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Attainment of optional low-density lipoprotein cholesterol goal of less than 70 mg/dl and impact on prognosis of very high risk stable coronary patients: a 3-year follow-up

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Objectives: We aimed to investigate the proportion of very high-risk patients with coronary heart disease (CHD) who achieve the optional low-density lipoprotein cholesterol (LDL-C) target of < 70 mg/dl (1.8 mmol/liter), the factors that influence the success rate and the impact on their prognosis.
Research design and methods: We enrolled 1337 consecutive patients with stable CHD. Fasting lipids were determined and all cardiovascular events were recorded during a median follow-up of 33 months.
Results: The majority (86.5%) of patients were taking lipid-lowering medication (95.5% statins), but only 50.6% had LDL-C levels of < 100 mg/dl (2.6 mmol/liter). In total, 941 (70.4%) patients were considered very high risk and only 15.1% of them had LDL-C levels of < 70 mg/dl. The use of intensive lipid-lowering medication was associated with 12-fold (95% CI 6.98 – 20.76; p < 0.001) higher possibility in achieving LDL-C levels of < 70 mg/dl. Attainment of LDL-C levels of < 70 mg/dl by patients at very high risk were independent predictors of all cardiovascular events (HR = 0.34, 95% CI 0.17 – 0.70; p = 0.003).
Conclusions: The vast majority of very high-risk patients do not achieve the optional LDL-C goal; this is mainly due to the suboptimal uptitration of statin dose and is translated into loss of clinical benefits.

Keywords: LDL cholesterol target, stable coronary heart disease, statins, very high-risk patients

Expert Opin. Pharmacother. (2011) ***12****(10):1481-1489*

1. Introduction

The management of dyslipidemia has been improved substantially over the last years mainly due to the increased use of statins [1-5]. The EUROASPIRE (European action on secondary prevention by intervention to reduce events) III survey conducted in 2006/2007 [1] showed that 88.8% of stable coronary heart disease (CHD) patients take hypolipidemic drug medication, while in EUROASPIRE II (1999/2000) [2] the proportion was 62.7% and in EUROASPIRE I (1995/1996) even lower (32.2%) [3]. The proportion of patients achieving cholesterol levels of < 175 mg/dl (4.5 mmol/liter; target set by the 2003 Joint European Societies guidelines on cardiovascular disease prevention) [4] increased to 53.8% in EUROASPIRE III from 23.3% in EUROASPIRE II and 5.5% in EUROASPIRE I.

There are sufficient data indicating than intensive lipid-lowering medication is associated with additional clinical benefits compared with moderate lipid-lowering

10.1517/14656566.2011.591379 © 2011 Informa UK, Ltd. ISSN 1465-6566

medication [6-9]. In 2004, the US National Cholesterol Education Program (NCEP) Adult Treatment Panel III guidelines were updated and an optional target for low-density lipoprotein cholesterol (LDL-C) of < 70 mg/dl (1.8 mmol/liter) was set in coronary patients who are at 'very high' risk [10]. This very high-risk group includes stable CHD patients with additional risk factors such as diabetes mellitus, smoking or metabolic syndrome. In addition, patients who manifest CHD as an acute coronary syndrome (ACS) are considered as very high risk.

There are few data exploring the proportion of very high-risk patients with stable CHD that attain the optional LDL-C target of < 70 mg/dl (1.8 mmol/liter). It has been reported that only a small proportion of very high-risk patients (15 – 21%) are at the optional therapeutic goal of LDL-C < 70 mg/dl (1.8 mmol/liter) [11-14] and this failure is associated with worse prognosis [15]. In our study we examined i) the proportion of very high-risk patients with stable CHD who achieve the optional goal of LDL-C < 70 mg/dl (1.8 mmol/liter); ii) the factors that influence the success rate; and iii) the impact on their prognosis.

2. Methods

2.1 Study population

All stable CHD patients that attended the outpatient cardiologic department of four large hospitals in Athens (University General Hospital 'Attikon', Athens General Hospital, General Hospital of Nikea and Western Attica General Hospital) between 2006 and 2010 were asked to participate in the study. We initially screened 1880 patients of whom 1337 satisfied the selection criteria and made up the final sample. Subjects were included in the study if they had been previously hospitalized for ACS (> 6 months), had undergone coronary artery bypass graft (CABG; > 6 months) or had undergone coronary angiography for chest pain and there was a documentation of CHD. Coronary artery stenosis was defined as ≥ 50% reduction in lumen diameter of any of the three coronary arteries or their primary branches.

Exclusion criteria were ACS or CABG within the previous 6 months, clinical evidence of heart failure (≥ class II according to the New York Heart Association), age > 75 years, chronic renal failure (creatinine levels > 2 mg/dl, 176.8 μmol/liter), coexistent malignancy or inflammatory disease.

All patients underwent clinical examination and special attention was paid to reporting the risk factors and their medication. The following definitions were used: hypertension, blood pressure ≥ 140/90 mmHg [16] and/or antihypertensive treatment; diabetes mellitus, fasting plasma glucose > 125 mg/dl (6.9 mmol/liter) [17] and/or glucose-lowering treatment and hypercholesterolemia, total cholesterol > 200 mg/dl (5.2 mmol/liter) and/or lipid-lowering agents. Intensive lipid-lowering medication was considered a medication that could achieve an LDL-C lowering of > 50% and this included the use of rosuvastatin 20 – 40 mg, atorvastatin 40 – 80 mg, simvastatin 80 mg daily or the combination of a statin at moderate or high dose with ezetimibe, bile acid sequestrant or niacin. The remaining modes of hypolipidemic treatment comprised the moderate or mild lipid-lowering medication. Smoking habits were recorded and body mass index (weight in kg/height^2 in meters) was also evaluated. Metabolic syndrome was defined according to the American Heart Association and National Heart, Lung, and Blood Institute definition [18]. Among stable CHD patients, very high risk patients were defined as those who were current smokers, had diabetes mellitus, metabolic syndrome or combined these characteristics. In addition, dietary habits, depressive symptomatology and physical activity were reported.

A special validated diet score that assesses adherence to Mediterranean dietary pattern was calculated [19]. The score is derived by a questionnaire that includes nine major food groups (nonrefined cereals, fruit, vegetables, legumes, potatoes, fish, meat and meat products, poultry, full-fat dairy products), as well as olive oil and alcohol intake. Each question is scored on a scale of 0 to 5 according to the frequency of food consumption per week, and the diet score ranges between 0 and 55. Higher values of this diet score indicate greater adherence to the Mediterranean diet.

Depressive symptomatology was assessed by a translated version of Zung Depression Rating Scale (ZDRS), a valid and sensitive research tool in measuring the severity of depression [20-22]. ZDRS consists of 20 items covering affective, psychological and somatic symptoms [20]. The patient specifies the frequency with which the symptom is experienced. Each question is scored on a scale of 1 to 4 (a little of the time = 1, some of the time = 2, a good part of the time = 3, or most of the time = 4) and the score ranges between 20 and 80.

Physical activity was assessed by a translated short version of the International Physical Activity Questionnaire (IPAQ), as index of weekly energy expenditure using frequency (times/week), duration (min/time) and intensity of physical activity. The IPAQ measures are expressed as metabolic equivalents (MET)-minutes.week^{-1} [23]. MET is defined as 3.5 ml $O_2 \times kg^{-1} \times min^{-1}$. We used the following MET estimates of IPAQ: vigorous physical activity = 8 MET, moderate = 4 MET, walking on average = 3.3 MET and sitting = 0 MET. For calculating the overall MET physical activity, each category was multiplied with its special MET estimate value. IPAQ has reasonable measurement properties for monitoring population levels of physical activity [23,24].

Patients were followed up by telephone interview by trained cardiologists. When a patient was not found, data were obtained by telephone interview with family members or the treating physician. All cardiovascular events (cardiovascular death, ACS, revascularization procedure due to clinical deterioration, stroke or arrhythmic event) were recorded.

The study was approved by the ethics committee of our institution and all subjects gave their informed consent.

2.2 Biochemical measurements

Peripheral blood samples were collected from patients after overnight fast between 0800 and 1000 h for assessing plasma concentrations of lipids. Total cholesterol and triglycerides were measured within 48 h by an enzymatic method in a Dimension of DATE BEHRING analyzer (Date-Behring Marburg GmbH, Marburg, Germany). High-density lipoprotein cholesterol (HDL-C) was assayed with the direct method of DATE BEHRING. LDL-C was calculated according to the Friedewald formula: LDL-C = total cholesterol - (triglycerides/5 + HDL-C).

2.3 Statistical analysis

Continuous variables were expressed as mean ± SD. Differences between means were compared with unpaired Student's t test and associations between categorical variables were tested using the chi-square test. Odds ratio (OR) and 95% confidence intervals (CIs) were calculated using logistic regression analysis. In univariate analysis, variables having significant association with dependent variable ($p < 0.05$) were inserted in a multivariate analysis model. Hazard ratio (HR) and corresponding 95% CIs were also calculated using Cox proportional hazards models. Event-free survival was analyzed by the Kaplan–Meier method and the log-rank test was used for the comparisons between groups. A p value of < 0.05 was considered significant. The SPSS version 13 (SPSS, Inc., Chicago, USA) statistical package was used.

3. Results

3.1 Risk factors status at interview

Table 1 presents the baseline characteristics of the population. The prevalence of metabolic syndrome, overweight and obesity was 47, 50.2 and 33.1%, respectively. In addition, 46% of the patients were recruited by a university hospital and 21.2% had a high educational (tertiary) level.

3.2 Lipid-lowering medication and achievement of LDL cholesterol < 100 mg/dl (2.6 mmol/liter)

Regular lipid-lowering medication was taken by 1157 patents (86.5%). The vast majority (95.5%) were taking statins either as monotherapy (86.4%) or as combination therapy (9.1%) with ezetimibe, bile acid sequestrant, fibrates or nicotinic acid. The rest were taking a non-statin hypolipidemic drug as monotherapy. The use of hypolipidemic drugs was favored by the history of CABG or percutaneus coronary intervention (PCI), higher educational level of the patient and attendance at a university hospital (**Table 2**). By contrast, higher ZDRS score was associated with lower possibility of using lipid-lowering medication.

The proportion of patients with LDL-C levels of < 100 mg/dl (2.6 mmol/liter) was 50.6%. **Table 3** shows the factors that influenced the achievement of the LDL-C target. The use of hypolipidemic drugs, higher educational level and male gender were independent predictors of having LDL-C levels of < 100 mg/dl (2.6 mmol/liter), while smoking was associated with a 50% lower possibility.

3.3 Very high-risk patients and achievement of the optional target of LDL-C of < 70 mg/dl (1.8 mmol/liter)

Of the studied population, 941 patients (70.4%) were considered very high risk. These patients were current smokers (43.6%) or diabetic (47.4%) or had metabolic syndrome (65%). Of the very high-risk patients, 142 (15.1%) had LDL-C < 70 mg/dl (1.8 mmol/liter). **Table 4** shows the factors that influenced the achievement of this target. The use of hypolipidemic drugs was associated with 2.8 times higher possibility in achieving the LDL-C goal, while smoking was associated with a 55% lower possibility.

Finally, patients on lipid-lowering medication were divided into two groups: those receiving intensive and those receiving moderate or mild lipid-lowering medication. Of those on hypolipidemic drug treatment, only 16% were on intensive lipid-lowering medication. In a logistic regression model that included the very high-risk patients on lipid-lowering medication (n = 826; **Table 5**), the use of intensive lipid-lowering medication was associated with 12 times (CI 6.98 – 20.76; $p < 0.001$) higher possibility in achieving the LDL-C target of < 70 mg/dl (1.8 mmol/liter).

3.4 Predictors of cardiovascular events among very high-risk patients during follow-up

The median period of follow-up was 33 months (interquartile range: 21 – 40 months). Follow-up data were not obtained in 151 patients owing to several reasons (wrong addresses, denied to participate, etc.), while 16 patients whose death was considered noncardiovascular were excluded. Therefore, analysis was confined to 1170 coronary patients of whom 251 (21.5%) presented cardiac events. Of these, 48 died (cardiovascular death; 4.1%), 106 developed ACS (9.1%), 65 (5.6%) had a revascularization procedure as a result of clinical deterioration, 4 had a stroke (0.32%) and 28 (2.4%) presented an arrhythmic event. Multivariate Cox regression analysis showed that achievement of LDL-C levels of < 70 mg/dl (1.8 mmol/liter) by 809 patients at very high risk were independent predictors of all cardiovascular events (HR = 0.34, 95% CI 0.17 – 0.70; $p = 0.003$) after adjustment for conventional risk factors (**Table 6**). **Figure 1** shows the event-free cardiovascular event rate during the follow-up period according to the LDL-C goal of < 70 mg/dl (1.8 mmol/liter) among very high-risk patients with stable CHD.

4. Discussion

In our study we found that, despite the high proportion of coronary patients on hypolipidemic drugs, mainly statins, the management of hypercholesterolemia continues to be suboptimal as half of them failed to meet the LDL-C target

Table 1. Baseline characteristics of the study population (n = 1337).

Age (years)	61.2 ± 9.5
Males	1146 (85.7%)
Current smokers	409 (30.6%)
Hypercholesterolemia	1227 (91.8%)
Triglycerides	142.5 ± 83.2 mg/dl (1.61 ± 0.94 mmol/liter)
HDL cholesterol	43.1 ± 10.6 mg/dl (1.11 ± 0.27 mmol/liter)
Hypertension	872 (65.2%)
Diabetes mellitus	446 (33.3%)
Family history for CHD	473 (35.4%)
Ejection fraction of LV (%)	50.9 ± 11.2
Previous ACS	1069 (80%)
CABG or PCI	993 (74.3%)
Body mass index (kg/m^2)	28.8 ± 4.5
ZDRS score	36.7 ± 9.1
Dietary score	31.7 ± 5.1
Physical exercise (METs-min.week^{-1})	3334.5 ± 5663
Antiplatelet treatment	1200 (89.8%)
Lipid-lowering medication	1157 (86.5%)
Beta-blockers	1090 (81.5%)
ACE inhibitors or AT$_1$ blockers	867 (64.8%)

Data are presented as mean ± SD or %.
ACE: Angiotensin converting enzyme; ACS: Acute coronary syndrome; CABG: Coronary artery bypass grafting; CHD: Coronary heart disease; HDL: High-density lipoprotein; LV: Left ventricle; MET: Metabolic equivalent total; PCI: Percutaneous coronary intervention; ZDRS: Zung Depression Rating Scale.

of < 100 mg/dl (2.6 mmol/liter). The therapeutic gap was even greater among the very high-risk coronary patients of whom only 15% achieved the guideline-recommended optional LDL-C target of < 70 mg/dl (1.8 mmol/liter). Receiving intensive lipid-lowering medication and being a nonsmoker were associated with higher likelihood of achieving the optional LDL-C target. Finally, attainment of the optional LDL-C goal was associated with better clinical outcome during a 3-year follow-up of stable coronary patients at very high risk.

4.1 Lipid-lowering medication and achievement of LDL-C < 100 mg/dl (2.6 mmol/liter)

In our study, 86.5% of coronary patients were taking lipid-lowering medication. This is in accordance with the high proportion (88.8%) of coronary patients treated with hypolipidemic drugs in the EUROASPIRE III survey (2006/2007). Compared with data obtained 10 – 15 years ago, the improvement in the treatment of hypercholesterolemia is more than obvious because the proportion of patients on lipid-lowering medication has increased by at least two times [1,14,25]. Factors that favored the use of hypolipidemic drugs in our population were the history of CABG or PCI, patients' higher educational level and attendance at a university hospital. We have previously reported that coronary patients with a history of coronary intervention are more likely to receive hypolipidemic drugs [25]. This may be due to the closer follow-up of these patients and the better perception of the severity of their disease, which might improve patients' adherence to drug treatment. It has also been shown that highly educated people are more likely to receive lipid-lowering medication than people with a low educational level [26,27]. In addition, there is some evidence that university hospitals offer a better quality of care, which might explain the higher prescription rate of hypolipidemic drugs in the university compared with the nonuniversity hospitals in our study [28]. Depression had a negative impact on receiving hypolipidemic treatment and this is in accordance with previous studies that have reported that depression is associated with medication nonadherence [29,30].

Despite this impressive increase in the prescription of lipid-lowering medication, only 50% of our coronary patients had LDL-C levels of < 100 mg/dl (2.6 mmol/liter). A similar degree of LDL-C target achievement was reported by the EUROASPIRE III [1]. In the NEPTUNE (NCEP evaluation project utilizing novel e-technology) II survey conducted in USA in 2003 [11], 57% of the coronary patients achieved the LDL-C treatment goal; while in Asians the goal attainment was lower, ranging between 30 and 38% [31,32]. In the CEPHEUS (centralized pan-European survey on the undertreatment of hypercholesterolemia) survey, conducted in eight European countries, the proportion of patients on lipid-lowering drugs for ≥ 3 months who reached the LDL-C target was 49.7% [12,33].

In our study, the use of hypolipidemic drugs, higher educational level of the patient and male gender were independent predictors of achieving the LDL-C target, while smoking was associated with a 50% lower likelihood of reaching the goal. Similar to our results, CEPHEUS [33] and EUROASPIRE [34] surveys reported that female gender was associated with an inverse likelihood of achieving LDL-C targets.

4.2 Very high-risk patients, achievement of LDL-C < 70 mg/dl (1.8 mmol/liter) and prognosis

A significant proportion of the coronary patients fulfilled the criteria of very high-risk patients. In particular, 7 out of 10 patients were at very high risk. Similarly, in the NEPTUNE II survey, among 1447 patients with cardiovascular disease 75% were classified as very high risk [11]. Therefore, the majority of the coronary patients were eligible for achieving the optional LDL-C target of < 70 mg/dl (1.8 mmol/liter).

In our study, only a small proportion (15.1%) of these patients achieved this target. This finding is consistent with other studies. In particular, in the NEPTUNE II survey [11], among very high-risk patients, 17.8% had an LDL-C level of < 70 mg/dl (1.8 mmol/liter), while in a prospective study [13] of 1968 diabetic patients with cardiovascular disease, 20.8% reached the goal. In the more recent CEPHEUS-Greece survey the proportion of very high-risk patients at goal was 14.7% [12].

Table 2. Multivariate logistic regression analysis: predictors of receiving hypolipidemic drug treatment patients with stable coronary heart disease (n = 1337).

Predictors	OR	95% CI	p
CABG or PCI	4.03	2.74 – 5.9	< 0.001
Hospital of attendance (university vs nonuniversity)	2.69	1.76 – 4.1	< 0.001
Education level (tertiary vs nontertiary)	3.05	1.61 – 5.78	0.001
Metabolic syndrome	0.84	0.57 – 1.24	0.387
Sex (male vs female)	0.67	0.39 – 1.16	0.153
ZDRS score	0.96	0.95 – 0.98	0.001

CABG: Coronary artery bypass grafting; CI: Confidence interval; OR: Odds ratio; PCI: Percutaneous coronary intervention; ZDRS: Zung Depression Rating Scale.

Table 3. Multivariate logistic regression analysis: predictors for achieving LDL cholesterol levels of < 100 mg/dl (2.6 mmol/liter) in patients with stable coronary heart disease (n = 1337).

Predictors	OR	95% CI	p
Hypolipidemic drug	2.59	1.71 – 3.93	< 0.001
CABG or PCI	1.24	0.91 – 1.69	0.175
Hospital of attendance (university vs nonuniversity)	1.09	0.83 – 1.43	0.529
Educational level (tertiary vs. nontertiary)	2.05	1.46 – 2.90	< 0.001
Metabolic syndrome	0.96	0.73 – 1.26	0.762
Sex (male vs. female)	1.74	1.15 – 2.63	0.009
ZDRS score	0.99	0.98 – 1.01	0.565
Marital status (married vs. nonmarried)	1.30	0.85 – 1.99	0.224
Current smoking	0.50	0.37 – 0.67	< 0.001

CABG: Coronary artery bypass grafting; CI: Confidence interval; LDL: Low density lipoprotein; OR: Odds ratio; PCI: Percutaneous coronary intervention; ZDRS: Zung Depression Rating Scale.

Table 4. Multivariate logistic regression analysis: predictors for achieving LDL cholesterol levels of < 70 mg/dl (1.8 mmol/liter) in very high risk patients with stable coronary heart disease (n = 941).

Predictors	OR	95% CI	p
Hypolipidemic drug	2.81	1.15 – 6.9	0.024
CABG or PCI	0.75	0.39 – 1.09	0.200
Hospital of attendance (university vs nonuniversity)	1.02	0.63 – 1.68	0.929
Metabolic syndrome	1.74	0.98 – 3.10	0.078
Smoking	0.45	0.26 – 0.78	0.004
Diet score	1.03	0.98 – 1.08	0.233

CABG: Coronary artery bypass grafting; CI: Confidence interval; LDL: Low-density lipoprotein; OR: Odds ratio; PCI: Percutaneous coronary intervention.

As one would expect, the use of hypolipidemic drugs was associated with 2.8-fold higher likelihood of achieving the optional LDL-C target. By contrast, smoking was associated with a 55% lower possibility. This might be due to the more negative attitude of smokers toward behavioral changes and less compliance with their medication [35]. In addition, smoking is associated with higher LDL-C levels, and this might contribute to the lower possibility of smokers of achieving the LDL-C target [36,37].

The importance of the appropriate dose of statins in achieving the optional and more stringent LDL-C goal of < 70 mg/dl (1.8 mmol/liter) was demonstrated by comparing the intensive with the nonintensive lipid-lowering medication. In multivariate analysis, intensive treatment was associated

Table 5. Multivariate logistic regression analysis: predictors for achieving LDL cholesterol levels of < 70 mg/dl (1.8 mmol/liter) in very high risk patients receiving hypolipidemic treatment (n = 826).

Predictors	OR	95% CI	p
Hypolipidemic drug (intensive vs moderate or mild treatment)	12.04	6.98 – 20.76	< 0.001
CABG or PCI	0.77	0.44 – 1.34	0.352
Hospital of attendance (university vs nonuniversity)	1.58	0.92 – 2.71	0.101
Metabolic syndrome	1.70	0.93 – 3.13	0.083
Smoking	0.49	0.27 – 0.87	0.015
Diet score	1.04	0.99 – 1.09	0.112

CABG: Coronary artery bypass grafting; CI: Confidence interval; LDL: Low-density lipoprotein; OR: Odds ratio; PCI: Percutaneous coronary intervention.

Table 6. Cox regression analysis: predictors of all cardiovascular events among 809 very high-risk patients with stable coronary heart disease during a 3-year follow-up.

Predictors	HR	95% CI	p
Attainment of LDL-C goal < 70 mg/dl (1.8 mmol/liter)	0.34	0.17 – 0.70	0.003
Gender (male vs female)	0.71	0.47 – 1.11	0.113
Diabetes mellitus	0.97	0.69 – 1.35	0.854
Hypertension	1.31	0.90 – 1.91	0.159
Smoking	1.01	0.72 – 1.42	0.947

CI: Confidence interval; HR: Hazard ratio; LDL-C: Low-density lipoprotein cholesterol.

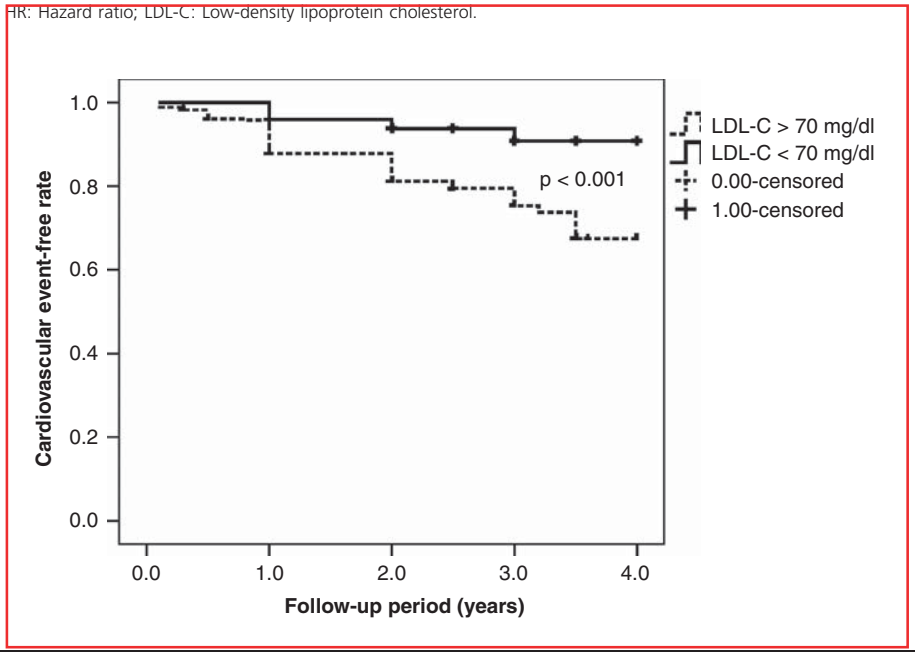

Figure 1. Kaplan–Meier survival estimates representing the cardiovascular event-free rate according to the achievement of the low-density lipoprotein cholesterol (LDL-C) target of < 70 mg/dl (1.8 mmol/liter) among very high-risk patients (n = 809).

with a 12-fold higher likelihood of achieving the goal. Therefore, submaximal doses of statins are an important reason of not achieving the optional LDL-C target. However, it should be emphasized that optimization of lipid-lowering medication and filling the gap between current guidelines and clinical practice is a complex issue with many interrelating factors such as patients' adherence to medication, physicians' awareness of guideline recommendations, cost of lipid-lowering drugs [38], etc. Another important factor is the high prevalence of unhealthy lifestyle trends among coronary

patients, such as smoking. In our study, one out of three patients were smokers, and smoking by itself puts stable coronary patients at very high-risk, setting the LDL-C target < 70 mg/dl (1.8 mmol/liter), and in addition adversely affects lipid levels, contributing to the gap between current practice and LDL-C goals.

The underuse of statins and failure to attain the current, recommended LDL-C target in very high-risk patients exposes them to a significant residual risk. In our study, achievement of the optional LDL-C goal was associated with fewer cardiovascular events during a 3-year follow-up of stable coronary patients at very high risk. In accordance with our data, Kim *et al.* reported that LDL-C levels of < 70 mg/dl (1.8 mmol/liter) were associated with a better clinical outcome in very high-risk patients treated with drug-eluting drugs [15]. Accordingly, there is sufficient evidence nowadays that intensive lipid-lowering therapy with statins in coronary patients at very high risk leads to extra clinical benefit. Therefore, it is imperative for the physicians to uptitrate the dose of statins aiming at an LDL-C level between 50 and 70 mg/dl (1.3 – 1.8 mmol/liter). Candidates for receiving the maximum dose of the most potent statins are all CHD patients at very high risk with pretreatment levels of LDL-C > 150 mg/dl (3.9 mmol/liter). However, maximal dose statins should be avoided in conditions that increase the risk of myopathy (advanced age, coadministration of cytochrome P-450 3A4 inhibitors, etc.), a dose-related side effect of statins [39,40].

4.3 Limitations

The main limitation of our study was the selection of coronary patients from outpatient cardiology hospital departments, and therefore the results cannot be extrapolated to all patients with CHD. However, this bias is likely to overestimate the extent to which coronary patients are being managed in general practice in relation to current guidelines where the majority of treating physicians are noncardiologists.

5. Conclusion

In conclusion, 7 out of 10 stable CHD patients are at very high risk for future cardiovascular events. This subgroup suffers from a wide therapeutic gap since < 20% achieve the optional LDL-C target of < 70 mg/dl (1.8 mmol/liter), and this is translated into loss of extra clinical benefits. Therefore, it is imperative for the physicians to bridge this therapeutic gap by carefully uptitrating statin dose until the target is achieved.

Declaration of interest

The authors state no conflict of interest and have received no payment in preparation of this manuscript.

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