Vascular Surgeon Pans Data Behind Carotid Stent Approval

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NEW YORK — The Stenting and Angioplasty With Protection in Patients at High Risk for Endarterectomy trial was flawed from its inception and should have been stopped because of its multiple shortcomings, according to Dr. Anthony J. Comerota.

Instead, the Food and Drug Administration used data from the SAPPHIRE trial in its decision to approve carotid stents in high-risk patients, and the results of the study were published in the New England Journal of Medicine (2004; 351:1493-501), "arguably the most influential medical journal in the world," said Dr. Comerota, who served on the FDA panel that reviewed the data.

SAPPHIRE was based on an improperly designed and executed feasibility study, which was undertaken to determine if carotid angioplasty and stenting (CAS) could be performed with less than two times the 6.7% stroke and death rate of carotid endarterectomy found in the North American Symptomatic Carotid Endarterectomy Trial (NASCET), Dr. Comerota argued.

However, only truly high-risk patients with symptomatic atherosclerosis were enrolled in NASCET, whereas the majority of patients in the SAPPHIRE feasibility study were asymptomatic, Dr. Comerota said at the Veith symposium on vascular medicine sponsored by the Cleveland Clinic. Fewer than 20% of CAS patients had more than 80% stenosis, 72% were asymptomatic, and 26% had recurrent stenosis. "These are low-risk patients," said Dr. Comerota, director of the Jobst Vascular Center, Toledo (Ohio) Hospital.

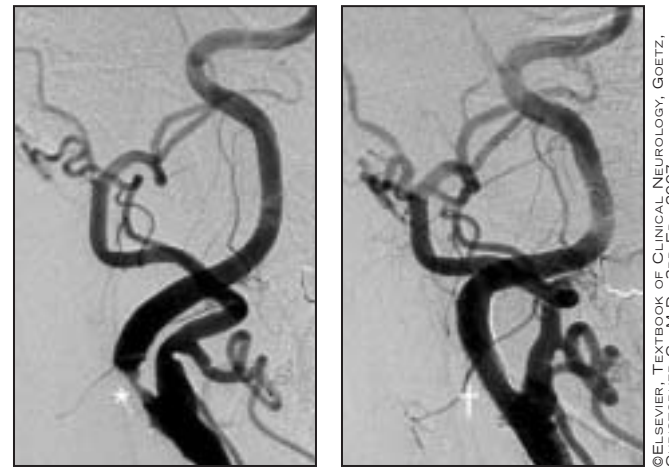
Furthermore, SAPPHIRE was designed as a randomized trial, yet a majority of patients were not randomized, but instead were entered into registries, and enrollment was terminated after only 334 of the target 2,900 had entered the study. "Termination was due to poor enrollment because of 'competing registries'—yet it was the sponsoring company's own registry that led to termination," Dr. Comerota said.

Another flaw in the study design was the inclusion of troponin-based MI as part of the primary end point, which also included stroke and death. The reason for this inclusion, according to the authors, was that patients with non–Q-wave MI have a 27-fold increased risk of an MI in the next 6 months. This was not borne out in the investigators' report of long-term outcomes, when there was no signal of an increased rate of MI, Dr. Comerota said.

"Furthermore, the statistical analysis was not done according to protocol, but rather was a unique triangular analysis I have not seen before or since SAPPHIRE," he added.

The FDA panel that reviewed the data for approval of the device included six cardiologists, two interventional radiologists, two vascular surgeons, and one neurologist. "There was no statistician on the panel, and the vote to recommend was 6-5. You can draw your own conclusions," said Dr. Comerota.

SAPPHIRE was supported by Cordis Corp., the manufacturer of the stent used in the study. ■



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Some consider carotid stenting to be the ideal solution (right) to stenosis (left) in high-risk patients, but the patients in the SAPPHIRE registry were not high risk, said Dr. Anthony J. Comerota. Fewer than 20% of CAS patients had more than 80% stenosis.