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The effects of obesity on surgical complications and postoperative prognosis of epithelial ovarian cancer: a meta-analysis

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Abstract

Objective To comprehensively evaluate and compare surgical outcomes of obese patients versus non-obese patients for surgical complications and postoperative prognosis due to epithelial ovarian cancer (EOC).

Methods Studies were obtained from database search systems of Medline (PubMed) and Embase. Data were analyzed by the meta-analysis method and the random-effect or fixed-effect model. The heterogeneity between the studies was evaluated by *I*2 index and the data were analyzed using STATA version 15.1 and Review Manager version 5.4.

Results 14 studies with 4858 cases of proven epithelial ovarian cancer who underwent extensive surgery were included. Obesity may be a risk factor of the low surgical complex score (RR1.08, 95% CI 1.01–1.15, $p=0.05$), but had no manifesting difference in the surgical complications score compared non-obesity group (RR 0.50, 95% CI 0.07–3.79, $p=0.501$ and RR 0.60, 95% CI 0.22–1.63, $p=0.316$). Obesity EOC patients who undergone surgery tended to be correlated with surgical complications, such as wound infection (RR 2.71, 95% CI 1.59–4.61, $p=0.000$), intestinal complications (RR 2.09, 95% CI 1.00-4.35, $p=0.000$), and 30-readmission rate (RR 1.84, 95% CI 1.16–2.93, $p=0.000$). Obese patients were more likely to have shorter prognosis free survival (PFS) (SMD 0.62-year, 95% CI-0.13 to 0.15), but the results did not discover a significant difference in overall survival (OS)between obesity and non-obesity. (SMD 0.01-year, 95% CI-0.13 to 0.15)

Conclusions Obesity affects the difficulty of ovarian cancer surgery, and a negative relationship between obesity and surgical complications is observed. Obesity is a potential risk factor for prognosis of EOC patients. Attention is played on determining what kind of case should be benefit most from this surgery to minimize the rates of operative complications and postoperative mortality.

PROSPERO registration number CRD 42,023,434,781.

Keywords Ovarian neoplasm, Obesity, Intraoperative complications, Prognosis, Meta-analysis

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Introduction

Ovarian cancer is the most common cause of gynecological cancer death lacking early diagnosis biomarkers and initial symptoms, so it is entitled of "silent woman killer" [1]. Because epithelial ovarian cancer (EOC) has the highest incidence, many scholars have conducted in-depth research on it. Nowadays, the incidence of obesity is increasing, and obesity is shown to be a risk factor for epithelial ovarian cancer [3]. Patients with epithelial ovarian cancer who undergone the surgery, obesity might be a factor in the significant risk of operative complications and perioperative mortality in some cases [5]. The Clavien-Dindo Grade represents the easiest assessment tool of postoperative situation that ranks complications [6]. This system represents an objective evaluation of outcomes from a surgical procedure by accurately and standardly defining surgical complications, especially ovarian cytoreductive surgery. While some scholars supporting the "obesity paradox" believed that this factor acts as a protective factor in the prognosis and operative complications of ovarian cancer patients [7]. Due to the lack of consensus, few meta-analyses assessed it in summary. A previous systematic review dates to year 2011 while a significant amount of literature has been published after that date [8]. Because of the severe surgical complications and high postoperative morality, how to reasonably evaluate the individual physical characteristics of patients especially obesity before operation was faced with confusions and difficulties. However, the effect of obesity still needs to be further elucidated. In addition, many studies may potentially be missed if literature searches are restricted to English-only sources. Therefore, we aim to evaluate the clinical effect, respectively for obesity and non-obesity in epithelial ovarian cancer with operative complications and postoperative outcomes.

Materials and methods

Search strategy

In this study, we searched the MEDLINE (PubMed) and EMBASE databases from Jan1st, 2006 to May31st, 2023 for relevant articles by the terms of "("BMI" OR "body mass index" OR "overweight" OR "obesity") AND ("ovarian cancer" OR "ovarian neoplasm" OR "ovarian carcinoma") AND ("surgery" OR "operation") AND ("survival analysis" OR "survival rate" OR "survival" OR "death" OR "mortality" OR "morbidity" OR "prognosis" OR "complications"). If the articles were written in English, they were eligible to be included in our research. To consider other potential sources for the study, references utilized in all publications that were found throughout the search were examined. Two authors separately assessed each of the retrieved papers and subsequently cross-checked them considering their conclusions. A third author will review the findings if there are any disagreements.

Inclusion and exclusion criteria

Inclusion criteria were: (1) observational studies or clinical trials; (2) studies evaluated the association of obesity status and women with surgical outcome; (3) patients with proven epithelial ovarian cancer who underwent extensive surgery served as the study subjects; (4) studies contained the experimental group (obesity)and the control group (Non-obesity); (5) measures of outcomes include things like mortality, complications from operation, and length of survival. Our exclusion criteria were: (1) comments, case series, reviews, letters, and editorials, articles about animal and cell studies; (2) no control or experimental group; (3) no details of participants; (4) patients with ovarian cancer who have not undergone major surgical treatment or opted for other treatments. We observed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) rules [9].

Data extraction

Data from the included studies were extracted and summarized independently by two of the authors [Jingjing Sheng (SJJ), Jiali Zhang (ZJL)]. Any disagreement was resolved by a third author [Yiping Huang (HYP)]. Data included the following: first author, publication year, country, study design, total sample size, each frequency of the cases (obesity) and control groups (non-obesity), follow-up year, the FIGO stage, mean diagnosis age, timing of BMI measurement, BMI category, adjustment variables, surgical procedures and complications, prognosis variables, preoperative commodities (see supplemental Table 1 [19] for details).

Quality assessment

The methodological quality of retrospective studies was assessed by the Newcastle–Ottawa Scale (NOS), which consist of three factors: patient selection, comparability of the study groups, and assessment of outcome (cohort studies). A score of 0–9 (allocated as stars) was allocated to each study. RCTs and observational studies achieving six or more stars were of high quality.

Data synthesis and analysis

For the effect of relationship between obesity and surgical complexity\complication risk\morality we used the Risks ratios (RRs) with 95% CIs. Standardized mean difference (SMD) and 95% confidence interval (95% CI) were used to estimate the relationship between obesity and overall survivals (OS)\recurrence free survivals (RFS). We evaluated statistical heterogeneity using the Cochran Chi-square ($X2$) and the $I2$ statistic. The random effect model based on generic inverse variance method was applied when heterogeneity was significant ($I2>50\%$). A p value <0.05 was considered significant heterogeneity for the $X2$ test. We used Funnel plot and Egger's test to explore the publication bias. Influence analysis was also conducted to determine whether an individual study affected the aggregate result or not. When the research only provided median and inter quartile range (IQR), the mean and the standard deviation (SD) were calculated by the formula given by Wan [24]. We performed subgroup analysis to explore the source of heterogeneity. We used sensitivity analysis to evaluate whether a single study affected the result. All statistical tests were two-sided, and statistical significance was defined as p value less than 0.05. We used The Rev Man 5.4 (Cochrane Collaboration, Oxford, UK) and STATA15.1 (Stata Corp, College Station, TX, USA) for statistical analyses.

Results

Study selection

Figure 1 is a flow diagram of the search process. A total of 1147 entries were found through the search. According to removal of duplicates 198 titles and abstracts were assessed and 26 articles appeared to be relevant for inclusion into the review. 12 articles were excluded for the following reasons: not EOC with surgery ($n = 1$), not about obesity ($n = 1$), with no details of subjects ($n = 4$), lack of data ($n = 6$).

Characteristics and quality assessment of included studies

The included articles reported results from three prospective cohort studies and eleven retrospective cohort studies. These eligible studies included a total of 4858 subjects. (see supplemental Table 1 [19] for details). Three of the studies were performed in Asia, four studies were performed in Europe and seven studies were performed in America. All the studies used comparative design. According to the NOS quality scale, all studies achieving six or more stars were of high quality. (see Supplementary Table 2 for details)

Obesity and surgical complex score

Two studies ($n = 2568$) which evaluated obesity and surgical complexity included in this part of meta-analysis. The result indicated that obesity may be a risk factor of the low surgical complex score (RR 1.08, 95% CI 1.01–1.15, $p = 0.05$). However, when it comes to moderate and high surgical complex score, obesity was not statistically significant. (RR 0.9, 95% CI 0.79–1.02, $p = 0.05$ and RR 0.77, 95% CI 0.55–1.08, $p = 0.05$) And there was no heterogeneity between the two studies ($I2 = 0\%$). (see Fig. 2 for details)

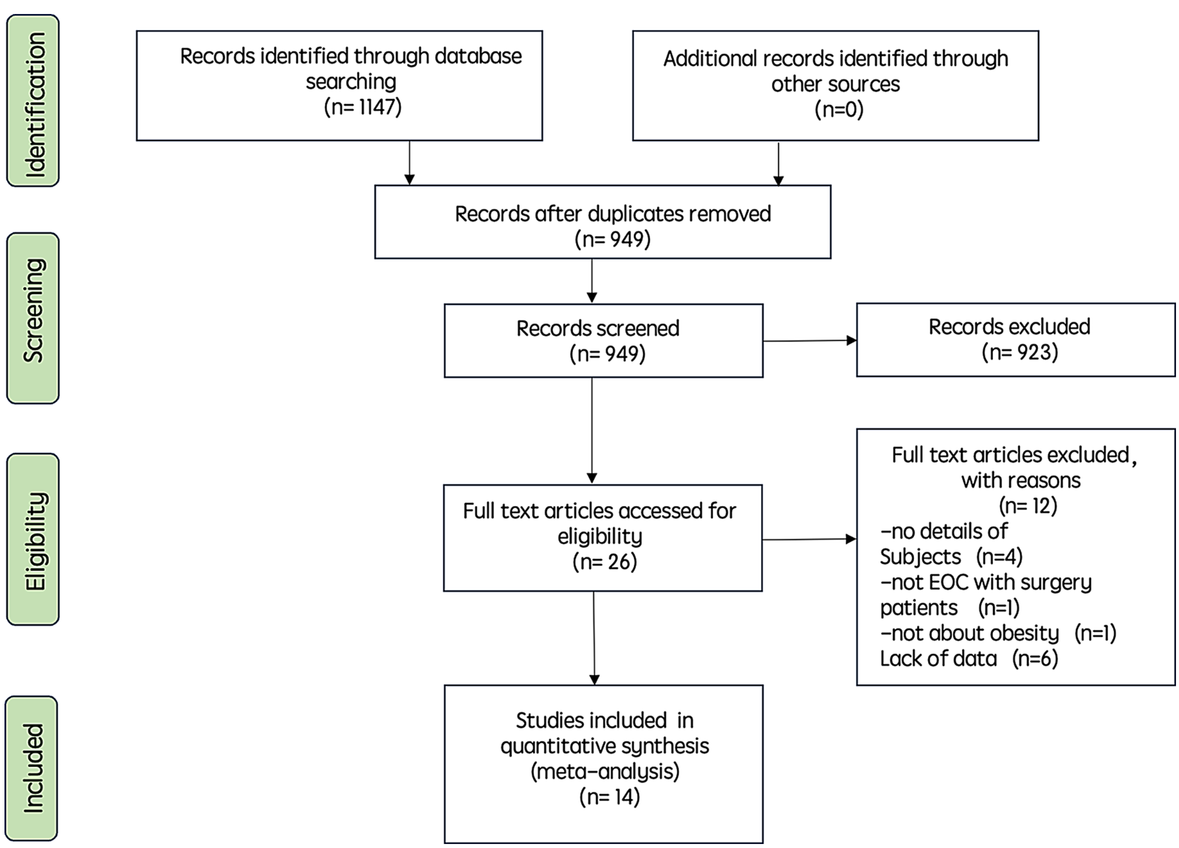

Fig. 1 Flow diagram of literature search and selection

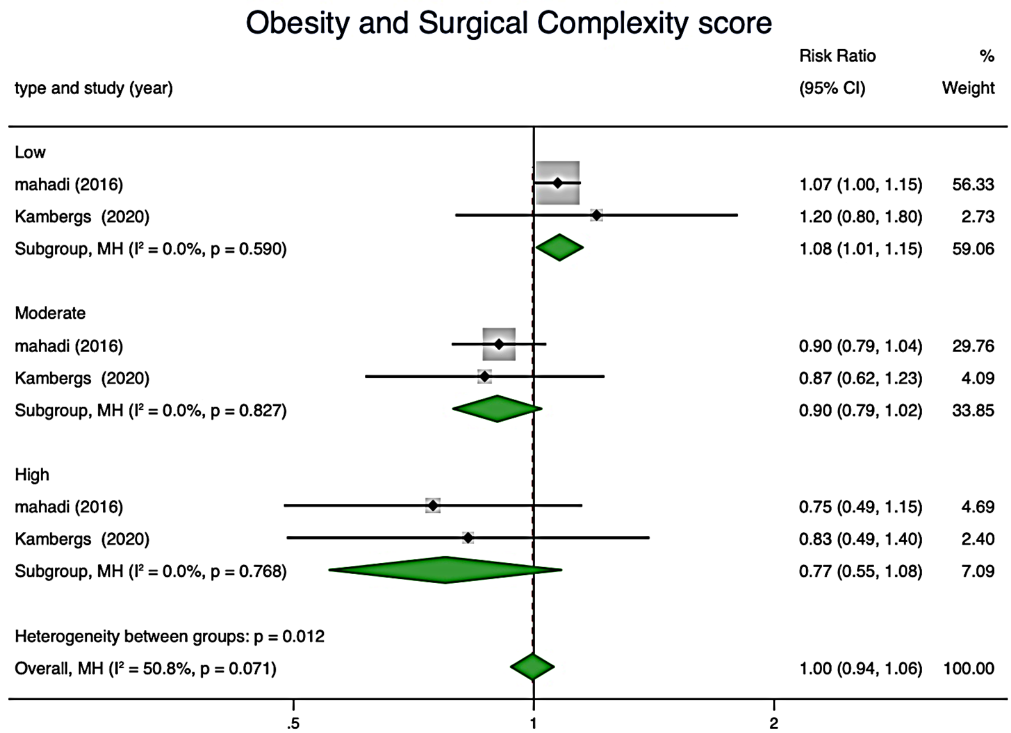

Fig. 2 Obesity and surgical complex score of Forest Plot

Obesity and surgical complications score(Clavien-Dindo grade)

Three studies ($n=1024$) investigated the association between obesity and surgical complications score(Clavien-Dindo grade). Two studies do not support a relationship between obesity and surgical complication score while the other one found obesity may be a risk factor of high Clavien-Dindo grade. Results of meta-analysis of the three studies indicated that obesity tended to be correlated with EOC surgical complications score. However, it was not statistically significant. (RR 0.50, 95% CI 0.07–3.79, $p=0.501$ and RR 0.60, 95% CI 0.22–1.63, $p=0.316$) Because heterogeneity was high among included studies, random effect model based on generic inverse variance method was applied, which let the heterogeneity decreased. (see Fig. 3 for details)

Obesity and surgical complications

Results of meta-analysis of the eight studies indicated obesity EOC patients who undergone surgery tended to be correlated with surgical complications, such as wound infection (RR 2.71, 95% CI 1.59–4.61), intestinal complications (RR 2.09, 95% CI 1.00-4.35) and 30-readmission rate. (RR 1.84, 95% CI 1.16–2.93) (see Fig. 4 for details).

Obesity and post-operative prognosis

Compared with non-obese patients after ovarian cancer surgery, the obese patients were more likely to have shorter prognosis free survival (PFS), (SMD 0.62-year, 95% CI-0.13 to 0.15) but the results did not discover a significant difference in overall survival (OS) between obesity and non-obesity. (SMD 0.01-year, 95% CI-0.13 to 0.15) But heterogeneity remained high. The subgroup analysis based on different mortality rate indicated that the mortality had no difference between two groups. (30-day: RR 1.03, 95% CI 0.98–1.09; 90-day: RR 2.69, 95% CI 0.99–7.30; 180-day: RR 0.81, 95% CI 0.58–1.12; 360-day: RR 0.95, 95% CI 0.77–1.18) The heterogeneity stayed high also. (see Figs. 5 and 6 for details)

Discussion

The overall goal of a meta-analysis is to combine the results of previous studies to arrive at a summary conclusion about a body of research. It is the most useful in summarizing prior research when individual studies are too small to yield a valid conclusion. In this study, we analyzed the associations between obesity and surgical complications and post-operative prognosis using a meta-analysis to obtain a powerful conclusion. To the best of our knowledge, this is the first meta-analysis providing comprehensive insights into the effects of obesity status and risk associated with surgical complexity and complication score. We were able to analyze the differences in PFS and OS between obese and non-obese patients. First, regarding PFS, we mentioned suggest that obese patients are more likely to have shorter PFS (SMD of 0.62 years, 95% CI of -0.13-0.15). This is consistent with findings, such as in a systematic review and

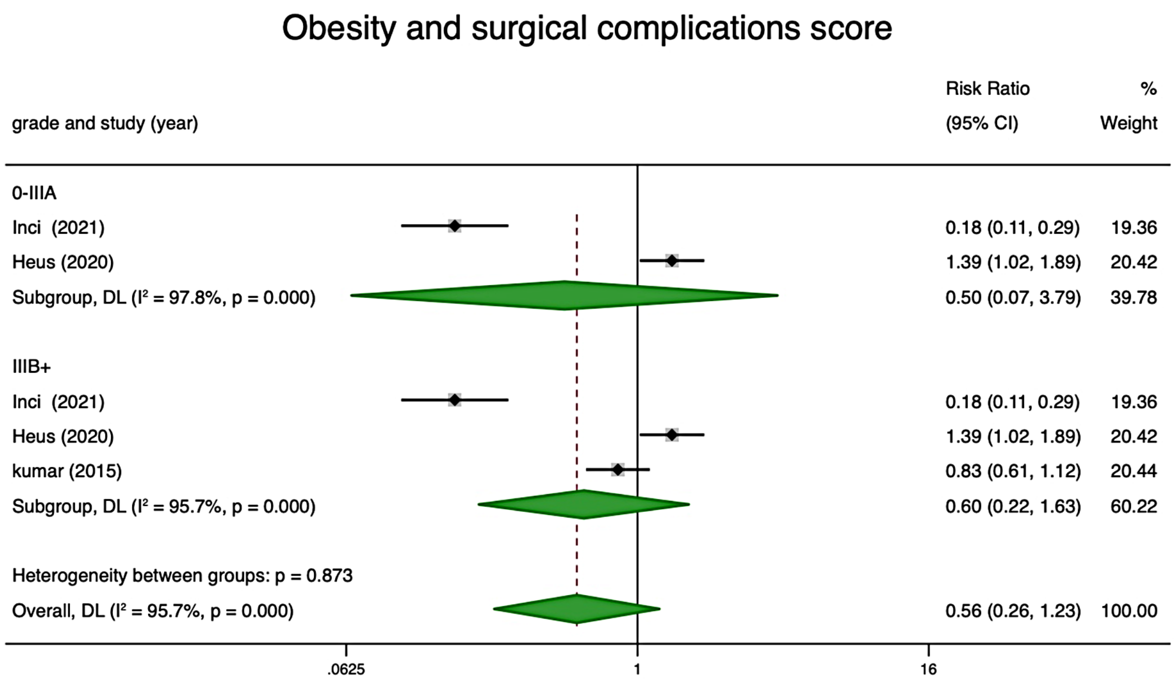

Fig. 3 Obesity and surgical complication score of Forest Plot

meta-analysis, that obesity was associated with reduced OS in cancer patients, but also with an increased risk of recurrence (HR of 1.13, 95% CI of 1.07–1.19). This suggests that obesity may have a negative impact on PFS in cancer patients. However, for OS, we mentioned did not find a significant difference between obese and non-obese (SMD of 0.01 years, 95% CI of -0.13 to 0.15). This is consistent with some studies, such as the Jackson Heart Study, which found inconsistencies between obesity and overall mortality when using different measures of obesity (BMI, WC, WHtR, and WHR), The association between BMI obesity and overall mortality was not significant (adjusted hazard ratio 1.14, 95% CI 0.96–1.35). In addition, another systematic review and meta-analysis also found that although obesity was associated with increased overall mortality in cancer patients (HR of 1.14, 95% CI of 1.09–1.19), survival outcomes were better in some specific types of cancer, such as lung cancer, renal cell carcinoma, and melanoma. Obesity may have a negative effect on PFS, but the effect on OS is less clear and there is some variation in the results from different studies. These findings suggest that the association between obesity and cancer survival may be influenced by several factors, including the type of cancer, how obesity is measured, and other clinical characteristics of patients. Results of our study also indicated that obesity is a risk factor of the low surgical complex score and tend to influence the surgical complication score. We found that Found by subgroup analysis heterogeneity was very low among included studies, low heterogeneity proved that this conclusion had sufficient probative value. It was well known that the difficulty of surgery was related to the possible complications during surgery, and our study also drew this possible conclusion, but due to the lack of specific groups of intraoperative complications, it was difficult to assess whether there was a certain correlation according to this study. Patients were obese before surgery tended to be with more severe surgical complications, such as wound infection, intestinal complications, and 30-readmission rate. We could see that obesity affected the occurrence of complications in surgical complications, but there was no significant statistical difference between them, and we found that heterogeneity was large, which might be related to the sample situation between the studies, our funnel plot and egger's test indicated that there was some publication bias in the included studies. After sensitivity analysis, we eliminated one of the most heterogeneous articles, and still saw no significant statistical difference between them (see Supplementary Figs. 1–2 for details). However, obesity did differ statistically significantly with other separately enumerated surgical complications such as deep vein thrombosis, incision infection, intestinal complications, and 30-readmission rate, and the heterogeneity was moderate. Compared with non-obese patients after ovarian cancer surgery, the obese patients were more likely to have shorter prognosis free survival. Even though most of the trials had small sample sizes and simple methodological quality, analysis of the pooled data showed a consistently superior effect of obesity combined with complications and prognosis in terms of total effectiveness, when compared to the control groups. As mentioned above, obesity

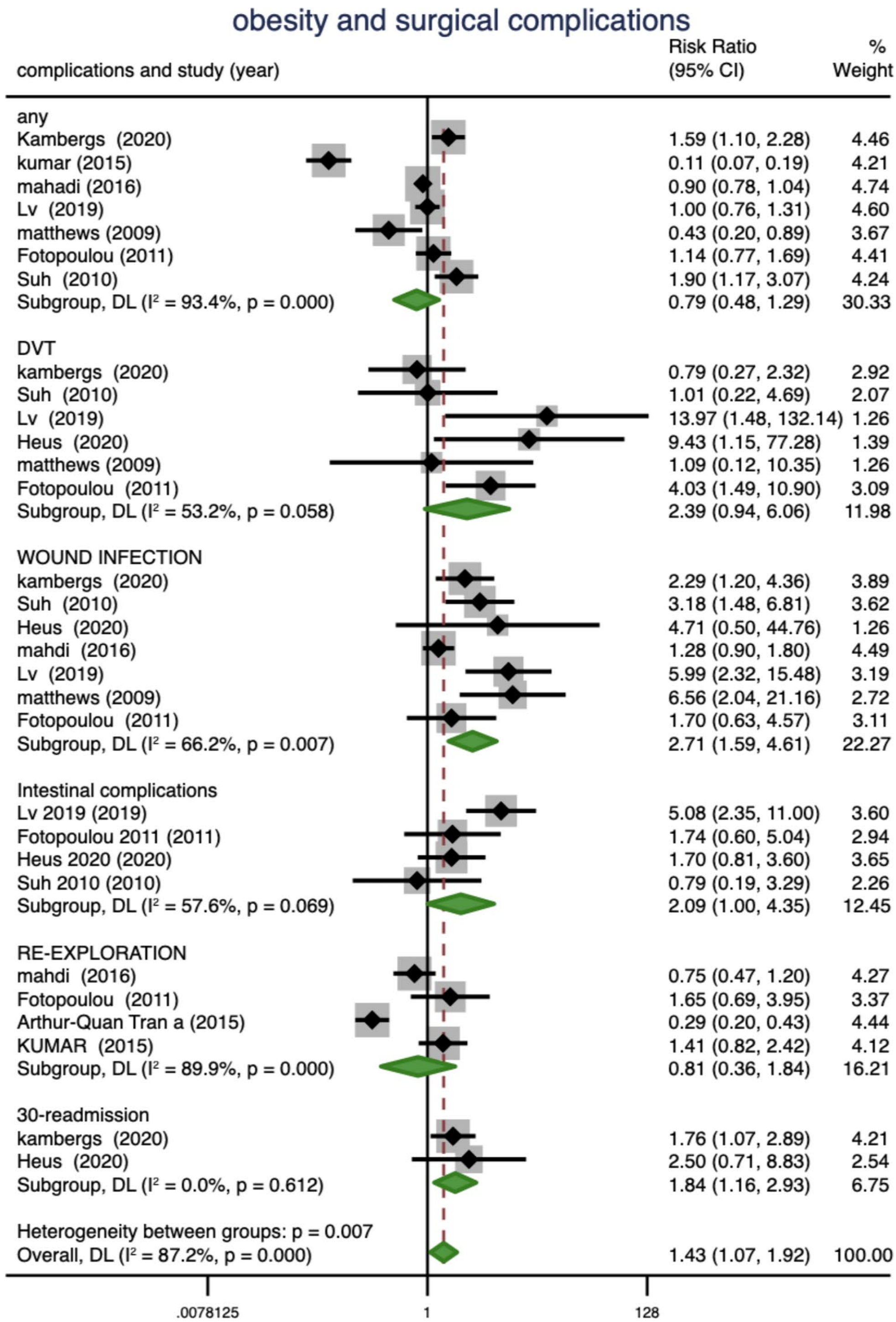

Fig. 4 Subgroup analysis of obesity status and surgical complication

was supposed to be related to more surgical complications, and obesity might be a potential risk factor for poor prognosis. The possible mechanisms were as follows: (1) Obesity and ovarian cancer: the impact of obesity itself on the occurrence, development, and prognosis of ovarian cancer, including metabolic factors and cytokine microenvironment factors [25]. However, due to the existence of the "obesity paradox", that is, some scholars believed that obesity could prolong the survival time of tumor patients to a certain extent and improve the prognosis of obese patients, but some scholars believed that it was not seen to have a significant correlation with ovarian cancer opposed to colon cancer [27]. (2) Obesity increased the occurrence of other comorbidities: obesity

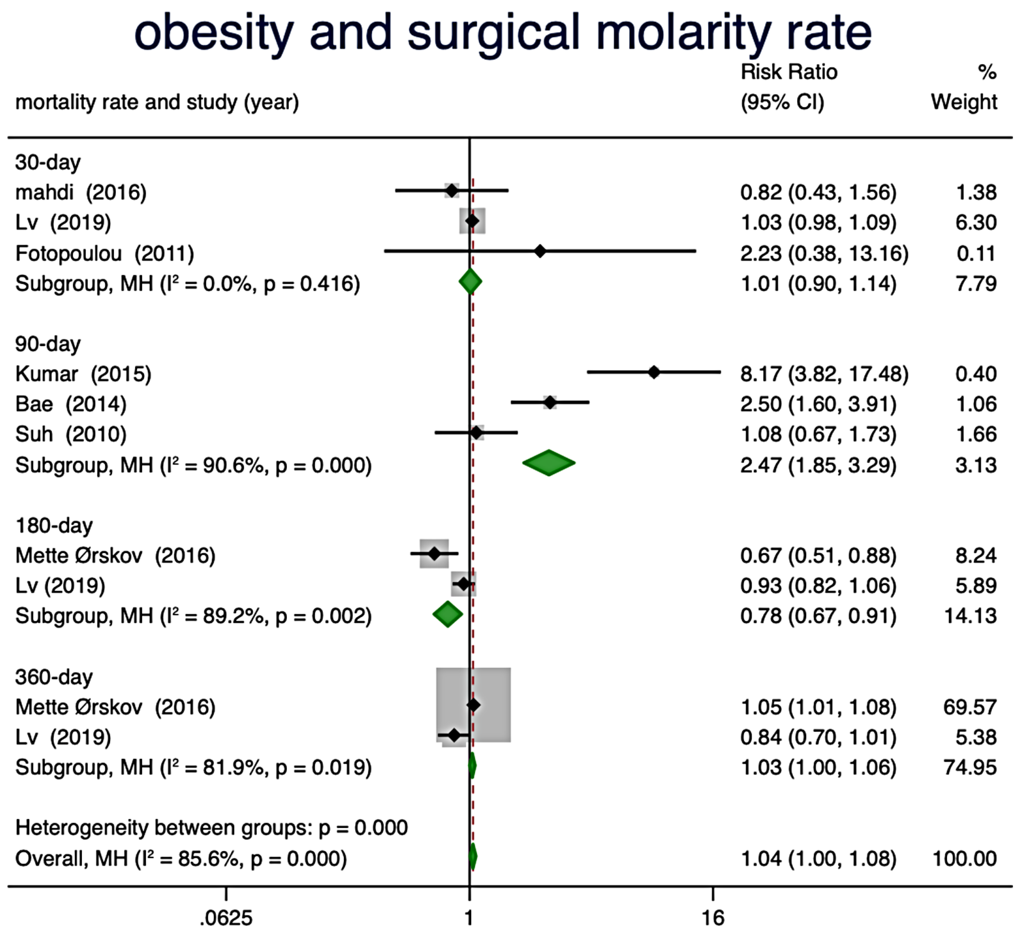

Fig. 5 Subgroup analysis of obesity status and morality rate

was accompanied by other obesity-related comorbidities, such as type 2 diabetes, hyperlipidemia, and other metabolic diseases, which affected the surgical complications and post-operative prognosis of obese patients with epithelial ovarian cancer to some extent [28]. (3) Obesity affects the operation complexity: obesity affects tissue exposure and separation during the operation process, increases the difficulty of surgery, prolongs the operation time, causes more intraoperative bleeding, affects healing, and increases the occurrence of related surgical complications, which is consistent with the results obtained by our research. However, at present, obese patients with early-stage ovarian cancer and young patients who need fertility-preserving surgery can reduce the occurrence of related surgical complications relatively through laparoscopic surgery, but it is not impossible. Therefore, there are often more restrictions in the selection of surgical methods and treatment methods, and more conservative treatment methods are usually chosen for efficacy and safety considerations, such as laparotomy and radiotherapy.

About preoperative evaluation, obesity may affect the diagnosis and staging of ovarian cancer. For example, excess abdominal fat may interfere with imaging tests, such as B-U CT scans and MRI, which can affect the accurate assessment of tumors. Obesity may also increase surgical risks, including the risk of anesthesia complications and surgical incision infections. Surgical planning needs to consider obesity-related physiological changes, such as increased abdominal pressure and changes in the position of internal organs, which may affect the difficulty and safety of surgery. More detailed preoperative preparation, including a nutritional assessment and weight management program, may be required. Obese patients may need closer postoperative monitoring after surgery because they may be at higher risk of complications such as deep vein thrombosis, lung complications, and wound healing problems. Post-operative rehabilitation programs may need to be specifically designed to help patients lose weight and improve quality of life.

Due to research limitations caused by inclusion factors and a variety of confounding factors, this meta-analysis did not include large sample randomization studies. As we all know, RCT is regarded as the gold standard for evaluating intervention effect, because it reduces the impact of confounding bias through the randomization

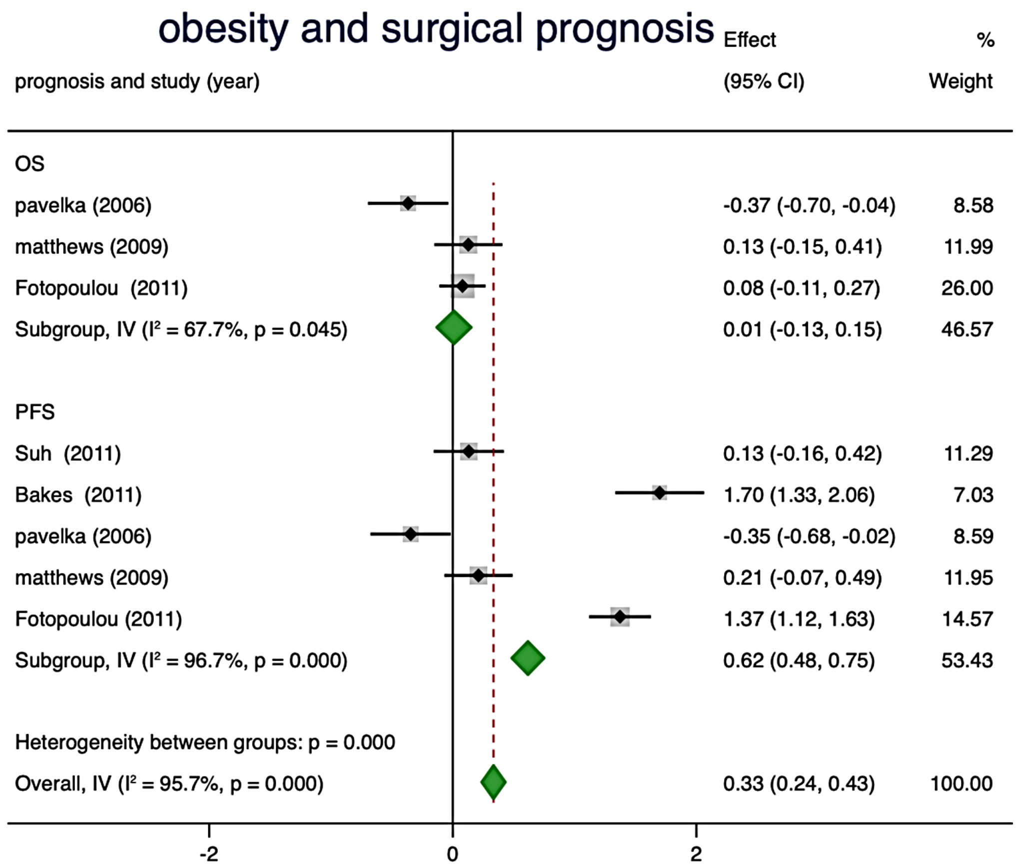

Fig. 6 Subgroup analysis of obesity status and surgical prognosis

process. However, the sample size of RCT is usually small and the diversity of subjects is limited. This may limit the extrapolation of the results. We know that different confounders may lead to systematic differences among the studies included in the meta-analysis, and the existence of heterogeneity complicates the combined results. Therefore, we tried our best to explore the sources of heterogeneity through subgroup analysis and Meta regression. However, due to the lack of methodological homogeneity in the original study, statistical adjustment is difficult to eliminate potential confounding bias, and the heterogeneity of confound-factor adjustment strategies may introduce new bias in the meta-analysis of case-control studies, affecting the accuracy of the combined effect size. This is also the limitation of our study, which needs to be demonstrated by further large-scale RCT studies and further detailed studies.

Strengths

In this work, we evaluated and compared surgical outcomes of obese patients versus non-obese patients for surgical complications and postoperative prognosis due to epithelial ovarian cancer. In this study, we analyzed the associations between obesity and intraoperative complications and post-operative prognosis using a meta-analysis to obtain a powerful conclusion. To the best of our knowledge, this is the first meta-analysis providing comprehensive insights into the effects of obesity status and risk associated with surgical complexity (surgical complex score) and complication score (Clavien-Dindo grade).

Limitations

The present meta-analysis has the following limitations that must be considered. Firstly, heterogeneity was substantial among studies although we performed a subgroup analysis to explore the source of it. This may be due to the study design (retrospective study), sample size, age and so on. Secondly, paucity of data in some included studies prevented us from evaluating influence of FIGO stage, differentiation grade, histological subtype, presence of ascites, CA125 levels, presence of distant metastases, intraoperative situation and receiving chemotherapy or not after surgery. Thirdly, potential publication bias is very likely to exist, despite no evidence obtained from our statistical tests and language of studies was limited to English, which may result in potential language bias.

Conclusion

Our study reveals that obesity affects the difficulty of ovarian cancer surgery, which may be a risk factor of the low surgical complex score when compared with controls, and a negative relationship between obesity and surgical complications is observed. In addition, obesity is a potential risk factor for prognosis of EOC patients. Therefore, attention is played on determining what kind of case should be benefit most from this surgery to minimize the rates of operative complications and postoperative mortality. Due to the small sample size of studies and lack of RCTs, more studies are needed to better clarify the effect of obesity in ovarian cancer surgery and explore the possible effect of mechanisms.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12893-025-02770-7.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

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Not applicable.

Author contributions
The literature search and data extraction were conducted by Jingjing Sheng (SJJ), Jiali Zhang (ZJL), and Yiping Huang (HYP). SJJ, ZJL, HYP and Yunxiao Zhou(ZYX) wrote the main manuscript text and Chu li prepared figures. Funding acquisition from Zujian Jin. All authors reviewed the manuscript. All authors contributed to the article and approved the submitted version.

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Data availability
All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate
This article does not address ethical review and informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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