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Lipid-lowering therapy and low-density lipoprotein cholesterol goal achievement in patients with acute coronary syndromes: The ACS patient pathway project

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A B S T R A C T

Background and aims: Post-acute coronary syndrome (ACS) patients are at very high risk for recurrent events and mortality, despite the availability of effective pharmacological approaches. Aim of this survey was to evaluate the compliance to ESC/EAS guidelines during the management of ACS patients and the effectiveness of secondary prevention in seven European countries.

Methods: By means of an online questionnaire, data on 2775 ACS patients (either acute case or follow-up patients) were collected, including data on lipid profile, medications, follow-up visit planning, screening for familial hypercholesterolemia.

Results: Lipid profiles were obtained for 91% of ACS patients in the acute phase, mostly within the first day of hospitalization (73%). During hospitalization, 93% of the patients received a lipid-lowering treatment; at discharge, only 66% of the patients received a high intensity statin therapy. At the first follow-up, most of the patients (77.6%) had LDL-C >70 mg/dL; among them, 41% had no change in their lipid-lowering therapies. Similar data were obtained during the second follow-up visit. The analysis of a subgroup of patients with at least 2 follow-up visits and known LDL-C levels showed that the percentage of patients at goal increased from 9% to 32%, and patients with LDL-C <100 mg/dL raised from 23% to 72%. Among acute cases, 44 were admitted with a diagnosis of familial hypercholesterolemia (FH); only 18% of the remaining patients were screened for FH.

Conclusions: Contemporary lipid management of very high CV risk patients is sub-optimal despite available treatments. Greater efforts are warranted to optimize cardiovascular prevention.

1. Introduction

Acute coronary syndromes (ACS) are a frequent clinical

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manifestation of coronary artery disease and include different types of events, such as unstable angina, and myocardial infarction with or without persistent ST-elevation on the ECG [1]. ACS remain a major cause of mortality and morbidity worldwide, despite a substantial progress in the prevention, treatment and management of these patients; in fact, post-ACS patients are at very high risk for recurrent events and mortality, despite the availability of optimal pharmacological treatments [2,3].

The benefit of statins in secondary prevention has been clearly demonstrated by a large number of clinical trials, and a meta-analysis of data from 170,000 patients showed that a more intensive statin therapy leads to a greater reduction in the incidence of major cardiovascular (CV) events (such as CV death, non-fatal myocardial infarction or ischemic stroke) compared with a moderate statin regimen [4]. For this reason, statins are recommended for all patients with ACS, should be started as early as possible, and should be continued after discharge [5]. For patients already on statin therapy before the event, statin dose should be increased (with the exception of individuals with intolerance to statins) [6]. Compared with previous guidelines, a more intensive reduction of LDL-C levels has been introduced in the new guidelines in secondary prevention for patients at very high risk (LDL-C reduction of $\geq$50% from baseline and an LDL-C goal of <55 mg/dL) [7]. These recommendations further extend the indications reported in the guidelines for the management of ACS, which indicate lipid-lowering as a major intervention in ACS patients and recommend to obtain a lipid profile as early as possible, and to re-evaluate it 4–6 weeks after the ACS event [6,8]. In patients who do not reach the LDL-C goal despite the highest tolerated statin dosage, ezetimibe is suggested as an add-on, as established by the IMPROVE-IT trial [9]. Moreover, the most recent anti-PCSK9 monoclonal antibodies (mAbs) can be considered for selected very high risk patients in whom LDL-C levels remain markedly elevated despite maximally tolerated statin and ezetimibe therapy [10]. The ODYSSEY OUTCOMES trial has in fact shown that targeting PCSK9 with alirocumab significantly reduces the risk of a composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization in patients who had a recent ACS (hazard ratio, 0.85) [11]. The highest absolute benefit of alirocumab was observed in patients who had a baseline LDL-C level $\geq$100 mg/dL [11].

Despite all the relevant indications provided for the treatment of patients with ACS, guidelines are only in part applied in everyday clinical practice. Several studies have, in fact, underlined an insufficient control of hypercholesterolemia in post-ACS patients, with most of them having LDL-C levels above the recommended target, despite improvement in the use of statin therapy for secondary prevention [12,13]. In addition, although the rate of initiation of lipid-lowering therapy is usually higher, the rates of statin uptritation or maximization (which associate with better clinical outcomes) are generally low [14]. These findings are suggestive of a non-optimal adherence to the guideline indications. In this context, surveys are an important tool to verify the real-life compliance of physicians to current guidelines, and allow to better define the gaps between the clinical practice and clinical recommendations. The EUROASPIRE V survey, which was conducted in patients who had been hospitalized for an acute event at least 6 months and at most 2 years prior to the interview, showed that most of them had an overall uncontrolled lipid profile, with a less than optimal management of LDL-C, which are far from the levels recommended by guidelines [15]. Our survey, which was conducted in 2018, was aimed at evaluating the compliance of cardiologists from seven European countries to guidelines for the management of dyslipidemia in patients at high CV risk (ACS patients), and the effectiveness of secondary prevention in these patients with respect to lipid lowering. Furthermore, previous studies have shown that among ACS patients the prevalence of familial hypercholesterolemia (FH) is higher than in the general population [16–20]; despite FH does not likely represent a risk factor in the post-ACS setting, we considered that ACS population represents an opportunity to increase the identification of patients with FH. For these reasons, we also evaluated the FH screening rate among patients in the acute phase.

2. Methods

The survey was performed in 7 European countries: France, Germany, Italy, Spain, United Kingdom, Switzerland and the Netherlands. Aim of this survey was to review the current clinical practice regarding the lipid management.

2.1. Recruitment process

Respondents were recruited via databases through a third party (commissioned by the sponsor to conduct the project) panel provider. The panel provider was briefed on the respondent type of interest (cardiologists), and eligible cardiologists from the panel were sent an e-mail to introduce the study and provide a link to the online survey. The respondents were asked to provide informed consent at the start of the online survey. As a standard procedure in market research, respondents received an incentive (based on fair market value and approved by the sponsor) for time spent to complete the survey. Based on data from 5 countries, the response rate (defined as the percentage of respondents who entered the survey among those invited) ranged from 28% to 64%. Research was double-blinded; participants and data were fully anonymized (participants cannot be identified and cannot identify the sponsor); there was no relationship between respondents and third party. The first part of the online survey was the 'screener', which determined whether the respondent matched the criteria we required for inclusion into the study.

Screening criteria for inclusion were: 1) interventional cardiologist or general cardiologist; 2) 3–35 years in practice as a cardiologist; 3) >70% of time spent in direct patient care; 4) >20 ACS patients treated per month. Cardiologists who matched the criteria and gave their consent then proceeded to the main survey.

2.2. Methodology

The main survey was administered as a 45-min online questionnaire that was completed independently by eligible respondents. The online questionnaire included a patient record form module in which each respondent provided data for the last 5 patients with ACS he/she has seen. Data was collected for the acute or the follow-up phase of the ACS journey, defined as follows:

- acute phase – data collected from hospital admission to discharge (patients who have been hospitalized and subsequently discharged within less than 1 month, with a hospitalization phase less than 7 days)
- follow up phase – data collected from discharge to 12 months of follow-up (patients discharged from hospital and receiving follow-up management within 12–18 after an ACS)

Online questionnaire did not allow for missing data. Data were collected during the period April–May 2018.

3. Results

The study enrolled a total of 2775 ACS patients, including 940 acute phase (34%) and 1835 follow-up patients (66%). Each country

recruited 500 patients, with the exception of Switzerland (125 patients) and the Netherlands (150 patients) (Supplemental Fig. 1).

A total of 555 physicians participated in this study; the sample (size and composition) was designed to be relevant and quantitatively meaningful to research objectives. Among participating physicians, 23% (N = 127) were interventional cardiologists and 77% (N = 428) general cardiologists. The distribution of physicians among the different countries involved in the study is represented in Supplemental Fig. 1.

Table 1 lists the patient characteristics. Mean age was 65.3y±12.5, and most patients were male (66.6%); many patients presented with co-morbidities, including hypertension (71.8%), obesity (28.5%) and diabetes (35.7%).

3.1. Acute phase

During the acute phase, 91% of the patients had lipid levels tested, with differences among participating countries, ranging between 83% in UK and 97% in Italy (Fig. 1 and Supplemental Table 1). Among the patients with lipid level tested, 73% patients were tested within the first day (31% at admission and 42% one day after admission), but 16% of the patients were tested after three or more days (average time 1.6 days) (Fig. 1 and Supplemental Table 1). In most cases, lipid levels were tested in fasting conditions (71%), but different countries showed significantly different percentages in this parameter, with 26% in the Netherlands up to >90% in Spain, Italy and France (Supplemental Table 1). LDL-C level was evaluated in 86% of the acute cases.

During hospitalization, 93% of the cases received a lipid-lowering treatment (LLT); among them, 37% were already under LLT, while 56% were statin-naïve patients (Fig. 1 and Supplemental Table 2). On average, statin therapy started at 2.3 days after admission, with 64% starting at day 1. Among the countries, statin therapy started after 1.4 days in Italy up to 3.8 days in Spain. At discharge, 67% received a high intensity statin (atorvastatin 40–80 mg or rosuvastatin 20–40 mg) with or without ezetimibe (Fig. 1); there was a great difference among the countries, with only 33% of patients receiving a high intensity statin ± ezetimibe in France versus 88% in UK. Low or moderate intensity statin ± ezetimibe was given to 25% of the patients (from 5% in UK up to 51% in France) (Supplemental Table 3).

Among patients who were not taking LLT at admission (56%, N = 528), 70% received high intensity statin therapy, of whom 8% also received ezetimibe in combination (Supplemental Table 4). Most (93%) of the patients admitted on high-intensity statin therapy alone were maintained on high-intensity statin ± ezetimibe regimen. Two-thirds of the patients admitted with low-to-moderate statin therapy were shifted to a high-intensity statin (Table 2).

At discharge, follow-up consultations were planned for 746 patients (79.4%), Italy and the Netherlands being the countries with the highest percentages of planned follow-up (93% and 94%, respectively) (Fig. 2 and Supplemental Table 5). However, only half of the patients had a rehabilitation/secondary prevention program planned during follow-up, with relevant differences among countries (28% Spain, 81% the Netherlands) (Fig. 2 and Supplemental Table 5). At discharge, only 64% of the patients received a letter for their physician containing lipid management guidance and therapeutic target indications (Fig. 2 and Supplemental Table 6).

Among acute cases, 44 were admitted with a known diagnosis of familial hypercholesterolemia (FH); only 18% (N = 171) of the remaining patients were screened for FH, ranging from 13.5% in the Netherlands to 20.6% in Spain (Supplemental Table 7). In the group of patients screened for FH, mean age was 62y (significantly younger than non-screened), 80% were male, 49% had a family history of premature cardiovascular disease, and most (93%) had LDL-C levels >70 mg/dL (of whom 46% had LDL-C levels >140 mg/dL), but only 36% were already on a LLT (Table 3). Among the patients screened, 76 (8% of acute patient sample) had a positive diagnosis for FH.

Table 1
Characteristics of the patients enrolled in the study.

Characteristics	N, (%)
N	2775
Acute cases	940
Follow-up cases	1835
Age [years], mean ± SD	65.3 ± 12.5
Male, N (%)	1848 (67%)
Smokers, N (%)	1988
Current smokers	1073 (39%)
Former smokers	915 (33%)
Comorbidities, N (%)	
Obesity	791 (29%)
Diabetes	990 (36%)
Hypertension	1993 (72%)
Familial hypercholesterolemia	208 (7%)
Previous CV event	295 (11%)
Stable CAD	398 (14%)
Polyvascular disease[a]	223 (8%)
Other	52 (2%)

CV = cardiovascular; CAD = coronary artery disease.
[a] Defined as the simultaneous presence of clinically relevant atherosclerotic lesions in at least two major vascular districts.

3.2. Follow-up

The time to the first follow-up from discharge was on average 3 months, with a low percentage of patients who had a follow-up 4–6 weeks after discharge (14%) (Fig. 3); the time to first follow-up visit varied among the countries (Supplemental Table 8). During the first follow-up consultation, a lipid test was performed in 86.4% of the patients; most of them (>60%) were evaluated for LDL-C, TC and HDL-C levels, with variations among the participating countries (Fig. 3 and Supplemental Table 9). For example, for LDL-C level measurement, ranged from 38% in the UK to up to 80% in Germany, Spain and Switzerland (Supplemental Table 9). Among patients with LDL-C levels tested at the first follow-up visit, only 22.4% (N = 224) had values < 70 mg/dL, 37.8% (N = 377) had values in the range 70–99 mg/dL, and 40% (N = 397) had values > 100 mg/dL (Fig. 3). This last percentage was highly variable among countries, ranging from 18% in Switzerland, to 54% in Italy (Supplemental Table 10). As a result, 77.6% (N = 774) of the patients tested at first follow-up had LDL-C> 70 mg/dL (ranging from 50% in France up to 92% in Germany). When data were analyzed based on the recently released ESC/EAS guidelines [7], which recommend an LDL-C goal of <55 mg/dL for very high risk patients in secondary prevention, only 10% of post-ACS patients had their LDL-C levels <55 mg/dL at first follow-up, which increased up to 16% at third follow-up; even lower was the percentage of patients reaching levels <40 mg/dL (Supplemental Fig. 3). Of note, most of the patients who achieved these goals were from France.

When considering patients not at goal, 59% had their therapies adjusted, either by increasing the dose of the same drug, or by adding another lipid-lowering agent, or switching to a different treatment (Fig. 3 and Supplemental Table 11); the remaining 41% had not change in treatment regimen or dose. At the second follow-up visit (N = 626), 68% of the patients (N = 423) were still not at goal (LDL-C >70 mg/dL), but with differences among countries, ranging from 44% in France up to 86% in UK (Fig. 4 and Supplemental Table 12). Therapies remained unchanged for 61% of not-at-goal patients (Fig. 4 and Supplemental Table 13). At the third

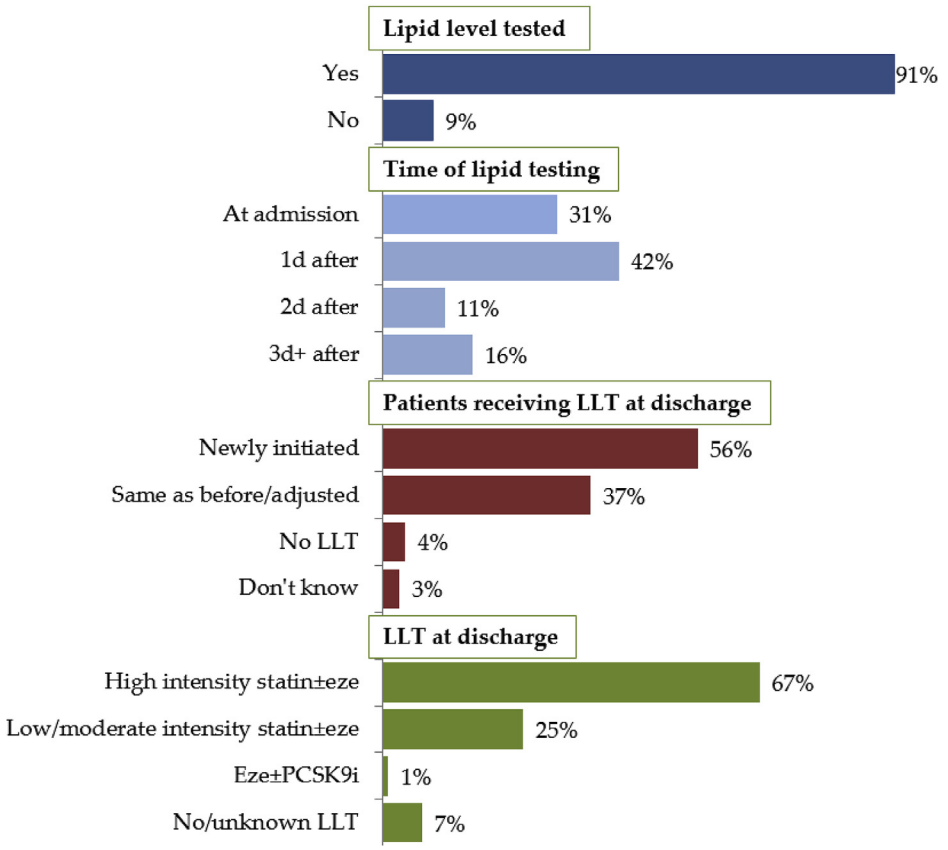

Fig. 1. Percentages of patients who had lipid levels tested and pharmacological approaches during acute phase. LLT: lipid-lowering therapy.

Table 2
Pharmacological approach in acute ACS patients without or with low/moderate intensity statin at admission.

Therapies at admission and after the acute event	N (%)
Patients without LLT at admission	528
started high-intensity statins (±ezetimibe)	370 (70.1%)
started low/moderate-intensity statins (±ezetimibe)	147 (27.8%)
started other LLT	6 (1.1%)
no LLT therapy	0 (0%)
don't know	4 (0.8%)
Patients with low/moderate-intensity statins at admission	222
started high-intensity statins (±ezetimibe)	148 (67.6%)
maintained on low/moderate-intensity statins (±ezetimibe)	68 (30.6%)
started other LLT	4 (1.8%)
no LLT therapy	0 (0%)
Patients with high-intensity statin at admission	72
started high-intensity statins (±ezetimibe)	67 (93.0%)
started low/moderate-intensity statins (±ezetimibe)	3 (4.2%)
started other LLT	2 (2.8%)
no/unknown LLT	0 (0%)

follow-up visit (N = 271), 62% (N = 168) of the patients were still not at goal (LDL-C >70 mg/dL) and most of them (67%) had not changed their pharmacological therapies (Fig. 4).

The analysis of a subgroup of patients with at least 2 follow-up visits with known LDL-C levels showed that, from the acute phase to the second visit, the percentage of patients at goal (<70 mg/dL) increased from 9% to 32%, and patients with LDL-C <100 mg/dL raised from 23% to 72% (Fig. 5a). This was probably mostly driven by the increased proportion of patients treated with a more effective therapy: while the percentage of patients on statin monotherapy was reduced, there was an incremental increase in those treated with a combination statin + ezetimibe (from 14% to 33% for the combination with high-dose statin, and from 0% to 9% for low/moderate intensity statin) (Fig. 5b). More importantly, the percentage of patients with LDL-C≥140 mg/dL was dramatically reduced (from 46% during acute phase to 7% at the second follow-up), and, overall, the percentage of patients with LDL-C≥100 mg/dL decreased from 77% to 27% (Fig. 5a).

Among the 998 patients with LDL-C tested at the first follow-up, 291 (29%) presented with values > 140 mg/dL, or LDL-C in the range 100–139 mg/dL in the presence of high risk factors despite already being on high-intensity statin ± ezetimibe or low/moderate statin + ezetimibe. These patients would have been eligible for therapy with anti-PCSK9 mAbs, based on the most recent recommendations from ESC/EAS Task force [10]. Only 14 of them were on anti-PCSK9 therapy at their first follow-up (Supplemental Fig. 2).

The survey also asked to indicate the LDL-C goal for the described patients. Data collected from this point show that for most of patients in the acute phase as well as for the follow-up phase, the LDL-C goals set by the cardiologists ranged between 70 and 99 mg/dL (Fig. 6). Only a small percentage of cardiologists gave an indication for an LDL-C goal "as low as possible" (Fig. 6).

4. Discussion

This survey, which was undertaken before the release of new ESC/EAS guidelines for the management of dyslipidemia, aimed at evaluating the compliance of cardiologists to guidelines during management of patients with an ACS, either during the acute phase and at follow-up. The main result is an overall sub-optimal lipid management and a lack of compliance with guidelines by the physicians. Several clinical trials have shown that early statin

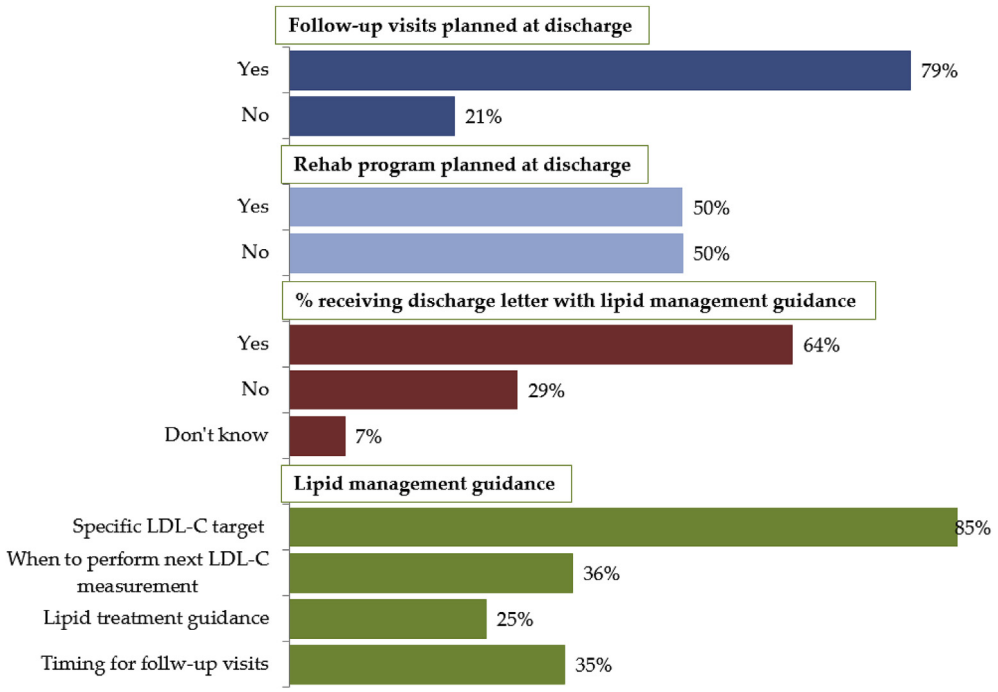

Fig. 2. Structured follow-up pathway: follow-up by physician, rehabilitation program, discharge letter with therapeutic targets and lipid management guidance.

Table 3
Subgroup of patients tested for FH.

Characteristics	N (%)
N	171
Age [years], mean ± SD	61.8 ± 11.5
Gender, N (%)	
Male	136 (79.5%)
Female	35 (20.5%)
Family history of premature[a] CV, N (%)	83 (48.5%)
LDL-C levels**, N (%)	
<70 mg/dL	9 (6.3%)
70–99 mg/dL	20 (14.1%)
100–139 mg/dL	47 (33%)
≥140 mg/dL	66 (46.5%)
Receiving LLT at admission, N (%)	61 (36%)

[a] Men: <55 years; women: <60 years; **data on 142 patients.

therapy reduces the risk of death or major cardiovascular events in patients with a recent ACS [21,22]. Moreover, cholesterol-lowering therapies are effective in secondary prevention [23]. Finally, a more intensive LLT induces a larger reduction of CV risk compared with less intensive regimens [4]. Based on these observations, the most recent guidelines for the treatment of ACS indicate the use of high intensity statin therapy in all patients with acute myocardial infarction (unless contra-indicated), and to obtain a lipid profile as early as possible after admission, which should be re-evaluated 4–6 weeks after the CV event [6] This will help to evaluate whether the pharmacological approach prescribed during hospitalization is appropriate, allowing for possible therapy adjustments. As patients with ACS are at very high CV risk, the pharmacological approach must aim to an LDL-C reduction of ≥50% from baseline, with an LDL-C goal of <55 mg/dL (which may be lowered to a goal of <40 mg/dL for patients experiencing a second vascular event within 2 years) [7].

In this survey, however, we observed that not all patients with an ACS had a lipid testing during the acute phase, and the percentage of those not tested varied widely among the countries included in the study. In fact, the percentage not tested was low in Italy (3%) but much higher in UK (17%). Furthermore, only 86% of acute phase patients had had their LDL-C levels measured. Finally, at first follow-up, the percentage of patients who had LDL-C levels measured was only 68%. This value may explain the high percentage of patients that were not at goal at first follow-up, with 78% of patients still having LDL-C levels >70 mg/dL, which was the threshold indicated by guidelines valid at the time of this survey; when these data were analyzed based on the targets of current guidelines [7], which recommend LDL-C levels <55 mg/dL or < 40 mg/dL, the percentage of patients who achieved these goals were even lower, which is suggestive of a significantly sub-optimal approach; even more worrisome is the observation that a large proportion of ACS patients had LDL-C levels >100 mg/dL not only at the hospitalization time, but also at follow-ups. Despite the very low percentage of patients reaching their LDL-C goal with the therapies established during hospitalization for the ACS event, at the first follow-up only 59% patients had their pharmacological therapies adjusted. Similar results were observed during the second and third follow-up visits. The lack of information regarding baseline LDL-C levels (i.e. before any lipid-lowering treatment), furthermore, did not help the cardiologists adjusting therapies efficiently to achieve the LDL-C goal. Moreover, many patients were discharged with an inappropriate pharmacological therapy, as only two-thirds of them received a high-intensity statin therapy, while ezetimibe in combination with a statin was only prescribed in a small number of patients, despite guideline recommendations to start high-intensity statin therapy as early as possible and to consider ezetimibe as add-on to statins [6]. Furthermore, a subgroup of patients presenting with elevated LDL-C levels despite high-intensity statin, with or without ezetimibe might have to be considered eligible for the treatment with PCSK9 inhibitors, in order to achieve a further reduction of the incidence of CV events [11,24]. Nevertheless, a very low number of patients were receiving an anti-PCSK9 monoclonal antibody at the first follow-up, which suggests that the use of these therapies is still low in the clinical

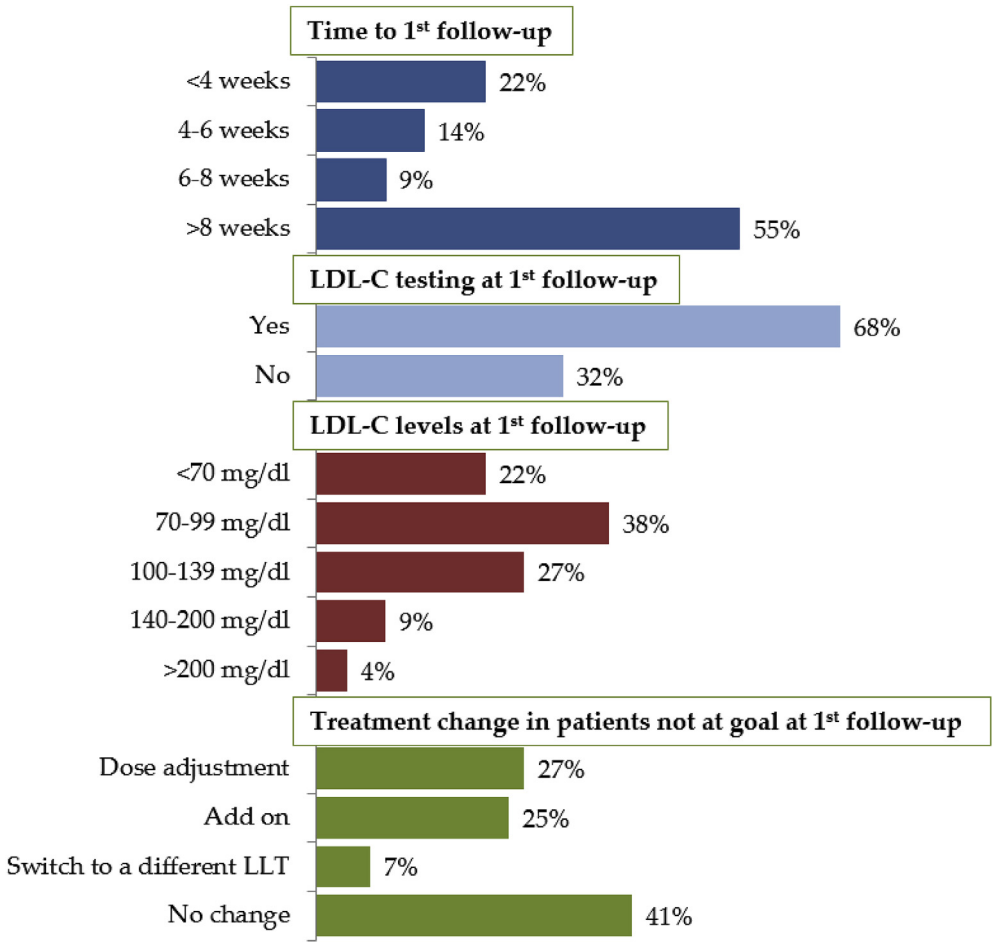

Fig. 3. Time to first follow-up, LDL-C profile and therapy changes in patients not at goal at 1st follow-up. LLT: lipid-lowering therapy; *>70 mg/dL.

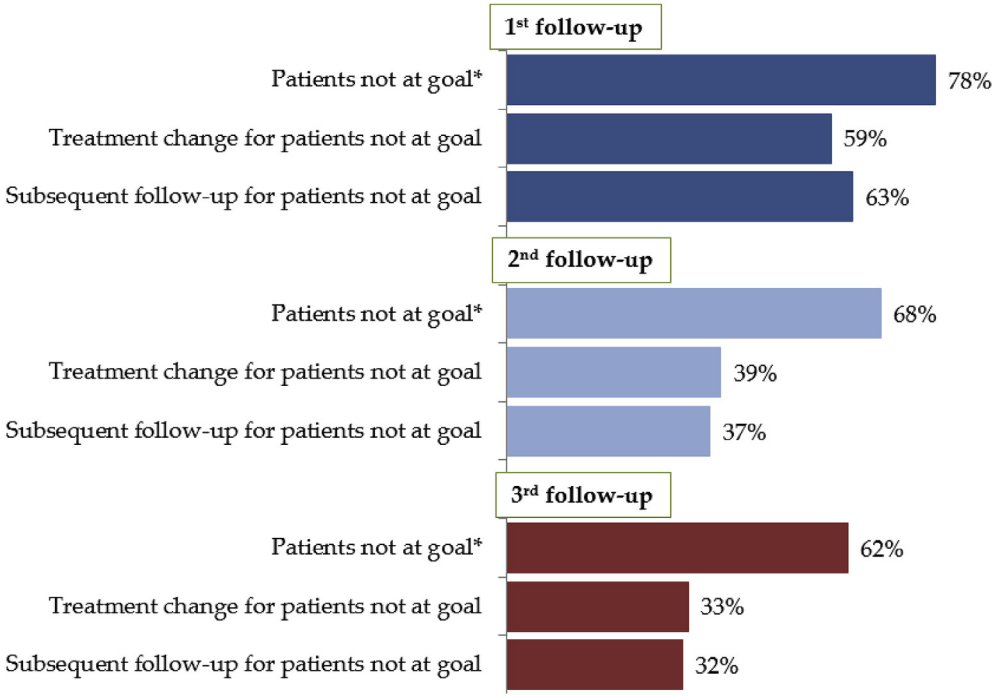

Fig. 4. Percentages of patients not at goal, treatment changes and subsequent follow-up planning during three follow-up visits. *>70 mg/dL.

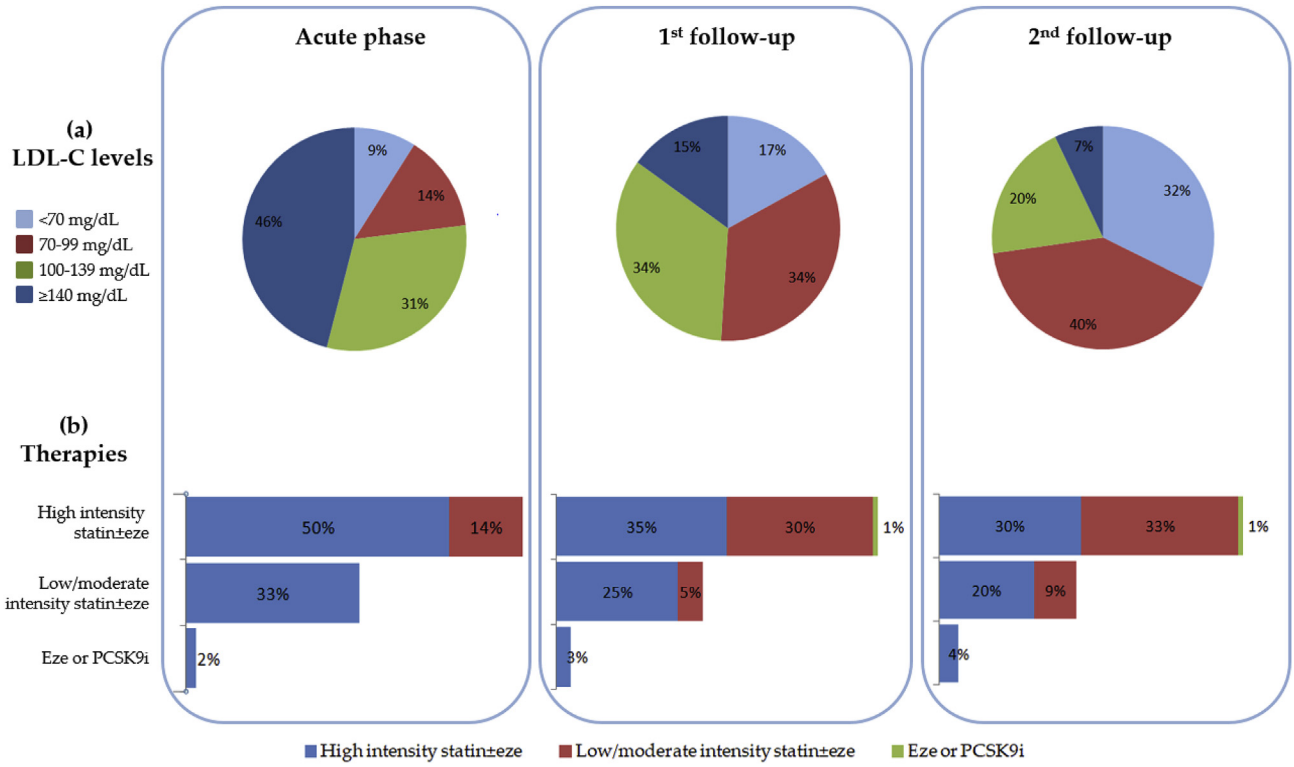

Fig. 5. LDL-C levels (a) and lipid-lowering therapies (b) in a subgroup of patients with at least 2 follow-up visits with known LDL-C levels. Eze: ezetimibe.

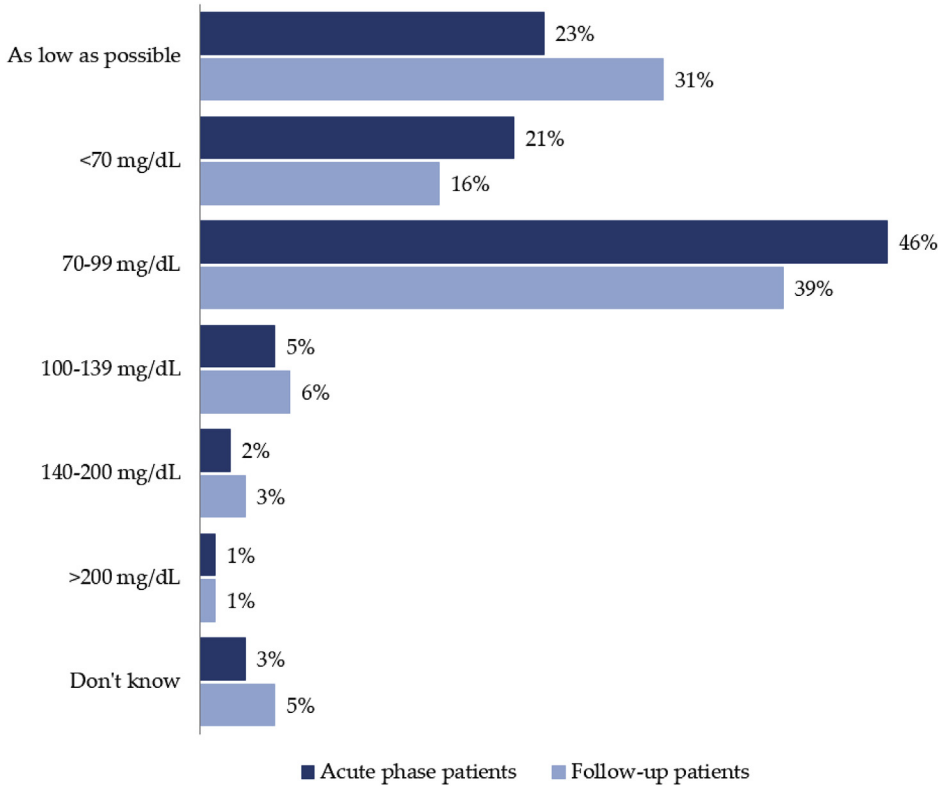

Fig. 6. LDL-C goal for acute phase and follow-up patients, as indicated by cardiologists during the survey.

practice. In agreement with the findings of our study, a recent study performed in ACS patients with a history of myocardial infarction or revascularization reported an overall underutilization of statins before hospitalization, with most patients not achieving LDL-C level

<70 mg/dL despite being at very high CV risk [25]. Although this survey was conducted before the release of new ESC/EAS guidelines, we must highlight that the percentage of patients able to achieve the new LDL-C set for this category of patients (now referred as to very-high risk), was very low. Similarly, the number of patients treated with a PCSK9 inhibitor in this survey was very low; in the new guidelines, for patients at very-high risk (such as those with a previous ACS) not achieving their goal on a maximum tolerated dose of statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended [7]. This new recommendation is based on the results of the ODYSSEY OUTCOMES study, that showed a significant reduction in the risk of major cardiovascular events in post-ACS patients treated with alirocumab [11], suggesting that an aggressive lipid-lowering treatment may safely reduce the CV risk in these patients. Furthermore, only few of the patients who had not their LDL-C levels well controlled were prescribed additional LLT at discharge [25]. Overall, it appears that cardiologists accept sub-optimal LDL-C levels for ACS patients. Our observations are in line with those reported by the EUROASPIRE V survey, which showed a suboptimal management of lipid profile in coronary patients, and a significant distance of LDL-C levels from those recommended for this very high risk category [15].

Patients with FH are at increased CV risk, due their lifelong exposure to elevated LDL-C levels, with CV complications at an early age, among which ACS represents a common clinical event [16–19,26]. On the other hand, among patients with an acute coronary syndrome, the prevalence of FH is significantly higher, (1 in 22 patients) [16–20], representing a great opportunity to identify patients with FH and initiate a cascade screening in family members. For this reason, patients presenting with an acute CV event, especially those experiencing the event at an early age, should be screened for FH, since patients with FH and CVD are classified by current guidelines as very-high risk, in order to both maximize the effects of the pharmacological approach and reduce cumulative lifetime risk, and identify family members who may be at high CV risk [26]. In the present study, however, only 18% were screened for FH; in this subgroup, only a very small number of patients were already under statin therapy despite having levels of LDL-C well above those recommended for their CV risk category. This finding further confirms the statement that FH is underestimated and undertreated [26], and there is compelling evidence that further efforts are required to improve the detection and management of this condition.

There may be some possible limitations in this study. As first, the survey was conducted only in seven countries of the European Union, thus it might not be representative of the entire EU. Being an online survey, we had not direct access to the patient records, thus all the evaluations were done based on the information provided by the physicians on the last 5 patients they have seen, which might be not representative of the type of patients commonly seen by the physicians. Another major limitation relies on differences in healthcare systems among participating Countries, which may have driven, or at least influenced, the therapeutic approach by physicians.

In summary, this multinational observational survey provides insights into the clinical profile and management of patients with ACS across Europe. Our study highlighted several gaps between evidence-based guideline recommendations [6,7] and clinical practice: about one fifth of patients were discharged without a planned follow-up visit; about one third of patients were discharged without a lipid management letter for their physician; half of the patients were discharged without a rehabilitation program; not all patients had LDL-C levels measured. These results clearly indicate that lipid management of very high CV risk patients is far from being optimal in contemporary conditions, and further efforts are required to correct this approach, and this is even more evident in light of the recommendations from the new guidelines. The use of appropriate strategies, which may include decision algorithms [27], will help to improve and facilitate the management of hypercholesterolemia in very high CV risk patients, such as those who experienced a recent ACS, in compliance with current guidelines.

CRediT authorship contribution statement

Ulf Landmesser: Supervision. **Angela Pirillo:** Conceptualization, Writing - original draft, Writing - review & editing. **Michel Farnier:** Supervision. **J. Wouter Jukema:** Supervision. **Ulrich Laufs:** Supervision. **François Mach:** Supervision. **Luis Masana:** Supervision. **Terje R. Pedersen:** Supervision. **François Schiele:** Supervision. **Gabriel Steg:** Supervision. **Marco Tubaro:** Supervision. **Azfar Zaman:** Supervision. **Pepe Zamorano:** Supervision. **Alberico L. Catapano:** Conceptualization, Supervision.

Declaration of competing interest

U. Landmesser has received speaker and advisory honorary from Sanofi, Amgen, Medicines Company, Berlin Chemie and Novartis; A. Pirillo has nothing to disclose; M. Farnier reports having received grants, consulting fees and/or honoraria and delivering lectures for Abbott, Akcea/Ionis, Amarin, Amgen, AstraZeneca, Daiichi-Sankyo, Eli Lilly, Kowa, Merck and Co, Mylan, Pfizer, Sanofi/Regeneron and Servier; JW Jukema/his department has received research grants from and/or was speaker (with or without lecture fees) on a. o.(CME accredited) meetings sponsored by Amgen, Athera, Astra-Zeneca, Biotronik, Boston Scientific, Dalcor, Daiichi Sankyo, Lilly, Medtronic, Merck-Schering-Plough, Pfizer, Roche, Sanofi Aventis, The Medicine Company, the Netherlands Heart Foundation, CardioVascular Research the Netherlands (CVON), the Netherlands Heart Institute and the European Community Framework KP7 Programme; U. Laufs reports fees for lectures/consulting from Amgen and Sanofi; F. Mach has nothing to disclose; L. Masana reports fees for lectures and advisory work from Amgen, Sanofi, MSD, Mylan, Daichii/Sankyo; T.R. Pedersen has nothing to disclose; F. Schiele reports personal fees from Sanofi-Aventis, Amgen, Pfizer, Astra Zeneca, MSD, BMS, and Bayer outside the submitted work; G. Steg reports research grant from Amarin, Bayer, Sanofi, and Servier and speaking or consulting fees from Amarin, Amgen, AstraZeneca, Bayer/Janssen, Boehringer-Ingelheim, Bristol-Myers-Squibb, Idorsia, Novartis, Novo-Nordisk, Pfizer, Regeneron, Sanofi, Servier; M. Tubaro reports speaker/consulting fees from Bayer, Bristol Myers Squibb and Pfizer; A. Zaman reports speaker/consulting fees and/or research grants from: Sanofi, Daiichi-Sankyo, BMS, Amgen, Pfizer, Boehringer, Bayer, Astra; P. Zamorano has nothing to disclose; A.L. Catapano reports grants from Sanofi, Regeneron, Merck, Mediolanum, grants from SigmaTau, Menarini, Kowa, Recordati, Eli Lilly, personal fees from Merck, Sanofi, Regeneron, AstraZeneca, Amgen, Sigma Tau, Recordati, Aegerion, Kowa, Menarini, Eli Lilly, Genzyme, outside the submitted work.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosissup.2021.01.009.

Appendix

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