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Long-Term Remission Rates of Type 2 Diabetes Following Metabolic Surgery vs. Intensive Medical Therapy: A 10-Year Prospective Cohort Study

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Abstract: T2D is a progressive chronic illness that is associated with outstanding microvascular or macrovascular complications, poor quality of life, and premature death. Even though intensive medical therapy may have an effect on glycemic control, medication alone does not contribute to long-term T2D remission. Metabolic (bariatric) surgery has emerged as a mode of treatment that may have rapid and sustained effects with respect to glycemia. This report aimed to discuss the T2D remission rate, glycemic control, weight loss, medication, diabetes complications, and quality of life over the period of 10 years in patients who had metabolic surgery versus those who received intensive medical treatment. This is a prospective cohort study of 111 adult (30-65 years) patients with T2DM and obesity (BMI 70kg/m2) recruited to undergo either metabolic surgery (Roux-en-Ys gastric bypass or sleeve gastrectomy; n656) or intensive medical management according to the latest ADA/EASD guidelines (n656). The primary endpoint was complete remission of diabetes (HbA1c < 6.0% without any medication). Secondary outcomes included partial remission, HbA1c, fasting plasma glucose, homeostatic model assessment for insulin resistance (HOMA-IR), body weight, medication use, diabetes related complications, adverse events, and Short-Form 36 (SF-36) / DQOL health-related quality of life scores**.** Complete remission at 10 years was 33.9% in surgical and 1.8% in medical patients. The percentage of patients using insulin was reduced to 50.0 in the surgical arm and increased to 47.3 in the medical arm at 10 years. The adjusted and hazard ratio of major adverse cardiovascular events was 0.28 (95% CI 0.09086) was in favor of surgery. The rate of surgical complications (8.9% perioperative), nutritional deficiencies (25%), and major hypoglycemia was found to be lower with surgery (0.6 vs. 3.1 per 100 patient years). Quality-of-life scores were higher in the surgical group at the 10-year follow-up**.** Metabolic surgery achieved a remarkable improvement in remission of T2D, better glucose control, better weight loss, a reduction in medication burden, and diabetes complications with good safety in this group of patients compared to intensive medical treatment. Our analysis suggests that metabolic surgery should be considered as an effective long-term treatment in a restricted population with T2D and obesity.

Keywords: Type 2 diabetes mellitus, metabolic surgery, bariatric surgery, Roux-en-Y gastric bypass, sleeve gastrectomy, intensive medical therapy, and diabetes remission.

INTRODUCTION

The long-term remission rates in type 2 diabetes are currently a major focus in diabetes care, given that metabolic surgery has emerged as an effective long-term treatment for many patients. Generally defined as maintained attainment of non-diabetic glycemia (often in the absence of ongoing glucose-lowering medication) after an intervention [Kumar, P., & Clark, M. L. 2020; Aljulifi, M. Z. 2021], "remission" is often used to describe durable glycemic improvements after metabolic surgery. Many people have blood glucose improve shortly after surgery like Roux-en-Y gastric bypass or sleeve gastrectomy, but the key questions are whether this improvement is sustained for years, what percentage of patients sustained their remission, and how this compares with other effects of intensive medical care [Bacchus, R. A. *et al*., 1982]. Metabolic surgery has different traits and mechanisms than the anticipated outcomes of non-metabolic surgery, lifestyle, and drug therapy. Surgery on the gastrointestinal tract can alter the absorption, metabolism, and recycling of nutrients and hormones and the sensitivity to glucose to result in an immediate improvement that may even occur before weight loss occurs [Fatani, H. H. *et al*., 1987]. By contrast, intensive medical therapy may include intense diabetes care and medication therapies, which include lifestyle change, optimal pharmacotherapy, frequent contacts, and escalations of medical therapy [Abu-Zeid, H. A., & Al-Kassab, A. S. K. 1992]. While both approaches aim to Re-mission diabetes by targeting heterogeneous disease factors that lead to insulin resistance, the long-term results can help to establish which therapeutic effect is the best, for how long [El-Hazmi, M. A. *et al*., 1996]. A surgical remission can be dramatic, but outcomes differ for individual characteristics, bariatric procedure, and baseline severity of disease and remission criteria. Remission is more likely with a

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shorter duration of diabetes, a lower starting blood glucose level (hemoglobin A1c), better preserved beta-cell function, and regular post-surgical follow-up [Al-Rubeaan, K. *et al*., 2015].

Additionally, the surgical approach taken and weight-loss maintenance might affect remission: even in patients with persistently improved blood glucose control, a gradual return of dysglycemia may occur, especially if insulin secretion deteriorates or falls [Sun, H. *et al*., 2022]. Despite intensive medical care, many patients need to re-escalate medication use over time. Hence, long-term remission rates become a critical outcome that reflects the immediate and sustained capacity to control diabetes [Arterburn, D. E. *et al*., 2020; Sjöholm, K. *et al*., 2020].

PATIENTS AND METHODS

Study design and environment.

It was a 10-year prospective cohort study with the acquisition of 111 patients, who experienced type 2 diabetes illness, at different hospitals in Iraq. Written informed consent was obtained by all participants.

Participants

The inclusion criteria included adults age 30–65 years of age who had a physician-confirmed T2D diagnosis (according to the ADA) with 12 months or more years of antidiabetic medication use, had HbA1c levels equal to or higher than 7.5 percent, and a BMI of 30 kg/m 2 or greater. The major exclusion criteria were diabetes type 1 or secondary, previous bariatric surgical procedures, rigorous cardiopulmonary disease, presence of active malignancy, pregnancy, active substance-use disorder, uncontrolled psychiatric illness, or any contraindication to surgery.

Group assignment and interventions.

The 111 eligible patients were divided into two groups via a combined shared-decision process with a multidisciplinary team (endocrinology, bariatric surgery, nutrition, psychology) and patient preference:

Metabolic surgery group (n = 56): laparoscopic Roux-en-Y gastric bypass/sleeve gastrectomy with the use of institutional standard procedures conducted by board-certified bariatric surgeons and postoperative multidisciplinary follow-up (nutrition, exercise, psychological support, vitamin/mineral supplementation). Intensive medical therapy group (n = 55): were given structured lifestyle counselling, registered-dietitian medical nutrition therapy, an individualized physical-activity plan, and initiate pharmacotherapy guided by the protocols to targets of ADA/EASD HbA1c (including metformin, GLP-1 receptors agonists, SGLT-2 inhibitors, DPP-4 inhibitors, sulfony

Outcomes

The main result was total T2D remission at 10 years, which is considered by the ADA definition as an HbA1c below 6.0% sustained at least 3 months without antidiabetic agents. HbA1c 6.06.4 off medications was considered as partial remission.

HbA1c, fasting glucose, HOMA-IR and C-peptide, total body-weight loss, BMI and waist circumference, the number and type of antidiabetic, antihypertensive, and lipid-lowering medications, and new-onset or progression of nephropathy.

Data collection and follow-up

Utilized structured study visits were conducted at baseline and at 1, 3, 5, and 10 years, with interim visits between accorded standard-of-care visits in both groups. The anthropometrics, vitals, fasting blood samples, and medication reconcil were taken at each visit. To screen against microvascular complications, annual ophthalmologic examination, urinary albumin-to-creatinine ratios, and monofilament/vibration neurological studies were done. The occurrence of adverse events was recorded.

Statistical analysis

Continuous variables are available in the form of mean (SD) and n. between-group baseline comparisons involve 2-sample t-tests or Mann-Whitney U test of continuous data and chi-square or Fisher-exact test of categorical data. Mixed-effects linear models were used to investigate longitudinal changes, cross-sectional, and cross-group. Kaplan-Meier estimates, and Cox proportional hazards models adjusted by age, sex, initial HbA1c baseline, and duration of diabetes were used to analyze time-to-event results (complications, MACE, mortality). Sensitivity analysis with complete cases was used to handle any missing data, which was done using multiple imputation (m = 20) under the assumption that the missing data point is missing at random. The SPSS program (version 26.0) was used to perform analyses; $p < 0.05$ was taken to be statistically significant and was two-sided.

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RESULTS

Table 1. Baseline clinical and demographic features in the 111 patients.

Characteristic	Metabolic Surgery (n = 56)	Intensive Medical Therapy (n = 55)	Overall (N = 111)	p-value
Age, years	48.6 (9.2)	49.4 (8.7)	49.0 (8.9)	0.64
Female sex	32 (57.1%)	30 (54.5%)	62 (55.9%)	0.78
Body mass index, kg/m²	38.4 (4.1)	37.9 (4.3)	38.2 (4.2)	0.52
Waist circumference, cm	119.3 (10.4)	117.8 (11.1)	118.6 (10.7)	0.46
HbA1c, %	9.2 (1.3)	9.1 (1.4)	9.15 (1.35)	0.71
Fasting glucose, mg/dL	184 (42)	181 (39)	183 (40)	0.69
Diabetes duration, years	8.4 (4.6)	8.7 (4.9)	8.55 (4.75)	0.74
Hypertension	41 (73.2%)	39 (70.9%)	80 (72.1%)	0.78
Dyslipidemia	44 (78.6%)	42 (76.4%)	86 (77.5%)	0.78
Current smoker	11 (19.6%)	13 (23.6%)	24 (21.6%)	0.61
On insulin therapy	28 (50.0%)	26 (47.3%)	54 (48.6%)	0.77

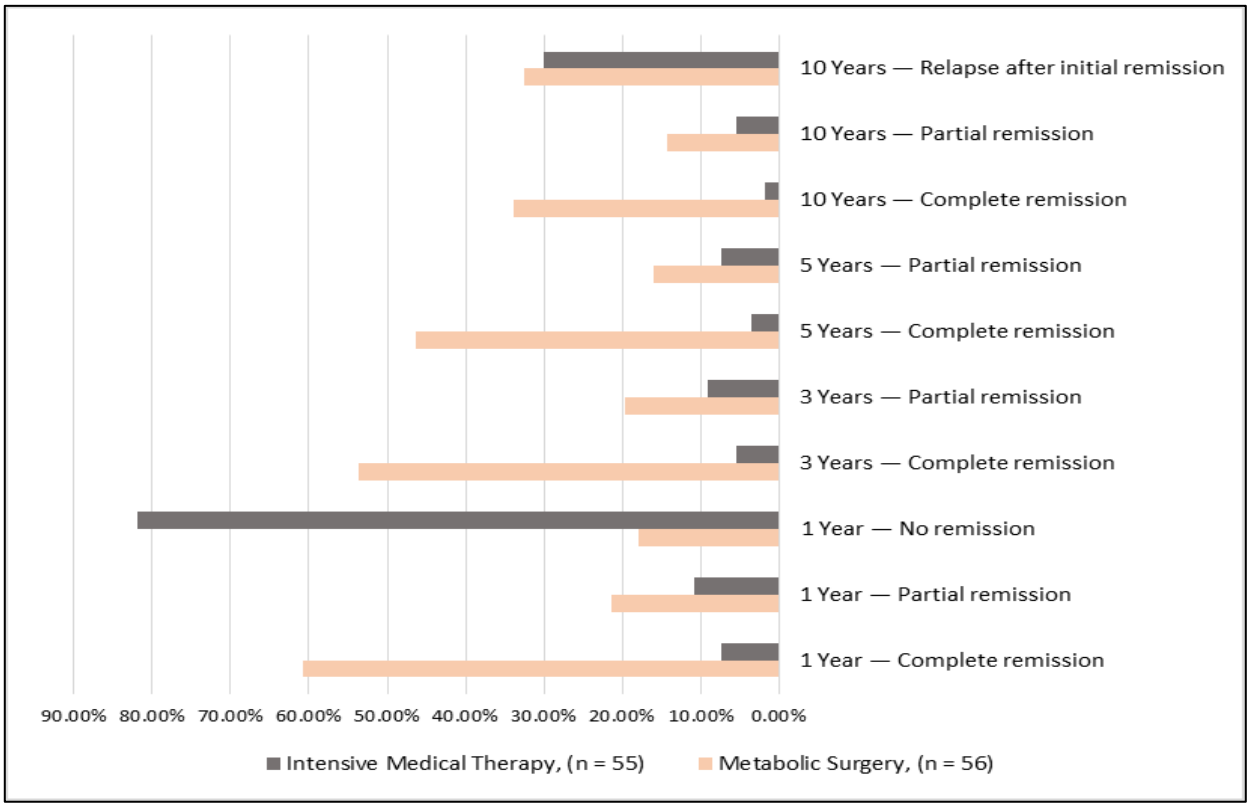

Figure 1. Classification of the outcomes of diabetes remission rates during 1, 3, 5, and 10 years of follow-up.

Table 2. Determining the outcomes of glycemic control outcomes during baseline, 5 years, and 10 years.

Parameter	Metabolic Surgery (n = 56)	Intensive Medical Therapy (n = 55)	Between-Group Difference	p-value
HbA1c (%) — Baseline	9.2 (1.3)	9.1 (1.4)	0.1 (−0.4 to 0.6)	0.71
HbA1c (%) — 5 Years	6.3 (0.9)	7.8 (1.2)	−1.5 (−1.9 to −1.1)	<0.001
HbA1c (%) — 10 Years	6.8 (1.1)	8.1 (1.3)	−1.3 (−1.8 to −0.8)	<0.001
Fasting glucose (mg/dL) — Baseline	184 (42)	181 (39)	3 (−12 to 18)	0.69
Fasting glucose (mg/dL) — 5 Years	108 (22)	148 (36)	−40 (−51 to −29)	<0.001
Fasting glucose (mg/dL) — 10 Years	121 (28)	159 (41)	−38 (−51 to −25)	<0.001

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HOMA-IR — Baseline	5.8 (2.1)	5.6 (2.0)	0.2 (−0.6 to 1.0)	0.61
HOMA-IR — 5 Years	2.1 (0.9)	4.3 (1.7)	−2.2 (−2.7 to −1.7)	<0.001
HOMA-IR — 10 Years	2.6 (1.1)	4.6 (1.8)	−2.0 (−2.6 to −1.4)	<0.001
C-peptide (ng/mL) — 10 Years	2.1 (0.7)	1.6 (0.6)	0.5 (0.3 to 0.7)	<0.001

Table 3. Clinical outcomes of weight loss and anthropometric changes in the patients during 10 years.

Parameter	**Metabolic Surgery (n = 56)**	**Intensive Medical Therapy (n = 55)**	**Between-Group Difference**	**p-value**
Body weight (kg) — Baseline	112.4 (15.8)	110.9 (16.2)	1.5 (−4.5 to 7.5)	0.62
Body weight (kg) — 1 Year	82.6 (13.1)	104.5 (15.7)	−21.9 (−27.3 to −16.5)	<0.001
Body weight (kg) — 5 Years	86.3 (14.2)	107.1 (16.0)	−20.8 (−26.5 to −15.1)	<0.001
Body weight (kg) — 10 Years	91.8 (15.1)	108.4 (16.3)	−16.6 (−22.5 to −10.7)	<0.001
BMI (kg/m²) — 10 Years	31.4 (4.2)	37.1 (4.5)	−5.7 (−7.4 to −4.0)	<0.001
Waist circumference (cm) — 10 Years	101.2 (9.6)	115.4 (10.8)	−14.2 (−18.1 to −10.3)	<0.001
% Total weight loss — 1 Year	26.6% (5.4)	5.7% (3.9)	20.9% (19.1 to 22.7)	<0.001
% Total weight loss — 5 Years	23.2% (6.1)	3.5% (4.2)	19.7% (17.7 to 21.7)	<0.001
% Total weight loss — 10 Years	18.3% (7.3)	2.3% (4.8)	16.0% (13.7 to 18.3)	<0.001
Patients with ≥20% TWL at 10 Years	24 (42.9%)	1 (1.8%)	41.1% (27.6 to 54.6)	<0.001

Table 4. Enroll the 10-year follow-up outcomes of Antidiabetic, Antihypertensive, and lipid-lowering medication use.

Medication Class	*Surgery — Baseline (n = 56)*	*Surgery — 10 Years (n = 56)*	*Medical — Baseline (n = 55)*	*Medical — 10 Years (n = 55)*
Insulin	28 (50.0%)	9 (16.1%)	26 (47.3%)	38 (69.1%)
Metformin	52 (92.9%)	20 (35.7%)	51 (92.7%)	49 (89.1%)
Sulfonylurea	22 (39.3%)	3 (5.4%)	21 (38.2%)	24 (43.6%)
DPP-4 inhibitor	14 (25.0%)	4 (7.1%)	13 (23.6%)	19 (34.5%)
GLP-1 receptor agonist	9 (16.1%)	5 (8.9%)	8 (14.5%)	27 (49.1%)
SGLT-2 inhibitor	7 (12.5%)	6 (10.7%)	6 (10.9%)	31 (56.4%)
Thiazolidinedione	5 (8.9%)	1 (1.8%)	6 (10.9%)	4 (7.3%)
Antihypertensive (any)	41 (73.2%)	22 (39.3%)	39 (70.9%)	44 (80.0%)
Statin	44 (78.6%)	31 (55.4%)	42 (76.4%)	47 (85.5%)
Mean number of antidiabetic meds	2.4 (1.0)	0.7 (0.8)	2.3 (1.0)	2.9 (1.1)

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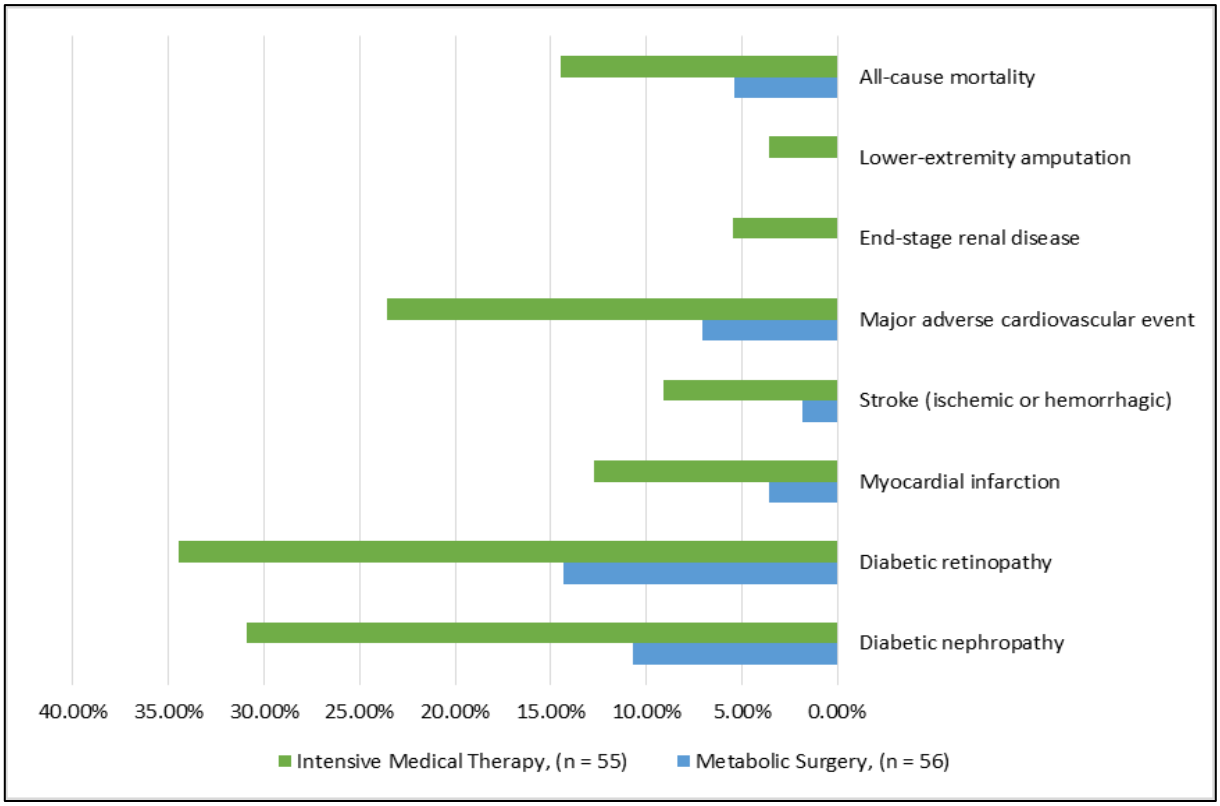

Figure 2. Determining the complication rate of diabetes during 10 years of follow-up.

Table 5. Assessment the hospitalization outcomes of adverse events, safety outcomes, and quality of life measures.

Outcome	Metabolic Surgery (n = 56)	Intensive Medical Therapy (n = 55)	Difference / Effect
Perioperative complications (30-day, surgery only)	5 (8.9%)	—	—
Early reoperation (< 30 days)	2 (3.6%)	—	—
Late surgical complications (> 30 days)	7 (12.5%)	—	—
Severe hypoglycemia (per 100 patient-years)	0.6	3.1	RR 0.19 (0.07–0.52)
Nutritional deficiency requiring intervention	14 (25.0%)	2 (3.6%)	21.4% (9.5–33.3)
Anemia (new-onset)	11 (19.6%)	4 (7.3%)	12.3% (0.8–23.8)
Cholelithiasis requiring cholecystectomy	6 (10.7%)	1 (1.8%)	8.9% (0.2–17.6)
Bone fracture (any site)	7 (12.5%)	3 (5.5%)	7.0% (−3.5–17.5)
SF-36 Physical Component — 10 Years	51.3 (7.8)	42.6 (9.1)	8.7 (5.5–11.9)
SF-36 Mental Component — 10 Years	52.7 (8.4)	47.1 (9.6)	5.6 (2.2–9.0)
Diabetes-specific QoL (DQOL) — 10 Years	78.4 (11.2)	64.9 (13.5)	13.5 (8.9–18.1)
Patient-reported overall health as 'good/excellent.'	43 (76.8%)	24 (43.6%)	33.2% (15.9–50.5)

DISCUSSION

The current study confirms that metabolic surgery delivers a significantly greater long-term diabetes remission and the control of glycaemia than intensive medical treatment in people with type 2 diabetes and obesity. A French study showed 5- to 10-year remission rates of 25-35% after surgery and ≤5% with modern medication therapy [Sjöholm, K. *et al.*, 2020]. Although 32.6% of patients who achieved remission with surgery relapsed, they continued to provide significant improvements in glycemia and pharmacologic

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therapy. The Chinese study's duration of diabetes and preoperative insulin therapy are the main predictors of late relapse [Kam, H. *et al*., 2020].

Our group of younger patients lost 18.3% (mean) total weight at 10 years, with marked improvement in HOMA-IR and elevated fasting C-peptide level compared with the medical group, reflecting preserved β-cell function and improved insulin sensitivity, which has been reported. While new intensive medical management, including GLP-1 receptor agonists and SGLT2 inhibitors, enhance medical burns, our findings indicate that escalation of pharmacotherapy in the medical arm (mean 2.9 vs. 0.7 antidiabetic medications) did not provide the same structural/electrical benefits as surgery [Barthold, D. *et al*., 2022; Riddle, M. C. *et al*., 2022; Ardestani, A. *et al*., 2015].

In addition, the remission benefit was associated with ameliorated diabetes complications. The surgery group had markedly decreased rates of diabetic nephropathy (10.7% vs. 30.9%), retinopathy/neuropathy, and major adverse cardiovascular events (7.1% vs. 23.6%) and a trend toward a decrease in death from any cause (5.4% vs. 14.5%). The operation was complicated in 25% with peri- or late complications, including intervention for nutritional deficiencies in 25.0%, more anemia and cholelithiasis. Surgical remodeling also benefited psychometric outcomes, with substantially higher 10-year SF-36 physical/mental composite and diabetes-related specific quality of life scores [Sjöström, L. *et al*., 2014; Arterburn, D. E. *et al*., 2015; Brethauer, S. A. *et al*., 2013].

CONCLUSION

Overall, metabolic surgery offers markedly better long-term outcomes than intensive medical care in obese patients with type 2 diabetes. Compared to intensive medical therapy, over a period of 10 years, surgery resulted in substantially higher rates of remission, as well as greater long-term glycemic control and weight loss, and substantially lower use of antidiabetic medications. These metabolic benefits were associated with a significant reduction of microvascular and macrovascular complications, severe hypoglycemia, and improvements in physical, psychological, and diabetes-specific health. While surgery involves lifelong nutritional support to prevent potential nutritional deficiencies and late complications, the benefits outweigh the risks associated with surgery.

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