

SUPPLEMENTARY FILE

Effectiveness of Bariatric Surgery on Acquired Hypothalamic Obesity: A Systematic Review and Meta-Analysis

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Table S1. Search strategy.

Table S2. Reasons of Exclusion

Table S3. Summary of the qualitative assessment according to Newcastle-Ottawa Scale

Table S4. Evidence profile assessment according to GRADE framework

Table S5. Summary of matching strategies.

Table S1. Search strategy.

Pubmed

("Craniopharyngioma"[Mesh] OR craniopharyngioma[tiab] OR "Brain Tumors"[Mesh] OR brain neoplasm*[tiab] OR "Hypothalamic Diseases"[Mesh] OR hypothalamus disease*[tiab] OR hypothalamic dysfunction[tiab])

AND

("Obesity, Morbid"[Mesh] OR "Obesity"[Mesh] OR morbid obesity[tiab] OR severe obesity[tiab] OR hypothalamic obesity[tiab] OR obesity[tiab])

AND

("Bariatric Surgery"[Mesh] OR bariatric surg*[tiab] OR bariatric operat*[tiab] OR "Gastric Bypass"[Mesh] OR gastric bypass*[tiab] OR gastroileal bypass*[tiab] OR gastrojejunostom*[tiab] OR gastropplast*[tiab] OR jejunoileal bypass*[tiab] OR ileojejunal bypass*[tiab] OR intestinal bypass*[tiab] OR biliopancreatic bypass*[tiab] OR biliopancreatic diversion*[tiab] OR duodenal switch*[tiab] OR pancreatobiliary bypass*[tiab] OR gastric banding*[tiab] OR stomach banding*[tiab] OR laparoscopic adjustable silicone banding*[tiab] OR bariatric operat*[tiab] OR bariatric procedure*[tiab] OR obesity surg*[tiab] OR obesity operat*[tiab] OR sleeve gastrectom*[tiab] OR gastric sleeve*[tiab] OR metabolic surg*[tiab] OR stomach surg*[tiab] OR weight loss operat*[tiab] OR weight loss surg*[tiab] OR weight reduction operat*[tiab] OR weight reduction surg*[tiab])

AND

("Weight Loss"[Mesh] OR weight low*[tiab] OR weight reduction*[tiab] OR weight loss[tiab] OR losing weight[tiab])

NOT

("Review" [Publication Type] OR "Systematic Review" [Publication Type] OR "Meta-Analysis" [Publication Type] OR "Editorial" [Publication Type] OR "Case Reports" [Publication Type] OR "Comment" [Publication Type])

AND

("Randomized Controlled Trial" [Publication Type] OR "Matched-Pair Analysis"[Mesh] OR "Case-Control Studies"[Mesh] OR "Propensity Score"[Mesh] OR "Cohort Studies"[Mesh] OR randomi*[tiab] OR randomly[tiab] OR trial[ti] OR cohort[tiab] OR Propensity Score*[tiab] OR MatchedPair*[tiab] OR matched-pair*[tiab] OR paired comparison*[tiab] OR case-control[tiab] OR retrospective*[tiab] OR prospective*[tiab] OR longitudinal*[tiab] OR observational*[tiab] OR follow-up[tiab])

Embase

('craniopharyngioma'/exp OR 'pituitary tumor'/exp OR (craniopharyngiom* OR 'pituitary adenoma' OR 'pituitary tumor*' OR 'brain tumor*'):ab,ti,kw)

AND

('hypothalamic obesity'/exp OR 'hypothalamus dysfunction obesity'/exp OR (hypothalam* AND (obesity OR 'weight gain' OR 'body mass index increase' OR BMI)):ab,ti,kw)

AND

('bariatric surgery'/exp OR 'gastric bypass surgery'/exp OR 'gastrojejunostomy'/exp OR 'stomach surgery'/exp OR 'collis gastroplasty'/exp OR 'vertical banded gastroplasty'/exp OR 'intestine bypass'/exp OR 'gastric sleeve'/exp OR 'endoscopic sleeve gastroplasty'/exp OR 'one-anastomosis gastric bypass'/exp OR ('bariatric surg*' OR 'bariatric operat*' OR 'gastric bypass*' OR 'gastroileal bypass*' OR gastrojejunostom* OR gastroplast* OR 'jejunoileal bypass*' OR 'ileojejunal bypass*' OR 'intestinal bypass*' OR 'biliopancreatic bypass*' OR 'biliopancreatic diversion*' OR 'duodenal switch*' OR 'pancreatobiliary bypass*' OR 'gastric banding*' OR 'stomach banding*' OR 'laparoscopic adjustable silicone banding*' OR 'bariatric operat*' OR 'bariatric procedure*' OR 'obesity surg*' OR 'obesity operat*' OR 'sleeve gastrectom*' OR 'gastric sleeve*' OR 'metabolic surg*' OR 'stomach surg*' OR 'weight loss operat*' OR 'weight loss surg*' OR 'weight reduction operat*' OR 'weight reduction surg*'):ab,ti,kw)

AND

('weight loss'/exp OR 'body weight change'/exp OR ('weight reduction*' OR 'weight loss*' OR 'losing weight*' OR 'body weight change*' OR 'body weight decrease*' OR 'body mass index change*' OR BMI):ab,ti,kw)

AND

('clinical trial'/exp OR 'cohort study'/exp OR 'case-control study'/exp OR 'observational study'/exp OR (trial OR cohort OR 'case control' OR observational OR prospective* OR retrospective* OR 'follow-up' OR study OR studies):ab,ti,kw)

NOT

('review'/exp OR 'meta-analysis'/exp OR 'editorial'/exp OR 'case report'/exp OR 'animal study'/exp OR 'comment'/exp OR 'letter'/exp OR 'note'/exp)

Table S2. Reasons of Exclusion

Article	Reason of exclusion
Duodenal-jejunal bypass normalizes pancreatic islet proliferation rate and function but not hepatic steatosis in hypothalamic obese rats ¹	Non-human subject.
Hormone substitution after gastric bypass surgery in patients with hypopituitarism secondary to craniopharyngioma ²	Intervention does not include bariatric surgery.
Bariatric surgery in the elderly: Results of a mean follow-up of five years ³	Not hypothalamus obesity
The swedish adjustable gastric banding (SAGB) for morbid obesity: 9 year experience and a 4-year follow-up of patients operated with a new adjustable band ⁴	Not hypothalamus obesity
Hypothalamic Obesity: 4 Years of the International Registry of Hypothalamic Obesity Disorders ⁵	No control group
Sleeve gastrectomy leads to easy management of hormone replacement therapy and good weight loss in patients treated for craniopharyngioma ⁶	No control group
Long-term follow-up of morbidly obese patients with childhood craniopharyngioma after laparoscopic adjustable gastric banding (LAGB) ⁷	No control group
First experiences with laparoscopic adjustable gastric banding (LAGB) in the treatment of patients with childhood craniopharyngioma and morbid obesity ⁸	No control group
Hypothalamic integrity is necessary for sustained weight loss after bariatric surgery: A prospective, cross-sectional study ⁹	Lack of follow-up data at 12 months or 24 months
Bariatric surgery for morbid obesity in craniopharyngioma ¹⁰	Control group not matched on pre-operative BMI
Hypothalamic obesity in children ¹¹	Review
Childhood craniopharyngioma ¹²	Review
Hypothalamic obesity: Causes, consequences, treatment ¹³	Review
Management of hypothalamic obesity during transition from childhood to adulthood ¹⁴	Review

Table S3: Summary of the qualitative assessment according to the Newcastle-Ottawa Scale for Case Control Studies

Studies Author/pub year	Selection				Comparability		Exposure			Conclusion
	1	2	3	4	1	2	1	2	3	
Faucher 2022	1	1	0	1	1	1	1	1	0	Good
Garrez 2020	1	1	0	1	1	1	1	1	0	Good
Van Santen 2021	1	0	0	0	1	1	1	1	0	Poor
Wijnen 2017	1	1	0	1	1	1	1	1	0	Good

The Newcastle-Ottawa scale accredits a 1 (=yes, when adequate quality was assessed) or 0 (=no) for specific point in three subcategories.

Selection

- 1- Is the case definition adequate?
- 2- Representativeness of the cases
- 3- Selection of Controls
- 4- Definition of Controls Comparability of cases and controls on the basis of the design or analysis
 - 1- The study controls for pre-operative BMI (the most important factor)
 - 2- Study controls for other factors

Exposure

- 1- Ascertainment of exposure
- 2- Same method of ascertainment for cases and controls
- 3- Non-Response rate

The Newcastle-Ottawa scales was than converted to good, fair, and poor quality study based on combining scores from these subcategories:

- Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
- Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
- Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

Table S4. Evidence profile assessment according to GRADE framework¹

Outcome	No. of studies (design)	Quality assessment					Summary of findings*			Quality
		Limitations	Inconsistency	Indirectness	Imprecision	Publications bias	Mean Difference (95% CI)	p-value	Plausible confounding	
TWL% at 12 months after operation	4 (observational studies)	No serious limitations	No serious inconsistency: I ² =0%, p=0.55	No serious indirectness	Very Serious imprecision: wide confidence intervals	No serious publication bias	-6.17 [-8.74, -3.60]	<0.001	No plausible confounding	Very low
TWL% at 24 months after operation	3 (observational studies)	No serious limitations	No serious inconsistency: I ² =0%, P=0.43	No serious indirectness	Very Serious imprecision: wide confidence intervals	No serious publication bias	-7.65 [-10.79% - -4.52%]	0.43	No plausible confounding	Very low

*Assessment of dose-response was not applicable in this systematic review and meta-analysis and was thus left out of the GRADE assessment

¹Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008 Apr 26;336(7650):924-6. doi: 10.1136/bmj.39489.470347.AD. PMID: 18436948; PMCID: PMC2335261.

Table S5. Summary of matching strategies.

1. Faucher et al. 2022

Matching standard: Subjects with craniopharyngioma were individually matched to two control subjects with common obesity. Matching was based on the type of bariatric procedure, gender, age (range: 10 years) at bariatric procedure, preoperative body mass index, and preoperative diabetes status

Loss of follow-up: unspecified

2. Garrez et al., 2020

Matching standard: The 5 included patients were individually matched to 2 control subjects with common obesity derived from the abovementioned database meeting the national reimbursement criteria for bariatric surgery: ≥ 18 years of age and a BMI > 40 kg/m² or a BMI > 35 kg/m² associated with one or more of the following comorbidities being type 2 diabetes mellitus needing pharmacological treatment, therapy resistant hypertension necessitating at least three anti-hypertensive drugs, or obstructive sleep apnea syndrome. Matching was based on type and date of bariatric procedure, gender, age at bariatric procedure, and preoperative BMI. Relevant clinical data were collected from the electronic patient files.

Loss of follow-up (2 years):

CP: 0

Control: 2

3. van Santen et al., 2021

Matching standard: Potential controls were first selected according to sex, type of bariatric surgery (Roux-en-Y gastric bypass or sleeve gastrectomy), preoperative type 2 diabetes, and pre-operative hypertension. Further matching was performed by year of obesity operation (10-year span category), age at obesity operation (10-year span category), and preoperative body mass index (BMI) (maximum of ± 5 different from the control). Controls were included only once. If fewer than 10 controls were found, the criteria for matching age at bariatric surgery were extended to ± 10 years of the patient's age instead of a certain age category, which was required in 5 patients. For one patient, the criteria for BMI were extended as this patient was an outlier because of an extremely high BMI: the best-matched controls were chosen without a limit to BMI criteria. All patients were matched with 10 controls except for 2 patients: nine

controls were found for 1 and 6 controls were found for the extreme outlier. This resulted in the selection of 155 optimally matched controls. Controls had follow-up data on body weight (in kilograms) available at 6 weeks, and at 1, 2, and 5 years after bariatric surgery.

Loss of follow-up (5 years):

CPs: 6

Controls: 59

4. Wijnen et al., 2017

Matching standard: Patients with craniopharyngioma were individually matched to 6–10 control subjects with ‘common’ obesity, which yielded a total of 75 control participants.

Matching was based on the type and date of bariatric procedure, age, gender, preoperative body mass index and preoperative morbidity (that is, presence of diabetes mellitus and/or hypertension).

Loss of follow-up (104 weeks)

CPs: 4

Controls: 50