Misperceptions regarding the long term safety of the AneuRx stent graft

On July 9, 2004, the Wall Street Journal reported that an article posted on the Journal of Vascular Surgery Web site was withdrawn from publication by the FDA as a result of lobbying by Medtronic. According to the Wall Street Journal, this article “raised concerns about the long term safety record of a device” which was the subject of a Public Health Notification (PHN) by the FDA in December 2003. We regret that the article will not be published for it would provide an opportunity to examine evidence upon which clinical practice decisions may be based. We hope that this letter will provide information on the long-term safety of the AneuRx stent graft that can be weighed against the FDA PHN and media interpretations.

In the PHN, the FDA reported its analysis of 942 patients treated with the AneuRx stent graft and found a 30-day abdominal aortic aneurysm (AAA) death rate of 1.5%, with 8 late AAA deaths during 3 follow-up years. The cumulative AAA death rate was 2.7% at 3 years, which was lower than the 3.1% AAA death rate reported for all 1193 patients treated during the AneuRx clinical trial, due to exclusion of high-risk patients from the FDA analysis. It was also lower than the 3% to 5% operative mortality for surgery, which the FDA found in the literature. However, rather than reassuring patients with these good results, the FDA suggested that “the risk of late AAA-related mortality associated with AneuRx may exceed that associated with open surgery...[and]...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.” How could the FDA arrive at this remarkable conclusion? Perhaps the supporting data appear in the “squelched” article, and these needs to be published.

From our reading of the PHN, it appears the FDA assumed that operative mortality for surgery is 1% to 2%, that late AAA death rate is 0.18% per year (as opposed to 0.4% per year for AneuRx), and that late adverse events for both increase linearly with time. We find little data to support these assumptions. There is, however, actual data with Kaplan-Meier analysis extending to 5 years for all 1193 AneuRx clinical trial patients. How do the FDA’s projections compare to these actual data? Since the FDA excluded high-risk patients, we excluded the 262 high-risk patients in the trial, leaving 931 patients, very similar to the 942 patients studied by the FDA. The AAA death rates for these 931 patients at 30 days and 1 to 5 years are as follows: 1.5%, 1.5%, 1.8%, 1.9%, 2.5%, and 2.5% (Kaplan-Meier analysis). Thus far, there have been no AAA deaths beyond 4 years, suggesting that AAA death for AneuRx patients does not increase linearly with time. Using the FDA’s estimate of 0.18% per year, and assuming operative mortality rates of 2% and 5% at 5 years, the AAA death rate for surgery would be 2.9% and 5.9%, both higher than the actual 2.5% 5-year AAA death rate for AneuRx. Thus, evidence for a late “cross-over” of results is lacking.

We call for publication of the article containing the evidence upon which the FDA has made practice-based recommendations in its PHN so that patients and physicians can judge the evidence and select the best treatment option.

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REFERENCES