



Safety and effectiveness of antireflux surgery in obese patients

A Tandon¹, R Rao², A Hotouras⁵, QM Nunes², M Hartley², R Gunasekera², N Howes²

¹Aintree University Hospital NHS Foundation Trust, UK

²Royal Liverpool and Broadgreen University Hospitals NHS Trust, UK

⁵Barts Health NHS Trust, UK

ABSTRACT

INTRODUCTION The incidence of gastro-oesophageal reflux disease and obesity has increased significantly in recent years. The number of antireflux procedures being carried out on people with a higher body mass index (BMI) has been rising. Evidence is conflicting for outcomes of antireflux surgery in obese patients in terms of its safety and efficacy. Given the contradictory reports, this meta-analysis was undertaken to establish the outcomes of antireflux surgery (ARS) in obese patients and its associated safety.

METHODS A systematic electronic search was conducted using the PubMed, MEDLINE®, Ovid®, Cochrane Library and Google Scholar™ databases to identify studies that analysed the effect of BMI on the outcomes of ARS. A meta-analysis was performed using the random effects model. The intraoperative and postoperative outcomes that were examined included operative time, conversion to an open procedure, mean length of hospital stay, recurrence of acid reflux requiring reoperation and wrap migration.

RESULTS A total of 3,772 patients were included in 13 studies. There was no significant difference in procedure conversion rate, recurrence of reflux requiring reoperation or wrap migration between obese and non-obese patients. However, both the mean operative time and mean length of stay were longer for obese patients.

CONCLUSIONS ARS in obese patients with gastro-oesophageal reflux disease is safe and outcomes are comparable with those in patients with a BMI in the normal range. A high BMI should therefore not be a deterrent to considering ARS for appropriate patients.

KEYWORDS

High body mass index – Antireflux surgery – Fundoplication – Obesity

Accepted 9 April 2017

CORRESPONDENCE TO

Ashutosh Tandon, E: drashutoshtandon@gmail.com

Gastro-oesophageal reflux disease (GORD) is increasingly encountered, having an estimated prevalence of up to 20% in the Western hemisphere.¹ Antireflux surgery (ARS) for GORD is cost effective compared with medical management in the long term,² with laparoscopic ARS being the gold standard.^{3,4}

Obesity has doubled globally in the last three decades, and epidemiological studies suggest an association between obesity and GORD⁵ as a result of distorted pressure gradients across the gastro-oesophageal junction.⁶ Consequently, ARS is increasingly being carried out on people with a higher body mass index (BMI). Evidence for outcomes of ARS on obese patients is conflicting in terms of its safety and efficacy.^{7–11} This systematic review and meta-analysis was undertaken with a view to informing future practice.

Methods

A systematic electronic search was undertaken using PubMed, MEDLINE®, Ovid®, Cochrane Library and Google Scholar™ according to PRISMA (Preferred Reporting Items

for Systematic Reviews and Meta-Analyses) guidance.¹² Search terms comprised “obesity” OR “high BMI” AND “antireflux surgery” OR “Nissen fundoplication” OR “fundoplication”. All search terms were combined with Boolean operators and searched as both keywords and Medical Subject Headings. The results were reviewed by two independent researchers (AT and QMN). The last search date was 10 October 2016.

Inclusion and exclusion criteria

Studies were included in this review if they looked at the effect of BMI on the outcome of laparoscopic fundoplication. Case reports, letters, editorials, conference abstracts, non-English articles and animal studies were excluded, as were studies investigating bariatric surgery as ARS.

Outcome measures

The World Health Organization classification of BMI was used: normal BMI 18.5–24.9kg/m², overweight ≥25kg/m² and obese ≥30kg/m².¹⁵ Outcomes included operative time, conversion to open procedure, mean length of hospital stay,

recurrence of acid reflux requiring reoperation and wrap migration. Data were also collected for preoperative assessment, including lower oesophageal pressure, total acid exposure time on 24-hour pH monitoring, DeMeester score, presence of Barrett's oesophagus, presence of reflux oesophagitis, type of fundoplication and follow-up duration.

Study selection

Two authors (AT and QMN) independently performed the search. Disagreements on study selection were resolved by consensus with the senior author (RG). If the issue of study selection was still not resolved, the lead author's (NH's) decision was considered final.

Statistical analysis

Statistical analysis was undertaken using RevMan version 5.3 (Nordic Cochrane Centre, Copenhagen, Denmark). Data were pooled and rate differences as well as standard mean differences (SMDs) with 95% confidence intervals (CIs) were calculated. The random effects model was used as the effects were expected to be heterogeneous owing to the variety of study populations and study designs included in the analysis.¹⁴ Heterogeneity was tested using the I^2 statistic.

Quality assessment

The methodological index for non-randomised studies (MINORS)¹⁵ was used to evaluate methodological quality and potential bias of included studies.

Results

Overall, 8,470 articles were identified. Following exclusion of duplicates, non-English articles and animal studies, 2,124 articles remained. The titles and abstracts were then reviewed, and a further 2,103 articles were excluded. Of the remaining 21 articles, 8 were excluded owing to being smaller case series and studies reporting inappropriate outcomes. Finally, 13 studies were left for review (Fig 1).^{7-11,16-25} No randomised controlled trials (RCTs) were identified. Eight of the studies were prospective^{7,9,10,16,18,19,21,25} and five were retrospective.^{8,11,17,20,22}

Study and patient characteristics

A total of 3,772 patients were included in the 13 studies. Seven studies reported on patients in all three categories of BMI,^{7,8,10,16,18,19,25} three studies reported on patients with BMI $<30\text{kg/m}^2$ and BMI $\geq 30\text{kg/m}^2$,^{9,17,20} and one study reported on patients with normal BMI and patients who were obese.¹¹ The mean or median age was reported in six studies.^{7,10,16,20,21,25} There were 1,942 male and 1,464 female patients in 12 studies (Table 1).^{7-11,16-19,21-25} Co-morbidities were not reported in any of the studies.

Conversion from laparoscopic to open procedure

Six studies reported conversion of laparoscopic procedures to open procedures.^{7,11,18,20,21,25} Two of these stated there were no conversions.^{11,25} The pooled data gave the rates of

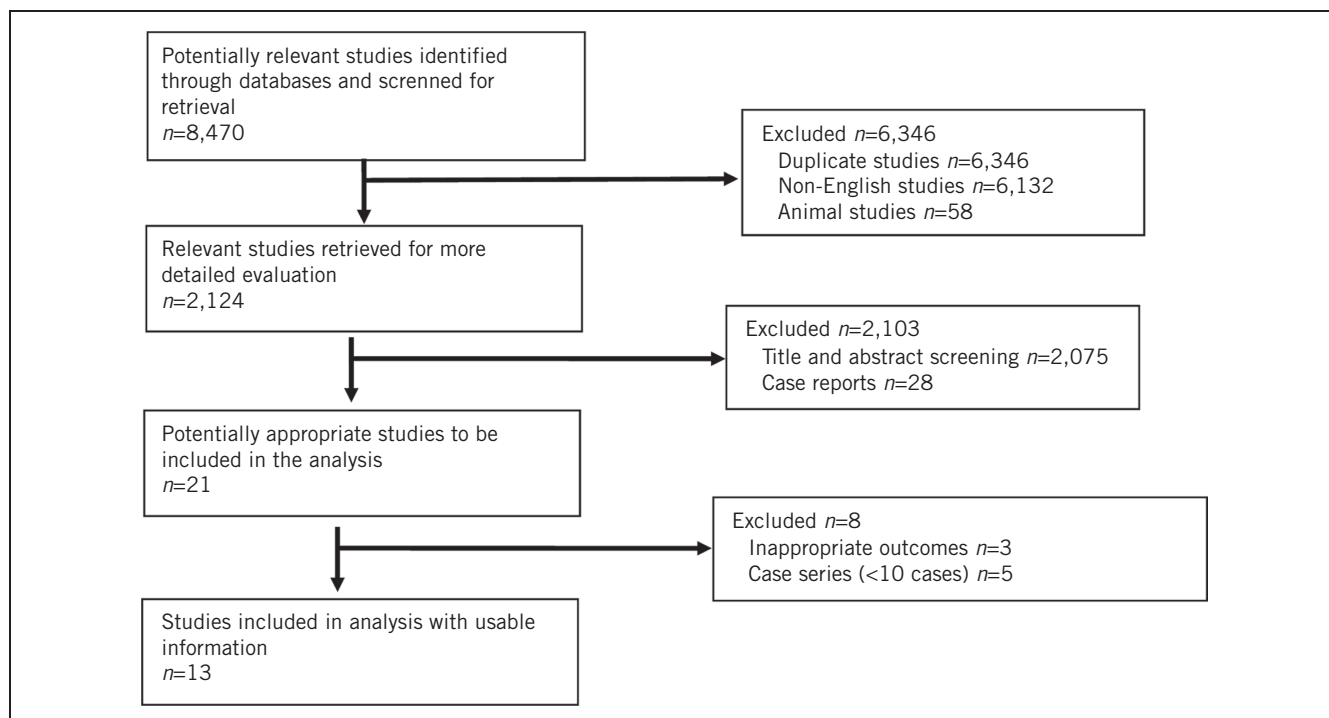


Figure 1 Flowchart of studies included in review

Table 1 Summary of studies and patient characteristics

Study	Design	MINORS score	Number of patients	BMI <24kg/m ²	BMI 25–30kg/m ²	BMI ≥30kg/m ²	Mean / median age in yrs	Sex ratio
Fraser, 2001 ⁷	Prospective	13/24	194	40 (21%)	88 (45%)	66 (34%)	Mean 46.9 (range: 17–74)	M=60%, F=40%
Perez, 2001 ⁸	Retrospective	14/24	224	89 (40%)	87 (39%)	48 (21%)		M=53%, F=47%
Anvari, 2006 ⁹	Prospective	23/24	140	70 (50%)		70 (50%)		M=50%, F=50%
Morgenthal, 2007 ¹⁰	Prospective	6/16	174	21 (12%)	47 (27%)	22 (13%)	Mean 47.1 ±13.9 (range: 12–77)	M=55%, F=45%
Luketina, 2015 ¹¹	Retrospective	21/24	80	40 (50%)	0 (0%)	40 (50%)		M=56%, F=44%
Campos, 1999 ¹⁶	Prospective	11/16	199	47 (24%)	BMI 25–35kg/m ² : 144 (72%)	BMI >35kg/m ² : 8 (4%)	Median 49 (range: 15–77)	M=70%, F=30%
Hahnloser, 2002 ¹⁷	Retrospective	10/16	126	75 (60%)		51 (41%)		M=56%, F=44%
Winslow, 2003 ¹⁸	Prospective	18/24	505	82 (16%)	210 (42%)	212 (42%)		M=52%, F=48%
D’Alessio, 2005 ¹⁹	Prospective	17/24	257	79 (31%)	116 (45%)	62 (24%)		M=45%, F=55%
Ng, 2007 ²⁰	Retrospective	13/24	366	292 (80%)		74 (20%)	Mean 44 (range: 12–86)	
Chisholm, 2009 ²¹	Prospective	14/24	481	103 (21%)	208 (43%)	170 (36%)	Mean 50.3 (range: 16–91)	M=58%, F=42%
Irino, 2010 ²²	Retrospective	12/16	26					M=65%, F=35%
Tekin, 2012 ²³	Prospective	19/24	1,000	484 (48%)	384 (38%)	132 (13%)	Mean 39.64 ±10.58	M=61%, F=39%

BMI = body mass index; MINORS = methodological index for non-randomised studies

conversion for BMI <30kg/m² and BMI ≥30kg/m² as 1.2% (23/1,931) and 1.4% (10/694) respectively with a combined risk ratio (RR) of 0.97 (95% CI: 0.46–2.07, *p*=0.94). Heterogeneity was 0% (Fig 2).

Recurrence of reflux requiring reoperation

Recurrence was compared in five studies.^{8,9,18,20,25} There was no significant difference in recurrence rate between the BMI <30kg/m² and BMI ≥30kg/m² groups (3.1% [53/1,698] vs 7.5% [40/536] respectively) with a combined RR of 1.99 (95% CI: 0.85–4.65, *p*=0.11). Heterogeneity was 62% (Fig 3).

Wrap migration

Four studies compared wrap migration at follow-up review.^{9,11,18,20} There was no significant difference in the number of patients who had wrap migration between the BMI <30kg/m² and BMI ≥30kg/m² groups (1.0% [7/694] vs 1.5% [5/396] respectively) with a combined RR of 1.25 (95% CI: 0.37–4.03, *p*=0.75). Heterogeneity was 0% (Fig 4).

Operative time

Seven studies reported the mean operative time with range or standard deviation.^{7–9,18,20,21,25} There was a significant

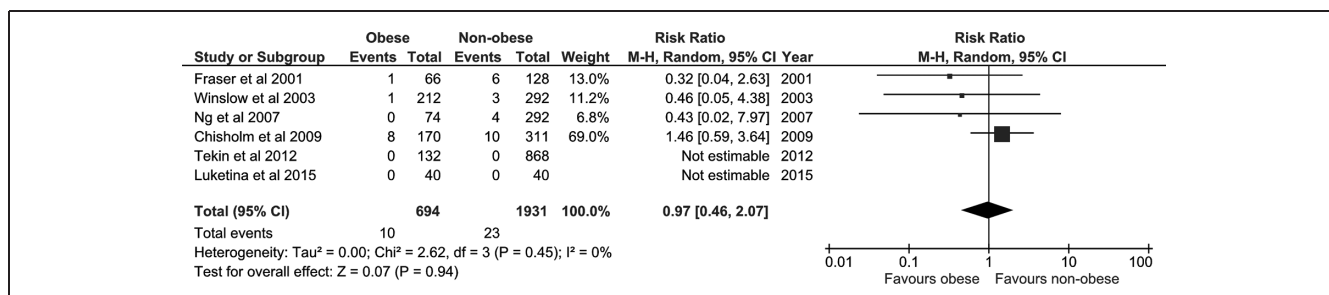


Figure 2 Forest plot comparing rates of conversion from laparoscopic to open fundoplication for body mass index (BMI) <30kg/m² and BMI ≥30kg/m². A random effects model was used for meta-analysis. Risk ratios are shown with 95% confidence intervals.

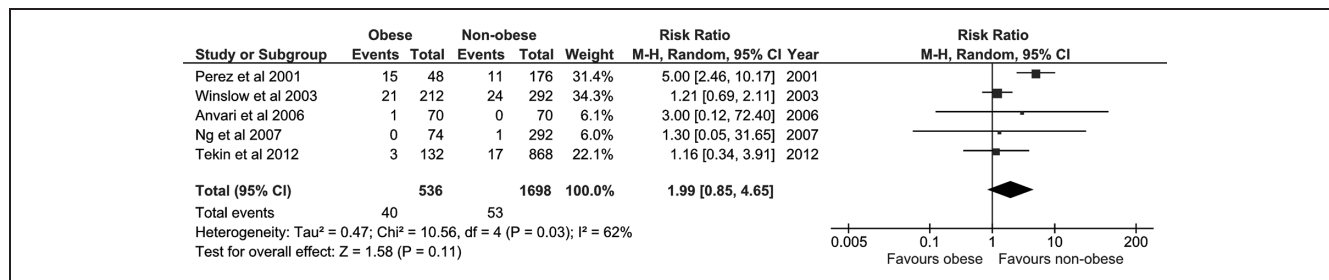


Figure 3 Forest plot comparing recurrence of reflux requiring reoperation for body mass index (BMI) <30kg/m² and BMI ≥30kg/m². A random effects model was used for meta-analysis. Risk ratios are shown with 95% confidence intervals.

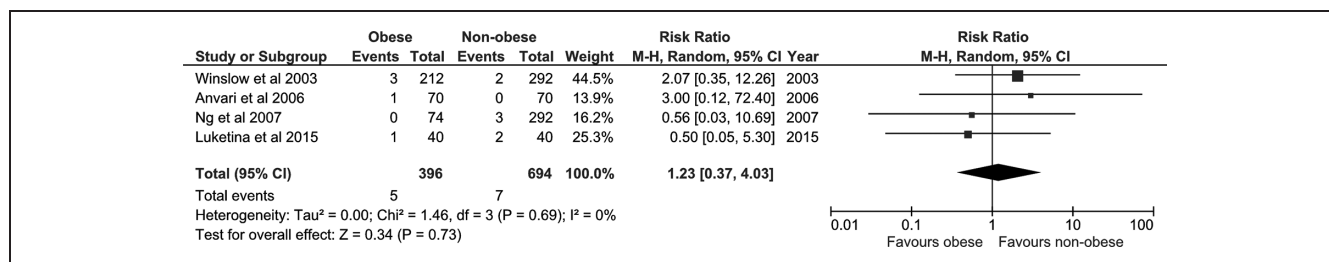


Figure 4 Forest plot comparing rates of migration of wrap for body mass index (BMI) <30kg/m² and BMI ≥30kg/m². A random effects model was used for meta-analysis. Risk ratios are shown with 95% confidence intervals.

difference, ranging from 55.9 minutes to 152 minutes in obese patients and 48.05 minutes to 144 minutes in patients with BMI <30kg/m² (SMD: 1.24 minutes, 95% CI: 0.46–2.02 minutes, *p*=0.002). Heterogeneity was 98% (Fig 5).

Length of stay

The mean length of hospital stay in both groups was reported in five studies.^{9,18–20,25} This was significantly lower in the normal weight group, ranging from 1.09 to 2.2 days compared with a range of 1.08–3.17 days in the obese group (SMD: 1.11 days, 95% CI: -0.16–2.06 days, *p*=0.020). Heterogeneity was 98% (Fig 6).

Follow-up duration

The mean or median follow-up duration was reported in 11 studies (Table 2).^{7–9,11,16–19,21–25} The minimum mean follow-up duration was 14.7 months,¹¹ the maximum being 96 months.²¹

Type of antireflux surgery

The type of ARS performed was reported in all studies (Table 2). In seven of the studies, laparoscopic Nissen fundoplication (LNF) was performed in all patients.^{7,9,10,16,17,19,20} Perez *et al* carried out LNF and Belsey Mark IV procedures, noting that the transthoracic approach in the latter operation was technically easier for obese patients.⁸ Although Chisholm *et al* chose LNF and laparoscopic anterior fundoplication for the majority of their patients, 2% underwent laparoscopic Toupet fundoplication (LTF).²¹ Their choice of

procedure was not influenced by BMI. In the remaining four studies, just LNF and LTF were performed, with Winslow *et al*¹⁸ and Tekin *et al*²⁵ favouring LNF while Luketina *et al*¹¹ and Irino *et al*²² favoured LTF.

Quality of studies

The quality of the studies was evaluated with the MINORS criteria (Table 1).¹⁵ The highest score achieved by a non-comparative study was 12/16.²² For comparative studies, the highest score was 23/24.⁹ Three studies concluded that ARS had a poor outcome in high BMI patients (Table 3).^{8,10,17}

Discussion

Laparoscopic fundoplication is the established gold standard for surgical treatment of GORD.^{4,24} ARS in obese patients is technically challenging owing to body habitus, the abundance of intraperitoneal fat and hepatic hypertrophy. As high BMI is the main precipitating factor for GORD, if it remains untreated, it could theoretically bring about failure of the ARS. Patients with a high BMI are prone to an increased rate of postoperative complications and a lower success rate.^{10,17} Bariatric operations are becoming more common and are associated with low complication rates. Roux-en-Y gastric bypass is the most frequently undertaken bariatric procedure, and it has been shown to be effective in achieving weight loss and also in treating reflux in these patients.²⁵ Conversely, however, many studies have reported that construction of a sound wrap in obese patients has outcomes

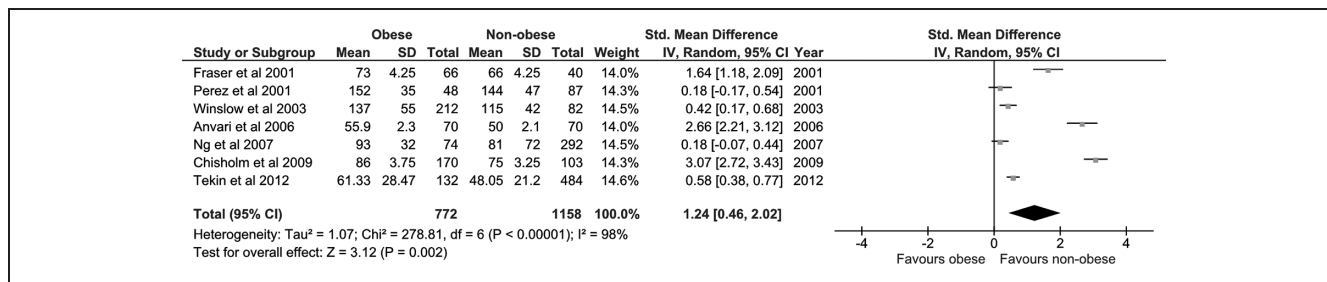


Figure 5 Forest plot comparing operative time for body mass index (BMI) <30kg/m² and BMI ≥30kg/m². A random effects model was used for meta-analysis. Risk ratios are shown with 95% confidence intervals.

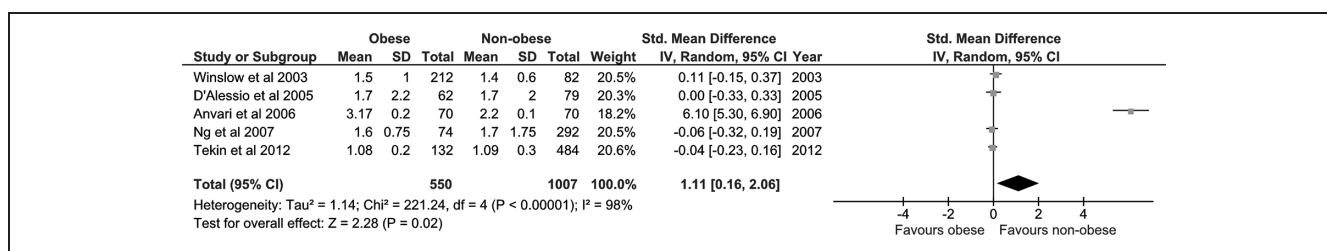


Figure 6 Forest plot comparing length of hospital stay for body mass index (BMI) <30kg/m² and BMI ≥30kg/m². A random effects model was used for meta-analysis. Risk ratios are shown with 95% confidence intervals.

that are comparable with those for people with normal BMI in terms of both complications and failure.^{9,11,18}

This review was undertaken to compare outcomes of ARS (operative time, length of stay and conversion rates) as well as complications for normal and high BMI patients. Our meta-analysis included eight prospective trials and five retrospective studies. Eight of these classified BMI into three categories^{7,8,10,11,16–19,21–25} while two studies grouped results by BMI <30kg/m² and BMI ≥30kg/m².^{9,20} None of the studies detailed any coexisting co-morbidities for their cohort. Obesity associated cardiovascular, respiratory and endocrine co-morbidities carry unique challenges when patients are considered for surgery, and they can influence outcomes.

In this meta-analysis, the mean operative time reported in seven studies was significantly longer for obese patients. Interestingly, conversion rates in six studies were similar for the BMI <30kg/m² and BMI ≥30kg/m² groups (1.2% vs 1.4% respectively, $p=0.94$), which may be indicative of the competent laparoscopic skills of the surgeons in these studies and their familiarity with operating on people with raised BMI. Only four studies reported on the occurrence of wrap migration (1.0% for BMI <30kg/m² vs 1.3% for BMI ≥30kg/m²) and the difference between the groups was not statistically significant. Follow-up duration was reported in 8 studies with a minimum mean of over 14 months.

In seven studies, LNF was carried out on all patients, making it the most common procedure. Perez *et al* compared the LNF and Belsey Mark IV procedures in 224 patients, reporting that the transthoracic procedure was technically easier in obese patients as it gave good exposure

of the hiatus.⁸ However, this was associated with a higher recurrence in the obese group. Chisholm *et al* reported outcomes in 481 patients, the majority of whom underwent LNF (67%) followed by laparoscopic anterior fundoplication (31%) and LTF (2%).²¹ The choice of wrap was not influenced by BMI and outcomes were not affected by BMI or sex of the patient. Irino *et al* undertook 14 LTF and 12 LNF procedures, and found patients with BMI >25kg/m² had better outcomes than those with BMI <25kg/m².²² Obesity was not associated with inferior outcomes when Luketina *et al* compared the outcomes of LTF ($n=58$) with LNF ($n=22$) although it should be noted that the follow-up period was only 12 months.¹¹ Winslow *et al* predominantly undertook LNF in their 505 patients, with longer operative times in obese patients.¹⁸

This meta-analysis comprised non-randomised studies as there is a dearth of RCTs on the subject. The inclusion of non-randomised studies in meta-analyses is a matter of ongoing debate.²⁶ While RCTs are considered the gold standard for evidence-based practice, non-randomised studies are increasingly being included in meta-analyses as both types of studies are associated with their unique strengths and weaknesses.²⁷ Designed to minimise bias, RCTs can be restrictive in their selection criteria. On the other hand, non-randomised studies tend to be more representative of patient populations seen in routine clinical practice.²⁸ The approach of analysing non-randomised studies in a systematic manner through a meta-analysis is becoming more prevalent as the resulting information can play an important role in informing practice and investigation.^{27,29,30}

Table 2 Preoperative assessment, type of antireflux surgery and follow-up duration

Study	Mean / median LOS pressure in mmHg	Mean / median acid exposure time over 24 hrs	Mean / median DeMeester score	Barrett's oesophagus	Oesophagitis	Type of antireflux surgery	Mean / median follow-up duration in mths
Fraser, 2001 ⁷						LNF 100%	Mean 38.4 (range: 12–72)
Perez, 2001 ⁸			BMI ≤24kg/m ² : 11.2% BMI 25–29kg/m ² : 19.7% BMI ≥30kg/m ² : 19.5%	BMI ≤24kg/m ² : 39.3% BMI 25–29kg/m ² : 37.9% BMI ≥30kg/m ² : 45.8%	BMI ≤24kg/m ² : LNF 88%, BMIV 12% BMI 25–29kg/m ² : LNF 85%, BMIV 15% BMI ≥30kg/m ² : LNF 73%, BMIV 27%	BMI ≤24kg/m ² : Mean 33.8 BMI 25–29kg/m ² : Mean 33 BMI ≥30kg/m ² : Mean 39.6	
Anvari, 2006 ⁹	BMI <30kg/m ² : 10.8 ±0.8 BMI ≥30kg/m ² : 6.0 ±0.6	BMI <30kg/m ² : 7.5% ±0.7% BMI ≥30kg/m ² : 9.2% ±0.7%			LNF 100%		BMI <30kg/m ² : Mean 48.2 ±3.0 BMI ≥30kg/m ² : Mean 41.6 ±2.8
Morgenthal, 2007 ¹⁰					LNF 100%		
Luketina, 2015 ¹¹	BMI <25kg/m ² : 9.70 ±4.99 BMI ≥30kg/m ² : 8.25 ±3.98	BMI <25kg/m ² : 22.07 ±11.88 BMI ≥30kg/m ² : 21.51 ±17.17			BMI ≤24kg/m ² : LNF 28%, LTF 72% BMI ≥30kg/m ² : LNF 27%, LTF 73% (p=0.93)		Mean 14.7 ±2.4
Campos, 1999 ¹⁶					LNF 100%		Median 15 (range: 6–74)
Hahnloser, 2002 ¹⁷					LNF 100%		Mean: 42
Winslow, 2003 ¹⁸	BMI ≤24kg/m ² : 10 ±7 BMI 25–29kg/m ² : 9 ±7 BMI ≥30kg/m ² : 9 ±6	BMI ≤24kg/m ² : 14% ±9% BMI 25–29kg/m ² : 12% ±7% BMI ≥30kg/m ² : 14% ±12%	BMI ≤24kg/m ² : 51 ±48 BMI 25–29kg/m ² : 57 ±60 BMI ≥30kg/m ² : 59 ±60	BMI ≤24kg/m ² : 11% BMI 25–29kg/m ² : 20% BMI ≥30kg/m ² : 12%	BMI ≤24kg/m ² : 51% BMI 25–29kg/m ² : 63% BMI ≥30kg/m ² : 53%	BMI ≤24kg/m ² : LNF 90%, LTF 10% BMI 25–29kg/m ² : LNF 91%, LTF 9% BMI ≥30kg/m ² : LNF 94%, LTF 6% (p=0.004)	BMI ≤24kg/m ² : Mean 35 ±24 BMI 25–29kg/m ² : Mean 36 ±24 BMI ≥30kg/m ² : Mean 37 ±24

D'Alessio, 2005 ¹⁹	BMI ≤24kg/m ² : 43.6 ±53.5 BMI 25-29kg/ m ² : 51.7 ±44.0 BMI ≥30kg/m ² : 51.0 ±35.4	BMI ≤24kg/m ² : 37% BMI 25-29kg/ m ² : 33% BMI ≥30kg/m ² : 42%	LNF 100%	BMI ≤24kg/m ² : Mean 28.8 ±24.7 BMI 25-29kg/m ² : Mean 21.8 ±23.1 BMI ≥30kg/m ² : Mean 28.3 ±23.9
Ng, 2007 ²⁰	BMI <30kg/ m ² : 9 (range: 2-30) BMI ≥30kg/m ² : 8 (range: 3-19)	BMI <30kg/m ² : 23% BMI ≥30kg/m ² : 22%	LNF 100%	
Chisholm, 2009 ²¹	BMI <30kg/ m ² : 9.5% (0.2- 61.8%) BMI ≥30kg/ m ² : 9.6% (2.3- 51%)]		LNF 67%, LAF 31%, LTF 2%	BMI ≤24kg/m ² : Mean 96 (range: 12-180) BMI 25-29kg/m ² : Mean 91.2 (range: 12- 180) BMI ≥30kg/m ² : Mean 79.2 (range: 12- 180)
Irino, 2010 ²²			LNF 46%, LTF 54%	Median: 30.5
Tekin, 2012 ²³	BMI ≤24kg/m ² : 9.78 ±9.6 BMI 25-29kg/ m ² : 7.78 ±9.17 BMI ≥30kg/m ² : 8.88 ±8.13	BMI ≤24kg/m ² : 7% BMI 25-29kg/m ² : 9.6% BMI ≥30kg/m ² : 10.6%	BMI ≤24kg/m ² : LNF 75%, LTF 25% BMI 25-29kg/m ² : LNF 69%, LTF 32% BMI ≥30kg/m ² : LNF 45%, LTF 55% (p<0.00001)	BMI ≤24kg/m ² : Mean 55.35 ±16.92 BMI 25-29kg/m ² : Mean 55.35 ±16.92 BMI ≥30kg/m ² : Mean 50.80 ±15.59
BMI = body mass index; BMIV = Belsey Mark IV; LAF = laparoscopic anterior fundoplication; LNF = laparoscopic Nissen fundoplication; LOS = lower oesophageal sphincter; LTF = laparoscopic Toupet fundoplication;				

Table 3 Study conclusions

Study	Conclusion
Fraser, 2001 ⁷	No correlation between BMI and outcome following LNF.
Perez, 2001 ⁸	Irrespective of surgical approach, obese patients have higher failure rate following ARS.
Anvari, 2006 ⁹	Morbid obesity does not adversely affect outcome following LNF.
Morgenthal, 2007 ¹⁰	Morbidly obese patients have higher risk of failure.
Luketina, 2015 ¹¹	Obesity does not affect success of laparoscopic ARS.
Campos, 1999 ¹⁶	Excellent or good outcome following LNF can be achieved in high BMI patients.
Hahnloser, 2002 ¹⁷	High BMI is a risk factor for complications following LNF.
Winslow, 2003 ¹⁸	Symptom relief, complication rates and anatomic failure rates are similar in obese and non-obese patients.
D'Alessio, 2005 ¹⁹	Perioperative morbidity, symptom reduction and patient satisfaction following LNF are similar in obese and non-obese patients.
Ng, 2007 ²⁰	Outcomes are similar in obese and morbidly obese patients following LNF.
Chisholm, 2009 ²¹	BMI does not influence clinical outcome after laparoscopic ARS.
Irino, 2010 ²²	Patients with BMI >25kg/m ² have higher satisfaction scores and are good candidates for laparoscopic ARS.
Tekin, 2012 ²³	Laparoscopic ARS is safe but more demanding in obese patients.

ARS = antireflux surgery; BMI = body mass index; LNF = laparoscopic Nissen fundoplication

Study limitations

There are several limitations to this review. The included studies were from single centres and were mostly retrospective. None of the studies fulfilled all of the MINORS criteria,¹⁵ meaning that firm conclusions cannot be drawn. The incidence of postoperative symptoms (dysphagia, food intolerance, belching), continued use of medications (proton pump inhibitors, H₂ blockers) and satisfaction scores were not reported adequately in the included studies. Furthermore, caution is advised in the interpretation of the results with respect to very severely obese patients (BMI >40kg/m²) undergoing ARS in clinical practice as all patients with BMI >30kg/m² were grouped together in a single obese category in the studies included in our analysis. However, given the lack of currently available literature, our review adds important information on antireflux surgery in obese patients.

Conclusions

Analysis of pooled data revealed that ARS in obese patients with GORD is safe and outcomes are comparable with those for patients with a BMI in the normal range. LNF is the most commonly undertaken procedure in obese patients, with acceptable conversion rates. The mean operative time and mean length of hospital stay were prolonged in the high BMI group but complication and reoperation rates were not significantly higher. Consequently, a high BMI should not be a deterrent to considering ARS for appropriate patients.

References

- Dent J, El-Serag HB, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut* 2005; **54**: 710–717.
- Faria R, Bojke L, Epstein D *et al*. Cost-effectiveness of laparoscopic fundoplication versus continued medical management for the treatment of gastro-oesophageal reflux disease based on long-term follow-up of the REFLUX trial. *Br J Surg* 2013; **100**: 1,205–1,213.
- Catarci M, Gentileschi P, Papi C *et al*. Evidence-based appraisal of antireflux fundoplication. *Ann Surg* 2004; **239**: 325–337.
- Peters MJ, Mukhtar A, Yunus RM *et al*. Meta-analysis of randomized clinical trials comparing open and laparoscopic anti-reflux surgery. *Am J Gastroenterol* 2009; **104**: 1,548–1,561.
- Friedenberg FK, Xanthopoulos M, Foster GD, Richter JE. The association between gastroesophageal reflux disease and obesity. *Am J Gastroenterol* 2008; **103**: 2,111–2,122.
- Pandolfino JE, El-Serag HB, Zhang Q *et al*. Obesity: a challenge to esophagogastric junction integrity. *Gastroenterology* 2006; **130**: 639–649.
- Fraser J, Watson DI, O'Boyle CJ, Jamieson GG. Obesity and its effect on outcome of laparoscopic Nissen fundoplication. *Dis Esophagus* 2001; **14**: 50–53.
- Perez AR, Moncure AC, Rattner DW. Obesity adversely affects the outcome of antireflux operations. *Surg Endosc* 2001; **15**: 986–989.
- Anvari M, Bamehriz F. Outcome of laparoscopic Nissen fundoplication in patients with body mass index ≥ 35 . *Surg Endosc* 2006; **20**: 230–234.
- Morgenthal CB, Lin E, Shane MD *et al*. Who will fail laparoscopic Nissen fundoplication? Preoperative prediction of long-term outcomes. *Surg Endosc* 2007; **21**: 1,978–1,984.
- Luketina RR, Koch OO, Köhler G *et al*. Obesity does not affect the outcome of laparoscopic antireflux surgery. *Surg Endosc* 2015; **29**: 1,327–1,333.
- Liberati A, Altman DG, Tetzlaff J *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med* 2009; **151**: W65–W94.
- Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* 2000; **894**: i–xii, 1–253.
- DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**: 177–188.
- Slim K, Nini E, Forestier D *et al*. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. *ANZ J Surg* 2003; **73**: 712–716.
- Campos GM, Peters JH, DeMeester TR *et al*. Multivariate analysis of factors predicting outcome after laparoscopic Nissen fundoplication. *J Gastrointest Surg* 1999; **3**: 292–300.

17. Hahnloser D, Schumacher M, Cavin R *et al*. Risk factors for complications of laparoscopic Nissen fundoplication. *Surg Endosc* 2002; **16**: 43–47.
18. Winslow ER, Frisella MM, Soper NJ, Klingensmith ME. Obesity does not adversely affect the outcome of laparoscopic antireflux surgery (LARS). *Surg Endosc* 2003; **17**: 2,003–2,011.
19. D'Alessio MJ, Arnaoutakis D, Giarelli N *et al*. Obesity is not a contraindication to laparoscopic Nissen fundoplication. *J Gastrointest Surg* 2005; **9**: 949–954.
20. Ng VV, Booth MI, Stratford JJ *et al*. Laparoscopic anti-reflux surgery is effective in obese patients with gastro-oesophageal reflux disease. *Ann R Coll Surg Engl* 2007; **89**: 696–702.
21. Chisholm JA, Jamieson GG, Lally CJ *et al*. The effect of obesity on the outcome of laparoscopic antireflux surgery. *J Gastrointest Surg* 2009; **13**: 1,064–1,070.
22. Irino T, Takeuchi H, Ozawa S *et al*. Age and body mass index: significant predictive factors for successful laparoscopic antireflux surgery. *Surg Today* 2010; **40**: 1,137–1,143.
23. Tekin K, Toydemir T, Yerdel MA. Is laparoscopic antireflux surgery safe and effective in obese patients? *Surg Endosc* 2012; **26**: 86–95.
24. Society of American Gastrointestinal and Endoscopic Surgeons. *Guidelines for Surgical Treatment of Gastroesophageal Reflux Disease (GERD)*. Los Angeles: SAGES; 2010.
25. Khan A, Kim A, Sanossian C, Francois F. Impact of obesity treatment on gastroesophageal reflux disease. *World J Gastroenterol* 2016; **22**: 1,627–1,638.
26. Shrier I, Boivin JF, Steele RJ *et al*. Should meta-analyses of interventions include observational studies in addition to randomized controlled trials? A critical examination of underlying principles. *Am J Epidemiol* 2007; **166**: 1,203–1,209.
27. Faber T, Ravaud P, Riveros C *et al*. Meta-analyses including non-randomized studies of therapeutic interventions: a methodological review. *BMC Med Res Methodol* 2016; **16**: 35.
28. Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. *N Engl J Med* 2000; **342**: 1,878–1,886.
29. Stroup DF, Berlin JA, Morton SC *et al*. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA* 2000; **283**: 2,008–2,012.
30. Tandon A, Pathak S, Lyons NJ *et al*. Meta-analysis of closure of the fascial defect during laparoscopic incisional and ventral hernia repair. *Br J Surg* 2016; **103**: 1,598–1,607.