

Comparing Endoscopy and Surgery: A Systematic Review of Early Colorectal Cancer Treatments

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Abstract:

Colorectal cancer is a major type of gastrointestinal cancer that significantly contributes to disease burden and mortality, particularly among younger people. Early colorectal cancer refers to the early stages of the disease that require early detection and treatment to improve the overall prognosis and survival. There are various treatment options available for early colorectal cancer, such as endoscopic resection, including methods like transanal endoscopic microsurgery (TEMs), endoscopic mucosal resection (EMR), or submucosal dissection (ESD), as well as surgical resection, including open and laparoscopic techniques. However, to make informed decisions about which approach is best, it is crucial to thoroughly understand the long-term outcomes associated with each option. We systematically reviewed the PubMed and Google Scholar databases from 2013 to August 11, 2023, to obtain such knowledge. We selected nine for in-depth analysis after carefully reviewing 2761 articles, including those written in English and focusing on human studies. The review focused on individual benefits, merits, and drawbacks, considering the extent of the disease, clinical outcomes, survival, and complication rates. Although endoscopic resection has the advantage of being less invasive and promoting faster patient recovery, it should be noted that its primary objective may not necessarily be achieving complete excision (R0). This is because there are potential obstacles, including inadequate lymph node removal and inaccurate T staging that may prevent the achievement of R0. Nevertheless, it is important to stress that both endoscopic and surgical resection ultimately share the goal of complete excision and curing the patient. Finally, this systematic review emphasizes the need for additional research to fill knowledge gaps, improve clinical decision-making, and promote the application of sophisticated technology. As the landscape of early colorectal cancer treatment evolves, a balanced integration of endoscopic and surgical resection procedures, together with emerging technologies, can improve patient outcomes and increase treatment efficacy.

Categories: Gastroenterology, Internal Medicine, General Surgery

Keywords: sigmoidoscopy, proctosigmoidectomy, hemicolectomy, endoscopic submucosal resection,

endoscopic submucosal dissection (esd), endoscopic resection, colonic surgery, colectomy, colorectal neoplasms, colorectal cancer

Introduction And Background:

Colorectal Cancer (CRC) is the third most prevalent cancer diagnosed worldwide, and nearly a quarter of cases diagnosed (23%) are in stage 1 [1,2]. Colorectal cancer screening is firmly established as a crucial method for early detection and management, contributing to the rising rates of early disease detection and influencing mortality outcomes [3-6]. According to the current American Joint Committee on Cancer TNM classification, early CRC is described as invasive neoplasia that does not invade the colonic wall beyond the mucosal and submucosal layers [3-6]. Due to the lack of a rich lymphatic network in the region, the probability of lymph node metastases following neoplastic invasion of the colorectal mucosa, lamina propria, muscularis mucosa, and superficial submucosa is low [3,6].

Early CRC therapy options include endoscopic treatments and surgical resection [1,7]. Surgical resection has long been considered the gold standard treatment (either open or laparoscopically assisted), but less invasive techniques (such as Transanal Endoscopic Microsurgery (TEMs), Endoscopic Mucosal Resection (EMR), or Endoscopic Submucosal Dissection (ESD)) are emerging as important and safe treatment options [3,8-10]. Nonetheless, there is little published evidence on the short and long-term effects of these novel and less intrusive treatments compared to typical surgical outcomes [3,8-10]. Local knowledge of both endoscopic and surgical teams largely dictates treatment decisions, and the findings are frequently published in the literature with no comparison of approaches [3,8-10]. Endoscopic procedures for managing CRC individuals with low-risk lymph node metastases include mucosal resection or submucosal dissection [1,7]. Patients with submucosal invasion depths greater than or equal to 1,000 micrometers, undifferentiated adenocarcinoma, lympho-vascular spread, and positively lateral and vertical excision margins should have a radical lymphadenectomy [1,7]. Because of its limited invasiveness, TEMs has been promoted as the preferable local excision technique for treating early lower rectal cancer [11]. It entails using

specialized devices such as an operating proctoscope, laparoscopic camera, and laparoscopic instruments, which allow the operator to access lesions in the mid and upper rectum [12].

However, more research is needed to compare the long-term oncologic outcomes of these two treatment options [1]. The purpose of this study is to collect and analyze existing data on the short and long-term outcomes of EMR or ESD compared to the gold-standard surgical technique (open or laparoscopic surgery) for treating patients with early CRC [3].

Review

Methods:

Figure 1 depicts the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards followed in this review [13]. The systematic review attempted to compare alternative therapy options for early colorectal cancer like endoscopic and surgical resection based on already published data, eliminating the need for approval from the ethics committee.

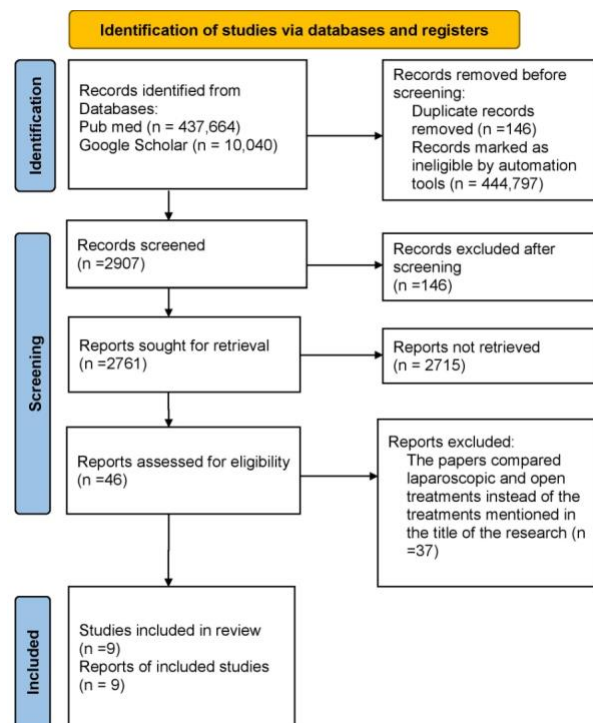


FIGURE 1: PRISMA flow diagram showing the systematic review's search method and selection process.

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Data sources and search strategy:

We framed a research question using the population, intervention/condition, control/comparison, and

outcome (PICO) strategy. We used keywords from the research question and related MeSH terms (depicted in Table 1) to recruit articles from electronic medical databases like PubMed, Medline, and Google Scholar. All possible combinations of results with MeSH terms were retrieved using Boolean operations (AND, OR) to narrow down the results.

Search Strategy	Database 1 with results	Database 2 with results
{(colorectal neoplasms OR sigmoid neoplasms OR colonic neoplasms OR early colorectal cancer [MeSH Terms])} AND [(colectomy OR colonic surgery OR hemicolectomy OR sigmoidoscopy OR rectosigmoidectomy) AND (endoscopic resection OR endoscopic treatment OR ESD OR endoscopy [MeSH Terms] OR endoscopic submucosal resection)]}	Pubmed-18,890	Google scholar-1700
(((((colorectal cancer [MeSH Terms]) AND ((surgery [MeSH Terms]))) OR ((surgical resection)))) AND ((Endoscopic resection)))) OR ((endoscopy [MeSH Terms]))	Pubmed-418,774	Google scholar-8340

Table 1: Showing the data sources used, with the search strategies and their results.

Systematic literature search and study selection criteria:

The study focused on comparative studies such as clinical trials, systematic reviews, and randomized controlled trials. This study only included papers performed on humans and written in English. The experimental intervention studies comparing open surgery versus laparoscopy, as well as just comparing ESD or ESR, were omitted. Abstracts and entire articles with data shortages were not assessed. Case reports, letters to the editor, and commentary were also excluded. The reviewers separately assessed the eligibility of all screened abstracts based on the inclusion and exclusion criteria stated in Table 2. The authors' disagreements were resolved through timely discussion.

Inclusion Criteria	Exclusion Criteria
Articles from 2013-2023	Articles before 2013
Age > 19 years	Age < 19 years
Human studies	Animal studies
English text papers	Non-English text papers
Free full text papers	Paid full text papers
Comparative studies	Case reports, letters to editor
Studies comparing laparoscopy and endoscopy	Studies comparing open and laparoscopic methods or comparison between ESD, EMR
Non gender specific studies	Gender specific studies

Table 2: Showing the Inclusion and Exclusion criteria adopted during the study.

Quality Appraisal:

The quality assessment for this systematic review was done using specific tools to check the validity and credibility of the studies included. Table 3 depicts the tools used for different types of studies and Table 5 shows quality assessment using the tools mentioned in table 3 for each study.

Critical Appraisal Tools	Study type
Amstar Checklist	Systematic Reviews and Meta-analyses
Cochrane Bias Tool Assessment	Randomized Control Trials
Newcastle-Ottawa Tool	Non-Randomized control trials and Observational studies
SANRA Checklist	Traditional reviews

Table 3: Showing all the different quality appraisal tools used during the risk of bias assessment.

Results:

In adherence to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, the results of this systematic review are presented below. We extracted 447,704 articles after inspecting three databases: PubMed, Medline, and Google Scholar. We then applied some primary filters like text availability, associated data, age limit, human studies, and English texted studies on PubMed, Medline and Google Scholar resulting in the exclusion of 444,797 articles. We excluded 146 of the remaining 2907 papers due to duplicates or unsuitable titles and abstracts. We scrutinized the remaining 2761 papers and rejected 2715, since their content did not match our inclusion criteria. Finally, we performed a thorough quality check on the nine papers that fulfilled our selection criteria. Each one of the selected studies has been outlined in Table 4.

Author/ Year	Country	Study design	Interventions compared	Conclusion
Kyeong et al., 2022 [1]	Korea	Retrospective data analysis	Endoscopic versus laparoscopic surgery	
Gustavo et al., 2016 [3]	Brazil (South America)	Systematic review and meta-analysis	Endoscopic versus surgical resection	Surgical resection for early CRC treatment has higher curative and en bloc rates, but higher complications compared to endoscopic resection, with shorter procedure times.
Silvia et al., 2016 [7]	Europe	Prospective data analysis	TAMIS versus TEMS	TAMIS - safe, short-learning technique for laparoscopic surgeons with single-port procedures, offering effective oncological outcomes compared to other techniques like TEMS.
Sajid et al., 2013 [11]	UK	Systematic analysis of trials	TEMS versus RR	Transanal endoscopic microsurgery appears to have clinically measurable advantages in patients with early rectal cancer.
Ailish et al., 2020 [12]	Europe	Systematic literature review and meta-analysis	Endoscopic versus transanal surgery	Endoscopic techniques are preferred for benign early rectal neoplasms due to reduced morbidity and cost-effectiveness, while transanal surgery is preferred for suspected malignancy due to superior R0 resection rate.
Franco et al., 2019 [14]	Europe	Systematic literature review	TAMIS versus TEMS	There is a need to homogenize or standardize functional and manometric outcome assessment after TEMS or TAMIS (transanal endoscopic or minimally invasive surgery)
Jen-Hao et al., 2020 [15]	East Asia	Systematic literature review and meta-analysis	ER versus surgery	The study suggests that endoscopic resection (ER) should be the primary treatment for T1 colorectal cancers, with additional surgery potentially yielding similar outcomes.
Bernard et al., 2017 [16]	Europe	Multicenter randomized controlled trial		The ETAP-GRECCAR 11 trial demonstrate the oncological safety and improved postoperative morbidity and quality of life following ETAP (endoscopic transanal proctectomy) for low rectal cancer compared with the standard LAP (Laparoscopic proctectomy)
Simon et al., 2020 [17]	UK	Randomized trial	TREC versus total mesorectal excision	Short-course radiotherapy combined with transanal endoscopic microsurgery improves organ preservation, quality of life, and safety in patients unsuitable for total mesorectal excision, requiring further evaluation.

Table 4: Showing the summary of all the papers included in the study.

<u>Study</u>	<u>Quality Appraisal Tool</u>	<u>Assessment summary</u>
Kyeong et al., 2022	Newcastle-Ottawa Tool	8 /9
Gustavo et al., 2016	Amstar	11/11
Silvia et al., 2016	Newcastle-Ottawa Tool	8/9
Sajid et al., 2013	Amstar	8/11
Ailish et al., 2020	Amstar	11/11
Franco et al., 2019	Amstar	8/11
Jen-Hao et al., 2020	Amstar	10/11
Bernard et al., 2017	Cochrane Bias tool	Low risk of bias
Simon et al., 2020	Cochrane Bias tool	Low risk of bias

Table 5: Summary of assessment for each study using quality appraisal tool.

- Newcastle-Ottawa tool has 3 domains – selection (one star for each; total questions = 4), Comparability (maximum of 2 stars; total questions= 1) and outcome/exposure (one star for each; total questions=4)
- Amstar checklist is a 11-question checklist; (yes scored as 1; No or can't answer scored as 0)
- Cochrane bias tool has 5 domains – selection, Performance, attrition, reporting, other and each domain is assessed as high, low, or unclear risk of bias.

Interpretation of Results:

After thoroughly examining various studies on treatments for early colorectal cancer, the collective results reveal a complex and detailed picture. According to Kyeong et al., (2022) [1], endoscopic resection has been shown to have comparable long-term oncological results to laparoscopic surgery, making it a highly promising early intervention that employs a multidisciplinary approach. Furthermore, Gustavo et al., (2016) [3] systematic review highlights the advantages of surgical resection, including higher rates of cure and complete removal of tumors. However, it should be noted that this approach also comes with the drawback of increased complications and longer operation times.

Studies by Silvia et al., (2016) [7] and Sajid et al., (2013) [11] have revealed the impressive safety and effectiveness of transanal techniques, such as TEMS and TAMIS, in dealing with rectal polyps and early rectal cancer. This has led to a notable shift in the surgical approach to these conditions. In fact, Ailish et al., (2020) [12] emphasize the growing preference for endoscopic techniques in benign cases and transanal surgery in suspected malignancies. This is supported by the superior R0 resection rate achieved through transanal surgery.

According to Franco et al., (2019) [14], it is imperative to establish a set of standardized outcome evaluations following TEMS or TAMIS procedures, as these could have significant functional consequences. Furthermore, Jen-Hao et al., (2020) [15] review emphasizes endoscopic resection as the preferred treatment for T1 colorectal cancers, with the possibility of additional surgery resulting in comparable results.

The 2017 ETAP trial by Bernard et al., [16] confirms the oncological safety and considerable benefits in postoperative morbidity and quality of life associated with ETAP for low rectal cancer over the traditional LAP approach. Similarly, Simon et al., (2020) [17] reveals the efficacy of combining short-course radiotherapy with transanal endoscopic microsurgery in preserving organs, enhancing quality of life, and ensuring safety for patients who cannot undergo total mesorectal excision.

Through a comprehensive review, it is evident that a personalized, collaborative approach is strongly recommended in tackling early colorectal cancer. This involves considering patient risk, lesion attributes, and the importance of consistent outcome evaluations. What's more, the constant progression of treatment methods further highlights the need for flexibility in our strategies.

Discussion:

Comparative Outcomes of Endoscopic and Surgical Treatments:

The study aimed at a broad comparison of endoscopic and surgical outcomes in early CRC treatment to aid with clinical decision-making. According to Kyeong et al., 2022 [1] retrospective data analysis study, patients who received endoscopic treatment had better short-term clinical outcomes, including shorter operating time and hospital stay, and comparable long-term oncologic outcomes to those who underwent laparoscopic surgery.

The findings of the study comparing outcomes among 60 patients undergoing endoscopic treatment and 38 patients undergoing laparoscopic surgery for early colorectal adenocarcinoma revealed that the endoscopic group experienced shorter operation times, quicker time to consumption of liquids, and shorter hospital stays [1]. Furthermore, the endoscopic group showed similar overall and disease-free survival rates (91.5%, 90.4%) to the laparoscopic group (87.4%, 87.4%), with a lower occurrence of systemic recurrences (1.6% vs. 2.0%) [1]. As a result, with a multidisciplinary approach, endoscopic treatment was advocated as a first option for early CRC [1].

Impact of TEM and TAMIS on Surgical Approach:

Because the rectal wall is partially removed and pelvic nerve damage is potentially avoided, TEM and TAMIS have significantly altered the surgical approach to rectal polyps and early rectal cancer [14]. According to the Franco et al., 2019 [14] systematic review, which included nearly 1300 patients, reported some

deterioration in manometric scores after both TEM (Transanal endoscopic microsurgery) and TAMIS (Transanal minimally invasive surgery), and suggested worsening in function at least in some items of the used scores, including de novo incontinence in some patients. However, the procedures do not have a major impact on QoL (Quality of Life) [14].

R0 Resection Rates in Transanal Surgery:

The key finding in Ailish et al., 2020 [12] systematic literature review and metaanalysis is that transanal surgery has a greater R0 resection rate when compared to endoscopic resection. However, it should be noted that there was no difference in the en bloc resection rate [12]. While the endoscopic arm had a greater rate of partial resection/residual adenoma, there was no difference in late recurrence rates [12]. These findings were strong and held up in the sensitivity analysis [12].

Comparison of Primary ER and Primary Surgical Treatments:

We discovered that the overall, disease-specific, and recurrence-free survival rates were comparable across primary ER (Endoscopic Resection) and primary surgical treatments in the Jen-Hao et al., 2020 [15] review. After combing through 19,979 patient cases; the study revealed no significant variances in overall survival, recurrence-free survival, or disease-specific survival when comparing the effectiveness of primary endoscopic resection (ER) versus primary surgery for T1 colorectal cancers [15]. Notably, primary ER showed a marked reduction in procedure-related adverse events (2.3%) compared to primary surgery (10.9%) [15]. Patients with T1 CRC who got ER alone showed worse results than those who received surgery if the lesions were high-risk (cancer recurrence of up to 10%) [15]. As a result, the advantages of extra surgery should be more pronounced in individuals with high-risk lesions [15]. In these individuals, further surgery was beneficial and had no additional harmful effects on prognosis when compared to patients who got main surgery [15].

The ETAP Trial: Transanal Endoscopic Proctectomy vs. Laparoscopic Proctectomy:

Bernard et al., 2017 [16] ETAP trial is the first to compare ETAP (Transanal endoscopic proctectomy) against a typical transabdominal laparoscopic procedure using an active inclusion technique. In this non-inferiority trial, the first patient, n°01001, was admitted on January 26, 2016, with the hypothesis that ETAP would have similar oncologic results (R1 resection rate) with significant improvements in dissection quality (mesorectal assessment and nerve preservation), morbidity, function, and quality of life compared to laparoscopic proctectomy [16].

TEMS Technique and Risk of Local Tumor Recurrence:

The TEMS (Transanal endoscopic microsurgery) technique for managing early rectal cancer is associated with a higher risk of local tumor recurrence [11]. Still, it is statistically equal to RR (Radical resection) in terms of terms of total mortality, overall survival, and the risk

of distant metastasis, according to the findings of the Sajid et al., 2013 [11] systematic review. Furthermore, TEMS relates to a shorter operation duration and length of hospital stay, as well as a lower risk of postoperative complications [11]. The combined analysis of all types of research and the combined analysis of solely randomized trials yielded comparable results [11]. Furthermore, the combined analysis of randomized trials alone and the combined analysis of observation studies alone yielded identical results [11].

Meta-Analysis on Endoscopic vs. Surgical Treatment:

Gustavo et al., 2016 [3] first meta-analysis that compiled all available data to compare endoscopic versus surgical treatment of early CRC. Even though only three studies passed the inclusion criteria, the total number of patients (768 for endoscopic resection and 552 for surgical resection) is large [3]. A rigorous systematic analysis revealed that, when individual study results were considered, all three trials obtained identical, statistically significant data outcomes involving en bloc resection, curative resection, and complications [3]. The meta-analysis illustrated in this study supports some of these findings and lays the groundwork for future larger-scale, better-designed studies, such as multicenter randomized controlled trials [3].

Limitations:

In our thorough examination of the literature, certain restrictions were imposed. Our inquiry was limited to recent English publications, and we only had access to freely available resources. Additionally, we concentrated solely on English papers delving into minimally invasive techniques for early colorectal cancer. However, it is important to note that our comparative analysis did not consider cancer staging. To arrive at more definitive and all-encompassing findings, further research incorporating a wider range of staging factors is vital.

Conclusions:

In conclusion, the study comparing endoscopic and surgical outcomes for early colorectal cancer reveals the promising advantages of endoscopic resection, particularly with innovative techniques such as TEMS and TAMIS. These methods have been shown to reduce operation times and hospital stays while resulting in similar long-term cancer outcomes as traditional laparoscopic surgery. However, care must be taken to account for individual factors, such as lesion characteristics, staging of cancer, and patient risk, to achieve complete removal of the cancer. This highlights the evolving nature of surgical methods, with transanal techniques demonstrating superior success rates in removing all cancerous tissue. While potential functional consequences must be acknowledged, the study suggests a customized and collaborative approach that combines both endoscopic and surgical techniques in the treatment of early colorectal cancer. Continual research and cross-disciplinary collaboration are essential in responding to the ever-evolving nature of treatment techniques and enhancing clinical decision-

making. Moreover, these findings serve as a building block for future extensive and well-designed investigations, including randomized controlled trials conducted across multiple centers.

Additional Information:

Disclosures:

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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