

Atorvastatin reduced stroke and CV events after recent stroke or TIA in patients with no known coronary heart disease

The SPARCL Investigators. High-dose atorvastatin after stroke or transient ischemic attack. *N Engl J Med.* 2006;355:549-59.

Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Geriatrics ★★★★★☆☆ Neurology ★★★★★☆☆

QUESTION

In patients with no known coronary heart disease (CHD) and recent stroke or transient ischemic attack (TIA), is atorvastatin more effective than placebo for reducing stroke?

METHODS

Design: Randomized placebo-controlled trial (Stroke Prevention by Aggressive Reduction in Cholesterol Levels [SPARCL] trial).

Allocation: {Concealed}†.*

Blinding: Blinded (clinicians, patients, data safety and monitoring committee, {data collectors, outcome assessors, and data analysts}†).*

Follow-up period: Median 4.9 years (range 4.0 to 6.6 y).

Setting: 205 centers in 27 countries.

Patients: 4731 patients > 18 years of age (mean age 63 y, 60% men) who had ischemic or hemorrhagic stroke or TIA 1 to 6 months before randomization, were ambulatory, had a modified Rankin score ≤ 3, and a low-density lipoprotein (LDL) cholesterol level 100 to 190 mg/dL (2.6 to 4.9 mmol/L). 69% of enrolled patients had had previous stroke. Exclusion criteria included atrial fibrillation, embolism from other cardiac sources, and subarachnoid hemorrhage.

Intervention: Atorvastatin, 80 mg/d ($n = 2365$), or placebo ($n = 2366$).

Outcomes: Fatal or nonfatal stroke. Secondary outcomes included all-cause death and 7 composite endpoints: stroke or TIA; cardiac death, nonfatal myocardial infarction, or resuscitation after cardiac arrest (major coronary event); stroke plus any major coronary event); stroke plus any major coronary event (major cardiovascular [CV] event); major coronary event or unstable angina (acute coronary event); acute coronary event plus coronary revascularization, unstable angina, or angina or ischemia requiring hospitalization (any CV event); coronary, carotid, or peripheral revascularization; and any previous composite endpoint plus peripheral vascular disease (any CV event).

nary event (major cardiovascular [CV] event); major coronary event or unstable angina (acute coronary event); acute coronary event plus coronary revascularization, unstable angina, or angina or ischemia requiring hospitalization (any coronary event); coronary, carotid, or peripheral revascularization; and any previous composite endpoint plus peripheral vascular disease (any CV event).

Patient follow-up: 96% (intention-to-treat analysis).

MAIN RESULTS

Atorvastatin reduced fatal or nonfatal stroke and all 7 secondary composite endpoints

more than did placebo (Table). Groups did not differ for all-cause death (9.1% vs 8.9%; hazard ratio 1.0, 95% CI 0.8 to 1.2).

CONCLUSION

In patients with no known coronary heart disease and recent stroke or transient ischemic attack, atorvastatin reduced stroke and coronary and cardiovascular events.

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*See Glossary.

†Information provided by author.

Atorvastatin vs placebo in patients with no known coronary heart disease and recent stroke or transient ischemic attack (TIA) at median 4.9 years†

Outcomes	Atorvastatin	Placebo	RRR (95% CI)	NNT (CI)
Fatal or nonfatal stroke	11%	13%	15% (0.9 to 28)	51 (28 to 817)
Composite endpoint of stroke or TIA	16%	20%	21% (11 to 31)	24 (17 to 46)
Major coronary event [§]	3.4%	5.1%	34% (13 to 50)	58 (40 to 156)
Major CV event	14%	17%	19% (7.3 to 29)	32 (21 to 80)
Acute coronary event¶	4.3%	6.4%	34% (16 to 49)	46 (32 to 101)
Any coronary event**	5.2%	8.6%	41% (26 to 53)	29 (22 to 45)
Revascularization	4.0%	6.9%	44% (27 to 56)	33 (26 to 54)
Any CV event††	22%	29%	23% (15 to 30)	16 (12 to 24)

‡CV = cardiovascular. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from control event rates and adjusted hazard ratios in article.

§Cardiac death, nonfatal myocardial infarction, or resuscitation after cardiac arrest.

||Stroke plus any major coronary event.

¶Major coronary event or unstable angina.

**Acute coronary event plus coronary revascularization, unstable angina, or angina or ischemia requiring hospitalization.

††Any previous composite endpoint plus peripheral vascular disease.

COMMENTARY

The SPARCL trial was the first to evaluate the effects of statins on patients with cerebrovascular disease but without known CHD. Patients who received atorvastatin, when compared with those who received placebo, had a 2.2% absolute risk reduction (ARR) in stroke and a 3.5% ARR in vascular events (stroke or major cardiac event) after 5 years. To put these numbers in perspective, this magnitude of ARR is similar to that of antiplatelet therapy (1).

Before SPARCL, the only available data on statins in patients with cerebrovascular disease were from a subgroup analysis of the Heart Protection Study (HPS) (2). HPS did not show a reduction in recurrent stroke rates, although there was a 5.1% ARR in vascular events over 5 years. SPARCL and HPS differ in 2 important ways. First, SPARCL enrolled patients much sooner after a cerebrovascular event than did HPS. Because recurrent stroke rates are highest in the first year, statins given sooner after a stroke may have a greater effect on reducing these rates. Second, patients in SPARCL received a larger dose

of a more potent statin than did patients in HPS. Accordingly, the mean LDL reduction was greater in SPARCL than in HPS (56 vs 39 mg/dL).

One caveat is that patients taking statins in both SPARCL and HPS had a higher absolute risk for hemorrhagic stroke by 0.6% to 0.9% over the duration of their studies.

SPARCL showed that statins modestly reduced risk for both stroke and vascular events in patients with recent stroke without known CHD. Along with antithrombotic and antihypertensive therapy, statins should be given to most patients with a recent cerebrovascular event to prevent further vascular events.

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References

1. Antithrombotic Trialist Collaboration. *BMJ.* 2002;324:71-86.
2. Collins R, Armitage J, Parish S, Sleight P, Peto R. *Lancet.* 2004;363:757-67.