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Perspectiva de los médicos de atención primaria sobre el manejo de la dislipemia en pacientes sin enfermedad cardiovascular aterosclerótica: estudio transversal

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Perspective of primary care physicians on the management of dyslipidaemia in patients without atherosclerotic cardiovascular disease: a cross-sectional study

Background: *Evidence suggests many dyslipidemic patients do not reach target low-density lipoprotein and cholesterol (LDL-C) levels in primary health care. Objective: We aimed to describe the pharmacologic therapeutic management of dyslipidemia in patients without established atherosclerotic cardiovascular diseases (ASCVD) from the primary care physician's perspective in Spain.* ***Material and Methods:*** *We conducted a cross-sectional study through an online survey directed to primary care physicians to explore their therapeutic management of dyslipidemia in patients without ASCVD, focusing on their knowledge and adherence to the 2019 European Society of Cardiology/ European Atherosclerosis Society (ESC/EAS) guidelines and their perspective concerning the barriers to achieving LDL-C therapeutic targets.* ***Results:*** *In total, 279 primary care physicians completed the survey. Most interviewees (80.65%) stated they had already adopted the 2019 ESC/EAS guidelines in their clinical practice. Nevertheless, around 30% adhered to therapeutic targets by previous ESC/EAS guidelines (2016), and most treated their patients mainly with statins in monotherapy, prescribing doses below the maximum tolerated. Additionally, 50.18% were classified as low adherence to the 2019 ESC/EAS guidelines, especially to the treatment algorithm. According to the physicians, the underestimation of patients' cardiovascular risk and the reluctance to increase doses or use combined therapy were the most critical barriers to achieving LDL-C targets.* ***Conclusions:*** *Although primary care physicians in our survey reported adherence to the 2019 ESC/EAS guidelines recommendations, our observations indicate they need to integrate them better into their clinical practice.*

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Keywords: *Cardiovascular Diseases; Hypercholesterolemia; Practice Guideline.*

RESUMEN

Antecedentes: *un alto porcentaje de pacientes con dislipemia no alcanza los objetivos terapéuticos de colesterol unido a lipoproteínas de baja densidad (C-LDL)*

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en el nivel primario de atención. ***Objetivo****: Describir el manejo terapéutico de la dislipemia en pacientes sin enfermedad cardiovascular aterosclerótica (ECA) establecida, desde la perspectiva del médico de atención primaria en España.* ***Material y Métodos****: Estudio transversal mediante encuesta electrónica dirigida a médicos de atención primaria para explorar su manejo terapéutico farmacológico de la dislipemia en pacientes sin ECA, que se centraba en su conocimiento y adherencia a las guías de la Sociedad Europea de Cardiología/Sociedad Europea de Aterosclerosis (ESC/AES) de 2019 y su perspectiva con respecto a las barreras para alcanzar los objetivos de C-LDL.* ***Resultados****: Un total de 279 médicos de atención primaria completaron la encuesta. La mayoría (80,65%) afirmaron que ya habían adoptado las guías de la ESC/EAS de 2019 en su práctica. Sin embargo, alrededor del 30% seguía los objetivos terapéuticos de las guías anteriores (2016) y muchos trataban a sus pacientes con estatinas en monoterapia y dosis menores a la máxima tolerada. Adicionalmente un 50,18% era poco adherente a las guías de la ESC/EAS de 2019, especialmente al algoritmo de tratamiento. Las barreras más importantes para alcanzar los objetivos de C-LDL eran la subestimación del riesgo cardiovascular y la reticencia a aumentar la dosis o a utilizar terapia combinada.* ***Conclusiones****: Aunque los médicos de atención primaria afirman que seguían las guías ESC/EAS de 2019, los resultados indican que no las habían integrado completamente en su práctica clínica.*

Palabras clave*: Enfermedades Cardiovasculares; Guía de Práctica Clínica; Hipercolesterolemia.*

Atherosclerotic cardiovascular diseases (ASCVD) and, especially, ischemic heart disease and cerebrovascular disease are the leading causes of death in Europe and Spain in particular[1, 2]. They account for the higher proportion of premature deaths (aged under 65 years)[3] and are one of the main causes of health-related quality of life deterioration and disability[3-5]. The prevention of ASCVD is mainly based on the promotion of a healthy lifestyle (regular physical activity, healthy nutrition) and the control of modifiable cardiovascular risk factors such as dyslipidaemia (elevated total or low-density lipoprotein cholesterol [LDL-C], or low high-density lipoprotein cholesterol [HDL-C]), high blood pressure, or type 1 and 2 diabetes mellitus [6]. Elevated levels of LDL-C have emerged as the primary target for ASCVD prevention[7], since prolonged lowering of LDL-C levels reduces the risk of ischemic heart disease considerably[8-10].

Given these findings, the 2019 European Society of Cardiology and European Atherosclerosis Society (ESC/EAS)[11] and, more recently, the 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice[12] have moved towards a stricter therapeutic target for LDL-C reduction and have set a new therapeutic algorithm to achieve LDL-C objectives. However, despite these efforts, real-world data reveal that a high percentage of patients with ASCVD still do not reach LDL-C objectives[13-18] and are undertreated[13-15].

Considering the unmet therapeutic needs above, we aimed to describe the therapeutic management of dyslipidaemia in patients without established ASCVD, from primary care physicians' perspective with the focus on the following aspects: physicians' knowledge of and degree of adherence to the 2019 ESC/EAS guidelines, their perception of the main barriers to achieving therapeutic LDL-C targets, and the actions that could improve adherence to the guidelines.

Material and Methods

Study design and participants

We conducted a cross-sectional study through an online survey targeting primary care physicians with experience in the management of dyslipidaemia in patients without established ASCVD and practising for at least five years in the Spanish public or private healthcare. We estimated a minimum sample size of 265 physicians (295 for a 10% drop-out rate) assuming the maximum

indeterminacy (with a 95% confidence interval and 6% accuracy), and considering the number of primary care physicians in the Spanish National Health System in 2018 (29 086)[19].

Questionnaire

Two experts in the management of dyslipidaemia (one primary care physician and one cardiologist) developed the questionnaire. The final version comprised 31 items covering the objectives of the study: 1) Management of dyslipidaemia in patients without established ASCVD, 2) 2019 ESC/EAS guidelines: knowledge and degree of adherence, 3) Barriers to achieving therapeutic targets (LDL-C) and actions to improve adherence to the guidelines (See Supplemental Table 1). The surveys were completed between September 24 and December 24, 2020, using Alchemer platform (https://www.alchemer.com/).

The degree of adherence to the 2019 ESC/EAS guidelines was estimated according to two clinical case studies and eight assumptions. Each physician was awarded one point for each correct answer and 0 points for each incorrect answer (minimum 0; maximum 8 points; see Supplemental Table **2** for correct answers). Accordingly, physicians were classified as low adherent: score ≤ 4; moderate adherent: score > 4 and ≤ 6; and high adherent: score > 6.

To characterise physicians who adhere less to guidelines, we grouped them according to their adherence, sociodemographic characteristics and their knowledge and opinion of the ESC/EAS guidelines.

Finally, to establish priority actions to improve adherence to the 2019 ESC/EAS guidelines, each physician ranked 6 actions according to their preferences. Each action was awarded a score (from 6 points to the most to 1 point to the least preferred). A final score was obtained for each option based on the sum of individual scores divided by the number of participants, ranging from 0 to 6.

The study protocol was approved by the Ethics Committees of the Hospital Universitario Puerta de Hierro Majadahonda (Madrid). All participants were informed about the study and consented to participate prior to inclusion.

Statistical analysis

Qualitative and quantitative study variables were collected in an electronic case report form and an anonymized database was created. Data were reviewed and verified to ensure quality. Missing data were properly identified in the database and were excluded from the analysis.

For the descriptive analysis, qualitative variables were estimated using absolute and relative frequencies. In contrast, quantitative variables were calculated by measures of central tendency and dispersion (mean, standard deviation [SD], percentile, maximum and minimum).

Physicians were classified into two subgroups based on guidelines adherences (adherent: score > 6; and non-adherent: score ≤6) and were compared using the Chi-squared test (see Supplemental methods).

The data analysis was performed using the STATA version 14 statistical software package. Results were considered statistically significant when $p < 0.05$.

Results

Description of the participants and the profile of patients without established ASCVD in primary care settings

In total, 279 experienced primary care physicians (mean of 25.74 [SD: 9.69] years of practising) completed the survey. According to their estimations, most of their patients with dyslipidaemia and without established ASCVD had two or three cardiovascular risk factors (92.48%), around 30% had moderate cardiovascular risk and approximately one-third had type 1 and 2 diabetes mellitus (See details in Table 1).

Management of dyslipidaemia in patients without established ASCVD in primary care settings

Most participants estimated the patient's cardiovascular risk in at least 75% of cases, and 79.04% used the SCORE scale. Approximately half responded that they always used a scale to measure cardiovascular risk in patients with type 1 and 2 diabetes mellitus or moderate chronic kidney disease (high cardiovascular risk). Also, over 50% of physicians considered that the therapeutic target for LDL-C should be < 70 mg/dL for these high cardiovascular risk patients (according to the 2019 ESC/EAS guidelines) and around 30% adhered to the previous therapeutic target (< 100 mg/dL) (Table 2).

Table 1. Physicians' sociodemographic characteristics and their view of the profile of patients with dyslipidaemia attending primary care consultations

Variables	N (279)
Physicians' sociodemographic characteristics	
Age (years), mean (SD)	54.02 (9.11)
Gender (male), n (%)	164 (58.78)
Time practising (years), mean (SD)	25.74 (9.69)
Work settings[I], n (%)	
Rural	23 (8.24)
Semi-rural	55 (19.71)
Urban	201 (72.04)
Profile of patients with dyslipidaemia attending primary care consultations according to physicians' view	
Patients assigned (last year), n (%)	
Less than 1,500	66 (23.66)
Between 1,500 and 2,000	178 (63.80)
More than 2,000	35 (12.54)
Patients with dyslipidaemia (one year), n (%)	
Less than 200	31 (11.11)
Between 200 and 400	167 (59.86)
More than 400	76 (27.24)
DK/NA	5 (1.79)
Patients without established ASCVD, n (%)	
Only one CVR factor	8 (2.87)
Usually two CVR factors	141 (50.54)
Usually three CVR factors	117 (41.94)
Four or more CVR factors	10 (3.58)
DK/NA	3 (1.08)
Patients without established ASCVD, mean % (SD)	
Moderate CVR[II]	35.20 (17.28)
High CVR[I]	21.38 (16.08)
Type 1 or 2 diabetes	31.35 (18.87)
Metabolic syndrome	28.03 (19.41)
Moderate chronic kidney disease[III]	18.73 (13.21)
Severe chronic kidney disease[IV]	7.93 (7.76)
Diabetic duration, years, mean (SD)	
Less than 10	32.29 (17.06)
Between 10 and 20	41.05 (14.82)
More than 20	26.66 (14.80)

ASCVD (atherosclerotic cardiovascular disease); CVR (cardiovascular risk); SD (standard deviation); [I]Rural (municipalities with population of less than 2,000 inhabitants); Semi-rural (municipalities with between 2,000 and 10,000 inhabitants); Urban (municipalities with a population of more than 10,000 inhabitants); [II]Measured by the SCORE chart. Available at: http://www.heartscore.org/es_ES/access; [III]Estimated Glomerular Filtration Rate [eGFR] 30-59 mL/min/1.73 m^2; [IV]Estimated Glomerular Filtration Rate [eGFR] 15-30 mL/min/1.73 m^2.

Table 2. Management of dyslipidaemia in patients without established ASCVD in primary care settings

Variables	n (%)	
Analytical determinations for diagnosing dyslipidaemia		
The determination of TC is sufficient	2 (0.72)	
It is necessary to determine TC and triglycerides	5 (1.79)	
It is necessary to determine the concentrations of LDL-C, HDL-C, and triglycerides	272 (97.49)	
Total	279 (100)	
Lifestyle recommendations before lipid-lowering treatment		
Yes, always	213 (76.34)	
Only if they have other CVR factors	64 (22.94)	
No, never	2 (0.72)	
Total	279 (100)	
Estimation of patient's CVR before deciding on lipid-lowering treatment		
Yes, always	124 (44.44)	
Yes, in about 75% of cases	114 (40.86)	
Yes, in about 50% of cases	30 (10.75)	
Yes, in about 25% of cases	4 (1.43)	
No, never	7 (2.51)	
Total	279 (100)	
Scale to calculate CVR		
Framingham	18 (6.62)	
REGICOR	37 (13.60)	
SCORE	215 (79.04)	
Others	2 (0.74)	
Total	272 (100)	
Use a scale to estimate CVR in patients with	**T1DM and T2DM**	**Chronic kidney disease**
Yes, always	133 (47.67)	122 (43.73)
Only if they have other CVR factors	64 (22.94)	76 (27.24)
No, I consider these patients as high CVR	82 (29.39)	81 (29.03)
Total	279 (100)	279 (100)
Therapeutic target for LDL-C for patients with	**T1DM and T2DMI**	**Moderate chronic kidney disease**
LDL-C levels < 55 mg/dL	10 (3.58)	38 (13.67)
LDL-C levels < 70 mg/dL	158 (56.63)	151 (54.32)
LDL-C levels < 100 mg/dL	106 (37.99)	85 (30.58)
LDL-C levels < 116 mg/dL	5 (1.79)	4 (1.44)
Total	279 (100)	278 (100)
Reasons to refer the patient to a specialist[III]		
Patient is not controlled on statin monotherapy	7 (1.60)	
Patient is not responding to treatment	64 (14.61)	
Patient has comorbidities that prevent him/her from responding to the treatment	106 (24.20)	
Patient has side effects from treatment	48 (10.96)	
Familial hypercholesterolemia or familial combined hyperlipidemia is suspected	205 (46.80)	
Other	8 (1.83)	
Total	438 (100)	

CVR (cardiovascular risk); HDL-H (high-density lipoprotein cholesterol); LDL-C (low-density lipoprotein cholesterol); T1DM (type 1 diabetes mellitus); T2DM (type 2 diabetes mellitus); TC (total cholesterol); [I]T2DM patient with 10 years duration, without organ damage and without other significant CVR factors; [II]patient with eGFR between 30-59 ml/min/1.73 m^2 and without other significant CVR factors; [III]multiple choice question where specialist had to choose one or more of the options given.

Physicians considered that 36.47% (SD: 17.75%) of their patients without established ASCVD did not achieve the lipid therapeutic goal. The most common lipid-lowering treatments prescribed were atorvastatin (24.37%-27.96%) and rosuvastatin (22.22%-24.19%) alone (See Supplemental Figure 1). Amongst those patients treated with statins, 37.23-47.06% were receiving the maximum dose of atorvastatin (40-80 mg/day) and 25.8-38.1% the maximum dose of rosuvastatin (20-40 mg/day) (Supplemental Table 3).

2019 ESC/EAS guidelines for the management of dyslipidaemia: primary care professionals' knowledge and degree of adherence

Of the participants who followed recommendations (97.13%), 83.03% followed the 2019 ESC/EAS guidelines, meaning that 80.65% of the total had adopted the new guidelines to their practice. Additionally, around 80% of physicians considered appropriate the new therapeutic targets for high or moderate cardiovascular risk. Regarding the treatment algorithm proposed by these guidelines, most of them reported following it to some extent (Figure 1).

Most physicians (91.76%) were classified as moderate or low adherent to the 2019 ESC/EAS guidelines, whereas the remaining 8.24% were in the high adherent group (details in Supplemental Table 4). Besides, the percentage of moderate and high adherent physicians was significantly higher among those who agreed with the 2019 ESC/EAS guidelines' therapeutic targets (p = 0.022). Supplemental Table 5 shows the subgroup analysis between adherence groups.

Barriers to achieving therapeutic targets (LDL-C), and actions to improve adherence to the guidelines

Barriers to achieving therapeutic targets

Participants believed that underestimating the patient's cardiovascular risk, and the reluctance to increase the dose of statins or to use combined therapy were the most critical physician-related barriers to achieving the lipid targets (Figure 2.A). The most important patient-related barriers were non-compliance with drug treatment and underestimating their illness (Figure 2.B).

Actions to improve adherence to dyslipidaemia management guidelines

The physicians considered that the discussion of patients' cases on the internet was the best action to improve adherence to dyslipidaemia guidelines (Figure 3).

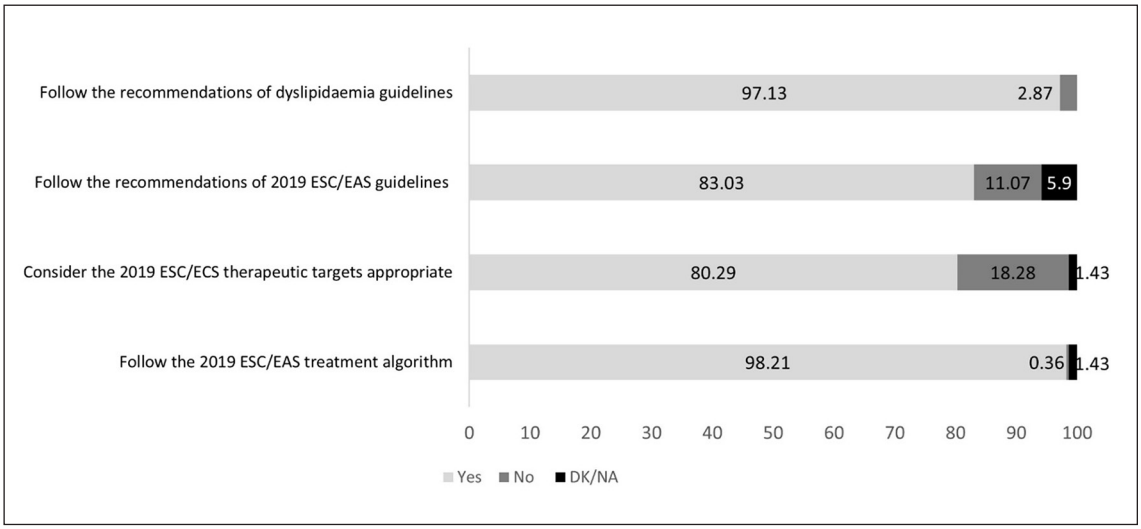

Figure 1. Knowledge and opinion of dyslipidaemia management guidelines. DK/NA (don't know/ no answer); ESC/EAS (European Society of Cardiology and European Atherosclerosis Society).

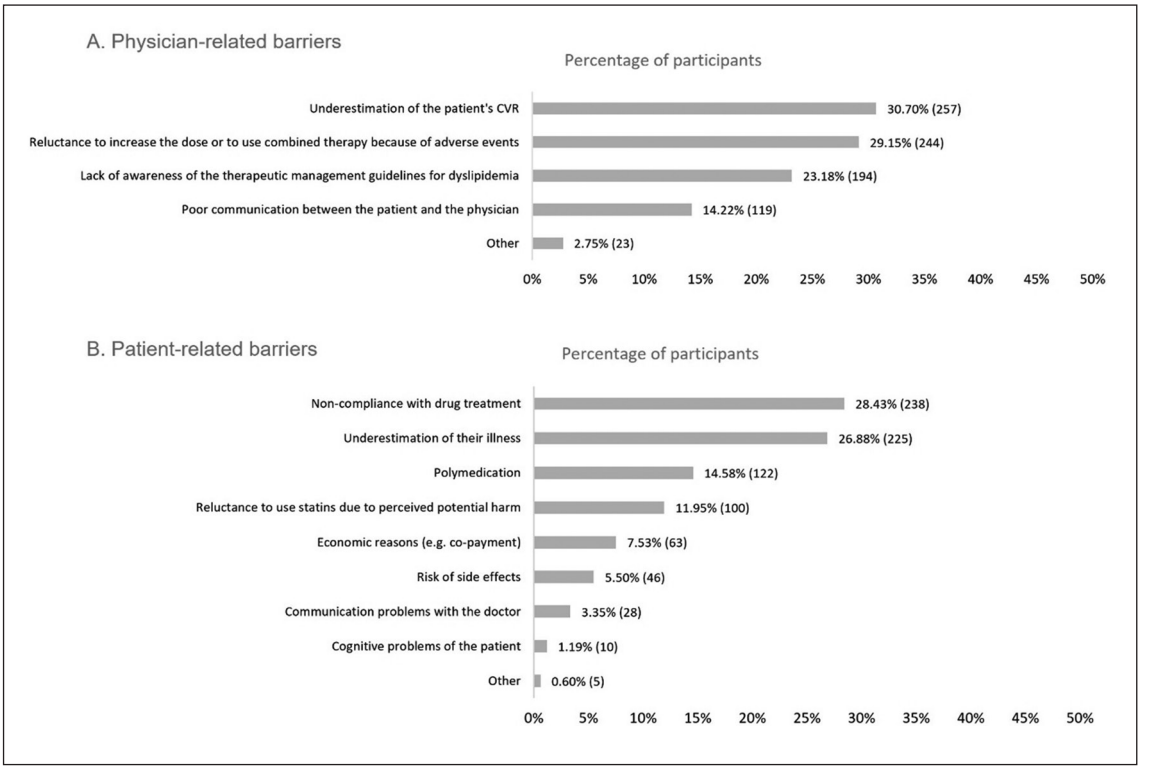

Figure 2. Barriers to the achievement of the lipid target related to physicians **(A)** and patients **(B)**. CVR (cardiovascular risk).

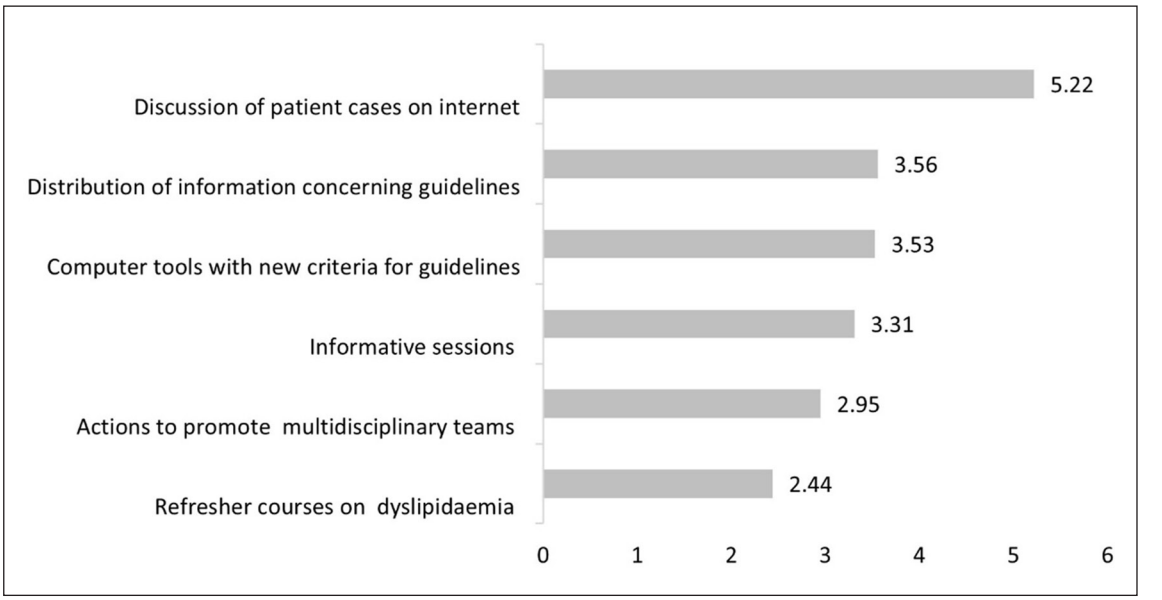

Figure 3. Actions to improve adherence to dyslipidaemia management guidelines. Ranked from a mean of 6 points (the most preferred) to 1 point (the least preferred)

Discussion

The ASCVD prevention is a key aspect of primary care and is mainly based on promoting a healthy lifestyle and treating modifiable cardiovascular risk factors, especially dyslipidaemia[6]. Most primary care physicians in our study stated that they made lifestyle recommendations to their patients without established ASCVD before prescribing lipid-lowering treatment, being in line with the 2019 ESC/EAS guidelines[11] and the statement by the Spanish Interdisciplinary Committee for Vascular Prevention (CEIPV)[20] and the recent Spanish Society of Arteriosclerosis guidelines[21].

As for the treatment of dyslipidaemia, the accurate assessment of the patient's cardiovascular risk is essential to decide on the subsequent therapeutic actions. Most physicians estimate cardiovascular risk in patients without established ASCVD regularly using the SCORE scale for low-risk cardiovascular risk populations. However, in its latest statement, the CEIPV[20] proposed recalibrating these tables as the cardiovascular mortality observed in this population was overestimated[22,23]. The updated SCORE algorithm(SCORE2[24]), was published in 2021 to avoid this overestimation and incorporated in the new ESC Guidelines on cardiovascular disease prevention[12].

Both the 2019 ESC/EAS guidelines[11] and the recent 2021 ESC Guidelines on cardiovascular disease prevention[12] have set therapeutic targets for LDL-C according to patients' cardiovascular risk levels (moderate-risk: < 100 mg/dl, high-risk: < 70 mg/dl, and very high-risk: < 50 mg/dl). These targets are based on the extensive evidence that shows that greater, earlier LDL-C reduction lowers the risk of cardiovascular events[8-10]. Most physicians in our survey currently followed these recommendations and considered these new therapeutic targets appropriate. However, when they were asked which LDL-C therapeutic targets best suited two high cardiovascular risk patients without ASCVD, 30% still adhered to the less strict ESC/EAS guidelines released in 2016[25] that recommended LDL-C values of <100 mg/dl for high-risk patients.

Physicians considered that a mean of 36.47% (SD: 17.75%) of their patients without established ASCVD did not achieve their therapeutic LDL-C goals. This percentage is lower than that observed in real-world studies for patients with established ASCVD, where 44.1-91.2% of them did not reach 2016 ESC/EAS guidelines LDL-C goals[13-18]. Furthermore, a recent multicenter study conducted in 18 different countries (including Spain)[26] showed that around 46% and 67% of patients did not achieve their 2016 and 2019 goals, respectively. This discrepancy between physicians' perception and real-world observations was previously pointed out by Fuster et al.[27]; in this study, 68.3% of primary care physicians considered more than 50% of patients with atherogenic dyslipidaemia achieved the therapeutic objectives.

The most common strategy to achieve LDL-C objectives is to use lipid-lowering treatment. When asked about this, the physicians acknowledged that over 60% of their patients with high cardiovascular risk were treated with monotherapy, mainly with atorvastatin or rosuvastatin. Besides, less than 40% of patients taking atorvastatin and rosuvastatin received the maximum statin doses, suggesting that a large percentage of high cardiovascular risk patients at the primary care level might remain on monotherapy or doses below those proposed by the 2019 ESC/EAS guidelines[11].

During the study period, the Spanish Society of Cardiology (SEC) released treatment algorithms for patients with[28] and without ASCVD[29] aimed to improve lipid control in Spain, Consisting of treatment options individualized to each patient's needs to ensure achieving LDL-C more rapidly. This approach might be especially interesting for primary care physicians as our results suggest that they are especially reluctant to intensify patients' treatment. This reluctance and underestimating patients' cardiovascular risk were the most critical barriers to achieving lipid objectives and are related to therapeutic inertia, which has been previously observed in specialized care in Spain[17, 30].

Finally, around half of the respondents were low adherents to the 2019 ESC/EAS guidelines. In this respect, only about 30% of physicians correctly answered the questions about the therapeutic choices for the clinical case studies. Both questions were related to the recommendation to treat patients with high potency statins and increase to the maximum tolerated dose when they are not achieving their therapeutic goals[11]. These adherence results are in keeping with the idea that integrating the 2019 ESC/EAS therapeutic algorithm into primary care practice in Spain

is still insufficient. The interviewees themselves recognized that the lack of awareness of the therapeutic management guidelines for dyslipidaemia –together with therapeutic inertia– was one of the main physician-related obstacles for achieving lipid targets.

Strengths and limitations

This study has some limitations. First, the ad-hoc questionnaire is not a standardized, validated questionnaire; hence, the results obtained may not be compared with or generalized to other locations. Second, the questionnaire might not have addressed all the aspects related to the management of dyslipidaemia from a primary care perspective; rather, we might have covered the most important, as a scientific committee composed of physicians with extensive experience in dyslipidaemia ensured the inclusion of the critical aspects connected with the treatment of this disease. Third, a convenience sampling technique was chosen to recruit the physicians. Although this sampling method can introduce bias, it was necessary to ensure that they had sufficient experience in the management of dyslipidaemia. Finally, extrapolating the present findings to other countries should be done with caution due to the possible influence of local treatment guidelines and the different degrees to which primary care physicians are involved in patient care. Despite these limitations, we believe the findings of our survey are meaningful in ours and similar contexts.

In conclusion, the results of this survey describe the current management of dyslipidaemia in Spain; most of the primary care physicians affirmed that they followed the 2019 ESC/AES guidelines for the management of dyslipidaemia however, some did not adhere to them especially to the therapeutic algorithm. Thus, although participants acknowledged these weak areas, they can still pose a significant barrier to achieving the 2019 ESC/EAS therapeutic goals in primary care settings.

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