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Long-term Safety and Efficacy of Closure of Mesenteric Defects in Laparoscopic Gastric Bypass Surgery
A Randomized Clinical Trial

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IMPORTANCE Short-term and midterm data suggest that mesenteric defects closure during laparoscopic Roux-en-Y gastric bypass (LRYGB) surgery reduces the risk of internal herniation with small bowel obstruction (SBO) but may increase risk of kinking of the jejunojejunostomy in the early postoperative period. However, to our knowledge, there are no clinical trials reporting long-term results from this intervention in terms of risk for SBO or opioid use.

OBJECTIVE To evaluate long-term safety and efficacy outcomes of closure of mesenteric defects during LRYGB.

DESIGN, SETTING, AND PARTICIPANTS This randomized clinical trial with a 2-arm, parallel, open-label design included patients with severe obesity scheduled for LRYGB bariatric surgery at 12 centers in Sweden from May 1, 2010, through November 14, 2011, with 10 years of follow-up after the intervention.

INTERVENTIONS During the operation, patients were randomly assigned 1:1 to closure of mesenteric defects beneath the jejunojejunostomy and at the Petersen space using nonabsorbable running sutures during LRYGB or to nonclosure.

MAIN OUTCOME AND MEASURES The primary outcome was reoperation for SBO. New incident, chronic opioid use was a secondary end point as a measure of harm.

RESULTS A total of 2507 patients (mean [SD] age, 41.7 [10.7] years; 1863 female [74.3%]) were randomly assigned to closure of mesenteric defects (n = 1259) or nonclosure (n = 1248). After censoring for death and emigration, 1193 patients in the closure group (94.8%) and 1198 in the nonclosure group (96.0%) were followed up until the study closed. Over a median follow-up of 10 years (IQR, 10.0-10.0 years), a reoperation for SBO from day 31 to 10 years after surgery was performed in 185 patients with nonclosure (10-year cumulative incidence, 14.9%; 95% CI, 13.0%-16.9%) and in 98 patients with closure (10-year cumulative incidence, 7.8%; 95% CI, 6.4%-9.4%) (subhazard ratio [SHR], 0.42; 95% CI, 0.32-0.55). New incident chronic opioid use was seen among 175 of 863 opioid-naive patients with nonclosure (10-year cumulative incidence, 20.4%; 95% CI, 17.7%-23.0%) and 166 of 895 opioid-naive patients with closure (10-year cumulative incidence, 18.7%; 95% CI, 16.2%-21.3%) (SHR, 0.90; 95% CI, 0.73-1.11).

CONCLUSIONS AND RELEVANCE This randomized clinical trial found long-term reduced risk of SBO after mesenteric defects closure in LRYGB. The findings suggest that routine use of this procedure during LRYGB should be considered.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT01137201

Visual Abstract

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Supplemental content

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The incidence of severe obesity is increasing worldwide, with associated increased risk for several metabolic comorbidities, new onset of cancer, mortality, and reduced quality of life.[1-3] Metabolic and bariatric surgery reduces weight and has been shown to have good long-term outcomes for many of the conditions associated with severe obesity.[4-6] Laparoscopic Roux-en-Y gastric bypass (LRYGB) is the second most common surgical treatment for obesity, with an estimated annual volume worldwide extending beyond 200 000 operations.[7] One of the most serious complications of this procedure has been internal herniation resulting in small bowel obstruction. Studies reporting long-term follow-up suggest a high incidence (10%-20%) of internal herniation and small bowel obstruction if no measures are taken to reduce the incidence.[8-11] Closure of mesenteric defects has been reported to reduce the risk of small bowel obstruction.[12,13] However, due to technical difficulties with this intervention, mesenteric defects may be insufficiently closed or may even open with time due to reduction of the amount of adipose tissue.[14] Closure of mesenteric defects has also been suggested to be associated with increased risk of chronic abdominal pain.[15] At present, 3 randomized clinical trials (RCTs)[12,13,16] including a total of 3013 patients have reported results of mesenteric defects closure 3 to 5 years after surgery, but to our knowledge, there are no RCTs reporting efficacy and safety outcomes over long-term follow-up. The aim of the present study was to evaluate safety and efficacy outcomes of mesenteric defects closure during LRYGB over long-term follow-up from a multicenter, registry-based RCT.

Key Points

Question What are the long-term safety and efficacy outcomes of mesenteric defects closure during laparoscopic Roux-en-Y gastric bypass (LRYGB) surgery?

Findings In this randomized clinical trial with a 2-arm, parallel design that included 2507 Swedish patients randomized to closure or nonclosure of mesenteric defects during LRYGB, at 10 years' follow-up, closure of mesenteric defects reduced the incidence of reoperation for small bowel obstruction from 14.9% to 7.8%.

Meaning In this trial, closure of mesenteric defects during LRYGB surgery effectively reduced the long-term risk for small bowel obstruction.

Methods

Study Design

This open-label, parallel, registry-based RCT (NCT01137201) including patients at 12 centers for bariatric surgery in Sweden was conducted from May 1, 2010, until November 14, 2011. Ethics approval was granted by the regional ethics committee in Uppsala. Written informed consent was obtained from all study participants. The trial protocol can be found in Supplement 1. The evaluation of new incident use of opioids was an amendment to the initial study design. The study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.

Participants

All adult patients (aged ≥18 years) who received bariatric surgery at any of the centers participating in the study and met the criteria for bariatric surgery as recommended by the Swedish National Board of Health and Welfare (body mass index [BMI] ≥35; calculated as weight in kilograms divided by height in meters squared) were considered for inclusion. Previous bariatric surgery was considered a criterion for exclusion.

Randomization and Masking

During the operation, a concealed, opaque envelope was opened, and the patient was randomized to either closure of the mesenteric defects or nonclosure. Patients were randomly assigned at a 1:1 ratio, with permuted blocks of different sizes (from 4 to 50) stratified by center.[12] As requested by the ethics committee, the study was open label after the operation.

Intervention

The laparoscopic gastric bypass procedure was highly standardized with an antecolic, antegastric Roux-en-Y gastric bypass with an approximately 100 cm–long alimentary limb and a 50 cm–long biliopancreatic limb.[17] To close the mesenteric defects beneath the jejunojejunostomy and at the Petersen space (the space between the mesentery of the transverse colon and the Roux limb), a braided, nonabsorbable running suture technique was used.[12] Patients were followed up at the hospital clinic with registrations in the Scandinavian Obesity Surgery Registry (SOReg). By use of the national personal identification numbers (unique to all Swedish citizens), the database was cross-linked with the nationwide National Patient Register, Total Population Register, and National Prescribed Drugs Register. The National Patient Register includes an inpatient component covering virtually all hospital admissions in public health care and an outpatient component covering about 96% of outpatient visits in specialized health care.[18] The Swedish National Prescribed Drugs Register contains all dispensed prescribed drugs in Sweden classified according to the World Health Organization Anatomical Therapeutic Chemical classification system.[19] The Total Population Register covers data on emigration and immigration and includes complete coverage of dates of birth and death for all individuals in Sweden.[20] The medical records and operative notes of all potential reoperations for bowel obstruction were reviewed to ensure a uniform classification of small bowel obstruction.

Outcomes

The primary end point was reoperation for small bowel obstruction at 3 years after surgery, with planned long-term follow-up at 10 years after surgery. Secondary end points included reoperation specifically for internal hernia. In addition, new chronic use of opioids was amended as a secondary end point when the current study was designed. Small bowel obstruction was defined as acute onset of abdominal pain with signs of obstruction at the time of an operation for this complication, dilatation of small bowel or gastric remnant, mesenteric lymphedema, or incarcerated bowel with or without

signs of ischemia.[12] Internal hernia was deemed to be the cause of small bowel obstruction if the bowel was herniated at the time of surgery with signs of small bowel obstruction. The assessors (E.S., I.N.) were masked with respect to study treatment at the time of evaluation. New incident chronic opioid use was defined as having 1 or more dispensed prescriptions of opioids during 2 consecutive 6-month periods at least 2 years after surgery while having no opioid prescription dispensed during the 2 years before surgery.

Statistical Analysis

Based on the reported incidence of small bowel obstruction at the time of planning the study, we did a power calculation assuming a clinically relevant reduction in surgery for small bowel obstruction from 5.0% to 2.5% after 3 years. To detect such a difference with 80% power at the 5% significance level, a minimum of 906 patients in each group was needed. Because of different incidence rates in previous studies, we decided to include 1200 patients in each group (Supplement 1). Categorical variables are presented as numbers and percentages and continuous variables as means and SD or medians with IQRs in the case of nonnormal distribution.

The main comparison was analyzed as intention to treat and secondarily as per protocol. We visualized time to reoperation for small bowel obstruction with the cumulative incidence function with all-cause mortality as a competing event. All patients were followed up from surgery to the first reoperation for small bowel obstruction or mortality and were censored at the time of death, emigration, after 10 years, or on June 30, 2021, whichever came first. We used competing-risk survival regression to compare the closure and nonclosure groups, adjusted for surgical center-presenting subhazard ratios (SHRs) with 95% CIs to estimate relative risks.[21] As the proportional hazards assumption was violated as shown by Schoenfeld residuals, we modeled the group variable interaction with follow-up time (0-30 days vs 31 days to 10 years) as an indicator variable to estimate time-dependent analyses in accordance with the concept of delayed entry.

The same strategy of analyses was performed for time to reoperation for internal herniation by which patients also were censored for small bowel obstruction due to reasons other than internal herniation. This analysis was divided by sex and age, and interaction tests by the intervention groups were performed (eTable 1 in Supplement 2).

Time-restricted Cox proportional hazards regression in which follow-up began at 1 year after surgery (to allow inclusion of postoperative weight loss) was conducted to assess the potential risk factors for internal hernia. Based on the results from previous studies,[12,22] we included age, sex, BMI, antireflux surgery, and postoperative total weight loss (TWL) (percentage TWL = 100 × [(initial weight - postoperative weight) / initial weight]) at 1 year after surgery and closure or nonclosure of mesenteric defects as potential risk factors. Age, BMI, and percentage of TWL were modeled as a restriction spline function with 4 knots at the 5th, 35th, 65th, and 95th percentiles according to Harrell's recommendations.[23] A sensitivity analysis with follow-up at surgery but excluding postoperative weight loss as a potential risk factor was conducted (eTable 2 in Supplement 2).

The data were analyzed with IBM SPSS, version 27 and Stata, release 17 (StataCorp LLC). A data monitoring committee from the secretariat of SOReg was involved in overseeing the data. Two-sided $P < .05$ was considered significant.

Results

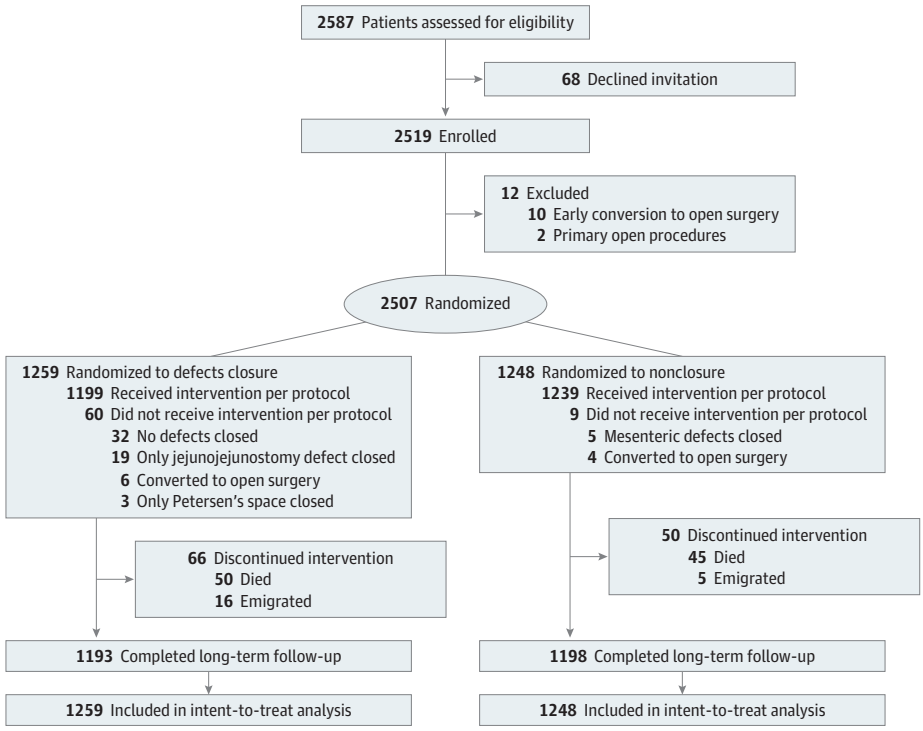
Patient inclusion has been presented in detail previously.[12] In brief, during the inclusion period from May 1, 2010, until November 14, 2011, 2519 patients were included in this study. After exclusion of 10 patients for whom laparoscopy was abandoned before randomization and 2 patients who were planned for primary open surgery, 2507 patients (mean [SD] age, 41.7 [10.7] years; 1863 females [74.3%] and 644 males [25.7%]) were randomized to either mesenteric defects closure (n = 1259) or nonclosure (n = 1248) (**Figure 1**). Significant adhesiolysis (>10 minutes) was required during the primary operation for 25 patients with nonclosure (2.0%) and 38 patients with mesenteric defects closure (3.0%).

At 1 year after surgery, 2439 patients (97.3%) had a registered clinical follow-up, with registration of weight for 2241 patients (89.4%). During the study period, 23 patients emigrated (0.9%) and 107 patients died (4.3%); 12 patients who later died (0.5%) were reoperated for small bowel obstruction at an earlier stage and unrelated to the later death (Figure 1). After censoring for death and emigration, 1193 patients in the closure group (94.8%) and 1198 in the nonclosure group (96.0%) were followed up until the study closed. The median follow-up time for small bowel obstruction was 10.0 years (IQR, 10.0-10.0 years) for both groups, with the shortest follow-up being 9.6 years for patients who did not emigrate, have small bowel obstruction, or die (Figure 1). The randomization generated 2 groups balanced in baseline characteristics (**Table 1**).

Small Bowel Obstruction

During the study period, 98 patients with closed mesenteric defects (10-year cumulative incidence, 7.8%; 95% CI, 6.4%-9.4%) and 185 with nonclosure (10-year cumulative incidence, 14.9%; 95% CI, 13.0%-16.9%) had a reoperation for small bowel obstruction (**Figure 2**A). An increased risk for small bowel obstruction during the first 30 postoperative days was seen among patients with closed mesenteric defects (SHR, 2.62; 95% CI, 1.16-5.91; $P = .02$). Closure of the mesenteric defects was associated with a reduced risk for small bowel obstruction after the initial 30 postoperative days (SHR, 0.42; 95% CI, 0.32-0.55; $P < .001$). The main cause of small bowel obstruction after day 30 was internal herniation, followed by adhesions (**Table 2**). At the time of reoperation, lymphedema was reported in 11 patients with closed mesenteric defects (23.9% of 46 patients with internal herniations for whom the severity could be retrieved) and 42 with nonclosure (27.6% of 152 patients with internal herniations for whom the severity could be retrieved). Among patients with closed defects, a further 8 patients were considered to have ischemia (17.4% of patients with internal herniations) compared with 25 patients with nonclosure (16.5% of patients with internal herniations). Two patients (1 of 47 patients with closed mesenteric

Figure 1. CONSORT Diagram



defects who had internal herniation [2.1%] and 1 of 159 patients with open mesenteric defects who had internal herniation [0.6%]) had nonreversible ischemia requiring small bowel resection. Among 206 patients with internal herniation, preoperative computed tomography (CT) was performed in 160 (77.7%). The findings of this examination were considered positive for 141 patients (88.1%), inconclusive for 9 (5.6%), and negative for 10 (6.3%). During the entire study period, closure of the mesenteric defects was associated with a reduced risk for internal herniation, with 47 patients with closed mesenteric defects undergoing a reoperation for internal herniation with small bowel obstruction compared with 159 among patients with open mesenteric defects (10-year cumulative incidence, 3.8% [95% CI, 2.9%-5.0%] vs 12.9% [95% CI, 11.1%-14.9%]; SHR, 0.28 [95% CI, 0.20-0.39]; $P < .001$) (Figure 2B). The results were similar when stratified by age and sex (eTable 1 in Supplement 2).

Among patients with open mesenteric defects, 85 (6.8%) had the mesenteric defects closed during another operation unrelated to a complication from the LRYGB over the follow-up period. In the per protocol analysis, closure of the mesenteric defects was associated with reduced risk for small bowel obstruction (after day 30: HR, 0.40; 95% CI, 0.30-0.53; $P < .001$) and for internal herniation (HR, 0.27; 95% CI, 0.20-0.39; $P < .001$). Open mesenteric defects, younger age, and higher TWL were associated with higher risk for small bowel obstruction due to internal hernia (**Table 3**).

New Chronic Use of Opioids

Of 863 patients with nonclosure who were opioid naive at baseline, 175 were considered chronic new incident opioid users during follow-up (10-year cumulative incidence, 20.4%; 95% CI, 17.7%-23.0%). Of 895 patients with closed defects who were opioid-naive at baseline, 166 were considered chronic new incident users during follow-up (10-year cumulative incidence, 18.7%; 95% CI, 16.2%-21.3%) (SHR, 0.90; 95% CI, 0.73-1.11; $P = .33$).

Discussion

In this RCT, we demonstrated that mesenteric defects closure reduced the risk of small bowel obstruction up to 10 years after surgery in patients undergoing LRYGB for obesity. The reduced incidence was due to a marked reduction in internal herniation.

The risk for internal herniation with small bowel obstruction appeared to be highest during the first 3 years after surgery, coinciding with the time of the greatest weight loss. Although the risk subsided slightly after this period, this complication continued to occur over time, and the incidence continued to diverge further between the groups over time. In the present study, the risk among patients with nonclosure of the mesenteric defects reached 14.9% for small bowel obstruction and 12.9% for internal herniation over 10 years of follow-up, supporting the findings previously reported in an observational study by Higa and colleagues.[10] Some studies[22,24,25] have reported even higher rates of internal herniation, but these studies have often used wider definitions of internal herniation, including situations when the mesenteric defects were open without signs of bowel obstruction and patients who improved after relaparoscopy with closure of the

mesenteric defects. However, it is likely that in a number of patients with symptoms suggestive of intermittent herniation, the bowel may not necessarily be herniated at the time of surgery. Including all patients with these unspecific signs is likely to overestimate the incidence of internal herniation. Moreover, it might overestimate the treatment effect from mesenteric defects closure as there may be other potentially explanatory factors for abdominal pain after surgery and the placebo effect during the first months after reoperation can be expected to be strong.[26]

In addition to mesenteric defects closure, younger age and higher postoperative weight loss were risk factors for internal herniation with small bowel obstruction. Most participants in this study were women, and many women with severe obesity have difficulty becoming pregnant. After bariatric surgery, many women have improved fertility, and pregnancy has been reported to be associated with an increased risk for small bowel obstruction after LRYGB, mainly due to internal herniation.[27] Younger age is also associated with higher postoperative weight loss.[28] The loss of intra-abdominal fat has also been associated with an increased risk for internal herniation and small bowel obstruction after LRYGB.[12,22]

Internal herniation is associated with risk of serious consequences, and the diagnosis, even in the case of small bowel obstruction, can be challenging. Computed tomography is often used to guide clinical decision-making, resulting in high frequency of use of these scans.[29,30] The sensitivity of CT is, however, low. In the present study, the radiologist failed to confirm the diagnosis in 6.3% of patients with internal herniation, and a further 5.6% of CT findings were inconclusive. These observations corroborate the results from a recent meta-analysis[31] reporting 82% sensitivity for internal herniation identified by CT after LRYGB. Early evaluation by a surgeon with significant experience in bariatric surgical complications with a low threshold for diagnostic laparoscopy may thus be warranted.

The efficacy of any intervention must always be weighed against the potential adverse effects. Closing the mesenteric defects with sutures is a technically challenging intervention previously reported to increase the risk of kinking of the jejunojejunostomy and secondarily to increase the rate of pulmonary complications.[12] To some extent, kinking of the jejunojejunostomy might be attributable to a learning curve effect and could therefore be expected to be less common over time. Moreover, a small increase in early small bowel obstruction might be considered a reasonable trade-off for the later reduction in internal hernia and small bowel obstruction. A different technique using clips instead of running, nonabsorbable sutures has been reported to be easier and have less influence on operation time[13,24] but was also associated with slightly higher risk for kinking of the jejunojejunostomy.[13,32]

A high proportion of patients report chronic abdominal pain after bariatric surgery.[33] While an increased risk of chronic pain has been reported after a variety of surgical procedures,[34] the risk appears to be particularly high after LRYGB.[33,35] There are many potential causes for this complication, and its pathophysiology may often be multifactorial and complex.[36] An association between mesenteric defects closure and postoperative pain has previously been suggested,[15] but in the present study, no difference in postoperative opioid use among patients naive to opioids at baseline was seen. We used chronic opioid intake as a proxy for chronic pain with the limitation of not being able to separate the source of chronic pain. However, our data are supported by previous studies reporting similar findings in the early postoperative period and during follow-up.[13,37]

Table 1. Baseline Characteristics

Characteristic	Patients[a]	
	Defects not closed (n = 1248)	Defects closed (n = 1259)
Sex		
Female	915 (73.3)	948 (75.3)
Male	333 (26.7)	311 (24.7)
Age at operation, mean (SD), y	41.7 (10.7)	41.7 (10.8)
Coexisting disorders with ongoing treatment	636 (51.0)	618 (49.1)
Sleep apnea	100 (8.0)	107 (8.5)
Hypertension	333 (26.7)	327 (26.0)
Diabetes	146 (11.7)	179 (14.2)
Dyslipidemia	150 (12.0)	139 (11.0)
Dyspepsia	127 (10.2)	117 (9.3)
Depression	174 (13.9)	175 (13.9)
Other	77 (6.2)[b]	83 (6.6)[c]
Previous venous thromboembolism		
Any	33 (3.4)	39 (3.9)
Missing data	266 (21.3)	251 (20.0)
Smoking		
Active	176 (16.4)	174 (16.3)
History	179 (16.7)	160 (15.0)
Missing data	178 (14.3)	193 (15.3)
BMI, mean (SD)	42.4 (5.2)	42.3 (4.9)
Waist circumference		
Mean (SD), cm	127.2 (13.4)	127.5 (13.1)
Missing data	124 (9.9)	115 (9.1)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

[a] Data are presented as number (percentage) of patients unless otherwise indicated.

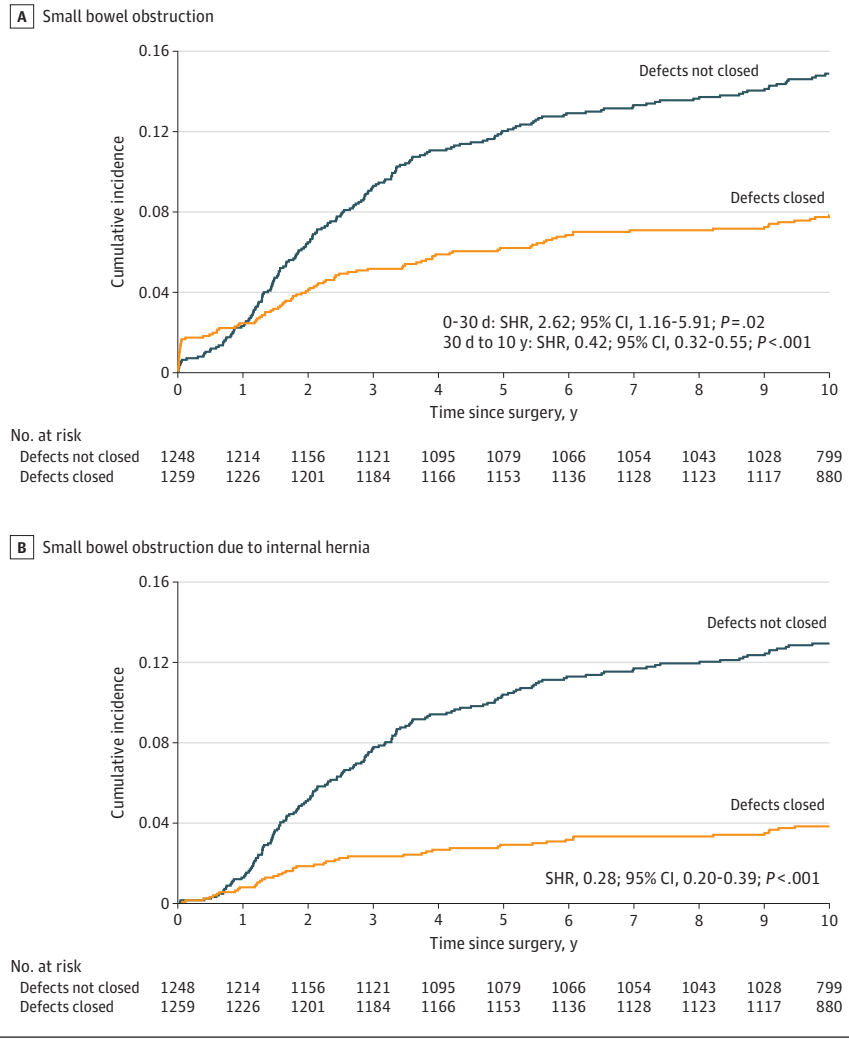
[b] Other disorders were cardiovascular disease (8 [0.6%]), pulmonary disease (6 [0.5%]), pain or mobility limitation (48 [3.8%]), systemic disease (8 [0.6%]), psychiatric disorder other than affective disorder (1 [0.1%]), and other (6 [0.5%]).

[c] Other disorders were cardiovascular disease (12 [1.0%]), pulmonary disease (5 [0.4%]), pain or mobility limitation (56 [4.4%]), systemic disease (5 [0.4%]), psychiatric disorder other than affective disorder (2 [0.2%]), and other (3 [0.2%]).

Strengths and Limitations

This study has strengths. This study was designed as a registry-based RCT. While traditional RCTs have been reported to overestimate efficacy of an intervention,[38] a registry-based RCT offers high inclusion rates and generalizability of the results,[39,40] suggesting that similar treatment effects of mesenteric defects closure can be expected in general practice outside the current study. This assumption is also supported by a previous comparison with patients who underwent surgery in Sweden outside this RCT.[41]

Figure 2. Cumulative Incidence of Small Bowel Obstruction Comparing Closure of Mesenteric Defects With Nonclosure



P values are based on Cox proportional hazards regression adjusted for surgical center. SHR indicates subhazard ratio.

Table 2. Causes of Small Bowel Obstruction

Cause	Patients, No. (%)					
	Day 0-30			After day 30		
	Defects not closed (n = 1248)	Defects closed (n = 1259)	*P* value[a]	Defects not closed (n = 1248)	Defects closed (n = 1259)	*P* value[b]
Kinking of jejunojejunostomy	3 (0.2)	16 (1.3)	.003	2 (0.2)	1 (0.1)	>.99
Internal hernia						
All	2 (0.2)	1 (0.1)	.62	157 (12.9)	46 (3.8)	<.001
Beneath jejunojejunostomy	2 (0.2)	1 (0.1)	.62	105 (8.9)	28 (2.3)	<.001
Petersen space	0	0	NA	39 (3.4)	17 (1.4)	.003
Combined or undefined	0	0	NA	13 (1.2)	1 (0.1)	.01
Adhesions	2 (0.2)	2 (0.2)	>.99	10 (0.9)	18 (1.5)	.17
Incisional hernia	1 (0.1)	2 (0.2)	>.99	1 (0.1)	0	>.99
Intussusception	0	0	NA	6 (0.6)	8 (0.7)	.66
Other or unknown	0	0	NA	1 (0.1)	4 (0.3)	.22

Abbreviation: NA, not applicable.

[a] Based on the χ^2 test or Fisher exact test as appropriate.

[b] Based on Cox proportional hazards regression.

Table 3. Risk Factor Analyses for Internal Herniation With Follow-up Beginning at 1 Year After Surgery[a]

Variable	Internal herniation, No./total No. (%)	Unadjusted[b]		Adjusted[c]	
		SHR (95% CI)	*P* value	SHR (95% CI)	*P* value
Mesenteric defects					
Open	130/1098 (11.8)	1 [Reference]	NA	1 [Reference]	NA
Closed	35/1087 (3.2)	0.26 (0.18-0.38)	<.001	0.25 (0.17-0.37)	<.001
Sex					
Female	123/1624 (7.6)	1 [Reference]	NA	1 [Reference]	NA
Male	42/561 (7.5)	0.98 (0.68-1.40)	.91	1.18 (0.81-1.72)	.39
Antireflux surgery					
No	164/2170 (7.6)	1 [Reference]	NA	1 [Reference]	NA
Yes	1/15 (6.7)	0.86 (0.11-6.75)	.89	0.96 (0.12-7.78)	.97
Age, y[d]					
25	NA	2.29 (1.51-3.48)	NA	2.18 (1.42-3.35)	NA
35	NA	1.87 (1.29-2.70)	NA	0.46 (0.32-0.67)	NA
45	NA	1 [Reference]	NA	1 [Reference]	NA
55	NA	0.79 (0.58-1.07)	NA	0.83 (0.61-1.13)	NA
65	NA	0.86 (0.35-2.13)	NA	0.95 (0.39-2.35)	NA
BMI[d]					
35	NA	0.79 (0.43-1.47)	NA	0.99 (0.55-1.79)	NA
40	NA	1 [Reference]	NA	1 [Reference]	NA
45	NA	1.03 (0.72-1.47)	NA	0.93 (0.65-1.33)	NA
50	NA	0.96 (0.63-1.47)	NA	0.81 (0.53-1.23)	NA
55	NA	0.88 (0.47-1.64)	NA	0.69 (0.37-1.27)	NA
60	NA	0.81 (0.31-2.09)	NA	0.59 (0.23-1.51)	NA
1-y TWL, %[d]					
20	NA	0.70 (0.42-1.14)	NA	0.75 (0.45-1.28)	NA
25	NA	0.78 (0.65-0.93)	NA	0.81 (0.67-0.98)	NA
30	NA	1 [Reference]	NA	1 [Reference]	NA
35	NA	1.39 (1.05-1.82)	NA	1.33 (1.00-1.77)	NA
40	NA	1.64 (1.18-2.29)	NA	1.58 (1.11-2.27)	NA
45	NA	1.80 (1.13-2.88)	NA	1.78 (1.07-2.96)	NA

Abbreviations: BMI, body mass index (calculated as weight in kilograms divide by height in meters squared); NA, not applicable; SHR, subhazard ratio; TWL, total weight loss.

[a] Including 2185 patients with measured weight loss at 1 year after surgery who were still at risk for internal herniation with small bowel obstruction (1098 in the nonclosure group and 1087 in the closure group). Subhazard ratios are from competing risk regression with all-cause mortality as the competing event.

[b] All unadjusted analyses were adjusted for center.

[c] Adjusted for all variables in the table and center.

[d] Age, BMI, and 1-year TWL were modeled by restricted cubic splines with 4 knots at the 5th, 35th, 65th, and 95th percentiles.

This study also has limitations. Clinical registries were used to retain high follow-up rates. While a risk for faulty registration exists, all the registries we used have high coverage with high validity of data.[18-20,42] In addition, the hospital medical records and operative notes of all patients who potentially underwent a reoperation for small bowel obstruction were reviewed to ensure a uniform classification of this complication in accordance with our prespecified definition. With the multicenter design, including several participating surgeons, the degree of standardization of the technique may be lower than in a proof-of-concept design within a single center. While measures were taken to ensure the implementation of a uniform technique,[12] individual differences in mesenteric defects closure techniques cannot be ruled out. Accordingly, the results should not be considered as the best possible achievable results from this intervention. Rather, the study might be considered pragmatic, reflecting daily clinical practice, and the results should therefore be generalizable to a wider group of patients with characteristics similar to those of patients included in this study. In addition, not all patients received their allocated treatment. The main reason for this was technical difficulties in closing one of the mesenteric defects, which would mainly underestimate the treatment effect of the intervention. A small group did not receive their allocated treatment for unknown reasons. However, this group represents a small proportion of the entire study group, with limited effects on the results. In addition, HRs used to estimate risks may introduce a built-in selection bias by censoring patients with events,[43] which might further increase the risk of underestimating the treatment effect of the intervention. Finally, as requested by the regional ethics committee, the study was unblinded after the intervention.

Conclusions

In this open-label, registry-based RCT in Sweden, closure of the mesenteric defects in LRYGB reduced the risk of small bowel obstruction up to 10 years after surgery. The findings suggest that routine use of this procedure in LRYGB operations should be considered.

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Invited Commentary

Closure of Mesenteric Defects During Gastric Bypass Reduces but Does Not Eliminate the Risk of Internal Hernia

I. Michael Leitman, MD

With the continued popularity of laparoscopic Roux-en-Y gastric bypass (LRYGB) for the treatment of severe obesity, the issue of how to prevent internal herniation (IH) appears to be settled. In this issue of *JAMA Surgery*, Stenberg and colleagues'[1] prospective randomized clinical trial assigned patients to either closure of the mesenteric defects beneath the jejunojejunostomy and at the Petersen space using nonabsorbable running sutures or nonclosure. Most of the 2519 patients were followed up for a median of 10 years. A significantly greater number without closure of the mesenteric defect required reoperation for small bowel obstruction (SBO) compared with those that had closure during their index operation (14.9% vs 7.8%). The main cause for SBO after day 30 was IH but almost half of the patients that had their mesenteric defect closed that developed SBO requiring surgery resulted from IH. A secondary outcome of postoperative chronic opioid use did not reach statistical significance. It is important to note that the 10-year cumulative incidence of intestinal obstruction of requiring surgery in the treatment group was still almost 8%.

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IH is reported to occur in as many as 9% of patients who undergo LRYGB.[2] It most typically occurs in the first few years after LRYGB, during the period of rapid weight loss and might represent the loss of mesenteric fat. This may occur whether the alimentary limb is brought to the gastric pouch in an antecolic or retrocolic fashion.[3] A drawback of the laparoscopic approach is the higher incidence of IH compared with the open approach, but most IH cases are able to be managed laparosopically.[4]

Similarly, the incidence of IH after gastrectomy ranges from 0.2% to 5.6% and the routine closure of the mesentery and the Petersen space after Roux-en-Y reconstruction should also be considered.[5] SBO following LRYGB is a serious problem with a mortality rate of 1% to 2%. Computed tomography scanning may identify most but not all cases of IH. Abdominal pain radiating pain to the back, postprandial pain, and elevated white blood cell count are predictors of IH and may require diagnostic laparoscopy or laparotomy to prevent intestinal necrosis. Pregnant patients are a special subgroup of patients at risk, due to anatomic changes that occur and signs that might be more subtle.[6] The current study by Stenberg et al[1] has settled this issue; however, neither primary nor secondary closure of mesenteric defects can completely eliminate the risk of IH.[7]

ARTICLE INFORMATION

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