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Hospitalist Update

Perioperative Statins in Non-cardiac Surgery

Robert Lancey MD

Preoperative cardiac risk stratification has taken on an important role in inpatient medicine. But perhaps of even greater importance is the subject of perioperative medical management. Given the mounting evidence that preoperative revascularization is largely ineffective for improving postoperative survival over medical management, perioperative medical therapy to reduce surgical morbidity and mortality has gained importance. The evidence in favor of perioperative beta-blockers has recently come into question but the literature looking at the benefit of HMG-CoA reductase inhibitors (statins) appears quite promising.

Perioperative statins have been studied extensively in the setting of cardiac surgery. A recent meta-analysis of multiple RCTs by Hindler et al (4) showed a perioperative mortality benefit of 39% for statins in cardiac surgery patients. The same meta-analysis showed a 59% relative risk reduction in favor of statins after high-risk vascular surgery. However, data on statins in intermediate-risk, noncardiac surgery is sparse, with only one large retrospective database survey available to evaluate the benefits of statins in this cohort of patients.

The data supporting the benefit of statins in noncardiac surgery includes one small randomized trial and several retrospective studies. In 2004, Durazzo et al (1) randomized 100 patients to either atorvastatin 20 mg qd or placebo, starting at least 30 days prior to elective major vascular surgery. Primary outcome measures included mortality and cardiovascular events; at 6 months, 8% of the atorvastatin group vs. 26% of the placebo group had met an endpoint ($p=0.03$). Similarly, a large retrospective chart review by Lindenhauer et al (3) demonstrated a significant reduction in mortality between patients on statins at the time of surgery versus those not on statins. In 2007, Le Manach et al (2) studied the question of what happens when statins are discontinued perioperatively; in their retrospective review of almost 700 patients who had undergone AAA repair, the occurrence of myonecrosis was assessed with troponin I levels. Patients who received continuous statin therapy had a 5-fold lower incidence of (cont)



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(cont) elevated troponins than did those patients whose statin therapy was discontinued for at least four days postoperatively.

In conclusion, the data thus far strongly suggests that perioperative statin therapy is beneficial in patients undergoing noncardiac surgery. Unfortunately, due to a lack of randomized trials, the evidence is far from definitive; nevertheless, the early evidence is compelling and may already be able to guide therapy in two areas. First, discontinuing statins perioperatively likely increases the rate of adverse cardiac events; second, starting statins at least four weeks prior to noncardiac surgery seems to provide cardiovascular benefit for patients who are at increased cardiac risk. More robust data is expected in the near future and, hopefully, will give hospitalists another management resource for their perioperative toolkit.

1. Durazzo et al., *Reduction in CV Events after Vascular Surgery with Atorvastatin: a Randomized Controlled Trial*, J Vasc Surg 2004; 39:967-976
2. Le Manach et al., *The Impact of Postoperative Discontinuation or Continuation of Chronic Statin Therapy on Cardiac Outcome after Major Vascular Surgery*, Anesth Analg 2007; 104:1326-1333
3. Lindenhauer et al., *Lipid-Lowering Therapy and In-Hospital Mortality following Major Noncardiac Surgery*, JAMA 2004; 291:2092-2099
4. Hindler et al., *Improved Postoperative Outcomes associated with Preoperative Statin Therapy*, Anesthesiology 2006; 105:1260-1272

CASE OF THE MONTH

Kyle Moylan MD

Orthopedic Surgery requested an inpatient Internal Medicine consultation for evaluation of an 81 year old woman with multiple vertebral fractures of possible pathologic origin. The patient had been in excellent health with no chronic medical problems and took no medications. Three months prior to admission, she presented to an outside ER with the acute onset of midline thoracic back pain that started immediately after lifting a gallon of milk. The pain was severe but she had no associated neurologic symptoms. A plain radiograph revealed a vertebral compression fracture (level not specified); no labs were obtained and she was sent home with analgesics and a referral to orthopedic clinic in one month. At that visit, she was prescribed Tylenol and offered vertebroplasty but the patient declined. She presented to the University Hospital ER one month later with worsening pain, uncontrolled by the Tylenol; a plain radiograph revealed severe T-6 and L-4 vertebral compression fractures; these were not present on films obtained one month prior. A T-11 anterior wedge deformity, presumably the original fracture, was unchanged. The patient was seen by Orthopedic Surgery in the ER; she was prescribed cyclobenzaprine, ibuprofen and a Jewett brace and was set up for an outpatient MRI and an orthopedic spine surgery appointment. There was some discussion of an inpatient evaluation but the patient had declined. With this management, the mid thoracic pain improved but she experienced worsening pain in the upper lumbar and thoracolumbar area.

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The MRI of the thoracic and lumbar spine was performed two weeks prior to admission. This revealed multiple zones of abnormal vertebral body signal, most prominent at T6, T11, L4 and in the sacrum. Additional innumerable punctuate zones of signal abnormality were also found throughout the vertebrae. There was no compression of the neural canal. These findings were interpreted as highly suggestive of metastatic disease and she was seen at the Spine Center later that day. Since malignancy was suspected, an outpatient bone scan was performed that demonstrated abnormal uptake in the bodies of L3 and T10 and in the posterior elements of T6. Abnormal foci were also seen in the right lateral 6th and 9th ribs and in the left 7th rib. A CT scan of the chest, abdomen and pelvis showed no evidence of a primary malignancy or of other metastases.

One week prior to admission, a vertebroplasty and biopsy was performed successfully at the T-11 vertebra; the biopsy was negative, consisting mostly of blood. On follow-up, the patient reported increasing pain and repeat radiography showed a new T12 anterior wedge deformity, consistent with an acute fracture. She was admitted for a T12 vertebroplasty and repeat biopsy attempt.

During this admission, Internal Medicine was consulted. The patient denied additional symptoms except for some anorexia and an unintentional 15 pound weight loss over the past year. She was taking Calcium 600mg +Vitamin D TID, ibuprofen 600 mg TID and prn cyclobenzaprine. She denied trauma, falls, lymphadenopathy, fever, night sweats, chills or breast mass. Physical findings were limited to tenderness over the thoracolumbar area; there were no neurological deficits and breast, rectal and lymph node exams were normal. Labs were remarkable for Hgb 11.0, MCV 90, WBC 12.1 (normal diff), BUN 23, Cr 1.4, Ca 12.0; LFTs, including AP, TP and Alb were normal. ESR was 39mm/hr and CRP was high at 1.3 mg/dl. Serum and urine protein electrophoresis had been performed and were normal.

Based on the patient's age, lack of primary tumor, hypercalcemia, anemia and renal dysfunction, the working diagnosis was multiple myeloma. Zoledronic acid 4mg IV was given for the hypercalcemia and the serum calcium normalized within 48 hrs. Her renal function improved (Cr 1.1 on discharge) and her pain was controlled with scheduled Tylenol 1000 TID and prn oxycodone; her appetite improved and she was ambulating in the halls prior to discharge.

Additional labs included serum beta-2 microglobulin 3.9 mg/L (normal 1.1-2.4), 24 hour urine for electrophoresis and immunofixation with 27.20 mg/dl of kappa light chains (normal .14-2.42) and a kappa:lambda ratio of 104.6 (normal 2-10). A skeletal survey showed no additional lytic lesions and the repeat biopsy confirmed multiple myeloma (monotonous sheets of mature plasma cells). Follow-up was arranged with Heme-Onc.

Discussion: Vertebral fractures are common in older patients and are usually due to osteoporosis. However, the physician should look for secondary causes and workup should include serum Ca and Phos, serum intact parathyroid hormone, serum 25-hydroxyvitamin D level and protein electrophoresis of serum and urine. As in this patient, multiple myeloma usually occurs in older patients (it is rare under 40) and common clinical features include anemia, elevated ESR, proteinuria, marrow failure, infection and renal impairment; other features may include hypercalcemia, hyperviscosity, neuropathy, amyloidosis and coagulopathy.

The primary pathology of multiple myeloma is a neoplastic transformation of a monoclonal plasma cell population which produce a monoclonal protein; intact immunoglobulin is most common (IgG 60%, IgA 20%). However, some patients, such as ours, have no detectable immunoglobulin by serum and urine electrophoresis and immunofixation; these cases represent nonsecretory myeloma or light chain disease. When clinical suspicion is high, a 24 hour urine collection is required to detect free light chains (Bence-Jones protein), which may be missed by spot urine testing. Serum beta-2 microglobulin is a new test that adds to our diagnostic arsenal and has prognostic significance. Ultimately, the diagnosis must be confirmed by bone marrow biopsy and aspiration. Zoledronic acid is effective at normalizing serum calcium and preventing additional fractures.

FROM THE JOURNALS**Syed Ahsan MD**

I have recently come across the following articles that should be of interest to Hospitalists:

House Staff Member Awareness of Older Inpatients' Risks for Hazards of Hospitalization

Fernandez, HM et al., Arch Intern Med, 2008, Feb 25; 168(4):390-396

This study showed that Internal Medicine house staff members are not aware of many of their patients' risk factors that contribute to the hazards of hospitalization.

Outcomes of Care by Hospitalists, General Internists and Family Physicians

Lindenauer, PK et al., NEJM, 2007, Dec 20; 357(25): 2589-2600; Center for Quality & Safety Research, Baystate Medical Center, Springfield, MA 01199

For common inpatient diagnoses, the hospitalist model is associated with a small reduction in the length of stay without adverse effect on rates of death or readmission.

Promoting Effective Transitions of Care at Hospital Discharge: A Review of Key Issues for Hospitalists

Kripalani, S et al., J Hosp Med, 2007, Sep; 2(5): 314-323

This article reviews several important challenges to providing high quality care upon discharge.

Acute Heart Failure Syndromes in Patients with Coronary Artery Disease: Early Assessment and Treatment

Flaherty, JD et al., Acute Heart Failure Syndromes International Working Group, J Am Coll Cardiol 2009, Jan 20; 53(3): 254-263

The initial in-hospital and after-discharge management of AHFS may be dependent on clinical presentation.

ID CORNER**William Salzer MD****Candidiasis Guidelines**

The IDSA has updated their practice guidelines for Candida infections; this includes candidemia, other invasive forms and superficial infections.

Pappas, PG et al., Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Disease Society of America, Clin Infect Dis 2009; 48:503-535

<http://www.journals.uchicago.edu/doi/pdf/10.1086/596757>

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MISSOURI HOSPITALIST CALENDAR

Arrhythmia Management for the Clinician, Am College Cardiology, Four Seasons Hotel, Philadelphia, PA, April 16-18, www.greatheartdoctors.com/ghd/page297.htm

American Geriatrics Society 2009, Hyatt Regency, Chicago, April 29—May 3, info and registration: www.americangeriatrics.org

47th Annual USC Weil Symposium on Critical Care and Emergency Medicine, May 17-21, Westin Mission Hills, Rancho Mirage, California; 800-USC-1119 or register online: www.peopleware.net/0128 (select course #2480)

Missouri ACP Meeting, to include a **Hospitalist Conference Luncheon**, focusing on **Hospital Acquired Infections**, September 24-27; details to follow.

The Academic Hospitalist Academy: Essential Skills for Education, Scholarship and Professional Success, Society of GIM, November 8-11, Atlanta, Peachtree Conference Center; for more info, contact Amy Woodward, woodwarda@sgim.org; **note that attendance will be capped at 100 participants (register early).**

COMMENTS FROM MEMBERS

None Received

Please direct all comments, ideas and newsletter contributions to the Editor:

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Please forward this newsletter to Missouri Hospitalists that you might know!