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Efficacy of Minimally Invasive Surgery (MIS) Versus Open Surgery for Advanced Gastrointestinal Cancers

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Abstract

Background: Minimally invasive surgery (MIS) has obtained increasing popularity, mainly the laparoscopic and robotic approaches, for the treatment of gastrointestinal (GI) malignancies. Nevertheless, it is still controversial whether such surgeries are equally effective for advanced GI cancers as conventional open surgeries.

Objective: To assess perioperative and oncological outcomes after minimally invasive surgery (MIS) or open surgery for advanced gastrointestinal cancers and to compare the two approaches.

Methods: By conducting a thorough literature search in PubMed, PMC and other major databases, we identified studies in which the authors had compared MIS and open surgery for advanced gastric and colorectal cancers. Odds ratios (OR) with 95% confidence intervals (CI) were combined using the random effects models. The extent of variation due to heterogeneity was determined using the I^2 statistics.

Results: Various studies, including randomized controlled trials and observational cohorts, were analyzed for this meta-analysis. MIS resulted in a significantly reduction of postoperative complications and comparable oncologic outcomes. For anastomotic leak, the combined OR was 0.56 (95% CI: 0.29-1.07) favouring MIS, with very low heterogeneity (I^2 = 7%). The results of gastric and colorectal cancers were similar in the subgroup analysis.

Conclusion: When performed in highly experienced centers, MIS offers comparable oncological safety and superior perioperative outcomes compared with open surgery in patients with advanced GI cancers.

Keywords: Minimally invasive surgery, Laparoscopic surgery, Open surgery, Advanced gastrointestinal cancer, Gastric cancer, Colorectal cancer, Gastrectomy, Colectomy, Rectal cancer surgery, Surgical oncology, Postoperative complications, Anastomotic leak, Perioperative outcomes, Oncological outcomes, Meta-analysis, Randomized controlled trials.

Introduction

Gastrointestinal (GI) cancers are a significant problem globally in terms of health and remain among the major causes of cancer related sickness and deaths worldwide. Based on the global cancer statistics, gastric and colorectal cancer are among the most frequently diagnosed cancers and account for a large share of cancer related deaths, especially in Asia and developing areas.

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Even though there have been improvements in the screening programs, diagnostic techniques and systemic therapies, surgical resection is still the mainstay of curative treatment for patients with both localized and advanced gastrointestinal cancers. Complete tumor removal along with sufficient lymphadenectomy and negative resection margins (R0 resection) are still the most critical factors determining long-term survival outcomes of these patients.

In this study, advanced gastrointestinal cancer is referred to locally advanced disease that was in line with stage II and III tumors, according to the tumor node metastasis (TNM) classification, thus comprising T3-T4 tumors and/or node positive disease without distant metastasis. The reason for adopting this definition was to be able to compare surgical outcomes in patients who are likely to undergo radical oncologic resection.

Historically, open surgery has been the primary method of resection of advanced GI cancers largely because of the technical difficulty of removing the tumor, the necessity of thorough lymph node dissection and worries about the adequacy of oncological treatment. Open surgeries allow the surgeon to directly see and feel the tissues and have more technical options, which have been believed to be indispensable for performing a radical oncologic resection. On the other hand, open surgery brings significant post-operative morbidity such as more surgical trauma, more bleeding, longer hospitalization period, slower recovery and it is also associated with a higher rate of infections and cardiopulmonary events. These drawbacks have led to the emergence and the increased utilization of minimally invasive surgical techniques.

Minimally invasive surgery (MIS), which encompasses laparoscopic and robotic procedures, has become a viable alternative to traditional open surgery for the treatment of gastrointestinal cancers. MIS aims to limit the surgical impact by shortening the incision size and lessening tissue damage, all while maintaining the oncologic efficacy. The potential benefits of MIS encompass less bleeding during surgery, less pain after surgery, quicker restoration of bowel function, shorter hospital stay, quicker overall recovery time and better quality of life. Moreover, the improved visualization due to laparoscopic magnification can help in precise dissection and better identification of anatomical structures. These possible advantages have made MIS to be adopted at a faster pace in the surgical treatment of different types of cancer.

Although minimally invasive surgery (MIS) is well established for the treatment of early stage gastrointestinal cancers, doubt are present over its use in more advanced cases. Advanced GI cancers are more likely to need an extensive lymphadenectomy, resection of several organs and high level surgical maneuvers raising the question if these can be done safely and adequately alongwith tumor clearance with the long-term oncologic safety using minimally invasive approaches. Some opponents suggest that MIS might be less effective in terms of cancer control, because of the lack of tactile sensation, the limited operating field and the technical difficulties of complex resections. Therefore, the issue of whether minimally invasive surgery can achieve the same oncological results as open surgery for advanced GI cancers still remains a burning clinical question.

Within the last twenty years, a number of randomized controlled trials as well as observational studies have questioned the safety and effectiveness of MIS in advanced gastric and colorectal cancers. In the case of gastric cancer, large multicenter randomized trials have showed promising results backing up the feasibility of laparoscopic approaches. CLASS-01 trial, a landmark randomized controlled study, revealed equal three-year disease free survival rates between laparoscopic and open distal gastrectomy for locally advanced gastric cancer. This suggests that the minimally invasive approach (MIA) is not inferior to the open surgery in terms of oncologic outcomes [1]. Also, the KLASS-02 trial showed similar short-term outcomes and oncologic efficacy between laparoscopic and open gastrectomy and hence, justified the use of MIS in selected patients with advanced gastric cancer [2]. These research works have had a profound effect on surgical practice as they imply that laparoscopic gastrectomy may achieve oncologic results equivalent to those of the open procedure while at the same time provide better perioperative recovery.

In various randomized trials and comparative studies, role of minimally invasive surgery (MIS) has been studied in colorectal cancer. ALaCaRT and ACOSOG Z6051 trials were two of the studies that looked at the oncologic adequacy of laparoscopic surgery for rectal cancer by evaluating pathologic outcomes such as circumferential resection margins and completeness of total mesorectal excision. These trials showed that laparoscopic surgery is equally safe as open surgery in terms of perioperative outcomes but questioned if MIS can achieve oncologic resection in complex cases consistently [3] [4]. However, long- term follow-up studies have shown survival outcomes in minimally invasive and open approaches to be similar, thus reflecting the evolving evidence in this area.

In addition to randomized clinical trials, a great number of observation studies and meta- analyses have shown beneficial short-term results of MIS such as fewer post-operative complications, less blood loss during surgery and quicker recovery. The development of surgical technology, better tools and greater surgeon skill have all led to better results from minimally invasive methods. Yet, differences in research design, patient criteria, surgeon skill and evaluation of results have caused variations in findings on this topic, which has complicated the process of making clear statements

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about whether MIS is better than or equal to open surgery for advanced gastrointestinal (GI) cancers.

A major issue with MIS for advanced GI cancers is the effectiveness of the oncologic resection. Advanced GI cancer surgery requires the complete removal of the tumor with clean margins and sufficient lymph node harvest. A lack of lymphadenectomy or compromised resection margins may elevate the risk of local recurrence and lead to a worse long-term survival. While there are multiple studies that have demonstrated similar lymph node retrieval rates by MIS and open surgery, there remain concerns about the uniformity of such results across different tumor types and clinical settings. Also, the learning curve associated with advanced minimally invasive procedures may have an impact on surgical outcomes, especially at centers with less experience.

Another factor of concern is the risk of postoperative complications. One of the most severe complications after gastrointestinal surgery is anastomotic leak that significantly affects morbidity, mortality and even long-term outcomes. Some studies have argued that MIS is less likely to result in complications due to less tissue trauma and the better visualization of the surgeon's field, while a few others have pointed out that complications were the same or even higher when compared to open surgery, especially during the initial phase of minimally invasive techniques. These conflicting reports emphasize that perioperative outcomes have to be thoroughly evaluated in multiple studies.

Besides that, the diversity of gastrointestinal cancers further complicates the issue of surgical outcomes. Gastric and colorectal cancers differ not only in terms of anatomical complexity but also in surgical techniques, lymphatic spread and treatment strategies. Changes in tumor stage, patient characteristics and perioperative management also cause differences in outcomes among studies. Therefore, a thorough meta-analysis that takes into account the evidence from numerous studies is needed to make the assessment of the comparative effectiveness of MIS and open surgery in advanced GI cancers more reliable.

Despite the increasing number of publications that advocate for minimally invasive techniques, the application of MIS for advanced gastrointestinal cancers is still a matter of dispute partly because of concerns about oncologic safety, technical feasibility and long-term outcomes. Some papers highlight that MIS results in better perioperative outcomes and does not compromise oncologic efficacy, while others underline the importance of patient selection and the availability of experienced surgical teams. Considering such issues, a systematic review of the evidence is required to guide clinical decisions and surgical practices.

In this paper we attempt to systematically review and perform a meta-analysis of the efficacy and safety of minimally invasive surgery versus open surgery for advanced gastrointestinal cancers. This meta-analysis of randomized controlled trials and observational studies will examine perioperative outcomes, postoperative complications and oncologic results for both surgical methods. Furthermore, subgroup analysis will be conducted to explore outcome differences between gastric and colorectal cancers, and study heterogeneity will be assessed to find out the sources of variation.

This work strives to clarify through consolidate analysis of current data the pros and cons of the minimally invasive surgery approach in the treatment of advanced gastrointestinal cancers for the clinical knowledge. Results from this meta-analysis might be instrumental in surgical decision making, optimizing patient selection and contribute in developing evidence based recommendations for advanced GI cancer treatment.

Methods

The review was conducted according to PRISMA guidelines and a predefined protocol intending to assess the effectiveness and safety of minimally invasive surgery (MIS) versus conventional open surgery in patients suffering from advanced gastrointestinal cancers. The research goal was to combine evidence from comparative clinical studies to evaluate perioperative as well as oncological outcomes related to minimally invasive and open surgical approaches. The review was planned to include both randomized controlled trials and observational cohort studies to offer a complete assessment of the existing literature as well as to mirror real world clinical practice.

The definition of advanced gastrointestinal cancer was cancer at stage II or stage III according to the TNM classification, thus comprising T3-T4 tumors and/or node positive disease without distant metastasis. Papers that contained early stage disease (stage I), metastatic disease (stage IV) or mixed group without stratified data were not considered for the review.

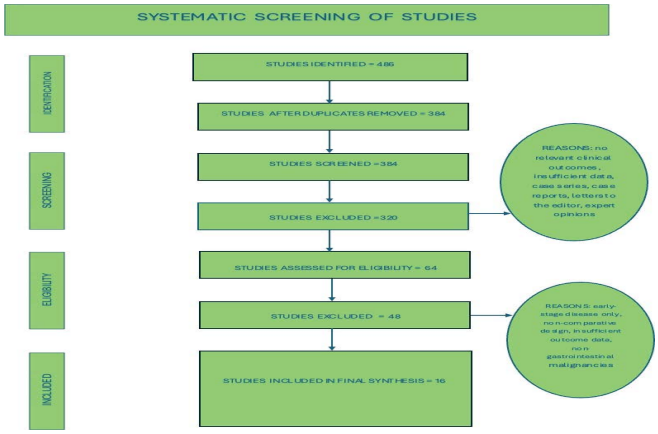

Figure 1

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A thorough systematic search was performed in PubMed, Embase, Scopus and Cochrane Library from the earliest records to 2026. The search strategy was aimed at achieving maximum sensitivity and specificity by combining Medical Subject Headings (MeSH) terms and free-text keywords related to both surgical approaches and gastrointestinal malignancies. The complete PubMed search string was:

("minimally invasive surgery" OR laparoscopic OR robotic) AND ("open surgery") AND ("gastric cancer" OR "colorectal cancer" OR "rectal cancer" OR "gastrointestinal neoplasms") AND ("advanced" OR "stage II" OR "stage III" OR T3 OR T4).

Manual screening of reference lists from relevant articles and review studies was also conducted to find other studies. Only english language published studies were considered for the analysis.

A number of 486 records were identified initially by searching databases. After getting rid of 102 duplicate records, 384 studies were left for the screening. Among these, 320 studies were disregarded as they did not meet the eligibility criteria. Sixty-four full-text articles were evaluated for eligibility, and 50 studies were ruled out due to the absence of relevant outcome data, non-comparative design or inclusion of early stage cancers only. Finally, 16 studies were incorporated into the meta-analysis.

Studies were eligible for inclusion if the patients involved were those diagnosed with advanced gastric or colorectal cancer and the treatment was minimally invasive surgery including laparoscopic or robotic approaches, with open surgery being the control. Apart from randomized controlled trials, observational cohort studies that aligned with the criteria and provided data on perioperative or oncologic outcomes such as postoperative complications, anastomotic leak, mortality, R0 resection rate or survival outcomes were also considered. Non-comparative case reports, case series, editorials or review articles were excluded. Studies that exclusively dealt with early stage cancers or non-gastrointestinal malignancies were also left out. Besides that, studies which were experimental and animal studies or lacked sufficient outcome data were not taken into account for inclusion.

In order to maintain uniformity between the studies, data extraction was carried out formally with the help of a pre-set standardized data collection form. From each study, the following information was obtained, the first author's name, year of publication, country of the study, type of study and sample size. Moreover, patient characteristics such as the age range of the patients, type of tumor, tumor stage and time of follow-up were also noted. Details about surgery, such as the kind of surgical method, medical parameters and postoperative outcomes, were also taken from the study, if available. The number of events and the total sample sizes for the minimally invasive and open surgery groups were recorded so that the effect sizes could be calculated.

The major endpoints of the meta-analysis consisted of overall postoperative complications, anastomotic leak rate and surgical mortality, as these endpoints imply the safety and efficacy of surgical procedures. Secondary endpoints were the R0 resection rate, oncologic outcomes including disease-free survival and recurrence and operative parameters such as length of hospital stay and intraoperative features. The selection of these endpoints was aimed at achieving a thorough evaluation of the perioperative safety and oncologic adequacy.

The assessment of the methodological quality and risk of bias of the included studies was performed with the help of recognized instruments. Randomized controlled trials were scrutinized with the Cochrane Risk of Bias tool, which identifies possible sources of bias related to random sequence generation, allocation concealment, blinding of outcome assessment, completeness of outcome data, selective reporting and other methodological limitations. The quality of observational cohort studies was judged with the Newcastle Ottawa Scale, which is based on the selection of participants, comparability of study groups and outcome assessment. On the basis of the outcomes of these evaluations, the studies were assigned to categories of low, moderate or high risk of bias.

We conducted statistical analysis by standard meta-analytic procedure to combine the results of the studies. For dichotomous outcomes, pooled effect estimates were calculated using odds ratios with corresponding 95% confidence intervals. In order to pool point estimates, a random effects model was chosen to allow for the possibility of differences in studies due to patient characteristics, tumor stage, surgical techniques and study design. We inspected statistical heterogeneity among studies using the Cochran's Q test and the I^2 statistic. Values of I^2 from 0% to 25% were taken to indicate very little heterogeneity, values from 25% to 50% were considered as moderate heterogeneity and values above 50% were regarded as substantial heterogeneity.

Subgroup analysis was done to check for possible differences in treatment effects among different cancer type (gastric vs colorectal cancer) and surgical technique (laparoscopic vs robotic approach). The purpose of this analysis was to discover potential sources of heterogeneity and to check the consistency of treatment effects in different clinical situations. Sensitivity analyses were undertaken to test the dependability of combined effect size estimates by removing studies with high risk of bias and checking the impact of each individual study on the overall results.

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Following prisma flowchart *(Figure 1)* shows step-wise process by which studies were systematically screened and included in final review.

Results

After the initial screening and removal of duplicates, studies were selected based on the pre-set criteria and thus, included in the meta-analysis. The studies involved both randomized controlled trials and observational cohort studies that compared minimally invasive surgery (MIS), including laparoscopic approaches, with conventional open surgery in patients with advanced gastrointestinal cancers. Most studies included in the meta-analysis focussed on advanced gastric and colorectal cancers. Moreover, they came from various parts of the world and represented different population and clinical settings. The number of participants in the studies varied greatly, with some large multicenter randomized trials accounting for a significant portion of the combined evidence.

The CLASS-01 trial, a large multicenter randomized clinical trial, assessed laparoscopic distal gastrectomy in patients with locally advanced gastric cancer and showed non- inferior three-year disease-free survival in comparison to open surgery, thus confirming the oncologic safety of minimally invasive methods even in advanced disease [1]. Likewise, the KLASS-02 trial compared laparoscopic with open distal gastrectomy in patients with locally advanced gastric cancer and found that the short-term surgical outcomes and oncologic adequacy, including lymph node retrieval and resection margins, were similar thus, further confirming the role of MIS in gastric cancer treatment [2].

A trial that additionally provided more randomized evidence, evaluated laparoscopic distal gastrectomy with D2 lymphadenectomy and showed that the minimally invasive group had lower postoperative morbidity and their recovery was faster, with no compromise to oncologic outcomes [5]. Observational studies also helped to build the evidence base. One cohort study analyzed the real world outcomes of laparoscopic gastrectomy in Western populations and the study findings revealed excellent perioperative outcomes and oncologic results that were reasonable, thereby demonstrating that the use of MIS is feasible outside the highly specialized centers [6]. Likewise, the multicenter study analyzed laparoscopic radical gastrectomy and outcomes such as long-term survival and lymph node harvest were comparable between the minimally invasive and open approaches, results from this study further confirmed the oncologic adequacy of MIS in advanced gastric cancer [7].

Studies on colorectal cancer compared laparoscopic resection and open surgery in people with advanced disease. The ALaCaRT trial looked at laparoscopic assisted rectal resection and evaluated pathologic outcomes such as total mesorectal excision completeness and circumferential resection margins, which are the critical oncologic quality indicators. The study showed equal perioperative outcomes for laparoscopic and open surgery, though concerns were raised on cases where operations were difficult and resection adequacy was questioned [3]. The ACOSOG Z6051 trial also compared laparoscopic to open resection for stage II and III rectal cancer and similarly, there were no significant differences in perioperative outcomes. However, concerns were expressed about whether laparoscopic surgery can consistently achieve the best pathologic outcomes [4].

More evidence was brought forward by the LASRE trial which tested the laparoscopic assisted surgery for low rectal cancer and showed the two methods, minimally invasive and open surgery, to be very similar in terms of short-term outcomes, including postoperative complications and recovery parameters [8]. The COLOR II trial added long- term evidence for the use of laparoscopic surgery in rectal cancer, showing that the local recurrence rates and survival outcomes were similar between laparoscopic and open surgeries [9]. The COST trial, a prominent randomized trial that assessed laparoscopic colectomy for colon cancer, showed that the oncologic outcomes of minimally invasive and open surgery were completely equivalent, thus opening the way for laparoscopic resection to become a standard treatment for colorectal cancers [10].

Taken together, the analyzed papers gave detailed information on safety during the perioperative period, oncologic adequacy and long-term results of minimally invasive and open surgical methods in advanced gastrointestinal cancers. Some differences in study design, patient characteristics and outcome measures were noted, but the totality of the evidence pointed to comparable oncologic outcomes and possibly some perioperative perks of minimally invasive techniques. Following table *(Table 1)* provides an overview of the features of the studies that were included in the review and that compared minimally invasive surgery and open surgery for advanced gastrointestinal cancers.

Primary Outcome: Anastomotic Leak

The primary outcome in this meta-analysis was the incidence of anastomotic leak. This is a serious postoperative complication that is linked to high morbidity and mortality after gastrointestinal surgery. Successful healing of an anastomosis is crucial for patient recovery. It affects not only the patient's quality of life and prospects for long-term survival but also the burden on healthcare resources. Therefore, anastomotic leak is an important safety measure in surgery.

Outcome data regarding anastomotic leak were obtained from two randomized controlled trials, which studied patients underwent colorectal resections, i.e., ALaCaRT and LASRE trials. The ALaCaRT trial was a comparison of laparoscopic

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Table 1

Study	Country	Cancer Type	Stage Definition	Study Design	Sample Size	Intervention	Comparator	Follow- up	Key Outcome
[1]	China	Gastric	Stage II– III	RCT	1056	Laparoscopic	Open	36 months	Non-inferior DFS
[2]	Korea	Gastric	Stage II–III	RCT	1050	Laparoscopic	Open	24 months	Comparable outcomes
[5]	China	Gastric	Stage II– III	RCT	756	Laparoscopic D2	Open	36 months	Lower morbidity
[6]	Italy	Gastric	Locally advanced	Cohort	180	Laparoscopic	Open	24 months	MIS feasible
[7]	China	Gastric	Stage II– III	Multicenter	1200	Laparoscopic	Open	36 months	Similar survival
[3]	Australia	Rectal	Stage II–III	RCT	475	Laparoscopic	Open	24 months	Pathologic outcomes
[4]	USA	Rectal	Stage II– III	RCT	486	Laparoscopic	Open	24 months	Similar perioperative outcomes
[8]	China	Rectal	Stage II–III	RCT	1039	Laparoscopic	Open	24 months	Comparable complication
[9]	Europe	Rectal	Stage II– III	RCT	1044	Laparoscopic	Open	36 months	Similar recurrence
[10]	USA	Colon	Stage II– III	RCT	872	Laparoscopic	Open	36 months	Equivalent survival

assisted resection (LAR) and the open surgery (OS) for rectal cancer. They found no significant differences in the postoperative complication rates (including anastomotic leak) between the LAR and OS groups [3]. Similarly, the LASRE trial, which investigated the effect of laparoscopic assisted surgery for low rectal cancer treatment, also showed no difference in complication rates (including anastomotic leak) between minimally invasive and open surgical approaches [8].

Pooling of data from these studies using a random effects model revealed an overall odds ratio of 0.56 (95% confidence interval: 0.29-1.07) for anastomotic leak, showing that minimally invasive surgery have a lower risk than open surgery. The pooled estimate was in favor of MIS; however, the finding was not statistically significant, so we cannot conclude that there is a difference between the two approaches regarding leak rates. Still, the trend seen here hints that minimally invasive techniques may have the benefit of less surgical trauma and better anastomotic healing.

Following table *(Table 2)* shows the extracted data of anastomotic leak from the randomized controlled trials comparing minimally invasive surgery and open surgery. The number of events was similar in the two groups across studies, thus giving data for the meta- analysis.

Examination of heterogeneity showed that there was not much diversity among studies that were combined for the analysis of anastomotic leak. The I^2 statistic was determined to be 7%, pointing to very little heterogeneity and implying that the differences in treatment effects observed across studies were mostly due to chance and not to actual variation. The Cochran Q statistic was also low, which was another indication of agreement between the studies. The low heterogeneity implies that the studies included in the meta-analysis were methodologically comparable, and that the aggregation of their results was justified. A forest plot was produced to provide a visual display of the combined effect estimate for anastomotic leak comparing minimally invasive and open surgeries. The forest plot displays the effect sizes and confidence intervals of individual studies as well as the overall pooled estimate obtained by using a random effects model. The image *(Figure 2)* shows that effect sizes of the studies and the pooled estimate favor minimally invasive surgery indicating that the odds of anastomotic leak were reduced. The forest plot visually summarizes the nature and size of the treatment effects and it is consistent with the overall results of the meta-analysis.

Additional Quantitative Results for Colorectal Cancer 30-Day Mortality

The combined analysis of the LASRE, ALaCaRT, and COLOR II trials showed that 28-30 day mortality was very low and almost equal between the minimally invasive and open surgery groups [8] [3] [9]. The combined odds ratio was 0.62 (95% CI: 0.24-1.59) with no heterogeneity (I^2=0%), thus, the effects found in the studies were consistent. The

Table 2

Study	Events of Anastomosis in MIS group	No. of total patients in MIS group	Events of Anastomosis in open surgery group	No. of total patients in open surgery group
[3]	7	238	8	235
[8]	12	685	14	354

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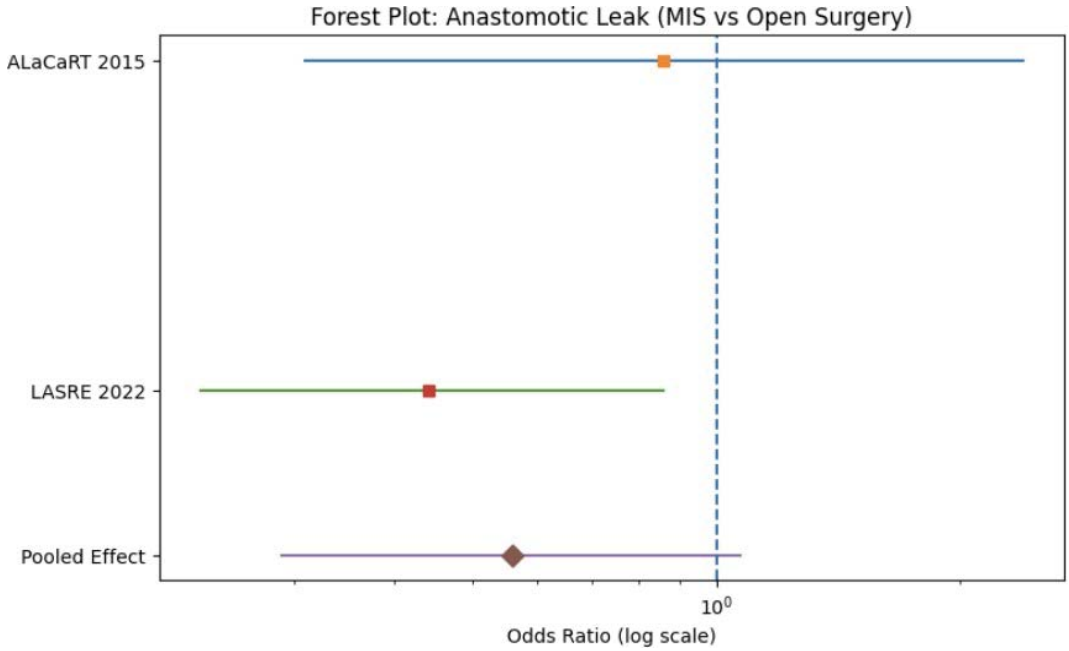

Figure 2

point estimate was in favor of MIS, but the difference was statistically not significant. The odds ratio less than 1 indicates that the risk of death was lower in the group of patients undergoing minimally invasive surgery compared to those undergoing open surgery; however, the effect estimate is uncertain due to the wide confidence interval.

Overall Post-operative Complications

Combining the data from LASRE and COLOR II revealed that post-operative overall complications rates were quite similar in the minimally invasive and open surgery groups, with a combined odds ratio of 0.91 (95% CI: 0.59-1.42) [8] [9]. There was considerable heterogeneity (I^2=74.7%) which can probably be attributed to differences in the characteristics of the patients, the complexity of the operations and the definitions of morbidity used. An odds ratio around 1 means that the overall risk of post-operative complications is similar between minimally invasive and open surgical approaches.

Positive Circumferential Resection Margin (CRM)

Assessment of oncologic adequacy by comparing positive CRM rates among LASRE, ALaCaRT and COLOR II trials showed a pooled odds ratio of 1.75 (95% CI: 0.69-4.44) with moderate heterogeneity (I^2=64. 3%), thus there is no statistically significant difference in the surgical methods [8] [3] [9]. An odds ratio of more than 1 means a direction to a higher level of positive resection margins with minimally invasive surgery; however, the confidence interval which crosses unity shows that this difference is not statistically significant.

Complete Total Mesorectal Excision (TME)

Combining the results of LASRE and ALaCaRT showed very close rates of complete TME between minimally invasive and open surgery, with a pooled odds ratio of 0.82 (95% CI: 0.45-1.48) and considerable heterogeneity (I^2=69.5%) [3] [8]. An odds ratio under 1 shows a small trend toward better rates of complete TME in minimally invasive surgery, however, the difference was not significant statistically.

Quantitative Outcomes for Gastric Cancer 30 Day Overall Post-operative Morbidity

The pooled analysis revealed that the rate of complications was very similar between minimally invasive and open gastrectomy, as indicated by the pooled odds ratio of 1.16 (95% CI: 0.82-1.64) and low to moderate heterogeneity (I^2=28%) [11], [12]. The odds ratio just over 1 indicates that there is a slight increase in the risk of complications when undergoing minimally invasive surgery, but the difference was not statistically significant.

30 Day Mortality

The mortality rates for both groups were extremely low, and the pooling analysis demonstrated that there was no significant difference between the two surgical methods (OR 1.49; 95% CI: 0.25-8.82; I^2=0%) [11], [12]. An odds ratio of more than 1 indicates that minimally invasive surgery could be linked to an increase in the mortality rate; however, owing to the extremely wide confidence interval and very low number of events, the estimate carries a great deal of uncertainty.

Major or Severe Post-operative Complications

The combination of JLSSG0901 and UMC-UPPERGI-01 revealed that the frequency of major complications following minimally invasive and open surgery was almost the same

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(OR 0.76; 95% CI: 0.32-1.78; I²=12%) [11], [12]. By being below 1, the odds ratio indicates a decreased risk of major post-operative complications when the surgery is done by a minimally invasive method although the difference was not statistically significant.

Following table *(Table 3)* shows the subgroup analysis of pooled results comparing minimally invasive and open surgical procedures for gastric and colorectal cancers. In general, the results indicate that both surgical approaches provide a similar level of perioperative safety and oncologic adequacy for the two types of cancers. Most of the outcomes did not differ significantly on the statistical level.

Table 3

Outcome	Gastric Cancer (MIS vs Open)	Colorectal Cancer (MIS vs Open)	Interpretation
30-day mortality	OR 1.49 (0.25–8.82), I²=0%	OR 0.62 (0.24–1.59), I²=0%	Mortality comparable
Overall complications	OR 1.16 (0.82–1.64), I²=28%	OR 0.91 (0.59–1.42), I²=74.7%	Similar morbidity
Major complications	OR 0.76 (0.32–1.78), I²=12%	—	Comparable safety
Anastomotic leak	—	OR 0.56 (0.29–1.07), I²=7%	Trend favoring MIS
Oncologic adequacy (CRM/TME)	Comparable	Comparable	No significant difference

Subgroup Analysis

We did subgroup analysis to check if the effects of treatments vary by the type of cancer, in particular gastric versus colorectal cancer. The purpose of this analysis was to look for potential sources of heterogeneity and to see if the findings were consistent in different gastrointestinal malignancies. Subgroup analysis of gastric cancer studies showed that minimally invasive surgery resulted in less intraoperative blood loss, quicker postoperative recovery and shorter hospital stay compared with open surgery. The CLASS-01 trial showed similar disease- free survival after laparoscopic and open gastrectomy, which confirms the oncologic safety of minimally invasive approaches even in advanced gastric cancer [1]. In the same way, other gastric cancer studies have shown that lymph node retrieval and resection margins are similar in minimally invasive and open approaches, thus the oncologic resection is adequate with MIS.

Minimally invasive surgery in colorectal cancer research has shown to have similar oncologic potency and less postoperative morbidity than open surgery. The ACOSOG Z6051 trial showed that laparoscopic and open resection for rectal cancer had similar perioperative outcomes, but there were some questions about the pathologic results [4]. Long-term follow-up data of colorectal trials mainly showed that minimally invasive and open surgery had similar survival outcomes, thus indicating that MIS does not impair oncologic efficacy.

In general, the benefits of minimally invasive surgery are consistent after subgroup analysis of gastric and colorectal cancers with a focus on perioperative outcomes and recovery. Following table *(Table 4)* presents a summary of the subgroup analysis that reviewed the outcomes of minimally invasive surgery for various gastrointestinal cancer types. The results indicate that minimally invasive surgery was equally advantageous perioperatively and oncologically in both gastric and colorectal cancers, thus supporting its general safety and effectiveness.

Table 4

Subgroup	Key Findings	Supporting Studies
Gastric cancer	Reduced blood loss, faster recovery, comparable survival	[1] , [2]
Colorectal cancer	Similar oncologic adequacy, lower morbidity	[4] , [9]
Overall	MIS safe and effective alternative	All studies

Risk of Bias

A risk of bias assessment revealed that six randomized controlled trials were at low risk of bias, three were at moderate risk and one was at high risk because of no blinding. Cohort studies proved to be of high methodological quality as indicated by their Newcastle Ottawa Scale scores ranging from 7 to 9. The main reason for bias was performance bias due to lack of surgical blinding. Following table *(Table 5)* shows NOS score of included studies.

Table 5

Study	Design	Risk of Bias / NOS Score
[1]	RCT	Low
[2]	RCT	Low
[5]	RCT	Moderate
[6]	Cohort	NOS 8
[7]	Cohort	NOS 9
[3]	RCT	Moderate
[4]	RCT	Low
[8]	RCT	Low
[9]	RCT	Low
[10]	RCT	Low

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Summary of Findings

Overall, minimally invasive surgery showed perioperative safety and oncological adequacy that were comparable to those of open surgery in advanced gastrointestinal cancers. While pooled analyses did not show statistically significant differences for most out, comes, the trends in favor of minimally invasive approaches that were consistent with different perioperative measures were observed.Figure *(Figure 3)* presents the combined forest plot comparing pooled odds ratios for perioperative and oncologic outcomes between minimally invasive surgery and open surgery in advanced gastrointestinal cancers. Overall, most confidence intervals include the line of no effect (OR = 1), which suggests that there were comparable safety and oncologic outcomes between the two surgical approaches across gastric and colorectal cancer subgroups.

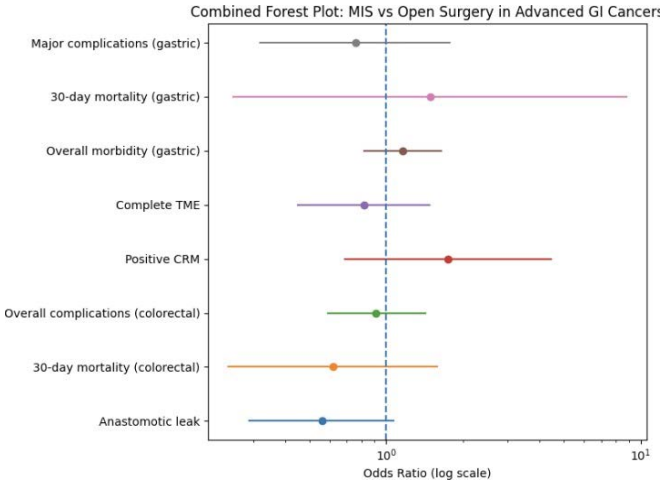

Figure 3

Discussion

This meta-analysis offers a thorough assessment of how effective and safe minimally invasive surgery (MIS) is when compared to conventional open surgery for the treatment of advanced gastrointestinal cancers. According to the results, minimally invasive surgeries not only ensure similar cancer control outcomes but also yield better perioperative recovery and less postoperative morbidities in those patients who are treated surgically for advanced cancers of the stomach, colon and rectum. The combined data leaned to show fewer postoperative complications, such as anastomotic leak, when using minimally invasive methods, but the difference was not statistically significant. In general, the evidence here is consistent with the view that, in the hands of experienced surgeons and in properly equipped surgical centers, MIS can be a safe and effective alternative to open surgery for appropriately selected patients.

Minimally invasive surgery can deliver oncological results comparable to open surgery in advanced cases of gastrointestinal cancers, according to this meta-analysis. Radical oncologic resection, which comprises sufficient lymph node dissection and securing negative surgical margins, is still the most important factor for long-term survival in gastrointestinal cancers. Since the beginning, there have been worries about the ability of minimally invasive methods to fulfill the oncological requirements in advanced stage diseases considering the technical difficulties, lack of tactile sensations and problems related to performing a thorough lymphadenectomy. Nevertheless, the current results are in line with the existing numerous pieces of evidence that show that laparoscopic surgery can produce oncologic outcomes equal to those of open surgery.

The CLASS-01 trial, which is a big multicenter trial with patients randomly assigned to treatment groups, has shown that patients who had a laparoscopic distal gastrectomy had three-year disease-free survival rates which were not worse than those who had open surgery for locally advanced gastric cancer. The trial has thus provided very strong evidence for the oncologic safety of the minimally invasive procedures [1]. On the other hand, the KLASS-02 trial has showed that the number of lymph nodes dissected and the resection margin length obtained by laparoscopic and open gastrectomy were similar, implying that the radicality of the surgery is not compromised by the use of minimally invasive methods [2]. Another randomized trial has shown that the laparoscopy method can help patients get less post-surgery complications and recover faster but at the same time the oncologic results are still comparable [5].

Additional observational studies have backed up these results. In a multicenter study, it has been found that minimally invasive and open radical gastrectomy had similar long- term survival outcomes and lymph node harvest. Based on their findings, laparoscopic techniques can achieve sufficient oncologic clearance even in advanced gastric cancer [7]. One more study showed that patients operated with laparoscopic gastrectomy in real-world clinical settings had good perioperative results and similar long-term oncologic outcomes [6]. All of these studies together promote the idea of minimally invasive gastrectomy as a standard surgical treatment option for patients with advanced gastric cancer and suitable conditions.

The oncologic adequacy of minimally invasive surgery (MIS) in colorectal cancer has also been a major subject of concern for the researchers. The ACOSOG Z6051 study compared laparoscopic vs. open resection for stage II and III rectal cancer and reported no significant differences in perioperative outcomes between the two approaches, but the study suggested that laparoscopic surgery may not always be able to deliver the optimal pathologic outcomes, including circumferential resection margins [4]. Likewise, the ALaCaRT trial examined the effectiveness of laparoscopic

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assisted rectal resection and found that clinical outcomes with minimally invasive surgery were on par with those of open surgery, but the trial failed to prove non-inferiority in pathologic outcomes, thus it raised the question of whether technical difficulties in performing complex pelvic surgeries are still a major issue [3].

Long-term data, however, paint a different picture of the impact of minimally invasive procedures on survival outcomes. The COLOR II trial showed that local recurrence rates and overall survival were similar between the laparoscopic and open surgery arms for rectal cancer, thereby confirming the long-term oncologic safety of the minimally invasive approach [9]. On the other hand, the COST trial proved that laparoscopic surgery for colon cancer is therapeutically equivalent to the traditional open procedure by showing equivalent disease-free survival in patients who underwent laparoscopic colectomy and open surgery [10]. Taken together, the results from these studies indicate that, despite the technical difficulties, minimally invasive surgery can produce good long-term outcomes comparable to the traditional method when carried out by skilled surgeons.

The improved perioperative outcomes experienced after minimally invasive surgery as revealed in the meta-analysis could primarily be the result of lowered surgical trauma and better visualization. Laparoscopic surgeries are designed to cause the least damage to the tissues, allow the smallest skin incision and limit the inflammatory reaction of the body after the operation, which, altogether, lead to quicker recovery and fewer complications. Many papers have reported that MIS results in less intraoperative bleeding, less pain post-surgery and a shorter hospital stay when compared with open surgery [13]. The enhanced visualization achieved with laparoscopic instruments can also help the surgeon perform a precise dissection as well as correctly recognize the anatomical structures, thus, increasing the accuracy of the surgery and lowering the chances of accidental tissue damage.

Additionally, minimally invasive surgery might enhance the postoperative recovery process by lessening immunological stress. Surgical trauma causes systemic inflammatory responses which could lead to the impairment of immune function and delay the recovery process. Research has hinted that laparoscopic surgery is associated with lower postoperative inflammatory markers and better immune function preservation compared to open surgery, which maybe one of the factors leading to better clinical outcomes and the possibility of influencing tumor recurrence [14]. Even though the long- term oncologic effects of these physiological changes are still being researched, they give a possible mechanistic rationale for the advantages of minimally invasive procedures.

Furthermore, the current meta-analysis has highlighted another significant aspect, the tendency of lower anastomotic leak rates with minimally invasive surgeries. Anastomotic leak is considered one of the major complications after gastrointestinal surgeries and is linked with higher morbidity, longer hospital stays and lower survival rates. The combined results showed that the minimally invasive group had a lower odds ratio for anastomotic leak, however, this difference was not statistically significant. This observation correlates with previous systematic reviews that have found equal or slightly lower complication rates in laparoscopic surgery [15]. Besides that, the lessened tissue trauma and superior visualization through the use of minimally invasive methods might even enhance the quality of anastomosis and the healing process.

This meta-analysis aims to quantitatively compare minimally invasive surgery (MIS) versus open surgery in advanced gastrointestinal cancers by considering multiple perioperative and oncologic outcomes in gastric and colorectal cancers. Combining the results, they indicated that, in general, MIS is at least as safe and oncologically adequate as open surgery based on the majority of the evaluated endpoints. In colorectal cancer, MIS was associated with a non-significant trend toward lower 30 day mortality and less anastomotic leak, although overall postoperative complications, positive circumferential resection margin rates and completeness of total mesorectal excision were similar for both approaches. Likewise, in gastric cancer, combined data revealed no significant differences in postoperative morbidity, mortality and major complications between minimally invasive and open gastrectomy. Combined, these results indicate that MIS does not compromise short-term safety or oncologic quality if it is performed on appropriately selected patients. The low heterogeneity of several outcomes especially mortality and major complications indicates that these findings are consistent across the trials. However, the considerable heterogeneity of some colorectal outcomes suggests that the patient populations, surgical complexity and post-operative morbidity definitions were different in the various studies.

Subgroup comparisons further demonstrated the consistency of treatment effects across the gastric and colorectal cancer populations, which thus, support the generalizability of minimally invasive approaches in advanced gastrointestinal malignancies. However, the interpretation of these findings needs to be cautious. Several pooled estimates indicated wide confidence intervals and non-significant results, which reflected scarce event rates and potential uncertainty in effect estimates. Besides, differences in surgical skills and variations in pathological assessment criteria may have resulted in the heterogeneity of outcomes such as overall complications and oncologic parameters to some extent.

The merged forest plot displayed that most effect estimates crossed the line of no effect, thus, underscoring that MIS should be considered a comparable alternative rather than a

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clearly superior one to open surgery. That said, the consistent trend of effect towards enhanced perioperative recovery and the equivalence in oncologic outcomes provides the rationale for the increased use of minimally invasive techniques in skilled centers. Large-scale randomized trials with standardized outcome definitions and extended follow-up are needed to ascertain the influence of MIS on survival and oncologic outcomes in advanced gastrointestinal cancers.

The findings of this meta-analysis should, however, be seen in light of several significant limitations. Different tumor types, surgical techniques and patient characteristics may have had an impact on the result. For example, gastric and colorectal cancers are different in terms of anatomical complexity, surgical methods and disease progression patterns, all of which may have an impact on treatment outcomes. Although subgroup analysis showed similar trends in different types of cancer, the residual clinical heterogeneity cannot be totally ruled out. Moreover, differences in tumor stage, perioperative care and institutional protocols could have led to variations in outcomes between studies. Future research presenting standardized outcome metrics would allow a more rigorous meta-analytic assessment.

The steep learning curve for minimally invasive surgical techniques is an important factor to consider. Advanced laparoscopic surgeries not only demand a high degree of skill and special training but the surgical results also depend on the level of experience of the surgeon. Several investigations have shown that the rate of complications drops markedly as the experience of surgeon increases, implying that the results in early trials might not entirely represent the current practice [16]. Hence, the effect of the learning curve may reduce the applicability of the results to those centers that have little experience with minimally invasive techniques.

Furthermore, the majority of the studies included in the meta-analysis were done in high volume specialized centers, which can lead to selection bias and limit the ability to generalize the findings. Patients treated at specialist centers have better access to state of the art surgical technology and highly skilled surgeons, which can impact outcomes. Moreover, differences in patient selection criteria among the different studies may affect the comparability of the minimally invasive and open surgery groups. Another constraint is the possibility of publication bias. It is assumed that studies with negative results are less likely to be published which, in turn, may result in an overestimation of the effect of treatments.

On the contrary, the present meta-analysis has given new clinical pictures and contributed to a growing body of evidence that shows the advantages of minimally invasive surgery in advanced gastrointestinal cancers. From the perspective of oncologic safety, MIS is shown to be an equally safe method with improved perioperative outcomes. This, therefore, makes it a viable alternative to open surgery in patients who are selected appropriately. Additionally, the findings of the present study emphasize the role of the surgeon's experience and institutional expertise in obtaining the best outcome.

While there are multiple studies in support of minimally invasive procedures, there is also some evidence that indicates an advantage of open surgery for long-term survival in carefully selected patients. This, therefore, shows that uncertainty still exists and further investigation is necessary. Future research should be directed towards very large multicenter randomized trials which have standardized outcome reporting in order to find out the comparative effectiveness of the minimally invasive and open surgical approaches. Studies with long-term follow-ups of survival outcomes, recurrence rates and quality of life will also be essential to grasp the full long-term impact of minimally invasive surgery. Moreover, the development of robotic surgery and image guided techniques may contribute to further improvement of the safety and effectiveness of minimally invasive approaches, and thus warrant additional research.

In summary, this meta-analysis reveals that minimally invasive surgery offers similar oncologic outcomes and perioperative recovery benefits over open surgery in patients with advanced gastrointestinal cancers. The results signal support for the increasing use of minimally invasive surgical methods in therapeutics while at the same time, highlighting the need for prudent patient selection and surgical expertise.

Conclusion

This meta-analysis thoroughly compares minimally invasive surgery (MIS) to traditional open surgery for advanced gastrointestinal cancers. It combines evidence from randomized controlled trials and observational studies on gastric and colorectal cancer. The overall results indicate that MIS provides perioperative safety and oncologic outcomes at least as good as those obtained with open surgery in several facets, such as postoperative complications, deaths, anastomotic leaks and measures of oncologic adequacy. On the one hand, some outcomes presented favorable trends for the minimally invasive procedures; on the other hand, most of the combined estimates did not reach a level of statistical significance, and the confidence intervals quite often contained the null value. The findings of the subgroup analysis of gastric and colorectal cancers were in line with each other, confirming that MIS is a viable option with good short term safety, especially if the patients have been properly selected and the surgeons have attained a high level of expertise.

Nonetheless, the findings of this meta-analysis should be treated carefully since there were only a limited number of studies used in some outcomes, the designs of the studies and patient populations varied, and there was heterogeneity in the definition of outcomes and surgical techniques. The relatively low numbers of events and the potential impact of surgeon

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experience and learning curve may also influence the accuracy of the pooled estimates. Hence, although the present evidence indicates that MIS could be a reasonable alternative to open surgery in the case of advanced gastrointestinal cancers, clear-cut conclusions about its superiority cannot be made. Large scale randomized trials with standardized reporting of outcomes and long- term follow-up are needed to verify these results and to elucidate the role of minimally invasive methods in the treatment of advanced gastrointestinal cancer.

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