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REVIEW

Laparoscopic Versus Open Gastrectomy for Advanced Gastric Cancer: A Meta-Analysis of Randomized Controlled Trials

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Abstract

Background Laparoscopy-assisted gastrectomy (LAG) is a well-established surgical technique in treating patients with early gastric cancer. However, the efficacy and safety of LAG versus open gastrectomy (OG) in patients with advanced gastric cancer (AGC) remains unclear.

Methods We systematically searched PubMed, Embase, and Cochrane Library in June 2023 for RCTs comparing LAG versus OG in patients with AGC. We pooled risk ratios (RR) and mean differences (MD) with 95% confidence intervals (CI) for binary and continuous endpoints, respectively. We performed all statistical analyses using R software version 4.3.1 and a random-effects model.

Results Nine RCTs comprising 3827 patients were included. There were no differences in terms of intraoperative complications (RR 1.14; 95% CI 0.72 to 1.82), number of retrieved lymph nodes (MD −0.54 lymph nodes; 95% CI −1.18 to 0.09), or mortality (RR 0.91; 95% CI 0.30 to 2.83). LAG was associated with a longer operative time (MD 49.28 minutes; 95% CI 30.88 to 67.69), lower intraoperative blood loss (MD −51.24 milliliters; 95% CI −81.41 to −21.06), shorter length of stay (MD −0.83 days; 95% CI −1.60 to −0.06), and higher incidence of pancreatic fistula (RR 2.44; 95% CI 1.08 to 5.50). Postoperatively, LAG was also superior to OG in reducing bleeding rates (RR 0.44; 95% CI 0.22 to 0.86) and time to first flatus (MD −0.27 days; 95% CI −0.47 to −0.07), with comparable results in anastomotic leakage, wound healing issues, major complications, time to ambulation, or time to first liquid intake. In the long-term analyses at 3 and 5 years, there were no significant differences between LAG and OG in terms of overall survival (RR 0.99; 95% CI 0.96 to 1.03) or relapse-free survival (RR 0.99; 95% CI 0.94 to 1.04).

Conclusion This meta-analysis of RCTs suggests that LAG may be an effective and safe alternative to OG for treating AGC; albeit, it may be associated with an increased risk for pancreatic fistula.

Keywords Laparoscopic-assisted gastrectomy · Open gastrectomy · Advanced gastric cancer

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Abbreviations

AGC	Advanced gastric cancer
CI	Confidence interval
EGC	Early gastric cancer
ICU	Intensive care unit
LAG	Laparoscopic-assisted gastrectomy
OG	Open gastrectomy
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
PROSPERO	International Prospective Register of Systematic Reviews
RCT	Randomized controlled trial
RR	Risk ratio

Introduction

Gastric cancer is one of the most prevalent cancers and a leading cause of mortality, ranking fifth among all malignant tumors worldwide [1]. Surgical resection with lymph node dissection is the most effective treatment for gastric cancer [2]. Since laparoscopy-assisted gastrectomy (LAG) was first described in 1994 by Kitano and colleagues [3], laparoscopic procedures have gained popularity for early gastric cancer (EGC) treatment, providing better short-term outcomes and similar survival rates compared with open gastrectomy (OG) [4–6].

The latest Japanese gastric cancer treatment guidelines recognize LAG as standard of care for patients with EGC [7]. This was mostly driven by the short-term benefits of LAG and established safety demonstrated by JCOG 0703 led by certified surgeons with substantial expertise in laparoscopic techniques [8]. Even so, the role of LAG versus OG for patients with advanced gastric cancer (AGC) rather than EGC remains unclear, since recent randomized controlled trials (RCTs) yielded conflicting results [5, 9].

Previous meta-analyses have addressed this matter and retrieved comparable short-term surgical outcomes and survival rates between LAG and OG for patients with AGC [10–15]. Nevertheless, some of them included RCTs and observational studies or combined data from early and advanced disease, as well as cases treated combining alternative surgical techniques, such as splenic hilar lymphadenectomy without gastrectomy [10–13]. This may have introduced bias and confounding to the analysis, retrieving less generalizable results for the specific population of patients with AGC [10] Moreover, these meta-analyses were unable to compare longer-term survival rates of LAG versus OG, which is a key component for the decision-making on surgical technique in the real-world setting [10, 11].

Recently, large RCTs on this topic released long-term post hoc analyses and shed light on more short-term outcomes of patients with AGC who underwent LAG versus OG [9, 16]. Therefore, we performed an updated meta-analysis evaluating the efficacy and safety of LAG compared with OG for patients with AGC, particularly exploring distal resection as a subgroup of interest.

Material and Methods

This systematic review, meta-analysis, and reporting were conducted in accordance with the Cochrane Handbook of Systematic Reviews of Interventions recommendations and Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [17, 18]. Its protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO) database under registration number CRD42023439925 on July 12, 2023.

Eligibility Criteria

We included restricted inclusion in this meta-analysis to the following eligibility criteria: (1) RCTs, (2) comparing LAG with OG, (3) in patients with AGC, and (4) reporting any of our outcomes of interest. We excluded observational studies, secondary analyses of included trials, and studies enrolling patients who underwent gastrectomy for EGC or benign lesions.

Search Strategy and Data Extraction

In accordance with PRISMA guidelines, we systematically searched PubMed, Embase, and Cochrane Library in June 2023 for RCTs comparing LAG versus OG in patients with AGC using the following search: "advanced gastric cancer," "GC," "AGC," "laparoscopic," "laparoscopy-assisted," "laparoscopy," "LADG," "LDG," "LG"," "gastrectomy," "open surgery," and "ODG." In addition, we performed a backward snowballing search using the references of included studies and systematic reviews. Two authors independently extracted data following predefined search criteria and quality assessment.

Endpoints and Subanalyses

Our outcomes of interest may be stratified as follows: (1) intraoperative outcomes; (2) postoperative complications; (3) in-hospital and short-term outcomes; (4) long-term survival rates. We performed a prespecified subanalysis in patients undergoing distal gastrectomy.

Quality Assessment

We performed quality assessment using the Cochrane Collaboration's tool for assessing risk of bias in randomized studies (Rob 2), which allows categorization of each study as low risk, some concerns, or high risk for bias in five domains: selection bias, performance bias, detection bias, attrition bias, and reporting bias [19]. Two authors (M.A.P.B. and K.M.R.) performed the risk of bias assessment independently, and disagreements were resolved through consensus. We further assessed potential small study effects (publication bias) using funnel plot analysis for the outcome of overall postoperative complications.

Statistical Analysis

We pooled risk ratios (RR) and mean differences (MD) with 95% confidence intervals (CI) for binary and continuous endpoints, respectively. A random-effects model was applied accounting for demographical and methodological heterogeneity among included RCTs, as per Cochrane recommendations [17]. Heterogeneity was evaluated through Cochran Q test and I^2 statistics; $I^2 \geq 25\%$ and p-values for heterogeneity inferior to 0.10 were considered significant for heterogeneity. High heterogeneity was explored using leave-one-out analyses. P-values inferior to 0.05 were considered statistically significant for treatment effects. We performed all statistical analyses following the intention-to-treat principle whenever available and using the meta and metafor packages in R software 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria).

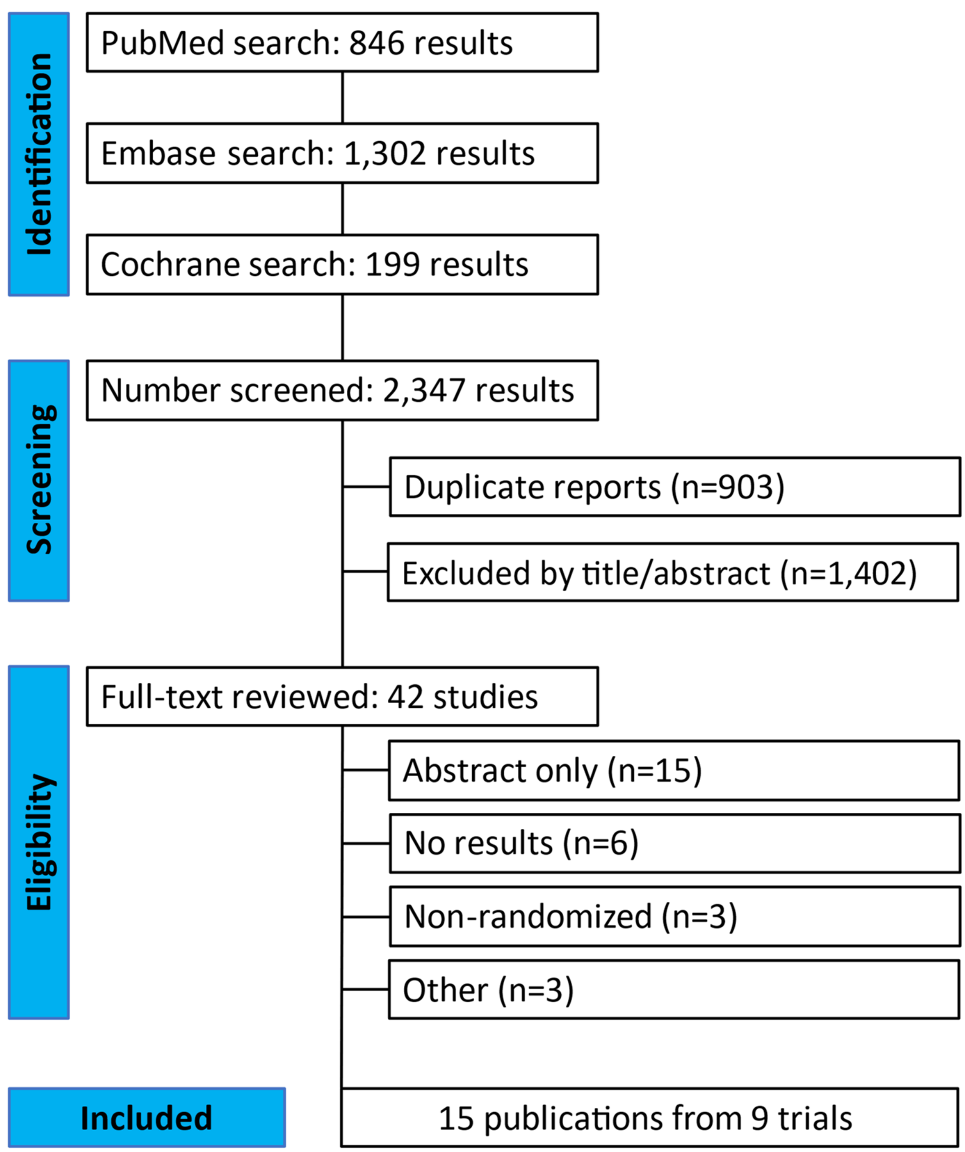
Results

Study Selection and Characteristics

As detailed in Fig. 1, 2347 studies were initially identified through our literature search. After removal of duplicate articles and unrelated studies, 42 were fully reviewed for the inclusion and exclusion criteria. Fifteen studies from nine trials comprising 3827 patients were included, of whom 1922 (50.2%) were randomized to LAG. Individual studies characteristics are displayed in Table 1 (Supplementary Material 1).

No significant differences in baseline characteristics were found and the total follow-up ranged from 30 days to 8 years. Operation techniques varied between each trial, and seven trials performed distal gastrectomy [9, 16,

Fig. 1 PRISMA flow diagram of study screening and selection



20–27]. One RCT focused on hand-assisted laparoscopic surgery [28, 29]. In addition, two included total or partial gastrectomy [30–32].

Of all the patients included, 2642 (69%) were male sex, and the age remained in the range of 60 years old. The tumor size was reported in five studies, ranging from 3.6 to 6.2 cm. Moreover, BMI was around 22 kg/m^2 in the patients, and most of them were classified as TNM stages I, II, or III in most of studies.

Pooled Analysis of All Studies

Intraoperative Outcomes

LAG was associated with a significantly longer operative time compared with OG (MD 49.28 minutes; 95% CI 30.88 to 67.69; $p<0.001$; $I^2=96\%$; Fig. 2a). In addition, patients undergoing LAG had a significantly lower intraoperative blood loss as compared with OG (MD −51.24 milliliters; 95% CI −81.41 to −21.06; $p<0.001$; $I^2=95\%$; Fig. 2b). Of note, there was a particularly high between-study heterogeneity in these outcomes.

There were no significant differences between groups with regards to intraoperative complications (RR 1.14; 95% CI 0.72 to 1.82; $p=0.576$; $I^2=2\%$), need for blood transfusion (RR 0.76; 95% IC 0.56 to 1.03; $p=0.075$; $I^2=32\%$), or absolute number of retrieved lymph nodes (MD −0.54 lymph nodes; 95% CI −1.18 to 0.09; $p=0.095$; $I^2=0\%$) (Fig. S1, Supplementary Material 2).

Postoperative Endpoints

Postoperative bleeding rates, both intra-abdominal and intra-luminal, were significantly lower in the LAG arm as compared with OG (RR 0.44; 95% CI 0.22 to 0.86; $p=0.017$; $I^2=0\%$; Fig. 3a), while there was a higher incidence of pancreatic fistula (RR 2.44; 95% CI 1.08 to 5.50; $p=0.032$; $I^2=0\%$; Fig. 3b). There was a comparable incidence of overall postoperative complications between LAG and OG (RR 0.82; 95% CI 0.66 to 1.01; $p=0.062$; $I^2=35\%$; Fig. 3c), anastomotic leakage (RR 1.18; 95% CI 0.68 to 2.06; $p=0.561$; $I^2=0\%$), and wound healing issues (RR 0.72; 95% CI 0.48 to 1.07; $p=0.107$; $I^2=0\%$) between groups (Fig. S2, Supplementary Material 2).

Major postoperative complications were evaluated using the Clavien-Dindo grade 3 or higher in most trials, but in the COACT 1001 trial was assessed using the Accordion Severity Classification of Postoperative Complications (ASCPC) [20]. There were no significant differences between groups in overall major complications

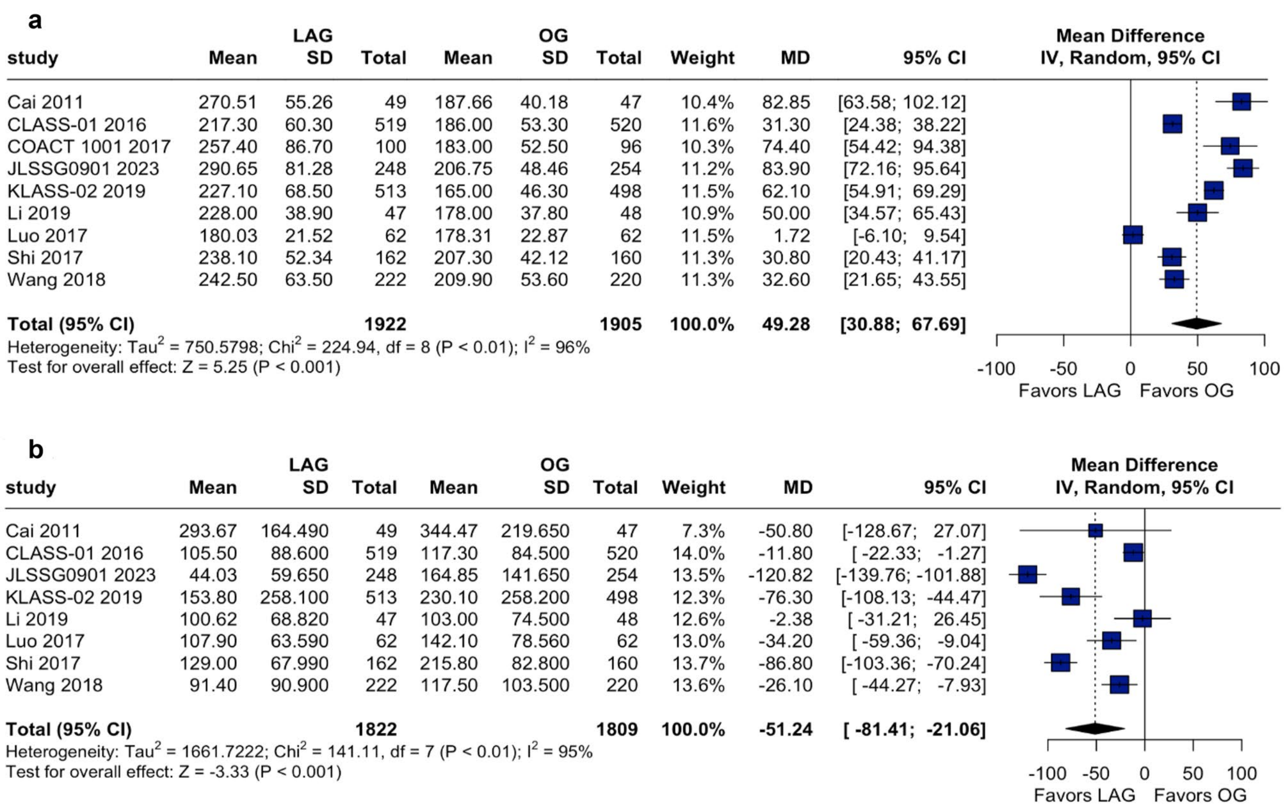


Fig. 2 **a** Operative time was significantly longer in the LAG group. **b** Intraoperative blood loss was significantly lower in the LAG group

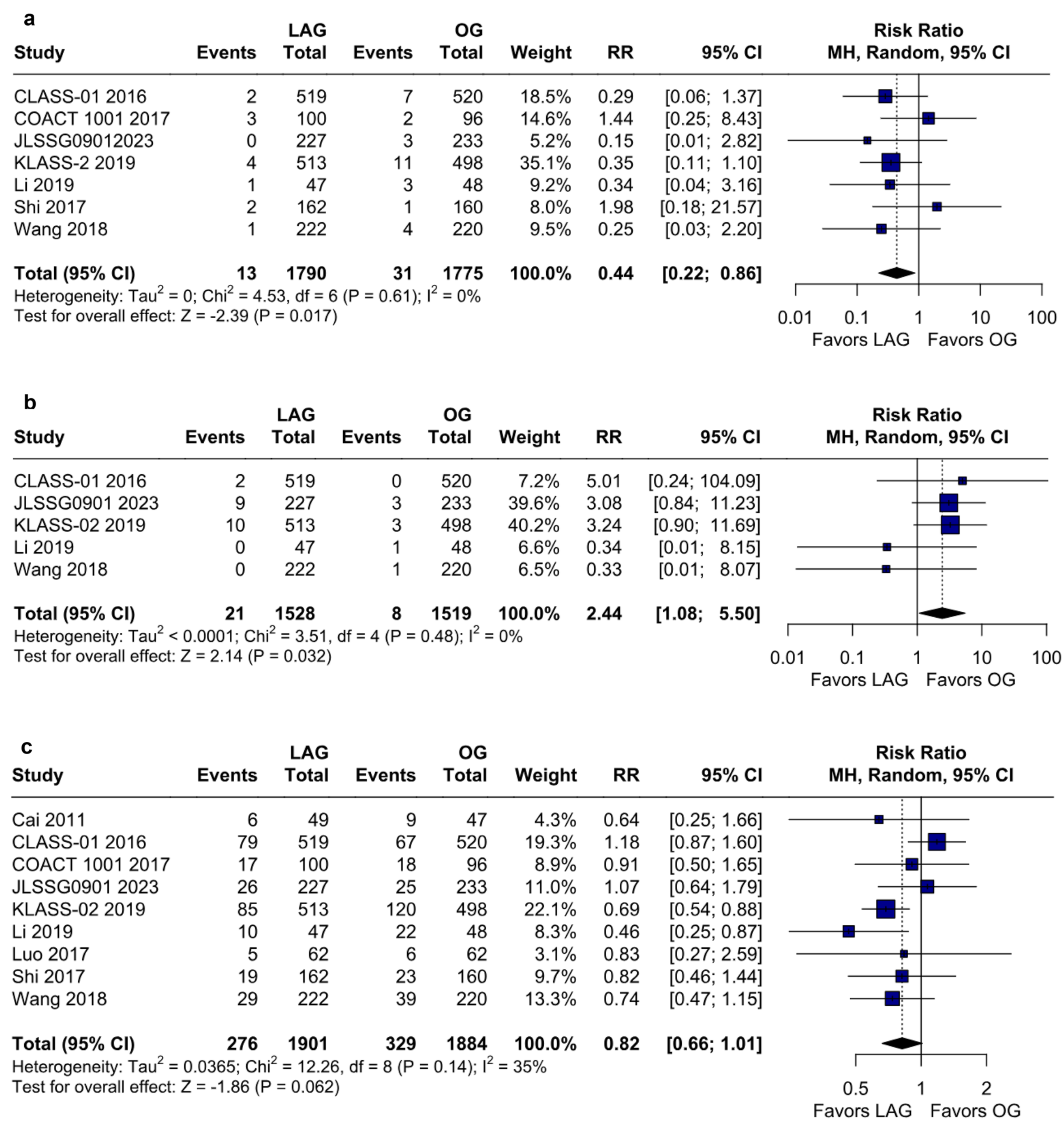


Fig. 3 **a** Postoperative bleeding was significantly lower in the LAG group. **b** Pancreatic fistula was significantly higher in the LAG group. **c** There were no differences between LAG and OG group

(RR 0.94; 95% CI 0.65 to 1.36; $p = 0.740$; $I^2 = 2\%$) and life-threatening complications requiring intensive care unit (ICU) admission (based on Clavien-Dindo grade 4; RR 1.29; 95% CI 0.47 to 3.52; $p = 0.622$; $I^2 = 0\%$) (Fig. S2, Supplementary Material 2).

In-Hospital and Short-Term Endpoints

There was no significant difference between laparoscopic and open techniques in 90-day mortality rates (RR 0.91; 95% CI 0.30 to 2.83; $p = 0.876$; $I^2 = 0\%$; Fig. 4a). Moreover, LAG

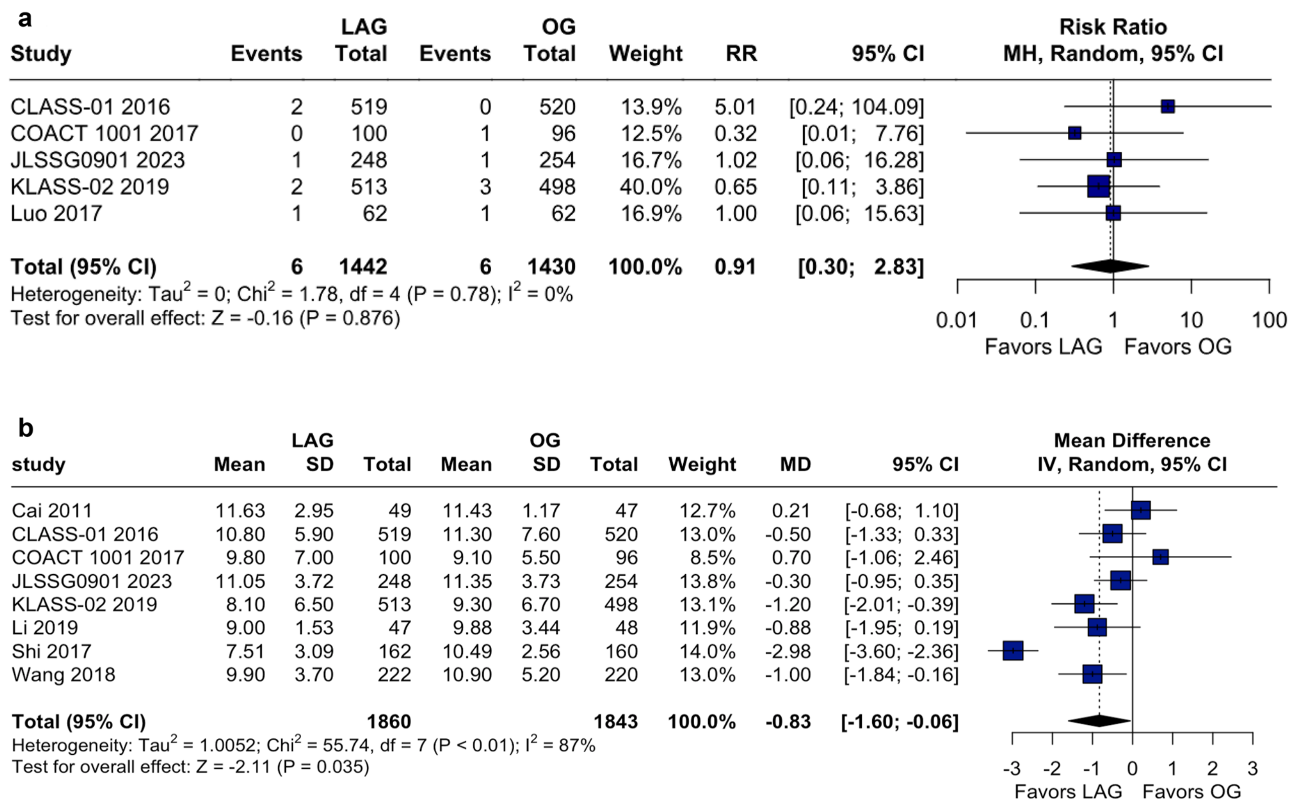


Fig. 4 **a** There were no differences between LAG and OG group. **b** The length of postoperative stay was significantly shorter in the LAG group

was associated with a significantly shorter length of stay as compared with OG (MD −0.83 days; 95% CI −1.60 to −0.06; $p=0.035$; $I^2=87\%$; Fig. 4b).

As for postoperative recovery, time to first flatus was significantly lower in the LAG group (MD −0.27 days; 95% CI −0.47 to −0.07; $p=0.009$; $I^2=81\%$), while there was no significant difference in time to ambulation (MD −0.44 days; 95% CI −1.00 to 0.13; $p=0.130$; $I^2=97\%$) or time to first liquid intake (MD −0.39 days; 95% CI −0.79 to 0.02; $p=0.061$; $I^2=83\%$) (Fig. S3, Supplementary Material 2).

Long-Term Survival

At 3 years, overall survival rates were comparable between LAG and OG (85.2% versus 85.5%; RR 1.00; 95% CI 0.96 to 1.03; $p=0.770$; $I^2=0\%$; Fig. 5a). The two techniques also yielded similar relapse-free survival rates (77.5% versus 78.6%; RR 0.99; 95% CI 0.94 to 1.03; $p=0.506$; $I^2=0\%$; Fig. 5b).

Results remained consistent at 5 years, with comparable overall survival (75.3% versus 76.4%; RR 0.99; 95% CI 0.96 to 1.03; $p=0.640$; $I^2=0\%$; Fig. 6a) and relapse-free survival rates (69.4% versus 70.2%; RR 0.99; 95% CI 0.94 to 1.04; $p=0.687$; $I^2=0\%$; Fig. 6b).

Subanalyses in Selected Populations

Predefined subgroup analyses were performed to evaluate the safety and efficacy specific to laparoscopic distal gastrectomy (LDG) and advanced distal gastric cancer. Intraoperative complications, operation time, blood loss, and blood transfusion were not significantly different in the subanalysis of LDG (Figs. S4 and S5, Supplementary Material 2). However, the number of retrieved lymph nodes was significantly lower in the LAG group (MD −1.04 lymph nodes; 95% CI −1.91 to −0.18; $p=0.018$; $I^2=0\%$; Fig. S5) in distal gastrectomy.

The length of stay and time to first flatus was significantly shorter in the LDG groups as compared to OG, and no differences were found between them in terms of time to first liquid intake (Fig. S6, Supplementary Material 2). As well as the overall postoperative complications, including type of complications, such as bleeding, anastomotic leakage, wound problems, and pancreatic fistula outcomes were not affected by distal gastrectomy approach (Figs. S7 and S8, Supplementary Material 2).

Similarly, no significant differences were found in terms of major complications, life-threatening complications requiring ICU management, and short-term mortality

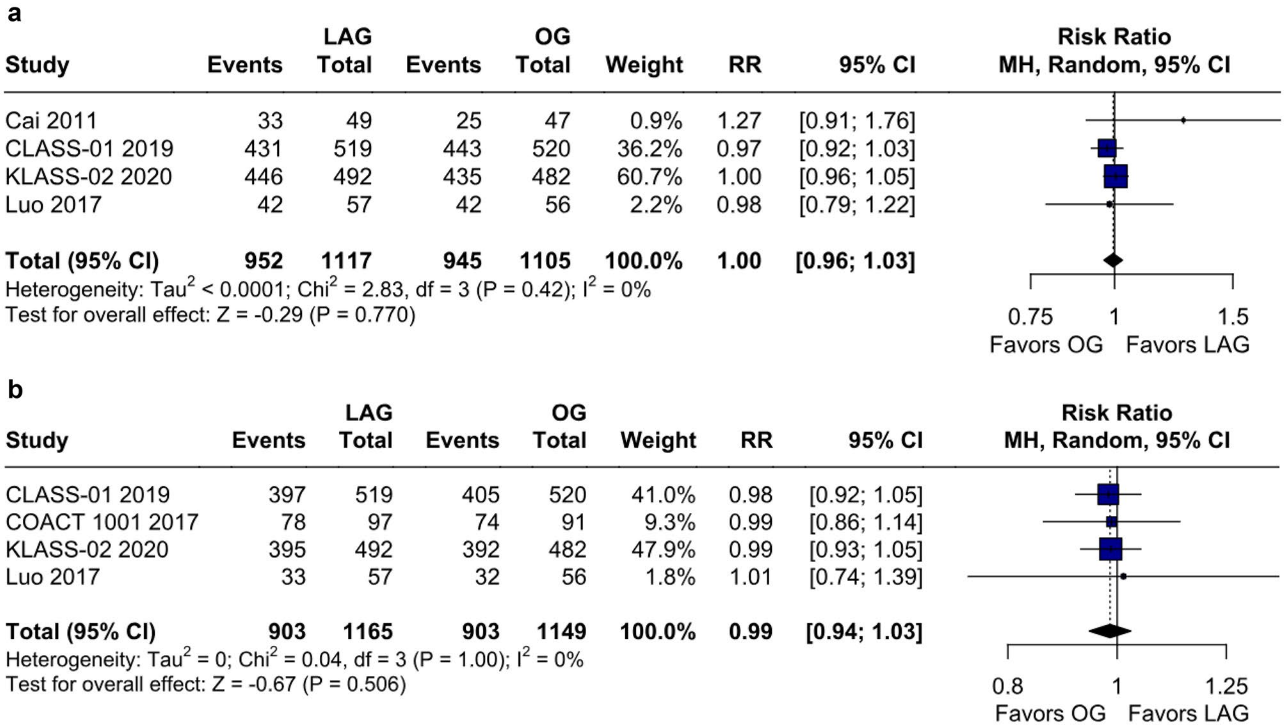


Fig. 5 **a** There were no differences between LAG and OG group. **b** There were no differences between LAG and OG group

between LDG and OG (Fig. S9, Supplementary Material 2). The extent of distal resection also had no effect in the long-term outcomes, such as 3-year RFS and 5-year OS (Fig. S10, Supplementary Material 2).

Quality Assessment

Supplementary Fig. S11 (Supplementary Material 2) outlines the quality appraisal of each individual RCT. One RCT

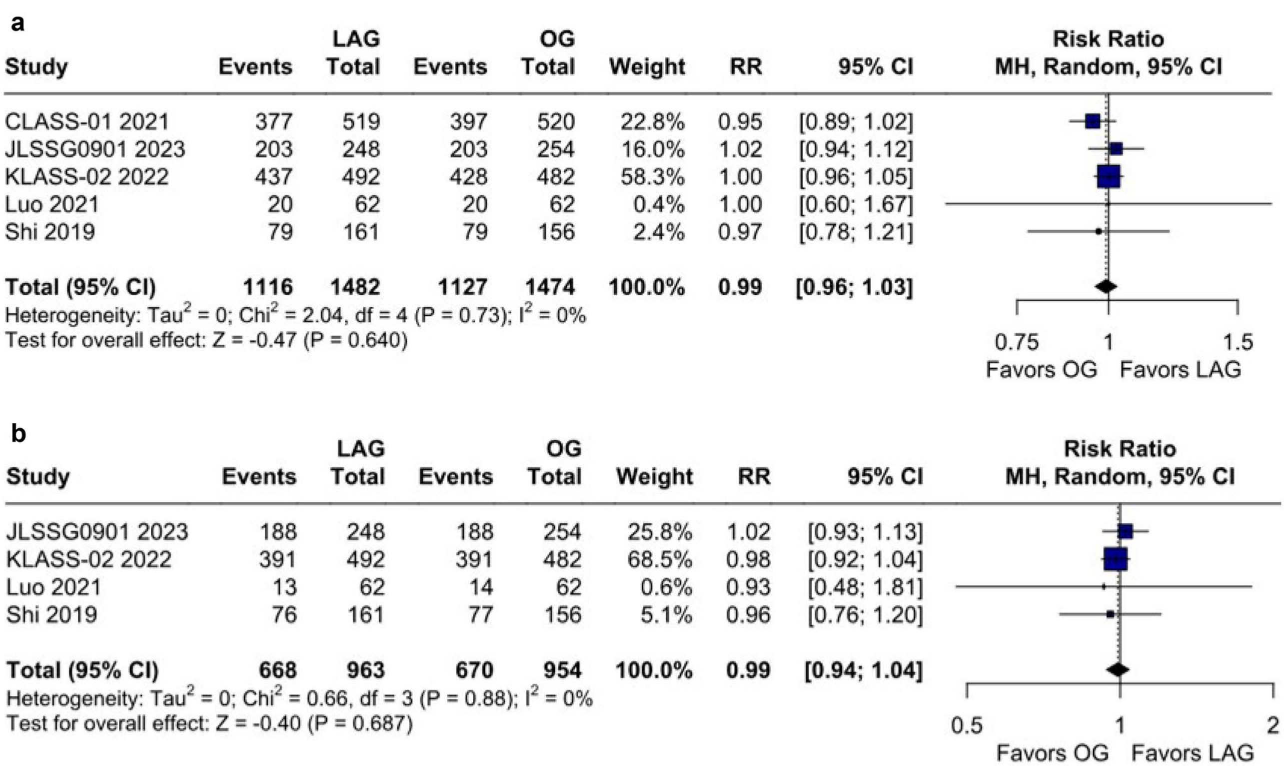


Fig. 6 **a** There were no differences between LAG and OG group. **b** There were no differences between LAG and OG group

was considered at high risk of selection bias because it was unclear whether the allocation sequence was concealed [32]. Two studies were judged to be at high risk of performance bias due to lack of information about the analysis used to estimate effect of assignment or adherence to intervention [29, 30], while one was considered at high risk of reporting bias due to retrospectively registering the trial protocol [29]. In addition, one was judged to be at high risk of reporting bias due to not citing a protocol or trial registration in the full text paper (Fig. S12, Supplementary Material 2) [30].

In the funnel plot analysis, there was a symmetrical distribution among the studies according to weight and converged to the pooled effect as weight increased. There was no evidence of publication bias demonstrated by Egger's regression test (Fig. S13, Supplementary Material 2). Leave-one-out analyses were performed for operative time, blood loss, and length of stay, revealing persistent high heterogeneity in all studies for each outcome (Figs. S14, S15, and S16, Supplementary Material 2). However, the results for blood loss and length of stay remained statistically significant in favor LAG group, even upon the exclusion of each individual study from the analysis.

Discussion

In this meta-analysis comprising 3827 patients and from nine RCTS, we compared outcomes after LAG versus OG for patients with AGC. Our main findings were as follows: LAG was associated with (1) lower intraoperative and postoperative blood losses; (2) higher operative time; (3) higher incidence of pancreatic fistula; (4) shorter in-hospital stay; (5) similar short and long-term survival rates as compared with OG.

Although the incidence of gastric cancer has decreased globally, it remains high in some regions, and there is a concerning trend of increasing risks and incidence rates in younger generations worldwide [33]. Despite considerable improvements, survival rates for this patient population remain low [34]. To address this public health issue, LAG and OG have been compared in patients with AGC, and it has been recently suggested that the two techniques have comparable cost-effectiveness [35]. Whether this translates into comparable long-term outcomes remains uncertain.

Previous meta-analysis of RCTs addressed this comparison with regards to intraoperative and short-term postoperative outcomes, mortality, and adverse events, but yielded conflicting results [13–15]. Worth mentioning, these meta-analyses included studies comprising patients with heterogeneous cancer staging and surgical approach, which may impair generalizability of the results to patients with AGC in particular. Our study addressed this limitation by comparing LAG with OG specifically in patients with AGC, further exploring long-term subanalyses and restricting inclusion to RCTs to avoid confounding. As a result, our meta-analysis stands as the most comprehensive analysis up to date. Overall, our findings are consistent with previous meta-analyses, demonstrating that LAG contributes with feasible short-term outcomes and further showing similar long-term outcomes compared to with OG for patients with AGC [10–15].

Hence, we herein reinforce the safety and efficacy of LAG as an alternative to OG in this patient population. Even so, operative time was significantly longer in the LAG arm with high between-study heterogeneity ($I^2 = 96\%$), which may suggest differences in performance owing to experience or center preferences. Achieving proficiency typically requires about 50 procedures performed, and surgeons have been shown to enhance surgical outcomes while reducing complications over time, as the number of procedures performed increases [36]. Of note, this higher mean operative time may be also attributable to the higher complexity of laparoscopy compared with open procedure, given the need to change instruments, lack tactile sensation, and the elaborateness of esophagojejunostomy [31, 37–39].

Our meta-analysis found no significant differences overall in postoperative complications. Noteworthy, there was a significantly higher incidence of pancreatic fistula in patients undergoing LAG. This may be partially explained by the unsuitable operating angle and field of view of surgical instruments associated with LAG [40]. On the other hand, blood losses may be halved by this technique owing to the more precise dissection, careful control, and wider surgical field provided by advanced instruments [21, 23]. Moreover, LAG was associated with a faster recovery, with a shorter length of postoperative stay and a shorter time to first flatus.

According to the current American Joint Committee on Cancer manual, it is recommended to retrieve a minimum of 16 lymph nodes during dissection, while obtaining 30 lymph nodes is considered preferable [41]. Of note, studies found that retrieving 29 lymph nodes is associated with benefits in survival rates in patients undergoing surgery for gastric cancer [42]. Interestingly, this association is indirectly corroborated by our findings, considering that there were no significant differences between LAG and OG both in number of lymph nodes retrieved and long-term survival. Therefore, LAG has shown promising results as an alternative with OG for this patient population.

Our study has limitations. First, the robustness of our findings may be hindered by our limited sample size, heterogeneous laparoscopic skills among surgeons across included trials, and lack of masking in study design. Second, all included trials were performed in East Asia, which could be a potential source of selection bias, impairing generalizability to a more diverse real-world population in western countries. Finally, the surgeons' experiences, surgical techniques and procedures, perioperative chemotherapy, and classifications systems for major complications were also heterogeneous among studies. Nonetheless, our meta-analysis further assessed subanalyses of distal gastrectomy and different definitions of post-operative complications, which retrieved consistent results.

Conclusion

In this meta-analysis of RCTs, LAG was superior to OG in reducing length of hospital stay, bleeding rates, time to first flatus, while yielding similar postoperative complication rates and long-term survival as compared to OG, albeit increasing risks of pancreatic fistula. This suggests that LAG may be an effective alternative to OG in treating AGC.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12029-024-01048-0.

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Author Contributions V.B. and M.F.B. planned, conducted, collected, and drafted the study. P.C.A.R. conducted, collected, and performed statistical analysis. M.A.P.B and K.M.R. contributed to analyzing the manuscript data and conducting the risk of bias. L.O.F. and G.B.C. contributed to analyzing and collecting the manuscript data. A.C.C., G.A., D.C.M. reviewed it critically for important intellectual content and contributed to interpretation of data. N.F. and M.P.G.C. contributed to conducting, reviewing critically, and interpreting the manuscript data.

Data Availability No datasets were generated or analysed during the current study.

Declarations

Competing Interests The authors declare no competing interests.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA A Cancer J Clinicians. 2021;71(3):209–49. https://doi.org/10.3322/caac.21660.
2. Smith JK, McPhee JT, Hill JS, et al. National outcomes after gastric resection for neoplasm. Arch Surg. 2007;142(4):387–93. https://doi.org/10.1001/archsurg.142.4.387.
3. Kitano S, Iso Y, Moriyama M, et al. Laparoscopy-assisted Billroth I gastrectomy. Surg Laparosc Endosc. 1994;4(2):146–8.
4. Katai H, Mizusawa J, Katayama H, et al. Short-term surgical outcomes from a phase III study of laparoscopy-assisted versus open distal gastrectomy with nodal dissection for clinical stage IA/IB gastric cancer: Japan Clinical Oncology Group Study JCOG0912. Gastric Cancer. 2017;20(4):699–708. https://doi.org/10.1007/s10120-016-0646-9.
5. Kim HH, Han SU, Kim MC, et al. Effect of laparoscopic distal gastrectomy vs open distal gastrectomy on long-term survival among patients with stage I gastric cancer: the KLASS-01 randomized clinical trial. JAMA Oncol. 2019;5(4):506–13. https://doi.org/10.1001/jamaoncol.2018.6727.
6. Katai H, Mizusawa J, Katayama H, et al. Survival outcomes after laparoscopy-assisted distal gastrectomy versus open distal gastrectomy with nodal dissection for clinical stage IA or IB gastric cancer (JCOG0912): a multicentre, non-inferiority, phase 3 randomised controlled trial. Lancet Gastroenterol Hepatol. 2020;5(2):142–51. https://doi.org/10.1016/S2468-1253(19)30332-2.
7. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition). Gastric Cancer. 2021;24:1–21. https://doi.org/10.1007/s10120-020-01042-y.
8. Katai H, Sasako M, Fukuda H, et al. Safety and feasibility of laparoscopy-assisted distal gastrectomy with suprapancreatic nodal dissection for clinical stage I gastric cancer: a multicenter phase II trial (JCOG 0703). Gastric Cancer. 2010;13(4):238–44. https://doi.org/10.1007/s10120-010-0565-0.
9. Etoh T, Ohyama T, Sakuramoto S, et al. Five-year survival outcomes of laparoscopy-assisted vs open distal gastrectomy for advanced gastric cancer: the JLSSG0901 randomized clinical trial. JAMA Surg. 2023;158(5):445–54. https://doi.org/10.1001/jamasurg.2023.0096.
10. Jiang J, Ye G, Wang J, et al. The comparison of short- and long-term outcomes for laparoscopic versus open gastrectomy for patients with advanced gastric cancer: a meta-analysis of randomized controlled trials. Front Oncol. 2022;12: 844803. https://doi.org/10.3389/fonc.2022.844803.
11. Yan Y, Ou C, Cao S, et al. Laparoscopic vs. open distal gastrectomy for locally advanced gastric cancer: a systematic review and meta-analysis of randomized controlled trials. Front Surg. 2023;10:1127854. https://doi.org/10.3389/fsurg.2023.1127854.
12. Chen X, Feng X, Wang M, et al. Laparoscopic versus open distal gastrectomy for advanced gastric cancer: a meta-analysis of randomized controlled trials and high-quality nonrandomized comparative studies. Eur J Surg Oncol. 2020;46(11):1998–2010. https://doi.org/10.1016/j.ejso.2020.06.046.
13. Zhu Z, Li L, Xu J, et al. Laparoscopic versus open approach in gastrectomy for advanced gastric cancer: a systematic review. World J Surg Oncol. 2020;18:126. https://doi.org/10.1186/s12957-020-01888-7.
14. Liao XL, Liang XW, Pang HY, et al. Safety and efficacy of laparoscopic versus open gastrectomy in patients with advanced gastric cancer following neoadjuvant chemotherapy: a meta-analysis. Front Oncol. 2021;11:704244. https://doi.org/10.3389/fonc.2021.704244.
15. Quan Y, Huang A, Ye M, et al. Comparison of laparoscopic versus open gastrectomy for advanced gastric cancer: an updated meta-analysis. Gastric Cancer. 2016;19(3):939–50. https://doi.org/10.1007/s10120-015-0516-x.
16. Son SY, Hur H, Hyung WJ, et al. Laparoscopic vs open distal gastrectomy for locally advanced gastric cancer: 5-year outcomes of the KLASS-02 randomized clinical trial. JAMA Surg. 2022;157(10):879–86. https://doi.org/10.1001/jamasurg.2022.2749.
17. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August 2023). Cochrane, 2023. Available from https://www.training.cochrane.org/handbook.
18. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372: n71. https://doi.org/10.1136/bmj.n71.

19. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. https://doi.org/10.1136/bmj.l4898.
20. Park YK, Yoon HM, Kim YW, et al. Laparoscopy-assisted versus open D2 distal gastrectomy for advanced gastric cancer: results from a randomized phase II multicenter clinical trial (COACT 1001). Ann Surg. 2018;267(4):638. https://doi.org/10.1097/SLA.0000000000002168.
21. Wang Z, Xing J, Cai J, et al. Short-term surgical outcomes of laparoscopy-assisted versus open D2 distal gastrectomy for locally advanced gastric cancer in North China: a multicenter randomized controlled trial. Surg Endosc. 2019;33(1):33–45. https://doi.org/10.1007/s00464-018-6391-x.
22. Li Z, Shan F, Ying X, et al. Assessment of laparoscopic distal gastrectomy after neoadjuvant chemotherapy for locally advanced gastric cancer: a randomized clinical trial. JAMA Surg. 2019;154(12):1093–101. https://doi.org/10.1001/jamasurg.2019.3473.
23. Lee HJ, Hyung WJ, Yang HK, et al. Short-term outcomes of a multicenter randomized controlled trial comparing laparoscopic distal gastrectomy with D2 lymphadenectomy to open distal gastrectomy for locally advanced gastric cancer (KLASS-02-RCT). Ann Surg. 2019;270(6):983–91. https://doi.org/10.1097/SLA.0000000000003217.
24. Hyung WJ, Yang HK, Park YK, et al. Long-term outcomes of laparoscopic distal gastrectomy for locally advanced gastric cancer: the KLASS-02-RCT randomized clinical trial. J Clin Oncol. 2020;38(28):3304–13. https://doi.org/10.1200/JCO.20.01210.
25. Hu Y, Huang C, Sun Y, et al. Morbidity and mortality of laparoscopic versus open D2 distal gastrectomy for advanced gastric cancer: a randomized controlled trial. J Clin Oncol. 2016;34(12):1350–7. https://doi.org/10.1200/JCO.2015.63.7215.
26. Huang C, Liu H, Hu Y, et al. Laparoscopic vs open distal gastrectomy for locally advanced gastric cancer. JAMA Surg. 2022;157(1):1–9. https://doi.org/10.1001/jamasurg.2021.5104.
27. Yu J, Huang C, Sun Y, et al. Effect of laparoscopic vs open distal gastrectomy on 3-year disease-free survival in patients with locally advanced gastric cancer. JAMA. 2019;321(20):1983–92. https://doi.org/10.1001/jama.2019.5359.
28. Luo G, Cao Y, Gong J, et al. Hand-assisted laparoscopic versus open surgery radical gastrectomy foradvanced distal gastric cancer: a prospective randomized study. Int J Clin Exp Med. 2017;10(3):5001–10.
29. Luo G, Wang X, Li Y, et al. Hand-assisted laparoscopic versus open surgery for radical gastrectomy in the treatment of advanced distal gastric cancer: long-term overall and disease-free survival (final results of a single-center study). J Int Med Res. 2021;49(9):03000605211047700. https://doi.org/10.1177/03000605211047700.
30. Cai J, Wei D, Gao CF, et al. A prospective randomized study comparing open versus laparoscopy-assisted D2 radical gastrectomy in advanced gastric cancer. Dig Surg. 2011;28(5–6):331–7. https://doi.org/10.1159/000330782.
31. Shi Y, Xu X, Zhao Y, et al. Short-term surgical outcomes of a randomized controlled trial comparing laparoscopic versus open gastrectomy with D2 lymph node dissection for advanced gastric cancer. Surg Endosc. 2018;32(5):2427–33. https://doi.org/10.1007/s00464-017-5942-x.
32. Shi Y, Xu X, Zhao Y, et al. Long-term oncologic outcomes of a randomized controlled trial comparing laparoscopic versus open gastrectomy with D2 lymph node dissection for advanced gastric cancer. Surg. 2019;165(6):1211–6. https://doi.org/10.1016/j.surg.2019.01.003.
33. Arnold M, Park JY, Camargo MC, et al. Is gastric cancer becoming a rare disease? A global assessment of predicted incidence trends to 2035. Gut. 2020;69(5):823–9. https://doi.org/10.1136/gutjnl-2019-320234.
34. Arnold M, Rutherford MJ, Bardot A, et al. Progress in cancer survival, mortality, and incidence in seven high-income countries 1995–2014 (ICBP SURVMARK-2): a population-based study. Lancet Oncol. 2019;20(11):1493–505. https://doi.org/10.1016/S1470-2045(19)30456-5.
35. van der Veen A, van der Meulen MP, Seesing MFJ, et al. Cost-effectiveness of laparoscopic vs open gastrectomy for gastric cancer: an economic evaluation alongside a randomized clinical trial. JAMA Surg. 2023;158(2):120–8. https://doi.org/10.1001/jamasurg.2022.6337.
36. Kikuchi S, Kagawa T, Kuroda S, et al. Accreditation as a qualified surgeon improves surgical outcomes in laparoscopic distal gastrectomy. Surg Today. 2021;51(12):1978–84. https://doi.org/10.1007/s00595-021-02309-2.
37. Wottawa CR, Cohen JR, Fan RE, et al. The role of tactile feedback in grip force during laparoscopic training tasks. Surg Endosc. 2013;27(4):1111–8. https://doi.org/10.1007/s00464-012-2612-x.
38. Campo R, Puga M, Furst R, et al. Excellence needs training "Certified programme in endoscopic surgery." Facts Views Vis ObGyn. 2014;6:240–4.
39. Hyung WJ, Song C, Cheong JH, et al. Factors influencing operation time of laparoscopy-assisted distal subtotal gastrectomy: analysis of consecutive 100 initial cases. Eur J Surg Oncol. 2007;33(3):314–9. https://doi.org/10.1016/j.ejso.2006.11.010.
40. Washio M, Yamashita K, Niihara M, et al. Postoperative pancreatic fistula after gastrectomy for gastric cancer. Ann Gastroenterol Surg. 2020;4(6):618–27. https://doi.org/10.1002/ags3.12398.
41. Amin MB, Greene FL, Edge SB, et al. The Eighth Edition AJCC Cancer Staging Manual: continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017;67(2):93–9. https://doi.org/10.3322/caac.21388.
42. Woo Y, Goldner B, Ituarte P, et al. Lymphadenectomy with optimum of 29 lymph nodes retrieved associated with improved survival in advanced gastric cancer: a 25,000 patient international database study. J Am Coll Surg. 2017;224(4):546–55. https://doi.org/10.1016/j.jamcollsurg.2016.12.015.