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Robotic beyond total mesorectal excision (TME) for locally advanced or recurrent rectal cancer: a systematic review protocol

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ABSTRACT

Introduction The surgical treatment for locally advanced or recurrent rectal cancer requires oncological clearance with a pelvic exenteration or a beyond total mesorectal excision (TME). The aim of this systematic review is to explore the safety and feasibility of robotic surgery in locally advanced and recurrent rectal cancer by evaluating perioperative outcomes, oncological clearance rates, and survival and recurrence rates postrobotic beyond TME surgery.

Methods The systematic review will include studies published until the end of December 2023. The MEDLINE, EMBASE and Scopus databases will be searched. The screening process, study selection, data extraction, quality assessment and analysis will be performed by two independent reviewers. Discrepancies will be resolved by consensus with a third independent reviewer. The risk of bias will be assessed with validated scores. The primary outcomes will be oncological clearance, overall and disease-free survival, and local and systemic recurrence rates post robotic or robot-assisted beyond TME surgery for locally advanced or recurrent rectal cancer. Secondary outcomes will include perioperative outcomes.

Ethics and dissemination No ethical approval is required for this systematic review as no individual patient cases are studied requiring access to individual medical records. The results of the systematic review will be disseminated with conference presentations and peer-reviewed paper publications.

PROSPERO registration of the study CRD42023408098.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A robust search strategy protocol of current databases will be used with the support of an experienced librarian to identify published work detailing the safety and feasibility of robotic beyond total mesorectal excision (TME) surgery for locally advanced or recurrent rectal cancer.
⇒ The literature search will be performed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Protocols guidelines.
⇒ Two independent reviewers will be involved in the whole systematic review process from the screening of studies to the data analysis.
⇒ The lack of high-quality clinical trials or prospective studies, due to the robotic approach being currently implemented for beyond TME surgery, may lead to limited good-quality evidence available for analysis.

INTRODUCTION

The management of rectal cancer is multimodal with surgery remaining the mainstay curative option. Total mesorectal excision (TME) is the standard operation for rectal cancer.[1 2] Oncological clearance is defined by a circumferential resection margin (CRM) greater than 1 mm, that is, a distance greater than 1 mm between the tumour and the mesorectal envelope. CRM involvement is the most important prognostic indicator negatively affecting overall survival in rectal cancer[3] and, therefore, oncological clearance is key in curative intent and patient survival.

Locally advanced rectal cancer, defined by the tumour involving the CRM or directly invading adjacent organs, requires an oncological resection in the form of a beyond TME or multiorgan en bloc resection.[4] In cases of recurrent rectal cancer, the CRM is no longer present due to previous surgery and, therefore, the margin for clearance may be more extensive and/or involving adjacent pelvic organs.[4] Early recurrence is defined as local recurrence within 12 months of the primary surgery. Approximately 40% of local rectal cancer recurrence cases occur 36 months post index procedure.[5] Hence, a beyond conventional TME approach or a pelvic exenteration (anterior, middle, posterior and total) is recommended in locally advanced or recurrent rectal cancer.

Minimally invasive surgical approaches have been shown to improve postoperative pain and facilitate recovery following pelvic

abdominal surgery.[6 7] However, laparoscopic surgery has significant limitations when working in a narrow pelvis with reduced access and lack of tactile feedback. Robotic surgery can overcome some of these limitations by offering additional benefits in accessing the pelvis with enhanced 3D vision and wristed instruments.[6–9] There have been several case reports and case series published worldwide on robotic pelvic exenterations and robotic beyond TME surgery suggesting that the robotic approach is safe and feasible for locally advanced or recurrent rectal cancer.[8 9]

This systematic review aims to investigate, evaluate and present an overview of the reported perioperative and oncological outcomes as well as the recurrence and survival data from robotic or robot-assisted beyond TME or exenterative surgery in locally advanced or recurrent rectal cancer. The review may provide insight into the safety and feasibility of the robotic approach for beyond TME surgery.

METHODS

Study eligibility criteria

The studies selected will be required to meet the following criteria: (1) studies reporting on locally advanced or recurrent rectal cancer outcomes following robotic or robotic-assisted beyond TME or exenterative surgery in patients aged ≥18 years of age; (2) studies comparing the robotic versus open surgery with regards to beyond TME or exenteration surgery; (3) randomised controlled trials, prospective or retrospective cohort studies, case series and case reports; (4) studies published up until the end of December 2023; (5) studies published in English. The reviewers will exclude (1) reviews, letters, commentaries, abstracts, editorials and videos; (2) studies without full text. Although a minimum follow-up time of 3 years is required, survival analyses may not be feasible with studies reporting various follow-up lengths. Therefore, the inclusion of studies with variable follow-up will be assessed on a case-by-case basis. If studies are identified that report outcomes from the same cohort of patients in different time scales, the study with the largest sample size and longest follow-up data will be included. It is intended that by following these eligibility (inclusion/exclusion) criteria we will capture all available studies for our research question.

Information sources and search strategy

The systematic review will be conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Protocols checklist.[10] The systematic search will be performed using the MEDLINE and EMBASE databases via OVID, and the SCOPUS database. The systematic review will also be informed of contemporary registered studies by searching the Clinical Trials database (clinicaltrials.gov) and the PROSPERO Registry (crd.york.ac.uk/prospero). A combination of search keywords and subject headings will be used for MEDLINE and EMBASE databases, whereas a combination of search headings will be used for the SCOPUS database (please see online supplemental file 1). This combination of keywords and/or subject headings forms our search strategy which will be supported by an experienced librarian. There will be no temporal limits placed on the search strategy other than including the studies published up until the search date. A limit placed on the search strategy will be that the included studies are published in English. Individual researchers may be contacted directly via e-mail to request clarification of data if no sufficient information is provided in the corresponding published literature.

Data management

Duplicates from the literature search results will be removed by using the reference manager Endnote (Clarivate, Philadelphia, PA, USA). The search results will then be uploaded to Rayyan QCRI web-based software management programme. Abstracts and articles will be uploaded as documents for the screening and study selection by the reviewers.

Study selection process

A flow diagram depicting the screening process as per PRISMA guidelines will be included.[11] Potentially eligible studies for inclusion will be identified by screening the titles and abstracts of studies before being uploaded to Rayyan QCRI for analysis. During screening, the studies will receive scores from each of the two reviewers based on the eligibility criteria, with the final inclusion of studies occurring after full-text screening by the two reviewers.

Data collection process

A Microsoft Excel file will be created when extracting the data in a standardised form and the two screening authors (IGP and AP) will extract the data from eligible studies for comparison on the Excel file. The data will include the study details, the patient demographics, the methods and the corresponding outcomes of interest.

Outcomes

The primary outcome of the systematic review will be to identify the reported oncological clearance rates, survival data and recurrence rates from robotic or robot-assisted beyond TME surgery in locally advanced or recurrent rectal cancer. Survival is defined as the time between surgery and death. Recurrence following robotic beyond TME or exenterative surgery for locally advanced or recurrent rectal cancer is defined as confirmation of local or distant recurrence based on clinical, radiological and/or histological assessment. Secondary outcomes will include the safety and feasibility of the robotic approach for beyond TME or exenterative surgery in locally advanced or recurrent rectal cancer and will be examined by assessing perioperative outcomes and identifying reported complications. The outcome data will be compared with the standard practice of open exenterative or beyond TME surgery for locally advanced or recurrent colorectal cancer. If further outcomes are evaluated

as important during the search, the systematic review protocol will be amended and these outcomes will be included in the systematic review report.

Quality assessment and risk of bias

The quality of the included studies will be assessed by the review authors (IGP and AP) independently. Disagreements will be resolved by consensus but if required a third reviewer will be invited (GNP). All authors have expertise in the management of rectal cancer. The methodological quality and the risk of bias at the study level will be assessed with the Cochrane RoB 2 Tool[12] for randomised controlled trials and with the ROBINS-I assessment tool[13] for observational or non-randomised studies. If a synthesis of the results of published case reports or case series is required due to lack of higher level of evidence, the 13-item Case Report (CARE) checklist[14] will be used for critical appraisal.

Data synthesis

A narrative synthesis of the review findings from the included studies will be provided. Outcomes will be presented in a structured or tabular form with a meta-analysis performed if more than three studies with the same outcome measures are identified. If a meta-analysis is not possible, descriptive statistics and primary effect measures will be used to synthesise the results of a small number of studies. The scarcity of prospective studies on the application of robotic surgery for beyond TME for locally advanced or recurrent rectal cancer may result in limited high-quality evidence and, therefore, a narrative review of the available evidence will be performed.

Statistical analysis

The statistical analysis will be performed using IBM SPSS Statistics or Graphpad Prism. Categorical data will be described with median values and interquartile ranges and will be analysed with χ^2 test. Continuous data will be described with mean values and standard deviations and will be analysed with the Kruskal-Wallis test. A $p<0.050$ will be considered statistically significant. If a meta-analysis is performed, standardised mean differences and descriptive statistics will be used to show the study data. Heterogeneity will be assessed with I^2 statistics (I^2 values of 25%, 50% and 75% will be low, moderate and high, respectively). A random effects model will be adopted to provide the pool estimates of mean differences in case of moderate or high heterogeneity in the included studies. If a random effects model is used, a sensitivity analysis will be performed.

Metabias(es)

The potential of publication bias will be assessed by accessing the studies' published protocols before the start of patient recruitment/inclusion. The potential of reporting bias will be assessed by comparing outcomes reported in the published study protocol with those reported in the corresponding published paper article.

Confidence in cumulative evidence

The strength of the body of evidence with regard to the research question will be assessed using the GRADE tool (Grading of Recommendations Assessment, Development and Evaluation).[15] The quality of the available evidence will be reported with the GRADE certainty ratings of high, moderate, low and very low.[16] This assessment will offer clear indications of the quality of the literature used in the systematic review.

Patient and public involvement

There was no formal patient and public involvement in the creation of the systematic review protocol. The results will be communicated with patients in lay language via patient organisations such as the patient representative body of the Association of Coloproctology of Great Britain and Ireland (ACPGBI).

Ethics and dissemination

No ethical approval has been obtained for this systematic review as no individual patient cases are studied requiring access to individual medical records. The results of the systematic review will be disseminated with conference presentations and peer-reviewed paper publications.

Study planning

The literature search will include studies published up until the end of December 2023. The data collection and analysis will be performed between January and February 2024. The systematic review will be written up by the end of April 2024.

Amendments

If an amendment is made to the systematic review protocol, the reason for the amendment and the date for the change will be provided.

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Contributors Substantial contributions to the conception and design of this systematic review protocol: IGP, MH, GAM and JSK. Drafting the protocol: IGP. Critical appraisal: AP, GNP, GAM, MH and JSK. Final approval of the version to be published: IGP, AP, GNP, MH, GAM and JSK. All authors agreed to be accountable for all aspects of the work included in this manuscript.

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