group (bradycardia which was determined to be related to medication for heart rate control). No significant differences in 30-day resource use (CCTA vs traditional care) were observed (Table 2).

**Table 2. Resource Utilization.**

| Use of Resources | CCTA-Based (%) | Tradtional Care (%) | 95% CI for Difference |
|---|---|---|---|
| Catheterization | 5.1 | 4.2 | -4.8 to 6.6 |
| Revascularization | 2.7 | 1.3 | -4.3 to 7.0 |
| Repeat ED visit | 8.0 | 7.5 | -5.2 to 6.2 |
| Re-hospitalization | 3.1 | 2.4 | -4.9 to 6.4 |
| Cardiologist visit | 7.1 | 3.8 | -2.4 to 9.0 |

Dr. Litt noted that this trial had a wider range of traditional care and "real world" management and disposition of patients, but the results only applied to low-to-intermediate-risk individuals. He concluded that a CCTA-first strategy for low–intermediate-risk potential ACS patients was safe and efficient, with increased ED discharge rates and reduced LOS. Larger randomized controlled trials are needed, as well as long-term follow-up on resource use and effects of CAD diagnosis on outcomes.

## Comparison of Bariatric Surgical Procedures and IMT for the Treatment of T2DM in Patients with Moderate Obesity: One-Year STAMPEDE Trial Results

*Written by Rita Buckley*

Results from the 1-year Surgical Therapy And Medications Potentially Eradicate Diabetes Efficiently trial [STAMPEDE; NCT00432809], comparing bariatric surgery with intensive medical therapy (IMT) for the treatment of type 2 diabetes (T2DM) in patients with moderate obesity, concluded that bariatric surgery is more effective than IMT. Philip Raymond Schauer, MD, Cleveland Clinic, Cleveland, Ohio, USA, who reported the results, noted that many of the surgical patients achieved glycemic control without the use of diabetic medications. In addition, improvement in cardiovascular (CV) risk factors after surgery allowed many of these patients to reduce their use of CV medications.

This was the first study to compare IMT with IMT plus bariatric surgery to achieve resolution of T2DM in moderate to severely obese patients (body mass index [BMI] >30 kg/m$^2$). IMT was based on 2011 American Diabetes Association clinical care guidelines but with an increased focus on reducing HbA1C to ≤6% through the use of diet and lifestyle counseling and potent diabetes medications (eg, insulin sensitizers, GLP-1 agonists, sulfonylureas, and insulin). All patients were evaluated and counseled by dieticians and psychologists in preparation for possible bariatric surgery and were instructed in frequent home glucose monitoring and self-titration of medications.

The primary endpoint was the success rate of achieving HbA1C ≤6% at 12 months. Secondary endpoints included changes in fasting plasma glucose (FPG), BMI, lipids, blood pressure, hsCRP, and the use of diabetic and CV medications, as well as safety and adverse events. Patients (n=150) were randomized to IMT alone, IMT plus gastric bypass, or IMT plus sleeve gastrectomy, a procedure that involves vertically stapling and excising the stomach to achieve approximately 75% to 80% stomach volume reduction, leaving a narrow tubular stomach. Both procedures are performed laparoscopically and require a very small abdominal incision, resulting in a hospital stay of about 2 days and recovery time of 2 to 4 weeks.

Eligible patients were aged 20 to 60 years with HbA1C >7% and BMI 27 to 43 kg/m$^2$. The average patient age was 49 years, average BMI was 37 kg/m$^2$, and average duration of diabetes was 8 years. Mean baseline HbA1C was 9.2±1.5%. Subjects were well treated at baseline, with the majority on at least 3 diabetes medications. Approximately half were on insulin; 80% were on a lipid-lowering agent, and 66% were on an ACEI/ARB.

The primary endpoint, HbA1C ≤6%, was achieved in 12% of IMT patients, compared with 42% of gastric bypass patients (p=0.002 relative to IMT) and 37% of sleeve gastrectomy patients (p=0.008 relative to IMT). All of the gastric bypass patients and 27% of the sleeve gastrectomy patients achieved the primary endpoint target without requiring an increase in their diabetes medications. Patients who were undergoing surgery had an average weight loss of 25 to 30 kg (55 to 65 lbs) compared with 4 to 5 kg (10 lbs) in patients who were receiving IMT. Changes in FPG, hsCRP, and triglycerides and increases in high-density lipoprotein cholesterol also favored surgery over IMT (Table 1). The average number of diabetes medications that were used was significantly reduced (p<0.001) in the surgery groups relative to IMT patients. At 12 months, insulin was withdrawn in 92% to 96% of the surgical patients compared with ~40% of the IMT patients.

In addition, at 12 months, 94% of gastric bypass and 71% of sleeve gastrectomy patients were on only 0 to 1 CV medications, while 72% of the IMT patients were on 3 or more CV medications. There were no differences

in final blood pressure between the 3 groups. There were no unexpected complications or deaths through 12 months. More serious adverse events (SAEs) that required hospitalization were seen in patients who were assigned to gastric bypass than sleeve gastrectomy or IMT (22% vs 9% vs 8%). Other SAEs that occurred more frequently in the surgery groups included reoperation (6% of gastric bypass patients and 2% of sleeve gastrectomy patients vs no patients in the IMT), intravenous treatment for dehydration (8% of gastric bypass and 4% of sleeve gastrectomy patients vs no IMT patients), and pneumonia, which occurred only in the gastric bypass group (4% of patients).

**Table 1. Secondary Efficacy Endpoints.**

| Parameter | IMT n=41 | Bypass n=50 | Sleeve n=49 | p value[1] | p value[2] |
|---|---|---|---|---|---|
| Change in FPG (mg/dL) | -28.0 | -87.0 | -63.0 | 0.004 | 0.003 |
| Change in BMI | -1.9.0 | -10.2 | -9.0 | <0.001 | <0.001 |
| % change in HDL | +11.3 | +28.5 | +28.4 | 0.001 | 0.001 |
| % change in TG | -14.0 | -44.0 | -42.0 | 0.002 | 0.08 |
| % change in hsCRP | -33.0 | -84.0 | -80.0 | <0.001 | <0.001 |

[1]Gastric bypass vs IMT; [2]Sleeve vs IMT; FPG=fasting plasma glucose; BMI=body mass index; HDL= high-density lipoprotein; TG=triglycerides; hsCRP=high-sensitivity C-reactive protein.

The investigators caution that the study is limited by its short duration but add that a 4-year extension is ongoing. This was also a single-center trial, and larger multicenter studies will be needed to determine whether observed improvements in glycemic control and CV risk factors and withdrawal of diabetes and CV medications translate into reductions in CV events and/or end organ failure from microvascular disease [Schauer PJ et al. *N Engl J Med* 2012].

## TAVR Associated with Increased Late Mortality from Paravalvular Regurgitation

*Written by Rita Buckley*

One-year data from the Placement of Aortic Transcatheter Valves Trial [PARTNER; NCT00530894] showed that survival rates were similar among high-risk patients with aortic stenosis (AS) who received either transcatheter aortic valve replacement (TAVR) or surgical replacement [Smith CR et al. *N Engl J Med* 2011; Vinall M. *MD Conference Express: ACC 2011*]. Susheel K. Kodali, MD, Columbia University Medical Center, New York, New York, USA, presented outcomes after 2 years of follow-up in the PARTNER trial [Kodali SK et al. *N Engl J Med* 2012].

Inclusion criteria were severe symptomatic AS; an echo-derived aortic-valve area (AVA) ≤0.8 $cm^2$ (or AVA index <0.5 $cm^2/m^2$) and a peak velocity ≥40 mm Hg (or peak jet velocity of >4.0 m/s); NYHA ≥II; and high surgical risk (ie, guideline-predicted risk of operative mortality ≥15%, as determined by site surgeon and cardiologist). The risk score threshold was an STS score ≥10 [http://riskcalc.sts.org/STSWebRiskCalc273/de.aspx].

The primary endpoint of the randomized, multicenter trial was all-cause mortality. Other endpoints included cardiovascular (CV) mortality, rehospitalization, strokes and transient ischemic attacks (TIAs), vascular and bleeding events, NYHA functional class, and echocardiographic measures of valve performance (including valve gradient/areas and postprocedural aortic regurgitation [AR]).

At 2 years, there were no significant differences in mortality from any cause between the TAVR group (33.9%; 95% CI, 28.9 to 39.0) and the SAVR group (35.0%; 95% CI, 29.8 to 40.2; p=0.78). CV mortality was also similar in the TAVR and SAVR groups (21.4% [95% CI, 16.8 to 26.0] and 20.5% [95% CI, 15.8 to 25.3], respectively; p=0.80).

The frequency of all neurological events (stroke or TIA) at 2 years was higher with TAVR than with surgical replacement (11.2% vs 6.5%; p=0.05). However, there was no significant difference in the number of overall strokes between the TAVR and SAVR groups (24 vs 20, respectively at 36 months; HR, 1.22; 95% CI, 0.67 to 2.23; p=0.52).

Moderate or severe paravalvular AR was more common after TAVR than after SAVR at both 1 and 2 years (7.0% vs 1.9% at 1 year; 6.9% vs 0.9% at 2 years; p<0.001 for both comparisons). The presence of paravalvular or any AR (mild, moderate, or severe vs none or trace) after TAVR was associated with increased late mortality (HR, 2.11; 95% CI, 1.43 to 3.10; p<0.001), underscoring the importance of close clinical follow-up and echocardiography in patients after TAVR.

Dr. Kodali concluded that TAVR should be considered an option for patients with severe symptomatic AS who are high risk for SAVR. He noted that TAVR remained equivalent to SAVR, with similar rates of all-cause and CV mortality, and that symptom improvement was similar in both groups. Although TAVR valve hemodynamics remained stable at 2 years, the more frequent late development of paravalvular and any significant AR following TAVR was associated with a doubling of late mortality.