

Roux-en-Y Helps Patients Meet Diabetes Treatment Goals

BY ALICIA AULT

Associate Editor, Practice Trends

SAN FRANCISCO — Roux-en-Y gastric bypass surgery is effective in helping people with type 2 diabetes meet the American Diabetes Association goals for hemoglobin A_{1c}, systolic blood pressure, and LDL cholesterol, according to a retrospective study presented at the annual meeting of the Endocrine Society.

Dr. Daniel Leslie of the University of Minnesota, Minneapolis, said that his study was the first to report on the effectiveness of Roux-en-Y in meeting treatment goals set by the American Diabetes Association (ADA) in 2004 for the management of type 2 diabetes.

Dr. Leslie and colleagues reviewed all Roux-en-Y gastric bypass procedures conducted at the University of Minnesota between 2001 and 2007. Of all the procedures, 85% were done laparoscopically. There were a total of 2,210 consecutive surgeries, and of those patients, 564 had type 2 diabetes.

But only 338 patients had all three measures—HbA_{1c}, systolic blood pressure, and LDL cholesterol—available at baseline. Only 169 patients had all three measures available both preoperatively and postoperatively, Dr. Leslie said.

The average age of the patients was 51 years; 79% (133) were women and 85% (143) were white. The average duration of diabetes was 9 years, although

39% (66) of the group had diabetes for more than 10 years. Patients were followed for an average of 26 months.

Dr. Leslie estimated that 32% (54) of the patients met the ADA goals after surgery. Only 9.5% (16) of patients had met those goals before gastric bypass. The duration of diabetes was not associated with meeting the goals.

The ADA goals included an HbA_{1c} of 7% or less, LDL cholesterol of 100 mg/dL or less, and systolic blood pressure of 130 mm Hg or less.

The HbA_{1c} value improved from 7.7% on average to 6.2% after the procedure. Systolic blood pressure dropped from an average of 136 mm Hg to 128 mm Hg. The use of oral antidiabetic medications and insulin dropped dramatically, Dr. Leslie noted.

Use of cholesterol-lowering and blood pressure-lowering drugs also fell, but the need for antihypertensives increased after about 24 months—a finding seen in other studies, Dr. Leslie said.

The mean body mass index dropped from 49 to 33 kg/m² after the surgery.

“Gastric bypass is a useful tool for improving diabetes treatment goals,” said Dr. Leslie, although he noted that the study was not controlled.

Dr. Leslie disclosed that his surgery division receives grant support from Covidien AG and Ethicon Endo-Surgery Inc., but said that he does not personally receive any industry grants. ■

Laparoscopic Banding Safe, Effective for BMI Under 35

BY JEFF EVANS

Senior Writer

PHILADELPHIA — Laparoscopic adjustable gastric banding in patients with a body mass index less than 35 kg/m² might be safe and effective for weight loss and improvement of obesity-related comorbidities, according to a review of over 50 patients.

The study is the first to evaluate the effect of laparoscopic adjustable gastric banding (LAGB) in U.S. patients with a BMI less than 35. This BMI value is the cutoff used in National Institutes of Health guidelines on patient selection criteria for weight-loss surgery in people with significant comorbidities, said Dr. Manish Parikh of the general surgery department at New York University.

Of the 53 patients in the study (mean age 47 years), 49 had at least one obesity-related comorbidity, and 44 were women.

The patients' mean preoperative BMI of 33 declined to 28 after 6 months and to 26 after 2 years. The patients lost 48% of their excess weight after 6 months and 70% after 2 years. More than 80% of the patients were available for follow-up at 2 years.

Overall, 75% of the patients had improvement or resolution of their comorbidities, Dr. Parikh reported at the annual meeting of the Society of American Gastrointestinal and Endoscopic Surgeons.

The weight loss and improvement in comorbidities seen in the study are important

when put into the context of a previous study in which researchers estimated a 25% increase in mortality and 3-4 years of life lost for individuals with a BMI of 25-35—about 20% of U.S. adults, Dr. Parikh said (JAMA 2003;289:187-93).

Previous studies of LAGB in patients with a BMI less than 35 outside the United States have reported similar results. A study of 210 Italian patients reported 72% excess weight loss at 5 years, 89% resolution of comorbidities, an 8% complication rate, and one death 20 months postoperatively due to sepsis stemming from the perforation of a dilated gastric pouch (Obes. Surg. 2004;14:415-8).

A previous study conducted by Dr. Parikh and his associates found that 93 Australian patients lost an average of 54% of their excess weight at 3 years, with improvement or resolution of comorbidities in most (Surg. Obes. Relat. Dis. 2006;2:518-22).

The “most compelling data” for operating on these patients, according to Dr. Parikh, come from a trial in which 80 Australian patients were randomized to undergo LAGB or an intensive nonsurgical weight loss program (Ann. Intern. Med. 2006;144:625-33). The LAGB patients lost a significantly greater percentage of excess weight at 2 years than the nonsurgical group did (87% vs. 22%).

Two of Dr. Parikh's coinvestigators are on the medical advisory board for Allergan Inc., which manufactures the Lap-Band system used in the study. ■

Genes Predict Treatment Response in Hepatitis C

BY KATE JOHNSON

Montreal Bureau

MONTREAL — A genetic signature involving 18 genes can reliably predict response to pegylated interferon α plus ribavirin therapy in patients infected with hepatitis C, reported Dr. Limin Chen at Canadian Digestive Diseases Week.

This finding “could form the basis for a diagnostic tool to encourage treatment compliance,” Dr. Chen said in an interview. The results also confirm the findings of *in vitro* studies by Dr. Chen's group from the University of Toronto.

His group previously identified gene expression differences in the pretreatment liver biopsies of hepatitis C virus (HCV) patients who subsequently responded and those who failed to respond to pegylated interferon α plus ribavirin, showing that these two groups “differ fundamentally in their innate [interferon] response to HCV infection” (Gastroenterology 2005;128:1437-44).

Upregulation of an 18-gene signature known as USP18 predicted lack of response to treatment, and another study by the same group showed that silencing this gene signature *in vitro* could improve treatment response.

“We were able to show that if we silence this USP18 gene, the virus actually gets more sensitive to interferon. In other words, we can use much less interferon to kill the virus,” Dr. Chen said.

The group's latest work validates the findings from a prospective cohort study of 78 HCV patients (mean age, 51 years): 23 nonresponders and 55 responders. Using pretreatment liver biopsies, “we confirmed that USP18 is more highly expressed in nonresponders,” he said.

The study showed that the genetic evaluation of pretreatment liver biopsies with regard to this gene signature can predict treatment response with a positive predictive value of 96%. However, the sensitivity was only 50%. “Therefore, you cannot use it to exclude patients from treatment,” he said.

Current combination treatment with pegylated interferon α plus ribavirin has only a 50% success rate, and patient compliance is jeopardized by the significant side effects and expense, Dr. Chen explained. Genetic markers such as USP18 that predict good treatment response might help physicians encourage compliance in certain patients, he said at the meeting, sponsored by the Canadian Association of Gastroenterology. ■

Unexplained Acute Liver Failure Is Often Acetaminophen Toxicity

BY ALICIA AULT

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SAN DIEGO — As many as 18%-20% of cases of indeterminate acute liver failure may be the result of unrecognized acetaminophen toxicity, according to a presentation at the annual Digestive Disease Week.

The etiology is unknown in about 15% of cases of acute liver failure (ALF), said Dr. Niraj Khandelwal of the University of Texas, Dallas. Using a novel assay that detects acetaminophen (APAP) protein adducts, the Acute Liver Failure Study Group had determined in a previous study that adducts were present in 7 (19%) of 36 cases diagnosed as indeterminate ALF. The APAP adduct levels were comparable with those seen in patients with known acetaminophen overdose (Gastroenterology 2006;130:687).

To further evaluate indeterminate ALF, the authors conducted a larger study using a newer assay—high-performance liquid chromatography with electrochemical detection (HPLC-EC)—that is more efficient and more sensitive, Dr. Khandelwal said.

The assays were conducted on sera from 113 patients in the ALF Study Group registry. The serum samples were taken on the first or second day after admission and were collected from 1998 to 2006.

Of the 113, there were 32 with known APAP overdose, 93 who were adduct negative, and 20 (18%) who were adduct positive (defined using a cut point of 1 nmol/mL). Of those 20 patients, 9 (45%) died or received transplants and 11 (55%) spontaneously survived. Eight patients were given *N*-acetylcysteine (NAC), and six (75%) of those eight patients survived. Only 5 patients (42%) of the 11 who spontaneously survived did so without NAC.

The clinical and lab findings of the patients who had adducts equal to 1 nmol/mL or greater were consistent with findings—including very high aminotransferases, low bilirubin, and favorable outcome—for known APAP overdose patients. The median bilirubin level was 5.05 mg/dL, compared with 24.5 mg/dL for patients with negative adducts (1 nmol/mL or less).

The study confirms previous data showing that as many as one in five patients with indeterminate ALF actually has unrecognized acetaminophen toxicity, Dr. Khandelwal said. Given these data and the lack of an adduct assay that can be used at the bedside in real time, NAC should be considered in patients with indeterminate ALF who match the biochemical profile for APAP overdose, he said.

Dr. Khandelwal had no disclosures. ■