obtained at each time point during the follow-up revealed a higher HUS for the ILI group only at Months 12 and 18 for HUI-2 scores and Months 6 and 12 for HUI-3 scores. However, SF-6D scores were always higher for the ILI group and were nearly always significantly different (ie, not at 0 and 5 years; $p < .05$ for all). FT scores were always significantly higher for the ILI group ($p < .05$ for all). HUI-2, HUI-3, and SF-6D values for all study participants tended to diminish with time, while FT values plateaued in the latter two thirds of follow-up.

Limitations included missing data not included in the analysis, potential reporting biases, and preferential weighting of HUSs that may not have been representative of the US population. The researchers concluded that an ILI is effective in improving quality of life. This estimated improvement will be used to assess the cost-effectiveness of this strategy.

Bariatric Surgery Confers Long-Term Protection for Patients With and Without Diabetes

Written by Brian Hoyle

Gastric banding surgery confers long-term (up to 17 years) protection from death and the development of cardiovascular diseases (CVD) and type 2 diabetes mellitus (T2DM) in patients with and without diabetes, according to the results of a study conducted by Antonio E. Pontiroli, MD, and colleagues, University of Milan, Milan, Italy.

Studies to date on the protection afforded by bariatric surgery have varied in their length of follow-up and number of patients and enrolled only a small number of patients with DM [Pontiroli AE, Morabito A. *Ann Surg* 2011] or have suffered from a lack of details or a high drop-out rate [Christou NV et al. *Ann Surg* 2004; Sjostrom L et al. *N Engl J Med* 2007; Busetto L et al. *Surg Obes Relat Dis* 2007; Adams TD et al. *N Engl J Med* 2007; Sowemimo OA et al. *Surg Obes Relat Dis* 2007]. The prolonged retention of patients in trials and the associated longer-term outcomes remain unclear. Furthermore, although bariatric surgery can apparently help prevent DM and lessen CVD risk [Pontiroli AE et al. *Diabetes Care* 2005; Heneghan HM et al. *Am J Cardiol* 2011; Johnson BL et al. *J Am Coll Surg* 2013; Busetto L et al. *Surg Obes Relat Dis* 2014], differences in outcomes between patients with and without diabetes remain unclear.

The present prospective, cohort record-linked study involved obese (body mass index [BMI] >35 kg/m^2) patients aged 18 to 65 years who underwent the same gastric banding procedure or received medical treatment from 1995 through 2001 at four centers in Milan. Medical records were examined for sex, age, clinical evidence of coronary heart disease (CHD) and retinopathy, anthropometric data (height, weight, BMI, systolic and diastolic blood pressures), and metabolic data (fasting blood glucose, HBA1C, total cholesterol, high- and low-density cholesterol, triglycerides, aspartate transaminase, alanine transaminase, creatinine, and estimated glomerular filtration rate). The limit date for deaths, patient exceptions, and hospital admissions was September 30, 2012. The analyses were on an intention-to-treat principle. Identification codes of all patients were entered into the Lumbardy Regional Database to ascertain patients alive, patients dead and cause of mortality, patients migrated elsewhere, and the development of new diseases.

The baseline characteristics differed between the patients who did and did not have gastric banding surgery, and therefore group matching was applied (Tables 1 and 2).

Table 1. Baseline Characteristics of Surgery and Non-Surgery Patients

Intervention	Surgery	No Surgery	p Value
Patients (M/W)	527	963	0.0001*
Age (years)	39.6	44.9	0.0001
BMI (kg/m^2)	43.0	39.8	0.0001
Systolic BP (mm Hg)	130.3	142.7	0.0001
Diastolic BP (mm Hg)	109.3	120.1	0.0021
On hypertension treatment	28	150	0.0001*
Blood glucose (mg/dL)	109.3	120.1	0.0021
On DM treatment	73	221	0.0001*
IFG	23	78	0.0001*
HbA1C (%)	6.0	7.8	0.0001*
Triglycerides (mg/dL)	133.8	158.2	0.0035
CHD	5	49	0.0001*
Died	17	92	0.0001*
% Died	3.2	9.6	0.0001*
Total Exemptions	133	402	0.0001*

BMI=body mass index; BG=blood glucose; BP=blood pressure; CHD=coronary heart disease; DM=diabetes mellitus; IFG=impaired fasting glucose; M=men; W=women.
*Chi-squared test.

Gastric banding was associated with significantly increased survival in both the entire patient cohort and among matched patients.

The survival advantage with surgery was evident for all patients with diabetes (OR, 0.37; 95% CI, 0.14 to 0.93; p=.035), matched patients with diabetes (OR, 0.33; 95% CI, 0.13 to 0.84; p=.020), and all patients without diabetes (OR, 0.39; 95% CI, 0.20 to 0.75; p=.005), and almost

Table 2. Baseline Characteristics of Surgery and Non-Surgery Patients After Matching for Age, Sex, BMI, and Blood Pressure

Intervention	Surgery	No Surgery	p Value
Patients (M/W)	385	681	0.689*
Age (years)	40.5	42.4	0.0095
On DM treatment	52	127	0.017*
IFG	16	50	0.033*
HbA1C (%)	6.0	7.8	0.0001
Triglycerides (mg/dL)	131.6	150.9	0.0367
CHD	4	35	0.0001*
Died	12	65	0.0001*
% Died	3.1	9.5	0.0001*
Total Exemptions	83	194	0.013*

BMI = body mass index; CHD = coronary heart disease; DM = diabetes mellitus; IFG = impaired fasting glucose; M = men; W = women.
*Chi-squared test.

achieved significance in matched patients without diabetes (OR, 0.44; 95% CI, 0.19 to 1.00; p = .052). The causes of death were not significantly different between patients who did or did not undergo gastric banding surgery.

The researchers concluded that the prevention of mortality following gastric banding continues for 15 (range, 11–17) years and is associated with the absence of the development of new diseases, in particular DM and CVD, over the same period in patients with and without diabetes. The researchers plan to undertake another round of assessments with the same cohort in 2017.

Characterizing Hypoglycemic Events During Saxagliptin Treatment in Type 2 Diabetes

Written by Emma Hitt Nichols, PhD

Treatment of type 2 diabetes mellitus (T2DM) with saxagliptin increased the risk of major and minor hypoglycemic events, but it enabled more patients to reach an HbA1C target of less than 7% without hypoglycemia. This is according to a subanalysis of the Does Saxagliptin Reduce the Risk of Cardiovascular Events When Used Alone or Added to Other Diabetes Medications? study [SAVOR-TIMI 53; NCT01107886]. Itamar Raz, MD, Hadassah Medical Center, Jerusalem, Israel, presented the results. The main results of this multicenter, randomized, double-blind, placebo-controlled Phase 4 study have been published [Scirica BM et al. *N Engl J Med* 2013].

Hypoglycemia is a serious complication of diabetes treatment, and patients with the greatest risk of hypoglycemia need to be identified. This subanalysis aimed to identify potential predisposing factors for hypoglycemia in patients with T2DM.

The SAVOR-TIMI 53 trial randomly assigned patients with documented T2DM and established cardiovascular disease (CVD) or multiple cardiovascular (CV) risk factors to receive saxagliptin 5 mg/day (dose adjusted for reduced renal function) or placebo. The median duration of follow-up was 2.1 years, with visits every 6 months. The composite primary end points were CV death, myocardial infarction, or ischemic stroke.

Hypoglycemia (any hypoglycemia, minor hypoglycemia, major hypoglycemia, or hypoglycemia requiring hospitalization) occurred more frequently in patients assigned to saxagliptin (Table 1). This excess risk, however, was statistically significant only in the subgroup of patients who were taking sulfonylureas at baseline. Sulfonylurea use without insulin was associated with a significantly higher rate of major hypoglycemia in the saxagliptin group versus the placebo group in patients with a baseline HbA1C level of < 7% (HR, 2.24).

Table 1. Rate of Hypoglycemia by Type With Saxagliptin and Placebo

	Saxagliptin	Placebo	p Value
Any hypoglycemia (%)	15.3	13.4	< .001
Minor hypoglycemia (%)	14.2	12.5	0.002
Major hypoglycemia (%)	2.1	1.7	0.047
Hypoglycemia requiring hospitalization (%)	0.6	0.5	0.33

Patients in the saxagliptin arm who were taking at baseline metformin alone, insulin alone, or a sulfonylurea plus insulin or metformin, but not a sulfonylurea alone, were more likely to achieve an HbA1C < 7% without experiencing a hypoglycemic event at 1 and 2 years and at the end of the trial (Figure 1).

In the overall study population, insulin, particularly short-acting insulin, was the strongest predictor for the development of hypoglycemia. In a multivariate analysis, insulin use, decreasing renal function, and increasing disease duration were all independently associated with an increased risk of hypoglycemia.

In conclusion, Prof. Raz stated that the results of this subanalysis of SAVOR-TIMI 53 indicate that insulin therapy is the strongest predictor of hypoglycemia. Treatment with saxagliptin increased the rates of major and minor hypoglycemia in the subgroups noted earlier but not the risk of hospitalization due to hypoglycemia.