Review Article Meta-analysis of perioperative outcomes between obese and non-obese patients on minimally invasive partial nephrectomy

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Abstract: Purpose: The safety and efficacy of minimally invasive partial nephrectomy (MIPN) on obese patients is controversial. The existing evidence lacks details about the differences in perioperative outcomes between obese and non-obese patients. This study aims to unveil the relationship between obesity and perioperative outcomes in MIPN. Methods: We conducted a systemic review and meta-analysis to clarify this relationship. Relevant studies were identified in four databases (PubMed, Cochrane Library, Web of Science and Embase), and twelve studies were included, with nine studies regarding laparoscopic partial nephrectomy (LPN) and four studies regarding robot-assisted laparoscopic partial nephrectomy (RLPN). Intraoperative outcomes included the operative duration (OD), estimated blood loss (EBL), warm ischemia time (WIT), transfusion rate, length of stay (LOS) and conversion to open surgery rate. Postoperative outcomes included the complication rate and the presence of positive margins. Results: The results showed that the obese group exhibited a longer OD, larger EBL, longer WIT and LOS, and higher ratio of total and minor complications than those of the non-obese group in RLPN (p<0.05). The results also demonstrated that the obese group had a larger EBL and higher ratio of total and minor complications: MIPN could be performed in obese patients with numerous advantages, but some perioperative outcomes need to be considered with discretion.

Keywords: Obesity, perioperative outcomes, body mass index, minimally invasive partial nephrectomy

Introduction

Renal cell carcinoma (RCC) is the most common kidney neoplasm in adults, and its incidence increases by nearly 2% per year over the last two decades [1, 2]. Although some patients with renal masses remain asymptomatic until the late stages of the disease, the majority of renal cell carcinoma cases are detected incidentally when abdominal ultrasound or computed tomography is carried out for physical examination or other medical reasons. Small renal masses (SRMs) are defined as contrastenhancing masses of 4 cm or less on abdominal imaging [3]. Minimally invasive partial nephrectomy (MIPN) is one of the standards of care for the management of SRMs, and it includes pure laparoscopic partial nephrectomy (LPN) and robot-assisted laparoscopic partial nephrectomy (RLPN) [4].

Obesity has been a global medical problem for decades. It is associated with an increased risk of many chronic diseases and several types of cancer [5-7]. Obesity was also reported as one of the etiological factors for RCCs [8]. However, whether obesity influences the perioperative outcomes of MIPN still remains unclear.

Previous meta-analyses reported that the incidence of major complication was higher in obese patients than non-obese patients who underwent LPN [9]. However, similar issues with RLPN have not been illustrated by high levels of evidence, such as systematic reviews or meta-analyses. We aimed to perform a Cochrane level, systematic review of the literature with a meta-analysis comparing the perioperative outcomes of obese and non-obese patients who underwent MIPN, performing the first evidence-based medical research of this topic on RLPN as well as updating the previous metaanalyses on LPN.

Materials and methods

Information sources and search strategies

A literature search was performed by all the authors on March 26, 2018 using PubMed, the Cochrane Library, the Web of Science and Embase. Meshed search headings with combined keywords were searched for in the (Title/ Abstract) section that included the words "obesity", "body mass index", "nephrectomy", "laparoscopy", "partial nephrectomy", "laparoscopic partial nephrectomy" and "robot-assisted partial nephrectomy". The related article functions were used to broaden the search, and they were searched for papers published in all available years of each database. All studies and abstracts were reviewed irrespective of language. Internet search was accompanied with the manual search of the reference lists of all retrieved studies, reviews, and conference abstracts. The search terms will be adapted with other bibliographic databases in combination with database-specific filters. There were no language, regional or publication status restrictions. Likewise, there were no restrictions regarding the types of study design eligible for inclusion.

The protocol and methods of this meta-analysis were conducted according to the recommendations of the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [10]. The protocol was registered in PR-OSPERO as International prospective registration of systematic review (Registration number: CRD42016046906) [11].

Inclusion criteria

Based on the principle of PICOS (participant, intervention, comparison, outcomes and study design) [10], the following criteria were used for

study selection. 1. Participants with small renal masses (of any nationality and ethnicity) who required minimally invasive partial nephrectomy, including laparoscopic partial nephrectomy or robotic-assisted partial nephrectomy, were included. 2. Obesity was defined as a BMI \geq 30 kg/m², while non-obesity was defined as a BMI <30 kg/m². 3. The measured outcomes included several perioperative indexes and parameters.

Exclusion criteria

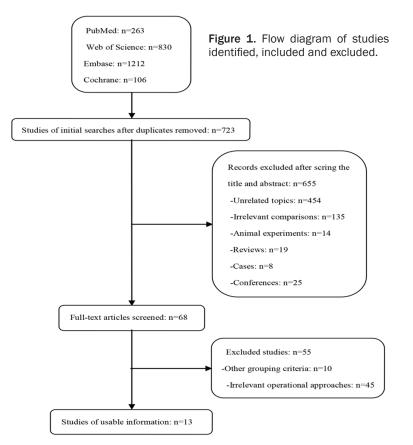
1. Studies were excluded when full information was unavailable, and could not be obtained from the authors. 2. Animal experiments, conference abstracts and irrelevant studies were likewise excluded from analysis. 3. Studies reporting combined data from MIPN and other kinds of nephrectomy were also excluded. 4. Patients who underwent radical nephrectomy, simple nephrectomy and open surgery were not included.

Data extraction

Intraoperative outcomes: The operative duration (OD), estimated blood loss (EBL), warm ischemia time (WIT), transfusion rate, length of stay (LOS) and conversion to open surgery rate were measured as intraoperative outcomes.

Postoperative outcomes: The total complications, major complications, minor complications and presence positive margins were recorded as postoperative outcomes.

Three authors independently screened the studies, read the full articles, and extracted the following data from the included studies using a pre-standardized data extraction form. The study inclusion criteria and sample size, methods of sampling and grouping, types of participants, interventions/comparisons, outcome measures, and statistical methods of the studies were recorded on this form. All data were checked twice by these three authors, and any discrepancy was resolved by the adjudicating senior author. In cases of missing data, we made attempts to contact the study investigators for further information. For continuous variables, the standard deviations (SDs) and means were estimated when the studies only provided sample sizes, ranges, and medians



[12, 13]; SDs of absolute changes from baseline were inputted and we used a correlation of r = 0.5 as described in the Cochrane Handbook for Systematic Reviews of Interventions. The consolidation of data from different BMI groups was based on equations from published materials [14].

Methodological quality assessment

According to the World Health Organization classification, all subjects in these reports could be divided into three BMI groups: the normal group (BMI <25 kg/m²), the overweight group ($25 \le BMI < 30 \text{ kg/m}^2$), and the obese group (BMI \geq 30 kg/m²). Based on the Clavien-Dindo grading system, postoperative complications were classified into five grades. Grade I and II were regarded as minor complications, which required pharmacological treatment but no invasive or radiological interventions. Major complications included grade III, IV and V complications. Grade III and IV complications needed the interventions mentioned in the minor complications and even ICU management for life-threatening complications. A grade V complication involved a patient death [15]. The methodological quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS] [16, 17], which contained three aspects of study design: patient selection, comparability of the study groups, and assessment of outcomes. A score of 0 to 9 (allocated as stars) was allocated to each study. Studies with a score of ≥ 6 stars were regarded as high-quality studies.

Statistical analysis

All meta-analyses were performed by Review Manager Version 5.3 (Cochrane Collaboration, Oxford, UK). The weighted mean difference (WMD) was used to analyze continuous variables, and odds ratios (ORs) were used to analyze dichotomous outcomes.

An OR of more than 1 indicated a higher risk in the obese groups. The estimation of OR was considered to be statistically significant if P was less than 0.05 and the 95% CI did not include a value of 1. All results were reported with a 95% confidence interval (CI).

Heterogeneity was quantified using the l^2 statistic, and statistical heterogeneity was evaluated by the chi-square test with significance set at P<0.10. The assumption of homogeneity between studies was regarded as invalid if the *p* value was less than 0.1 and the randomeffects models were reported after exploring the causes of heterogeneity. Otherwise, the fixed-effects models were reported. A two-tailed *p* value of less than 0.05 was considered statistically significant.

Sensitivity analyses were performed for highquality studies. Studies with six or more stars on the modified Newcastle-Ottawa scale were included in sensitivity analysis. Funnel plots were used to screen for potential publication bias. Revman 5.3 were used to conduct funnel plots in this study.

Surgery	Authors	Voar	Country	BMI, kg/	Study	Patients	s, n.	Mean [SD]	Mean [SD]	Mean [SD]	Right:	Malignant,	Matching*	Quality score
procedures	Autions	ieai	Country	m ²	design	Non-Obesity	Obesity	age, years	BMI, kg/m²	tumor size, cm	Left, n	n	watching	Quality Score
RLPN														
	Abdullah N	2015	US	<30 >30	R	1030	806	61 [2.83] vs 59 [2.33]	26 [0.83] vs 33.8 [1.07]	2.5 [0.28] vs 2.9 [0.33]	NA	NA	1, 2, 3, 6, 8	****
	Isac WE	2012	US	<30 >30	R	147	103	59.49 [12.2] vs 57.66 [11.2]	NA	2.44 [0.27] vs 3.09 [0.47]	NA	NA	1, 2, 3, 4, 6, 8	*****
	Kiziloz H	2012	US	<30 >30	R	162	108	61 [12.21] vs 57.42 [10.45]	25.93 [2.66] vs 34.68 [4.05]	2.83 [1.19] vs 3.08 [1.35]	NA	94 vs 73	1, 3, 8, 9	****
	Naeem N	2011	US	<30 >30	RP	48	49	60.2 [13.25] vs 58.9 [9]	25.7 [2.3] vs 36.2 [4.68]	2.3 [1.8] vs 2.5 [1.28]	20:28 vs 19:30	40 vs 46	1, 2, 3, 4, 5, 6, 7, 8, 9	******
Total LPN						1387	1066							
	Anast JW	2004	US	<30 >30	R	32	12	NA	NA	NA	21:11 vs 8:4	NA	1, 2, 3, 4, 5, 6, 7, 8, 9	******
	Bensalah K	2008	US	<30 >30	R	33	28	56 [12] vs 58 [12]	NA	2.4 [0.9] vs 3 [1.4]	NA	NA	1, 2, 3, 6, 8, 9	*****
	Colombo JR Jr	2007	US	<30 >30	R	238	140	60.2 [13.5] vs 57.6 [11.2]	25.7 [2.6] vs 35.7 [6.4]	2.8 [1.3] vs 2.8 [1.1]	131:107 vs 76:64	139 vs 92	1, 2, 3, 4, 6, 8, 9	******
	Eaton SH	2011	US	<30 >30	R	77	48	55.61 [12.26] vs 54.02 [12.16]	NA	2.64 [2] vs 2.74 [1.37]	27:50 vs 21:27	NA	1, 2, 3, 4, 6, 8	*****
	George AK	2015	US	<30 >30	R	254	181	58.69 [9.75] vs 58.9 [9.17]	25.83 [2.75] vs 35.7 [6.75]	3.25 [1.99] vs 3 [1.97]	NA	NA	1, 2, 3, 6, 7, 8, 9	******
	Romero FR	2008	US	<30 >30	R	56	56	58 [11] vs 55.4 [10.8]	25.5 [2.5] vs 36.6 [7.2]	3.1 [0.9] vs 3.1 [1.2]	28:28 vs 30:26	42 vs 45	1, 3, 4, 5, 6, 8, 9	******
	Sharma V	2014	US	<30 >30	R	1126	892	NA	NA	NA	NA	NA	1, 2, 3, 6	****
	Gong EM	2006	US	<30 >30	RP	47	38	NA	NA	NA	NA	NA	1, 2, 3, 4, 7, 8	*****
	Wiens EJ	2017	Canada	<30 >30	NA	85	102	59.72 [9.6] vs 56.2 [11.8]	NA	2.97 [1.1] vs 3.42 [1.4]	NA	NA	1, 2, 3, 6, 7, 8	*****
Total						1948	1497							

 Table 1. Characteristics of included studies

R = retrospective; RP = retrospective data collection; NA = not available; *Matching: 1 = age; 2 = gender; 3 = body mass index; 4 = tumor side; 5 = clinical stage; 6 = American Society of Anesthesiologists score; 7 = previous abdominal surgery history; 8 = tumor size; 9 = The pathological nature.

A Forest plot of Operative duration.

	0	bese		Nor	n-obese	Ð		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Fixed, 95% CI	IV. Fixed, 95% CI
Abdullah 2015	176	11.67	806	156	11.33	1030	88.5%	20.00 [18.94, 21.06]	
Isac 2012	189.08	13.31	103	180	11.63	147	9.8%	9.08 [5.90, 12.26]	-
Kiziloz 2012	213.27	55.69	108	192.02	42.18	162	0.7%	21.25 [8.90, 33.60]	
Naeem 2011	265	31.5	49	242.5	18.5	48	0.9%	22.50 [12.24, 32.76]	
Total (95% CI)			1066			1387	100.0%	18.96 [17.96, 19.96]	•
Heterogeneity: Chi ² = 4		•			3%				-20 -10 0 10 20
Test for overall effect:	Z = 37.18	(P < 0.	00001)						Obese Non-Obese

B Forest plot of Estimated blood loos.

	c	bese		No	n-obese	,		Mean Difference		Mean D	fference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Fixed. 95% CI		IV. Fixe	d. 95% CI	
Abdullah 2015	150	25	806	100	20.83	1030	94.5%	50.00 [47.86, 52.14]				
Isac 2012	213.59	50.96	103	185.37	38.53	147	3.2%	28.22 [16.57, 39.87]				
Kiziloz 2012	358.61	357.9	108	252.94	217.94	162	0.1%	105.67 [30.29, 181.05]				
Naeem 2011	150	43.75	49	100	25	48	2.2%	50.00 [35.86, 64.14]			—	
Total (95% CI)			1066			1387	100.0%	49.34 [47.26, 51.43]			•	
Heterogeneity: Chi ² =					%				-100	-50	0 50	100
Test for overall effect:	Z = 46.39	(P < 0.	00001)							Obese	Non-Obese	

C Forest plot of Warm ischamia time.

	0	bese		No	n-obes	е		Mean Difference	Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, F	ixed, 95%	CI	
Abdullah 2015	19	1.5	806	19	1.67	1030	91.2%	0.00 [-0.15, 0.15]					
Isac 2012	19.27	2.41	103	17.35	2	147	6.0%	1.92 [1.35, 2.49]					
Kiziloz 2012	22.52	9.22	108	23.19	11.08	162	0.3%	-0.67 [-3.11, 1.77]	_			_	
Naeem 2011	26.5	2	49	22.5	2.38	48	2.5%	4.00 [3.12, 4.88]					
Total (95% CI)			1066			1387	100.0%	0.21 [0.07, 0.35]		2	•		
Heterogeneity: Chi ² = Test for overall effect:				00001);	l ² = 97%	6			-4	-2	0	2	4
rest for overall effect.	2 - 3.01	(5.003)							Obe	se Non-	Obese	

D Forest plot of Length of stay.

	0	bese		Nor	1-obes	se		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	otal Mean SD Tota			Weight	IV. Fixed, 95% CI	IV. Fixed, 95% CI
Isac 2012	3.27	0.5	103	3	0.22	147	69.9%	0.27 [0.17, 0.37]	
Kiziloz 2012	3.71	1.23	108	3.22	1.02	162	9.4%	0.49 [0.21, 0.77]	
Naeem 2011	2	0.5	49	2	0.45	48	20.7%	0.00 [-0.19, 0.19]	_
Total (95% CI)			260			357	100.0%	0.23 [0.15, 0.32]	•
Heterogeneity: Chi2	= 9.55, df	= 2 (P	= 0.008	B); I ² = 7	'9%				-0.5 -0.25 0 0.25 0.5
Test for overall effect	t: Z = 5.35	(P < (0.00001	1)					-0.5 -0.25 0 0.25 0.5 Obese Non-Obese

E Forest plot of Total complications.

	obes	е	Non-ob	ese		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random. 95% CI
Abdullah 2015	50	806	55	1030	57.0%	1.17 [0.79, 1.74]	
Isac 2012	38	103	36	147	29.4%	1.80 [1.04, 3.12]	
Kiziloz 2012	10	108	8	162	9.6%	1.96 [0.75, 5.15]	
Naeem 2011	5	49	3	48	4.0%	1.70 [0.38, 7.57]	
Total (95% CI)		1066		1387	100.0%	1.42 [1.05, 1.91]	◆
Total events	103		102				
Heterogeneity: Tau ²	= 0.00; Chi ²	= 2.12	, df = 3 (P	= 0.55); $ ^2 = 0\%$	-	
Test for overall effect							0.2 0.5 1 2 5 Obese Non-Obese

F Forest plot of Minor complications..

	e	Non-ob	ese		Odds Ratio	Odds Ratio				
Study or Subgroup	Events	Total	Events Total		Weight	M-H. Random, 95% CI	M-H. Random, 95% CI			
Isac 2012	23	103	14	147	80.2%	2.73 [1.33, 5.61]				
Naeem 2011	6	49	3	48	19.8%	2.09 [0.49, 8.90]				
Total (95% CI)		152		195	100.0%	2.59 [1.36, 4.94]				
Total events	29		17							
Heterogeneity: Tau ² = Test for overall effect:				= 0.75); I ² = 0%	-	0.2 0.5 1 2 5			
rest for overall effect.	2 - 2.09 (- 0.0	04)				Obese Non-Obese			

Association between obesity and perioperative outcomes undergoing MIPN

Figure 2. Forest plots of obese versus non-obese patients following robot-assisted laparoscopic partial nephrectomy in terms of intraoperative outcomes. A. Operative duration. B. Estimated blood loss. C. Warm ischemia time. D. Length of stay. E. Total complications. F. Minor complications. Squares are the point estimates of the treatment effect [OR, WMD], with 95% CI indicated by horizontal bars. Diamonds are the summary estimate from the pooled studies with 95% CI.

Results

Results of data mining and characteristics of inclusions

1688 studies were found in initial search after removal of duplication. The search strategy was demonstrated in a flow diagram (Figure 1). For LPN, the results were updating a previous meta-analysis in 2011, and the inclusions of LPN were expanded from 4 studies to 9 studies [9]. 5898 participants were enrolled, with 2563 patients in the obese group and 3335 patients in the non-obese group. No randomized controlled trial (RCT) was included. 2 studies were retrospective with prospective data collection [18, 19], and 10 studies were retrospective [20-29]. All inclusion characteristics and quality scores are represented in Table 1. The results of every outcome were analyzed in the LPN and RLPN subgroup, respectively.

Outcomes in robot-assisted laparoscopic partial nephrectomy

The operation duration was longer in the obese group (P<0.05, WMD 18.96 min, 95% CI 17.96 to 19.96) (Figure 2A), and the estimated blood loss was also larger in the obese group (P< 0.05, WMD 49.34 ml, 95% CI 47.26 to 51.43) (Figure 2B). Warm ischemia time was longer in obese group (P<0.05, WMD 0.21 min, 95% CI 0.07 to 0.35) (Figure 2C). Only three studies reported the length of stay (LOS) [19, 21, 22], and the LOS was longer in the obese group (P<0.05, WMD 0.23 days, 95% CI 0.15 to 0.32) (Figure 2D). The total complication rate was higher in the obese group (P<0.05, OR 1.42, 95% CI 1.05 to 1.91) (Figure 2E). Minor complications were only reported in two studies [19, 21], and they were higher in the obese group (P<0.05, OR 2.59, 95% CI 1.36 to 4.94) (Figure 2F). The statistical difference (shown in Supplementary RLPN) was not significant for the transfusion rate (P = 0.47, OR 1.17, 95% CI 0.77 to 1.78), conversion to open surgery rate (P = 0.64, OR 1.30, 95% CI 0.43 to 3.99), major complication rate (P = 0.3, OR 1.26, 95% CI 0.81 to 1.95), or presence of positive margins

(P = 0.36, OR 1.28, 95% CI 0.76 to 2.15) (**Table** 2).

Outcomes in laparoscopic partial nephrectomy

The estimated blood loss (EBL) was reported by six studies [23, 25-28, 30], and the EBL in the obese group was larger than that in the nonobese group (P<0.05, WMD 60.58 ml, 95% CI 25.99 to 95.17) (Figure 3A). The total complication rate was higher in obese group (P<0.05, OR 1.34. 95% CI 1.08 to 1.67) (Figure 3B). Five studies reported the minor complication rate [18, 23, 26, 27, 29], which was higher in the obese group than in the non-obese group (P<0.05, OR 1.34, 95% CI 1.02 to 1.76) (Figure 3C). Other outcomes (shown in Supplementary LPN) showed no significant difference between the two groups in terms of the operative duration (P = 0.06, WMD 7.49 min, 95% CI -0.36 to 15.34), warm ischemia time (P = 0.34, WMD -0.51 min, 95% CI -1.54 to 0.53), transfusion rate (P = 0.58, OR 1.33, 95% CI 0.48 to 3.64), length of stay (P = 0.43, WMD -0.10 days, 95% CI -0.34 to 0.14), conversion to open surgery rate (P = 0.05, OR 4.17, 95% CI 1.02 to 17.14), major complication rate (P = 0.1, OR 1.39, 95% CI 0.94 to 2.04), and presence of positive margins (P = 0.63, OR 1.63, 95% CI 0.22 to 11.98] (Table 2).

Sensitivity analysis and publication bias

Ten studies [18, 19, 21, 23-28, 30] with six or more stars on the modified Newcastle-Ottawa scale were included in sensitivity analysis (**Table 3**). No changes in significance of all outcomes was found except total complications in RLPN that was show to be no significantly (OR: 1.37; 95% CI, 1.00 to 1.88; p = 0.05), and minor complications in LPN that was show to be no significantly (OR: 1.26; 95% CI, 0.80 to 2.00; p = 0.32). These two subcategories showed no significant statistical difference between obese and non-obese group. The sensitivity analysis of conversion rate was not available with only one study.

Figure 4 showed two funnel plots of inclusions in this meta-analysis. The funnel plot for total

Outcomes of interest	Surgery	Studies,	Pat	ients, n.		nyoluc	Stu	dy h	eterog	geneity
Outcomes of Interest	procedures	No	Obesity	Non-Obesity	WMD/OR, [95% CI]	p value	X ²	df	l², %	p value
	RLPN			·						
Operative duration [min]		4	1066	1387	18.96† [17.96, 19.96]	<0.00001	41.25	3	93	<0.0000
Estimated blood loss [ml]		4	1066	1387	49.34† [47.26, 51.43]	<0.00001	15.15	3	80	0.002
Warm Ischemia Time [min]		4	1066	1387	0.21† [0.07, 0.35]	0.003	115.45	3	97	<0.0000
Transfusion rate		2	909	1177	1.17* [0.77, 1.78]	0.47	0.21	1	0	0.64
Length of stay [days]		3	260	357	0.23† [0.15, 0.32]	<0.00001	9.55	2	79	0.008
Conversion rate		2	914	1192	1.30* [0.43, 3.99]	0.64	NA	NA	NA	NA
Total complications		4	1066	1387	1.42* [1.05, 1.91]	0.02	2.12	3	0	0.55
Major complications		3	958	1225	1.26* [0.81, 1.95]	0.3	0.11	2	0	0.95
Minor complications		2	152	195	2.59* [1.36, 4.94]	0.004	0.1	1	0	0.75
Positive Margins		2	855	1078	1.28* [0.76, 2.15]	0.36	0.04	1	0	0.85
	LPN									
Operative duration [min]		5	437	657	7.49† [-0.36, 15.34]	0.06	5.03	4	21	0.28
Estimated blood loss [ml]		6	539	742	60.58† [25.99, 95.17]	0.0006	3.97	5	0	0.55
Warm Ischemia Time [min]		5	527	710	-0.51† [-1.54, 0.53]	0.34	2.3	4	0	0.68
Transfusion rate		4	381	601	1.33* [0.48, 3.64]	0.58	5.17	3	42	0.16
Length of stay [days]		7	567	775	-0.10† [-0.34, 0.14]	0.43	14.61	6	59	0.02
Conversion rate		3	208	326	4.17* [1.02, 17.14]	0.05	0.14	1	0	0.71
Total complications		8	1395	1863	1.34* [1.08, 1.67]	0.008	5.31	7	0	0.62
Major complications		5	1171	1536	1.39* [0.94, 2.04]	0.1	1.49	4	0	0.83
Minor complications		5	1171	1536	1.34* [1.02, 1.76]	0.03	2.86	4	0	0.58
Positive Margins		1	48	77	1.63* [0.22, 11.98]	0.63	NA	NA	NA	NA

Table 2. Results of Meta-analysis Compariso	on of Obese and Non-Obese under MIPN
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Abbreviations: NA = not available; OR = odds ratio; WMD = weighted mean difference; CI = confidence interval; df = degrees of freedom; *OR; †WMD.

complication rate of RLPN was shown in **Figure 4A**, and outcomes were within the 95% CIs and symmetrically distributed, showing no evidence of publication bias. The funnel plot for total complication rate of LPN was shown in **Figure 4B**, the outcomes were also within the 95% CIs and symmetrically distributed, showing no evidence of publication bias.

Discussion

This article is a meta-analysis of 13 studies with 5898 enrolled subjects. In LPN, the current research expanded the study inclusion of previous meta-analysis and challenged previous research on this topic by Aboumarzouk et al. [9]. We found there was a significant difference in the estimated blood loss, total complication rate and minor complication rate between the obese group and non-obese group, and no difference in other outcomes. It is implied that not only were major complications higher in obese patients as a previous meta-analysis reported, the total complication rate was also higher in the obese group.

In RLPN, our results indicated a great difference between the two groups in many out-

comes for the first time, including the operative duration, estimated blood loss, warm ischemia time, length of stay, and total and minor complication rates, which could demonstrate what might occur during the management of obese patients who underwent RLPN. In robotic laparoscopy, obese individuals can pose a challenge for two reasons in peritoneal access. First, surface anatomical landmarks can vary significantly in relation to the underlying anatomy. For example, the distortion of the umbilicus, a landmark and access point for the laparoscopic procedure, is common in morbidly obese individuals, in whom the thickness of the abdominal wall limits the method of access. The greater depth of the wound also requires larger incisions. Furthermore, the trocar length and external interference also become issues in morbidly obese or super-obese patients. All in all, obesity and distorted surface anatomy not only makes initial peritoneal access more challenging but also increase the risk of intraperitoneal and retroperitoneal injuries [31].

Numerous studies have reported adverse effects or necessary considerations for MIPN patients with high BMI [32-36]. Oh T et al. reported increased BMI was associated with a higher

	c	besity		non-obesity				Mean Difference	Mean Difference				
Study or Subgroup	Mean	SD	Total	Total Mean		Total	Weight	IV, Fixed, 95% CI	I IV, Fixed, 95%			6 CI	
Anast 2004	427	637	12	189	189	32	0.9%	238.00 [-128.31, 604.31]		-			
Colombo 2007	309	666	140	249	318	238	8.7%	60.00 [-57.49, 177.49]			+-	_	
Eaton 2011	290.76	228.6	48	238.42	365.52	77	11.0%	52.34 [-51.81, 156.49]				-	
George 2015	318.7	249.17	181	285.76	270.86	254	49.3%	32.94 [-16.33, 82.21]					
Romero 2008	391.7	308.6	56	280.9	202.1	56	12.8%	110.80 [14.18, 207.42]					
Wiens 2017	261	360	102	162.5	212.1	85	17.3%	98.50 [15.35, 181.65]			-	_	
Total (95% CI)			539			742	100.0%	60.58 [25.99, 95.17]			•		
Heterogeneity: Chi ² =	3.97, df =	5 (P = 0	.55); l²	= 0%						250		250	500
Test for overall effect:	Z = 3.43	(P = 0.00	006)						-500	-250 obe	sity non-	250 obesity	500

A Forest plot of Estimated blood loss.

B Forest plot of Total complications.

	Obese	e	Non-Ob	ese		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
Anast 2004	3	12	8	32	2.0%	1.00 [0.22, 4.63]	
Bensalah 2008	4	28	2	33	1.5%	2.58 [0.44, 15.30]	
Colombo 2007	27	140	40	238	16.1%	1.18 [0.69, 2.03]	- -
Eaton 2011	15	48	19	77	7.3%	1.39 [0.62, 3.09]	
George 2015	42	181	37	254	19.5%	1.77 [1.09, 2.89]	
Gong EM 2006	12	38	13	47	5.4%	1.21 [0.47, 3.08]	
Romero 2008	10	56	15	56	5.7%	0.59 [0.24, 1.47]	
Sharma 2014	78	892	73	1126	42.5%	1.38 [0.99, 1.93]	
Total (95% CI)		1395		1863	100.0%	1.34 [1.08, 1.67]	◆
Total events	191		207				
Heterogeneity: Tau ² =	0.00; Chi ²	= 5.31	df = 7 (P	= 0.62); l² = 0%		
Test for overall effect:	Z = 2.66 (P	P = 0.0	08)	,			0.1 0.2 0.5 1 2 5 10 Obese Non-Obese

C Forest plot of Minor complications.

	Obese		Non-Ob	ese		Odds Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C		M-H, Ran	dom, 95% Cl	
Anast 2004	1	12	5	32	1.4%	0.49 [0.05, 4.70]			+	
Eaton 2011	10	48	15	77	9.1%	1.09 [0.44, 2.67]				
George 2015	27	181	25	254	21.6%	1.61 [0.90, 2.87]			+	
Gong EM 2006	2	38	5	47	2.5%	0.47 [0.09, 2.55]	-	· · ·	+	
Sharma 2014	77	892	72	1126	65.4%	1.38 [0.99, 1.93]				
Total (95% CI)		1171		1536	100.0%	1.34 [1.02, 1.76]			•	
Total events	117		122							
Heterogeneity: Tau ² =			, ,	= 0.58); I² = 0%		+ 0.05	0.2	1 5	20
Test for overall effect:	Z = 2.12 (P = 0.0	3)					Obese	Non-Obese	

Figure 3. Forest plots of obese versus non-obese patients following laparoscopic partial nephrectomy in terms of intraoperative outcomes. A. Estimated blood loss. B. Total complications. C. Minor complications. Squares are the point estimates of the treatment effect [HR, OR, WMD], with 95% CI indicated by horizontal bars. Diamonds are the summary estimate from the pooled studies with 95% CI.

estimated blood loss in patients undergoing simple or radical laparoscopic nephrectomy [34]. For patients undergoing radical nephrectomy with concomitant IVC thrombectomy for RCC, obesity was reported to represent an adverse prognosticator for operative blood loss [36]. Kurzer et al. have quantified the risk of complications in laparoscopic renal surgeries for obese patients, and found that with every unit increases in the BMI, the risk of a major complication increases by 14% [33]. Hua X et al. reported that patients were more likely to experience complications after nephrectomy as BMI increases, and metabolic disorders, such as obesity, hypertension and diabetic mellitus were closely related to a greater number of complications of varying degrees after nephrectomy [32]. Richards KA et al. reported that the BMI was an independent risk factor for worsening kidney function following MIPN [35].

Other studies emphasized the benefits and feasibility of MIPN for obese patients [4, 37-41]. Klingler HC et al. demonstrated that patients with a higher BMI benefited more from laparoscopy in respect to postoperative pain and morbidity, but did not experience more complications [39]. Christopher Reynolds et al. founded

Outcomes of interest	Surgery	Studies,	Pat	ients, n.		n volue	Stu	dy h	eterog	geneity
Outcomes of interest	procedures	No	Obesity	Non-Obesity	- WMD/OR, [95% CI]	p value	X ²	df	l², %	p value
	RLPN									
Operative duration [min]		3	958	1225	18.94† [17.94, 19.94]	<0.00001	41.11	2	95	< 0.00001
Estimated blood loss [ml]		3	958	1225	49.30† [47.22, 51.39]	<0.00001	13	2	85	0.002
Warm Ischemia Time [min]		3	958	1225	0.22† [0.08, 0.36]	0.002	114.94	2	98	<0.00001
Conversion rate		1	806	1030	NA	NA	NA	NA	NA	NA
Length of stay [days]		2	152	195	0.21† [0.12, 0.30]	<0.00001	6.04	1	83	0.01
Total complications		3	958	1225	1.37* [1.00, 1.88]	0.05	1.64	2	0	0.44
	LPN									
Total complications		7	503	737	1.31* [0.99, 1.75]	0.06	5.26	6	0	0.51
Major complications		4	279	410	1.76* [0.99, 3.13]	0.06	0.32	3	0	0.96
Minor complications		4	279	410	1.26* [0.80, 2.00]	0.32	2.76	3	0	0.43

Table 3. Sensitivity analysis comparison of obese and non-obese patients undergone MIPN

Abbreviations: NA = not available; OR = odds ratio; WMD = weighted mean difference; Cl = confidence interval; df = degrees of freedom; *OR; †WMD

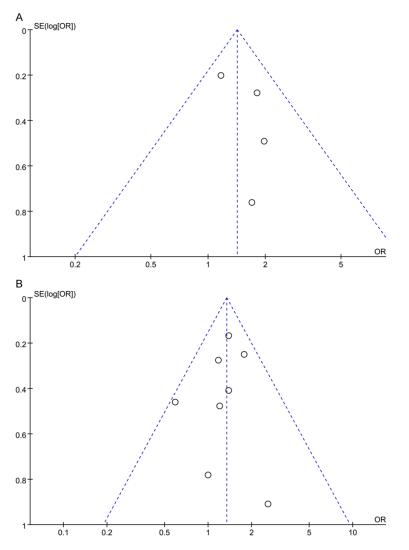


Figure 4. Funnel plots for assessing publication bias (A). Funnel plot showing approximation symmetry indicative of no evidence of publication bias for total complication rate of RLPN and (B). Funnel plot showing symmetry indicative of no evidence of publication bias for total complication rate of LPN.

out that increasing nephrometry score was the sole variable associated with perioperative complications rather than BMI [4]. Nita G et al. suggested that proper trocar site selection and greater insufflation pressures were critical for successful MIPN for obese patients [41]. Additionally, a number of researchers also reported obesity was related to less-aggressive disease profiles for RCC and superior cancer-specific survival [42-44]. Even though it warrants further exploration, this association suggests that surgeons should pay more attentions to the topic.

Once MIPN has failed, the procedure is converted to an open partial nephrectomy (OPN), which has been the main surgical operation for RCC in the 20th century. OPN served as the last approach for all kinds of difficulties and that is why we do not compare those outcomes under OPN. The fact that MIPN has many advantages over OPN in obese patients was reported in numerous studies. MIPN resulted in a significantly decreased blood loss, shorter operating time, and quicker return of bowel function, lower analgesic requirements, shorter convalescence and reduced hospital stay in treating obese patients with RCC when compared with those of OPN [28, 29, 37, 45-47]. In addition to medical outcomes, obesity could influence the costs in some patients who underwent OPN [24]. The length of stay seems to be the main determinants of economic costs in renal surgery.

However, there were some limitations in this analysis. First, all the inclusion studies were retrospective, and no randomized controlled trials were included. Retrospective studies might have selective bias from the subjects by the researchers. Second, even if we expanded inclusions for LPN compared with previous analysis and conducted the first meta-analysis of RLPN on this topic, more studies with larger samples would still be required for solid and detailed clinical outcomes and conclusion. Third, a thorough understanding of one operation and its indications not only needs perioperative outcomes but also relies on long term postoperative and oncological outcomes and prognoses. None of the included studies provided prognosis or long-time postoperative outcomes on this topic.

Conclusion

For LPN, obese patients have a higher likelihood of total and minor complications and a larger EBL. For RLPN, obese patients have a longer OD, WIT, and LOS. They also have a larger EBL and higher likelihood of total and minor complications than non-obese patients. For this reason, MIPN should be performed on obese patients with caution.

Disclosure of conflict of interest

None.

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А

Forest polt of Transfusion rate. obese Non-obese Odds Ratio Odds Ratio M-H, Random, 95% CI Study or Subgroup Events Total Events Total Weight M-H, Random, 95% Cl Abdullah 2015 30 806 35 1030 72.2% 1.10 [0.67, 1.81] 1.37 [0.62, 3.06] Isac 2012 13 103 147 27.8% 14 Total (95% CI) 909 1177 100.0% 1.17 [0.77, 1.78] Total events 43 49 Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 1 (P = 0.64); $I^2 = 0\%$ 0.5 0.7 1.5 2 1 Test for overall effect: Z = 0.72 (P = 0.47) Obese Non-Obese

В

Forest plot of Conversion rate.

	obes	е	Non-ob	ese		Odds Ratio		Od	ds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C		M-H, F	ixed, 95% Cl	
Abdullah 2015	0	806	0	1030		Not estimable				
Kiziloz 2012	6	108	7	162	100.0%	1.30 [0.43, 3.99]				
Total (95% CI)		914		1192	100.0%	1.30 [0.43, 3.99]				
Total events	6		7							
Heterogeneity: Not ap	plicable						+	0.5		
Test for overall effect:	Z = 0.46 (P = 0.6	4)				0.2	0.5 Obes	se Non-Obese	5

С

Forest plot of Major complications.

	obes	е	Non-ob	ese		Odds Ratio	Odds Ratio					
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI					
Abdullah 2015	34	806	35	1030	83.2%	1.25 [0.77, 2.03]						
Isac 2012	5	103	5	147	12.0%	1.45 [0.41, 5.14]						
Naeem 2011	2	49	2	48	4.8%	0.98 [0.13, 7.24]						
Total (95% CI)		958		1225	100.0%	1.26 [0.81, 1.95]	-					
Total events	41		42									
Heterogeneity: Tau ² =	0.00; Chi ²	= 0.11	, df = 2 (F	9 = 0.95); I² = 0%	-		- I				
Test for overall effect:	Z = 1.03 (P = 0.3	0)				0.2 0.5 1 2 Obese Non-Obe	5 ese				

D

Forest plot of Positive margins.

	obes	е	Non-ob	ese		Odds Ratio			Odds Ratio					
Study or Subgroup	Events	Events Total		Total	Weight	M-H, Random, 95% Cl			М-Н,	Rand	lom, 9	95% CI		
Abdullah 2015	28	806	28	1030	96.5%	1.29 [0.76, 2.19]				_	┼══╌	-		
Naeem 2011	1	49	1	48	3.5%	0.98 [0.06, 16.12]								
Total (95% CI)		855		1078	100.0%	1.28 [0.76, 2.15]						•		
Total events	29		29											
Heterogeneity: Tau ² =	= 0.00; Chi ²	= 0.04	, df = 1 (P	= 0.85); I² = 0%					+	1		+	+
Test for overall effect: Z = 0.91 (P = 0.36)							0.1	0.2	-).5 bese	Non	z -Obese	5 9	10

Supplementary RLPN. Forest plots of obese versus non-obese patients following robot-assisted laparoscopic partial nephrectomy in terms of intraoperative outcomes. A. Transfusion rate. B. Conversion rate. C. Major complications. D. Positive margins.

A Forest plot of Operative duration.

	C	bese		Noi	1-Obes	е		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Anast 2004	260	51	12	233	78	32	3.8%	27.00 [-12.53, 66.53]	
Colombo 2007	205.2	57.9	140	205.2	59.1	238	29.0%	0.00 [-12.18, 12.18]	
Eaton 2011	220.16	46.38	48	201.49	42.02	77	19.0%	18.67 [2.54, 34.80]	
George 2015	142.5	46.17	181	138.74	60.27	254	37.5%	3.76 [-6.25, 13.77]	
Romero 2008	195.2	59.8	56	181.1	62.4	56	10.7%	14.10 [-8.54, 36.74]	
Total (95% CI)			437			657	100.0%	7.49 [-0.36, 15.34]	
Heterogeneity: Tau ² =	16.71; Cl	hi² = 5.0	3, df =	4 (P = 0.	28); I² =	21%			-20 -10 0 10 20
Test for overall effect:	Z = 1.87	(P = 0.0	6)						-20 -10 0 10 20 Obese Non-Obese

В

Forest plot of Warm ischemia time.

_	o	besity		non-obesity				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Colombo 2007	31.7	10	140	32.3	10.1	238	24.3%	-0.60 [-2.70, 1.50]	
Eaton 2011	29.33	6.27	48	29.81	5	77	24.3%	-0.48 [-2.58, 1.62]	
George 2015	16.7	8.83	181	17.1	9.75	254	34.5%	-0.40 [-2.16, 1.36]	
Romero 2008	28.2	10.5	56	31	9.9	56	7.5%	-2.80 [-6.58, 0.98]	
Wiens 2017	27.24	13.4	102	26.14	10.2	85	9.3%	1.10 [-2.29, 4.49]	
Total (95% CI)			527			710	100.0%	-0.51 [-1.54, 0.53]	-
Heterogeneity: Chi ² =	2.30, df	= 4 (P	= 0.68)	; I ² = 0%	6				-4 -2 0 2 4
Test for overall effect:	Z = 0.96	(P = (0.34)						-4 -2 0 2 4 obesity non-obesity

С

•
2
-

D

Forest plot of Length of stay.

	o	besity		non	-obes	ity		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Anast 2004	4.5	3.7	12	3.1	2.8	32	1.1%	1.40 [-0.91, 3.71]	
Bensalah 2008	2.3	1.5	28	2.5	1.1	33	12.7%	-0.20 [-0.87, 0.47]	
Colombo 2007	2.8	1.5	140	3.5	4.5	238	14.7%	-0.70 [-1.32, -0.08]	
Eaton 2011	3.72	1.05	48	3.77	2	77	19.9%	-0.05 [-0.59, 0.49]	
George 2015	2.3	2.17	181	2.65	2.82	254	26.0%	-0.35 [-0.82, 0.12]	
Romero 2008	3.2	2.2	56	3.2	1.6	56	11.3%	0.00 [-0.71, 0.71]	
Wiens 2017	4.11	2.9	102	3.29	1.35	85	14.3%	0.82 [0.19, 1.45]	
Total (95% CI)			567			775	100.0%	-0.10 [-0.34, 0.14]	•
Heterogeneity: Chi ² =	14.61, d	f = 6 (F	P = 0.02	2); I ² = 5	59%				-2 -1 0 1 2
Test for overall effect: Z = 0.79 (P = 0.43)									-2 -1 0 1 2 Favours [experimental] Favours [control]

Е

Forest plot of Conversion rate.

	Obes	e	Non-ob	ese		Odds Ratio					
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H,	Random, 9	5% CI	
Anast 2004	2	12	1	32	31.8%	6.20 [0.51, 75.84]					
Colombo 2007	4	140	2	238	68.2%	3.47 [0.63, 19.20]					
Romero 2008	0	56	0	56		Not estimable					
Total (95% CI)		208		326	100.0%	4.17 [1.02, 17.14]					
Total events	6		3								
Heterogeneity: Tau ² =	0.00; Chi ²	= 0.14	, df = 1 (F	9 = 0.71); I² = 0%		0.01	0.1	1	10	100
Test for overall effect:	Z = 1.98 (P = 0.0	5)				0.01		bese Non-o	10 obese	100

F

Forest plot of Major complications.

	Obes	е	Non-Ob	ese		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Anast 2004	2	12	3	32	4.0%	1.93 [0.28, 13.30]	
Eaton 2011	5	48	4	77	8.0%	2.12 [0.54, 8.33]	
George 2015	15	181	12	254	24.2%	1.82 [0.83, 3.99]	
Gong EM 2006	5	38	5	47	8.5%	1.27 [0.34, 4.77]	
Sharma 2014	28	892	31	1126	55.3%	1.14 [0.68, 1.92]	P
Total (95% CI)		1171		1536	100.0%	1.39 [0.94, 2.04]	◆
Total events	55		55				
Heterogeneity: Tau ² =	0.00; Chi ²	= 1.49	, df = 4 (P	= 0.83); I² = 0%		
Test for overall effect:	Z = 1.66 (P = 0.1	0)				0.1 0.2 0.5 1 2 5 10 Obese Non-Obese

G

Forest plot of Positive margins.

	Obes	e	Non-ob	oese		Odds Ratio		C	dds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H, Fixed, 95% Cl				
Eaton 2011	2	48	2	77	100.0%	1.63 [0.22, 11.98]			╶┤┻┛╴			
Total (95% CI)		48		77	100.0%	1.63 [0.22, 11.98]						
Total events	2		2									
Heterogeneity: Not ap	plicable						0.01	0.1	1	10	100	
Test for overall effect:	Z = 0.48 (P = 0.6	3)				0.01		ese Non-o		100	

Supplementary LPN. Forest plots of obese versus non-obese patients following laparoscopic partial nephrectomy in terms of intraoperative outcomes. A. Operative duration. B. Warm ischemia time. C. Transfusion rate. D. Length of stay. E. Conversion rate. F. Major complications. G. Positive margins.