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Original Article

Poor attainment of lipid targets in patients with symptomatic peripheral artery disease

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BACKGROUND: Patients with peripheral artery disease (PAD) are at very high risk of future cardiovascular (CV) events. Strict lipid-lowering therapy is recommended. However, data on target level attainment are scarce.

OBJECTIVE: The objective of the study was to investigate guideline equitable lipid lowering in a large observational study of symptomatic PAD patients.

METHODS: Single-center observational study including 1109 patients with symptomatic PAD planned for revascularization at a tertiary university center. Between 2010 and 2017, guideline target level attainment trends over time and the association of statin therapy with CV mortality were analyzed.

RESULTS: Atorvastatin (52.3%) and rosuvastatin (23.5%) were the most frequently prescribed statins and amounted to an average simvastatin equivalent of 52 mg/d. Attainment rates of low-density lipoprotein cholesterol (LDL-C) and of non–high-density lipoprotein cholesterol goals were as low as 27% and 33%, respectively. Although there was a significant improvement of LDL-C from 2010 to 2017 (mean LDL-C 110 vs 80 mg/dL, $P < .0001$ for trend), attainment remained poor, that is, only 42% in 2016 and 45% in 2017 achieved the <70 mg/dL goal. CV mortality was significantly lower (4% vs 11%, $P < .01$) in statin-treated patients over a median follow-up period of 50 ± 26 months.

CONCLUSION: There is a remarkable undertreatment of LDL-C and non–high-density lipoprotein cholesterol in patients with symptomatic PAD, although LDL-C decreased significantly from 2010 to 2017. As statin treatment was associated with a reduced CV mortality rate, our findings call for an increased awareness in clinical lipidology regarding symptomatic PAD patients.

Introduction

International guidelines[1–3] consider established peripheral artery disease (PAD) as very high cardiovascular (CV) risk. It has been shown that patients with PAD are at a higher risk for CV events than patients with coronary artery disease (CAD),[4–7] possibly due to dyslipidemia and

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the increased inflammatory state of the disease, as has been demonstrated based on levels of C-reactive protein, which are higher in PAD than in coronary patients.[8,9]

Guidelines recommend strict risk factor control, in particular and among others of low-density lipoprotein cholesterol (LDL-C) and non–high-density lipoprotein cholesterol (HDL-C).[1,2,10–12] In randomized, controlled clinical trials, statin treatment has been proven to reduce CV events in patients with PAD.[13,14]

Nevertheless, it has been reviewed that adherence to statins in general remains is poor,[15] which contrasts strongly to the well-documented benefits of this treatment modality. Even more, in contrast to the literature on patients with CAD, there are scant clinical data on adherence to lipid-lowering therapy (LLT) and target level attainment in patients with PAD. We therefore aimed at defining treatment practices in a large observational study of consecutive, unselected patients with symptomatic PAD undergoing lower limb revascularization at a large tertiary care university center. Trends in LDL-C target level attainment over time and relation to CV mortality rates were evaluated.

Materials and methods

Study design

This cross-sectional, observational, single-center study has the purpose of investigating lipid levels, lipid target attainment as recommended by European Society of Cardiology (ESC) guidelines, status of LLT (statins mono/combination therapy), and CV death rate in patients with symptomatic PAD. Data from a total of 1109 consecutive patients, being referred to the Swiss Cardiovascular Center between January 2010 and September 2017, were analyzed. The lipid values of these 1109 patients were obtained at the admission for the peripheral intervention. A subset of 598 patients from the total study cohort was seen for a second lipid reading at an interval of 50 ± 26 months.

From 2016, the Division of Angiology instituted an outpatient clinic for lipid therapy. Data were derived from a consecutive, prospective database and were retrospectively analyzed. The database and participant informed consent form on research involving humans were approved by the Swiss Ethics Committee. Each patient's written informed consent was obtained before inclusion.

Intermittent claudication (IC) was defined as a symptomatic deficiency in blood supply to exercising muscle relieved during resting classified by the Fontaine stage II. Critical limb ischemia (CLI) was defined according to the Second European Consensus Document[16] as persistently recurring ischemic rest pain requiring regular adequate analgesia for > 2 weeks or ulceration or gangrene of the foot or the toe associated with an ankle systolic pressure ≤ 50 mm Hg or a toe systolic pressure of ≤ 30 mm Hg or both, classified as Fontaine stage III (rest pain) or IV (ulceration/gangrene).

Patients with PAD presenting with trophic skin lesions or delayed wound healing, or both, but without hemodynamic evidence of CLI were grouped with IC patients for statistical evaluation. CV risk factors and comorbidities were assessed at baseline. The definition for the assessed risk factors is provided elsewhere.[17]

Lipid target levels were defined according to the ESC and National Lipid Association (NLA) guidelines with a recommended target level for LDL-C in high-risk CV patients of < 70 mg/dL.[2,10] Non–HDL-C was defined as an estimation for all atherogenic lipoproteins in plasma calculated from total cholesterol minus HDL-C. The recommended goal for non–HDL-C being used was < 100 mg/dL.[2,10]

Statin intolerance was defined as muscular complaints caused by at least two different statins having occurred within 4 to 6 weeks. The muscle complaints had to be typically symmetrical and proximal and generally affecting large muscle groups including the thighs, buttocks, calves, and back muscles.[18]

Intensity of statin treatment was categorized as high, moderate, and low. Based on the American College of Cardiology (ACC) guidelines,[11] we defined LLT with atorvastatin 40–80 mg and rosuvastatin 20–40 mg as high-intensity therapy. Atorvastatin 10–20 mg, fluvastatin 40 mg twice daily, pravastatin 40–80 mg, rosuvastatin 5–10 mg, and simvastatin 20–40 mg were defined as moderate-intensity therapy. Finally, fluvastatin 20–40 mg, pravastatin 10–20 mg, and simvastatin 10 mg were categorized as low-intensity therapy.

Inclusion criteria

Consecutive patients with chronic, symptomatic PAD (Fontaine stage II, III, or IV) due to atherosclerotic disease referred for primary endovascular lower limb revascularization were included. Written informed consent was given.

Exclusion criteria

Patients with nonatherosclerotic arterial obstructive disease, endovascular redo procedures (restenosis), acute or embolic PAD, known vasculitis, or other than atherosclerotic PAD were excluded. Patients aged below 40 years with high probability of nonatherosclerotic PAD were excluded.

Data collection

Consecutive database

Patient's fasting blood test at the time of referral for revascularization was used to measure serum lipid levels. LLT was recorded and data on statin type, dose, and other lipid-modifying therapies were collected. Statin potency was normalized to simvastatin to allow for comparison between compounds.[19] Data were entered into the department's database on PAD patients.