Years Later, AHA Program Hasn't Saved Lives

The 'Get With the Guidelines' program has cost millions of dollars but to little effect, critics say.

BY DAVID MONAGAN

After 9 years and tens of millions of dollars, Get With the Guidelines—the American Heart Association's push for new standards of excellence for follow-up treatment of acute cardiovascular events—appears to have yielded murky gains at best in terms of saving lives, according to a new analysis.

A total of 3,909 medical centers participated in the Get With the Guidelines (GWTG) program. Of these, 355 (9%) received a nonmonetary achievement award for either heart failure or acute myocardial infarction (AMI) follow-up care.

The report compared the risk-adjusted 30-day mortality figures for the top 355 hospitals with those of the remaining participating centers, and found no statistically significant difference in heart failure mortality. A modest 0.19% superiority in the top hospitals' survival rates following AMI was reduced by 43% after the data were adjusted for confounding factors (Am. Heart J. 2009;158:546-53).

Dr. Paul A. Heidenreich of the Veterans Affairs Palo Alto (Calif.) Health Care System and his fellow authors, all from the GWTG steering committee, acknowledged that the best-performing hospitals tended to be ones that were exceptionally well funded before the program began. Overall, "it is unclear if outcomes are better in those hospitals recognized by the GWTG program for their processes of care," they wrote.

Further, differentials in the 30-day mortality for the third component of GWTG—follow-up-care for stroke—were unclear. Recognition on all three measures of excellence, the core aim of GWTG, was achieved by 15 of the 3,909 hospitals in the program.

The program now costs as much as $12 million per year. At the AHA scientific sessions in 2005, Dr. Gray Ellrodt, lead author of an interim review of the initiative, said the program was the start of a new era of systematic excellence in cardiovascular care. "Men and women, young and old, showed dramatic improvements in care," said Dr. Ellrodt, an internist at Berkshire Medical Center, Pittsfield, Mass.

In an interview, Dr. Heidenreich called this claim "an accurate statement. The improvements in process of care were dramatic given that many quality interventions have no improvement."

Yet despite dramatic changes in care—including greater assessment of left ventricular function, use of ACE inhibitors, and rigorous discharge counseling for heart failure patients; rapid onset of thrombolytics for MI patients and emergency percutaneous coronary intervention where necessary; and more consistent use of aspirin and beta-blockers at every stage—the benefits in terms of improved mortality remained small. ■

Telmisartan Approved for High-Risk Patient Indication

BY ELIZABETH MECHCATIE

Telmisartan was approved by the Food and Drug Administration for a new indication last month: reducing the risk of myocardial infarction, stroke, or death from cardiovascular causes in patients 55 years or older who are at high risk of developing major cardiovascular events and cannot take ACE inhibitors.

Also approved by the FDA was a tablet formulation combining telmisartan with the calcium channel blocker amlodipine for treating hypertension.

Telmisartan, an angiotensin-II receptor blocker (ARB) marketed as Micardis, is manufactured by Boehringer Ingelheim Pharmaceuticals Inc. It was initially approved as an antihypertensive in 1998.

In one study, incidence of the primary end point was similar in patients treated with telmisartan (16.7%) and those treated with ramipril (16.5%) over a mean of 54 months.

The revised label for telmisartan includes a statement that patients at high risk for cardiovascular (CV) events can use it with other needed treatments, such as antihypertensive, antiplatelet, or lipid-lowering therapy, but that use with an ACE inhibitor is not recommended. The approved dose for the cardiovascular risk reduction indication is 80 mg once daily.

The approval for CV risk reduction is supported by two studies involving patients aged 55 years and older who were at high CV risk, according to the revised label. In both, the primary end point was a composite of death from CV causes, MI, stroke, and hospitalization for heart failure; the secondary end point was a composite of CV death, MI, and stroke.

In ONTARGET (Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial), which compared 80 mg of telmisartan, 10 mg of ramipril, or the combination in 25,620 patients who did not have a history of intolerance to ACE inhibitors, the incidence of the primary end point was similar in patients treated with telmisartan (16.7%) and those treated with ramipril (16.5%) over a mean of about 54 months.

In TRANSCEND (Telmisartan Randomized Assessment Study in ACE Intolerant Subjects With Cardiovascular Disease), which compared 80 mg of telmisartan with placebo in almost 6,000 patients who had a history of intolerance to ACE inhibitors (mostly due to cough), the incidence of the primary end point was also similar in the two groups over a mean of 56 months: 15.7% among those on telmisartan and 17% among those on placebo. The incidence of the secondary end point, which did not include heart failure hospitalization, was significantly lower among those on telmisartan than in those on placebo (13% vs. 14.8%).

Although the rates of events in ONTARGET were similar between patients on telmisartan and those on ramipril, "the results did not unequivocally rule out that Micardis may not preserve a meaningful fraction of the effect of ramipril in reducing cardiovascular events," the label states, but the results of both studies "do adequately support Micardis being more effective than placebo would be in this setting."

The telmisartan-amlodipine combination tablet will be marketed under the trade name Twynsta, according to the company. There are four strengths: 40 mg of telmisartan with 5 mg or 10 mg of amlodipine and 80 mg of telmisartan with 5 mg or 10 mg of amlodipine. ■

Many CABG Outcomes Worse With Off-Pump Procedures

BY MARY ANN MOON

A variety of outcomes were poorer with off-pump than with on-pump coronary artery bypass graft in a large clinical trial directly comparing the two procedures, said A. Laurie Shroyer, Ph.D., of Northport (N.Y.) Veterans Affairs Medical Center and associates.

In the Randomized On/Off Bypass trial, both short-term and 1-year mortality, as well as rates of major complications, MI, revascularization procedures, and graft patency, all were worse with the off-pump approach. Most surprisingly, rates of neuropsychological sequelae were not significantly different.

"Our trial did not show any overall advantage to the use of the off-pump" coronary artery bypass graft (CABG), the authors wrote (N. Engl. J. Med. 2009;361:1827-37).

The prospective study involved 2,203 patients undergoing elective or urgent CABG between 2002 and 2008 at 18 VA medical centers. Most (over 99%) were white men who were current or former smokers and had at least one comorbid condition; over 40% had diabetes. A majority had three-vessel coronary artery disease and normal left ventricular function.

The study subjects were randomly assigned to on-pump (1,099 patients) or off-pump (1,104 patients) surgery while waiting in the preoperative holding area.

The primary short-term end point was a composite of death or major complications such as reoperation, new mechanical support, cardiac arrest, coma, stroke, or renal failure requiring dialysis within 30 days. The primary long-term end point was death from any cause, nonfatal MI, or repeat revascularization within 1 year.

The short-term composite outcome was not significantly different between the two groups, affecting 7.0% of the off-pump group and 5.6% of the on-pump group. In contrast, the long-term composite outcome was significantly higher in the off-pump group (9.9%) than in the on-pump group (7.4%).

A subsequent sensitivity analysis of the data "showed even stronger advantages for on-pump procedures," the investigators said.

The rate of graft patency at 1 year was significantly lower for the off-pump group (82.6%) than the on-pump group (87.8%). Significantly more patients in the off-pump group (36.5%) had at least 1 occluded graft than in the on-pump group (28.7%).

Among those with no occluded grafts, the primary 1-year composite outcome was lower in the on-pump group than in the off-pump (3.3% vs. 6.4%). The researchers speculated that this was because "there was less complete revascularization in the off-pump group."

A subset of 1,156 study subjects had completed a battery of neuropsychological tests at baseline and was retested at 1 year. Dysfunctions in attention, memory, and visuospatial skills were assessed.

Unexpectedly, there were no significant differences between the two treatment groups on these measures, and the changes in individual test scores either were minimal or showed improvement after surgery for both groups, Dr. Shroyer and colleagues said.

"A number of studies have suggested that cardiopulmonary bypass causes permanent neurologic dysfunction or decreases cognition and motor abilities. Our trial did not show a cognitive decline within 1 year after surgery in either group," they noted.

Dr. Shroyer reported no potential conflicts of interest. ■