REVIEW

Short Versus Long Roux-Limb Length in Roux-en-Y Gastric Bypass Surgery for the Treatment of Morbid and Super Obesity: a Systematic Review of the Literature

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Abstract Because of an important burden of disease, obesity is a major public health challenge in the twenty-first century. Where medico-psychological management has shown its limitations, bariatric surgery is now acknowledged as the most efficient therapy potentially offered to severely obese patients. Among other options, Roux-en-Y gastric bypass (RYGBP) is the most frequently performed procedure. The objective of this review is to systematically evaluate the effect of the Roux-(alimentary) limb length on postoperative weight loss after RYGBP in severely obese patients. MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CEN-TRAL) were searched using terms related to Roux-limb, gastric bypass and obesity. To be included, studies had to be either randomized controlled trials, quasi-randomized controlled trials or prospective cohort studies comparing a shorter to a longer Roux-limb. Studies were critically appraised with regard to methodological components. Eight studies were reviewed. Variations in methodology, operation design and outcome assessment among studies caused considerable clinical heterogeneity, preventing us from performing a metaanalysis. The overall quality was questionable, owing to lack of rigor in methodological components reporting. Results were heterogeneous, but we identified a trend supporting that the construction of a longer Roux-limb is more efficient in super

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obese patients. This review suggests that the tailoring of a longer Roux-limb might only be efficient in super obese patients. The overall limited quality of the included studies prompts to call for improvement in trial design in surgery.

Keywords Obesity \cdot Super obesity \cdot Anastomosis \cdot Roux-en-Y \cdot Gastric bypass \cdot Limb length \cdot Weight loss

Introduction

Obesity is a global public health challenge and there is worldwide concern about this health condition. During the past two decades, bariatric surgery has been repeatedly shown to be beneficial to severely obese patients, by safely achieving outcomes such as weight loss and co-morbidity control [1-4]. Accordingly, bariatric surgery is now recognized as the main component of morbid obesity treatment and can be dichotomized into two main kinds of procedure: restrictive and malabsorptive [5]. Roux-en-Y gastric bypass (RYGBP), the most commonly performed procedure, combines both aspects, as it consists of the creation of a small gastric pouch combined with a gastrointestinal bypass [6-8]. Even though most of its effects are believed to be caused by restriction, the bypassing of a large proportion of the stomach, the duodenum and various lengths of the jejunum is also likely to contribute to weight loss [9, 10]. Initially designed for morbidly obese patients, RYGBP has been shown to be less efficient in super obese populations [11-13]. This finding encouraged surgeons aiming at more satisfying results to imagine variations of RYGBP. Among the various components of the RYGBP that can be modified, lengthening the portion of the intestine within which absorption is limited-because of a lack of interaction of food with bile and pancreatic enzymes-appears as an appealing opportunity to improve weight loss profile.

Objectives

The objective of this review is to assess the evidence regarding the efficacy of tailoring a longer as compared to a shorter Roux-limb for improving weight loss profile in morbidly obese (BMI \geq 35 kg/m²) patients undergoing RYGBP surgery. More in-depth questions to be addressed in this review are:

- Does the construction of a longer Roux-limb improve long-term weight loss results?
- Is Roux-limb length a determinant of postoperative weight loss in both morbidly and super obese (cf. definitions below) patients?
- Does the Roux-limb length have an effect on obesity related co-morbidities, such as type 2 diabetes (T2DM), dyslipidaemia, hypertension (HTN), sleep apnea syndrome (SAS) and gastroesophageal reflux disease (GERD)?
- Is there a relationship between the risk of nutritional deficiencies after RYGBP and Roux-limb length?

Methods

Types of Studies

Studies included were randomized controlled trials (RCTs) comparing long vs. short Roux-limb in severely obese patients treated with RYGBP, regardless of the surgical technique (laparoscopy vs. open surgery). Anticipating the paucity of available literature, it was decided to include quasirandomized controlled trials and prospective cohort studies as well. To be included, studies had to have at least a 12-month follow-up. Studies were included irrespective of publication status. The assessed literature was written in either English, French, Italian or Spanish. Exclusion criteria were: any kind of study design that included retrospectively collected data; studies that did not compare different intervention groups (one long Roux-limb vs. one short Roux-limb): for instance case series, studies assessing Roux-limb length variation in other setting than RYGBP (e.g. biliopancreatic diversion with or without duodenal switch) or secondary analyses based on previously published reports.

Patients

All the patients included in this review were adults $(\geq 18 \text{ years old})$ who met the criteria for surgical treatment. With respect to obesity, included participants had to fall in one of the following categories:

• Morbid obesity, defined as a BMI \ge 40 kg/m² (or \ge 35 with clinically relevant obesity related co-morbidities/

high health risk) or an absolute body weight \geq 45 kg higher than ideal body weight, depending on the studies considered

- Super obesity, defined as a BMI≥50 kg/m² or an absolute body weight ≥90 kg higher than ideal body weight, depending on the studies considered
- Super-super obesity, defined as a BMI \geq 60 kg/m²

Types of Outcomes and Their Measurements

Outcomes of interests were of three types:

- Weight loss indicators, such as mean weight loss (MWL) (kilogram), mean absolute weight (MAW) (kilogram), excess weight loss (%EWL), success rate (defined as the percentage of patients achieving a %EWL≥50%), mean absolute BMI (MAB) (kilogram per square metre) and mean BMI loss (or change) (kilogram per square metre).
- Co-morbidity indicators such as, respectively:

T2DM control (fasting glucose level <100 mg/dl, random glucose level <200 mg/dl, glycated haemoglobin <6%, achievement of treatment interruption); T2DM improvement (no insulin necessary or decreased drug dosage of diabetes medications) [14, 15]

Dyslipidaemia control (total cholesterol <200 mg/dl, LDL-cholesterol <100, 130 and 160 mg/dl with respectively existing coronary artery disease, two or more risk factors and fewer than two risk factors for coronary artery disease, HDL-cholesterol <35 mg/dl, fasting triglycerides <20 mg/dl, achievement of treatment interruption); dyslipidaemia improvement (lipid profile normalized by medication) [15]

HTN control (systolic and/or diastolic blood pressure <140 and 90 mmHg, respectively, with diet or diuretic medications only); HTN improvement (blood pressure normalized by medication) [15]

 Nutritional status and/or deficiencies, assessed by repeated blood level measurement of nutrients such as Haemoglobin; albumin; vitamins A, B₁, B₆, B₁₂ and D; folates; electrolytes (iron, calcium, magnesium, zinc)

Search Strategy

Firstly, we searched the following electronic databases: MEDLINE (1966 onwards), EMBASE (1980 onwards) and The Cochrane Central Register of Controlled Trials (Clinical Trials; CENTRAL). The search terms used for MEDLINE were the following¹: 1 morbid obesity.mp. OR Obesity, Morbid/ OR Obesity/ OR (superobese or super-

¹ "/" defining MeSH term and "mp." defining a random keyword term

obese or super obese or superobesity or super-obesity or super obesity).mp. 2 Gastric Bypass/ OR anastomosis, roux-en-y/ OR gastroenterostomy/ 3 long limb.mp. OR short limb.mp. OR limb length.mp OR (limb lengthening or limb extending).mp OR distal.mp. Then, we combined these terms in a query formulated as "1 AND 2 AND 3".

We also used additional resources to identify further relevant trials: the manually scanned reference lists of all papers retrieved from electronic search; the hand-search of journals with specialized interest in the concerned subject such as *Obesity* (2000 onwards), *International Journal of Obesity* (1997 onwards), *Obesity Surgery* (1991 onwards), *Surgery for Obesity and Related Diseases* (2005 onwards) and *Obesity Research & Clinical Practice* (2007 onwards). Finally, we attempted to find relevant studies not yet/or not published through the web site www.clinicaltrial.gov and the grey literature.

Results

Search

The electronic search yielded a result of 172 articles (125 in MEDLINE, 47 in EMBASE, CENTRAL providing only articles already retrieved from the two former sources). Hand scanning the reference lists of the relevant articles,

Fig. 1 Flow chart of the inclusion/exclusion process

searching articles in specialized journals and the grey literature provided one potentially includable article. After careful reading of the titles and abstracts, we decided to exclude 155 articles, based on either retrieving the same paper from several sources or irrelevant subject. Out of the 18 remaining articles, 9 were excluded: 7 for inappropriate design (retrospective case series) [16–22], 1 was a narrative review [23] and 1 used a fixed Roux-limb length, evaluating common limb length as the primary exposure variable [24]. Details of the inclusion/exclusion process can be found in Fig. 1.

Characteristics of Studies

Nine articles met the inclusion criteria [25–33]. Out of these, five were RCTs [25, 27, 29, 30, 33] and four were prospective cohort studies [26, 28, 31, 32]. See ESM Table A1 for details of the included studies. After thorough reading of the papers, it appeared that two studies [26, 28] had overlapping author lists and had been conducted in the same medical centre. We contacted the author, who confirmed that the study populations of the two papers were derived from the same cohort. Therefore, we further excluded one article [26]. We had the same impression regarding two other RCTs [27, 29]. Again, we contacted the author, who excluded overlapping of the two study populations; thus, we kept both papers.



In addition to our critical appraisal, the quality of the studies was graded according to the five-point Jadad score [34] (see Table 2).

Six studies were performed in the USA [25, 27–31], one in Brazil [33] and one in Switzerland [32]. Publication dates ranged from 1992 [25] to 2008 [28, 31, 33].

Number of Patients

Overall, these 8 studies comprised a total of 699 patients (391 in RCTs).

No study reported having conducted an a priori power analysis. The study by Inabnet [30] was the only one stating the a priori sample size goal (n=100), although it failed to provide the rationale of it.

Patients

Four studies mentioned adhering to NIH Consensus Development Conference Panel on gastrointestinal surgery for severe obesity [27, 29, 31, 33]. Three studies included only super obese patients [25, 28, 33]. One study focused on patients with BMI<50 [30]. Otherwise, both morbid and super obese patients were eligible. Demographic characteristics are presented in the ESM Table A1. Only the study by Ciovica showed some uneven distribution of baseline characteristics among intervention arms [28]. Muller compared two subsequent groups of patients treated differently and randomly matched each of the two groups for sex, age and baseline BMI. Paired analysis was conducted, comparing patients drawn from each of the two groups [32].

Data of all the included studies were prospectively collected.

Surgical Procedures

The operative protocols were thoroughly described in all the included studies. With regard to the Roux-limb lengths, there was clinical heterogeneity (or variability) in intervention design: Brolin compared limbs of 75 to 150 cm. Choban and Flancbaum stratified patients according to their initial BMI, obtaining four groups: among patients with BMI<50, they compared lengths of 75 to 150 cm, and among those with BMI>50, they compared 150 to 250 cm [27, 29]. Two studies tailored limbs of either 100 or 150 cm [28, 30]. Pinheiro allocated patients to Roux-limb length of either 150 or 250 cm [33]. Muller opted for an original design, comparing a proximal gastric bypass procedure with a distal one [32]. In the former procedure, a Roux-limb of 150 cm was created, whereas in the latter the distance from the Roux-en-Y anastomosis to the ileocaecal valve (the common limb) was fixed at 100-150 cm. Lee evaluated the relationship between weight loss and varying Roux-limb lengths in a continuum: for patients with BMIs \leq 40, Roux-limb were 100 cm; for every unit of BMI over 40, the surgeon added 5 cm extra limb length. For example, a patient with BMI of 42 was given a Roux-limb length of 110 cm. The maximum length was limited to 150 cm [31].

The technique used for limb length measurement was described in five papers. Three used a pre-cut measurement tape [27, 30, 31], one measured 10 cm steps using a marked laparoscopic forceps with the bowel held taut but not stretched [32] and one reported only measuring the distance between gastrojejunostomy and jejunojuejunostomy hold-ing the bowel on a stretch, omitting to describe the measurement scale [25].

Outcomes and Effect of Intervention

It is worthwhile to notice that some authors chose to report results at specific time points and not regularly throughout follow-up; for instance, Inabnet [30] and Ciovica [28] provided MWL at 12 months post-surgery only. On the other hand, Muller [32] reported results of a 4-year follow-up analysis. See Table 1 for outcome reporting.

Weight Loss Profile

MWL and MAB were reported in (or could be deduced from the results of) four [25, 27, 29, 30] and six studies [25, 27, 28, 30–32], respectively. The five RCTs and the study by Ciovica [28] described EWL%. Success rate was discussed by Brolin (at 24 months only) and Choban [25, 27].

In his 1992 landmark paper, Brolin compared short (Roux-limb 75 cm, biliopancreatic limb 15 cm) vs. long limbs (Roux-limb 150 cm, biliopancreatic limb 30 cm) in 45 super obese patients [25]. The MWL was greater among the long limb group throughout the whole follow-up, with a statistically significant difference observed at 24 and 36 months. MAB followed the same trend, with statistical significance at 24 months only.

After stratified randomization, Choban showed that success rate was significantly higher at 18 months in super obese patients that had been allocated to the long limb group [27]. This association was not observed among morbidly obese patients. All the other assessed outcomes failed to show statistical significance.

Flancbaum performed an RCT assessing weight loss profile in four groups of patients [29], using the same stratified randomization scheme as Choban [27]. Flancbaum did not detect any statistical evidence for difference in MWL or EWL% at 12-months of follow-up in either morbidly obese or super obese patients [29].

The study by Inabnet assessed the effect of Roux-limb length in 48 patients with a BMI \leq 50 kg/m². The Roux-limb was either 100 or 150 cm. This study failed to show

| Table 1 Ou | tcomes invo | estigated in | the | included | studies |
|------------|-------------|--------------|-----|----------|---------|
|------------|-------------|--------------|-----|----------|---------|

| Study design | | Outcomes | | | | | | | | |
|------------------------|-----------------------------|------------------------------------|--------------------------------|---|---|---------------------------------|---------------------|--|--|--|
| | | Postoperative weight loss | | | | | | Surgical | T2DM- | |
| | | Mean absolute weight (kg) | Mean weight loss (kg) | Mean absolute BMI (kg/m ²) | Mean BMI change (kg/m ²) | Excess weight loss (%) | Success rate (%) | complications/ mortality/ nutritional complications | dyslipidaemia/ hypertension/sleep apnea/GERD | |
| Brolin 1992 [25] | RCT | _ | + | + | + | + | + | +/+/+ | +/+/+/- | |
| Flancbaum 1998 [29] | RCT | - | + | - | _ | + | - | _/_/+ | _/_/_/_ | |
| Choban 2002 [27] | RCT | - | + | — | + | + | + | +/+/+ | _/_/_/_ | |
| Inabnet 2005 [30] | RCT | + | - | + | — | + | - | +/+/+ | _/_/_/_ | |
| Lee 2006 [31] | Prospective cohort study | _ | + | — | + | _ | _ | _/_/+ | _/_/_/_ | |
| Pinheiro 2008 [33] | RCT | - | - | — | - | + | - | _/+/+ | +/+/+/+ | |
| Ciovica 2008 [28] | Prospective cohort study | - | + | + | + | + | — | _/_/_ | _/_/_/_ | |
| Muller 2008 [32] | Prospective cohort study | _ | _ | + | + | _ | _ | +/+/ | +/+/-/- | |

"+" means that the item was reported in—or imputable from—the study under consideration; "-" means that the item was not reported in—or imputable from—the study under consideration

evidence to support the intervention in a non-super obese population; in fact, there was a non-statistically significant difference in MAW, EWL% and MAB between short and long limb groups, respectively, at 3, 6, 12 and 24 months [30].

Pinheiro did not find any significant difference in EWL % between the two study groups [33].

Ciovica provided the reader with several positive results supporting the intervention in a super obese population. The following indicators were improved at 12 months postsurgery in the intervention group [28]:

- MWL (55.3 (95% CI 52.2–58.5) vs. 68.5 (61.3–73.9)) (p<0.01)
- MAB in kg/m² (40 (95% CI 39–41) vs. 36 (34–38)) (p<0.01)
- Mean BMI change in kg/m² (21 (95% CI 20–22) vs. 25 (23–27)) (p=0.03)
- EWL% (53% (95% CI 50–56) vs. 64% (58–69)) (p=0.02)

Muller observed a BMI decrease from 45.9 to 31.7 kg/m^2 in the proximal group and from 45.8 to 33.1 kg/m^2 in the distal group. This represents a 3% difference in percentage BMI between the two groups. These results did not reach statistical significance [32].

Finally, Lee demonstrated that there was a linear relationship between Roux-limb length and both MWL and mean BMI change (p=0.0025 and 0.0011, respectively) [31]. These regression models show relatively flat slopes (0.075 and 0.19), meaning that each additional centimetre in Roux-limb length would lead to a slight increase in either BMI change or absolute weight loss.

Co-morbidities

Improvement of co-morbidities was investigated in the studies by Pinheiro, Brolin and Muller [25, 32, 33]. T2DM improvement or control, improvement in lipid disorders and HTN were assessed in the three papers. As opposed to that, SAS and GERD were variably taken into account. Pinheiro showed that during the first 12 weeks following intervention, T2DM control was achieved in 93% vs. 58% of patients allocated to long and short limb, respectively (p <0.05). Dyslipidaemia was improved in 70% of patients within the long limb group, whereas only 57% of the short limb group showed improvement (p < 0.05). There was no statistical evidence for improvement in HTN. Both groups were declared to be cured of GERD symptoms and SAS [33]. Brolin provided details of the incidence of pre- and postoperative obesity co-morbidities, but the study was underpowered to detect any statistically significant difference among intervention groups [25]. Muller showed that T2DM, dyslipidaemia and HTN were reduced in all intervention groups, although no statistical significance for the difference between groups was found [32].

Nutritional Outcomes

Six studies took nutritional outcomes into account [25, 27, 29–31, 33]. Inabnet obtained the results of 56% and 52% patients in the short and long limb groups, respectively, and there were no formal comparative results reported in the manuscript or tables [30]. Flancbaum found no association

between Roux-limb length and measured resting energy expenditure [29].

No study found significant difference regarding nutritional outcomes between groups. See ESM Table A1.

Risk of Bias in the Included Studies

Of the five RCTs, none reported either the method used for generation of allocation sequence or whether the actual allocation sequences were concealed from study practitioners. No RCT declared to have analysed the data according to the intention-to-treat principle.

The study by Inabnet was the only one to report blinding of the surgical team, operating room staff, ancillary staff, consultants and patients to group allocation [30].

Discussion

Out of eight studies, four provided some evidence supporting the construction of a long Roux-limb at improving postoperative weight loss profile. The results of these studies suggest that the benefit is strictly restricted to super obese patients. These results are consistent with several retrospective analyses that were not included in this paper [19–21]. The apparent lack of efficiency of constructing a long Roux-limb in the morbidly non-super obese patients could be interpreted as either a lack of statistical power (or type II error) of the individual studies or as bias introduced by some unexplored variables. For example, intestinal adaptation, a pattern of morphostructural and functional changes compensating for the loss of digestive and absorptive capacity after small bowel resection and malabsorptive surgery [35, 36], might have shifted the results toward the null hypothesis, limiting the impact of a long gastrointestinal bypass and acting as a negative confounder.

Because a mixture of study designs (RCTs and cohort studies), extra care would have been necessary if a meta-

| | fable | 2 | Methodology | of | the | included | studies |
|--|-------|---|-------------|----|-----|----------|---------|
|--|-------|---|-------------|----|-----|----------|---------|

analysis had been carried out. Furthermore, the eight included articles showed clinical heterogeneity, limiting the relevance of performing a meta-analysis. Heterogeneity was found in three main aspects. First, definition of "short" and "long" limb varied, as did the techniques used to measure limb length. Accordingly, some studies considered a given Roux-limb length as a short one, and others as a long one [25, 33], potentially introducing misclassification. Secondly, different kinds of patients were included, some studies focusing on particular sub-populations such as super obese patients [25, 28, 33] or diabetic [33], and others allowing for more permissive inclusion criteria [27, 29, 31, 32]. Thirdly, follow-up duration and time points chosen for hypothesis testing were varied. Besides Brolin's, Pinheiro's and Muller's studies [25, 32, 33], there was limited followup and short follow-up durations might not be adequate for studies dealing with weight loss profile after RYGBP. There are two main reasons for this: first, it is likely that a substantial proportion of the weight loss occurring after RYGBP-especially during the first postoperative year-is actually attributable to the restrictive part of the procedure, in other words, the tailoring of a small gastric pouch [31, 37, 38]. Secondly, gastric bypass and more generally bariatric surgery procedures are not punctual interventions that resolve a specific pathological condition; they are interventions that must be put into the context of a more holistic approach, including medical, surgical and behavioural aspects. Therefore, short follow-up studies might draw insufficient conclusions, considering the realistic and complex conditions entailed in long-term management of severe obesity. Although not formally included in this review, the retrospective analysis of Christou and colleagues skilfully addressed time-to-intervention issues by providing data of more than 10 years of follow-up [39]. Patients in this series were either treated with a long (100 cm) or a short (40 cm) Roux-limb. There was evidence supporting that after a nadir occurring at 2.2 postoperative years on average, MAB starts to rise again.

| | Study design | Adequate allocation sequence | Allocation concealment | Blinding | Jadad score | |
|---------------------|--------------------------|------------------------------|------------------------|----------------|----------------|--|
| Brolin 1992 [25] | RCT | ? | No | No | 2 | |
| Flancbaum 1998 [29] | RCT | ? | No | No | 1 | |
| Choban 2002 [27] | RCT | ? | No | No | 1 | |
| Inabnet 2005 [30] | RCT | ? | No | Yes | 3 | |
| Lee 2006 [31] | Prospective cohort study | Not applicable | Not applicable | Not applicable | Not applicable | |
| Pinheiro 2008 [33] | RCT | ? | No | No | 1 | |
| Ciovica 2008 [28] | Prospective cohort study | Not applicable | Not applicable | Not applicable | Not applicable | |
| Muller 2008 [32] | Prospective cohort study | Not applicable | Not applicable | Not applicable | Not applicable | |

Super obese patients lost weight significantly more quickly and subsequently gained weight more quickly as well. Overall, Christou and colleagues found no evidence suggesting that a long Roux-limb provided more satisfying results than a short one.

Finally, other methodological weaknesses such as lack of allocation sequence description and concealment status among RCTs undermined the overall validity of the results reported (see Table 2).

Conclusions

This review revealed that the body of literature comparing long to short Roux-limb in RYGBP was poor in quantity and of questionable quality, owing to a lack of rigour in reporting important methodological components. The large clinical variability in both intervention design and outcome reporting epitomized the weak consensus among bariatric surgery centres. The heterogeneity in results was notable and is, in our opinion, attributable to both systematic (bias) and random errors.

The results collected here suggest that the construction of a long Roux-limb might be efficacious at improving postoperative weight loss in super obese (BMI>50 kg/m²) patients only. Moreover, it does not seem that an increased limb length jeopardizes the vitamin and mineral absorption more than a standard RYGBP.

Finally, this paper is an opportunity for us to call surgeons with research interest for an improvement in the rigour of their trial design, in order to gain in validity and interpretability. Such an effort should particularly make the results of surgical trials more amenable to meta-analyses, which, thanks to their increased statistical power, guide clinical practice more than any other research design.

Conflict of Interest We declare we have no conflict of interest.

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