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Incidence of colonic fistulas in patients with colon cancer submitted to robotic surgery versus laparoscopic colorectal surgery: a systematic review and meta-analysis protocol

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ABSTRACT

Introduction Up to the present time, the laparoscopic approach for colon cancer is considered the gold standard. However, robotic surgery has been appraised in modern medicine. It is essential to evaluate the differences between laparoscopic and robotic surgery, owing to the significant impact they cause in postoperative morbidity and mortality. This article aims to perform a systematic review and meta-analysis of the literature to compare robotic versus laparoscopic colectomies in patients with colon cancer in terms of the incidence of colonic fistulas.

Methods and analysis PubMed, Embase, Scopus, Web of Science, Science Direct, Cochrane Central Register of Controlled Trials, CINAHL, LILACS and Clinical trials databases will be searched for randomised clinical trials investigating the incidence of colonic fistulas in patients with colonic cancer, submitted to robotic surgery compared with a laparoscopic approach. No language or publication period restrictions will be imposed. The primary outcome will be the incidence of colonic fistulas in patients with colon cancer in different surgical approaches. The secondary outcomes will be the incidence of infection, sepsis, mortality, length of hospitalisation and malnutrition. Three independent reviewers will select the studies and extract data from the original publications. The risk of bias will be assessed using The Risk of Bias 2 tool, and the evidence's certainty will be made using the Grading of Recommendations Assessment, Development and Evaluation. Data synthesis will be performed using the Review Manager software (RevMan V.5.2.3). To assess heterogeneity. We will compute the I^2 statistics. In addition, a quantitative synthesis will be performed if the included studies are sufficiently homogeneous.

Ethics and dissemination This study will review the published data; thus, it is not necessary to obtain ethical approval. The findings of this systematic review will be published in a peer-reviewed journal.

PROSPERO registration number CRD42021295313.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The results obtained in this systematic review will evaluate the effectiveness of the robotic surgery intervention in preventing colonic fistulas postcolectomy compared with standard care.
⇒ Our sample will include only oncological patients, limiting generalisability for other colectomies.
⇒ Three independent reviewers will select the studies included in this review, extract data without different variables and assess the risk of bias.
⇒ Potential limitations include a small sample size and a limited number of studies, which may influence the validity and reliability of the findings.

INTRODUCTION

Colorectal cancer is the second most common type of neoplasm globally, whose only curative strategy is through colectomy.[1] In this group of patients, postoperative complications occur in more than 50% of the situations, negatively impacting patients' morbidity and mortality and causing increased costs for health systems.[1]

Colectomy remains the main therapeutic strategy in the management of colon cancer, which requires, therefore, a particular focus in literature to investigate the safest and most effective way to perform a given procedure in search of the best prognosis for the patients.[2]

The latter generates intense debates in the medical community regarding possible changes in operative procedures considered the gold standard, which revolves around comparing robotic and laparoscopic surgery.[3 4]

The evolution of robotic surgery is considered a significant innovation in modern medicine, as it provides an alternative to a surgical approach in different scenarios.[5] Although some studies select it as more time-consuming and expensive than laparoscopy, they suggest that it allows for a faster recovery of bowel function, shorter hospital stay, less blood loss and lower rates of complications and wound infections compared with the standard laparotomy.

On the other hand, they consider some technical disadvantages of the laparoscopic approach, such as the limited range of motion of instruments and related loss of dexterity, fixed instrument tips and an inadequate visual field associated with an unstable view of the camera and traction of the assistant.[2 3]

Currently, the laparoscopic approach is considered the gold-standard treatment method for colon cancer.[6 7] Therefore, it is essential to confirm whether laparoscopy remains the strategy that brings the most benefits or whether robotic surgery, with new techniques and an advanced therapeutic arsenal, enables more favourable outcomes for patients.[3]

Although laparoscopic is the gold-standard approach for treating malignant and benign colon diseases, it has some limitations, such as the two-dimensional view of the operating field, physiological tremor of the camera operator and lack of ergonomic design of the instruments.[8]

Robotic technology was introduced in 2002 to overcome technical difficulties faced during a laparoscopic approach. The main advantages of robotic surgery include its three-dimensional magnification and stable vision, convenient movements of the robotic arms, endo wrist instruments with seven df, ambidextrous capability, tremor filtering and indocyanine green fluorescence imaging through the Firefly Imaging System.[8]

Also, it facilitated dissection with hand-like motions of the instruments and offered the surgeon an ergonomically comfortable position to sit.[9 10]

Depending on the tumour staging, colectomy is considered a medium to large operation.[2] Thus, postoperative complications, such as wound infection, sepsis and malnutrition, increase the length of hospital stay and the morbidity and mortality of operated patients.[4] However, one of the most worrying and difficult-to-manage complications is the dehiscence of anastomoses and colonic fistulas.[11]

Dehiscence of anastomoses corresponds to a structural dysfunction of the intestinal wall close to the suture's site, forming the communication between intra and extraluminal spaces. On the occasions that the dehiscence progresses with the communication between two adjacent organs of the gastrointestinal tract or between them and the external environment, it is called a digestive fistula. Its diagnosis is clinical but may require additional exams, such as radiography and CT, to aid in the differential diagnosis. Due to the interference in homoeostasis, this condition and treatment represent a challenge.[11]

Mortality for most elective surgical procedures is less than 2%. However, in patients with digestive fistula, mortality varies from 6% to 48%, even after advances observed in their treatment.[12 13]

The results presented by this and other epidemiological studies reveal the seriousness of this problem and demonstrate that data on patients with colonic fistulas are still scarce and inaccurate.[14 15] That is why the search for a more detailed understanding of the incidence of this complication among patients with cancer, a vulnerable group subject to several postoperative complications, becomes so relevant.

Therefore, this study aims to compare laparoscopic colectomies to colectomies performed by robotic surgery concerning the appearance of colonic fistulas in patients with colon cancer undergoing curative oncologic surgery.

Review questions?

1. What is the incidence of colonic fistulas after colectomy?
2. Are the colonic fistulas more incident on laparoscopic or robotic-assisted surgery?
3. What are the other complications associated with colectomies?

Objectives

This systematic review will aim to estimate the incidence of colonic fistulas in robotic versus laparoscopic colectomies in patients with colon cancer.

MATERIALS AND METHODS

The systematic review and meta-analysis in question will be developed following the guidelines of the Meta-analysis of Observational Studies in Epidemiology[16] and Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).[17 18] This protocol is listed in the International Prospective Registry of Systematic Reviews (PROSPERO) (CRD42021295313).

Inclusion criteria

This systematic review will include the following studies: Randomised clinical trials that evaluated the incidence of colonic fistulas in patients submitted to laparoscopy or robotic surgery; studies involving patients (age >18) with colon cancer; studies without time restriction and published in any language.

Exclusion criteria

Case reports, meeting abstracts, review papers, observational studies (cohort, case–control, transversal) and commentaries.

The PECOT strategy

- Population: patients with colon cancer submitted to colectomy.
- Intervention: laparoscopic colorectal surgery.
- Control: robotic surgery.
- Outcome: incidence of colonic fistulas.

- Type of studies: randomised clinical trials.

Types of patients

Studies included patients aged >18 with colon cancer in the postoperative period of colectomy.

Types of exposures

Studies where the patients realised laparoscopic and robotic-assisted colectomy.

Types of outcome measures

Fistulas in the postoperative period of colectomy for colon cancer are frequent and significant health problems for this population.

Secondary outcome

Incidence of infection, sepsis, mortality, length of hospitalisation and malnutrition.

Patient and public involvement

This is a protocol for a systematic review and meta-analysis; the research will be conducted based on a comprehensive literature search from relevant databases; the individual patient data will not be included. Thus, patients will not be involved while setting the search terms, determining outcome measures, implementing the study design and analysing the results.

Search strategy

The strategy will be performed in the databases PubMed, Embase, Scopus, Web of Science, Science Direct, LILACS, Cochrane Central Register of Controlled Trials, CINAHL and clinical trials databases (www.trialscentral.org; www.controlled-trials.com, ClinicalTrials.gov), without language restrictions. 'Grey literature' will be searched on www.opengrey.eu and Google Scholar. No language or publication period restrictions will be imposed. The databases will be searched until July 2023.

The Medical Subject Headings (MeSH) terms will be: ((Colonic Neoplasm OR Colonic Cancer OR Cancer of Colon) AND (Laparoscopic Colectomy OR Right Colectomy OR Sigmoidectomy OR Hemicolectomy) AND (Robotic Surgical Procedures OR Robot OR Robot-assisted) AND (Digestive System Fistula OR Intestinal Fistula OR Infection OR Sepsis OR Mortality OR Length of Hospitalization OR Malnutrition)) (table 1).

Table 1 Presents the search strategy for Medline

Search items	
1	Colonic Neoplasm
2	Colonic Cancer
3	Cancer of Colon
4	1–3/OR
5	Laparoscopic Colectomy
6	Right Colectomy
7	Left Colectomy
8	Sigmoidectomy
9	Hemicolectomy
10	5–9/OR
11	Robotic Surgical Procedures
12	Robot
13	Robot-assisted
14	11–13/OR
15	Digestive System Fistula
16	Intestinal Fistula
17	Infection
18	Sepsis
19	Mortality
20	Length of Hospitalization
21	Malnutrition
22	15–21/OR
23	4 AND 10 AND 22

Other sources

Eligible studies may also be selected from the reference lists of retrieved articles. That is, the scope of the computerised literature search may be enlarged based on the reference lists of retrieved articles.

Data collection and analysis

Selection of studies

Three authors, PVOV, VRDM and CAA, will independently screen the search results using titles and abstracts using the software Rayyan (https://www.rayyan.ai). Duplicates and reviews will be removed from the database. The articles will be included in an Excel table (Google Drive). The same authors will review the full text to determine whether the studies meet the inclusion criteria. A fourth reviewer, HPMA, will resolve any discrepancies. The selection of studies will be summarised in a PRISMA flow diagram (figure 1).

Data extraction and management

A standardised data extraction form will be developed and tested. Data from each included study will be extracted independently by two reviewers (HPMA and TCLS), and any subsequent discrepancies will be resolved through discussion with a third reviewer (IA-F). The data extracted will include the type of study, main objectives, population, type of surgery, follow-up of participants, surgical intervention, colonic fistula, infection, sepsis, mortality, length of hospitalisation and malnutrition. Furthermore, participant characteristics (eg, mean age, gender). Information about the authors, year of publication, and study location will be used for study identification.

Data extraction and management

A standardised data extraction form will be developed and tested. Data from each included study will be extracted independently by two reviewers (HPMA and TCLS), and any subsequent discrepancies will be resolved through discussion with a third reviewer (IA-F). The data extracted

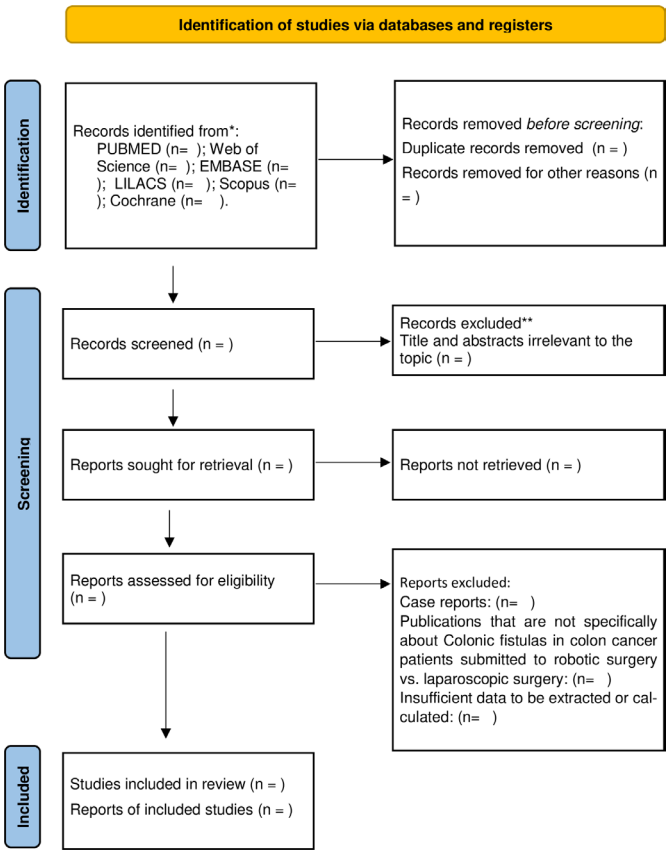

Figure 1 PRISMA flow diagram for systematic review and meta-analysis. *Databases will be searched. **Records excluded by title and abstracts irrelevant to the topic. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

will include the type of study, main objectives, population, type of surgery, follow-up of participants, surgical intervention, colonic fistula, infection, sepsis, mortality, length of hospitalisation and malnutrition. Furthermore, participant characteristics (eg, mean age, gender). Information about the authors, year of publication, and study location will be used for study identification.

Addressing missing data

In the case of missing data, the authors of this article will contact the corresponding authors or coauthors of the article by phone or email. If we do not receive the necessary information, the data will be excluded from our analysis and will be covered in the discussion section.

Risk of bias assessment

The quality of articles will be analysed by two independent researchers (CAA and VRDM) using The Risk of Bias 2 tool.[10]

Assessment of heterogeneity

The heterogeneity between the results of the studies will be evaluated using a standard $\chi 2$ test with a significance level of $p<0.1$. To assess heterogeneity, we planned to calculate the I^2 statistic, which is a quantitative measure of inconsistency between studies. A value of 0% indicates the absence of heterogeneity, while values of I 2≥50% indicate a substantial level of heterogeneity; however, heterogeneity will only be assessed if it is appropriate to perform a meta-analysis.

Analysis

The data will be entered in the Review Manager software (RevMan V.5.2.3). This software allows the user to enter protocols; complete reviews; include text, study characteristics, comparison tables and study data; and perform meta-analyses.

For dichotomous results, we will extract or calculate the OR and 95% CI for each study. In case of heterogeneity (I^2≥50%), the random effects model will be used to combine the studies to calculate the OR and 95% CI, using the DerSimonian-Laird algorithm in the meta for the package, which provides functions to drive meta-analyses in R.

Other study characteristics and results will be summarised narratively if the meta-analysis cannot be performed for all or some of the included studies. Sensitivity analysis will be used to explore the robustness of the findings concerning study quality and sample size. The latter is only possible if we can perform a meta-analysis. Sensitivity analysis will be presented in a summary table.

Grading quality of evidence

Assessment of the certainty of the evidence will be made by using the Grading of Recommendations Assessment, Development and Evaluation[10] method or an equivalent methodology that will be clearly described and documented.

DISCUSSION

Colectomy is the gold-standard treatment in the management of colon cancer. However, it has disadvantages and needs improvement to achieve better results and reduce rates of postoperative complications. Laparoscopic and robotic approaches are comparatively studied to meet these expectations.[2 6 7]

Compared with a laparoscopic approach, robotic colectomy provides a significantly shorter time to first flatus, a shorter length of hospital stay, less intraoperative blood loss and a significant reduction in the rate of overall postoperative complications and wound infections.

No statistically significant differences were found in the conversion to open surgery rate, the number of harvested lymph nodes and the rate of both anastomotic leak and postoperative ileus, but right colectomy required a higher operative time and cost than laparoscopy.[2]

Colonic fistulas are one of the main complications of this operation. The severity of the condition is due to the loss of volume of body fluids, which contain essential substances for life, promoting malnutrition and hydroelectrolytic disorders, in addition to increasing the susceptibility of patients to infections and sepsis, the main cause of mortality in these patients.[11 19 20]

They can be classified according to anatomical location, output (high >500 mL, moderate 200–500 and low <200 mL/24 hours), origin (congenital or acquired) or even according to aetiology.[8 13]

In the postoperative period, in addition to the presence of drains and foreign bodies, systemic factors are also relevant, such as malnutrition and the use of corticosteroids10. Furthermore, they are associated with high morbidity and mortality, longer hospital stays and costs, and a higher risk of reoperations and permanent ostomies.[11 13]

In an epidemiological study conducted by Wercka *et al*, with a sample of 1148 operated patients in different specialties, the incidence of fistula was 5.5%. Among these, 22% of fistulas were colonic, and the mortality rate of patients with fistula was 25.4%. Thirty-two patients (51%) evolved with malnutrition, and 11 (18%) required parenteral nutrition for more than 7 days. The diagnosis of sepsis was observed in 46 patients (73%). In 32 cases (51%), intensive care unit (ICU) admission was needed. There were 16 deaths, with a mortality rate of patients who developed postoperative complications of 25.4%.[12]

Consequently, colonic fistulas represent a great challenge for patients and surgeons since they present a complex and time-consuming treatment, increasing the rates of worsening prognosis after surgical intervention.[11]

Therefore, understanding which surgical technique is associated with a lower incidence of colonic fistulas in the postoperative period is of extreme interest to prevent as many cases as possible. It is essential to know if laparoscopy remains the best option for patients with cancer in the colectomy scenario or if robotic surgery, of more recent origin, has more advantages.[4 5]

This definition is highly relevant since it can influence important decisions about the destination of resources and if one should invest in one technique or another, depending on which one represents a better outcome for patients. At the same time, it encourages caution and careful analysis of new technologies inserted in the health area, revealing the need to always be submitted to the scientific method so that their effectiveness and safety are proven.[21]

It is expected that accurate data collection and analysis will be carried out on the subject of the study and that, through this, the therapeutic strategy with lower rates of adverse secondary complications will be guided in the literature as preferred to improve morbidity and mortality and quality of life of patients undergoing surgery for colon cancer.

ETHICS AND DISSEMINATION

Ethical approval is not required because this review will draw on publicly available scientific literature. The findings of this systematic review will be published in a peer-reviewed journal, and updates will be conducted if there is enough new evidence that may cause any changes in the conclusions of the review. Any amendments made to the protocol during the conduct of the review will be reported in the manuscript.

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