



REVIEW ARTICLE

The role of statins in atherosclerotic peripheral arterial disease

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Abstract The use of statins for secondary prevention in patients with peripheral (extracoronary) arterial disease is not widespread. Their possible use has only relatively recently been studied and data in the literature are sometimes controversial or are not disclosed.

The aim of this paper is to review the recent literature and to discuss possible reasons for using statins in patients with extracoronary atherosclerotic arterial involvement, focusing on the areas in which they have been investigated.

The main conclusions are that statins should be prescribed with the objective of reducing coronary and cerebrovascular morbidity and mortality in patients with carotid disease, abdominal aortic aneurysm and lower limb occlusive disease. There is sufficient evidence to suggest a reduction in the perioperative risk of vascular surgery when statins are used, and in patients with carotid stenosis they also appear to reduce perioperative risk in endarterectomy. Nevertheless, there are insufficient data to recommend the use of statins to control post-endarterectomy restenosis.

In patients with intermittent claudication, statins improve walking distance and may be used for this purpose.

Finally, there is insufficient evidence to recommend statins to prevent restenosis in lower limb revascularization procedures, to control progression of abdominal aortic aneurysms, or to reduce the severity of renal artery stenosis or renal dysfunction.

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PALAVRAS-CHAVE

Estatinas;
Doença arterial
periférica

Prevenção secundária com estatinas na patologia arterial periférica aterosclerótica

Resumo A utilização de estatinas em prevenção secundária na patologia arterial periférica (extra-coronária) não é universal. As razões para a sua eventual utilização são relativamente recentes e os dados da literatura são, por vezes, controversos ou não se encontram divulgados.

O objectivo deste trabalho consiste em rever a literatura recente e discutir as razões eventuais para uma maior utilização de estatinas em doentes com patologia do foro vascular «extra-coronário» tendo sido seleccionadas as áreas em que estes fármacos têm sido estudados.

Conclui-se que as estatinas devem ser utilizadas com o objectivo de reduzir a morbilidade e a mortalidade de causa coronária em doentes com patologia carotídea, aneurisma da aorta e doença oclusiva dos membros inferiores. Há evidência suficiente que comprova a redução do risco per-operatório em Cirurgia Vasculare e a sua utilização em doentes com estenose carotídea é também recomendada com o objectivo de reduzir o risco per-operatório da endarterectomia. No entanto, não há dados que permitam recomendar o uso de estatinas para controlo da re-estenose após endarterectomia carotídea.

Há evidência que sugere um papel benéfico das estatinas nos doentes com claudicação intermitente, em termos de melhoria da distância de marcha, pelo que a sua utilização com este objectivo é recomendada.

Finalmente, não há evidência suficiente que permita recomendar a utilização de estatinas com o objectivo de prevenir a re-estenose e melhorar a *performance* dos procedimentos de revascularização convencional dos membros inferiores, de controlar a progressão dos aneurismas da aorta abdominal nem de melhorar a gravidade da estenose ou da disfunção renal.

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Introduction

Secondary prevention in vascular surgery always includes correction of risk factors for atherosclerosis, antiplatelet therapy, and in some cases oral anticoagulation. Although the use of statins is well established in secondary prevention of ischemic heart disease and cerebrovascular disease, and is included in the international guidelines, they are less frequently used in other areas of medicine, such as vascular surgery, and there is evidence from various countries that their use in the treatment of “peripheral” atherosclerotic disease is not widespread¹⁻⁴.

The aim of this paper is to analyze the recent literature and to discuss possible reasons for using statins in patients with extracoronary atherosclerotic arterial involvement⁵.

We should first clarify the term peripheral arterial disease (PAD), since it is used in two senses in the literature: extracoronary atherosclerotic disease, and lower limb occlusive disease. In the present review we use it with the first meaning, but regarding cerebrovascular disease, it is only mentioned with reference to the current use of statins in occlusive disease of the extracranial arteries, particularly the carotid bifurcation.

Statins (3-hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase inhibitors) significantly reduce LDL cholesterol and are highly effective in preventing

coronary and cerebral ischemic events. Besides their lipid-lowering properties, they have been shown to have parallel (pleiotropic) effects, notably in reducing inflammation.

The beneficial effects of statins, and the fact that they are generally well tolerated, mean they play an important role in secondary prevention of coronary and cerebrovascular disease.

With regard to secondary prevention in peripheral vascular disease, their value has been investigated in the following areas:

- Reduction of global cardiovascular risk in vascular patients: prevention of major vascular events in coronary, cerebral and lower limb arterial territories.
- Reduction of perioperative cardiac and non-cardiac complications of revascularization surgery.
- Reduction of risk associated with atheromatous plaques in the carotid bifurcation.
- Reduction of risk of carotid restenosis after endarterectomy.
- Treatment of chronic lower limb occlusive disease, particularly intermittent claudication.
- Improvement of patency of infrainguinal bypass grafts and reduction of limb loss rates.
- Reduction of abdominal aortic aneurysm (AAA) expansion.
- Benefit in renovascular disease and perioperative renal dysfunction.

The reasons for the use of statins for each of the above clinical goals will now be discussed in the light of the available evidence.

Reduction of global cardiovascular risk in vascular patients: prevention of major vascular events

Patients with chronic obstruction of the lower limb arteries, carotid stenosis or AAA have a lower life expectancy than those of the same age without peripheral arterial disease⁶. This is due mainly to greater prevalence of risk factors and occlusive disease in other territories, especially the coronaries^{7,8}.

A diagnosis of PAD should be followed by proactive intervention to control risk factors and to identify and treat lesions in other territories, since this will have clear benefits on survival. With this in mind, statin therapy has been analyzed in various trials in PAD patients. In 1998 the Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) trial⁹ was published, including 9014 patients with a history of myocardial infarction or angina, followed for six years. Of these, 995 had intermittent claudication; of these 38% suffered a coronary, cerebral or peripheral event and 13% died of cardiovascular cause, as opposed to 27.5% and 8% respectively in the group without claudication. In those with claudication, the use of 40 mg/day of pravastatin reduced the risk of coronary, cerebral or peripheral events ($p=0.039$) compared with placebo.

In 2002, Aronow and Ahn published a randomized study¹⁰ of patients with peripheral arterial disease, including critical ischemia, of whom 318 were treated with statins and 342 received placebo; follow-up was 39 months. The incidence of new coronary events in those receiving statins was 48% compared to 73% in the control group ($p < 0.001$). Such a high incidence of events may have been due to the advanced age (mean 80 years [60-99]) of the subjects. There were also highly significant reductions in sudden death ($p < 0.0005$), new coronary events ($p < 0.001$) and fatal myocardial infarction (MI) ($p < 0.007$) in the statin group and in patients with and without previous MI.

The same year also saw the publication of the Heart Protection Study (HPS)¹¹, which made a significant contribution to clarifying the role of statins in reducing risk in patients with peripheral arterial disease. Of the 20 536 patients enrolled, 2701 presented peripheral arterial obstruction without coronary disease and 4047 had evidence of lower limb occlusive disease as well as coronary disease. In both groups the use of 40 mg/day simvastatin reduced the relative risk of major vascular events by 24% ($p < 0.00001$) and need for extracoronary revascularization, mainly carotid and lower limb, by 16% ($p=0.006$). The study's data indicate that the use of simvastatin for five years would prevent 70 major vascular events per 1000 patients¹². The long-term effect of statins was confirmed in an observational study by Feringa et al.¹³, in which there was still benefit after eight years of follow-up.

Similar results have been seen in other trials analyzing patients with peripheral arterial disease. In the LEADER study¹⁴, bezafibrate led to reduced risk for nonfatal coronary events, more marked in younger patients (under 65 at enrollment), but had no effect on the combined incidence of coronary heart disease and stroke. Mohler et al.¹⁵, in a randomized double-blind trial with 354 subjects, also found a significant reduction ($p=0.003$) in vascular accidents at 12 months in patients treated with atorvastatin vs. placebo. A study by Schillinger et al.¹⁶ showed lower risk of death (RR 0.52, 95%CI 0.3-0.91, $p=0.022$) and cumulative risk of death and MI (RR 0.48, 95%CI 0.29-0.79, $p=0.004$) in patients medicated with statins.

Cardiovascular risk is also higher in patients with carotid stenosis. The National Cholesterol Education Program (NCEP) classified carotid artery disease, like peripheral artery disease, as "coronary heart disease risk equivalent" in 2001 and 2004, and recommended keeping LDL cholesterol below 100 mg/dl^{17,18}. The same approach was adopted by the American Stroke Association in 2004¹⁹.

Patients with AAA have similar risk for coronary accidents to those with lower limb disease and carotid stenosis (according to the NCEP)¹⁸, with 2-year risk of cardiovascular death of 6.3%¹⁷ and 8-year risk of 28% as seen in the UK Small Aneurysm Trial²⁰.

Several studies have confirmed the benefit of statins in reducing global cardiovascular risk in patients with AAA; in a follow-up of 4.7 years, patients treated with statins had 2.5 times lower overall mortality and over 3 times lower vascular mortality²¹.

To summarize, there is clear evidence (level 1) of a significant reduction in coronary morbidity and mortality in patients with PAD when treated with statins, and recent guidelines recommend their intensive use^{22,23}.

Reduction of perioperative cardiac and non-cardiac complications of conventional or endovascular revascularization surgery

The idea of using statins to reduce perioperative complications in vascular surgery arose from the observation that they decrease the recurrence of early ischemic events after acute coronary syndromes and following coronary revascularization, and hence could also reduce risk in other vascular procedures²⁴. Some studies have shown this benefit in general surgery and in lower limb revascularization²⁵.

In 2003 Poldermans et al.²⁶ published a retrospective study of 2816 patients undergoing major vascular surgery (elective and emergent treatment of AAA, carotid endarterectomy and lower limb revascularization). Mortality was compared between those treated with statins and controls; 160 subjects (5.7%) died, of whom only 8% were treated with statins, as opposed to 25% of controls (OR 0.22, 95%CI 0.10-0.47, $p < 0.001$). There

was thus a 4-fold reduction in risk of death in the treated group.

In a prospective, randomized, double-blind trial, Durazzo et al.²⁷ compared the effect of 20 mg/day of atorvastatin in 50 patients with a placebo group of the same size, using the endpoint of occurrence of cardiovascular events following elective vascular surgery. Subjects were treated perioperatively for 45 days and were operated an average of 31 days, and not less than two weeks, after randomization. In a 6-month follow-up there was a clear reduction of coronary events in the treatment group (atorvastatin 8% vs. placebo 26%, $p=0.031$), a more than 3-fold risk reduction.

In 2004 Kertai et al.²⁸ studied 570 patients undergoing resection of AAA with a combined endpoint of mortality and MI, which occurred in 8.9%. Risk was lower in the statin group than in the non-statin group (3.7% vs. 11%, OR 0.31, 95% CI 0.13-0.74, $p=0.01$), even after adjustment for other variables (OR 0.24, 95% CI 0.10-0.70, $p=0.01$). The use of beta-blockers was also associated with lower risk.

Also in 2004, Lindenauer et al.²⁵ published a retrospective study of 780 591 patients undergoing non-cardiac surgery, of whom 65 399 underwent vascular surgery and 13 862 were medicated with statins. Statins were associated with a significant reduction in perioperative mortality ($p < 0.001$) in all procedures (vascular and non-vascular).

Finally, the StaRRS (Statins for Risk Reduction in Surgery) study²⁹ included retrospective data on 1163 patients undergoing carotid endarterectomy, aortic surgery or lower limb revascularization over a period of two years. The incidence of complications was significantly lower ($p=0.001$) in patients taking statins (9.9%) than in the others (16.5%); the greatest differences were seen in reduction of myocardial ischemia and congestive heart failure. The beneficial effect of statins remained after adjustment for age, gender, type of surgery, acuity of surgery, left ventricular dysfunction and diabetes.

The mechanism by which statins reduce perioperative risk is presumably through stabilization of vulnerable atheromatous plaques, particularly in the coronaries and the brain.

Although there are no level 1 studies specifically designed for this purpose, there is strong evidence for the perioperative use of statins in vascular surgery, and this should therefore be included in treatment protocols.

Carotid stenosis: reduction of perioperative risk and control of restenosis after endarterectomy

The use of statins in cerebrovascular disease will not be discussed in depth in this paper. However, it is important to mention that their use is recommended, several studies having demonstrated an overall reduction in relative risk for stroke, including a meta-analysis of over 90 000 patients³⁰.

With regard to the role of lipid-lowering therapy in patients with carotid stenosis, recent studies have

suggested that they reduce neurological risk associated with carotid plaques, as well as reducing overall cardiovascular risk³¹.

A retrospective study by McGirt et al.³² analyzed 1566 patients undergoing carotid endarterectomy performed by 13 surgeons; 42% of plaques were symptomatic and 42% of patients were medicated with statins at least one week before surgery. In the statin group there was less perioperative stroke (1.2% vs. 4.5%, $p < 0.01$) and perioperative transient ischemic attack (1.5% vs. 3.6%, $p < 0.01$), and lower overall mortality (0.3% vs. 2.1%, $p < 0.01$). Multivariate analysis correcting for other factors confirmed that statins independently reduced the risk of stroke three-fold (OR 0.35, 95% CI 0.15-0.85, $p < 0.05$) and of death five-fold (OR 0.20, 95% CI 0.04-0.99, $p < 0.05$) compared to the control group.

Kennedy et al.³³, in a 2005 retrospective study of 2031 patients undergoing carotid endarterectomy, found that statins reduced the risk of perioperative stroke two-fold (OR 0.55, 95% CI 0.32-0.95) and of death four-fold (OR 0.25, 95% CI 0.07-0.90) in symptomatic patients, although this effect was not seen in asymptomatic patients.

These results are interesting in that they suggest that the benefit seen in symptomatic patients may be related to the anti-inflammatory action of statins in stabilizing atheromatous plaques, reducing their vulnerability to rupture, and making them less liable to become symptomatic. By contrast, asymptomatic plaques are generally more stable, as shown in many studies³⁴. This hypothesis is supported by a study by Molloy et al.³⁵, which showed a lower incidence of symptomatic plaques in patients who took statins in the month prior to surgery ($p=0.0049$) and a lower rate of ipsilateral cerebral embolization on transcranial Doppler ultrasound ($p=0.0459$). Gomez-Hernandez et al.³⁶ performed histochemical analysis of carotid plaques and found that those retrieved from patients taking statins had a lower content of matrix metalloproteinases, particularly MMP-1 ($p=0.0176$) and MMP-9 ($p=0.0018$), and interleukin-6 ($p=0.0005$). These findings support the idea that the mechanism behind the plaque stabilization attributed to statins is their ability to reduce inflammation, angiogenesis and proteolysis^{37,38}.

An important retrospective study³⁹, published in 2007, on the medication to use in patients undergoing carotid endarterectomy (660 symptomatic and 901 asymptomatic), found that those treated with statins or diuretics were less likely to suffer cerebrovascular symptoms, irrespective of their initial clinical status.

Another line of research that appears to confirm the direct effect of statins on the arterial wall and atheromatous plaques concerns control of progression, or even regression, of intima-media thickening (IMT) or of the lesions themselves as measured by ultrasound⁴⁰. Direct modulation of the arterial wall and plaques by statins was demonstrated in a large meta-analysis³⁰ that showed a correlation between regression of IMT and lowering of LDL cholesterol ($r=0.65$, $p=0.004$). Another meta-analysis of 3445 patients confirmed the role of statins in reducing the rate of progression of carotid atherosclerosis⁴¹.

Furthermore, there is evidence to suggest that the echogenicity of carotid atheroma increases after statin use⁴², which implies a higher calcium⁴³ and collagen content and hence a more stable structure.

These data show how statins contribute to remodeling of carotid atherosclerotic lesions, reducing IMT and plaque progression and improving plaque stability.

There is thus evidence that treatment with statins reduces perioperative neurological risk in patients with carotid stenosis. However, the level of evidence is not strong, and the largest studies with the most conclusive results were retrospective. There is a need for level 1 trials to fully clarify this question, but there are ethical problems involved, since statin therapy has unquestioned benefit in reducing overall vascular risk⁴⁴.

In conclusion, statins are recommended in patients with carotid stenosis in order to reduce perioperative risk in endarterectomy.

Another question is the role of lipids in restenosis after carotid endarterectomy and the capacity of lipid-lowering drugs to reduce its incidence. A link between hyperlipidemia and greater risk of restenosis has been postulated since the 1980s, and a study by LaMuraglia et al.⁴⁵ suggested that cholesterol could be a marker of early restenosis. The lipid-lowering function of statins, as well as their anti-inflammatory properties, may reduce the intimal hyperplasia that accompanies scar formation after surgical procedures. However, this is far from proven, and the role of lipids in restenosis and its control remains the subject of debate. Thus, statins cannot currently be recommended for control of post-endarterectomy restenosis.

Treatment of chronic lower limb occlusive disease (intermittent claudication)

Chronic lower limb ischemia, caused by obstruction of one or more arterial segments, can have various clinical manifestations, for which there are different therapeutic approaches. In critical ischemia surgical or endovascular revascularization is essential to save the limb. In patients with intermittent claudication, the main problem is limited walking distance and hence reduced quality of life. In this case treatment is basically medical, with intervention only in patients with disabling claudication, and consists of correction of risk factors, exercise programs, and drug therapy with antiplatelets and peripheral vasodilators. We now discuss the addition of statins to treatment protocols.

Intermittent claudication, which affects 2-7% of those aged over 55⁴⁶, is a benign stage in the natural history of lower limb occlusive disease in which three-quarters of patients remain stable, or see improvement in walking distance, with medical therapy, exercise and control of risk factors for atherosclerosis. Only 5-10% will require revascularization, and less than 1% will undergo major amputation. However, given the generalized nature of atherosclerosis, intermittent claudication is an indicator of disease in other territories^{8,46} that is associated with

2-4 times higher cardiovascular (coronary and cerebral) mortality than in the general population without lower limb ischemia. In 2002 the American Heart Association defined peripheral arterial disease as a "coronary heart disease risk equivalent" and recommended the use of statins⁴⁷ in view of their benefit in reducing major vascular events and mortality.

Various studies have pointed to the possible impact of lipid-lowering therapy on clinical improvement in lower limb ischemia. The Program on the Surgical Control of the Hyperlipidemias (POSCH) study⁴⁸, which assessed the effect of cholesterol lowering by partial ileal bypass in 838 patients with previous MI and hyperlipidemia, found a significant reduction in *de novo* intermittent claudication at four years in the treated group (RR 0.66, 95% CI 0.20-0.90, $p=0.009$). In 1998 a post-hoc analysis of the Scandinavian Simvastatin Survival Study⁴⁹ showed that in patients with coronary disease followed for 5.4 years, statins reduced *de novo* intermittent claudication or worsening of previous claudication by 38% ($p=0.008$).

These findings, together with increasing awareness of the importance of lipid lowering in reducing the risk of atherosclerotic manifestations in the coronary and cerebral territories, have prompted studies focusing on other areas affected by atherosclerosis.

The Lower Extremity Arterial Disease Event Reduction (LEADER) trial⁵⁰, a randomized trial of bezafibrate (400 mg) compared with placebo that included 783 men in each arm and a mean follow-up of 4.6 years, showed significant improvement in symptoms of intermittent claudication for up to three years. Other trials on peripheral arterial disease followed, which provided important conclusions, although with small patient numbers. A multicenter randomized double-blind trial by Mohler et al.¹⁵ involved 354 patients in three groups: atorvastatin (10 mg or 80 mg) and placebo. No significant differences were seen in the endpoint of maximal walking time in a 12-month follow-up, although pain-free walking time increased significantly ($p=0.025$) in the 80 mg atorvastatin group. Physical activity and quality of life were assessed by questionnaires, with both treatment groups showing an improvement in physical activity ($p=0.011$), but there was no significant difference in responses to the quality of life questionnaires.

Using objective parameters to quantify pain-free treadmill exercise, Aronow and Ahn¹⁰ showed that treatment with simvastatin was associated with increased walking distance.

A study by McDermott et al.⁵¹ assessing the relation between clinical improvement (and motor function) and lipid lowering by statins in patients with intermittent claudication found improved walking speed and performance score in treated patients, independently of other factors including cholesterolemia and treatment with antiplatelets, ACE inhibitors, beta-blockers and vasodilators. These findings suggest that the pleiotropic effects of statins have an important role.

In a randomized double-blind trial of only 86 patients with lower limb ischemia and cholesterolemia >220 mg/dl, Mondillo et al.⁵² set out to assess the

immediate effect of statin therapy, the study population being randomized to two groups, each of 43 patients: 40 mg/day simvastatin and placebo. There was a mean improvement in total walking distance of 126 meters (95% CI 101-151, $p < 0.001$) and in pain-free walking distance of 90 meters (95% CI 64-116, $p < 0.005$) in the simvastatin group. Using an objective measure of hemodynamic status, ankle-brachial index (ABI), they found that the simvastatin group presented an increase in resting ABI of 0.09 (95% CI 0.06-0.12, $p < 0.01$) and post-exercise ABI of 0.19 (95% CI 0.14-0.24, $p < 0.005$). Thus, as well as subjective improvement in symptoms of intermittent claudication, there was also objective evidence of hemodynamic improvement quantified non-invasively.

In conclusion, there appears to be evidence suggesting a beneficial effect of statins in intermittent claudication, with improved walking distance. This, together with their clear benefit in preventing vascular events, has led to statins being recommended in patients with chronic lower limb ischemia, which should be reflected in treatment protocols.

Prevention of restenosis in lower limb revascularization procedures

It has been suggested that statins may help prevent early restenosis of infrainguinal bypass grafts, with some studies indicating that they may increase patency in these grafts and improve limb salvage rates.

In a retrospective analysis of 293 patients with critical ischemia undergoing 338 infrainguinal bypass procedures, Henke et al.⁵³ found that statins were associated with increased graft patency. Similarly, Abbruzzese et al.⁵⁴ performed a retrospective analysis of 189 infrainguinal venous grafts, divided into a group treated with statins ($n=94$) and a control group ($n=95$). Perioperative mortality did not differ between the groups, while at two years primary assisted patency was greater in the statin group (94% vs. 83%, $p < 0.02$), as was secondary patency (97% vs. 87%, $p < 0.02$). Multivariate analysis showed risk of graft failure to be 3.2 times greater in the control group.

Despite these retrospective analyses, the role of statins in improving graft patency has not been proved; level 1 trials will be required, and on the basis of current evidence the use of statins is not recommended for this purpose.

Reduction of abdominal aortic aneurysm expansion

The etiopathogenesis of AAA is multifactorial, with hemodynamic, genetic, inflammatory and biochemical factors being implicated, but there is as yet no theory unifying the different mechanisms, nor is there a known underlying cause for the arterial dilatation.

Degenerative alterations in the arterial wall in AAA appear to be dependent on biochemical mechanisms related to systemic and local proteolysis in the extracellular matrix. In general, inflammatory processes are closely linked to enzyme balance in the wall, a relation that, as in atherosclerotic disease, appears to be one of the central mechanisms in the pathogenesis of arterial dilatation.

The importance of inflammation led to the hypothesis that suppression of inflammatory phenomena and pharmacological control of metalloproteinase synthesis could result in control of dilatation. One approach involved the use of statins, and Nagashima et al.⁵⁵ demonstrated reduced metalloproteinase activity in human aortic aneurysm wall with cerivastatin. In an experimental study on aortic aneurysms induced in mice, Kalyanasundaram et al.⁵⁶ found that aneurysms in mice treated with simvastatin were significantly smaller; they also found reduced MMP-P activity and evidence that several mediators of inflammation, matrix remodeling, and oxidative stress were downregulated. Other studies^{57,58} have confirmed these findings, and Steinmetz et al.⁵⁹ have suggested that the mechanism by which statins control arterial dilatation is independent of lipid lowering.

In view of the evidence from small observational and experimental studies, the role of statins in medical treatment of AAA has not been established, and therefore they cannot yet be recommended for this purpose⁶⁰.

Renovascular disease and perioperative renal dysfunction

Some studies have analyzed the possible benefit of statins in renal artery stenosis, and suggest reduced severity and improved survival in patients following stenting⁶¹.

This conclusion, based on sparse data, was not confirmed by the AURORA study⁶² in patients undergoing hemodialysis, in whom there was no significant clinical benefit, despite clear reductions in LDL cholesterol levels.

It has also recently been suggested that statins protect against renal dysfunction in patients undergoing endovascular repair of AAAs with suprarenal endograft fixation⁶³.

In conclusion, the effects of statins in patients with renal artery stenosis are not fully known and so they cannot be recommended for this purpose.

Questions awaiting clarification

As pointed out above, different studies have used different statins in varying dosages and often with diverse patient groups. For this reason, questions concerning the best drug, ideal doses, and lipid targets for different categories of patients, remain the subject of debate.

Conclusion

The current role of statins in secondary prevention in patients with vascular disease can be summarized as follows:

- Statins should be prescribed with the objective of reducing coronary and cerebrovascular morbidity and mortality in patients with carotid disease, abdominal aortic aneurysm and lower limb occlusive disease;
- Statins should be used perioperatively in vascular surgery with the aim of reducing surgical risk;
- The use of statins in patients with carotid stenosis is recommended in order to reduce perioperative risk in endarterectomy, but there is insufficient evidence to recommend their use to control restenosis;
- There are studies that suggest statins are beneficial in intermittent claudication by improving walking distance and can therefore be prescribed for this purpose;
- There is insufficient evidence to recommend statins to prevent restenosis in lower limb revascularization procedures, to control progression of abdominal aortic aneurysms, or to reduce the severity of renal artery stenosis or renal dysfunction.

In view of the above, medication with statins is currently recommended in patients with peripheral vascular disease, which has recently been recognized by the TransAtlantic Inter-Society Consensus (TASC II) group⁶⁴ and in the 2009 European Society for Vascular Surgery guidelines on carotid disease²³.

Conflicts of interest

The authors have no conflicts of interest to declare.

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