Effect of Statins on Early and Late Clinical Outcomes of Carotid Endarterectomy and the Rate of Post-Carotid Endarterectomy Restenosis

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BACKGROUND: This study analyzed the effect of statins on clinical outcomes after carotid endarterectomy (CEA) and the rate of restenosis.

STUDY DESIGN: We performed a retrospective analysis of prospectively collected data on 500 consecutive CEAs followed at 1, 6, and 12 months and every year.

RESULTS: There were 299 patients on statins vs 201 without. Combined perioperative MI/death rates were 2.7% vs 4% ($p = 0.416$) and MI/stroke/death rates were 4% vs 5% ($p = 0.607$) for statins vs no statins. At mean follow-up (27 months), MI, stroke, and death rates were: 9.7%, 2.3%, and 2.3% vs 9%, 2.5% and 4.5% ($p = 0.18$) for statins vs no statins, respectively. Diabetic patients not on statins had 4 times more deaths (8.5% vs 2.3%) and twice as many strokes/deaths (10.2% vs 5.3%). Patients with hypercholesterolemia who were not on statins had twice as many deaths (4.3% vs 2.2%). Rates of freedom from stroke/MI/death at 1, 2, 3, and 4 years were: 94%, 90%, 85% and 77% vs 94%, 89%, 85%, and 82% ($p = 0.87$) for statins vs no statins, respectively. Rates of freedom from death only for patients on statins vs no statins at 1, 2, 3, and 4 years were: 98%, 98%, 97.4% and 97.4% vs 98%, 96%, 94.8% and 94.8%, respectively ($p = 0.191$). For diabetic patients, rates of freedom from death at 1, 2, 3, and 4 years were 99%, 99%, 97%, and 97% for statins vs 97%, 90%, 90%, and 90% without statins, respectively ($p = 0.048$). Post-CEA restenosis rates $\geq$50% were not significantly different between statins vs no statins ($p = 0.64$).

CONCLUSIONS: Statins significantly lowered death rates in patients with diabetes and tended to lower both death and stroke rates in diabetic patients and patients with hypercholesterolemia. Statins had no effect on post-CEA restenosis. (J Am Coll Surg 2015;220:481−487. © 2015 by the American College of Surgeons)

The pleiotropic effects of statins on the vascular system have resulted in several studies examining their use in several cardiovascular disorders such as coronary artery disease, peripheral artery disease, aneurysmal disease, stroke, and, more recently, in patients undergoing carotid endarterectomy (CEA).[1-8]

The Heart Protection Study (HPS) randomized patients into simvastatin (40 mg) vs placebo and concluded that patients on statin therapy with a previous history of cerebrovascular events conferred a 24% risk reduction in the composite endpoint of myocardial infarction (MI), stroke, vascular death, and the need for revascularization.[8] However, the incidence of late stroke alone was not reduced by statins, which was thought to be explained by the fact that patients probably gained more benefit from cardiac protection. Statins have also been shown to prevent stroke in clinical trials in different settings[2] and have been associated with a reduction in adverse events in noncardiac surgery. Others have reported that

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statins have putative neurologic protective effects[8]; therefore, statins have been recommended for cardiovascular risk modification in many medical and surgical patients. However, only a few studies have reported on their benefits in patients undergoing CEA. This study analyzed the effects of statins on perioperative and late clinical outcomes after CEA and the rate of post-CEA restenosis.

METHODS

This is a retrospective analysis of data collected prospectively on 500 consecutive patients who had CEAs over a recent 3-year period performed by vascular surgeons at the Vascular Center of Excellence at Charleston Area Medical Center/West Virginia University, Charleston, WV. The data were collected from the electronic medical records, including operative procedures, perioperative notes, and routine follow-up notes at the Vascular Center of Excellence. Additional data were sought from family physicians, if necessary, in regard to reports related to major adverse events (stroke, MI, and/or death). The death data were also supplemented by checking the Social Security Death Index. This study was approved by the Institutional Review Board of West Virginia University/Charleston Area Medical Center, Charleston, WV.

Patient demographics and clinical characteristics were recorded, including age, sex, hypertension, diabetes mellitus, coronary artery disease, hypercholesterolemia, smoking, COPD, and chronic renal insufficiency. The indications for CEA were also recorded, whether symptomatic (transient ischemic attack [TIA] or stroke) or asymptomatic. Redo CEAs, CEAs combined with coronary artery bypass, or CEAs associated with other brachiocephalic reconstructions were excluded from analysis. Patients were classified according to statin use at the time of admission to the hospital for the procedure. Statin use was defined as any type of statin therapy at any dosage. It was presumed that each statin would have an equal effect on the outcome; therefore, all statin users were counted as a single variable for the sake of analysis. Patients were not assessed for medication adherence at any point and there was no attempt to collect data on the dosage, perioperative duration of treatment, or potential complications of statin use. However, all patients who were on preoperative statin therapy were continued on statins postoperatively at discharge.

All CEAs were done under general anesthesia with systemic heparin, routine carotid patching, and intraluminal shunting. They were given preoperative aspirin (325 mg or 81 mg daily) within a few days of surgery, and it was continued indefinitely postoperatively.

Table 1. Demographic and Clinical Characteristics

	No statins (n = 201)		Statins (n = 299)		
Characteristic	**n**	**%**	**n**	**%**	**p Value**
Sex, male	111	55	154	52	0.414
Race, white	199	99	295	99	1
Hypertension	161	80	252	84	0.2266
History of stroke	35	17	41	14	0.2585
Coronary artery disease	76	38	128	43	0.2648
Hyperlipidemia	116	58	228	76	<0.0001
Diabetes mellitus	59	29	131	44	0.0011
Chronic renal insufficiency	24	12	31	10	0.5817
COPD	45	22	63	21	0.7255
Current smoker	74	37	97	32	0.312
Previous smoker	47	23	68	23	0.8675
All smokers	121	60	165	55	0.2665

Both 30-day perioperative and late major adverse events were recorded and analyzed, including stroke, MI, and/or death. These adverse events were compared between patients who were on statins vs no statins. Major adverse events, specifically death, were also compared in patients with diabetes mellitus and hypercholesterolemia, according to their intake of statins. All strokes were confirmed using brain CT scanning or MRI, and these patients were evaluated by a neurologist. An MI was defined as the presence of an abnormal electrocardiogram associated with chest pain and/or elevated plasma troponin with a value above 99% of the upper reference limit.

Definition of comorbidities

Coronary artery disease was defined as a history of angina, MI, coronary artery bypass graft, or coronary percutaneous transluminal angioplasty or stenting. Hypertension was defined as medical treatment for hypertension or consistent blood pressure of >150 mmHg systolic or >90 mmHg diastolic. Diabetes mellitus was defined as a history of medical treatment for diabetes.

The definition of COPD was the routine use of inhalers or a previous diagnosis of obstructive pulmonary disease or medical therapy for COPD. Chronic renal insufficiency/end-stage renal disease was defined as renal failure requiring chronic renal replacement therapy. Hyperlipidemia was defined as the need for medical treatment for hyperlipidemia or total cholesterol above 200 mg/dL.

Regarding post-CEA carotid duplex surveillance protocol, all patients underwent immediate postoperative duplex ultrasound, which was repeated at 1, 6, and 12 months, and every year thereafter. The presence of