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ORIGINAL ARTICLE

Use of statins and associated factors in nonagenarians in the Community of Madrid, Spain

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Abstract

Background The role of statins in the management of dyslipidemia in elderly patients with different cardiovascular risks remains unclear.

Objective To study use of statins and associated factors in subjects aged 90 or over in the Community of Madrid, Spain.

Methods Observational, cross-sectional study that included all people aged 90 or more residing in the Community of Madrid as of December 31, 2015. The clinical information was obtained from the database that contains the electronic medical records collected by family doctors in primary care. Comorbidity data are collected according to the International Classification of Primary Care, Second Edition (ICPC-2).

Results The study population comprised 59,423 subjects, with a mean age of 93.3 (2.5) years (25.8% males). Slightly more than one quarter of the population (28.2%) was in treatment with statins, 21.9% were in primary prevention, and 48.1% in secondary prevention. The multivariate analysis revealed the factors independently associated with statin treatment to be younger age, not being institutionalized, a higher Barthel score, a lower Charlson score, a higher body mass index, and a history of diabetes, dyslipidemia, chronic kidney disease, and cardiovascular disease.

Conclusions A significant percentage of nonagenarians—mainly less frail patients with more comorbidities—in the Community of Madrid receive statin treatment. No clear efficacy has been demonstrated in reducing cardiovascular events in an age group with such a short life expectancy.

Keywords Nonagenarians · Statins · Associated factors

Introduction

Genetic, epidemiological, and interventional studies (clinical trials) show that LDL-cholesterol is a causal factor in atherosclerotic cardiovascular disease [1]. Cholesterol concentrations increase progressively from puberty until the age of 60 years and then gradually decline [2]. Given that the close relationship between cholesterol and cardiovascular disease in middle age tends to weaken with older age and disappears in those over 75 years of age, it is not helpful in predicting cardiovascular risk [3].

Statins are safe drugs that inhibit cholesterol synthesis and reduce plasma LDL-cholesterol concentrations by up to 60%. Numerous clinical trials and several meta-analyses demonstrate that lowering LDL-cholesterol with statins is associated with a significant reduction in cardiovascular events [4–6]. Thus, for each 1 mmol/L decrease in LDL-cholesterol, the risk of a major cardiovascular event is reduced by about 20% [5, 6]. This benefit is maintained with

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increasing age in patients in secondary prevention of cardiovascular disease, although it becomes less evident in older patients (over 75 years) without cardiovascular disease [7].

Nonagenarians are frail and have multiple comorbid conditions and a short life expectancy. The percentage who are taking statins has received little attention in the literature, although it is probably low, given that clinical trials and cohort studies that prove their efficacy are lacking. In addition, the factors associated with their prescription are unknown.

This study aimed to evaluate the use of statins in people aged 90 years or older. We also analyzed the factors associated with their prescription and use in primary care centers in the Community of Madrid (Spain).

Methods

Study design and data source

We performed an observational, cross-sectional study of all persons aged 90 years or older living in the Community of Madrid on December 31, 2015. Of the 6,466,966 inhabitants registered on that date, a total of 59,913 (0.93%) were aged 90 years or older. Clinical information was obtained from the database containing primary care electronic medical records collected by 3,881 family physicians working in the 262 primary care centers and 162 local clinics.

Study population

Available information included age, sex, cardiovascular risk factors, presence and type of cardiovascular disease, comorbidity, and current medication (December 31, 2015). Comorbidity data are collected according to the International Classification of Primary Care, Second Edition (ICPC-2). The quality of the diagnoses collected in the electronic medical records has been validated elsewhere [8]. The Barthel Index is an ordinal scale used to measure performance in activities of daily living (ADL). Ten variables describing ADL and mobility are scored, a higher number being a reflection of greater ability to function independently. The Charlson comorbidity Index predicts the risk of mortality at 10 years according to age and a series of comorbidities (diabetes, chronic liver disease, chronic renal failure, acquired immunodeficiency syndrome, cancer, leukemia or lymphoma, heart failure, previous acute myocardial infarction, chronic obstructive pulmonary disease, peripheral vascular disease, cerebrovascular disease, dementia and connective tissue diseases).

Analytical data were included if determinations had been performed in the previous two years (2014 and 2015). Likewise, anthropometric measurements, smoking habit, and the measurement of functional capacity using the Barthel index were only taken into account if the information had been collected in the previous two years.

Statistical analyses

In the descriptive statistics of the study population, quantitative variables are presented as mean and standard deviation, while qualitative variables are presented as relative and absolute frequencies. Prevalence was calculated as the ratio between the number of patients with each diagnosis and the total number of patients. The Kolmogorov–Smirnov test was used to verify the normal distribution of the variables. Quantitative variables were compared using an unpaired t test. Qualitative variables were compared using the χ^2 test.

To identify variables independently associated with statin use, logistic regression analysis was performed to estimate odds ratios, which were interpreted as prevalence ratios and expressed with their 95% confidence interval. The variables included in the explanatory model were those for which $p < 0.10$ in the univariate analysis and those that, for theoretical reasons or because of their potential confounding effect, were considered appropriate. The statistical analyses were performed using IBM SPSS Statistics version 19.0 (IBM Corp, Armonk, New York, USA).

Results

The study population comprised 59,423 subjects aged 90 years or more, with a mean (standard deviation) age of 93.3 (2.5) years. Of these, 25.8% were male. Table 1 shows the demographic and clinical-biological characteristics of the population. Slightly more than one quarter (28.2%) were taking statins (30.8% of men and 27.3% of women). Of the 45,121 subjects with no known cardiovascular disease, 21.9% were taking statins, in contrast with 48.1% of patients in secondary prevention. Figure 1 shows the percentage of statin use in the different population subgroups. The clinical characteristics of the participants according to whether or not they took statins are shown in Table 2.

Regarding total cholesterol and LDL-cholesterol, the participants on statin treatment had lower values than those not treated, although they had higher HDL-cholesterol and triglyceride values. Subjects on statin treatment were more likely to be men and younger and had a higher prevalence of cardiovascular risk factors, atrial fibrillation, heart failure, and chronic kidney disease. In contrast, those not taking statins more frequently lived in nursing homes and had a higher dependency score (lower Barthel index score), a higher prevalence of dementia, and lower comorbidity (lower Charlson index score) than those taking statins. In the multivariable logistic regression

Table 1 Baseline demographic and clinical characteristics of the study population (59,423 nonagenarians)

Age m (SD), years	93.3 (2.7)
Male sex (%)	25.8%
Living in a nursing home (%)	14.1
Arterial hypertension (%)	71.4
Diabetes mellitus (%)	19.6
Dyslipidemia (%)	36.8
Current smoker (%)	1.6
History of cardiovascular disease (%)	24.1
Atrial fibrillation (%)	17.0
Heart failure (%)	11.2
Chronic kidney disease (%)	12.0
Dementia (%)	13.5
Cancer (%)	6.6
Barthel index score m(SD)	62.7 (29.0)
Charlson index score, m(SD)	6.3 (1.3)
Body mass index, m(SD), kg/m^2	26.5 (4.5)
Total cholesterol, m(SD), mg/dl	177 (38)
LDL-cholesterol, m(SD), mg/dl	104 (31)
HDL-cholesterol, m(SD), mg/dl	52 (15)
Triglycerides, m(SD), mg/dl	110 (52)

m (SD) mean (standard deviation)

analysis, the factors independently associated with statins were younger age, not living in a nursing home, history of diabetes, dyslipidemia, chronic kidney disease, prior history of cardiovascular disease (secondary prevention), having a higher Barthel index score (lower dependency), having a lower Charlson index score (higher comorbidity), and having a higher body mass index (Table 3).

Discussion

Almost one in three nonagenarians in Madrid is taking statin treatment, a percentage that increases to 48.1% in subjects with known cardiovascular disease. In the subgroup of persons over 75 years of age in the SPRINT study (mean age of 79.9 years and high cardiovascular risk), 52% of participants took statins [9], this percentage is similar to the percentage we report in secondary prevention. In a British series with 3900 patients over 80 years of age discharged after acute myocardial infarction between 1999 and 2016, 66.5% left hospital taking statins [10], although it is likely that up to 40% abandoned treatment at 1 year of follow-up [11]. In the ASPREE study, which included patients in primary prevention (mean age, 74.2 years), 31.1% received statin treatment [12]; this percentage is similar to the one we report, although the study population was younger. In a study of North American veterans aged over 75 years without cardiovascular disease, 14.8% received statins, a percentage that decreased to 10.1% in those over 90 years of age [13], that is, three times less than patients of the same age group in our study. Part of the difference can be explained by the dates of the study—2002–2012—when the indication and objectives of statin treatment were different.

Meta-analyses of clinical trials have confirmed that treatment with statins [5] or with lipid-lowering agents in general [6] reduces cardiovascular events in patients aged over 75 years. However, when differentiating between patients with and without previous cardiovascular disease, the beneficial effect did not reach statistical significance in those undergoing primary prevention and aged over 70 years [6]. In the last two years, numerous retrospective studies have been published to determine the effect of statins in patients over 75 years of age without cardiovascular disease [13–15]. Using the database of primary care in Catalonia (Spain),

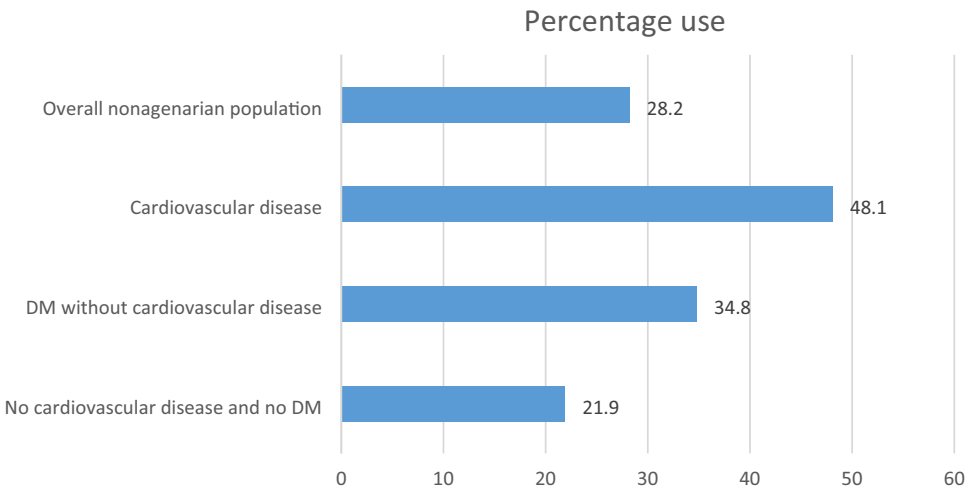

Fig. 1 Percentage of statin use in nonagenarians overall and according to cardiovascular risk subgroup

Table 2 Comparison between groups according to the use of statins

	No statins $n=42,659$	Statins $n=16,764$	p value
Age, m (SD), years	93.5 (2.8)	92.5 (2.1)	<0.001
Male sex (%)	24.9	28.2	<0.001
Living in a nursing home (%)	15.8	9.9	<0.001
Arterial hypertension (%)	68.0	80.1	<0.001
Diabetes mellitus (%)	16.1	28.5	<0.001
Dyslipidemia (%)	23.5	70.5	<0.001
Current smoking (%)	1.7	1.5	0.040
History of cardiovascular disease (%)	17.4	41.0	<0.001
Atrial fibrillation (%)	16.2	18.8	<0.001
Heart failure (%)	10.5	12.9	<0.001
Chronic kidney disease (%)	10.3	16.4	<0.001
Dementia (%)	14.7	10.5	<0.001
Cancer (%)	6.8	7.0	0.379
Barthel index score, m(SD)	60.0 (30.2)	68.4 (27.1)	<0.001
Charlson index score, m(SD)	6.1 (1.2)	6.6 (1.4)	<0.001
Body mass index, m(SD), kg/m^2	26.2 (4.4)	27.1 (4.3)	<0.001
Total cholesterol, m(SD), mg/dl	180 (37)	170 (40)	<0.001
LDL-cholesterol, m(SD), mg/dl	108 (29)	95 (32)	<0.001
HDL-cholesterol, m(SD), mg/dl	52 (15)	53 (15)	<0.001
Triglycerides, m(SD), mg/dl	107 (49)	117 (80)	<0.001

m (SD) mean (standard deviation)

Table 3 Factors significantly and independently associated with statin use in nonagenarians (logistic regression analysis)

Variable	B	p	OR (95% CI)
Age (per unit of increment)	−0.120	<0.001	0.887 (0.868 – 0.905)
Male sex (vs. female)	0.096	0.065	1.101 (0.994 – 1.220)
Living in nursing home (yes vs. no)	−0.334	0.001	0.716 (0.592 – 0.865)
Diabetes mellitus (yes vs. no)	0.701	<0.001	2.016 (1.802 – 2.255)
Dyslipidemia (yes vs. no)	2.058	<0.001	7.827 (7.137 – 8.583)
Cardiovascular disease (yes vs. no)	1.464	<0.001	4.324 (3.877 – 4.822)
Chronic kidney disease (yes vs. no)	0.133	<0.001	1.299 (1.115 – 1.514)
Barthel index (per unit of increment)	0.007	<0.001	1.007 (1.005 – 1.009)
Charlson index (per unit of increment)	−0.077	0.002	0.926 (0.883 – 0.972)
Body mass index (per unit of increment)	0.036	<0.001	1.037 (1.027 – 1.047)

Ramos et al. reported that initiation of statins in patients aged over 75 years only had a cardiovascular benefit in patients with diabetes mellitus aged between 75 and 85 years [14]. In contrast, in studies conducted in Korea [15] and the United States [13], initiation of statins in this age group was associated with decreased cardiovascular events and mortality. Finally, in a study conducted in France, the withdrawal of lipid-lowering treatment in primary prevention patients aged over 75 years was associated with a significant increase in cardiovascular admissions in the following two years [16]. Therefore, data from observational studies and meta-analyses appear to support lipid-lowering treatment in the elderly without cardiovascular disease, although we must await the conclusions of several clinical trials currently underway to resolve this issue.

Consistent with our findings, data from other authors reveal less frequent prescription of statins with increasing age in elderly patients, probably related to the progressive increase in frailty and lower life expectancy [17–19]. Similarly, most studies show that statins are taken less frequently by women, regardless of age [17–19]. This is because they are perceived by health care personnel as having a lower cardiovascular risk and, therefore, receive less treatment and less intensive treatment [20] and partly because of a higher rate of discontinuation of statin treatment [21]. In our study, being male was associated with

statin therapy, this association was almost significant in the multivariate analysis ($p = 0.065$). As expected, the presence of established cardiovascular disease is closely associated with statins in elderly patients [19]. In our population of nonagenarians, slightly more than half of the patients in secondary prevention received statins, whereas fewer than one in four did so among those with no known cardiovascular disease. The presence of diabetes mellitus, is also related to greater use of statins owing to its higher associated cardiovascular risk, as has also been shown elsewhere both in primary [19] and in secondary prevention [18]. In our study, not being institutionalized, lower dependency, as calculated by the Barthel index, and higher body mass index, as markers of good health and longer life expectancy, were associated with a higher probability of receiving treatment with statins. Therefore, statins in nonagenarians are associated with high cardiovascular risk and better health status.

Among the limitations of our study, we highlight those inherent to any cross-sectional study, namely, that it is not possible to establish causal relationships between the associations found. Likewise, the quality of the data could vary between physicians or primary care centers, although the quality of some of the diagnoses has previously been validated [8]. On the other hand, the main strength of our study is the inclusion of all nonagenarians in the Community of Madrid, thus avoiding selection bias.

We conclude that almost one in three nonagenarians in the Community of Madrid is receiving statin treatment, although more than half have no known cardiovascular disease. The factors associated with prescription are presence of cardiovascular disease, comorbidities (dyslipidemia, diabetes mellitus, chronic kidney disease), and lower frailty. Further evidence is needed to justify the use of statins in the very elderly people with no prior cardiovascular disease or diabetes mellitus.

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Author contributions MASF and JCV contributed to the study design or concept and secured funds. JMP and CLR performed the statistical analyses and edited the manuscript. CLR and MASF drafted the initial manuscript. All authors read and approved the final manuscript. All the authors met the criteria for authorship.

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Availability of data and materials The datasets used and/or analyzed during the current study are not publicly available owing to institutional restrictions but are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare that they have no competing interests.

Ethical approval Given that this study is retrospective and contains de-identified information, informed consent from the participants was waived by the Research Ethics Committee of Ramon y Cajal Hospital in Madrid, Spain (approval identification code: 113/16) on 22 April 2016. In addition, administrative permission to access electronic clinical records was acquired from the Central Research Committee of Madrid Regional Health Service (SERMAS), Primary Health Care (Madrid, Spain). The study complies with the International Guidelines for Ethical Review of Epidemiological Studies (Geneva, 1991).

Consent to participate Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Consent for publication Not applicable.

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