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# Duodenal Switch Provides Superior Resolution of Metabolic Comorbidities Independent of Weight Loss in the Super-obese (BMI≥50 kg/m$^2$) Compared with Gastric Bypass

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**Abstract**
*Objective* Increased body mass index is associated with greater incidence and severity of obesity-related comorbidities and inadequate postbariatric surgery weight loss. Accordingly, comorbidity resolution is an important measure of surgical outcome in super-obese individuals. We previously reported superior weight loss in super-obese patients following duodenal switch (DS) compared to Roux-en-Y gastric bypass (RYGB) in a large single institution series. We now report follow-up comparison of comorbidity resolution and correlation with weight loss.
*Methods* Data from patients undergoing DS and RYGB between August 2002 and October 2005 were prospectively collected and used to identify super-obese patients with diabetes, hypertension, dyslipidemia, and gastroesophageal reflux disease (GERD). Ali–Wolfe scoring was used to describe comorbidity severity. Chi-square analysis was used to compare resolution and two-sample *t* tests used to compare weight loss between patients whose comorbidities resolved and persisted.
*Results* Three hundred fifty super-obese patients [DS ($n$=198), RYGB ($n$=152)] were identified. Incidence and severity of hypertension, dyslipidemia, and GERD was comparable in both groups while diabetes was less common but more severe in the DS group (24.2% vs. 35.5%, Ali–Wolfe 3.27 vs. 2.94, $p<0.05$). Diabetes, hypertension, and dyslipidemia resolution was greater at 36 months for DS (diabetes, 100% vs. 60%; hypertension, 68.0% vs. 38.6%; dyslipidemia, 72% vs. 26.3%), while GERD resolution was greater for RYGB (76.9% vs. 48.57%; $p<0.05$). There were no differences in weight loss between comorbidity "resolvers" and "persisters".
*Conclusions* In comparison to RYGB, DS provides superior resolution of diabetes, hypertension, and dyslipidemia in the super-obese independent of weight loss.

**Keywords** Morbid obesity · Super-obesity · Comorbidity resolution · Duodenal switch · Gastric bypass · Bariatric surgery · Diabetes · Gastroesophageal reflux · Biliopancreatic diversion

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## Introduction

Obesity has dramatically increased over the past several decades both in the USA and worldwide. According to a representative sample of nearly 14,000 individuals in the National Health and Nutrition Examination Survey, the prevalence of obesity among adults in the USA, defined as body mass index (BMI) ≥30 kg/m$^2$ [calculated as weight (kilograms) divided by the square of the height (meter)] increased from 13% in 1960 to 1962[1] to 32% in 2003 to 2004, with 3% of men and 7% of women classified as being severely obese (BMI≥40 kg/m$^2$) in the most recent estimate.[2] Strikingly, a disproportionate increase in the prevalence of superobesity (BMI≥50 kg/m$^2$) is evident when specifically examining trends in severe obesity, with a nearly tenfold increase in the prevalence of superobesity between 1986 and 2005 as compared to a twofold increase

in obesity (BMI≥30 kg/m$^2$) and fivefold increase in severe obesity (BMI≥40 kg/m$^2$) during this period.[3]

BMI is itself a strong predictor of overall mortality, with a progressive excess in mortality noted above the optimum BMI of 22.5–25. In a recent collaborative analysis of 900,000 adults enrolled in 57 studies, at a BMI of 30–35 kg/m$^2$, median survival was reduced by 2–4 years; at a BMI of 40–45 kg/m$^2$, it was reduced by 8–10 years. Furthermore, for each 5 kg/m$^2$ increase in BMI greater than 25, there was a nearly 30% increase in all-cause mortality due mainly to metabolic and vascular disease.[4] Indeed, the prevalence of metabolic comorbidities, including diabetes, hypertension, and dyslipidemia, increases significantly with increasing BMI.[5–7] The relationship between BMI and prevalence of comorbidities is not absolute, however: Not all severely obese or super-obese individuals have these conditions, and not all individuals with these conditions are overweight or obese. Furthermore, in comparison to individuals 40 years ago, the prevalence of hypertension and dyslipidemia (but not diabetes) as defined by levels of control in overweight and obese individuals has actually decreased,[8] although this appears to be due in large part to the increased use of anti-hypertensive and lipid-lowering medications. Despite these improvements in cardiovascular risk management, however, obesity-associated disability has actually increased by over 40% over the past decade.[9]

Even bariatric surgery, the most effective means of achieving significant and sustained weight loss in individuals with severe obesity,[10–13] may be less effective in achieving adequate weight loss as BMI exceeds 50 kg/m$^2$. Indeed, the initial concept of superobesity proposed by Mason et al.[14] was based on the observation that patients with BMI≥50 kg/m$^2$ undergoing vertical-banded gastroplasty often failed to achieve satisfactory weight loss after surgery, and this difference in weight loss outcome between patients with severe obesity and superobesity has since been demonstrated following Roux-en-Y gastric bypass (RYGB).[15–18]

The increase in the prevalence of superobesity, recognition of inadequate weight loss following RYGB in super-obese patients, and weight loss comparisons between bariatric operations in two recent meta-analyses[10,12] have prompted a growing interest in the biliopancreatic diversion with duodenal switch (DS) as a potentially advantageous procedure in the super-obese. The DS, developed by Hess and Hess[19] and Marceau et al.[20,21] is a hybrid operation that combines the DS of DeMeester et al.,[22] initially developed for the treatment and prevention of bile reflux, with the Scopinaro biliopancreatic diversion.[23] The greater technical complexity (particularly when performed laparoscopically) and perceived perioperative[24] and nutritional[25,26] risks of DS in comparison to RYGB, however, have limited the widespread adaptation of DS among bariatric surgeons. We have previously demonstrated superior weight loss with the DS in direct comparison to RYGB without significant difference in morbidity and mortality in 350 consecutive super-obese patients.[27] As such, the added technical difficulty of the DS procedure and greater potential for nutritional deficiency of DS may be justified by the higher likelihood of significant and sustained weight loss.

Weight loss itself, however, is only one of the goals of bariatric surgery. An equally important outcome measure following a bariatric procedure is its impact on obesity-related comorbidities, particularly those associated with increased cardiovascular risk. Indeed, the cost-effectiveness of laparoscopic gastric bypass at 2 years after surgery is in large part predicated on a reduction in comorbidity-associated medication use, hospitalizations, and physician visits.[28] Numerous studies suggest an important linkage between weight loss and comorbidity improvement by showing that that a relatively modest amount of weight loss (10%) may result in significant improvement, and in some cases, resolution, of comorbidities.[29,30] Given that the observed weight loss following both DS and RYGB is often three to five times that amount, one would not anticipate substantial differences in comorbidity resolution between the two procedures. Furthermore, both RYGB[31] and DS[32–34] lead to dramatic improvement of obesity-related comorbidities. Nonetheless, given the differences that have been noted in the effects on comorbidities of the various bariatric procedures,[10,12] factors including the magnitude of weight loss and/or the physiology of the surgically altered anatomy may play an important role in their etiology. We herein report our follow-up comparison of comorbidity resolution and correlation with weight loss in super-obese patients following DS and RYGB.

## Material and Methods

We conducted a retrospective review of an Institutional Review Board-approved, prospectively maintained database containing the demographic and anthropomorphic data of patients undergoing RYGB, biliopancreatic diversion with DS, and laparoscopic adjustable gastric banding (LAGB) between August 5, 2002 and November 10, 2005. The initial date was chosen, as it corresponds to the first DS performed at our institution. Patients underwent extensive multidisciplinary preoperative evaluation by a board-certified surgeon (VNP or JCA), dietician, and psychologist and were found to be appropriate candidates for bariatric surgery based on current NIH criteria [severe obesity (BMI≥40 kg/m$^2$ or 35–40 kg/m$^2$ with significant obesity-related comorbidities), history of multiple previous non-surgical weight loss attempts, adequate comprehension and support, and absence of

active substance abuse or poorly controlled psychologic disorders].[11] Eligibility for inclusion in this study included all consecutive patients undergoing standardized primary RYGB or DS with a preoperative BMI≥50 kg/m$^2$. Patients who had previous bariatric procedures or who underwent staged bariatric operations were excluded. Patients undergoing LAGB were excluded from analysis, as there were no super-obese patients who underwent banding during this 3-year period (the first LAGB at our institution was performed in March, 2005). The database was used to identify patients with preoperative diabetes (DM), hypertension (HTN), dyslipidemia (DL), and gastroesophageal reflux disease (GERD), and the Ali–Wolfe scoring scheme (AORC)[35] was used to describe comorbidity severity at the time of surgery and during follow-up and are shown in Table 1. DM, HTN, and DL were included in this study given their impact on cardiovascular risk, while GERD was chosen as an "internal control" given the recognized effectiveness of RYGB for the treatment of refractory GERD in severely obese patients who have failed other anti-reflux operations.[36] Comorbidity severity scoring was performed retrospectively based on chart review for visits that took place before the publication of the AORC scheme in 2006.

## Procedure Selection

The relative advantages and disadvantages of the procedures were extensively discussed with the patient by the surgeon, and a general recommendation was made based on the severity of obesity, comorbidities present, and the patient's preference. While specific mention was made of the potential advantage of the DS with regards to weight loss in superobese patients, the final decision with regards to the procedure performed was made by the patient. In many instances, because the patient's insurance would not cover the DS, patients elected to proceed with the RYGB rather than attempt to appeal the decision of the insurance company, despite the patient's preference for DS. The patient's primary care physician was notified in writing regarding the decision by the bariatric surgery team and the patient. Any necessary preoperative testing or treatments were performed. Mandatory preoperative weight loss or special diet was not routinely required.

## Surgical Technique

Details regarding the techniques used to perform RYGB and DS have been previously described.[27] RYGB was performed in 152 super-obese individuals with a 40–50-cm biliopancreatic limb and a 100-cm ($n$=27) or 150-cm ($n$=125) Roux limb. The shorter Roux limb was used when mandated by insurance coverage. DS was performed in 198 super-obese individuals with a 100-cm common channel and 150-cm alimentary limb (distance from duodenoileostomy to ileoileostomy). Procedures were typically performed by an attending surgeon and senior surgical resident with a medical student operating the laparoscopic camera.

Intraoperative endoscopy with Roux (RYGB) or alimentary limb (DS) occlusion and air insufflation was used to test the integrity of the staple lines of the gastric reservoir and proximal anastomosis. A single 19-F Blake drain was placed near the proximal anastomosis extending up into the left upper quadrant, with removal taking place during the first postoperative visit (8–10 days postoperative). Patients were routinely admitted to the intermediate care unit with telemetry and continuous pulse oximetry after discharge from the recovery room and occasionally to the intensive care unit at the discretion of the surgeon and anesthesiologist. Patient-controlled intravenous narcotic analgesia was used for pain control. Low carbohydrate clear liquids at 30 mL/h were initiated on the morning of postoperative day 1, and enoxaparin 40–100 mg SQ bid was started and titrated to achieve a serum level just below therapeutic. Diet was

**Table 1** Assessment of Obesity-Related Comorbidity Scale (adapted from Ali et al.[35])

| Score | Diabetes | Hypertension | Dyslipidemia | GERD |
|---|---|---|---|---|
| 0 | Not present | Not present | Not present | Not present |
| 1 | Hyperinsulinemia without hyperglycemia | Borderline/intermittent/ diagnosis not confirmed | Borderline | Intermittent or variable symptoms, not requiring a response |
| 2 | Diabetes diagnosed, controlled by diet and exercise | Controlled by diet and exercise | Controlled by lifestyle changes: step 1, step 2 diet | Intermittent medication |
| 3 | Controlled by oral medications | Treatment with single medication | Controlled by low-dose medication | Regular medication ($H^2$ blockers or low-dose PPI) |
| 4 | Controlled by insulin | Treatment with multiple medications | Controlled by high-dose medication | High-dose PPI |
| 5 | Poorly controlled or severe complications | Poorly controlled or severe complications | Not controlled by medication | Meet criteria for antireflux operation or prior operation for GERD |

advanced to pureed foods on postoperative day 2 as tolerated, and patients were discharged after demonstration of diet tolerance and return of bowel function. Enoxaparin was continued for 2–3 weeks after discharge.

### Follow-up

Patients were seen 1.5 weeks postoperative for drain removal and 2.5 weeks postoperative for diet advancement and initiation of vitamin supplements (prenatal multivitamin, B12, and calcium citrate with vitamin D). Patients were seen by the surgeon and a bariatric dietician at each visit and by psychologists as needed. While the diet contents and progression were identical for both procedures, DS patients were instructed to achieve 75–85 g protein intake/day as opposed to 60–65 g protein/day for the RYGB patients. Subsequent follow-up appointments took place 1, 3, and 6 months, then yearly thereafter. Comorbidity assessments were performed at each postoperative visit and follow-up phone conversation, and nutritional parameters were measured at the 3-month, 6-month, and yearly visit, with supplementation adjusted accordingly. Resolution of comorbidity was defined as discontinuation of medications used for treatment with the absence of symptoms. All adjustments to medications used in the treatment of any comorbidity were made by the referring or primary care physician. Attempts were made by phone and by mail to contact patients who failed to keep follow-up appointments, moved, or whose insurance was no longer accepted at the University of Chicago Medical Center.

### Statistical Analysis

Ideal body weight (IBW) was calculated using the formula $\mathrm{IBW} = [(2.3 \times (\text{height in inches}) - 60)) + A) \times 2.2]$, where $A$ is 45.5 for females and 50 for males, with excess body weight (EBW)=measured weight−IBW. Comparison of the demographic data was performed using two-tailed pooled $t$ tests for continuous data (age, weight, BMI, and EBW) except length of stay, for which the Satterthwaite $t$ test was used due to unequal variances. Chi-square analysis was used to compare the rate of resolution for each of these comorbidities except when a low number of observations required Fisher exact test, and two-sample $t$ tests used to compare weight loss between patients whose comorbidities resolved and those whose comorbidities remained. Non-parametric Wilcoxon tests were used to compare the mean AORC score at various postoperative time points against their preoperative mean AORC score. Weights and comorbidity status were recorded at the time of clinic visit or telephone conversation. For purposes of analysis, weights and comorbidity status recorded between 4 and 8 months were grouped as "6 months postoperative," 9–15 months as "12 months," 16–20 months as "18 months," 21–30 months as "24 months," and 31–60 months as "36 months." If more than one visit occurred for an individual patient during any of these periods, the latest visit was used and the others excluded.

## Results

Three hundred fifty super-obese (BMI≥50 kg/m$^2$) patients underwent DS ($n$=198) or RYGB ($n$=152) over a 39-month period with equal 30-day mortality (DS, 1/198 (0.51%) and RYGB, 0/133, $p$=NS). Demographics of the two groups are shown in Table 2. Mean age and gender were similar in both groups, while mean preoperative weight (368.2 vs. 346.3 lbs, $p$=0.0002) and BMI (58.8 vs. 56.4 kg/m$^2$, $p$=0.0014) were significantly greater in the DS group compared to the RY group. The prevalence and severity of HTN, DL, and GERD was comparable in both groups ($p$=NS), while DM was less prevalent but more severe in the DS group.

The number of individuals for whom comorbidity scoring was available and their mean AORC score at each time point is shown in Table 3. Non-parametric Wilcoxon tests were used to compare the mean AORC score at various postoperative time points to the mean baseline AORC score, and all comparisons were found to be highly significant ($p$<0.05). Resolution rates for DM, HTN, and DL were greater for DS [DM: 18 months, 79.3% vs. 47.6%; 24 months, 91.2% vs. 50%; 36 months, 100% vs. 60%; HTN: 24 months, 56.5% vs. 28.6%; 36 months, 68.0% vs. 38.6%; DL: 36 months, 72% vs. 26.3%; $p$<0.05)], while GERD resolution was greater for RYGB (36 months, 76.9% vs. 48.57%; $p$<0.05; Table 4).

There were no statistically significant differences in mean weight loss noted between DS patients whose comorbidities resolved (AORC score 0) compared to DS patients whose comorbidities persisted (AORC score≥1). Similarly, no differences in weight loss were noted in RYGB patients whose comorbidities resolved and RYGB patients whose comorbidities persisted (data not shown). Finally, when comparing the weight loss of RYGB patients whose comorbidities resolved to the weight loss of DS patients whose comorbidities persisted, the weight loss for the DS patients whose hypertension and GERD did not resolve was greater than the RYGB patients whose hypertension and GERD did in fact resolve (Fig. 1).

## Discussion

Given the exponential increase in the prevalence of super-obesity within the population of patients who may be

**Table 2** Age and Gender Were Well-Matched

| | | DS | RYGB | *p* value |
|---|---|---|---|---|
| Number of patients | | 198 | 152 | |
| Age (years) | Mean±SD<br>Range | 40.4±9.5<br>18–61 | 40.5±10.9<br>21–68 | NS[a] |
| Gender | (% F) | 82.3% | 84.2% | NS[c] |
| Weight (lbs) | Mean±SD<br>Range | 368.2±52.3<br>267.4–596.5 | 346.3±55.2<br>239.8–504.9 | *0.0002*[a] |
| BMI (kg/m$^2$) | Mean±SD<br>Range | 58.8±6.7<br>49.6–96.3 | 56.4±6.8<br>49.5–84.2 | *0.0014*[a] |
| EBW (lbs) | Mean±SD<br>Range | 233.9±42.5<br>162.2–408.1 | 215.9±43.9<br>159.9–379.5 | *0.0001*[a] |
| Diabetes | Number of patients (prevalence) | 48 (24.2%) | 54 (35.5%) | *<0.05*[a] |
| | Mean AORC score | 3.27 | 2.9 | *<0.05*[a] |
| Hypertension | Prevalence | 133 (67.2%) | 101 (66.5%) | NS[a] |
| | Mean AORC score | 3.02 | 2.98 | NS[a] |
| Dyslipidemia | Prevalence | 62 (31.3%) | 55 (36.2%) | NS[a] |
| | Mean AORC score | 2.71 | 2.65 | NS[a] |
| GERD | Prevalence | 84 (42.4%) | 51 (33.6%) | NS[a] |
| | Mean AORC score | 2.54 | 2.52 | NS[a] |
| Mortality | (%) | 1/198 (0.51%) | 0.0% | 1.0000[b] |
| LOS (days) | (Mean±SD)<br>Range | 4.86±5.9<br>2–68 | 3.83±2.6<br>2–25 | *0.0300*[d] |
| LOS (days) | Median | 4.00 | 3.00 | |
| LOS>4 | | 48 (24.24%) | 30 (19.74%) | 0.3154[c] |

DS patients were heavier than RYGB in all measures. Mortality rate was not significantly different, but LOS was 1 day longer for DS. Equivalent proportions of patients had hospital stays> 4 days. The prevalence and severity of HTN, DL, and GERD was comparable in both groups (p=NS), while DM was less prevalent but more severe in the DS group. *p* values<0.05 are indicated in italics

*SD* standard deviation, *LOS* length of stay

[a] Pooled two-tailed *t* test

[b] Fisher's exact *p* value

[c] $\chi 2$ test

[d] Satterthwaite *t* test

**Table 3** Patients Available for Follow-up

| | | Months postoperation | | | | | |
|---|---|---|---|---|---|---|---|
| | | Pre | 6 | 12 | 18 | 24 | 36 |
| Diabetes | | | | | | | |
| Number of patients | DS | 48 | 45 | 44 | 29 | 34 | 21 |
| AORC | | 3.27 | 1.8 | 0.98 | 0.45 | 0.18 | 0 |
| Number of patients | RY | 54 | 43 | 37 | 21 | 28 | 20 |
| AORC | | 2.94 | 2.4 | 1.54 | 1.33 | 1.29 | 1 |
| Hypertension | | | | | | | |
| Number of patients | DS | 133 | 123 | 116 | 79 | 85 | 75 |
| AORC | | 3.06 | 2.59 | 2.04 | 1.7 | 1.16 | 0.83 |
| Number of patients | RY | 101 | 81 | 76 | 41 | 49 | 44 |
| AORC | | 3 | 2.54 | 2.22 | 1.76 | 2.06 | 1.75 |
| Dyslipidemia | | | | | | | |
| Number of patients | DS | 62 | 55 | 52 | 40 | 40 | 25 |
| AORC | | 2.71 | 2.31 | 1.65 | 1.18 | 0.68 | 0.56 |
| Number of patients | RY | 55 | 41 | 39 | 20 | 25 | 19 |
| AORC | | 2.65 | 2.44 | 1.72 | 1.6 | 1.32 | 1.68 |
| GERD | | | | | | | |
| Number of patients | DS | 84 | 76 | 69 | 49 | 50 | 35 |
| AORC | | 2.55 | 1.87 | 1.57 | 1.12 | 1.08 | 1.17 |
| Number of patients | RY | 51 | 43 | 34 | 20 | 26 | 26 |
| AORC | | 2.53 | 1.58 | 1.12 | 0.8 | 0.88 | 0.58 |

The number of patients with the particular comorbidity and the mean AORC score at each time point for whom follow-up data is available is shown

**Table 4** Resolution of Comorbidities Following DS and RYGB. Resolution of Comorbidity was Defined as Discontinuation of Medications Used for Treatment and the Absence of Symptoms of that Comorbidity

| | | Months postoperation | | | | |
|---|---|---|---|---|---|---|
| | | 6 | 12 | 18 | 24 | 36+ |
| DM | | | | | | |
| %Resolved | DS | 33.3 | 59.1 | 79.3 | 91.2 | 100 |
| | RY | 9.52 | 37.84 | 47.6 | 50 | 60 |
| *p* value | | 0.05 | 0.25 | 0.05 | 0 | 0.04 |
| HTN | | | | | | |
| %Resolved | DS | 7.4 | 24.1 | 32.9 | 56.5 | 68 |
| | RY | 8.8 | 19.7 | 31.7 | 28.6 | 38.6 |
| *p* value | | 0.58 | 0.62 | 0.69 | 0.01 | 0 |
| DL | | | | | | |
| %Resolved | DS | 7.27 | 32.7 | 45 | 70 | 72 |
| | RY | 10 | 33.3 | 35 | 52 | 26.3 |
| *p* value | | 0.89 | 0.46 | 0.5 | 0.02 | 0.01 |
| GERD | | | | | | |
| %Resolved | DS | 22.4 | 29 | 42.9 | 48 | 48.6 |
| | RY | 34.9 | 50 | 65 | 61 | 76.9 |
| *p* value | | 0.14 | 0.06 | 0.1 | 0.93 | 0.04 |

Adjustments to medications used in the treatment of any comorbidity were made by the referring or primary care physician. DM, HTN, and DL resolution was greater for DS at 24 months and 36 months, while GERD resolution was greater for RYGB at 36 months

potential candidates for bariatric surgery, determining the "best" surgical treatment for super-obesity is an important task facing the bariatric surgical community. The optimal procedure should have acceptably low morbidity and mortality rates, result in significant and durable weight loss, and lead to improvement or resolution of obesity-related comorbidities as well as quality of life.

We have previously demonstrated that DS provides a significant advantage over RYGB when comparing weight loss, percentage of EBW lost, decrease in BMI, and likelihood of achieving at least 50% EBW loss without significantly increased perioperative morbidity and mortality.[27]

The main focus of this report is the comparison of comorbidity resolution following DS and RYGB. We demonstrate that DS provides greater resolution of DM, HTN, and DL, while RYGB provides better resolution of GERD. The finding regarding DM is particularly striking given the greater preoperative severity of DM in the DS group (AORC, 3.27 vs 2.9, $p<0.05$). Furthermore, the relative advantage for DS in the treatment of HTN and DL cannot be explained by a difference in preoperative comorbidity severity, given the equivalent AORC scores in DS and RYGB patients (Table 2).

We chose to focus on resolution, rather than improvement, of comorbidities in this study in part to attempt to better characterize this rather dramatic effect of bariatric surgery. Modest weight loss (8–10%) is clearly associated with significant improvement of cardiovascular disease-associated comorbidities but rarely leads to their resolution.[30] Additionally, it is the reduction in medication requirements, hospital admissions, and clinic visits associated with comorbidity resolution that is the primary contributor to the cost-effectiveness of bariatric surgery[28] and as such the comparative differences in comorbidity resolution may impact cost-effectiveness in different ways. For example, giving preferential consideration to DS in the setting of super-obesity and severe diabetes may be appropriate given the higher likelihood of successful weight loss and diabetes resolution.

It is important to recognize, however, that the term "resolution," particularly when applied in the context of metabolic obesity-related comorbidities, is controversial. "Remission" may in fact be a more broadly acceptable term to non-surgical medical specialists to describe these phenomena until longer term data become available. Furthermore, we did not obtain objective measurements of comorbidities (e.g., homeostasis model assessment–insulin resistance and euglycemic clamp for glucose homeostasis, 24-h pH study for GERD, etc.) to determine whether a

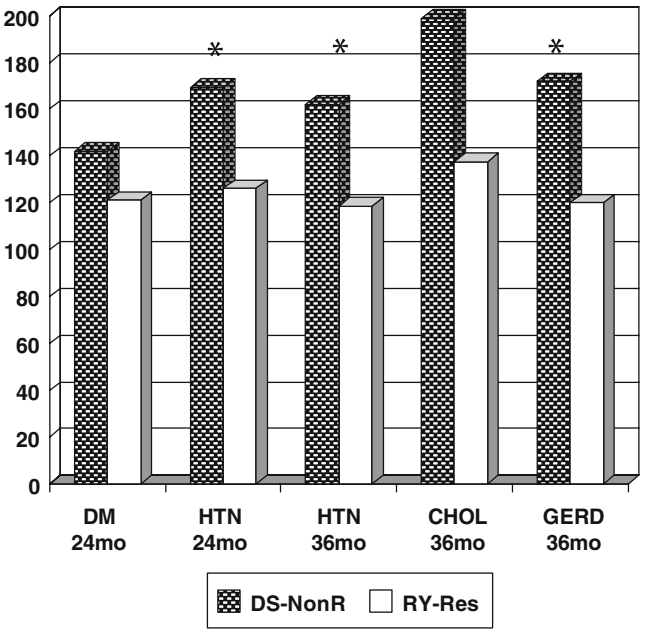


**Figure 1** Weight loss comparison between RYGB "Resolvers" and DS "Non-resolvers". When comparing the weight loss of RYGB patients whose comorbidities resolved to the weight loss of DS patients whose comorbidities persisted, the weight loss for the DS patients whose hypertension and GERD did not resolve was greater than the RYGB patients whose hypertension and GERD did in fact resolve. *$p<0.05$.

comorbidity had in fact resolved physiologically. Indeed, reliance on the accuracy and appropriateness of medication discontinuation on the part of a broad range of referring physicians and primary care providers introduces potential for error in our data. Finally, the strong incentives to discontinue medications on the part of both the patient (financial, convenience) and the surgeon (improvement in measured outcome to reporting bodies) may inadvertently reduce adherence to evidence-based guidelines for tighter "triple endpoint" control of HbA1c, blood pressure, and triglycerides, as adherence to treatment recommendations, which have demonstrable benefit with regards to reduced cardiovascular risk, may require the continued use of medications.

The lack of a demonstrable difference in weight loss between patients whose comorbidities resolved and those whose comorbidities persisted was a surprising finding. Unfortunately, our data are underpowered to assess whether those patients whose comorbidities persisted had higher preoperative AORC scores and how demographic factors, such as sex, age, and race impact the response of comorbidities to surgery. Nonetheless, when comparing the weight loss of RYGB patients whose comorbidities resolved to the weight loss of DS patients whose comorbidities persisted, the weight loss for the DS patients whose hypertension and GERD remained unresolved was greater than the RYGB patients whose hypertension and GERD did in fact resolve. The greater GERD resolution seen with RYGB despite reduced weight loss compared to DS suggests differences in the physiologic effects of altered surgical anatomy independent of weight loss per se. In the absence of objective physiologic data, we speculate that the modest amount of acid produced in the small volume gastric pouch combined with minimal bile reflux given a Roux limb length exceeding 100 cm may account for the marked improvement in GERD seen following RYGB. In contrast, the gastric sleeve of the DS has greater acid-producing capacity compared to the RYGB pouch, and the small caliber of the sleeve may result in increased resistance to flow of acid from the proximal sleeve and clearance of refluxate in the distal esophagus. Similarly, there is currently great interest in the role that alterations in gut hormones such as ghrelin, leptin, peptide YY, and glucagon-like peptide-1 (GLP-1) play in surgical weight loss and comorbidity physiology. The latter two hormones are secreted by L cells in the distal small bowel and may be major factors in inducing satiety through central mechanisms as well as through delayed gastric emptying and increased intestinal transit time.[37,38] Additionally, GLP-1 is a potent incretin that lowers blood glucose levels by enhancing insulin secretion, reducing glucagon levels, and delaying gastric emptying.[39] RYGB has been shown to result in an increase in both hormones,[40–42] and it may be that differences between the two procedures in their neurohormonal response may account for both the differences in weight loss and diabetes resolution following DS as compared to RYGB. As such, shifting attention from the effects of weight loss per se to the comparative physiology of the two operations promises to yield important insights into the mechanisms by which the procedures exert their effects as well as the pathophysiology (and potential development of non-surgical therapy) of these comorbidities.

Because the selection of the procedure performed was not randomized, a significant limitation of this study is selection bias. We generally recommended DS for all super-obese patients, particularly if their BMI was $\geq$60 kg/m$^2$ ($n$=109). Of the patients who ultimately underwent RYGB, about half did so because their insurer considered the DS to be "investigational" and they did not want to initiate a lengthy appeals process; about half did so because the DS was "too radical" or because an acquaintance or family member had a good outcome with RYGB. DS was not recommended in a few instances when patients had frequent or loose stools at baseline. Despite the lack of randomization, patient age and gender distribution did appear to be closely matched. Additionally, while there were variations in surgical technique with regards to the method of access and creation of anastomoses, the measured lengths used for small intestinal reconstruction were standardized to the extent possible. Finally, with the exception of a slightly greater daily protein requirement for DS patients, the perioperative management and follow-up regimen was purposefully kept the same for both procedures in an effort to minimize the influence that differences in postoperative care may have had on outcomes.

The loss of patients to follow-up is another factor that limits the quality of our data. While the rate of follow-up 1 year after DS and RYGB was 80% and 60%, respectively, at 3 years, the follow up was about 50% for both groups. This disappointing follow-up may have limited our ability to more accurately assess the likelihood of comorbidity resolution 2–3 years after surgery. While our follow-up rate is less than the 80–99% follow-up obtained in studies performed in the Canadian heath care system,[34,21] they are comparable to those seen in many American series.

Our previous direct comparison of short-term weight loss outcomes of DS to RYGB demonstrated that the DS provides superior weight loss in the super-obese compared to gastric bypass. This current study extends these findings by comparing the intermediate-term effects of these operations on the resolution of significant obesity-related comorbidities and demonstrates that weight loss per se may not be the primary determinant of comorbidity resolution. Further study and follow-up will be needed to confirm and extend the present findings, and a long-term assessment and comparison of nutritional outcomes

and quality of life will allow the development of an evidence-based rationale for procedure selection in this challenging patient population.

## Conclusion

In comparison to RYGB, DS provides superior resolution of diabetes, hypertension, and dyslipidemia in the super-obese independent of weight loss.

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### Discussant

**Dr. J. Chris Eagon (Washington University, St. Louis):** That was a wonderful presentation. I guess one of the questions I had was, "do you think that the duodenal switch operation is worse off in terms of GERD resolution because of the anatomical configuration of the sleeve?" Or is there some other effect there that is present that is making that difference?

Second of all, I was a little surprised about the relative lack of effect of gastric bypass compared to duodenal switch in terms of diabetes resolution.

Do you have any ideas about how to detect why that is the case? Are there some hormonal differences in the fact that the nutrients are being pushed a little bit farther downstream in the GI tract as a reason for that?

### Discussant

**Dr. Vivek Prachand (University of Chicago):** Even though the sleeve gastrectomy does result in resection of a significant amount of the gastric parietal cell mass, I suspect that the amount of acid production in the remaining pouch or sleeve is substantially greater than the small 20-cc pouch that is made during gastric bypass.

Combining this increased acid production with the relative resistance to forward flow given the long tubular structure of the sleeve—thinking about Poiseuille's law—I think that there may be impaired esophageal clearance of acid. I think that both operations are very effective at controlling biliary reflux given the Roux limb length of greater than 100 cm.

With regards to the resolution of diabetes, I think that there are contributions both from decreased fat cell mass, as well as the neurohormonal effects of these operations that contribute to the resolution.

It may very well be that the differential stimulation and increased release of GLP 1 and peptide YY with a greater amount of distal delivery of nutrients in the duodenal switch may, in part, account for the difference that we see.

### Discussant

**Dr. Michael Sarr:** Are there some people you would not do a duodenal switch on, such as someone who is in the weight category but has severe gastroesophageal reflux?

### Closing discussant

**Dr. Vivek Prachand (University of Chicago):** I think that is a patient that I would have serious reservations about performing a duodenal switch on. However, if they were a very bad diabetic, hypertensive, and so forth, then I still would probably lean more toward a duodenal switch than a bypass.

One of the questions that we do ask preoperatively is, "what is their typical bowel habit pattern beforehand?" If they are already having two to four bowel movements a day regularly, which is typically the pattern that we see after DS, I am also hesitant to offer duodenal switch to those patients.

### Discussant

**Dr. Michael Sarr:** What about a distal gastric bypass? Do you think that these patients lose the same amount of weight as a duodenal switch? That operation would get rid of the reflux problem.

### Discussant

**Dr. Vivek Prachand (University of Chicago):** I think your group has demonstrated that the weight loss is pretty similar to the duodenal switch and that might be a good option in a patient with reflux.

### Discussant

**Dr. Manfred Prager (Austria):** How do the comorbidities contribute to the overall effect of the duodenal switch. Is it the length of the biliopancreatic and/or the nutritional limb? Or is it also that you have the duodenal-jejunal anastomosis and that you leave the pyloric valve?

Does the pyloric valve have a positive effect on the efficacy of the duodenal switch?

### Discussant

**Dr. Vivek Prachand (University of Chicago):** I could speculate that, again, thinking about the distal gut hormones

and how they impact on gastric emptying, having an intact antropyloric mechanism may in part contribute to those sorts of effects. With regards to the biliopancreatic limb versus alimentary limb, as I mentioned, there are some groups that use fixed limb lengths as we do versus those that use proportionately tailored limbs. I think the answer is that we really do not know.

We chose to use fixed lengths because they are something that we could control, and be consistent with, and standardize. But I think that it is probably unrealistic and naive to think about the biliopancreatic limb as just being a passive conduit of biliopancreatic secretion when we know there is a lot of reabsorption and inactivation of enzymes that occurs.