Bariatric surgery

An updated systematic review and meta-analysis, 2003-2012

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[Intervention Protocol]

Bariatric surgery: an updated systematic review and meta-analysis, 2003-2012

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To examine the effectiveness and risks of bariatric surgery using up-to-date, comprehensive data and appropriate meta-analytic techniques.

BACKGROUND

This protocol is written following the Guidelines for Preparation of Review Protocols.[1] The protocol will be posted for five months and in this time we will actively seek open feedback and criticism of the methods to be employed. All feedback will be logged and publicly posted (unless privacy is requested), and responded to. In the light of feedback, the protocol may be amended upon agreement of all review authors. Any amendments to the protocol will be detailed in full along with the reasons. Feedback can be submitted by email to the corresponding author.

Description of Bariatric Surgery

As the prevalence of obesity increases globally,[2] the demand for bariatric surgery has risen dramatically in recent years. The total number of operations performed in the United States and Canada reached 220,000 in 2008 to 2009.[3,4] Bariatric surgery includes a variety of procedures, e.g., Roux-en-Y gastric bypass, biliopancreatic diversion with duodenal switch (BPD-DS), adjustable gastric banding, vertical banded gastroplasty, sleeve gastrectomy. Some procedures are restrictive; some are malabsoptive; and others have both a restrictive and malabsorptive component.

Why it is important to do this review

While clinical trial data for specific surgical procedures does exist, general questions regarding the effectiveness of bariatric surgery as an obesity treatment, as well as which type of bariatric surgery is the most advantageous for patients, remain unanswered. Previous reviews, e.g., Buchwald et al.[5] and Maggard et al.,[6] provided comprehensive analyses, but included data from clinical trials and studies published before 2003. A recent systematic review and meta-analysis conducted by Padwal and colleagues[7] focused only on randomized 66 controlled trials (RCTs). Their data included recently published trials, but did not exclude early publications. Due to advances in the technology of bariatric surgery and the increased knowledge and experience of surgeons, information provided in previous reviews is outdated. Therefore, it is necessary to reassess surgical treatments using more up-to-date data.

OBJECTIVES

To quantify the risks and benefits of various bariatric surgery procedures focusing on adult patients, specifically reporting the risks (defined as peri- and post-operative mortality, complications, and reoperations) and the effectiveness (defined as weight loss and remission of obesity-related diseases).

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs) and observational studies (OBSs) reporting bariatric surgical procedure performed and at least one outcome of interest resulting from that surgery will be included in this review.

Types of participants

Adult patients aged >18 years who underwent bariatric surgery or non-surgical intervention in the controlled arm will be included.

Types of Bariatric Surgery

Types of Bariatric Surgery will be grouped into five categories: (i) gastric bypass (GB), which will include laparoscopic Roux-en-Y Gastric Bypass (LRYGB), open RYGB, LRYGB with presurgery weight loss, laparoscopic biliopancreatic diversion with duodenal switch (LBD-DS), and biliopancreatic diversion with RYGB (BPD-RYGB); (ii) adjustable gastric banding (AGB), which will include laparoscopic gastric banding (LAGB)—Lapband, and LAGB—Swedish; (iii) vertical banded gastroplasty (VBG), (iv) sleeve gastrectomy (SG), which will include laparoscopic sleeve gastrectomy (SG); (v) nonsurgical interventions (Control).

Types of outcome measures

Types of outcome measures:

1. mortality (peri- and post-operative)
2. surgical complication rate
3. reoperation rate
4. obesity-attributable comorbidity remission rates

Operative mortality will be defined in terms of deaths occurring within 30 days of the surgery and deaths occurring after 30 days of the surgery. Unclear timing of death will be treated as if deaths were observed at the latest follow-up time.
Surgical complications included in the study will comprise all adverse events associated with Bariatric surgery reported in the articles included, such as bleeding, stomal stenosis, leak, vomiting, reflux, gastrointestinal symptoms, and nutritional and electrolyte abnormalities. Reoperations will include subsequent bariatric surgeries done after the initial surgical procedure, on a given patient. Remission of comorbidities will be defined as the report that a comorbid condition, associated with obesity, was either resolved or improved after surgery.

Search methods for identification of studies

Electronic Searches

A search strategy will be created by an MLIS qualified librarian. Comprehensive searches of the literature will be performed on MEDLINE, EMBASE, SCOPUS, COCHRANE, and CLINICALTRIALS.GOV. The timeframe used will be January 1st, 2003 to March 31st, 2012. Searches will be performed using the Firefox browser, and results will be imported to EndNote X5. Search terms are detailed in the Appendix.

Data collection and analysis

Selection of Studies

After an initial search, article abstracts will be reviewed and screened for the following exclusion criteria: publication of abstracts only, case reports, letters, comments, reviews, or meta-analyses; animal studies; languages other than English; duplicate studies; no surgical intervention; lack of outcomes of interest (weight change, surgical mortality and complications, and disease impacts); and not population of interest (adults aged>18 years). After removing excluded abstracts, full articles will be obtained and studies will be screened again more thoroughly using the same exclusion criteria. Three reviewers will independently review the studies, abstract data, and resolve disagreements by consensus.

Data extraction and management

An extraction form will be created in Excel and tested for consistency across reviewers. Studies will be included in data extraction if they report surgical procedure performed and at least one outcome of interest resulting from that surgery. If more than one procedure was performed in the study, data will be presented separately by surgical procedure. Study characteristics including study design, country of origin, publication year, follow-up length, and surgical procedures performed will be extracted. Initial study population size and sample size at all data collection points will be recorded. Characteristics of the starting study sample, such as age, race, sex, and weight information will be collected when available. Pre- and post-surgery data regarding comorbid conditions, body composition, and any other pertinent category will be extracted. The target obesity-related comorbidities will include type-2 diabetes mellitus, cardiovascular disease, hypertension, dyslipidemia, and sleep apnea. Conversion of units to maintain consistent data will be performed when necessary. Extracted studies will include RCTs and OBSs. Three reviewers will independently review the studies, abstract data, and resolve disagreements by consensus. Qualitative characteristics will be generated from the studies.

Assessment of study quality in included studies

All studies will be evaluated for quality using a six-category scoring system (range 0-6).[8] The categories will be (1) clear definition of surgeries; (2) clear time points given for outcomes; (3) adjustment for potential confounders in analysis (for OBSs only) and adequate randomization (for RCTs only); (4) defined a priori sample size calculations; (5) loss to follow up less than 20%; (6) reports of funding sources/conflicts of interest.[29,34-37] For categories 1-4, studies will receive a score of 1 if the study fulfills the criteria, and 0 otherwise. For categories 5 and 6, studies could receive a score of 0, 0.5, or 1. For category 5, a score of 0 will indicate that no information regarding loss to follow up was given, a score of 0.5 indicating that loss to follow up information was given, but loss to follow up was >20%, and a score of 1 indicating that loss to follow up was <20%. For category 6, a score of 0 will indicate that the article gave no information regarding funding sources or conflicts of interest, a score of 0.5 will indicate that the article was funded by surgical-related industry, and a score of 1 will indicate that funding and conflicts of interest were declared, and there was no link to industry. A higher score will indicate a higher quality study. Categories 3-6 will assess the risk of study bias

Measures of outcomes of operative mortality, complication rate, and obesity-related diseases improvement

For operative mortality, we will run separate analyses on studies which identified the deaths occurring within 30 days of the surgery and studies which identified the deaths occurring after 30 days of the surgery. Unclear timing of death will be treated as if deaths were observed at the latest time of follow-up. Deaths of unspecified causes were not excluded in any mortality analyses. Surgical complications will include all adverse events associated with surgery reported in the studies, such as bleeding, stomal stenosis, leak, vomiting, reflux, gastrointestinal symptoms, and nutritional and electrolyte abnormalities. Only overall complication rate will be collected and analyzed because specific surgical complications were variably reported and difficult to catalog.[5] Data on reoperation incidences will be separately collected and analyzed. Percentage of remission of comorbidities is defined as the proportion of the surgery patients who reported the target comorbid condition being either resolved or improved after surgery.

Measures of weight loss outcomes

All yearly post-surgery weight outcomes will be compared to the pre-surgery weight outcomes. Using the Frequentist approach, FE and RE models will be constructed. We will report post-surgery ΔBMI and %EWL for both study designs. A meta-regression of ΔBMI will be conducted to account for patient characteristics (e.g., pre-surgery BMI, gender composition, and age), study design and quality, surgical procedure, and geographic location. A preliminary meta-regression will be conducted, using overall quality scores to determine if analyses of ΔBMI should be limited to studies with higher scores. Next, a main meta-regression analysis will be conducted, using scores for each quality category. A mixed treatment comparison (MTC) with repeated measurement meta-analysis[9] will be conducted, using a Bayesian approach, targeting all RCTs from which we extracted data. This analysis will utilize the information on repeated measurements of ΔBMI at different study time points in the trials and compare and contrast the findings in Padwal et al.[7] Four MTC models will be considered. We will estimate post-surgery ΔBMI compared to the reference (relative surgery effect) in these models, taking advantage of

the direct and indirect comparisons within study arms of RCTs. The first two models will assume the following: Model 1 will assume that the mean post-surgery ΔBMI for the first arm was estimated independently for each time point of each study, but the relative surgery effects will be assumed to be constant over time, and Model 2 will assume the effects of surgical procedures in the same category to be similar.

Assessment of risk of bias in included studies

Categories 3-6 will assess the risk of study bias.

Unit of analysis issues

To maintain consistent data, unit conversions will be performed when necessary.

Dealing with missing data

We will impute the missing values by conducting a separate meta-analysis to estimate the distribution of standard deviations and then using the estimated distribution to predict the missing values. When a statistical test was conducted in the original study to compare the pre- and post- surgery BMI, we will compute standard deviation from the reported 95% confidence intervals or exact p-values.

Assessment of heterogeneity

The I^2 index will be computed to quantify the degree of study heterogeneity.[45,46] We will present the estimation results and I^2 index, measuring the percentage of variation, across studies, that is due to heterogeneity rather than random chance.

Assessment of reporting biases

Publication bias will be evaluated using funnel plots and Egger's test.[47,48] Publication bias will be evaluated for yearly BMI change outcomes of all surgical procedures for which at least two study arms were included.

Data synthesis

After data extraction is complete, amount and types of data extracted will be reviewed and specific outcomes that are able to be meta-analyzed will be chosen. The Frequentist approach will be used to perform FE and RE meta-analyses using STATA (SE/11.2, Stata Corp, College Station, TX). Bayesian RE meta-analysis will be conducted by R (2.14.0, R Development Core Team, Vienna, Austria) and JAGS, "runjags" package (0.9.9-2). Bhaumik estimates and the numerical solutions of the standard errors will be obtained using MATLAB (7.11, R2012a, MathWorks Inc, Natick, MA). MTC meta-analyses will be conducted using WinBUGS 1.4.3 (The BUGS Project, Cambridge, UK). We will report the means for RE, the relative surgery effect for MTC, and the estimates for meta-regression for weight outcomes. For the remaining outcomes, we will report the means for Bayesian RE models. 95%

confidence/credible intervals (CIs) associated with the Frequentist/Bayesian estimates will be reported in brackets.
Mortality, complication, and comorbidity remission rates were estimated by Bayesian random-effects meta-analysis method[10,11] to avoid statistical problems caused by zero or rare events in each study.[12-14] In addition, simple averaging method proposed by Bhaumik et al.[14] was conducted as an alternative to the Bayesian RE meta-analysis. Both methods are detailed in the Appendix (Section 2).

Subgroup analysis and investigation of heterogeneity

If there is sufficient data, statistical heterogeneity will be explored using subgroup analyses. Subgroups will be divided by surgical procedures, outcomes of interest, time points, or study designs.

PLANS FOR UPDATING THE REVIEW

Once the review is completed, Chang S-H will be responsible for updating the review. Updates will be performed annually when necessary.

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STATEMENTS CONCERNING CONFLICT OF INTEREST

None.

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