males attained better optimal control of LDL-C levels (<130, <100 and 70 mg/dL, respectively) than females, both in primary and secondary prevention. Of 8455 patients with blood pressure values available, 3118 (36.9%) achieved the optimal blood pressure target (<130/80 mm Hg) and 5521 (65.3%) a less strict target (<140/90 mm Hg). Except for the strictest control in secondary prevention (<130/80 mm Hg), optimal control of blood pressure was more common in males, both in primary and in secondary prevention. The ABC goal (A, HbA1c <7%; B, blood pressure <140/85 mm Hg; C, LDL-C <100 mg/dL) was reached by 10.6% of patients, although this percentage was higher in males than in females (13.4 vs 9.5%; p<0.01) and in secondary prevention with respect to primary prevention (12.4% vs 9.7%; p<0.01).

The prevalence of hypertension was 81.4% (n=9483), and 4632 patients were taking ACE inhibitors or ARBs (48.8%), that is, our optimal criteria for treatment of hypertension.

In secondary prevention, 24% of patients with lipid data available from the clinical history had LDL-C >130 mg/dL, and 34% were receiving statins, with no differences between the sexes. However, differences were observed in patients with no history of cardiovascular events, given that 21.3% of males received statins compared with 31% of women (p=0.02). After adjusting for sex, age and dementia, the factor most associated with adequate use of statins was a low Charlson Index (table 3).

Lastly, 5026 (43.2%) subjects had previously had cardiovascular events and/or chronic atrial fibrillation and, therefore, were candidates for antithrombotic treatment, which was prescribed appropriately in 86.3% of cases. Adherence was significantly better in males (table 4) for

Table 1 Sociodemographic, clinical characteristics, and therapeutic profile of 11 645 nonagenarian living with type 2 diabetes mellitus

	Available values, %	All	Females	Males	P value	Effect size
No (%)	100	11 645	8507 (73.1)	3138 (26.9)	–	–
Age (years), mean (SD)	100	92.9 (2.5)	93 (2.6)	92.5 (2.2)	<0.01	0.21*
Living in a nursing home (%)	100	1587 (13.6)	1301 (15.3)	286 (9.1)	<0.01	0.08†
Basic activities of daily living	48.4					
Barthel Index, mean (SD)		61.5 (29.7)	58.8 (29.7)	68.7 (28.5)	<0.01	0.34*
Barthel Index categories						
Functionally independent (%)		562 (10)	324 (7.8)	238 (16)	<0.01	0.16†
Instrumental activities of daily living	47.9					
Lawton and Brody Index, mean (SD)		3.6 (2.5)	3.4 (2.5)	3.8 (2.4)	<0.01	0.16*
Lawton and Brody categories (%)						
Functionally independent (%)		501 (9)	350 (8.6)	151 (10)	<0.01	0.09†
Smoking	64.5					
Current smoker (%)		121 (1.6)	36 (0.7)	85 (4)	<0.01	0.16†
Former smoker (%)		97 (1.3)	27 (0.5)	70 (3.3)		
Never smoker (%)		7294 (97.1)	5325 (98.8)	1969 (92.7)		
History of						
Hypertension (%)	100	9483 (81.4)	7204 (84.7)	2279 (72.6)	<0.01	0.14†
Coronary artery disease (%)	100	1744 (15)	1068 (12.6)	676 (21.5)	<0.01	0.12†
Myocardial infarction (%)	100	786 (6.7)	438 (5.1)	348 (11.1)	<0.01	0.11†
Stroke (%)	100	1876 (16.1)	1357 (16)	519 (16.5)	0.44	0.01†
Peripheral arterial disease (%)	100	464 (4)	198 (2.3)	266 (8.5)	<0.01	0.14†
Heart failure (%)	100	1706 (14.7)	1266 (14.9)	440 (14)	0.24	0.01†
Chronic atrial fibrillation (%)	100	2270 (19.5)	1611 (18.9)	659 (21)	0.01	0.01†
Dyslipidaemia (%)	100	5500 (47.2)	4207 (49.5)	1293 (41.2)	<0.01	0.07†
Chronic kidney disease (%)	100	1876 (16.1)	1290 (15.2)	586 (18.7)	<0.01	0.04†
Albuminuria (%)	29.6	1625 (40.4)	1085 (37.8)	540 (46.8)	<0.01	0.08†
Dementia (%)	100	1550 (13.3)	1255 (14.8)	295 (9.4)	<0.01	0.07†
Charlson Comorbidity Index, mean (SD)	100	7.37 (1.39)	7.30 (1.33)	7.57 (1.2)	<0.01	0.10*
Anthropometric variables						
SBP (mm Hg), mean (SD)	72.6	131.1 (17.1)	131.7 (17.2)	129.4 (16.7)	<0.01	0.14*
DBP (mm Hg), mean (SD)	72.6	70,1 (9.5)	70.6 (9.5)	68.9 (9.4)	<0.01	0.18*
BMI (kg/m^2), mean (SD)	46.2	27 (4.5)	27.2 (4.8)	26.6 (4)	<0.01	0.14*
BMI categories	46.2					
BMI <25 Kg/m^2, n (%)		1824 (33.9)	1243 (33.4)	581 (35)	<0.01	0.10†
BMI 25–29 kg/m^2, n (%)		2317 (43.1)	1515 (40.7)	802 (48.3)		
BMI ≥30 kg/m^2, n (%)		1240 (23)	961 (25.8)	279 (16.8)		
Laboratory measures						
Fasting plasma glucose (mg/dL), mean (SD)	77.3	120.1 (40.7)	120.1 (42.7)	120.1 (40.7)	0.97	0.00*
HbA1c (%), mean (SD)	68.4	6.8 (1.1)	6.8 (1.2)	6.8 (1.1)	0.50	0.00*
HDL-cholesterol (mg/dL), mean (SD)	70.4	49.1 (14.3)	50.4 (14.7)	45.3 (12.4)	<0.01	0.38*
Total cholesterol (mg/dL), mean (SD)	76.6	168.5 (37.8)	173.5 (37.9)	154.7 (34)	<0.01	0.52*
LDL-cholesterol (mg/dL), mean (SD)	70.1	95.6 (31)	98.2 (31.6)	88.2 (27.9)	<0.01	0.33*
Triglycerides (mg/dL), mean (SD)	75.2	125.2 (61.8)	130.8 (63.6)	109.5 (53.6)	<0.01	0.36*
Albumin (g/dL), mean (SD)	46	3.90 (0.4)	3.88 (0.4)	3.94 (0.5)	<0.01	0.13*
Creatinine, mg/dL, mean (SD)	76.4	1.00 (0.4)	0.96 (0.4)	1.19 (0.5)	<0.01	0.51*
eGFR <60 mL/min/1.73 m^2 (%)	46.4	2650 (49.1)	2088 (52.1)	562 (40.2)	<0.01	0.10†

Continued

Table 1 Continued

	Available values, %	All	Females	Males	P value	Effect size
Use of						
Diuretics, n (%)	100	5520 (47.4)	4139 (48.7)	1381 (44)	<0.01	0.04†
Antiplatelet agents, n (%)	100	5279 (45.3)	3770 (44.3)	1509 (48.1)	<0.01	0.03†
Anticoagulants, n (%)	100	2536 (21.8)	1801 (21.2)	735 (23.4)	0.01	0.02†
Beta-blockers, n (%)	100	2312 (19.9)	1639 (19.3)	673 (21.4)	0.01	0.02†
Calcium antagonists (%)	100	3101 (26.6)	2359 (27.7)	742 (23.6)	<0.01	0.04†
ACEI or ARB (%)	100	5135 (44.1)	3765 (44.3)	1370 (43.7)	0.56	0.01†
Statins, n (%)	100	4776 (41)	3420 (40.2)	1356 (43.2)	<0.01	0.03†
Primary prevention (n=8043), n (%)	100	2795 (34.8)	2175 (35.4)	620 (32.6)	0.03	0.03†
Secondary prevention (n=3602), n (%)	100	1981 (55)	1245 (52.7)	736 (59.4)	<0.01	0.06†
Oral antidiabetic drugs, n (%)	100	6086 (52.3)	4371 (51.4)	1715 (54.7)	<0.01	0.04†
Insulin, n (%)	100	1332 (11.4)	1027 (12.1)	305 (9.7)	<0.01	0.04†
Oral antidiabetic drugs+Insulin, n (%)	100	1352 (11.6)	968 (11.4)	384 (12.2)	<0.01	0.04†

*Cohen's d.
†Cramer's V.
ACEI, ACE inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; DBP, diastolic blood pressure;eGFR, estimated glomerular filtration rate; HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.

each previous criterion of evidence-based cardiovascular preventive therapies.

DISCUSSION

Life expectancy at 90 years of age is only a few years and is almost equal in men and women (6.6 years in men and 7.9 years in women, at 85 years and over, according to Eurostat data for Spain),[32] with lower gender differences in mortality rates for coronary heart diseases after 75 years.[33] Therefore, it is reasonable to think that at 90 years or over, there would be fewer gender differences in cardiovascular risk and physician-prescribed preventive treatments than at previous ages.

T2DM is accentuated in older people. In general, the prevalence of T2DM is higher among males than females in all age groups, except in persons aged ≥85 years.[34] However, in our study, the prevalence of diabetes in nonagenarians remained significantly higher in males. This preponderance of T2DM in males is due to their visceral and hepatic fat, which is greater than that of females.[35] The prevalence of T2DM among nonagenarians in other Spanish studies[36] and European studies[37] was lower in both males and females.

Furthermore, in the present study, as in other Spanish studies,[38 39] the percentage of older people living in a nursing home was lower than in an unselected population of nonagenarians living in central and northern Europe,[40] for two reasons. First, the prevalence of dementia (13.3%) was lower than in previous studies in older persons,[41] probably owing to the association between adherence to a Mediterranean diet (widespread in southern Europe) and slower cognitive decline and lower risk of dementia.[42]

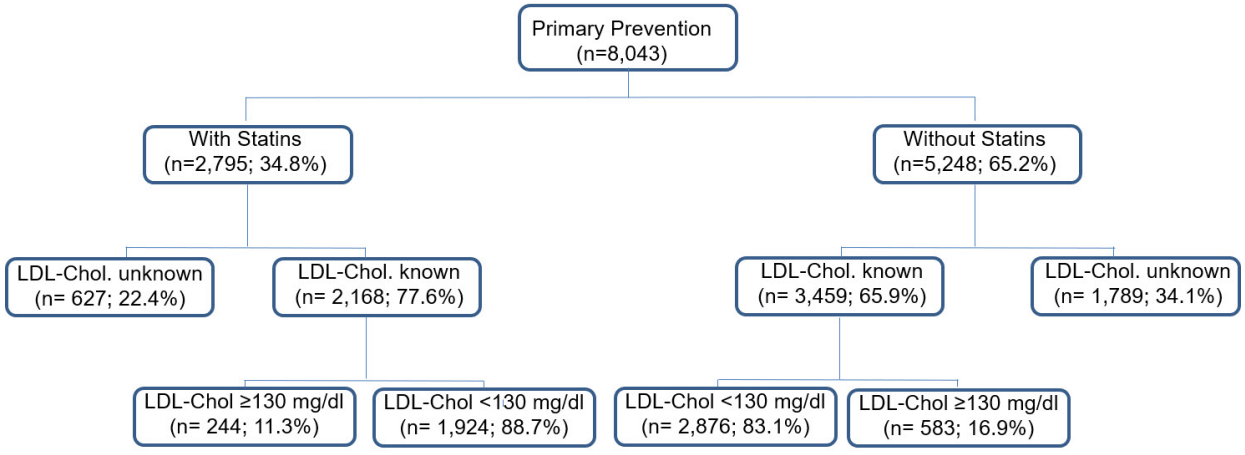

Figure 1 Proportion of nonagenarians with type 2 diabetes mellitus, free of cardiovascular events, who meet LDL-cholesterol goal, stratified by use of statins. LDL, low-density lipoprotein.

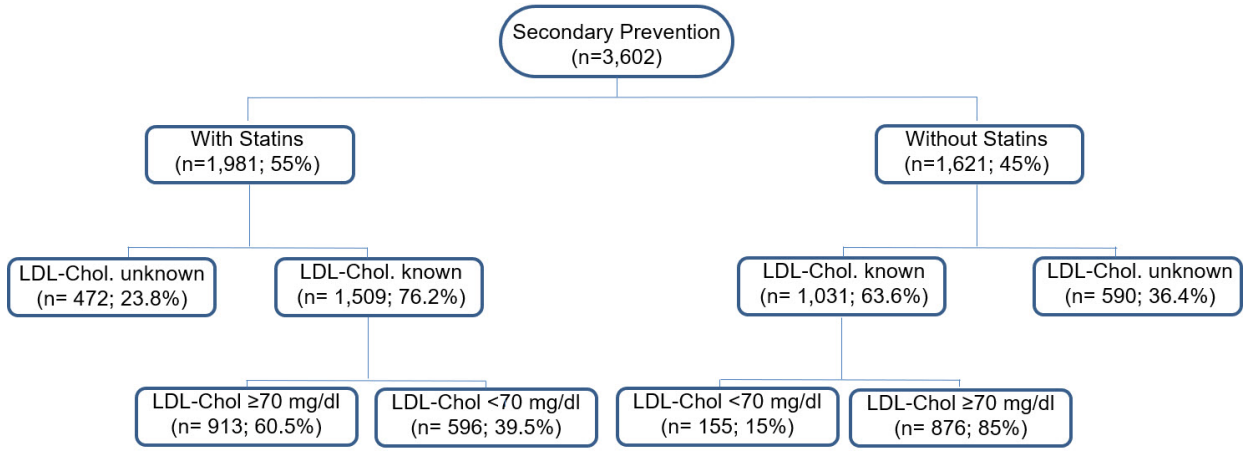

Figure 2 Proportion of nonagenarians with type 2 diabetes mellitus, on secondary prevention, who meet LDL-cholesterol goal, stratified by use of statins. LDL, low-density lipoprotein.

Second, as a result of the low supply of public nursing homes (free of charge from regional health services), the lack of family income to pay for private nursing homes, and the ability of families, friends, neighbours and other community-based caregivers to provide support,[43] family and social support is more common in Spain than in other countries in the Organisation for Economic Cooperation and Development.[39]

The prevalence of coronary artery disease and peripheral artery disease were lower in females than in males, as reported in other studies both in Spain[44] and elsewhere.[45] The sex differences in atherosclerotic disease in middle and advanced age are not yet completely understood. A possible explanation is that smoking is more prevalent in males, and this is a known risk factor for coronary artery disease and peripheral artery disease. We agree with other authors that diabetes in females aged less than 60 years is more strongly associated with myocardial infarction than the presence of diabetes in females over the age of 60 years.[46] On the other hand, diabetes attenuates the protective effect of female sex and increases the incidence of cardiovascular events to the extent that is more pronounced than in males.[8 47] The Framingham Heart Study and the Framingham Offspring Study (follow-up of 20 years) found that the adjusted HR for coronary artery disease mortality among diabetic people free of prior coronary artery disease was higher in females than in males (3.8 (95% CI 2.2 to 6.6) vs 2.1 (95% CI 1.3 to 3.3)).[48] Survival has long been poorer in diabetic females than in diabetic males at 28 days and 1 year after myocardial infarction,[49] probably owing to disparities between females and males in terms of cardiac procedures.[50] Our findings could be explained by a probable survival bias: at 90 years of age, fewer females than males would have survived after previously having a myocardial infarction. Nevertheless, Vaccarino *et al* showed that the odds of death were 11.1% greater for females than for males with every 5-year decrease in age (95% CI 10.1% to 12.1%).[50]

As in the present study, prior investigations have shown that from the sixth decade of life, diabetic females have a worse risk profile associated with cardiovascular disease[45] and achieve fewer treatment targets for HbA1c, LDL-C, high-density lipoprotein cholesterol (HDL-C) and systolic blood pressure,[51] even after controlling for age, body mass index and medication use.[52 53]

The discordance between poorer control of lipids and blood pressure in women and less coronary artery disease and peripheral artery disease is a paradoxical phenomenon. There are various possible explanations for this issue: first, abdominal fat accumulation, which is more prevalent in males, is associated with cardiovascular risk factors, such as diabetes, hypertension and dyslipidaemia. It is also linked with all-cause and cardiovascular mortality in the elderly aged ≥80 years, thus partly explaining the lower presence of vascular complications in women. Second, as previously commented, numerous studies carried out in the cardiovascular field[54 55] showed poorer use of diagnostic procedures when evaluating ischaemic heart disease and peripheral arterial disease in women. This issue may be due to gender bias in the manifestation of symptoms of ischaemia. In addition, clinicians may evaluate these symptoms without resorting to invasive tests that confirm the diagnosis and therefore to undertreatment.

In Spain, a cross-sectional study of 286 791 patients with T2DM aged 31–90 years showed a similar degree of control between males and females for HbA1c <7%, HbA1c <8%, systolic blood pressure <130 mm Hg and systolic blood pressure <140 mm Hg. However, findings were worse for LDL-C <130 mg/dL and LDL-C <100 mg/dL in females than in males.[44]

Poorer adherence to evidence-based cardiovascular preventive therapies in women than in men is compatible with a low prevalence of coronary artery disease and peripheral artery disease, as described in another Spanish study with similar methodology.[56]

Despite the time with T2DM, the proportion of subjects in our study who met their ABC goals was low, although similar to that reported in other studies with younger patients with T2DM .[9] Rawshani *et al* recently found that patients with T2DM who had five risk factors within the

Table 2 Achievement goals of 11 645 nonagenarians living with T2DM, stratified by presence of dementia and type of prevention (primary or secondary)

	Available values (%)	All	Females	Males	P value
HbA1c <7%, n (%)	68.4	5129 (64.4)	3779 (64.7)	1350 (63.6)	0.36
Dementia (n=1550), n (%)	63.6	647 (65.6)	523 (67.1)	124 (59.9)	<0.01
Without dementia (n=10 095), n (%)	69.1	4482 (64.3)	3256 (64.3)	1226 (64)	0.80
Primary prevention (n=8043), n (%)	72	3590 (65.4)	2745 (65.1)	845 (66.1)	0.54
Secondary prevention (n=3602), n (%)	74.1	1539 (62.4)	1034 (63.6)	505 (59.9)	0.07
HbA1c <8%, n (%)	68.4	6860 (86.2)	5012 (85.8)	1848 (87.1)	0.15
Dementia (n=1550), n (%)	63.6	847 (85.9)	670 (86)	177 (85.5)	0.85
Without dementia (n=10 095), n (%)	69.1	6013 (86.2)	4342 (85.8)	1671 (87.3)	0.12
Primary prevention (n=8043), n (%)	72	4760 (86.7)	3631 (86.2)	1129 (88.3)	0.05
Secondary prevention (n=3602), n (%)	74.1	2100 (85.1)	1381 (85)	719 (85.3)	0.84
BP <130/80 mm Hg, n (%)*	72.6	3118 (36.9)	2169 (35.7)	949 (39.9)	<0.01
Primary prevention (n=8043), n (%)	72	2067 (35.7)	1511 (34.6)	556 (39.1)	<0.01
Secondary prevention (n=3602), n (%)	74.1	1051 (39.4)	658 (38.5)	393 (40.9)	0.22
BP <140/85 mm Hg, n (%)†	72.6	5413 (64)	3808 (62.7)	1605 (67.4)	<0.01
Primary prevention (n=8043), n (%)	72	3648 (63)	2701 (61.9)	947 (66.6)	<0.01
Secondary prevention (n=3602), n (%)	74.1	1765 (66.2)	1107 (64.9)	658 (68.5)	0.05
BP <140/90 mm Hg, n (%)‡	72.6	5521 (65.3)	3888 (64)	1633 (68.6)	<0.01
Primary prevention (n=8043), n (%)	72	3730 (64.4)	2762 (63.2)	968 (68.1)	<0.01
Secondary prevention (n=3602), n (%)	74.1	1791 (67.2)	1126 (66)	665 (69.3)	0.08
LDL-cholesterol <130 mg/dL, n (%)	70.1	7078 (86.7)	5100 (84.8)	1978 (91.8)	<0.01
Primary prevention (n=8043), n (%)	70	4800 (85.3)	3634 (83.8)	1166 (90.2)	<0.01
Secondary prevention (n=3602), n (%)	70.1	2278 (89.7)	1466 (87.4)	812 (94.2)	<0.01
LDL-cholesterol <100 mg/dL, n (%)	70.1	4828 (59.1)	3343 (55.6)	1485 (68.9)	<0.01
Primary prevention (n=8043), n (%)	70	3113 (55.3)	2287 (52.8)	826 (63.9)	<0.01
Secondary prevention (n=3602), n (%)	70.1	1715 (67.5)	1056 (62.9)	659 (76.5)	<0.01
LDL-cholesterol <70 mg/dL, n (%)§	70.1				
Primary prevention (n=8043), n (%)	70	941 (16.7)	674 (15.6)	267 (20.6)	<0.01
Secondary prevention (n=3602), n (%)	70.1	751 (29.6)	444 (26.5)	307 (35.6)	<0.01
ABC goals: HbA1c <7% and BP <140/85 mm Hg and LDL-cholesterol <100 mg/dL, n (%)	73.9	1549 (19.1)	1033 (17.3)	516 (24.2)	<0.01
Primary prevention (n=8043), n (%)	73.9	993 (17.7)	691 (16)	302 (23.3)	<0.01
Secondary prevention (n=3602), n (%)	74.1	556 (22.3)	342 (20.6)	214 (25.6)	<0.01

*Recommendations of the Joint National Committee on Prevention Detection, Evaluation and Treatment of High Blood Pressure (2003).
†Recommendations of the European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension (2013).
‡Recommendations of the American Diabetes Association for older adults (2015).
§Recommendations of European Society of Cardiology guidelines on the management of diabetes developed in collaboration with the European Association for the Study of Diabetes for secondary prevention.[42]
BP, blood pressure; HbA1c, haemoglobin A1c; LDL, low-density lipoprotein; T2DM, type 2 diabetes mellitus.

target ranges (HbA1c, LDL-C, albuminuria, blood pressure and smoking) appeared to have little or no excess risk of death, myocardial infarction or stroke, compared with the general population.[57] Importantly, the protection derived from control of risk factors occurred in a stepwise fashion, so that, for example, individuals who met two targets had better outcomes than those who met one target. Therefore, we believe it is necessary to improve the degree of control of ABC regardless of age.

As for therapeutic profile, our data show that females were taking oral antidiabetic drugs, antiplatelet agents, anticoagulants agents, statins, ACE inhibitors, beta-blockers and oral glucose-lowering drugs in a lower proportion than males. These results are coincident with

Table 3 Influence of comorbidity on adequate use of statins after adjusting for gender, age and dementia

	OR	95% CI	P value
Charlson Index	0.83	0.76 to 0.92	<0.01
Male sex	1.27	0.90 to 1.79	0.18
Age	1.04	0.98 to 1.09	0.19
Dementia	0.74	0.52 to 1.05	0.09

Among 1089 T2DM nonagenarians whose most recent LDL-cholesterol reading was ≥130 mg/dL.
LDL, low-density lipoprotein; T2DM, type 2 diabetes mellitus.

those of other studies.[9 45 53] In secondary prevention, the percentage of patients with poor control of LDL-C who were taking statins was similar for both sexes. However, in primary prevention and cases of poor control of LDL-C, statins were taken significantly more frequently by females.

In secondary prevention, men received statins more frequently than women. This circumstance highlights the inconsistency between available evidence and prescription under usual clinical conditions. Statins are effective in women for secondary prevention of cardiovascular disease[58] and there is much doubt surrounding primary prevention in women at low to intermediate cardiovascular risk,[59] so much so that the number needed to treat (NNT) to prevent one coronary heart disease event is 77 for men[60] and 140 for women.[58] However, for secondary prevention, the NNT is similar for men and women, around 25[58 61] for major coronary events.

Nevertheless, we found room for improvement in the use of statins. Approximately, a quarter of patients who take statins had an LDL-C reading from the previous year. This situation is less logical in secondary prevention, given that is not possible to know the effect of treatment and, therefore, adjust the dose. In the primary prevention, there is not enough evidence to support treatment.

Table 4 Adherence to evidence-based cardiovascular preventive therapies by sex

	All	Females	Males	P value
Hypertensive patients with albuminuria who were taking ACE inhibitors or ARBs, %	42.4	39.1	50.4	<0.01
Patients with dyslipidaemia and prior cardiovascular events who were taking statins, %	41.5	36.4	54.3	<0.01
Patients with prior cardiovascular events or chronic atrial fibrillation who were taking antithrombotic drugs, %	86.3	85.9	87.2	<0.01

ARBs, angiotensin II receptor blockers.

The differences between studies may be due, in part, to ethnic differences, unequal access to health resources, different priorities in the management of T2DM between countries, and disparities in the type of insurance (public or private) used to pay for treatment.[9]

Treatment of hypertension was optimal in only half of the study patients. This finding clearly reveals an area for improvement, given that patients with diabetes and hypertension should be treated with ACE inhibitors or ARBs, especially if they have albuminuria.[62]

Our study is subject to a series of limitations. First, its cross-sectional design prevents us from establishing causal relationships between variables. Second, many data are missing for variables such as blood pressure, body mass index, estimated glomerular filtration rate, albumin, HbA1c, HDL-C, LDL-C and fasting plasma glucose. However, it is important to remember that this study was carried out under real conditions of clinical practice, with little time per patient in a primary care office visit. Third, the duration of physician visits is similar across the age groups,[63] and given that elderly patients have more comorbidities and are prescribed more medications than younger patients, they require specific monitoring and counselling, with the result that recording of variables in their clinical history may be poorer. Therefore, the quality of data collection is not comparable to that of studies based on controlled conditions, such as clinical trials. Although findings are consistent with those from previous studies, there may still be bias due to missing data. Lastly, data on the therapeutic profile were based on the drugs prescribed; therefore, we did not have data on adherence.

The main strength of the study is that it is based on all persons with diabetes in our region, thus preventing recruitment bias. In addition, data from real-life clinical practice in primary care increase the knowledge of health workers and healthcare policy-makers and make it possible to improve the clinical management of patients and reorient clinical practice.

In conclusion, our study revealed sex differences in nonagenarians with T2DM. These took the form of a higher prevalence of cardiovascular risk factors (hypertension, dyslipidaemia and obesity), significantly higher blood pressure and body mass index, and worse values in total cholesterol, LDL-C, triglycerides, albumin and estimated glomerular filtration rate in females than in males. Furthermore, females were less likely to achieve ABC goals, and the proportion of females treated with antiplatelet drugs, lipid-lowering drugs and oral glucose-lowering drugs was lower than that of males. Lastly, adherence to evidence-based cardiovascular preventive therapies was poorer among females. Our findings indicate that sex differences in younger patients with T2DM persist in patients aged ≥90 years and that there is considerable room for improvement in standards of preventive care in nonagenarians with T2DM, especially women.

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