

Laparoscopic partial nephrectomy in obese patients: a systematic review and meta-analysis

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- To compare the safety and efficacy of laparoscopic partial nephrectomy (LPN) in obese and non-obese patients.
- We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1966 to November 2011), EMBASE (1980 to November 2011), CINAHL, Clinicaltrials.gov, Google Scholar, reference lists of articles and abstracts from conference proceedings without language restriction for studies comparing LPN in obese and non-obese patients.
- Four observational cohort studies were included for 256 obese patients compared with 403 non-obese patients who underwent LPN.
- There was no difference in operative duration (mean difference [MD] 5.64, 95% confidence interval [CI] -3.80 to 15.09), warm ischaemic time (MD -1.04, 95% CI -2.68 to 0.59), estimated blood loss (MD 53.73, 95% CI 0.72-106.74) or

What's known on the subject? and What does the study add?

The literature yielded only four studies on the subject; however, no clear outcome can be taken from individual studies.

This review adds a meta-analysis of these four studies to make the patient cohort larger and to allow for a greater understanding of the procedure in this select group of patients.

hospital stay (MD -0.04, 95% CI -0.30 to 0.22).

- There was no difference in complications in total (odds ratio [OR] 1.02, 95% CI 0.70-1.49), intraoperative complications (OR 0.68, 95% CI 0.30-1.53), or postoperative complications (OR 1.15, 95% CI 0.75-1.77).
- The obese group had significantly more Clavien grade III complications (OR 3.95, 95% CI 1.36-11.42), despite the low absolute incidence, with 4.3% (11/256) in the obese group vs 1.5% (6/403) in the non-obese group.

- Experienced laparoscopic surgeons can safely and efficiently perform PN for obese patients with comparable results to those of non-obese patients.
- The likelihood of major (Clavien Classification \geq III) complications is higher for the obese patient.

KEYWORDS

laparoscopy, partial nephrectomy, renal cell carcinoma, obesity, systematic review, meta-analysis

INTRODUCTION

Worldwide, obesity is on the rise and is now considered an epidemic with >300 million people afflicted [1]. About 25-34% of the adult population of the USA are considered obese [2-7]. Evidence suggests that the incidence of RCC increases with obesity, but that obese patients might have a better prognosis compared with non-obese patients [3,4,6]. With advances in imaging technology the detection of smaller RCCs has increased, leading to current figures of up to 60% of RCC being <4 cm [8,9]. The identification of smaller renal tumours has

led to an increase in the number of patients who are candidates for partial nephrectomy (PN) resulting in decreased renal insufficiency [8,10].

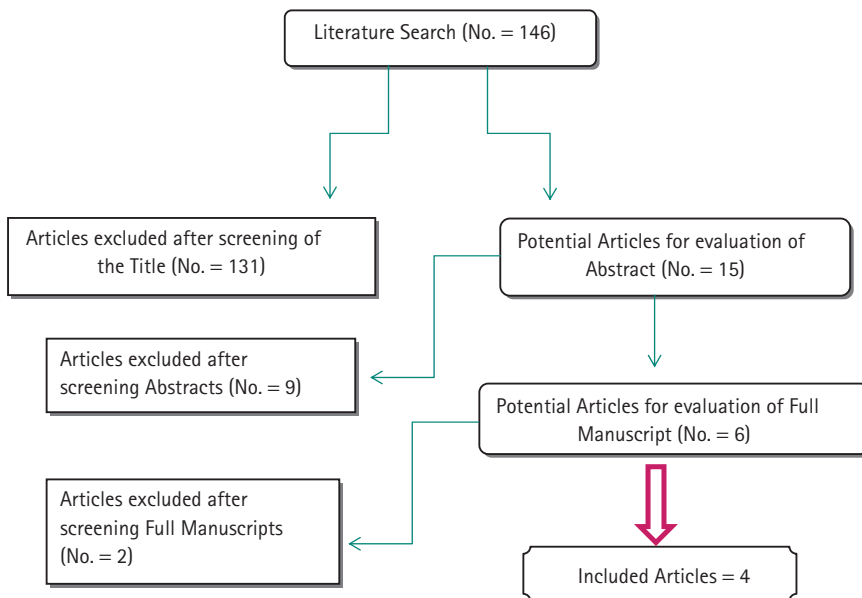
With advances in laparoscopic techniques, equipment, and operator skill, laparoscopic PN (LPN) has emerged as a viable alternative to open PN with comparable oncological outcomes, less morbidity, and faster recovery [8,9,11]. However, there are certain circumstances that may make LPN more challenging, e.g. operating on obese patients [6]. These patients not only tend to have a prolonged procedure but also often have

multiple co-morbidities with a higher risk of intra and postoperative complications [3-6].

With the rising incidence of obesity in society, laparoscopy has been increasingly used for PN in obese patients [2-6]. Nevertheless, controversy still remains about the safety of the laparoscopic approach despite evidence of more rapid recovery and equivalent oncological results with laparoscopy [5].

Therefore, we aimed to conduct a Cochrane level, systematic review of the literature with a meta-analysis of the results to

FIG. 1. Flowchart for article selection process of the review.



evaluate the safety and efficacy of LPN compared with the standard open PN.

The primary aim was to compare the efficacy of LPN in obese and non-obese patients; specific outcomes include the operative duration, the warm ischaemic time (WIT), estimated blood loss (EBL), and hospital stay. Our secondary objectives were to compare the safety of LPN between the two groups, with outcomes such as complications, conversion rates, and transfusion rates.

MATERIALS AND METHODS

SEARCH STRATEGY AND STUDY SELECTION

The systematic review was performed according to the Cochrane reviews guidelines and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [12].

The search strategy was conducted to find relevant studies from MEDLINE (1966 to October 2011), EMBASE (1980 to October 2011), Cochrane Central Register of Controlled Trials – CENTRAL (in The Cochrane Library Issue 1, 2011), CINAHL (1982 to October 2011), Clinicaltrials.gov, Google Scholar and Individual urological journals. The search was conducted in October 2011.

Terms used included: 'Laparoscopic', 'Laparoscopy', 'Partial', and 'Nephrectomy', and 'Obesity'.

Medical Subject Headings (MeSH) phrases included:
 (('Laparoscopy'[MeSH]) AND 'Obesity'[MeSH]) AND 'Nephrectomy'[MeSH]
 (('Obesity'[MeSH]) AND 'Nephrectomy'[MeSH])

Papers in languages other than English were included if data was extractable, also references of searched papers were evaluated for potential inclusion. Authors of the included studies were contacted wherever the data was not available or not clear.

Three reviewers (O.A., B.S., and R.S.) identified all studies that appeared to fit the inclusion criteria for full review. Each reviewer independently selected studies for inclusion in the review. Disagreement between the extracting authors was resolved by consensus or referred to a third author (G.H.).

DATA EXTRACTION AND ANALYSIS

The objectives were to evaluate the efficacy and safety of LPN for obese compared with non-obese patients. Obesity was defined as having a body mass index (BMI) of ≥ 30 kg/m².

The following variables were extracted from each study: patient demographics, tumour size, laterality, BMI, operating duration, ischaemic time, blood loss, transfusion rates, hospital stay, conversion rates, RCC rate, positive margins, and complications which were classified according the Clavien postoperative classification [13]. The data of each study was grouped into a meta-analysis, in an intention-to-treat basis, to allow a numerical representation of the results. Only similar results that were pooled from the included studies were meta-analysed [14]. For dichotomous data a Mantel-Haenszel chi-square test was used and expressed as odds ratios (ORs) with 95% CIs and for continuous data an inverse variance was used and the mean difference (MD) used, or the standardised mean difference (SMD), if different scales have been used [14].

There was no heterogeneity between the studies that were analysed using a chi-square test on N-1 degrees of freedom, with an alpha of 0.05 used for statistical significance and with the I² test [14,15]. I² values of 25%, 50% and 75% correspond to low, medium and high (significant) levels of heterogeneity [14]. Data was pooled using the fixed-effect model as there was no statistically significant heterogeneity (I² > 50% was considered as significant heterogeneity) existing between studies [14]. We used Review Manager (RevMan 5.0.23) to calculate the comparisons and plot the quality assessment tables.

QUALITY ASSESSMENT

We intended to assess the methodological quality of the included studies by using the National Health Service's Critical Appraisal Skills Programme (CASP) amalgamated with Newcastle-Ottawa scale checklist for methodology quality assessment [16].

RESULTS

The study selection process depicted in Fig. 1 shows that 146 titles were reviewed for potential inclusion. Of which, 140 were excluded due to irrelevance from the title or abstract. Of the remaining six, four were included, the remaining two were excluded [2–7]. The Naeem *et al.* [7] study was on robot-assisted PN in obese patients rather than laparoscopy. While the Gong *et al.* [5]

article was a review of the impact BMI has on the outcomes of laparoscopic surgery in general rather than focusing on just PN.

CHARACTERISTICS OF THE INCLUDED STUDIES

Four studies were included with 659 patients of which 256 were obese and were compared with 403 non-obese patients [2,4,6,7]. All the studies were retrospective studies in English language publications and conducted between 1998 and 2010. All the studies compared LPN between obese and non-obese patients.

Three of the studies were included in the meta-analysis of the patients' age and tumour size [3,4,6]. All the studies reported on the laterality of the tumours. Only two studies reported on the means of the BMI of the patients and the RCC rate [3,4]. Anast *et al.* [2] conducted a comparison of laparoscopic radical, partial, and simple nephrectomies in obese and non-obese patients and had not differentiated between the three procedures in numerous outcomes of this review and therefore their data was not included in those sections.

All the studies reported on the operative duration, WIT, EBL, and hospital stay. Although, one study did not report the WIT and therefore no data available for the meta-analysis [2]. Furthermore, only one study reported positive margins [6].

All the studies reported on complication rates. However, two of the studies divided their complications into intra and postoperative [3,4]. Eaton *et al.* [6] classified the complications accord to the Clavien system, while Anast *et al.* [2] classified the complications as minor and major. Minor complications are those classified as Clavien I or II while, major complications are Clavien \geq III.

All the studies reported on conversion rates [2–4], while three reported on transfusion rates [2,3,6].

QUALITY ASSESSMENT

In the absence of randomised controlled trials dealing with the issue, a meta-analysis of observational studies can be considered vital to fill the void [17]. Assessment of quality of observational studies is more

FIG. 2. Quality assessment (risk of bias summary: review authors' judgements about each risk of bias item for each included study).

	Did the study the study Title and Abstract indicate the study purpose?	Was the study conducted by using a review board approved protocol?	Did the authors define the objectives of the study?	Was there a clear definition of the outcomes measured?	Were the cases and controls subject to same ascertainment?	Was an appropriate statistical method used?	Did the results reflect the aim of the study?	Any missing or Incomplete outcome data?	Did the authors report complications without bias?	Any selective reporting?	Did the authors adequately discuss their results?	Was the conclusion a reflection of the results and discussion?	Any other source of Bias?	Any Confounding Issues?
Anast 2004[2]	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Colombo 2007[3]	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Eaton 2011[6]	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Romero 2008[4]	+	+	+	+	+		+	+	+	+	+	+	+	

difficult than that of randomised controlled trials and there is a lack of validated assessment tools available [17]. Despite this, the Cochrane Non-Randomized Studies Methods Working group recommend the use of the Newcastle-Ottawa Scale checklist to assess these types of studies [17,18]. Therefore, we have made a checklist that depicts all the important points that observational studies need to address (Fig. 2 [2–4,6]).

Although all the studies are limited by being retrospective and have a potential risk of selection bias, we found no other potential sources of bias in any of the studies. However, one study had a confounding issue, which was not made clear by the corresponding author despite attempts to contact him. Romero *et al.* [4] presented their data in both median (range) in the results section and again as mean \pm SD in the tables. There was no mention of which data set was used for the statistical comparison between the two groups and to

why both data sets were used. However, this did not alter the meta-analysis of this review.

EFFECTS OF INTERVENTION

There was no difference between the two groups for tumour size, laterality, and RCC rate ($P = 0.86, 0.75, 0.63$, and 0.18). There was of course significantly higher BMI within the obese group ($P < 0.001$). The obese group additionally had a younger cohort of patients compared with the non-obese group ($P = 0.01$; Table 1).

Concerning the primary objective of the present review, the efficacy, there was no statistically significant difference between obese and non-obese patients in any of the parameters considered. Both groups were statistically similar for operative duration ($P = 0.24$; MD 5.64, 95% CI –3.80 to 15.09), WIT ($P = 0.21$; MD –1.04, 95% CI –2.68 to 0.59), EBL ($P = 0.05$; MD 53.73, 95% CI 0.72–106.74) or hospital stay ($P = 0.76$; MD

TABLE 1 Table showing study results non-obese vs obese

Reference	No. of patients	Mean (SD) age, years	Mean (SD) tumour size, cm	Right:left, n	Mean (SD) BMI, kg/m ²	Malignant, n	Mean (SD) operating time, min	Mean (SD) WIT, min	Mean (SD) EBL, mL	Positive margins, n	Mean (SD) hospital stay, days
Anast <i>et al.</i> 2004 [2]	32 vs 12	NA	NA	21:11 vs 8:4	NA	NA	233 (78) vs 260 (51)	NA	189 (189) vs 427 (637)	2/77 vs 2/48	3.1 (2.8) vs 4.5 (3.7)
Colombo <i>et al.</i> 2007 [3]	238 vs 140	60.2 (13.5) vs 57.6 (11.2)	2.8 (1.3) vs 2.8 (1.1)	131:107 vs 76:64	25.7 (2.6) vs 35.7 (6.4)	139 vs 92	205.2 (59.1) vs 205.2 (57.9)	32.3 (10.1) vs 31.7 (10)	76:249 (318) vs 45:210 (213)	NA	76:2.5 (1.6) vs 45:2.4 (1)
Romero <i>et al.</i> 2008 [4]	56 vs 56	58 (11) vs 55.4 (10.8)	3.1 (0.9) vs 3.1 (1.2)	28:28 vs 30:26	25.5 (2.5) vs 36.6 (7.2)	42 vs 45	181.1 (62.4) vs 195.2 (59.8)	31 (9.9) vs 28.2 (10.5)	162:222 (241) vs 95:354 (787)	NA	162:3 (1.6) vs 95:3 (1.6)
Eaton <i>et al.</i> 2011 [6]	77 vs 48	55.61 (12.26) vs 54.02 (12.16)	2.64 (2) vs 2.74 (1.37)	27:50 vs 21:27	NA	64 vs 39	201.49 (42.02) vs 220.16 (46.38)	29.81 (5) vs 29.33 (6.27)	238.42 (365.52) vs 290.76 (228.6)	NA	3.77 (2) vs 3.72 (1.05)

NA, not available.

−0.04, 95% CI −0.30 to 0.22) (Table 1 and Fig. 3 [2–4,6]). Furthermore, two of 48 patients in the obese group vs two of 77 in the non-obese group had positive margins; however, this was not statistically significant ($P = 0.63$).

The secondary objective was to compare the safety of LPN between the groups. There was no statistically significant difference between obese and non-obese patients for complications in total ($P = 0.9$; OR 1.02, 95% CI 0.70–1.49), intraoperative complications ($P = 0.36$; OR 0.68, 95% CI 0.30–1.53), or postoperative complications ($P = 0.51$; OR 1.15, 95% CI 0.75–1.77).

Furthermore, there was no significant difference for procedure conversions ($P = 0.05$; OR 4.13, 95% CI 1.00 to 16.97) or blood transfusion rates ($P = 0.28$; OR 1.60, 95% CI 0.68–3.74) (Fig. 4 [2–4,6]).

Interestingly, when we group the complications according to the Clavien classification of postoperative complications, we found that for Clavien I and II there was no significant difference between the groups with 52/403 complications in the non-obese group and 38/256 in the obese ($P = 0.03$; OR 1.10, 95% CI 0.69–1.73). However, the obese group had significantly more complications classified as Clavien III with 11/256 complications compared with six of 403 in the non-obese group ($P = 0.01$; OR 3.95, 95% CI 1.36–11.42).

DISCUSSION

The present review found no difference between the obese and non-obese groups for tumour size, laterality, or cancer incidence (Table 1). However, evidence suggests that obesity is a risk factor for RCC due to the elevated concentration of insulin-like growth factor-I, free oestrogens and lipid peroxidation [3,6]. However, a quantitative review by Bergstrom *et al.* [19] reported that 27% and 29% of RCC among women and men respectively was related to excess weight or obesity. Despite the increased incidence of RCC in the obese group, studies have suggested a better prognosis in the obese group [3,4,6].

The better prognosis encourages the aggressive management of obese patients with RCC. However, due to the accompanying co-morbidities and difficulty

in anaesthetising these patients, risks of major complications have to be considered.

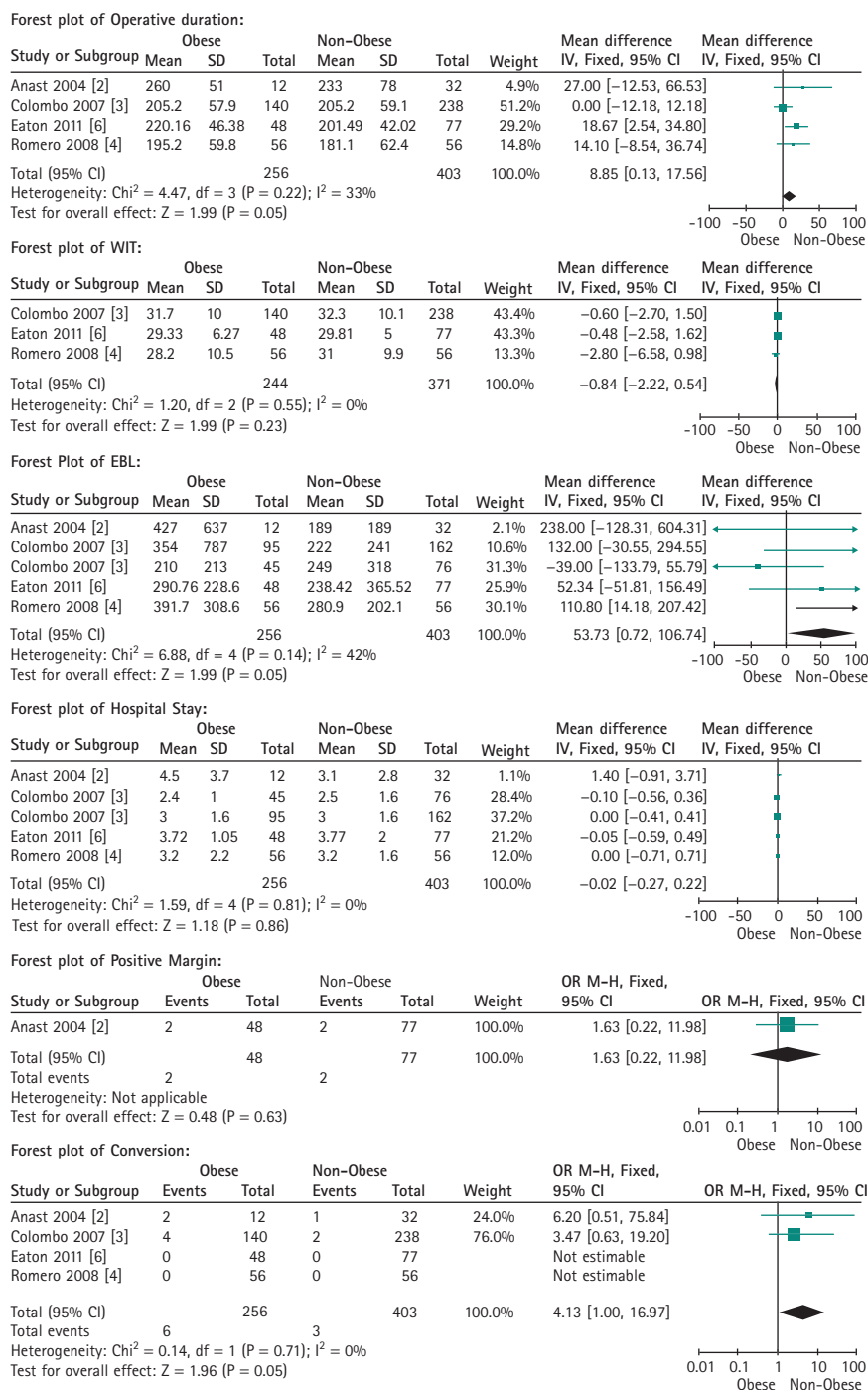
Matin *et al.* [20] conducted a study to evaluate age and comorbidities as risk factors after laparoscopic procedures. They reported that laparoscopy is well tolerated with no increased risk of complications in patients aged ≥ 65 years; however, is associated with a prolonged hospital stay in this population. The present review found that the non-obese patients were older; however, no difference was found between the groups for hospital stay (Fig. 3).

While Gong *et al.* reported that obesity is associated with increased operative difficulty and prolonged operative durations with increased intraoperative complications, we found no difference between the two groups for operative duration (Fig. 3) [5]. We also found no evidence to suggest that obese patients are more likely to develop intraoperative complications (Fig. 4). However, when a sub-group analysis was conducted to classify the complications according to the Clavien classification; we found that obese patients were significantly more likely to develop Clavien III complications compared to the non-obese patients (Fig. 4). There was no difference between obese and non-obese for Clavien I and CII complications (Fig. 4).

Furthermore, there was no difference in conversion rates, but there was a higher trend in the obese group for conversions (six of 256 vs three of 403). There was also no difference in the intraoperative EBL (Fig. 3). By contrast, to Jacobs *et al.* [21] reported that obese patients had longer operative durations and increased blood loss.

Numerous comparative studies comparing obese and non-obese patients have shown a variety of results, but no conclusive report has been published in this regard [2–6]. The present review, meta-analysed four studies that met the inclusion criteria and the only significant difference found between the obese and non-obese patient undergoing LPN was the greater risk of developing a major complication class Clavien \geq III (Fig. 4). This in itself should alert surgeons to be especially vigilant when managing obese patients intra- or postoperatively. However, the incidence of Clavien III complications was still low at 4.3% (11/256).

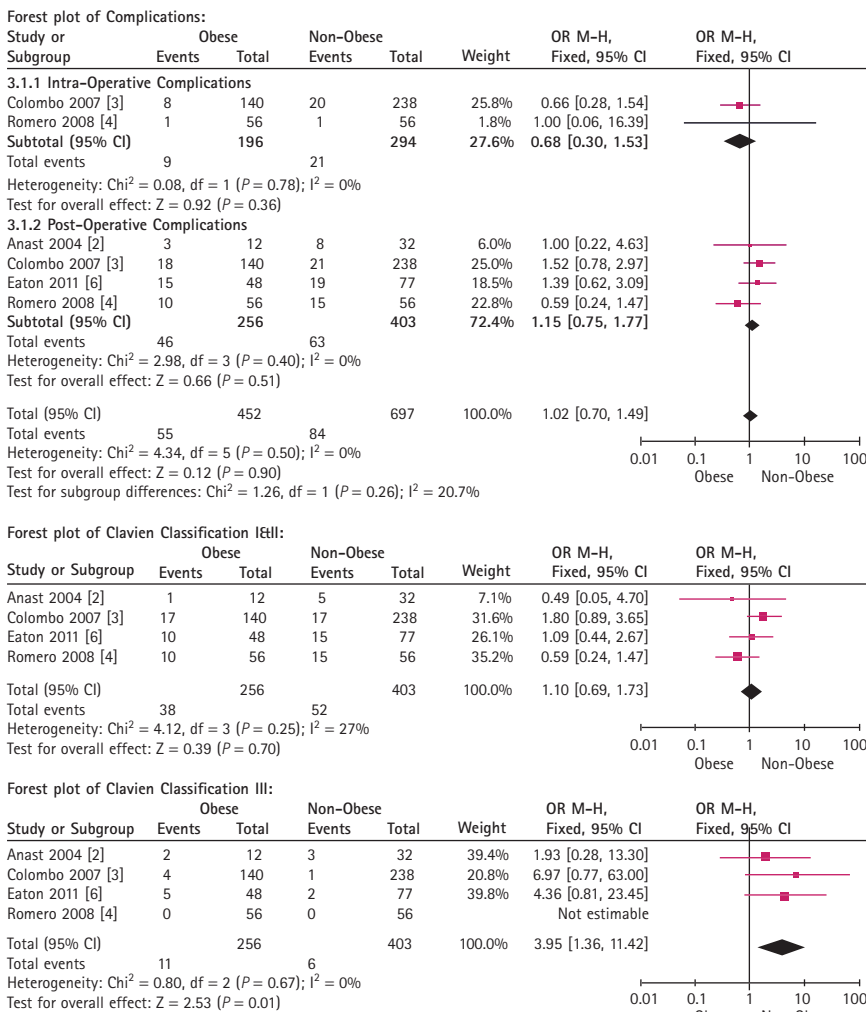
FIG. 3. Forest plots of outcomes.



Limitations of the present review are that the studies meta-analysed are observational control studies. However, due to the nature of the procedure in question, LPN, and looking at two distinct groups of patients, the obese and non-obese, randomisation and 'blinding' are not feasible options. To this end, the present review is an accurate

depiction of the comparison between these two cohorts for LPN. The studies also did not detail nephrometry scoring of renal tumours and therefore comparison corrected for similar tumour characteristics is not possible. A further limitation is the differing experience of the surgeons conducting the procedures, although none of the

FIG. 4. Forest plots of complications and Clavien classifications.



studies mention the level of expertise, all the studies were conducted in high-volume centres.

As more centres conduct these procedures, a prospective multi-centred, protocol-driven study would be useful. Including various centres with different levels of operator experience would be more representative of the standard Urological cross-section of practice. Furthermore, sub-group analysis comparing different levels of obesity to normal-weighted patients will allow a more robust comparison.

CONCLUSION

Based on the findings of the present meta-analysis, LPN can be safely and efficiently performed for obese patients with

comparable results to those for non-obese patients. Nevertheless, although still uncommon, the likelihood of major complications is higher for obese patients.

CONFLICT OF INTEREST

None declared.

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Abbreviations: (L)PN, (laparoscopic) partial nephrectomy; WIT, warm ischaemic time; EBL, estimated blood loss; BMI, body mass index; OR, odds ratio; (S)MD, (standardised) mean difference.