

MINDFUL PRACTICE

EVAR for Patients Ineligible for Open Repair

BY JON O. EBBERT, M.D., AND ERIC G. TANGALOS, M.D.

The Problem

You have been expectantly managing a 91-year-old man with an abdominal aortic aneurysm (AAA) and have monitored him with serial radiologic examinations. He is admitted to the hospital for severe microcytic anemia and is found to have Cameron ulcers and antral erosions. A CT scan reveals that his AAA has enlarged to 5.9 cm in maximum dimension with no evidence of bleeding. You continue to follow him, and a repeat ultrasound shows that the AAA has enlarged to 6.8 cm. At your institution, endovascular aneurysm repair (EVAR) is more commonly performed than open intervention. However, before presenting this option to your patient, you decide to review the literature.

The Question

Among patients ineligible for open AAA repair, does EVAR reduce mortality and improve quality of life, compared with usual care?

The Search

You log on to PubMed (www.pubmed.gov), enter search term "EVAR," and limit results to randomized controlled trials. You find a relevant study. (See box at right.)

Our Critique

This study was conducted to fill in knowledge gaps about patients in clinical practice who have significant medical comorbidities preventing them from undergoing open AAA repair. Importantly, the clinical characteristics of subjects refusing enrollment in this study did not differ significantly from those who agreed to be enrolled. Of the patients randomized to best medical treatment, 27% ultimately underwent aneurysm repair. This phenomenon may partly relate to the observations that the investigators made of "fitness inflation," in which patients not deemed fit for surgery were subsequently found to be so when the aneurysm got larger. Overall, this study suggests that with EVAR, the number of procedures in nonsurgical candidate patients is increased without clearly improving survival. This study also provides important prognostic information for expectantly managed AAA patients, a population estimated to have aneurysm-related mortality of 19% and all-cause mortality of 62% by 4 years.

Clinical Decision

You share the information with the patient, but his son presses for a consultation with the vascular surgeons. A CT scan reveals that his aneurysm is 7.5 cm in diameter. The vascular surgeons offer him EVAR. He does well post operatively, and you make plans to monitor him with CT annually.

DR. EBBERT and DR. TANGALOS are with the Mayo Clinic in Rochester, Minn. They report having no conflicts of interest. To respond to this column or suggest topics for consideration, write to Dr. Ebbert and Dr. Tangalos at our editorial offices or e-mail them at imnews@elsevier.com.

**EVAR trial participants.**

Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2). *Lancet* 2005;365:2187-92.

► **Design and setting:** Randomized clinical trial done at 31 hospitals in the United Kingdom.

► **Patients:** Patients were eligible for enrollment if they were at least 60 years old, had an aneurysm measuring at least 5.5 cm in diameter on any plane on a CT scan, and were medically unfit for open repair. Fitness for surgery was determined by the surgeon, radiologist, anesthesiologist, or cardiologist. General guidelines used included cardiac status (myocardial infarction or new-onset angina in last 3 months or unstable angina), cardiac valvular disease, significant arrhythmia, heart failure, poor respiratory status (FEV₁ less than 1.0 L), or elevated serum creatinine (2.3 mg/dL).

► **Intervention:** Patients were randomized to both EVAR and best medical treatment, or best medical treatment alone. Once enrolled, patients were expected to undergo aneurysm repair within 30 days.

► **Outcomes:** Patients with large AAAs considered unfit for open repair were followed for AAA growth and rupture. The primary outcome was all-cause mortality, and a blinded end point committee assigned the cause of death. Secondary outcomes included aneurysm-related mortality, incidence of postoperative complications of aneurysm repair and secondary interventions, health-related quality of life, and hospital costs. Aneurysm-related mortality was defined as deaths within 30 days of AAA surgery unless overruled by post mortem findings or unless a subsequent procedure unrelated to the aneurysm was attributed as the cause of death.

► **Results:** Between September 1999 and December 2003, 457 patients were identified as being unfit for open repair, and 338 of these were randomized (166 to EVAR, 172 to medical treatment). Groups were comparable at baseline. In the EVAR group, mean age was 77 years, 85% were men, 77% were former smokers, 65% had cardiac disease, AAA diameter was 6.4 cm, and average FEV₁ was 1.6 L. Notably, 47 patients (27%) assigned to no intervention underwent aneurysm repair, including 12 patients who had open repair. Over a median of 2.4 years of follow-up, 142 patients died; 42 deaths (30%) were aneurysm related. No differences were observed between groups with respect to aneurysm-related mortality and all-cause mortality. In the intention-to-treat analysis, 43% of patients in the EVAR group had at least one postoperative complication by 4 years, compared with 18% in the medical treatment group (hazard ratio 5.3; 95% confidence interval 2.8-10; *P* less than .0001). The overall intervention rate was higher for EVAR patients as well (HR 5.8; 95% CI 2.4-14.0; *P* less than .001). Quality of life did not differ by group.

Prospective Study of Vitamin D to Launch

BY DOUG BRUNK

SAN DIEGO — The ability of vitamin D to reduce the risks of cardiovascular disease and cancer are about to be put to the test in a randomized, controlled study.

January will bring the launch of the vitamin D and omega-3 trial (VITAL), a 20,000-participant study that will examine whether daily dietary supplements of vitamin D (about 2,000 IU) or fish oil (about 1 g of omega-3 fatty acids) reduces the risk of developing cancer, heart disease, and stroke.

Speaking at the annual meeting of the North American Menopause Society, Dr. Edward Giovannucci said that observational studies have validated vitamin D status as predictive of cardiovascular disease



'There could possibly be an age gradient for vitamin D where the level might be more important for older women.'

DR. GIOVANNUCCI

and cancer risks. The next step is therapeutic intervention with "various ranges of vitamin D. We need to know the dose-response better. We can learn a lot from intermediate end points such as inflammatory markers, but ultimately we need to look at hard end points such as cardiovascular disease and cancer."

The best studies to date suggest that serum vitamin D levels of 30 ng/mL or more are optimal for reducing the risk of cardiovascular disease and cancer, said Dr. Giovannucci, professor of nutrition and epidemiology at Harvard School of Public Health, Boston.

"There is no credible evidence of any risk associated with this level of intake," he said, but "we need to weigh benefits and risks" of vitamin D supplementation. Hypothetical associations between vitamin D deficiency and cardiovascular disease include increased levels of vascular calcification, vascular smooth cell proliferation, parathyroid hormone, tumor necrosis factor- α , and interleukin-6.

The research also could influence understanding of the pathophysiology of diseases, Dr. Giovannucci said. Elevated parathyroid hormone levels, for example, may contribute to hypertension and left ventricular hypertrophy.

In the Framingham Offspring Study, for example, a vitamin D level of 30 ng/mL or

greater was associated with a 50% reduction in risk for a cardiovascular event (*Circulation* 2008;117:503-11). "The risk flattened off at vitamin D levels of 20-25 ng/mL," he said.

In the Health Professionals Follow-up Study, a nested case-control study of myocardial infarction or fatal coronary heart disease, Dr. Giovannucci and his associates followed 454 cases and 900 controls for 10 years (*Arch. Intern. Med.* 2008;168:1174-80). After the investigators controlled for lifestyle factors, cardiovascular disease factors, lipids, and

inflammatory markers, the relative risk for MI in those with serum vitamin D levels of 15 ng/mL or less was twice as high as in those with levels of 30 ng/mL or more.

"We also found a very strong association between cases of sudden death and low levels of vitamin D," Dr. Giovannucci said.

A much larger cohort analysis, the Ludwigshafen Risk and Cardiovascular Health (LURIC) study, found strong associations between vitamin D status and all-cause and cardiovascular mortality (*J. Endocrinol. Metab.* 2008;93:3927-35). For example, about 35% of patients with vitamin D levels less than 15 ng/mL and 10% of those with levels greater than 30 ng/mL had died after nearly 8 years, he said.

As for vitamin D's effect on cancer risk, the evidence is strongest in colorectal cancer, he said. In breast cancer there have been some negative studies, but the Nurses' Health Study showed a link with borderline significance between vitamin D status and breast cancer risk in women aged 60 and older (*Cancer Epidemiol. Biomarkers Prev.* 2005;14:1991-7).

"There could possibly be an age gradient for vitamin D where the level might be more important for older women," he commented.

Dr. Giovannucci said that he had no relevant financial disclosures. ■