LDL Cholesterol Targets in Patients Undergoing Peripheral Revascularization

Metas de colesterol LDL en pacientes sometidos a revascularización periférica

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ABSTRACT

Background: Patients with peripheral vascular disease represent a group at high risk of cardiovascular events, and must therefore achieve the secondary prevention goals recommended in the guidelines.
Objectives: Primary: To determine what percentage of patients undergoing peripheral revascularization surgery reached LDL cholesterol goals at 6 months of the intervention compared with patients undergoing coronary artery bypass grafting. Secondary: To determine the percentage of patients reaching these levels at 18 months of follow-up, the percentage of patients with total cholesterol dosage and lipid fraction (LDL-C, HDL-C and TG) assessment at 6 and 18 months of follow-up and the percentage of statin use during the previous year and during the long term follow-up after surgery.
Methods: The degree of lipid control in a retrospective cohort of patients undergoing peripheral revascularization surgery was compared with another group of patients undergoing coronary artery bypass grafting at 6 months and 18 months of the procedure.
Results: A total of 468 individuals, 98 undergoing surgery for peripheral vascular disease and 370 for coronary artery disease were followed up for a period of 18 months. Mean LDL-C at 6 months of surgery was significantly higher in the vascular than in the coronary patients (98.8 ± 35 mg/dl vs. 84.7 ± 25 mg/dl, p=0.001), but lost significance at 18 months (93.3 ± 23 mg/dl vs. 88 ± 26 mg/dl, p=0.25). The percentage of patients achieving LDL-C targets <100 mg/dl was 27.5% vs. 48.6% (p <0.0001) at 6 months in the vascular and coronary patients, respectively, and 22.5% vs. 37.3% (p=0.006) at 18 months.
Conclusion: A lower percentage of patients undergoing surgical procedures for peripheral revascularization achieve LDL-C targets compared with those undergoing coronary revascularization.

Key words: Peripheral Vascular Diseases - Cholesterol, LDL - Intermittent Claudication - Peripheral Vascular Diseases/Surgery - Endarterectomy

RESUMEN

Introducción: Los pacientes con enfermedad vascular periférica representan un grupo de riesgo alto de eventos cardiovasculares, por lo que deben alcanzar las metas de prevención secundaria recomendadas en las guías.
Objetivos: Primario: Determinar qué porcentaje de pacientes sometidos a cirugía de revascularización periférica alcanzan las metas de colesterol LDL a los 6 meses de la intervención en comparación con los pacientes sometidos a cirugía de revascularización coronaria. Secundarios: Determinar el mencionado porcentaje a los 18 meses de seguimiento. Determinar el porcentaje de dosage de colesterol total y fracciones de lípidos (C-LDL, C-HDL y TG) a los 6 y 18 meses de seguimiento. Determinar el porcentaje de uso de estatinas durante el año previo y durante el período de seguimiento alejado de la cirugía.
Material y métodos: Se comparó el grado de control de lípidos de una cohorte retrospectiva de pacientes sometidos a cirugía de revascularización periférica con otra de pacientes sometidos a cirugía de revascularización coronaria luego de 6 meses y 18 meses del procedimiento.
Resultados: Se siguieron 468 individuos, 98 operados por enfermedad vascular periférica y 370 por enfermedad coronaria por un período de 18 meses. La media de LDL a los 6 meses de la cirugía fue significativamente mayor en los vasculares que en los coronarios ($98,8 \pm 35$ mg/dl vs. $84,7 \pm 25$ mg/dl; p = 0,001). Esta diferencia perdió significación a los 18 meses ($93,3 \pm 23$ mg/dl vs. 88 ± 26 mg/dl; p = 0,25). El porcentaje de alcance de la meta de LDL < 100 mg/dl a los 6 meses en los vasculares y coronarios fue 27,5% vs. 48,6% (p < 0,0001) y a los 18 meses fue 22,5% vs. 37,3% (p = 0,006).
Conclusión: Los pacientes sometidos a procedimientos quirúrgicos de revascularización periférica alcanzan las metas de C-LDL en un porcentaje menor en comparación con los sometidos a revascularización coronaria.

Palabras clave: Enfermedades vasculares periféricas - Colesterol LDL - Claudicación intermitente - Enfermedad vascular periférica/Cirugía - Endarterectomía

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Abbreviations

HDL-.C	High-density lipoprotein cholesterol		**PVD**	Peripheral vascular disease
LDL-C	Low-density lipoprotein cholesterol		**TG**	Triglycerides

INTRODUCTION

The presence of atherosclerosis in non-coronary vascular territories can cause as much or more morbidity and mortality than coronary heart disease. (1) Patients with peripheral vascular disease (PVD) represent a subgroup at high-risk for coronary events. (2) There is consistent evidence to recommend that patients with PVD achieve low-density lipoprotein cholesterol (LDL-C) levels below 100 mg/dl and even below 70 mg/dL. (3, 4) Although different studies have shown that patients with PVD are treated less aggressively than patients with coronary atherosclerosis, (2, 5-6) we do not know if this phenomenon is repeated in the subgroup of vascular patients who have undergone a surgical revascularization procedure.

The primary endpoint of the study was to assess whether patients undergoing peripheral revascularization (carotid, aortic and lower limb) surgery were able to achieve the LDL-C goals postulated by clinical practice guidelines in the same percentage as patients undergoing coronary artery bypass grafting after 6 months of intervention. (7-9) The secondary endpoints were to assess LDL-C at 18 months of follow-up, the rate of lipid dosage and its fractions during follow-up and the percentage of statin use at baseline and during follow-up.

METHODS

An observational, retrospective study was performed in a cohort of patients belonging to the Health Plan of the Hospital Italiano de Buenos Aires undergoing peripheral revascularization surgery and another cohort undergoing coronary artery bypass grafting. The first cohort included consecutive patients with no previous history of coronary artery events or coronary artery procedures who were discharged after undergoing carotid endarterectomy, abdominal aorta replacement, or peripheral artery bypass grafting at Hospital Italiano de Buenos Aires between 2007 and 2011. The other cohort included patients discharged after coronary artery bypass grafting performed in the same period in the same center. Lipid values were compared at 6 (±1.5) and 18 (±3) months of follow-up. The use of lipid-lowering medication during the year prior to surgery was also compared with its use during the period comprised between 12 and 18 months after surgery, taking as proxy of consumption the purchase of medication from pharmacies.

Statistical analysis

ICategorical variables were expressed as frequency and percentages, using the chi square test or Fisher exact test to statistically analyze the groups, as appropriate. Continuous variables were expressed as mean and standard deviation or median and interquartile range according to the observed distribution, using Student's t test or the Wilcoxon rank sum test to compare between groups, as appropriate.

A p value <0.05 for two-tailed tests was defined as statistically significant.

Ethical considerations

The study was performed following the recommendations of the Guidelines for Good Clinical Practice and current regulations; with the approval of the institutional Review Board.

RESULTS

A total of 468 individuals, 98 undergoing peripheral revascularization surgery and 370 coronary artery bypass grafting, were followed-up for a period of 18 months since the surgical date in each patient. The baseline characteristics of the population are described in Table 1.

The proportion of patients lost to follow-up at 18 months was similar in both groups, 17.3% in the peripheral revascularization surgery group and 15.4% in the coronary artery bypass grafting group (p=0.63).

The dosage of the different lipid fractions [(LDL-C, high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG)] at 6 and 18 months was significantly lower among patients in the peripheral vascular surgery group than in the coronary artery bypass grafting group (Table 2).

Mean LDL-C at 6 months of surgery was significantly higher among patients undergoing vascular surgery than coronary surgery (98.8±35 vs. 84.7±25 mg/dl, p=0.001). The percentage of vascular and coronary patients achieving the LDL-C<100 mg/dl target at 6 months was 27.5% and 48.6%, respectively (p<0.0001) (Table 3).

During follow-up, mean HDL-C was also significantly higher among vascular patients than among coronary artery patients, with a HDL-C value of 45±14 mg/dl vs. 37±9 mg/dl at 6 months (p<0.001) and 46±12 mg/dl vs. 42±9.6 mg/dl at 18 months (p=0.03), respectively.

The percentage of patients who reached the recommended guideline levels of HDL-C at 6 months was 16.3% among vascular patients and 6.5% among coronary artery patients (p<0.02), and 13.3% and 12.2%, respectively, at 18 months, albeit without statistical significance (p=0.77). This difference was neither significant at 18 months.

Regarding lipid-lowering medication, 52% of vascular patients and 64% of coronary artery patients were registered buying statins in institution-based pharmacies during the year prior to their surgical intervention (p=0.034). During the period following the year of surgery, statin purchase remained unchanged in vascular patients (52%), although it increased significantly among coronary artery patients (84%) (p<0.001).

Table 1. Baseline characteristics of the population

	Peripheral vascular disease n=98	Coronary artery disease n=370	p
Male gender, %	70.4	76.7	0.19
Age, mean±SD	72±10	70±10	0.04
Smoking, %	33.7	20	0.004
DM, %	13.2	16.4	0.43
Stroke and/or TIA, %	19.4	2.43	<0.0001
Dyslipidemia, %	46.9	46.4	0.94
HTN, %	72.4	71.6	0.87
CRF, %	8.16	5.14	0.25
COPD, %	11.2	2.7	<0.0001
Baseline lipid-lowering medication			
Statins, %	52	64	0.034
Ezetimibe, %	11.2	13.2	0.59
Fibrates, %	1	2.4	0.39
Baseline lipid profile			
	mg/dl±SD	**mg/dl±SD**	**p**
Total cholesterol	184 ±37	185 ± 42	0.84
LDL-C	115 ± 34	115 ± 36	0.92
HDL-C	43 ±13	41 ± 11	0.07
TG	136 ±131	133 ± 65	0.76

SD: Standard deviation. DM: Diabetes mellitus. TIA: Transient ischemic attack. HTN: Hypertension. CRF: Chronic renal failure. COPD: Chronic obstructive pulmonary disease. LDL-C: Low-density lipoprotein cholesterol. C-HDL: High-density lipoprotein cholesterol. TG: Triglycerides.

Table 2. Number of patients with total cholesterol and lipid fraction determinations at 6 and 18 months of surgery.

	Peripheral vascular disease		Coronary artery disease		
	n	%	n	%	p
TC 6 m	73	85	301	92	0.049
TC 18 m	55	67	226	72	0.37
LDL-C 6 m	47	55	238	73	0.001
LDL-C 18 m	38	47	196	62	0.01
HDL-C 6 m	50	58	249	76	0.001
HDL-C 18 m	42	51	204	65	0.02
TG 6 m	48	56	238	73	<0.0001
TG 18 m	42	51	200	64	0.0003

TC: Total cholesterol. LDL-C: Low-density lipoprotein cholesterol. C-HDL: High-density lipoprotein cholesterol. TG: Triglycerides. m: Months

Table 3. Percentage of patients who reached the LDL-C<100 mg/dl target at 6 and 18 months of surgery

p	Peripheral vascular disease	Coronary artery disease	p
6 months	27.5%	48.6%	<0.0001
18 months	22.4%	37.3%	0.005

DISCUSSION

Our study showed that following coronary artery bypass grafting, a lower percentage of patients with PVD reached the LDL-C targets recommended by secondary prevention guidelines compared to coronary artery patients. This is of relevance if we consider that the risk of cardiovascular events in patients with PVD is similar to or greater than that of coronary artery disease patients and that statin use has been associated with a reduction in major cardiovascular events. (10, 11)

Although the percentage of patients in both groups who had at least one total cholesterol dosage was similar, when we consider the determinations of the lipid fractions we can see that both the measurement of LDL-C, HDL-C and TG was significantly lower in the vascular group of patients. These findings are similar to those reported by Pereg et al. (12) who observed that while 81% of patients undergoing coronary ar-

tery procedures presented with a complete lipid profile, only in 63% (p<0.001) of vascular patients all lipid fractions had been measured. From this observation it would appear that, at least in part, the problem would not be the lack of patient follow-up, but also the medical doctors' commitment to reach all the recommended lipid goals. A study in which patients were randomized to either routine treatment or to receive a telephone call in which they were encouraged to ask the treating physician to intensify their lipid control showed that the latter improved lipid control significantly. (13) The fact that there is less awareness on the part of the medical community regarding the implementation of secondary prevention strategies in PVD patients is a universal phenomenon. This is demonstrated by the results of the PARTNERS study which showed that only 49% of physicians who treated patients with diagnosed PVD had the pathology of their patients present. (14)

The REACH registry enrolled more than 68,000 patients with atherosclerotic disease. (15) In this study the control of all risk factors was significantly lower in patients with PVD than in coronary artery disease patients. Unlike the REACH study, which included vascular patients with intermittent claudication and an ankle-brachial index of less than 0.9, our study analyzed only surgically revascularized patients, i.e. a sub-group that can be presumed to be sicker, since it was submitted to a surgical revascularization procedure. We did not find in the literature another study that focuses on vascular patients with surgical revascularization.

The difficulty in the control of cholesterol levels among patients undergoing vascular procedures would be multifactorial. There is evidence linking the specialty of the treating physician and the degree of control of the risk factors. (16) While most patients with coronary artery interventions are followed-up by cardiologists, this would not be the case of vascular patients. Moreover, patients with PVD underestimate the risk of cardiovascular events and minimize the benefit derived from lipid-lowering treatment. (17) On the other hand, unlike the control of arterial pressure, where the patient can be monitored and the results derived from the therapeutic interventions can be observed, the lipid-lowering treatment is not related to immediate tangible results. This highlights the importance of multidisciplinary team training and the need to educate patients in the knowledge of their own disease, given the strong evidence showing that reducing LDL-C levels translates into a reduction in mortality and major cardiovascular events. (18, 19)

Our study found a lower proportion of diabetic patients than other studies of vascular patients, which may be due to the fact that until a few years ago diabetes was considered as a pre-existing disease, limiting patients' access to medical prepaid systems (20)

Although this is a single center study, its results would seem to be repeated at all latitudes. We believe that it is imperative to acknowledge patients with vascular disease as a risk group that merits the implementation of all available therapeutic resources. (21)

Finally, it must be considered that since it is a retrospective study registry there may be biases. However, the information referred to the primary endpoint (LDL-C) was collected directly from the hospital´s computerized central laboratory database. For the prescription of the lipid-lowering medication, data was acquired from the medical registries of the electronic clinical record, and although there could be underreporting, this was estimated of the same magnitude in both groups. Regarding medication adherence, data was taken from drug purchase in institution-based pharmacies, assuming that if the patient was willing to pay the cost of the drugs then he must have taken them.

CONCLUSIONS

Patients undergoing peripheral revascularization surgery achieve a lower percentage of LDL-C goals compared to those undergoing coronary artery bypass grafting. It is necessary to determine the causes of this phenomenon to improve secondary prevention strategies.

Conflicts of interest

None declared. (See authors' conflicts of interest forms on the website/Supplementary material).

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