Original Article

Foregut bypass *vs.* restrictive bariatric procedures for nonalcoholic fatty liver disease: a meta-analysis of 3,355 individuals

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Background: Bariatric surgery represents an important treatment option for severely obese patients with nonalcoholic fatty liver disease (NAFLD). However, there remains inadequate data regarding the effects of different bariatric procedures on various NAFLD parameters, especially for histological outcomes. Thus, this meta-analysis aimed to compare the effects of restrictive bariatric procedures and foregut bypass on the metabolic, biochemical, and histological parameters for patients with NAFLD.

Methods: Medline and Embase were searched for articles relating to bariatric procedures and NAFLD. Pairwise meta-analysis was conducted to compare efficacy of bariatric procedures pre- *vs.* post-procedure with subgroup analysis to further compare restrictive against foregut bypass procedures.

Results: Thirty-one articles involving 3,355 patients who underwent restrictive bariatric procedures (n=1,460) and foregut bypass (n=1,895) were included. Both foregut bypass (P<0.01) and restrictive procedures (P=0.03) significantly increased odds of fibrosis resolution. Compared to restrictive procedures, foregut bypass resulted in a borderline non-significant decrease in fibrosis score (P=0.06) and significantly lower steatosis score (P<0.001). For metabolic parameters, foregut bypass significantly lowered body mass index (P=0.003) and low-density lipoprotein (P=0.008) compared to restrictive procedures. No significant differences were observed between both procedures for aspartate aminotransferase (P=0.17) and alkaline phosphatase (P=0.61). However, foregut bypass resulted in significantly lower gamma-glutamyl transferase

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than restrictive procedures (P=0.01) while restrictive procedures resulted in significantly lower alanine transaminase than foregut bypass (P=0.02).

Conclusions: The significant histological and metabolic advantages and comparable improvements in biochemical outcomes support the choice of foregut bypass over restrictive bariatric procedures in NAFLD management.

Keywords: Bariatric surgery; non-alcoholic fatty liver disease (NAFLD); obesity; fibrosis; endoscopy

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is a growing public health crisis (1) which is rapidly increasing in parallel with the global obesity epidemic (2,3). The spectrum of NAFLD ranges from simple steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis (4). NASH is the clinically aggressive variant of NAFLD and up to one-third of patients with NASH can progress to fibrosis and 20% to cirrhosis (5,6). NASH-related cirrhosis is currently the leading indication for liver transplantation among women (7,8). Furthermore, the incidence of hepatocellular carcinoma and liver-related deaths due to NASH are expected to increase by 137% and 178% respectively by the next decade (9).

Current guidelines recommend weight loss via lifestyle interventions as first line treatment for NASH (10,11). A previous study by Vilar-Gomez *et al.* demonstrated that patients with a weight loss of 7–10% resulted in improvements in histological outcomes (12). However, the adherence and maintenance of diet and lifestyle modifications to achieve weight loss often prove difficult in practice. In turn, bariatric surgery or endoscopic bariatric procedures have been proposed as alternatives to achieve substantial and durable weight loss among obese individuals (13). Restrictive procedures such as sleeve gastrectomy (SG) shrink the stomach capacity and promote satiation via stretch mechanoreceptor activation to induce weight loss, with additional metabolic effects related to lower secretion of ghrelin, an orexigenic hormone (14). Comparatively, foregut bypass procedures including Roux-en-Y gastric bypass (RYGB) and duodenal-jejunal bypass liner (DJBL) reduce weight via a bypass of the proximal small bowel to deliver nutrients directly into the hindgut (*Figure 1*). Foregut bypass has been associated with improvements in glucose tolerance and insulin resistance when compared to restrictive procedures (15,16) and has been shown to influence gut hormone modulation and gut microbiota involved in the pathogenesis of obesity (17).

While observational studies have suggested the superiority of RYGB over SG in improving NAFLD parameters (18,19), the data on the histopathological outcomes are less clear (20,21) especially for liver fibrosis. To date, there is still no consensus on the optimal choice of bariatric procedure in ameliorating histological outcomes in obese patients with NASH. Thus, this study aimed to conduct a systematic review and meta-analysis to compare the effects of restrictive procedures against foregut bypass for metabolic, biochemical, and histological parameters for patients with NAFLD. We present this article in accordance with the PRISMA reporting checklist (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-21-520/rc).

Methods

Search strategy

With reference to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines (22), a search was conducted on Medline and Embase databases for articles relating to bariatric surgery among patients with NAFLD from inception to 11 August 2021 without any date filter. The search strategy used search terms including 'non-alcoholic fatty liver disease', 'bariatric surgery', 'endoscopic bariatric metabolic therapy' and other related terms in titles and abstracts. The full search strategy is included in Appendix 1. All references were imported into Endnote X9 for duplicate removal. The references of included articles were also screened manually for a comprehensive search. The review was not registered.

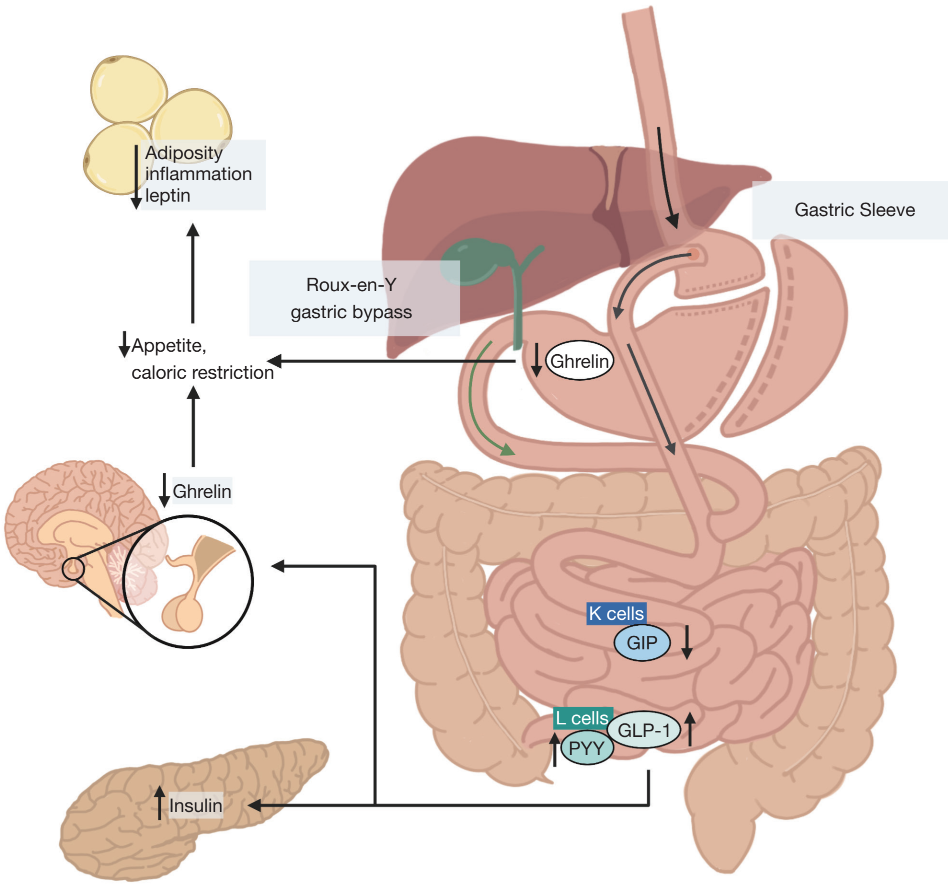

Figure 1 Mechanism of restrictive bariatric procedures versus foregut bypass. GIP, gastric inhibitory peptide; PYY, peptide YY; GLP-1, glucagon-like peptide-1.

Eligibility and selection criteria

Six authors (Lim WH, Lin SY, Ng CH, Tan DJH, Xiao J, Tay PWL) independently screened abstracts and conducted full text reviews to check the eligibility for inclusion, with disputes being resolved by obtaining the consensus of a seventh independent author (Muthiah MD). Only original studies in the English language were considered for inclusion, including retrospective and prospective studies, and randomized controlled trials (RCTs). Systematic reviews, meta-analyses, conference abstracts, case series, correspondence, and editorials were excluded. Duplicate studies inferring results from the same databases and paediatric studies were also removed. Studies were included if they (I) evaluated NAFLD/NASH patient cohort, and (II) reported any post-bariatric outcomes related to metabolic, biochemical, or histological parameters. Studies that failed to separate outcomes of NAFLD patients from non-NAFLD cohort (18), and those that did not provide sufficient granularity in outcomes according to specific type of bariatric procedure [i.e., RYGB, SG, adjustable gastric banding (AGB), intragastric balloon (IGB), DJBL, vertical banded gastroplasty] were excluded from the analysis (23-25).

Data extraction

Two pairs of authors (Lim WH and Lin SY, Ng CH and Tan DJH) independently extracted relevant data from the included articles onto a structured pro forma. Study characteristics including but not limited to author, year, country, study design, NAFLD diagnostic modality, and type of surgical procedure, patient characteristics including sample size, age, gender, and race, and finally, outcomes of bariatric procedures including metabolic parameters [e.g., body mass index (BMI), hemoglobin A1C (HbA1c), high-density lipoprotein (HDL), and low-density lipoprotein (LDL)], biochemical parameters [e.g., aspartate aminotransferase (AST), alanine transaminase (ALT), gamma-glutamyl transferase (GGT), and alkaline phosphatase (ALP)], and histological parameters [e.g., fibrosis, steatosis, ballooning, inflammation] were extracted. HDL and LDL were reported in milligrams per deciliter (mg/dL) while liver enzymes were reported in units per liter (U/L). The histological outcomes were largely classified according to the NASH activity score (NAS), as proposed by the Pathology Committee of the NASH Clinical Research Network where a composite score consists of: steatosis (grade 0 to 3), lobular inflammation (grade 0 to 3), and ballooning (grade 0 to 2); ranging from 0 to 8 (26). Fibrosis score of 0 indicates no fibrosis, 1= zone 3 perisinusoidal fibrosis only, 2= zone 3 perisinusoidal fibrosis with focal/extensive portal fibrosis, 3= zone 3 perisinusoidal fibrosis with focal/extensive bridging fibrosis, and 4= cirrhosis. Transformation of values were carried out using pre-existing formulae, in which mean and standard deviations were estimated from median and range using the widely adopted formula by Wan *et al.* (27).

Clinical endpoints

The different bariatric procedures were categorized into restrictive procedures and foregut bypass procedures. Restrictive bariatric procedures included SG, AGB, and vertical banded gastroplasty. Foregut bypass procedures included RYGB and DJBL. The primary histological endpoints were resolution of clinically significant fibrosis, resolution of steatosis, resolution of ballooning, and resolution of inflammation. Resolution of clinically significant fibrosis was defined as patients with fibrosis stage of F2, F3 or F4 on pre-procedure liver biopsy regressing to a fibrosis stage of F0 or F1 on interval biopsy. Resolution of steatosis, inflammation and ballooning were defined as patients with at least grade 1 of the above histologic parameters on pre-procedure liver biopsy resolving to grade 0 on interval biopsy. Secondary endpoints included reduction in biochemical (e.g., AST, ALT) and metabolic parameters (e.g., BMI, HbA1c, LDL, HDL).

Statistical analysis

All analyses were conducted in R Studio (version 4.0.3) using the *meta* package and statistical significance was considered for outcomes with a P value ≤0.05. Pairwise meta-analysis was conducted to compare efficacy of bariatric procedures pre- versus post-procedure in DerSimonian and Laird to obtain the odds ratio (OR) and mean difference (MD) for dichotomous and continuous variables respectively in corresponding 95% confidence interval (CI). Subgroup analysis was conducted to compare the difference between restrictive and foregut bypass procedures with further stratifications for SG and RYGB. The Hartung-Knapp estimator was used to stabilize the variance (28). Statistical heterogeneity was assessed via I^2 and Cochran Q test values, where an I^2 value of 0% to 40% indicates low heterogeneity, while values of 30% to 60%, 50% to 90%, and 75% to 100% indicates moderate, substantial, and considerable heterogeneity respectively (29,30). A Cochran Q test of $P<0.10$ was considered significant for heterogeneity. All analyses were conducted in random effects regardless of heterogeneity measures as it has been shown to be produce more robust estimates compared to the fixed effects models (31).

Quality assessment and publication bias

Four reviewers (Lim WH, Lin SY, Xiao J, Yong JN) independently assessed risk of bias of the included articles using the Newcastle-Ottawa Scale (NOS) for cohort studies (32) and the Cochrane Risk-of-Bias tool for RCTs (33). The NOS appraisal tool evaluates studies based on several parameters including appropriateness of sample frame, sampling method, ascertainment of exposure, demonstration that outcome of interest was not present at start of study, comparability of cohorts, methods for assessment of outcomes, duration of follow-up and adequacy of follow-up (32), while the Cochrane Risk-of-Bias tool for RCTs evaluates seven domains including random sequence generation, allocation concealment, masking of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other sources of bias (33). Disagreements were resolved by consensus or appeal to a fifth author (Muthiah MD). Publication bias was assessed through Egger's test where sufficient studies (k=10) were available (34,35).

Results

Summary of included articles

A systematic search of the literature yielded 1,598 articles after removal of duplicates. After 1,462 articles were excluded based on study title and abstract, 136 articles were selected for full text review, of which 31 articles met

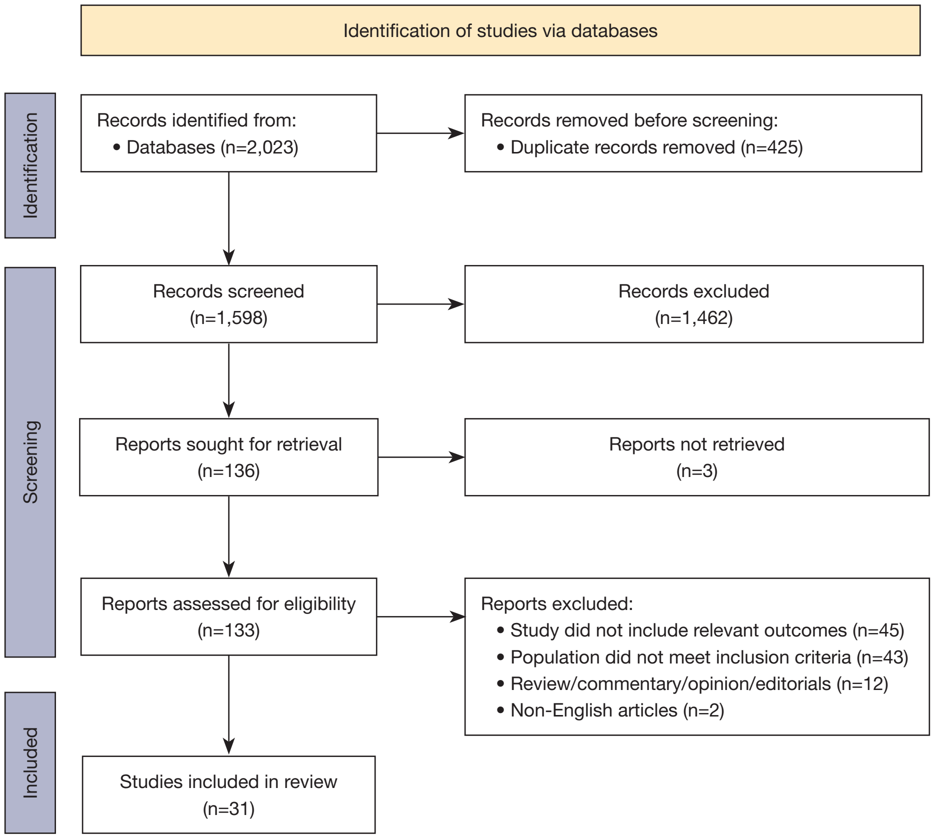

Figure 2 PRISMA flow diagram.

the final inclusion criteria (*Figure 2*). In total, five articles originated from the United States (36-40), six from Brazil (41-46), four from France (18,47-49), two from Poland (50,51), Australia (52,53) and Japan (54,55) respectively and one each from Denmark (56), Canada (57), Germany (58), Greece (59), India (60), Israel (61), The Netherlands (62), Saudi Arabia (63), Taiwan (64) and Turkey (65). Of the 31 included articles, there were 20 single-arm and 11 double-arm studies. The large majority of included articles were retrospective (n=12) and prospective cohort studies (n=18) with only one RCT. The online table (available at https://cdn.amegroups.cn/static/public/hbsn-21-520-1.pdf) summarizes the key characteristics and quality assessment for the included articles. A total of 3,355 NAFLD patients who underwent bariatric procedure were included in our analysis, comprising 1,460 patients who underwent restrictive bariatric procedures and 1,895 patients who underwent foregut bypass. Mean follow-up time was 20.1 months. All studies were assessed to have a low (n=23) to moderate (n=8) risk of bias based on the NOS and Cochrane Risk-of-Bias appraisal tools.

Primary endpoints

Reversal of clinically significant fibrosis

Both foregut bypass (OR: 3.23, 95% CI: 1.80 to 5.79, P<0.01; *Table 1*) and restrictive procedures (OR: 4.55, 95% CI: 1.42 to 14.55, P=0.03) significantly increased the odds of resolution of clinically significant fibrosis. However, subgroup analysis showed that only RYGB (P<0.01) resulted in significantly higher odds of fibrosis resolution, but not SG (P=0.10; *Figure 3*). Additionally, comparison between the two procedures showed that foregut bypass resulted in a borderline non-significant decrease in fibrosis score compared to restrictive procedures (MD: −0.58, 95% CI: −1.20 to 0.04 versus MD: −0.17, 95% CI: −1.52 to 1.18; P=0.06).

Resolution of steatosis

Both foregut bypass (OR: 75.40, 95% CI: 31.17 to 182.41,

Table 1 Comparison of primary endpoints between restrictive procedures and foregut bypass

Grade	Restrictive procedures					Foregut bypass					Subgroup difference
	No. of studies	OR (95% CI)	Cochran Q	I^2	P value	No. of studies	OR (95% CI)	Cochran Q	I^2	P value	
F0/F1	4	4.55 (1.42 to 14.55)	0.3	18.60%	0.03*	10	3.23 (1.80 to 5.79)	0.81	0.00%	<0.01*	0.44
S0	4	14.42 (1.35 to 153.57)	0.03	65.60%	0.04*	10	75.40 (31.17 to 182.41)	0.37	8.30%	<0.01*	0.05*
I0	3	6.25 (1.27 to 30.81)	0.4	0.00%	0.04*	8	15.99 (5.65 to 45.27)	0.25	22.10%	<0.01*	0.10
B0	2	27.44 (0.00 to 70.13)	0.04	75.60%	0.27	6	17.17 (6.25 to 47.15)	0.54	0.00%	<0.01*	0.77

*, P value ≤0.05 denotes statistical significance. F0/F1 represents reversal of clinically significant fibrosis; S0, I0, and B0 represents resolution of steatosis, lobular inflammation, and ballooning respectively. OR, odds ratio; CI, confidence interval.

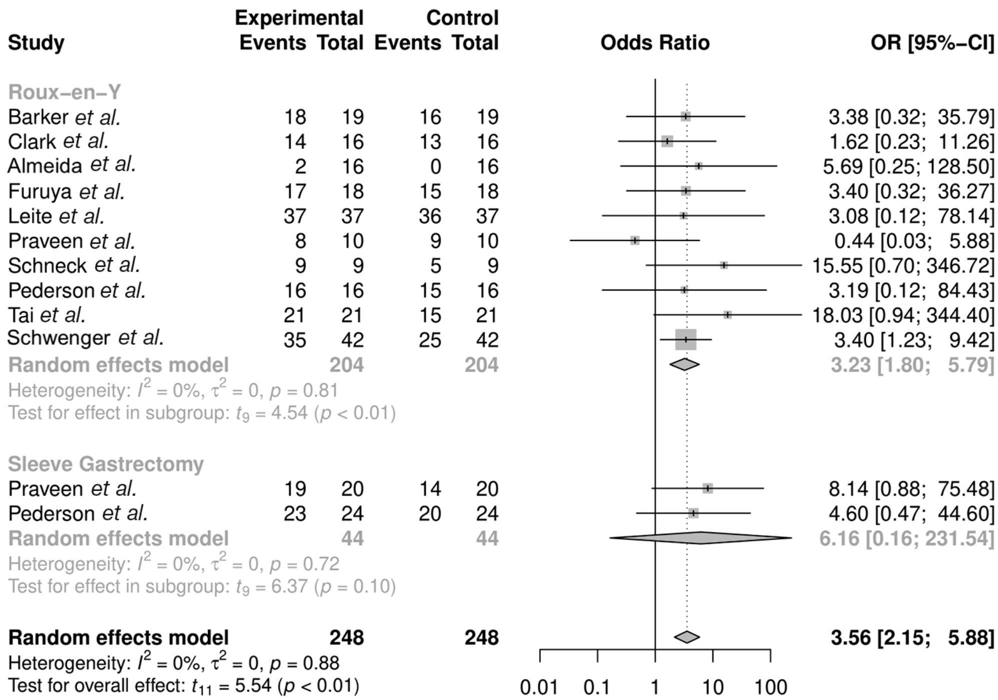

Figure 3 Fibrosis grade (F0/F1) after sleeve gastrectomy versus Roux-en-Y gastric bypass.

P<0.01; *Table 1*) and restrictive procedures (OR: 14.42, 95% CI: 1.35 to 153.57, P=0.04) significantly increased the likelihood of steatosis resolution. Foregut bypass resulted in significantly higher odds of steatosis resolution compared to restrictive procedures (P=0.05). Further subgroup analysis showed that only RYGB (P<0.01) resulted in significantly higher odds of resolution of steatosis, but not SG (P=0.36). Additionally, foregut bypass resulted in a significant decrease in steatosis score (MD: −1.92, 95% CI: −3.16 to −0.68, P=0.03), but not restrictive procedures (MD: −0.52, 95% CI: −1.83 to 0.80, P=0.23). Comparison between both procedures showed that foregut bypass resulted in a significantly lower steatosis score than restrictive procedures (P<0.001).

Resolution of lobular inflammation

Both foregut bypass (OR: 15.99, 95% CI: 5.65 to 45.27, P<0.01; *Table 1*) and restrictive procedures (OR: 6.25, 95% CI: 1.27 to 30.81, P=0.04) significantly increased odds of resolution of lobular inflammation. No significant difference was observed between both groups (P=0.10). However, subgroup analysis showed that only RYGB

Table 2 Comparison of metabolic and biochemical parameters between restrictive procedures and foregut bypass

Outcomes	Restrictive procedures					Foregut bypass					Subgroup difference
	No. of studies	MD (95% CI)	Cochran Q	I^2	P value	No. of studies	MD (95% CI)	Cochran Q	I^2	P value	
AST	15	−7.76 (−12.07 to −3.46)	<0.01	85.40%	<0.01*	16	−4.22 (−7.63 to −0.82)	<0.01*	90.10%	0.02	0.17
ALT	14	−19.66 (−26.30 to −3.46)	<0.01	85.20%	<0.01*	12	−10.11 (−16.31 to −3.90)	<0.01*	93.70%	<0.01*	0.02*
GGT	10	−11.30 (−16.41 to −6.19)	<0.01	72.90%	<0.01*	7	−20.40 (−27.56 to −13.22)	0.05	53.30%	<0.01*	0.01*
ALP	9	−12.84 (−24.96 to −0.73)	<0.01	86.60%	0.04*	8	−8.42 (−24.68 to −7.83)	<0.01*	93.10%	0.26	0.60
BMI	11	−11.20 (−12.95 to −9.45)	<0.01	83.60%	<0.01*	17	−15.79 (−18.60 to −12.97)	<0.01*	98.20%	<0.01*	0.003*
HbA1c	6	−0.97 (−1.40 to −0.54)	<0.01	76.30%	<0.01*	2	−0.70 (−0.96 to −0.44)	0.75	0.00%	0.02*	0.10
HDL	10	7.94 (4.78 to 11.10)	<0.01	81.60%	<0.01*	9	9.25 (4.57 to 13.93)	<0.01*	85.40%	<0.01*	0.60
LDL	10	−3.85 (−10.16 to 2.46)	<0.01	60.90%	0.20	7	−16.77 (−26.51 to −7.02)	0.04*	53.60%	<0.01*	0.01*

*, P value ≤0.05 denotes statistical significance. MD, mean difference; CI, confidence interval; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; BMI, body mass index; HbA1c, haemoglobin A1c; HDL, high density lipoprotein; LDL, low density lipoprotein.

(P<0.01) resulted in significantly higher odds of resolution of lobular inflammation, but not SG (P=0.15). In terms of lobular inflammation scores, no significant difference was observed between foregut bypass and restrictive procedures (P=0.65).

Resolution of ballooning

Foregut bypass significantly increased odds of resolution of ballooning (OR: 17.17, 95% CI: 6.25 to 47.15, P<0.01; *Table 1*), but not restrictive procedures (P=0.27). No significant difference was observed between both groups (P=0.77). Foregut bypass resulted in a significant decrease in ballooning score (MD: −1.14, 95% CI: −2.15 to −0.13, P=0.04), but not restrictive procedures (MD: −0.99, 95% CI: −3.91 to 1.92, P=0.14). No significant difference was observed between both groups (P=0.55).

Secondary endpoints

Biochemical parameters

A total of 31 studies involving 3,150 patients and 26 studies involving 1,847 patients reported AST and ALT changes following restrictive bariatric procedures and foregut bypass respectively. Restrictive procedures resulted in a significant decrease in AST (MD: −7.76, 95% CI: −12.07 to −3.46, P<0.01), ALT (MD: −19.66, 95% CI: −26.30 to −3.46, P<0.01), GGT (MD: −11.30, 95% CI: −16.41 to −6.19, P<0.01) and ALP (MD: −12.84, 95% CI: −24.96 to −0.73, P<0.01) while foregut bypass resulted in a significant decrease in AST (MD: −4.22, 95% CI: −7.63 to −0.82, P=0.02), ALT (MD: −10.11, 95% CI: −16.31 to −3.90, P<0.01) and GGT (MD: −20.40, 95% CI: −27.56 to −13.22, P<0.01), but not ALP (P=0.26). Foregut bypass resulted in significantly lower GGT compared to restrictive procedures (P=0.01) while restrictive procedures resulted in significantly lower ALT compared to foregut bypass (P=0.02). No significant difference was observed for AST (P=0.17) and ALP (P=0.61). Egger's test revealed no publication bias for both AST (P=0.33) and ALT (P=0.90). A summary of the biochemical parameters can be found in *Table 2*.

Metabolic parameters

Both restrictive bariatric procedures (MD: −11.20, 95% CI: −12.95 to −9.45, P<0.01) and foregut bypass (MD: −15.79, 95% CI: −18.60 to −12.97, P<0.01) resulted in a significant decrease in BMI. However, foregut bypass resulted in a greater decrease in BMI compared to restrictive procedures (P=0.003) although publication bias was noted (P=0.05). A significant decrease in HbA1c was observed following both restrictive procedures (MD: −0.97, 95% CI: −1.40 to −0.54, P<0.01) and foregut bypass (MD: −0.70, 95% CI: −0.96 to −0.44, P=0.02). No significant difference was observed between both procedures (P=0.11). Additionally, foregut bypass (MD: −16.77, 95% CI: −26.51 to −7.02, P<0.01) significantly improved LDL parameters but not restrictive procedures (MD: −3.85, 95% CI: −10.16 to 2.46, P=0.20). Comparison between the two groups showed a significant improvement of LDL in foregut bypass compared to restrictive procedures (P=0.007). Both restrictive procedures (MD: 7.94, 95% CI: 4.78 to 11.10, P<0.01) and foregut bypass (MD: 9.25, 95% CI: 4.57 to 13.93, P<0.01) also significantly increased HDL. However, no significant

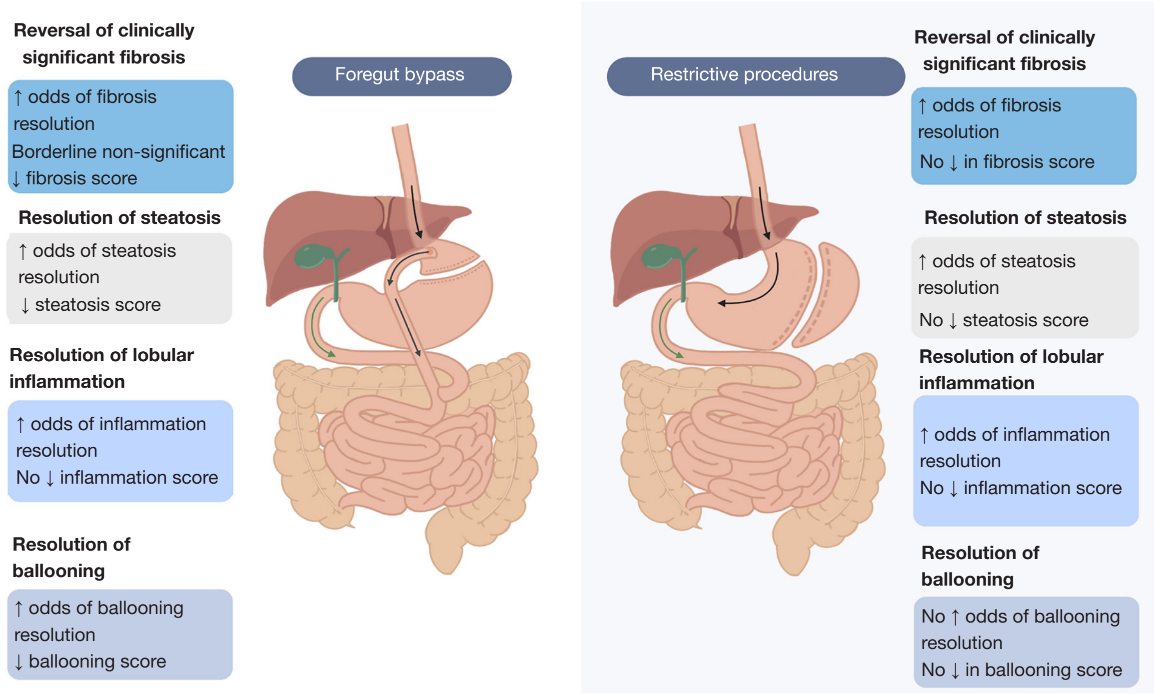

Figure 4 Summary of overall outcomes between restrictive bariatric procedures and foregut bypass.

difference was observed between both procedures (P=0.60). A summary of the metabolic parameters can be found in *Table 2*.

Discussion

The obesity epidemic has resulted in an unprecedented rise in NAFLD which affects up to 70% of obese individuals and over 90% of patients with morbid obesity (2). Bariatric surgery thus represents an important treatment option for patients with NAFLD and obesity. Until recently, RYGB was regarded as the standard bariatric procedure for its efficacy and duration of effects. However, restrictive bariatric procedures such as SG have been gaining popularity in recent years, in part due to the relatively less demanding learning curve and easier surgical technique (66). In NASH, Pais *et al.* demonstrated that despite similar weight loss, patients who underwent SG were more likely to have persistent fibrosis on interval repeat biopsies compared to patients who underwent RYGB (19). This meta-analysis of 3,355 patients provides evidence that foregut bypass yields better liver histological outcomes than restrictive bariatric procedures among patients with NAFLD. Furthermore, foregut bypass also confers significant advantages in the improvement of metabolic parameters compared to restrictive procedures among this group of patients (*Figure 4*).

A trend in lower fibrosis score favouring foregut bypass over restrictive procedures was observed. Foregut bypass also increased the likelihood of steatosis resolution in contrast to restrictive bariatric procedures. In addition, improvements in lobular inflammation and ballooning degeneration generally favoured foregut bypass over restrictive bariatric procedures (Tables S1-S3). These results suggest that foregut bypass results in superior histological outcomes compared to restrictive procedures as a surrogate endpoint for NAFLD improvement. While histological improvements were more prominent with bypass procedures, reductions in liver enzymes were generally found to be similar between restrictive and bypass bariatric procedures. However, transaminases may not be an accurate surrogate to monitor improvements in NAFLD given that a study by the NASH Clinical Research Network found that 19% of patients with stage 2 to 3 fibrosis and 7% of patients with stage 4 cirrhosis had normal liver enzymes levels (67).

Notably, foregut bypass also demonstrated superiority over restrictive bariatric procedures in improving metabolic parameters. Of which, bypass procedures were associated with larger improvements with BMI and LDL. Bypass of the foregut has been proposed to improve glucose profiles by enhancing the incretin response (68). Specifically, postprandial response of glucagon-like peptide-1 and glucose dependent insulinotropic polypeptide has been shown to increase after bypass procedures over and above restrictive procedures (69). The effect of bypass is probably more extensive so that, in addition to a restrictive effect, improvement of the enteroinsulinar axis may be achieved via reduction in stanniocalcin-2 and insulin-like growth factor binding protein 4 in a pregnancy-associated plasma protein-A dependent manner (70). While weight reduction is essential in the treatment of NAFLD (12), changes induced by lifestyle interventions are often challenging. With bypass procedures, a larger sustained reduction in BMI in turn reduces cardiovascular and metabolic risks (71). Importantly, cardiovascular morbidity and mortality remains the leading cause of death among patients with NAFLD regardless of other competing traditional cardiovascular risk factors (72,73). Previous studies have associated the reduction in BMI with decrease in atherosclerosis and coronary artery disease which are highly prevalent in NAFLD patients (74). A recent meta-analysis demonstrated that up to 37% and 55% of patients with NAFLD are associated with subclinical and clinical coronary artery disease respectively (75). Additionally, the added benefit of a greater reduction in LDL experienced by bypass patients may further decrease the burden of cardiovascular morbidity and mortality for those with NAFLD.

However, foregut bypass is not without its limitations. Internal hernia, a potentially dangerous complication, is present in up to 3% of patients post RYGB (76). Other causes for reoperation after RYGB include small bowel obstruction or late dumping, complications that less frequently occur after SG. In contrast, SG has been shown to exacerbate gastric reflux with recently published reports indicating development of Barrett mucosa in up to 17% of asymptomatic patients (77,78). Additionally, bariatric surgery has also been associated with adverse effects on mental health (79) and may potentiate the relationship between NAFLD and depression (80). Given the invasive nature and potential procedure-related adverse events after bariatric surgery, the emergence of non-surgical duodenal bypass potentially represents an important therapeutic opportunity in the future management of NAFLD (81).

Strengths and limitations

To our knowledge, this is the largest meta-analysis to date providing a comprehensive head-to-head comparison of restrictive bariatric procedures against foregut bypass for metabolic, biochemical, and histopathological outcomes among patients with NAFLD. However, several limitations should be accounted for when interpreting the study results. Firstly, the analysis of histological improvements was assessed based on the resolution of clinically significant fibrosis, steatosis, lobular inflammation and ballooning. While it would have been ideal to report a one-point change in histology, the sparsity of reporting prevented such an analysis. Previous meta-analyses on bariatric surgery in NAFLD have predominantly reported the proportion of patients for each respective parameter after bariatric procedures (82). It is also important to note that a limited number of studies reported continuous data for histopathological outcomes between the two procedures, thus the results should be interpreted with caution. Furthermore, most included studies did not provide sufficient granularity to delineate patients with NAFLD from NASH and cirrhosis which limited further analysis. Other parameters including the changes in liver volume, controlled attenuation parameter (CAP), ratio of liver to spleen (L/S ratio), magnetic resonance elastography (MRE) liver stiffness, AST to Platelet Ratio Index score (APRI) and Fibrosis-4 (FIB-4) score could not be evaluated owing to a sparsity of data. Finally, majority of studies did not have long-term follow-up and future longitudinal studies are warranted to better assess histological changes across longer timespan.

Conclusions

In conclusion, the significant histological and metabolic advantages and comparable improvements in biochemical outcomes support the choice of foregut bypass over restrictive bariatric procedures in the management of NAFLD. Development of new modalities for foregut bypass may provide novel strategies for the treatment of obese patients with NASH.

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Footnote

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