DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

December 17, 2003

FDA Public Health Notification: Updated Data on Mortality Associated with Medtronic AVE AneuRx® Stent Graft System

(You are encouraged to copy and distribute this information)

Dear Colleague:

In April 2001, we issued a public health notification on problems associated with endovascular grafts for repair of abdominal aortic aneurysm (AAA) (http://www.fda.gov/cdrh/safety/aaa.html). This notification is to provide you with updated information on the mortality risks associated with the AneuRx® Stent Graft System when implanted for the prevention of AAA rupture, so that you can make a more informed decision about using this product to treat your patients. This information is based on an analysis of the extension of an investigational premarket study, which began in March of 1996, and involved a subgroup of 942 patients, followed through October 24th, 2002.

This Public Health Notification focuses on the AneuRx® device, as it is the only currently marketed device with long-term clinical follow-up. Two other commercially available stent graft systems are not included in this notice because appropriate long-term data are not currently available for these devices.

Background

Our earlier notification identified several serious adverse events, including aneurysm ruptures, in patients treated with the AneuRx® Stent Graft. Since then, we have worked with the manufacturer, Medtronic AVE, as well as other sources, to obtain more complete follow-up data for the premarket cohort of patients who received the flexible model of the AneuRx® Stent Graft. These patients were considered good candidates for treatment with conventional open surgery. Certain categories of high risk patients were excluded from the study: American Society of Anesthesiology grade above IV; morbid obesity; acute renal failure or chronic dialysis; active systemic infection; less than one year of life expectancy; leaking aneurysm; aortic dissection; and aortic-iliac occlusive disease[1].

Our analysis assessed aneurysm-related death rates in patients treated with the AneuRx® Stent Graft. We defined aneurysm-related death to include deaths from rupture of the AAA or from any procedure intended to treat the AAA. If a death occurred within one month of any procedure intended to treat the AAA, it was presumed to be aneurysm-related, unless there was evidence to the contrary.

Study results

The analysis showed that the perioperative (within 30 days) aneurysm-related death rate associated with the AneuRx® Stent Graft was 1.5% (14/942). Following implantation, an additional 8 AAA related deaths were identified during the subsequent 3 years of follow-up covering 2,080 patient years, for an annualized late mortality rate of 0.40% per year. This FDA analysis estimates an AAA-related death rate of 1.9% at one year post-implant, 2.2% at two years post-implant, and 2.7% at three years post-implant.

Discussion:

Analysis of perioperative mortality associated with both endovascular and open surgical repair is complex, and may vary as a function of the patient's age, comorbidities and aneurysm morphology, surgeon, and hospital. Adding to this complexity, studies of open surgical repair typically include patients from all risk levels, whereas the investigational premarket study excluded many high-risk categories. Published literature from multi-center studies including population-based series employing statewide and national databases, states that the mortality rates for open surgical repair range between 3-5% at 30 days[2,3,4,5] This range is also consistent with the mortality for open surgery observed in two *small aneurysm* trials, the VA Cooperative Study[6] and the UK Small Aneurysm Trial[7], which reported operative mortality rates of 2.7% and 5.8%, respectively. Operative mortality rates reported in single center studies range between 0-5% [8, 9, 10, 11,12,13,14]. Results from multi-center studies may provide a better estimate of expected clinical outcome, as results from single center studies cannot typically be generalized to larger populations.

Repair of AAA also involves late mortality risk. This risk appears to be less for open surgery than for procedures using the AneuRx® stent graft. A review of late mortality associated with open surgical repair of AAA indicates the potential for mortality from pseudo-aneurysms developing at the aortic suture line and from infections[15]. Several individual studies suggest long term aneurysm-associated mortality rates associated with open surgical repair of AAA ranging from 0 % to 0.34 % per year, averaging approximately 0.18 % per year[3,6,8,9,13,14,16,17]. It should be noted that data from these studies have met varying standards of scientific rigor associated with different follow-up and diagnostic methodologies.

Recommendations

The results summarized above underscore the importance of following the manufacturer's instructions regarding careful selection and follow-up monitoring of patients with endovascular stent grafts, as stated in our April 2001 Public Health Notification.

Based on the findings of the present study, we recommend that the AneuRx® Stent Graft be used only in patients who meet the appropriate risk-benefit profile and who can be treated in accordance with the instructions for use.

In determining the risk-benefit profile for patients with AAA disease and the appropriate treatment option, among the factors to consider are:

- Long term AAA-related mortality, especially due to AAA rupture. The information above suggests that the risk of late AAA-related mortality associated with AneuRx® may exceed that associated with open surgery in some institutions. Because of this, the *overall* AAA-associated mortality from the AneuRx® Stent Graft is likely to cross-over and exceed the AAA-associated mortality from open surgery at some point in time.

- The experience of the institution or the physician. If open or endovascular surgery is performed in institutions or by physicians with little experience with open or endovascular AAA repair, the mortality rate may be considerably higher than average.

- Surgical risk factors for the individual patient. In patients who have substantial surgical risk factors such as age[18] and comorbidities (e.g., cardiac, renal and pulmonary), the mortality rate for open resection of AAA may be considerably higher than average. For example, the predicted operative mortality for a 70-year old could range from 2% if no risk factors were present to over 40% if multiple co-morbidities were present[19].

- The patient's life expectancy. Treatment with an endovascular graft may be preferable for patients with a shortened life expectancy.

- The patient's willingness to comply with the follow-up schedule for the endovascular graft.

Clinical updates of this investigational cohort are made available annually by Medtronic as a condition of AneuRx® approval. Practitioners can review the most recent information on the long term outcomes of AneuRx® patients enrolled in this investigation online, at www.Medtronic.com, and may request reprints from the Medtronic Customer Service Number, (800) 961-9055.

Reporting Adverse Events to FDA

The Safe Medical Devices Act (SMDA) of 1990 requires hospitals and other user facilities to report deaths and serious injuries associated with the use of medical devices, including endovascular stent grafts for AAA repair. You should follow the procedures established by your facility for such mandatory reporting.

We also encourage you to report any AAA stent graft malfunctions. You can report these directly to the device manufacturer. You can also report to MedWatch, the FDA's voluntary reporting program. You may submit reports to MedWatch one of four ways: online at http://www.accessdata.fda.gov/scripts/medwatch/ by telephone at 1-800-FDA-1088; by FAX at 1-800-FDA-0178; or by mail to MedWatch, Food and Drug Administration, HF-2, 5600 Fishers Lane, Rockville, MD 20857.

Future Public Health Notices will be provided as needed to update clinical information regarding the endovascular treatment of abdominal aortic aneurysm. The inputs from the above surveillance programs provide valuable resources for this purpose.

Getting More Information

If you have questions regarding this letter, please contact Laura Alonge, Office of Surveillance and Biometrics (HFZ-510), 1350 Piccard Drive, Rockville, Maryland, 20850, by fax at 301-594-2968, or by e-mail at phann@cdrh.fda.gov. Additionally, a voice mail message may be left at 301-594-0650 and your call will be returned as soon as possible.

All of the FDA medical device postmarket safety notifications can be found on the World Wide Web at http://www.fda.gov/cdrh/safety.html. Postmarket safety notifications can also be obtained through e-mail on the day they are released by subscribing to our list server. You may subscribe at http://list.nih.gov/archives/dev-alert.html.

Sincerely yours,

David W. Feigal, Jr., MD, MPH
Director
Center for Devices and Radiological Health
Food and Drug Administration

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