



FDA Action Allows More Obese Patients to Qualify for a Bariatric Procedure

Mike Mitka

THE US FOOD AND DRUG ADMINISTRATION (FDA) has expanded the eligibility criteria for patients to undergo a certain type of weight loss surgery.

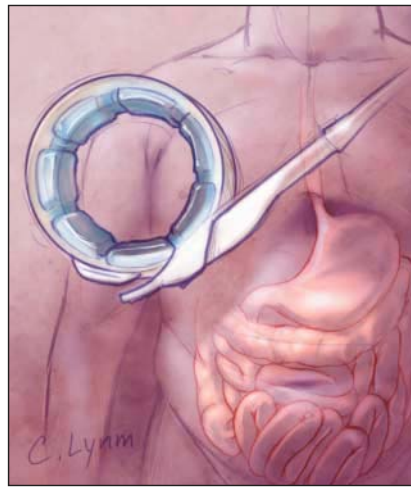
Proponents of the surgery applauded the FDA's February 16 action, saying an estimated 27 million more individuals will have access to a proven method to reduce weight and avoid the comorbidities associated with obesity, such as type 2 diabetes and hypertension. But critics of the agency's decision worry that the approval is based primarily on a small study that does not answer long-term safety and efficacy questions.

At issue is the Lap-Band Adjustable Gastric Banding System by Allergan, Inc, of Irvine, Calif, which had FDA approval for use in individuals with a body mass index (BMI) of at least 40, patients with a BMI of at least 35 and an existing severe condition associated with their obesity, or those who are overweight by at least 45 kg. Lap-Band reduces food intake by creating a smaller stomach pouch.

The FDA expanded approval for Lap-Band use to include individuals with a BMI of at least 30 who also have an existing condition related to their obesity. The agency rejected Allergan's request to allow Lap-Band surgery for patients with BMIs of at least 35 without comorbidities. The FDA's decisions reflected the recommendations made in December by the Gastroenterology and Urology Devices Panel of the agency's Medical Devices Advisory Committee.

Bruce M. Wolfe, MD, president of the American Society for Metabolic and Bariatric Surgery, who testified at the panel's December meeting, said the FDA's actions are appropriate. "The clinical evidence is strong to support the conclusion that obesity defined as BMI of

30 and above is a disease; it shortens life and is associated with multiple comorbid conditions," said Wolfe, who is also a professor of surgery at the Oregon Health & Science University in Portland. "The evidence that weight loss is helpful is strong. [Weight loss] does have some impact on diabetes and high blood pressure."



Gastric banding leads to weight loss by creating a smaller stomach pouch to reduce food intake, but some question the procedure's long-term efficacy and safety.

Philip R. Schauer, MD, director of the Bariatric and Metabolic Institute at the Cleveland Clinic, agreed that the FDA's decision is warranted, but he questioned how much impact the decision actually will have in the clinical setting. "It remains to be seen whether a single person will benefit from the FDA ruling because currently, surgeons can, and have, offered this procedure for patients with lower BMI, but it has been done off label," said Schauer, who is also a past president of the American Society for Metabolic and Bariatric Surgery. "This is more of a legal issue and takes away some of the surgeons' liability."

Wolfe admitted that evidence of benefit from surgery in patients with

BMIs between 30 and 35 is not as robust, and that is why critics remain cautious. The unpublished data presented in December that helped convince the majority of panel members to vote to expand the eligibility requirements came from a prospective single-arm, nonrandomized, 5-year multicenter study. That study, which began in 2007, involved 143 individuals with BMIs of 30 or greater and less than 40 who underwent the procedure. At 12 months, 83.9% of participants had lost at least 30% of their excess weight (the defined percentage representing clinically meaningful weight loss), and 65% of individuals were no longer obese. The weight loss was maintained in the second year of the study.

Joseph J. Cullen, MD, a professor of surgery at the University of Iowa Hospitals and Clinics in Iowa City, served on the devices panel in December and voted against expanding the eligibility criteria. He was concerned that the Allergan trial enrolled only 14 men and that 77% of the enrollees were white, hampering efforts to judge safety and efficacy across the entire population. Cullen also criticized the FDA for its presentation at the panel meeting. "The FDA did a poor job presenting other data from some European and US studies that showed no benefit," Cullen said. "I was really disappointed in the FDA's review."

Diana Zuckerman, PhD, president of the National Research Center for Women & Families, testified at the meeting against expanding the eligibility criteria. She noted that the Allergan study did not include persons older than 55 years, making general safety and efficacy statements problematic. "Will there be an FDA warning that it has not been tested on people over age 55?" Zuckerman asked. "I do not think Medicare should pay for Lap-Band



over age 55 if there is no study showing how safe it is in that population.”

Edward Livingston, MD, a professor of surgery at the University of Texas Southwestern Medical Center in Dallas and a *JAMA* contributing editor, questioned the value of performing a life-altering surgery on

individuals with lower BMIs. “There is a lack of efficacy when treating low BMIs, and the question becomes then, what are you treating,” Livingston said. “About 80% of the patients who fall in this lower BMI range are young healthy women who probably do not have too much risk from obe-

sity; they tend to tolerate obesity quite well.”

The FDA is requiring Allergan to provide annual reports and to conduct 2 postmarket studies to evaluate the long-term effectiveness and the incidence of adverse events associated with the device’s use. □

Reducing Door-to-Needle Time for tPA Use Remains an Elusive Goal in Stroke Care

Mike Mitka

HOSPITALS CONTINUE TO EXPERIENCE delays in administering a potentially lifesaving drug to patients presenting with acute ischemic stroke.

At issue is tissue-type plasminogen activator (tPA), the only thrombolytic therapy proven to reduce ischemic stroke mortality and morbidity. But the drug is strongly time dependent. Some researchers estimate that among 100 patients given tPA within the 1- to 3-hour treatment window, every 10-minute delay in the start of therapy reduces by 1 the number of patients having an improved disability outcome.

In light of this time sensitivity, national initiatives, such as the American Heart Association/American Stroke Association Get With the Guidelines–Stroke, recommend that hospitals complete clinical and imaging evaluation of a patient and initiate tPA therapy, if appropriate, within 1 hour of patient arrival. The Joint Commission wants primary stroke centers to administer tPA within 1 hour of patient presentation in 80% of cases.

The reality is quite different. A study presented at the American Stroke Association’s International Stroke Conference, held in Los Angeles in February, found that in 2009, only 29.1% patients treated with tPA had door-to-needle times of no more than 60 minutes, a slight improvement over the 19% figure from 2003 (Fonarow GC et al. *Circulation*. 2011;123[7]:

750-758). The study looked at data from 25 504 patients with acute ischemic stroke treated with tPA within 3 hours of symptom onset in 1082 hospitals participating in the Get With the Guidelines–Stroke program.

Gregg C. Fonarow, MD, lead author of the study and professor of cardiovascular medicine at the University of California, Los Angeles, found the results disappointing, especially because the study focused on hospitals that had joined the stroke association’s quality improvement efforts. “The results were in many ways surprising, as they also highlight a great opportunity for improvement,” Fonarow said. “We only saw modest improvements over time, plus we saw wide disparities across hospital and patient characteristics.”

The researchers found that hospitals treating patients with tPA in greater volume were better at meeting the 60-minute

target than hospitals treating fewer patients. Patients had a higher probability of being treated within 60 minutes upon arrival at an emergency department if they were younger, male, or white; if they had not had a previous stroke; or if they arrived by ambulance.

Another factor affecting treatment speed is how quickly the patient arrives at the emergency department after first experiencing the symptoms of stroke. Current guidelines say tPA should be given only in the first 3 hours after stroke onset. After that point, increased bleeding risks associated with the drug begin to outweigh the clot-busting benefits. (Newer studies are suggesting benefit of tPA given up to 4.5 hours after stroke onset, but the US Food and Drug Administration has yet to approve use of tPA during this expanded window.)

Mathew J. Reeves, PhD, DVM, a coauthor of the study and an associate profes-



Reducing the time needed to deliver clot-busting tissue-type plasminogen activator to patients with ischemic stroke presenting to an emergency department remains a difficult task.