

Impact of body mass index on short-term outcomes of laparoscopic gastrectomy in Asian patients: A meta-analysis

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Abstract

AIM

To perform a meta-analysis to investigate the correlation between body mass index (BMI) and the short-term outcomes of laparoscopic gastrectomy (LG) for gastric cancer (GC) in Asian patients.

METHODS

The PubMed, Cochrane, EMBASE, and Web of Science databases were searched for studies that focused on the impact of obesity on the short-term outcomes of LG for GC in Asian patients who were classified into a high BMI (BMI \geq 25 kg/m²) or low BMI group (BMI < 25 kg/m²). The results are expressed using the pooled odds ratio (OR) for binary variables and standard mean difference (SMD) for continuous variables with 95%

confidence interval (CI), and were calculated according to the fixed-effects model while heterogeneity was not apparent or a random-effects model while heterogeneity was apparent.

RESULTS

Nine studies, with a total sample size of 6077, were included in this meta-analysis. Compared with the low BMI group, the high BMI group had longer operative time (SMD = 0.26, 95%CI: 0.21 to 0.32, $P < 0.001$), greater blood loss (SMD = 0.19, 95%CI: 0.12 to 0.25, $P < 0.001$), and fewer retrieved lymph nodes (SMD = -0.13, 95%CI: 0.18 to 0.07, $P < 0.001$). There was no significant difference between the high and low BMI groups in postoperative complications (OR = 1.12, 95%CI: 0.95 to 1.33, $P = 0.169$), the duration of postoperative hospital stay (SMD = 0.681, 95%CI: -0.05 to 0.07, $P = 0.681$), postoperative mortality (OR = 1.95, 95%CI: 0.78 to 4.89, $P = 0.153$), or time to resuming food intake (SMD = 0.00, 95%CI: -0.06 to 0.06, $P = 0.973$).

CONCLUSION

Our meta-analysis provides strong evidence that despite being associated with longer operative time, greater blood loss, and fewer retrieved lymph nodes, BMI has no significant impact on the short-term outcomes of LG for GC in Asian patients, including postoperative complications, the duration of postoperative hospital stay, postoperative mortality, and time to resuming food intake. BMI may be a poor risk factor for short-term outcomes of LG. Other indices should be taken into account.

Key words: Obesity; Body mass index; Laparoscopic gastrectomy; Gastric cancer; Meta-analysis

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Core tip: The impact of body mass index (BMI) on the short-term outcomes of laparoscopic gastrectomy (LG) for gastric cancer in Asian patients have been controversial due to inconsistent results of previous studies. Our meta-analysis demonstrates that despite being associated with longer operative time, greater blood loss, and fewer retrieved lymph nodes, a high BMI could not be significantly associated with short-term outcomes of LG in Asian patients. BMI may be a poor risk factor for short-term outcomes of LG. Other indices should be taken into account.

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INTRODUCTION

Gastric cancer (GC), the second most prevalent cause of cancer-related deaths worldwide, has been a source of increasing concern^[1]. Since 1994, when laparoscopic technique was first used for GC^[2-6], laparoscopic gastrectomy (LG) has become increasingly popular for treating early GC (EGC) due to decreased intraoperative blood loss, less pain, and shorter hospital duration^[7-10]. The prevalence of obesity is increasing steadily in Asian countries. Obesity may increase the risk of health disorders, such as hypertension, cardiovascular disease, and type 2 diabetes mellitus^[11,12], and is regarded as a risk factor for worse surgical outcomes of complicated surgical procedures^[13]. Furthermore, patients with obesity have a higher risk of operative difficulties, as well as wound infection^[14-16]. Recently, the impact of obesity on short-term outcomes of LG in patients has been controversial due to inconsistent results of several studies. Obesity leads to a longer duration of postoperative hospital stay and time to resuming food intake in studies performed by Chen *et al.*^[17] and Yang *et al.*^[18], while Jung *et al.*^[19] reported that obesity was not a risk factor for these impacts. The studies performed by Chen *et al.*^[20], Shimada *et al.*^[21], and Yamada *et al.*^[22] suggested that the association between obesity and LG was significant, while Shin *et al.*^[23] and Oki *et al.*^[24] reported the opposite conclusion.

To date, although several studies used the body mass index (BMI) to assess the impact of obesity on the short-term outcomes of LG, the results have been controversial and limited. Hence, we conducted this meta-analysis to summarize all of the available evidence.

MATERIALS AND METHODS

Search strategy

The PubMed, Cochrane, EMBASE, and Web of Science databases were searched up to July 30, 2018 using the search terms (obesity) OR (metabolically benign) OR (obesity, morbid) OR (pediatric) OR (overweight) AND (body mass index) OR (index, body mass) OR (Quetelet index) OR (index, Quetelet) OR (Quetelet's index) OR (Quetelets index) AND (stomach neoplasms) OR (neoplasm, stomach) OR (stomach neoplasm) OR (gastric neoplasms) OR (gastric neoplasm) OR (neoplasm, gastric) OR (neoplasms, gastric) OR (cancer of stomach) OR (stomach cancers) OR (gastric cancer) OR (cancer, gastric) OR (cancers, gastric) OR (gastric cancers) OR (stomach cancer) OR (cancer, stomach) OR (cancers, stomach) OR (cancer of the stomach) OR (gastric cancer, familial diffuse) AND (laparoscopy) OR (laparoscopies) OR (celioscopy) OR (celioscopies) OR (peritoneoscopy) OR (peritoneoscopies) OR (surgical procedures, laparoscopic) OR (laparoscopic surgical procedure) OR (procedure, laparoscopic surgical) OR (procedures, laparoscopic surgical) OR (surgery, laparoscopic) OR (laparoscopic

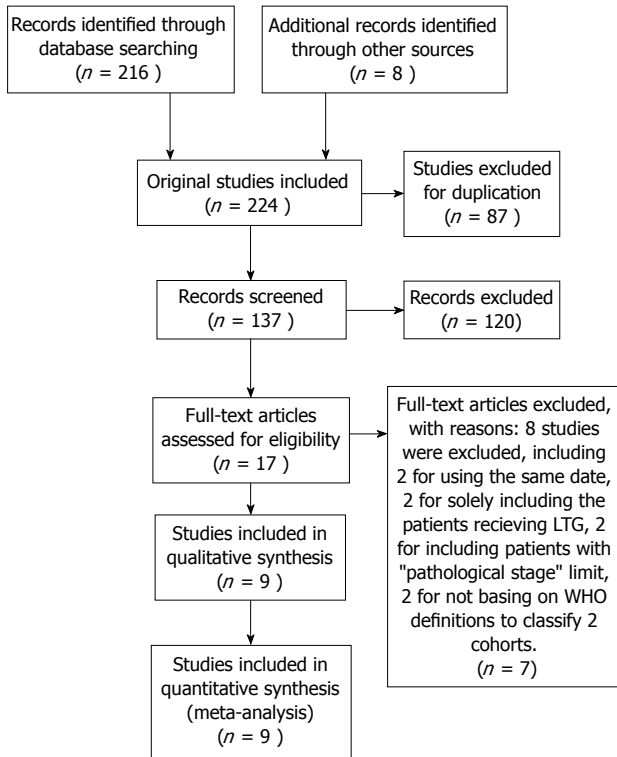


Figure 1 Flowchart of study selection in the meta-analysis. LTG: Laparoscopic total gastrectomy.

surgical procedures) OR (laparoscopic surgery) OR (laparoscopic surgeries) OR (surgeries, laparoscopic) OR (surgical procedure, laparoscopic) AND within the "Title/Abstract" and "Asian" limits. No restrictions were applied for language, country, or publication date. Moreover, lists of all relevant review articles were manually screened to identify further studies.

Selection criteria

Studies were included if they met the following predefined criteria: (1) all patients underwent LG; (2) all patients were diagnosed by esophagogastroduodenoscopy, postoperative pathological diagnosis, endoscopic ultrasound, or computed tomography (CT); (3) all studies were included without "age" or "pathological stage" limit; and (4) the risk estimates were adjusted for other confounding factors. Meeting abstracts, systematic reviews, case reports, studies without usable or extractable data, and those solely focusing on laparoscopic total gastrectomy (LTG) were all excluded. Publications with smaller data sets were excluded while the data were presented in more than one publication.

Outcome measures analyzed

Operative time, blood loss, and the number of retrieved lymph nodes were defined as indices of difficulties in LG. Postoperative complications, the duration of postoperative hospital stay, postoperative mortality, and time to resuming food intake were estimated as indices to assess the impact of BMI on the short-term outcomes

of LG. The cutoff points to divide patients into a high BMI and a normal BMI group were based on World Health Organization definitions (overweight, BMI ≥ 25 kg/m²; healthy-weight, BMI < 25 kg/m²)^[25,26]. Postoperative complications were defined as those requiring surgical or conservative treatment according to the Clavein-Dindo classification system. All of the postoperative complications observed in the included studies conform to this definition.

Data extraction and quality assessment

Data were extracted from the included studies by two independent investigators, and disagreements were resolved through consensus or consultation with a third investigator. Study characteristics such as the authors' names, year of publication, number of participants, operative time, blood loss, number of retrieved lymph nodes, postoperative complications, duration of postoperative hospital stay, postoperative mortality, and time to resuming food intake were recorded. The Newcastle-Ottawa Scale was used to assess the quality of the included studies.

Statistical analysis

The pooled odds ratio (OR) for binary variables and standard mean difference (SMD) for continuous variables with 95% confidence interval (CI) were calculated using a fixed-effects model while heterogeneity was not apparent or a random-effects model while heterogeneity was apparent. *P* for *I*² statistic was used to evaluate the heterogeneity in this meta-analysis, with *P* < 0.05 suggesting substantial heterogeneity among the included studies. The *Galbraith plot* test was performed to assess the potential source of heterogeneity. A sensitivity analysis was performed (when the number of included studies ≥ 9) to evaluate the stability of the results by excluding each study from the meta-analysis one by one. Publication bias was evaluated using funnel plots and the Egger's test (when the number of included studies ≥ 9). Duval's trim and fill method was used to solve publication bias. Statistical analyses were performed using STATA 12.1 (StataCorp, Texas, United States). A *P*-value < 0.05 indicated statistical significance.

RESULTS

Of the 224 studies identified using the predefined search strategy, 207 were excluded after screening titles and abstracts because they did not meet the predefined criteria; they were duplicate; or their full-text could not be accessed and insufficient data to make calculations from the abstracts. After performing full-text evaluations, eight studies were excluded, including two for using the same date, two for solely including the patients receiving LTG, two for including patients with "pathological stage" limit, and two for not being based on WHO definitions to classify the two cohorts. Thus, nine studies^[17-24,27] with a sample size of 6077 were included in the meta-analysis

Table 1 Characteristics of nine studies included in the meta-analysis

Study	Country	Study type	Inclusion period	Sample size	Type of gastrectomy	BMI cutoff point	Adjustment	Quality
Chen <i>et al</i> ^[20]	China	RC	2007-2010	531	LG	25	1, 3, 5	9
Chen <i>et al</i> ^[17]	China	RC	2004-2016	1691	LAG TLG	25	1, 2, 4, 5, 6, 7	8
Jung <i>et al</i> ^[19]	South Korea	RC	2006-2012	1512	LDG	25	1, 2, 3, 4, 6, 7	8
Lee <i>et al</i> ^[27]	South Korea	RC	-2005	1485	LAG	25	1, 2, 3, 4, 5, 7	9
Oki <i>et al</i> ^[24]	Japan	RC	2005-2009	138	TLDG	25	1, 2, 4, 5, 6, 7	8
Shimada <i>et al</i> ^[21]	Japan	RC	2007-2014	173	LADG	25	1, 2, 3, 4, 5, 6, 7	8
Shin <i>et al</i> ^[23]	South Korea	RC	2003-2005	192	LG	25	1, 2, 5, 6, 7	8
Yamada <i>et al</i> ^[22]	Japan	RC	1999-2005	141	LADG	25	1, 5, 6, 7	9
Yang <i>et al</i> ^[18]	China	RC	2009-2012	214	LAG	25	1, 2, 3, 5, 6, 7	8

1: Postoperative complications; 2: Postoperative hospital stay; 3: Mortality; 4: Time to resuming food intake; 5: Operative time; 6: Blood loss; 7: Retrieved lymph nodes. BMI: Body mass index; RC: Retrospective cohort; LG: Laparoscopic gastrectomy; TLG: Totally laparoscopic gastrectomy.

Table 2 Summary statistics of pooled odds ratio on various postoperative complications comparing high body mass index and normal body mass index groups receiving laparoscopic gastrectomy

Complication variable	No. of studies	No. of pooled patients	Pooled OR	95%CI	Test of heterogeneity		Test of overall effect	
					<i>P</i> value	<i>P</i> value		
Overall complications	9	6077	1.12	0.95-1.33	0.734	0.169		
Anastomotic leakage	6	3939	1.31	0.62-2.79	0.642	0.476		
Anastomotic stricture	4	3587	0.85	0.27-2.66	0.489	0.775		
Anastomotic bleeding	5	3798	0.63	0.27-1.45	0.942	0.277		
Abdominal abscess	5	3801	1.56	0.91-2.67	0.615	0.103		
Pancreatic leakage	6	3937	0.52	0.20-1.35	0.581	0.179		
Ileus	4	3584	1.96	0.79-4.83	0.382	0.144		
Wound	6	3939	1.77	0.92-3.42	0.289	0.087		

OR: Odds ratio; CI: Confidence interval.

(Figure 1). The outcomes of the quality assessment are shown in Table 1. All of the included studies obtained at least eight points, meaning that they were defined as high-quality.

Meta-analysis

Correlation between BMI and short-term outcomes of LG: There was no significant difference between the two cohorts in overall postoperative complications (OR = 1.12, 95%CI: 0.95 to 1.33, $P = 0.169$; Figure 2A), various postoperative complications (Table 2), the duration of postoperative hospital stay (SMD = 0.681, 95%CI: -0.05 to 0.07, $P = 0.681$; Figure 2B), postoperative mortality (OR = 1.95, 95%CI: 0.78 to 4.89, $P = 0.153$; Figure 2C), or time to resuming food intake (SMD = 0.00, 95%CI: -0.06 to 0.06, $P = 0.973$; Figure 2D). Heterogeneity was not apparent in any of these outcome results according to the fixed-effects model. Sensitivity analysis demonstrated that no study could affect the pooled OR for postoperative complications (Figure 3A). Visual assessments of the funnel plots (Figure 4A) and the Egger's test (Figure 5A) showed no evidence of publication bias for postoperative complications ($P = 0.849$).

Correlation between BMI and difficulties in LG:

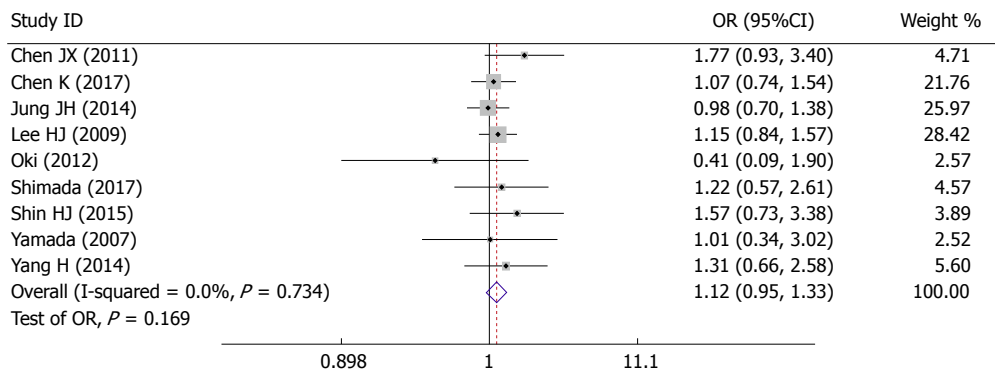
The high BMI group had longer operative time (SMD = 0.26, 95%CI: 0.21 to 0.32, $P < 0.001$; Figure 2E), greater blood loss (SMD = 0.19, 95%CI: 0.12 to 0.25,

$P < 0.001$; Figure 2F), and fewer retrieved lymph nodes (SMD = -0.13, 95%CI: 0.18 to 0.07, $P < 0.001$; Figure 6). Heterogeneity was not apparent in any of these outcome results according to the fixed-effects model. Sensitivity analysis demonstrated that no study could affect the pooled SMD for the operative time (Figure 3B). Visual assessment of the funnel plots (Figure 4B) and the Egger's test (Figure 5B) showed no evidence of publication bias for the operative time ($P = 0.887$).

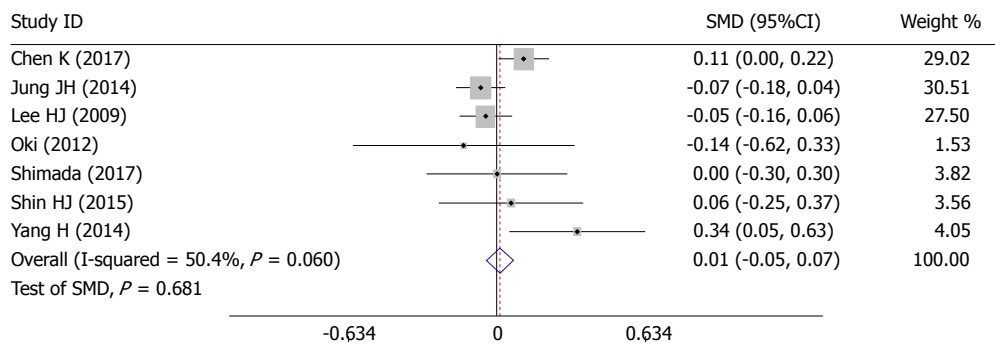
DISCUSSION

Obesity is traditionally considered a challenge for many surgeons who perform abdominal operations^[28-30]. Until now, the impact of obesity on the short-term outcomes of LG for GC has been controversial^[29,31]. This meta-analysis, including nine retrospective cohorts, aimed to investigate the correlation between obesity and the short-term outcomes of LG. Patients included were divided into a high BMI (≥ 25 kg/m²) and a normal BMI (< 25 kg/m²) group based on the World Health Organization definition of obesity. Splenic hilar lymph node dissection is necessary for LTG, but it is difficult to expose the deep location of the splenic hilum and complicated vessels. LTG has been regarded as a risk factor for short-term outcomes of LG for GC^[17]; therefore, studies solely focusing on LTG were excluded. Additionally, owing to the insufficient representativeness of the sample in the study with "pathological stage" limit, we excluded two studies

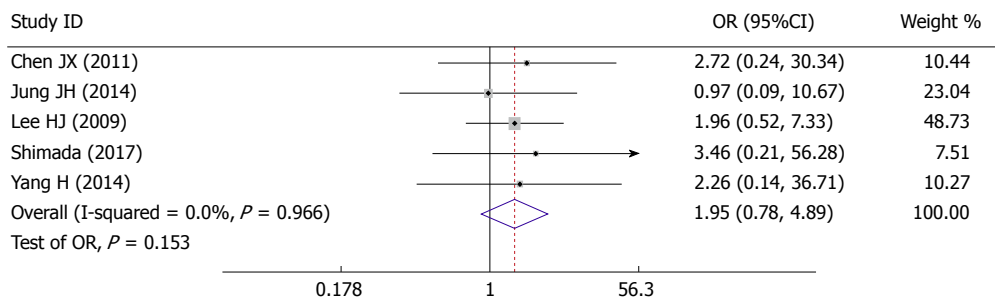
A



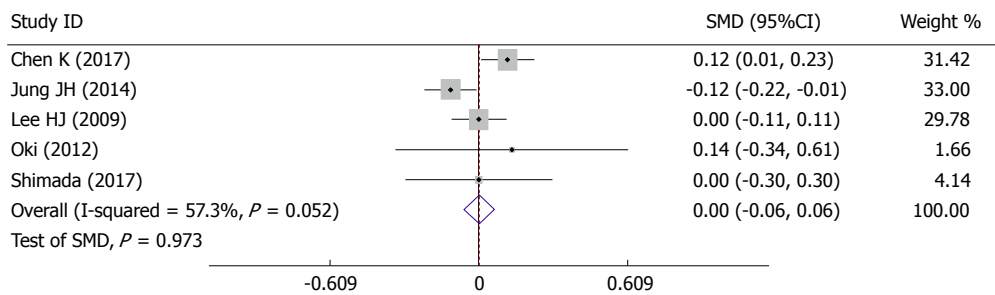
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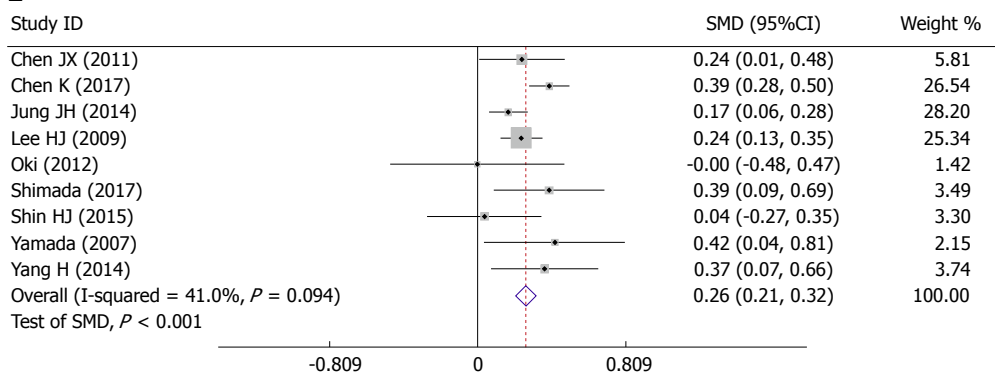
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E



F

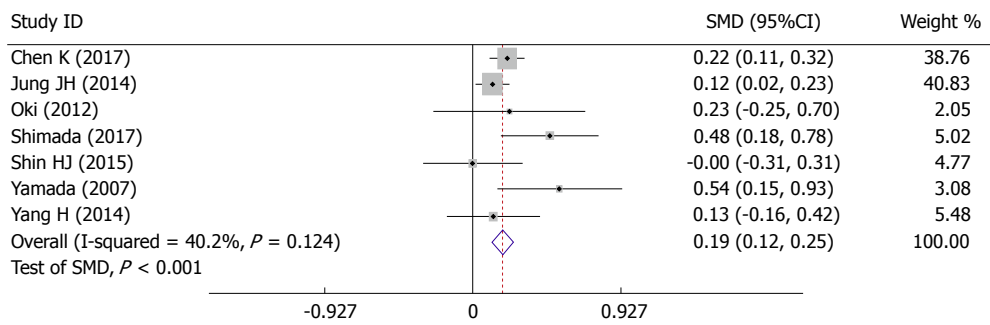
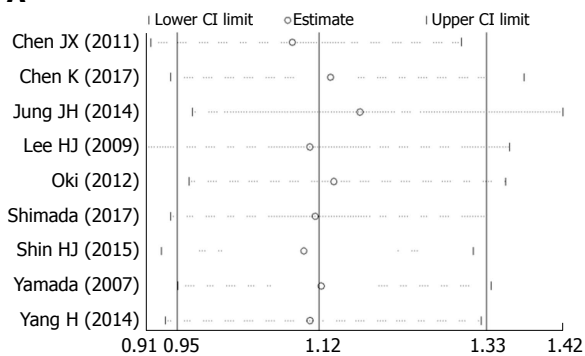


Figure 2 Correlation between body mass index and short-term outcomes/difficulties in laparoscopic gastrectomy. A: Correlation between body mass index (BMI) and postoperative complications in laparoscopic gastrectomy; B: Correlation between BMI and the duration of the postoperative hospital stay; C: Correlation between BMI and postoperative mortality; D: Correlation between BMI and the time to resuming food intake; E: Correlation between BMI and the operative time; F: Correlation between BMI and blood loss. SMD: Standard mean difference.

A

Meta-analysis estimates, given named study is omitted



B

Meta-analysis estimates, given named study is omitted

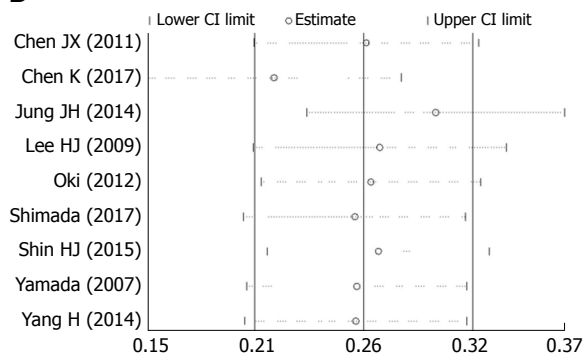
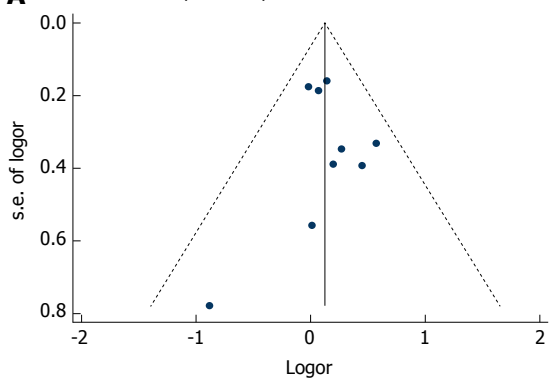


Figure 3 Sensitive analysis of association of postoperative complications and operative time with body mass index. A: Sensitive analysis of correlation between body mass index (BMI) and postoperative complications in laparoscopic gastrectomy; B: Sensitive analysis of correlation between BMI and the operative time.

A

Funnel plot with pseudo 95% confidence limits



B

Funnel plot with pseudo 95% confidence limits

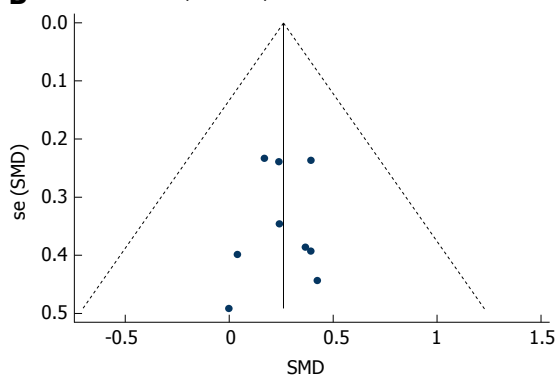


Figure 4 Funnel plot analysis of association of postoperative complications and operative time with body mass index. A: Funnel plot analysis of correlation between body mass index (BMI) and postoperative complications in laparoscopic gastrectomy; B: Funnel plot analysis of correlation between BMI and the operative time. SMD: Standard mean difference.

with this limit (one for solely including patients with early stage GC and the other for solely including patients with advanced GC).

Operative time, blood loss, and the number of retrieved lymph nodes were defined as indices of difficulties in LG. Our study has clearly demonstrated that the correlation between BMI and operative difficulties was

significant. Patients undergoing LG with a high BMI have longer operative time (SMD = 0.26, 95%CI: 0.21 to 0.32, $P < 0.001$), greater blood loss (SMD = 0.19, 95%CI: 0.12 to 0.25, $P < 0.001$), and fewer retrieved lymph nodes (SMD = -0.13, 95%CI: 0.18 to 0.07, $P < 0.001$). Likely due to hindered exposure to the stomach and pancreas, LG performed in patients with obesity is more technically

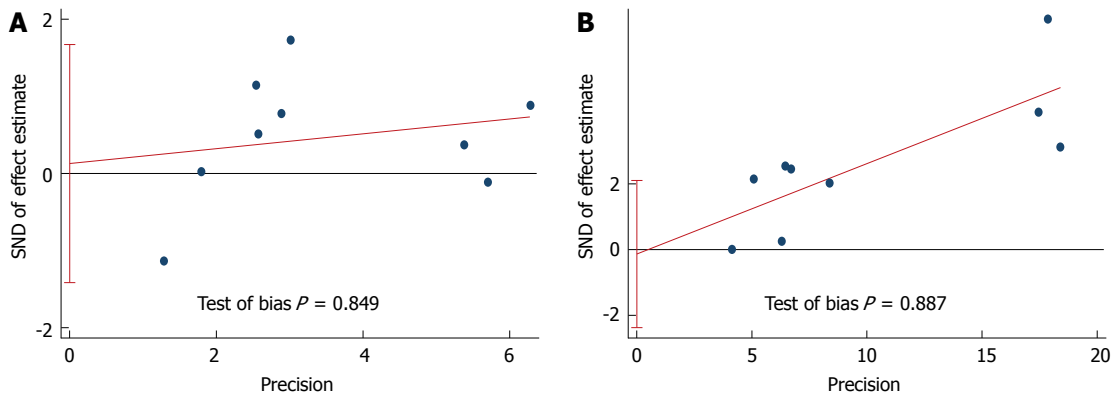


Figure 5 Egger's test of association of postoperative complications and operative time with body mass index. A: Egger's test of correlation between body mass index (BMI) and postoperative complications in laparoscopic gastrectomy; B: Egger's test of correlation between BMI and the operative time.

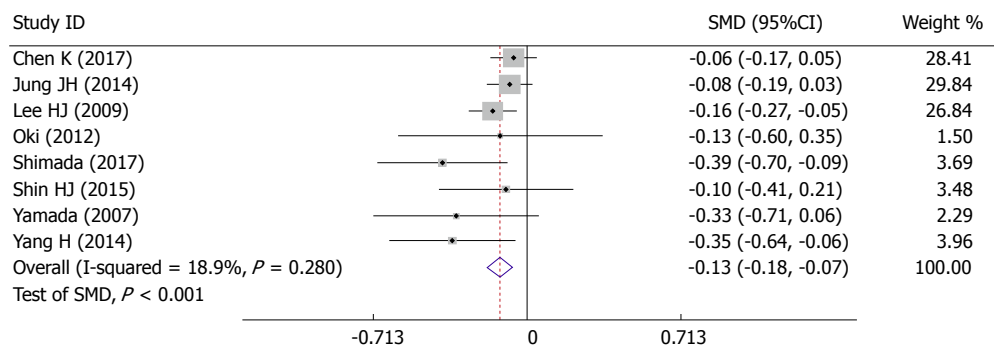


Figure 6 Correlation between body mass index and the number of retrieved lymph node. SMD: Standard mean difference.

demanding. The thickened mesentery, omentum, and ligamentum are very common in obese patients under certain circumstances and may lead to difficulties in the operative procedure, especially in ligation, dissection, or anatomy of the vessels and lymph nodes. Fatty stomach and omentum can also result in severe challenges owing to the stomach pulled by the surgeon. Blood bleed during the operation, caused by excessive incassate and fat mesenteries, is hard to stop in this narrow area surrounded by adipose tissue. It can be inferred that sensation recovery from anesthesia would be delayed in virtue of distribution of anesthetic agents affected by increased technical difficulties during exposure of an adequate operative field. Each of these potential factors contributes to longer surgical time and increased blood loss^[19]. As to the lower number of retrieved lymph nodes, it may be conferred that dissection of lymph nodes for patients with obesity could be limited by excess adipose tissue and structures. Obtaining lymph nodes from a mass of fat tissue could be more difficult than normal tissue and may be regarded as the other contributing factor to fewer retrieved lymph nodes; however, in all studies, the number of retrieved lymph nodes in the obese group was greater than the standard (> 15) recommended by the National Comprehensive Cancer Network (NCCN) guidelines, which suggests that LG can also ensure the curative effect in obese patients with GC.

Postoperative complications, the duration of

postoperative hospital stay, postoperative mortality, and time to resuming food intake were estimated as the impact of BMI on the short-term outcomes of LG. Our meta-analysis provided strong evidence that the correlation between BMI and postoperative short-term outcomes was not significant. In addition, anastomotic leakage, anastomotic stricture, anastomotic bleeding, abdominal abscess, pancreatic leakage, ileus, and wound infection would also be included in subgroup analysis. The results showed that BMI is not significantly associated with either overall postoperative complications or a particular one. The most critical factor contributing to this condition would be anastomosis. The excessive torsion of remnant stomach and duodenum could be avoided during the procedure of anastomosis performed by an experienced surgeon, especially in totally laparoscopic gastrectomy (TLG) which is becoming prevalent in Asian areas^[25]. In addition, the lower number of retrieved lymph nodes resulting from increased surgical difficulties also indicated that surgeons would be more careful and cautious during the operative procedure, and the injury of tissues and structures would be avoided to some extent. High-quality pre- and postoperative management could also help surgeons improve the patients' overall conditions and identify minor problems through observed indices on time, such as the amount of intro-abdominal bile drainage and the wound healing condition. Milder procedures and smaller wounds as well as careful pre-

and postoperative management result in lower rates of postoperative complications^[21]. Furthermore, to an extent, the results suggest that the assessment of obesity based solely on BMI may be insufficient. The distribution and amount of abdominal fat in an individual patient may not be accurately reflected by BMI, since it is a simple calculation based on weight and height^[23]. For instance, patients with a large amount of subcutaneous fat may have normal amounts of visceral and intra-abdominal fat that would not alter the difficulties and short-term outcomes of LG. Recent studies confer that visceral fat area is a more accurate predictor of intra- and postoperative outcomes than high BMI in obese patients due to its feasibility to evaluate the distribution of intra-abdominal fat^[32-34].

Limitations

Although we have searched recent publications using a rigorous search strategy, there are still some limitations to this meta-analysis. First, although all of the included studies obtained at least eight points, almost all of them were retrospective cohort studies. Although the randomized clinical trials (RCTs) are the gold standard for study design, it is hardly feasible to allocate patients with different BMIs randomly. Second, nine studies were included with a total sample size of 6077, which is relatively small. A larger sample size is needed to support the evidence. Third, as patients in Western countries have a higher BMI compared to Asian patients, our results should be considered carefully when being applied to other races, and more relevant studies should be performed worldwide.

In conclusion, our meta-analysis clearly supports that although high BMI in Asian patients with GC could increase the difficulties in LG with regard to operative time, blood loss, and the number of retrieved lymph nodes, there was no significant association between BMI and postoperative short-term outcomes, including postoperative complications, the duration of the postoperative hospital stay, postoperative mortality, and time to resuming food intake in Asian patients. It strongly demonstrates that a high BMI may not be a risk factor for short-term outcomes of patients undergoing LG if performed by an experienced surgeon with careful pre- and post-operative management, in contrast with the perspectives reported by previous studies. It may not be enough to estimate difficulties and postoperative outcomes in patients with GC undergoing LG using BMI as the only index to assess obesity. Other indices, for instance, VSA, should be taken into account.

patients with obesity have a higher risk of operative difficulties, as well as wound infection.

Research motivation

Recently, the impact of obesity on the short-term LG in patients has been controversial due to several studies. For instance, some studies reported that the association between obesity and LG was significant, while others reported the opposite conclusion.

Research objectives

To date, although several studies evaluating the body mass index (BMI) as an index to assess obesity and short-term outcomes of LG, the results have been controversial and limited. Hence, we conducted this meta-analysis to summarize all of the available evidence.

Research methods

The PubMed, Cochrane, EMBASE, and Web of Science databases were searched for studies that focused on the impact of obesity on the short-term outcomes of LG for GC in Asian patients who were classified into a high BMI (BMI ≥ 25 kg/m²) or low BMI group (BMI < 25 kg/m²). The results are expressed using the pooled odds ratio (OR) for binary variables and standard mean difference (SMD) for continuous variables with 95% confidence interval (CI), and were calculated according to the fixed-effects model while heterogeneity was not apparent or a random-effects model while heterogeneity was apparent.

Research results

Nine studies, with a total sample size of 6077, were included in this meta-analysis. Compared with the low BMI group, the high BMI group had longer operative time (SMD = 0.26, 95%CI: 0.21 to 0.32, $P < 0.001$), greater blood loss (SMD = 0.19, 95%CI: 0.12 to 0.25, $P < 0.001$), and fewer retrieved lymph nodes (SMD = -0.13, 95%CI: 0.18 to 0.07, $P < 0.001$). There was no significant difference between the high and low BMI groups in postoperative complications (OR = 1.12, 95%CI: 0.95 to 1.33, $P = 0.169$), the duration of postoperative hospital stay (SMD = 0.681, 95%CI: -0.05 to 0.07, $P = 0.681$), postoperative mortality (OR = 1.95, 95%CI: 0.78 to 4.89, $P = 0.153$), or time to resuming food intake (SMD = 0.00, 95%CI: -0.06 to 0.06, $P = 0.973$).

Research conclusions

Our meta-analysis provides strong evidence that despite the longer operative time, greater blood loss, and fewer retrieved lymph nodes, the association between BMI and the short-term outcomes of laparoscopic gastrectomy for GC, including postoperative complications, the duration of postoperative hospital stay, postoperative mortality, and time to resuming food intake was not significant. BMI could be a poor risk factor for short-term outcomes of LG. Other indices should be taken into account.

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ARTICLE HIGHLIGHTS

Research background

Gastric cancer (GC) is the second most prevalent cause of cancer-related deaths worldwide. Since 1994, laparoscopic gastrectomy (LG) has become increasingly popular for treating early GC in patients. The prevalence of obesity is increasing steadily in Asian countries. Obesity is regarded as a risk factor for worse surgical outcomes of complicated surgical procedures. Furthermore,

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