Metabolic Syndrome Affects Bariatric Outcomes

BY ELIZABETH MECHCATIE
Senior Writer

A patient's gender and ethnicity, as well as the presence of metabolic syndrome, affect the risk of death after bariatric surgery but not the risk of in-hospital complications, according to a retrospective study of more than 30,000 patients.

The findings "suggest that the presence of the metabolic syndrome negatively affects interethnic and gender-specific outcomes after bariatric surgery," Dr. Javier Esteban Varela said in an interview.

Dr. Varela of the University of Texas at Dallas was the lead investigator of the study and presented the results at the Academic Surgical Congress.

The investigators evaluated in-hospital clinical data on 30,954 patients with and without metabolic syndrome, who underwent bariatric surgery over a 5-year period (2003-2007). The data were obtained from the University HealthSystem Consortium database. The procedures performed included laparoscopic gastric bypass, open gastric bypass, and laparoscopic gastric banding. Most of the patients (85%) were women, 81% were white, 14% were black, and 5% were Hispanic. The researchers defined metabolic syndrome as morbid obesity plus two or more of the following: hypertension, diabetes, and hyperlipidemia.

The main results of the study—which analyzed gender, ethnicity, morbidity, and mortality—were the following:

- The prevalence of metabolic syndrome among bariatric surgery patients was higher than previously reported by the National Health and Nutrition Examination Survey (NHANES) III study (27% vs. 23%).
- Overall morbidity after bariatric surgery was significantly higher in patients with metabolic syndrome than in morbidly obese patients without metabolic syndrome (8.6% vs. 5.8%). Mortality was similar between the two groups (0.04% vs. 0.01%).
- Hispanics with metabolic syndrome had the highest morbidity rates, followed by blacks and whites. Males had higher mortality than females.
- In-hospital bariatric surgery outcomes were significantly better in patients who had laparoscopic gastric banding than in those who had gastric bypass. Laparoscopic gastric banding was associated with fewer complications (3% vs. 10%), shorter length of stay (1 vs. 3 days), and lower in-hospital costs ($9,000 vs. $13,000) than was gastric bypass.

The higher complication rates in patients with metabolic syndrome indicate that these patients might benefit from less-invasive procedures, such as laparoscopic gastric banding, said Dr. Varela, who also is director of minimally invasive surgery for the VA North Texas Health Care System. He added, however, that this hypothesis needs to be tested further before any clinical recommendations can be made. Long-term studies evaluating the efficacy of these bariatric procedures in resolving metabolic syndrome in morbidly obese patients are warranted, he said.

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In-hospital outcomes were better and costs were lower with gastric banding, Dr. Javier Esteban Varela said.

The finding that metabolic syndrome was higher among the Hispanic population had been observed previously, he noted.

Asked to comment on the results, Dr. Myriam Curet, a bariatric surgeon and professor of surgery at Stanford (Calif.) University, said that common obesity-related comorbidities—components of what is now called metabolic syndrome—have previously been recognized as risk factors for increased complications after any type of surgery, including bariatric surgery. But the findings of this study are helpful because they demonstrate the association using a large clinical database, and are therefore more translatable to a broad range of practices than are the results of studies from single institutions with a few hundred patients.

She also found the ethnic differences noteworthy. It has been recognized that after bariatric surgery, men do worse than women, and black women tend to do worse than white women, so the data on the ethnic differences are "pretty powerful," she said.

These results reveal other issues that need to be investigated, Dr. Curet said in an interview. For example, it is important to determine whether something can be done before surgery to reduce risk and to properly counsel patients with the risk factors identified in the study.

"Defining who are the appropriate candidates [and] who are high-risk candidates, and deciding what we can do for those high-risk candidates to make them lower-risk candidates are clearly important issues," Dr. Curet said. She cautioned against assuming that less-invasive procedures are more appropriate for higher-risk patients, however, pointing out that although some complications with laparoscopic banding are less severe than with gastric bypass procedures, other complications and the need for reoperation are the same as or higher than they are with laparoscopic banding. ■

Postop Ileus Drug Gets FDA Panel Vote Despite Concerns

BY ELIZABETH MECHCATIE
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SILVER SPRING, MD. — The majority of a Food and Drug Administration advisory panel agreed that the mu-opioid receptor antagonist alvimopan hastened gastrointestinal recovery in patients undergoing bowel resection and receiving opioids for pain. But when the panel weighed the benefits of the drug against its risks, panel members only narrowly voted in favor of the drug.

The FDA's Gastrointestinal Drugs Advisory Committee voted 13-0, with 2 abstentions, that clinical studies evaluating the effects of the drug on postoperative ileus (POI) were "clinically meaningful," and agreed that reductions in recovery time of 12 and 24 hours were significant.

However, the panel voted by a narrower margin of 9-6 that the beneficial effects of the drug outweighed its potential risks.

The manufacturer, Adolor Corp., has proposed that alvimopan, an oral medication, be approved for "acceleration of time to upper and lower gastrointestinal recovery following partial large or small bowel resection surgery with primary anastomosis." If approved, alvimopan would be the first drug approved for this indication, although surgeons use several drugs off-label for this use. The FDA usually follows the recommendations of its advisory panels, which are not binding.

According to Adolor, alvimopan is a "peripherally acting mu-opioid receptor antagonist that reverses opioid-induced changes in the GI tract without affecting opioid-induced analgesia." The company plans to market the drug under the trade name Entereg if approved. The recommended dose is one 12-mg capsule taken before surgery, then 12 mg twice daily until discharge for a maximum of 15 doses.

Because of safety concerns raised in a 12-month study of alvimopan as a chronic treatment for opioid-induced bowel dysfunction in patients with chronic, noncancer pain, Adolor has proposed that the drug be limited to short-term, in-hospital use in patients receiving open bowel surgery. The company has proposed a risk management plan aimed at preventing off-label use, long-term use, and use outside acute care hospitals.

In the long-term study of 750 patients, 500 patients received alvimopan 0.5 mg twice daily and 250 received placebo. Compared with the placebo group, the alvimopan group had a greater number of serious cardiovascular events (mostly MI), benign and malignant neoplasms, and bone fractures over a period of 1 year.

However, in short-term POI studies, where patients were treated for 7 days or less, the number of adverse cases was small, and there was no imbalance of these events between placebo and treatment groups, according to Adolor.

In another vote, eight panelists said they remained concerned about the potential risk of cardiovascular events with short-term use, while six panelists, including the cardiologists, said they were not concerned with the risks associated with short-term use. (There was one abstention.)

The nine panel members voting in favor of the overall-risk benefit profile of the drug in this population included the cardiologists and surgeons on the panel, but panelists supported long-term monitoring of cardiovascular effects of the drug and agreed that the risk management plan as proposed by the company was not adequate for monitoring its safety potential.

Cardiologist Dr. A. Michael Lincoff, professor of medicine at the Cleveland Clinic Foundation, said that in his view, there was no hint of any cardiovascular signal in the short-term follow-up and that he was not concerned about the cardiovascular risks for the short-term indication, even though patients would be taking a higher dose than was used in the long-term trials.

The acting chair of the panel, Dr. Alan L. Buchman, professor of medicine and surgery, division of gastroenterology at Northwestern University, Chicago, said that even though the drug had some physiologic and clinical beneficial effects, they were marginal and POI is a benign condition, so "the risk potential does at a minimum slightly outweigh the potential benefit for the patient."

Panel members cited the economic benefits of reducing hospital stays by 24 and even 12 hours, opening up more hospital beds for other patients.

The company presented pooled data from four phase III North American studies of more than 1,400 patients undergoing bowel resection (714 on alvimopan 12 mg twice daily and 695 on placebo). The mean age of the patients was about 60 years, and they received opioids via intravenous patient-controlled anesthesia. Alvimopan treatment accelerated GI recovery and reduced the time for the discharge order to be written by about 1 day (18-26 hours).

The proportion of those on alvimopan who met the GI recovery end point, defined as time to tolerating first food (upper GI recovery) and time to first bowel movement (lower GI recovery) by the fifth postsurgical day was 12%-18% higher among those on alvimopan over placebo. The GI recovery time, using this definition, was 13-26 hours faster than with placebo. In addition, the hospital discharge order was written for 85%-89% of those on alvimopan before the seventh day after surgery, compared with 68%-76% for placebo. Moreover, 12% of those on placebo had a nasogastric tube placed, compared with 7% of those on alvimopan, a highly significant difference.

Studies of the drug for chronic opioid-induced bowel dysfunction, conducted by GlaxoSmithKline Inc., are on hold. ■