

Start a statin prior to vascular surgery. *J Fam Pract.* 2010;59:108-110.

Potential PURL Review Form: Randomized controlled trials

SECTION 1: IDENTIFYING INFORMATION

1. Citation Schouten O, Boersma E, Hoeks SE, et al; for the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. Fluvastatin and perioperative events in patients undergoing vascular surgery. *N Engl J Med.* 2009;361:980-989.
2. Hypertext link to PDF of full article <http://content.nejm.org/cgi/reprint/361/10/980.pdf>
3. First date published study available to readers September 3, 2009
4. PubMed ID 19726772
5. Nominated By Jim Stevermer
6. Institutional Affiliation of Nominator University of Missouri
7. Date Nominated October 22, 2009
8. Identified Through EBP Review
9. PURLS Editor Reviewing Nominated Potential PURL Kate Rowland
10. Nomination Decision Date October 27, 2009
11. Potential PURL Review Form (PPRF) Type Randomized controlled trial
12. Other comments, materials or discussion
13. Assigned Potential PURL Reviewer Kate Rowland
14. Reviewer Affiliation University of Chicago
15. Date Review Due November 5, 2009
16. Abstract

BACKGROUND: Adverse cardiac events are common after vascular surgery. We hypothesized that perioperative statin therapy would improve postoperative outcomes. **METHODS:** In this double-blind, placebo-controlled trial, we randomly assigned patients who had not previously been treated with a statin to receive, in addition to a beta-blocker, either 80 mg of extended-release fluvastatin or placebo once daily before undergoing vascular surgery. Lipid, interleukin-6, and C-reactive protein levels were measured at the time of randomization and before surgery. The primary end point was the occurrence of myocardial ischemia, defined as transient electrocardiographic abnormalities, release of troponin T, or both, within 30 days after surgery. The secondary end point was the composite of death from cardiovascular causes and myocardial infarction. **RESULTS:** A total of 250 patients were assigned to fluvastatin, and 247 to placebo, a median of 37 days before vascular surgery. Levels of total cholesterol, low-density lipoprotein cholesterol, interleukin-6, and C-reactive protein were significantly decreased in the fluvastatin group but were unchanged in the placebo group. Postoperative myocardial ischemia occurred in 27 patients (10.8%) in the fluvastatin group and in 47 (19.0%) in the placebo group (hazard ratio, 0.55; 95% confidence

interval [CI], 0.34 to 0.88; $P=0.01$). Death from cardiovascular causes or myocardial infarction occurred in 12 patients (4.8%) in the fluvastatin group and 25 patients (10.1%) in the placebo group (hazard ratio, 0.47; 95% CI, 0.24 to 0.94; $P=0.03$). Fluvastatin therapy was not associated with a significant increase in the rate of adverse events. **CONCLUSIONS:** In patients undergoing vascular surgery, perioperative fluvastatin therapy was associated with an improvement in postoperative cardiac outcome. (Current Controlled Trials number, ISRCTN83738615.) Massachusetts Medical Society

17. Pending
PURL Review
Date

SECTION 2: CRITICAL APPRAISAL OF VALIDITY

- | | |
|--|--|
| 1. Number of patients starting each arm of the study? | 250 to fluvastatin, 247 to placebo |
| 2. Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc.)? | Inclusion: age >40, preop from vascular surgery (AAA repair, aortoiliac reconstruction, lower-limb arterial reconstruction, CEA, no history of statin use, score of at least 51 on a risk index.
Exclusion: on a statin, contraindication to a statin, emergency surgery, reoperation within 30 days of a previous operation, unstable coronary artery disease, stress test positive for left main disease. |
| 3. Intervention(s) being investigated? | Fluvastatin 80 mg |
| 4. Comparison treatment(s), placebo, or nothing? | Placebo |
| 5. Length of follow up? Note specified end points e.g. death, cure, etc. | 30 days |
| 6. What outcome measures are used? List all that assess effectiveness. | Postoperative myocardial infarction (MI), death from cardiovascular (CV) causes or MI. |
| 7. What is the effect of the intervention(s)? Include absolute risk, relative risk, NNT, CI, P -values, etc. | deaths (from CV causes): 6 (4) in fluvastatin vs 12(8) in placebo, absolute risk reduction (ARR) death: 2.4%; number needed to treat (NNT): 41.
CV causes: ARR: 1.16% NNT: 62.5.

ARR to prevent 1 case of myocardial ischemia: 12 (unclear if truly patient-oriented). |
| 8. What are the adverse effects of intervention compared with no intervention? | |
| 9. Study addresses an appropriate and clearly focused question - select one | Well covered |
| 10. Random allocation to comparison groups | Well covered |
| 11. Concealed allocation to comparison groups | Well covered |
| 12. Subjects and investigators kept "blind" to comparison group allocation | Well covered |

13. Comparison groups are similar at the start of the trial	Well covered
14. Were there any differences between the groups/arms of the study other than the intervention under investigation? If yes, please indicate whether the differences are a potential source of bias.	Well covered
15. Were all relevant outcomes measured in a standardized, valid, and reliable way?	Well covered
16. Are patient oriented outcomes included? If yes, what are they?	MI, death
17. What percent dropped out, and were lost to follow up? Could this bias the results? How?	Not addressed
18. Was there an intention-to-treat analysis? If not, could this bias the results? How?	Yes, ITT.
19. If a multi-site study, are results comparable for all sites?	N/A
20. Is the funding for the trial a potential source of bias? If yes, what measures were taken to insure scientific integrity?	Funded by Novartis, with investigator independence.
21. To which patients might the findings apply? Include patients in the study and other patients to whom the findings may be generalized.	High-risk cardiac patients undergoing vascular surgery.
22. In what care settings might the findings apply, or not apply?	Primary care, cardiology.
23. To which clinicians or policy makers might the findings be relevant?	Primary care, cardiologists, CV surgery.

SECTION 3: REVIEW OF SECONDARY LITERATURE

1. DynaMed excerpts

2. DynaMed citation/access date Perioperative cardiac management of noncardiac surgery. In: DynaMed [database online]. Available at: www.DynamicMedical.com Last updated October 29, 2009. Accessed November 4, 2009.

3. Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences) Cites this study and 2 others.

4. UpToDate excerpts

5. UpToDate citation/access date

6. Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences)

7. PEPID PCP excerpts Does not seem to be addressed.

8. PEPID citation/access data

9. PEPID content updating

10. Other excerpts (USPSTF; other guidelines; etc.)

Class I

1. For patients currently taking statins and scheduled for noncardiac surgery, statins should be continued. (Level of Evidence: B)

Class IIa

1. For patients undergoing vascular surgery with or without clinical risk factors, statin use is reasonable. (Level of Evidence: B)

Class IIb

1. For patients with at least 1 clinical risk factor who are undergoing intermediate-risk procedures, statins may be considered. (Level of Evidence: C)

11. Citations for other excerpts American College of Cardiology Foundation (ACCF), American Heart Association (AHA). ACC/AHA guideline update on perioperative cardiovascular evaluation for noncardiac surgery. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee to Update the 1996 Guidelines). Bethesda, MD: American College of Cardiology Foundation; 2002.

12. Bottom line recommendation or summary of evidence from Other Sources (1-2 sentences) May be evidence to back up AHA recommendations.

SECTION 4: CONCLUSIONS

1. Validity: How well does the study minimize sources of internal bias and maximize internal validity? Give one number on a scale of 1 to 7

(1=extremely well; 4=neutral; 7=extremely poorly)

2. If 4.1 was coded as 4, 5, 6, or 7, please describe the potential bias and how it could affect the study results. Specifically, what is the likely direction in which potential sources of internal bias might affect the results?

3. Relevance: Are the results of this study generalizable to and relevant to the health care needs of patients cared for by “full scope” family physicians? Give one number on a scale of 1 to 7 (1=extremely well; 4=neutral; 7=extremely poorly)

4. If 4.3 was coded as 4, 5, 6, or 7, please provide an explanation.

5. Practice changing potential: If the findings of the study are both valid and relevant, does the practice that would be based on these findings represent a change from current practice? Give one number on a scale of 1 to 7 (1=definitely a change from current practice; 4=uncertain; 7=definitely not a change from current practice)

6. If 4.5 was coded as 1, 2, 3, or 4, please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit.

I'm not sure that there are that many patients undergoing vascular surgery who aren't on a statin. Researchers reviewed 1669 patients for the study and rejected 789 because they were already on a statin.

7. Applicability to a Family Medical Care Setting:

Is the change in practice recommendation something that could be done in a medical care setting by a family physician (office,

hospital, nursing home, etc), such as a prescribing a medication, vitamin or herbal remedy; performing or ordering a diagnostic test; performing or referring for a procedure; advising, educating or counseling a patient; or creating a system for implementing an intervention? Give one number on a scale of 1 to 7 (1=definitely could be done in a medical care setting; 4=uncertain; 7=definitely could not be done in a medical care setting)

8. If you coded 4.7 as a 4, 5, 6 or 7, please explain.

9. Immediacy of Implementation: 1

Are there major barriers to immediate implementation? Would the cost or the potential for reimbursement prohibit implementation in most family medicine practices? Are there regulatory issues that prohibit implementation? Is the service, device, drug or other essentials available on the market? Give one number on a scale of 1 to 7 (1=definitely could be immediately applied; 4=uncertain; 7=definitely could not be immediately applied)

10. If you coded 4.9 as 4, 5, 6, or 7, please explain why.

11. Clinical meaningful outcomes or patient oriented outcomes: 1

Are the outcomes measured in the study clinically meaningful or patient-oriented? Give one number on a scale of 1 to 7 (1=definitely clinically meaningful or patient-oriented; 4=uncertain; 7=definitely not clinically meaningful or patient-oriented)

12. If you coded 4.11 as a 4, 5, 6, or 7 please explain why.

13. In your opinion, is this a Pending PURL? Give one number on a scale of 1 to 7 4

(1=definitely a Pending PURL;
4=uncertain; 7=definitely not a
Pending PURL)

Criteria for a Pending PURL:

- Valid: Strong internal scientific validity; the findings appears to be true.
- Relevant: Relevant to the practice of family medicine
- Practice changing: There is a specific identifiable new practice recommendation that is applicable to what family physicians do in medical care settings and seems different than current practice.
- Applicability in medical setting:
- Immediacy of implementation

14. Comments on your response in 4.13 Not sure it is a practice changer.

SECTION 5: EDITORIAL DECISIONS

1. FPIN PURLs editorial decision (select one) Pending PURL—Forward to JFP Editor

2. Follow up issues for Pending PURL Reviewer None

3. FPIN PURLS Editor making decision Kate Rowland

4. Date of decision November 5, 2009

5. Brief summary of decision We felt that this was a significant decrease in mortality in a setting where cardiac and noncardiac deaths are common. We were concerned that there might not be a lot of people who present for vascular surgery without being on a statin, but the investigators found about 50% of those screened for participation were not on a statin.