FACULDADE DE MEDICINA DA UNIVERSIDADE DE COIMBRA

MESTRADO INTEGRADO EM MEDICINA – TRABALHO FINAL

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Control of cardiovascular risk factors in high-risk patients after a secondary prevention program

ARTIGO CIENTÍFICO

ÁREA CIENTÍFICA DE CARDIOLOGIA

Trabalho realizado sob a orientação de:

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ABRIL/2018

CONTROL OF CARDIOVASCULAR RISK FACTORS IN HIGH-RISK PATIENTS AFTER A SECONDARY PREVENTION PROGRAM

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RESUMO

Introdução: As doenças cardiovasculares continuam a constituir a principal causa de morte na Europa. Embora os fatores de risco cardiovascular (FRCV) sejam bem conhecidos e existam intervenções efetivas na sua prevenção, o seu grau de controlo continua a ser muitas vezes inadequado. O objetivo deste estudo foi avaliar a evolução e controlo dos FRCV em doentes de alto risco, 10 meses após a conclusão de um programa de prevenção secundária integrado no ensaio clínico FOURIER.

Métodos: Estudo retrospetivo com recurso à base de dados do ensaio clínico FOURIER desenvolvido na Unidade de Investigação em Cardiologia do Centro Hospitalar e Universitário de Coimbra, bem como aos processos clínicos dos doentes. Na última consulta do programa de prevenção secundária, variáveis demográficas e dados relativos aos hábitos tabágicos, peso, história de hipertensão arterial (HTA), dislipidemia, diabetes e eventos cardiovasculares anteriores foram registados. Os valores das variáveis adesão terapêutica, índice de massa corporal (IMC), tensão arterial (TA), hemoglobina glicada A1c (HbA1c), colesterol total e suas frações (HDL-c e LDL-c), triglicerídeos, lipoproteína (a) (Lp(a)), apolipoproteína (Apo) A1 e B e rácio Apo B/Apo A1 foram aferidos na última consulta e comparados com os obtidos 10 meses após o término do programa. Ocorrência de eventos cardiovasculares e necessidade de intervenção coronária percutânea (ICP) neste período foram também avaliadas.

Resultados: Foram incluídos neste estudo 121 doentes (n=121), com 81% da amostra constituída por doentes do sexo masculino e com uma média de idades de 67,72 anos. Na primeira avaliação, 6,6% dos doentes eram fumadores e 81% apresentavam um IMC superior ao normal. Todos os doentes tinham uma história de dislipidemia e 97,5% apresentavam um diagnóstico prévio de HTA. Adicionalmente, 84,3% sofreram um enfarte agudo do miocárdio (EAM) prévio, 18,2% um acidente vascular cerebral (AVC) anterior e 67,5% foram

submetidos a ICP previamente. Após 10 meses, verificou-se um aumento significativo dos valores de colesterol total, LDL-c, triglicerídeos, Apo B, rácio Apo B/Apo A1, Lp(a) e HbA1c. Uma redução estatisticamente significativa foi encontrada para os níveis de HDL-c e Apo A1. Alterações na TA e IMC não se mostraram estatisticamente significativas. Houve ainda uma diminuição da percentagem de doentes que atingiram os valores alvo de controlo para todos os FRCV, sendo esta redução estatisticamente significativa para as variáveis HDL-c e LDL-c. Foram realizadas duas ICP e foram registadas duas hospitalizações por AVC, duas por EAM e cinco por angina instável.

Conclusão: A manutenção dos resultados após a intervenção mostrou-se difícil para a maioria dos doentes, tendo sido verificada uma tendência de diminuição do controlo dos FRCV. Mais estudos são necessários para determinar como os programas de prevenção secundária podem integrar sistemas de suporte que possibilitem resultados mais duradouros e, desta forma, identificar a melhor forma de intervenção para otimizar o controlo dos FRCV.

Palavras-chave: Doenças cardiovasculares, fatores de risco cardiovascular, prevenção secundária.

ABSTRACT

Background: Cardiovascular diseases remain the leading cause of death in Europe. While cardiovascular risk factors (CVRFs) are well established and effective preventive interventions are available, they are frequently subject to inadequate control. This study aimed to assess the progress and control of CVRFs in high-risk patients ten months after the conclusion of a secondary prevention program within the FOURIER trial.

Methods: Retrospective study using the FOURIER trial database developed within the Cardiology Investigation Unit in the Centro Hospitalar e Universitário de Coimbra, as well as patient clinical charts. At baseline, demographic variables and data regarding smoking habits, weight, hypertension medical history, dyslipidemia, diabetes and prior cardiovascular events were recorded. Therapeutic compliance, body mass index (BMI), blood pressure (BP), glycated hemoglobin levels (HbA1c), total cholesterol and its fractions (HDL-c, LDL-c), triglycerides, lipoprotein (a) (Lp(a)), apolipoprotein (Apo) A1 and B, and Apo B/Apo A1 ratio were evaluated and compared at the baseline and ten months after. Cardiovascular clinical events and the need for myocardial revascularization in this period were also collected.

Results: 121 patients were analyzed, with 81% of the sample consisting of men and an average age of 67.72 years. At baseline, 6.6% of patients were smokers and 81% had a BMI higher than normal. All patients had a history of dyslipidemia, with 97.5% presenting prior hypertension diagnosis. Additionally, 84.3% previously suffered acute myocardial infarction (MI), 18.2% had experienced a stroke before, and 67.5% had been formerly submitted to PCI. After ten months, a statistically significant increase in total cholesterol, LDL-c, triglycerides, Apo B, Apo B/Apo A1 ratio, Lp(a) and HbA1c was observed. There was also a statistically significant reduction in HDL-c and Apo A1 levels. Changes in BP and BMI were not shown to be statistically significant. There was a decrease in the percentage of patients that reached

the control rate goals for all evaluated CVRFs, yet the contrast was only statistically significant for HDL-c and for LDL-c. Two PCIs were performed and there were two recorded hospitalizations for strokes, two for MI and five for unstable angina.

Conclusion: Maintaining the results post-intervention proved challenging for most of the patients, with a trend towards a decrease in risk factor control rate. Further research is required to determine how secondary prevention programs can use support systems for more lasting results, and thus identify the optimal intervention path for risk control.

Keywords: Cardiovascular diseases, cardiovascular risk factor, secondary prevention.

INTRODUCTION

Cardiovascular diseases (CVD) can be defined as pathologies of the heart and blood vessels, which can take the form of coronary heart, cerebrovascular, peripheral arterial, rheumatic and congenital heart diseases, as well as deep vein thrombosis and pulmonary embolism.[1]

With decades worth of studies in atherosclerotic diseases and progress in cardiovascular event prevention, the fact remains that the incidence of CVD and its associated costs are, to this day, a significant global public health challenge.[2,3]

CVD persists as the leading cause of death, representing 31% of global mortality. Each year, these diseases accounts for 45% of all deaths across Europe, surpassing 4 million. The majority of CVD fatalities can be attributed to coronary heart and cerebrovascular diseases, being responsible for 1.8 million and 1.0 million deaths, respectively. Furthermore, despite CVD-related mortality and disability-adjusted life years (DALYs) experiencing a decline in most European countries over the last decade, CVD is responsible for the loss of more than 64 million DALYs in Europe.[3] The global rate of CVD is expected to rise as the risk factors prevalence in countries previously deemed as low risk begins to increase.[4]

Therefore, determining more effective prevention strategies for such diseases has taken an imperative role.

Compelling evidence that atherosclerotic CVD is largely preventable has been provided by both epidemiologic studies and randomized clinical trials, leading many European cardiac societies to add provisions promoting secondary prevention within their practice guidelines.[5]

Over the past decade, secondary prevention programs for CVD have entailed increasingly complex interventions. The most recent programs to show effectiveness have focused on multidisciplinary approaches with self-care components tailored for each risk factor. The goal

is to stunt disease progression and lower the recurrence of cardiovascular events by controlling modifiable cardiovascular risk factors (CVRFs). As per behavioral change models, comprehensive lifestyle interventions are employed, focusing on helping patients quit smoking, make healthier dietary choices such as opting for a Mediterranean diet (high intake of vegetables, fruits, whole grains, nuts, fatty fish and olive oil), exercise regularly, control their weight and manage stress levels. Other integral parts of this strategy include effectively reaching target levels for blood pressure, lipids and glucose, as well as ensuring the appropriate prescription and adherence to cardioprotective drugs.[6,7]

Even with clinical guidance and effective interventions targeting these modifiable CVRFs, they are still too poorly implemented in clinical practice and the degree of self-control observed among patients continues to produce suboptimal results.[7]

Patients with atherosclerotic diseases, such as coronary heart disease, are the highest priority for clinical prevention and should be intensively treated to achieve the stablished goals.[5] Low-density lipoprotein cholesterol (LDL-c) treatment aims for values below 1.8 mmol/L or a 50% decline if baseline LDL-c is found to be between 70 and 135 mg/dL (1.8 – 3.5 mmol/L). Lifestyle intervention and concomitant high-intensity statins such as Atorvastatin 40-80 mg or Rosuvastatin 20-40 mg will generally result in an LDL-c reduction of over 50%. If target level is not reached with maximally dosed high-intensity statins, ezetimibe should be added. Adding PCSK9 (proprotein convertase subtilisin/kexin type 9) inhibitor in selected high-risk patients can also be considered for further reduction.[8]

Evolocumab is a fully human monoclonal IgG2 antibody that inhibits PCSK9, blocking the binding of this proprotein to the extracellular compartment of the LDL receptor (LDL-R). This keeps LDL-R lysosomal degradation from occurring, which results in an increased

receptor density on the hepatocyte surface. As such, there is an increased clearance of LDL-c, resulting in lower LDL-c blood levels.[9,10]

The clinical efficacy and safety of Evolocumab when in tandem with statin therapy in patients with clinically evident atherosclerotic CVD was assessed in a randomized, double-blind, placebo-controlled, multinational clinical trial, the Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk (FOURIER). This trial concluded that LDL-c levels were lowered to a median of 0.78 mmol/L (30 mg/dL) and the risk of cardiovascular events was reduced.[11]

The aim of the current study was to assess whether high-risk patients that underwent a specialized secondary prevention program were successful in sustaining their results from the FOURIER clinical trial in CVRFs control, ten months after its conclusion.

METHODS

Study design and sample

This is a retrospective study that resorts to the database for the FOURIER multinational clinical trial developed within the Cardiology Clinical Investigation Unit of the Centro Hospitalar e Universitário de Coimbra, as well as patient clinical charts.

In this study, 121 patients at high-risk for CVD were included, aged between 40 and 85 years, who attended and completed a specialized secondary prevention program over the course of three years (from February 2013 to November 2016), within the FOURIER clinical trial.

To be eligible to participate in the FOURIER trial, patients had to present clinically evident atherosclerotic cardiovascular disease at high risk for a recurrent event, determined as a history of acute myocardial infarction (MI), non-hemorrhagic stroke or symptomatic peripheral arterial disease. Furthermore, other inclusion criteria include fasting triglycerides ≤4.5 mmol/L and LDL-c level ≥1.8 mmol/L or high-density lipoprotein cholesterol (HDL-c) ≥2.6 mmol/L, despite optimized stable lipid-lowering therapy.[11]

Follow-up visits of the secondary prevention program were led by a cardiologist with the assistance of a nurse every 12 weeks for three years. Patients were evaluated for the occurrence of adverse events, changes in their regular medication, assessment of lifestyle interventions and underwent a physical examination with the cardiovascular system as its focal point. Each visit also focused on reinforcing the importance of adequate dietary habits, physical exercise and medication compliance.

Assessed variables

For the purpose of this study, patients were examined on two different occasions: the last appointment within the FOURIER clinical trial (baseline) and the follow-up ten months later. Demographic details (such as age and gender), smoking habits, medical history of hypertension, dyslipidemia, previous acute MI, stroke and percutaneous coronary intervention (PCI) data were collected at baseline. Patients were classified as current smokers when they had smoked one or more cigarettes a day within the previous year; hypertensive when indicated in their medical history or when on antihypertensive medication; diabetic when there was a prior medical diagnosis or taking antidiabetic drugs; having dyslipidemia when previously diagnosed or taking lipid-lowering drugs; overweight when BMI was over 25 kg/m^2 and under 30 kg/m^2; obese when BMI was over 30 kg/m^2.

Variables that were recorded on both occasions included therapeutic compliance and degree of control of CVRFs, particularly body mass index (BMI), determination of blood pressure (BP), glycated hemoglobin levels (HbA1c), total cholesterol and its fractions (HDL-c, LDL-c), triglycerides, lipoprotein (a) (Lp(a)), apolipoprotein A1 (Apo A1) and apolipoprotein B (Apo B). Apo B/ Apo A1 ratio was also calculated.

Therapeutic compliance was measured using the 4-item Morisky Medication Adherence Scale (MMAS-4), as shown in Table 1. This instrument is a generic self-report extensively used and validated in a wide range of diseases. It contains four questions with closed dichotomous (yes / no) answers, meant to avoid the positive response bias from patient questionnaires made by health professionals. Patients score one point for every 'No' answer and zero points for every "Yes" answer. The patients were then scored from 0 to 4: a total of 4 indicates high adherence; a score of 2 or 3 indicates intermediate adherence; and a score of 0 or 1 indicates low adherence.[12,13]

Table 1. 4-Item Morisky Medication Adherence Scale (MMAS-4).

Questions		***Yes***	***No***
1	Do you ever forget to take your medicine?	0	1
2	Are you careless at times about taking your medicine?	0	1
3	When you feel better, do you sometimes stop taking your medicine?	0	1
4	Sometimes if you feel worse when you take the medicine, do you stop taking it?	0	1

Changes in the assessed variables (therapeutic compliance, BMI, BP, HbA1c, total cholesterol, HDL-c, LDL-c, triglycerides, Lp (a), Apo A1, Apo B and Apo B/ Apo A1 ratio) were checked for at baseline and it was evaluated whether these changes were sustained ten months after the end of the specialized secondary prevention program.

Control of cardiovascular risk factors

The control of the modifiable CVRFs was evaluated at baseline and at the follow-up appointment. In order to be deemed under control, patients should display the following parameters:

- Blood pressure: systolic blood pressure below 140 mmHg and diastolic blood pressure below 90 mmHg. BP targets in diabetic patients were systolic blood pressure below 140 mmHg and diastolic blood pressure below 85 mmHg.
- Diabetes: HbA1c under 7%.
- Dyslipidemia: total cholesterol under 4.5 mmol/L (175 mg/dL), LDL-c under 1.8 mmol/L (70 mg/dL), HDL-c over 1.0 mmol/L (40 mg/dL) in men and over 1.2 mmol/L (45 mg/dL) in women, triglycerides under 1.7 mmol/L (150 mg/dL).
- Obesity: BMI under 25 Kg/m^2.

Emergency room admissions

Emergency room admissions during this ten-month period due to unstable angina, acute myocardial infarction or stroke, as well as the need for myocardial revascularization intervention were also recorded. For this effect, the ALERT® informatic system was used.

Statistical Analysis

Qualitative variables are described as absolute frequency and relative frequency. The quantitative variables are represented by the median, first and third quartiles (Q1 and Q3), minimum and maximum. The normal distribution of quantitative variables was assessed using the Shapiro-Wilk test. For pairs of variables where both presented normal distribution, the paired t-Student parametric test was applied. Otherwise, the nonparametric paired Wilcoxon test was used. McNemar test was used to analyze paired nominal data. Statistical analysis was performed using the IBM SPSS Statistics software, v23. The level of significance was set at 5% ($p<0.05$).

RESULTS

Characteristics of the sample at the baseline

Demographics and clinical characteristics of the 121 patients enrolled in this study are shown in Table 2. The sample was predominantly constituted by males (81%) with a median age of 67.72 years. At the last appointment of the FOURIER clinical trial, eight patients were current smokers (6.6%) and 98 had a BMI higher than normal (81%). All patients had a history of dyslipidemia and 118 had a previous medical diagnosis of hypertension (97.5%). In addition, 102 patients had previously suffered acute MI (84.3%), 22 had previously suffered a stroke (18.2%) and 82 were previously submitted to PCI (67.5%).

Table 2. Demographic and clinical baseline characteristics of the study sample (n=121).

	Frequency (n)	**Percentage (%)**
Gender		
Male	98	81.0
Risk factors		
Hypertension	118	97.5
Dyslipidemia	121	100.0
Current smoking	8	6.6
Overweight	58	47.9
Obesity	40	33.1
Diabetes	42	34.7
Previous acute MI	102	84.3
Previous stroke	22	18.2
Previous PCI	82	67.5

Comparison of assessed variables at baseline and follow-up

The variables analyzed in the current study at the baseline and ten months later are displayed in Table 3.

The changes found in therapeutic compliance, HbA1c, total cholesterol and its fractions, triglycerides, Lp (a), Apo A1, Apo B and Apo B/Apo A1 ratio were statistically significant at ten months post-baseline. HbA1c was increased by 0.2% in non-diabetic and diabetic patients ($p=0.017$ and $p=0.002$ respectively), total cholesterol increased by 0.48 mmol/L ($p<0.001$), HDL-c reduced by 0.05 mmol/L ($p=0.001$), LDL-c increased by 0.45 mmol/L ($p<0.001$), triglycerides increased by 0.11 mmol/L ($p<0.001$), Lp(a) increased by 13 nmol/L ($p<0.001$), Apo A1 reduced by 0.08 g/L ($p<0.001$), Apo B increased by 0.16 g/L ($p<0.001$) and ApoB/Apo A1 ratio increased by 0.16 ($p<0.001$). Changes in blood pressure, both systolic and diastolic, and in BMI were not statistically significant.

Control of cardiovascular risk factors

Changes in the risk factor control rates between baseline and follow-up are described in Figure 1. The percentage of participants who achieved the control rate goals declined for all CVRFs after ten months. The differences observed in the control of total cholesterol, triglycerides, HbA1c, SBP, DBP and BMI were not statistically significant. The difference was, however, statistically significant for both HDL-c and LDL-c. The proportion of patients who reached the control goals at follow-up visit were 69.4% for total cholesterol, 64.5% for HDL-c, 20.7% for LDL-c, 66.1% for triglycerides, 73.8% for HbA1c, 44.6% for BP and 18.2% for BMI.

Table 3. Evolution of the risk factors measured at baseline and follow-up.

	Baseline				Follow-up				Change	P value
Variables	**Median**	**Q1**	**Q3**	**min-max**	**Median**	**Q1**	**Q3**	**min-max**		
Total Cholesterol (mmol/L)	3.66	2.53	4.28	1.74 – 5.65	4.14	3.71	4.67	2.59 – 7.8	0.48	< 0.001^{++}
HDL – c (mmol/L)	1.27	1.11	1.49	0.73 – 2.46	1.22	1.01	1.44	0.52 – 2.28	-0.05	0.001^{++}
LDL – c (mmol/L)	1.78	0.60	2.27	0.13 – 3.78	2.23	1.90	2.69	0.96 – 5.23	0.45	< 0.001^{++}
Apo A1 (g/L)	1.44	1.32	1.60	0.94 – 2.46	1.36	1.22	1.52	0.82 – 1.95	-0.08	< 0.001^{++}
Apo B (g/L)	0.66	0.35	0.83	0.22 – 1.13	0.82	0.71	0.94	0.46 – 1.73	0.16	< 0.001^{++}
Apo B/ Apo A1 ratio	0.45	0.24	0.56	0.12 – 0.90	0.61	0.52	0.71	0.28 – 1.20	0.16	< 0.001^{++}
Lp (a) (nmol/L)	47.00	14.50	148.50	5.00 – 361.00	60.00	18.00	183.50	2.00 – 436.00	13.00	< 0.001^{++}
Triglycerides (mmol/L)	1.17	0.87	1.69	0.41 – 3.77	1.28	0.86	1.84	0.53 – 8.93	0.11	< 0.001^{++}
SPB (mmHg)	136	122.50	146.50	101 – 183	138	124	148	89 – 196	2.00	0.225^{+}
DBP (mmHg)	80	73	87	50 – 101	80	72.50	89	49 – 115	0	0.306^{+}
BMI (Kg/m^2)	28.78	25.74	31.30	17.27 – 39.80	28.70	25.69	31.56	17.19 – 43.28	-0.08	0.905^{+}
HbA1c (%)										
Non – Diabetic	5.60	5.40	5.90	4.80 – 6.60	5.80	5.70	6.00	4.70 – 6.90	0.20	0.017^{++}
Diabetic	6.00	5.60	6.80	5.10 – 7.60	6.20	5.80	7.10	5.00 – 8.00	0.20	0.002^{++}
Therapeutic compliance	4	3	4	2 – 4	4	3	4	0 – 4	0	< 0.001^{++}

Changes were expressed as the difference of medians

$^{+}$ Student's t-test for paired samples; $^{++}$ Wilcoxon test for paired samples

LDL-c – low density lipoprotein cholesterol; HDL-c – high-density lipoprotein cholesterol; Apo A1 – apolipoprotein A1; Apo B – Apolipoprotein B; Lp(a) – lipoprotein (a); SBP – systolic blood pressure; DBP – diastolic blood pressure; HbA1c – glycated hemoglobin; BMI – body mass index

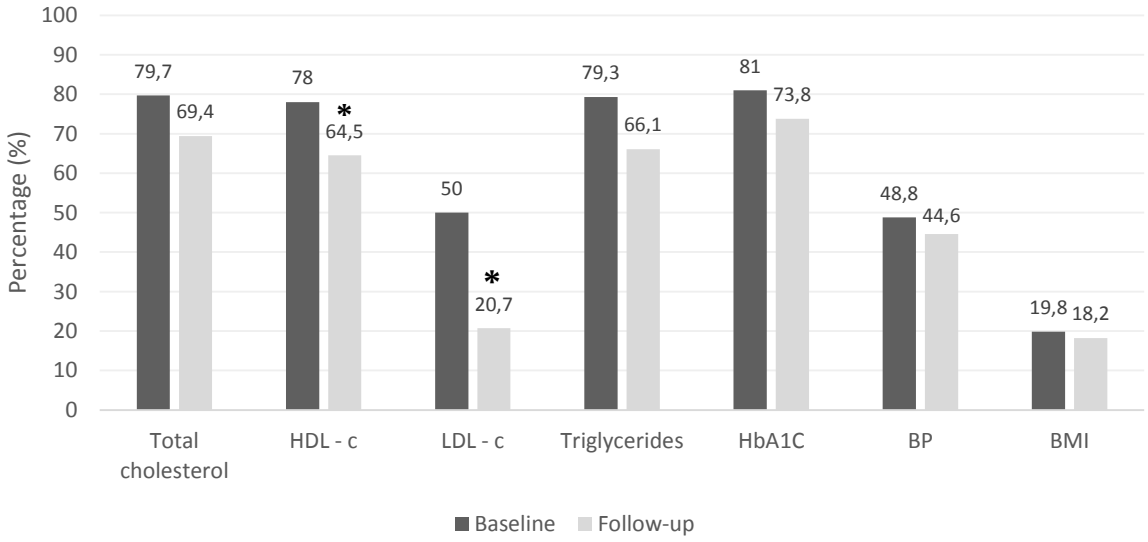

Figure 1. Evolution of the degree of control of modifiable cardiovascular risk factors at baseline and follow-up.

The percentage of the bars indicates the degree of controlled patients. Statistical significance: * $p<0.05$.

HDL-c – high-density lipoprotein cholesterol; LDL-c – low-density lipoprotein cholesterol; HbA1c – glycated hemoglobin; BP – blood pressure; BMI – body mass index.

Emergency room admissions

During the ten-month period, nine cardiac hospitalizations of cardiovascular origin occurred, specifically two for stroke, two for MI and five for unstable angina. In addition, during this period, two PCIs were performed.

DISCUSSION

CVD prevention seeks to reduce morbidity and premature mortality, while simultaneously increasing quality of life and longevity. Abundant scientific evidence indicates that the cornerstones of secondary prevention lie in a lifestyle shift towards cardioprotective behaviors, as well as managing CVD risk factors to reduce the recurrence of atherosclerotic events in high-risk patients.[14,15]

In this study, ten months post-baseline, hypertension was found to be less strictly managed, though this was not statistically significant. However, it is important to note that only 44.6% of the patients had achieved the recommended blood pressure targets, reflecting a suboptimal BP control in the study sample. It is widely accepted that high systolic BP accounts for the largest contribution out of all medical risk factors towards CVD mortality.[3] Moreover, a large meta-analysis has shown that managing hypertension is crucial because for every 10 mmHg SBP reduction, major CVD events were reduced by 20%, coronary heart disease by 17% and stroke by 27%.[16]

All patients had a medical history of hyperlipidemia at baseline. High levels of total cholesterol and LDL-c and low levels of HDL-c are strongly associated with a higher risk of CVD.[8,17] Within the context of this study, a statistically significant increase in LDL-c levels and a decrease in HDL-c concentrations was observed. The percentage of patients controlled decreased from 50% to 20.7% for LDL-c and from 78% to 64.5% for HDL-c and this reduction was statistically significant. European studies reported that, in spite of being treated with statins, antithrombotic medications, and angiotensin-converting enzyme inhibitors, over 80% of patients with a medical history of cardiovascular events present LDL-c values exceeding the advised level of 1.8 mmol/L.[18,19] These results are in agreement with those reported in the present study, at both baseline and follow-up.

An increase in total cholesterol and triglycerides levels was observed, along with a decrease in the control rate of these risk factors, although nearly two-thirds of patients were within the target values. The decrease in control rate was not statistically significant.

According to the results of this study, there was also an increase in Lp(a) concentrations, with more than 25% of patients having Lp(a) levels greater than 125 nmol/L. It is important to note that concentrations of Lp(a) above 125 nmol/L are associated with a higher risk of ischemic and coronary arterial disease. However, there are no randomized clinical trials showing the positive effects of lowering levels of this marker.[20]

Apo B/Apo A1 ratio represents the balance between atherogenic and cardioprotective lipoproteins. A statistically significant increase in the ApoB/Apo A1 ratio was observed in this study. Though evidence to support this variable as a treatment goal remains scarce, several large prospective studies have shown that this ratio performs as well or even better than traditional lipids as a risk indicator, exhibiting a strong correlation with a greater risk for MI, stroke and other cardiovascular events.[21,22]

The changes verified in lipid levels may be attributed to the fact that a portion of the patients were no longer undergoing treatment with Evolocumab in association with high dose statins. It is however important to note that only half of the patients were treated with this therapeutic regimen. In fact, the other half were treated with a placebo associated with high dose statins.

Diabetes mellitus control was also assessed, as it is associated with a two-fold increase in CVD risk. Furthermore, CVD remains the leading cause of morbidity and mortality in diabetic patients, and is also responsible for the greatest impact in its direct and indirect costs.[23] A statistically significant increase in HbA1c levels was observed in both diabetic and non-diabetic patients. The percentage of diabetic patients with HbA1c within

recommended levels at the time of the follow-up decreased from 81% to 73.8%, though this reduction was not statistically significant.

Nearly half of the patients in this study were overweight and close to one third were obese. There was an increase in BMI levels as well as a reduction in the percentage of controlled patients ten months after baseline. None of these changes was, however, statistically significant. At the population level, overweight and obese patients are at a greater risk for cardiovascular events and CVD-associated mortality. Among those with an established CVD, these patients seem to have a more favorable prognosis than leaner patients. In spite of this obesity paradox, overwhelming data still supports the importance of weight reduction in the prevention and treatment of CVD.[24]

To summarize, it was possible to verify a trend towards a decrease in risk factor control rate ten months post-baseline. Possible explanations could be: (1) patients were not capable of maintaining healthy lifestyle behaviors. Frequent physical exercise and healthy dietary habits are vital in managing weight, blood lipids and diabetes; (2) therapeutic non-compliance. In fact, a statistically significant decrease in adherence to prescribed medication regimens between baseline and follow-up was verified.

Studies have highlighted a high prevalence of deficient treatment plans and poor CVRFs management, with a stark contrast between nations. Most high-risk patients fail to meet the guideline standards for secondary prevention, instead presenting high blood pressure and lipid levels, with most patients being diabetic and overweight or obese. Even when there is a high reported use of therapeutic approaches, risk factor control is defective.[18,19]

In this regard, scientific evidence demonstrates that better outcomes are obtained through secondary prevention programs that prioritize health behaviors and therapeutic compliance.[25,26]

However recent cross-sectional survey, EUROASPIRE IV, showed that while many evidence-based guidelines for optimal strategies to limit event recurrence in patients with CVD are available, their effective implementation is lacking.[18]

Therefore, it becomes evident that there is a considerable gap between evidence-based guidelines and clinical practice. The results obtained in the present study are consistent with previous reports that underscored how sustaining the results after a specialized prevention program was challenging for many patients.[7,27,28]

In order to solve this problem, specialized prevention programs and patient consultations should focus their approach on increasing the involvement of the patients in the decision-making process, tailoring target behavioral changes to the life, priorities and expectations of each individual patient.[29] Psychosocial management should be an important core component in this programs.[30] Personal investment in the lifestyle changes increases the likelihood of them being maintained, as well as a more durable support system which could be provided from within primary care or found in community maintenance programs.[30]

In the last few years, new types of interventions have emerged as potential preventive strategies for CVD in high-risk patients. Providing counselling and support over the telephone, the internet and even message reminder systems could be helpful in increasing patient adherence to secondary prevention in populations with limited access to health care services. This would be helpful in bridging the gap between current scientific knowledge and common practice. Previous trials have shown that these approaches could prove as affective, while also being more scalable and likely to be accepted by the patients.[31]

A plan to outline and roll out an accreditation program for clinics carrying out cardiac rehabilitation, secondary prevention and sports cardiology has been announced by the

European Association for Preventive Cardiology. Its goal is to encourage greater quality, participation and reach of CVD secondary prevention in the continent.[32]

Study limitations

One of the limitations in this study was the reduced sample size, as well as the fact that it was a convenience sample and, as such, not representative of the population. Thus, the results can not be generalized to all patients with CVD, but only to those with a profile similar to that of the analyzed sample.

A lesser control of all risk factors was observed ten months after the end of the secondary intervention program. However, as this was an early follow-up, many of these reductions were not statistically significant, though it's possible to detect a trend towards control to decrease.

Additionally, because this was a retrospective study that depended on a pre-existing data and on patient clinical records, the lack of objective information regarding certain lifestyle interventions, particularly dietary habits and physical activity, kept these variables from being part of the study.

Lastly, the data concerning therapeutic compliance was collected through an MMAS-4 scale which is meant to detail how patients approach their medication. Yet, this approach does not appear to produce a comprehensive assessment of predictors for therapeutic adherence, potentially leading to a flawed association between the scale and objective clinical outcome measures.[13]

CONCLUSION

Ten months after the secondary prevention program reached its conclusion, many patients were unable to achieve the target levels for the control of cardiovascular risk factors. Maintaining the results proved challenging for most of the patients, with a trend towards a decrease in risk factor control rate.

While effective therapeutic options are currently available, it remains crucial to optimize secondary prevention programs for a greater impact. Indeed, future secondary prevention programs should integrate drug compliance interventions with physiological procedures and strategies specifically tailored towards preventing relapse and maintaining positive behavioral changes.

Further research is required to determine how secondary prevention programs can use support systems for more lasting results, and thus identify the optimal intervention path for optimal risk control.

ACKNOWLEDGMENTS

I would like to thank Professor Doctor Pedro Monteiro for his professionalism, availability and practical sense with which he always guided me throughout this project.

I would also like to thank the entire Cardiology Investigation Unit of the Centro Hospitalar e Universitário de Coimbra for all their help and support.

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