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Cost analysis and cost-effectiveness of open versus laparoscopic versus robot-assisted versus transanal total mesorectal excision in patients with rectal cancer: a protocol for a systematic review

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ABSTRACT

Introduction Nowadays, most rectal tumours are treated open or minimally invasive, using laparoscopic, robot-assisted or transanal total mesorectal excision. However, insight into the total costs of these techniques is limited. Since all three techniques are currently being performed, including cost considerations in the choice of treatment technique may significantly impact future healthcare costs. Therefore, this systematic review aims to provide an overview of evidence regarding costs in patients with rectal cancer following open, laparoscopic, robot-assisted and transanal total mesorectal excision.

Methods and analysis A systematic search will be conducted for papers between January 2000 and March 2022. Databases PubMed/MEDLINE, EMBASE, Scopus, Web of Science and Cochrane Library databases will be searched. Study selection, data extraction and quality assessment will be performed independently by four reviewers and discrepancies will be resolved through discussion. The Consensus Health Economic Criteria list will be used for assessing risk of bias. Total costs of the different techniques, consisting of but not limited to, theatre, in-hospital and postoperative costs, will be the primary outcome.

Ethics and dissemination No ethical approval is required, as there is no collection of patient data at an individual level. Findings will be disseminated widely, through peer-reviewed publication and presentation at relevant national and international conferences.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The literature search for this systematic review will be performed with the support of an experienced librarian and will be performed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines.
⇒ This review includes only prospectively collected data, as retrospective data on costs are associated with recall bias, excluding studies with limited quality of evidence.
⇒ In order to limit the effects of missing data, authors will be contacted and requested to provide additional data if needed.
⇒ The systematic review will be performed with support of a European expert in the field of health economics.
⇒ The scarcity of high-quality prospective studies evaluating total costs of the different techniques may lead to limited quality of evidence.

INTRODUCTION

The primary treatment for extraperitoneal rectal adenocarcinoma consists of surgical resection according to the total mesorectal excision (TME) principle, often preceded by (chemo)radiotherapy.[1] This procedure can be performed using open TME, laparoscopic TME (L-TME), robot-assisted TME (R-TME) and transanal TME (TaTME).[2] As of yet, no clear differences regarding intraoperative, postoperative or oncological outcomes have been described between the three minimally invasive techniques.[3–7] Currently all three minimally invasive techniques are performed as standard of care. As treatment of rectal cancer is primarily focused on oncological outcomes, less attention has been paid to the costs of the four TME techniques, consisting of all theatre, in-hospital and postoperative costs. However, cost-effectiveness of open TME, L-TME, R-TME and TaTME is of significant importance, particularly as robot-assisted surgery is said to be associated with significant implementation costs.[8–10]

Some authors suggest costs of R-TME are higher compared with L-TME as a result of high implementation costs and longer operating times.[8–10] Contrastingly, recent studies suggested that operating times may be equal between these techniques. TaTME was reported to be associated with shorter operating times compared with L-TME, when performed by two surgical teams.[3 7 11 12] However, it is important to consider that two teams working, that is often used in TaTME surgery, yield higher costs.[13] There are no studies comparing costs of R-TME and TaTME and the level of evidence of literature comparing the cost-effectiveness of the minimal invasive techniques is limited.

Currently, insight into the costs of the different procedures and level of evidence of cost-analysis studies is limited. An analysis and overview of the evidence on costs is, therefore, needed in order to assess the (minimal) invasive TME techniques. This systematic review aims to create an overview of the existing literature regarding the costs for open TME, L-TME, R-TME and TaTME and may provide recommendations for use and future cost-effectiveness studies. This is particularly important regarding the cost-containment discussion. Since all techniques are currently being performed, including cost considerations in the choice of treatment technique may significantly impact future healthcare costs.

METHODS

Patients, interventions, control, outcome and research question

Patients: patients with rectal cancer.

Interventions: open TME, L-TME, R-TME and TaTME

Control: -

Outcome: total costs, consisting of but not limited to theatre costs, in-hospital costs and postoperative costs.

Research question: What are the total costs, consisting of but not limited to theatre costs, in-hospital costs and postoperative costs, of open, laparoscopic, robot-assisted and TaTME for the surgical treatment of patients with rectal cancer?

Search strategy

This review will be performed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines (online supplemental file 1). A systematic search will be conducted on PubMed/MEDLINE, EMBASE, Scopus, Web of Science and Cochrane Library databases, using a predefined search strategy consisting of a combination of standard search headings and medical subject headings related to open TME, L-TME, R-TME and TaTME for treatment of rectal cancer (online supplemental file 2). The search will be supported by an experienced librarian. No limits based on study design or setting will be imposed on the search. For literature saturation, reference lists of included studies and the function 'related article' in PubMed will also be used to identify articles.

Additionally, databases of ongoing (unpublished) trials (ie, WHO Registry Network (including ClinicalTrials.gov), PROSPERO, EMBASE) will be searched. Should the available data presented in primary studies be insufficient for analysis or specifics on treatment details or outcomes of interest be missing, the corresponding authors of the study will be requested for additional data.

Study eligibility criteria

Studies will be selected if they meet the following eligibility criteria: (1) studies reporting on total costs, which includes, but is not limited to, theatre costs (personnel, consumables, conversions), in-hospital costs (ward, laboratory, imaging, pharmacy, Post Anesthesia Care Unit (PACU), Intensive Care Unit (ICU) and postoperative costs (complications, reinterventions), after open TME, L-TME, R-TME or TaTME for rectal cancer; (2) prospective studies or retrospective cohort studies with prospective collection of cost data; (3) studies with a minimal follow-up time of 3 months; (4) were published between January 2000 and March 2022 and finally and (5) studies published in English, French, German and Spanish.

Excluded will be: (1) reviews, (conference) abstracts, commentaries, letters (however, not randomized controlled trials (RCTs) published as 'letters to the editor'), editorials, case series and case reports; (2) studies including only patients with recurrent rectal carcinoma; (3) studies including less than 10 patients and finally (4) studies without full text available.

Retrospective studies with retrospectively collected data will be excluded, as these are associated with recall bias and, therefore, result in low evidence in term of cost evaluation. However, retrospective studies that collected cost data prospectively will be included. As substantial progression has been made during the first years following introduction of R-TME and TaTME, arguments could be made to opt for omitting early studies (ie, start the search from 2005 onwards). However, since it has been assumed that articles on costs of R-TME and TaTME are relatively scarce, we will include studies published between January 2000 and March 2022. As follow-up is essential for determining costs, a minimal follow-up time of 3 months is required. Studies reporting various follow-up lengths will be evaluated on a case-by-case basis for eligibility for inclusion.

Outcomes

The primary outcome of this systematic review will be total costs, consisting of but not limited to, theatre, in-hospital and postoperative costs. Due to potential variation in definition of total costs, this variable will be extracted and reported as described in individual studies. Different reporting outcomes will be evaluated for inclusion on a case-by-case basis.

Data management

The results from the literature search will be uploaded in Rayyan QCRI, a web-based software management programme that helps facilitate the screening and study

selection process of authors of systematic reviews. Duplicates will be removed and abstracts and full-text articles will be uploaded as Portable Document Formats. In studies reporting from the same sample of patients in different years, the study with the largest sample size and longest length of follow-up will be included.

Study selection process

Potentially eligible records will be identified through title and abstract screening by four independent review authors (RTJG, MB, BPAS and TGFL). Articles will receive scores based on the predefined eligibility criteria. Studies will then be selected for final inclusion through full-text screening. A flow diagram describing the screening process will be made.

Data collection process

A standardised data extraction form will be developed in Microsoft Excel. Review authors (RTJG, MB, BPAS, TGFL) will extract data from eligible studies independently. Instructions on use of the extraction form will be provided to increase consistency between authors. Extracted data will consist of study details, patient demographics, details of interventions used, methodology and relevant outcomes. Study characteristics will be tabulated in detail.

Data items and outcomes

The following data will be extracted from eligible studies: reference and title details (first author, journal, year of publication, country, study type, funding received), characteristics of study population (gender, age, number of patients, minimal invasive technique used), characteristics of disease (cT/cN/cM stage, neoadjuvant therapy, tumour types (colon vs rectal), characteristics of surgery (number of surgeons performing treatment, surgeon experience, type of procedure), methodological characteristics (economic evaluation type, perspective, length of follow-up, discount rate, costs, model assumptions, primary economic outcomes and sensitivity analyses), cost-effectiveness outcomes used (ie, complications, readmission rate, local recurrence, systematic recurrence, disease-free survival, overall survival) and main findings. The following cost components (if present) will be extracted from the individual studies; total costs, total theatre costs, conversion costs, instrumentation costs, consumable costs, personnel costs, costs for theatre per hour, costs of reinterventions, total in-hospital non-theatre costs, ward costs, complication costs, lab costs, imaging costs, pharmacy costs, PACU costs, ICU costs, rehabilitation costs, costs of community services and loss of productivity costs.

Risk of bias and quality assessment

Review authors (RTJG, MB, BPAS, TGFL) will independently assess the quality of included studies. All eligible studies will be assessed for quality using The Consensus Health Economic Criteria (CHEC) list.[14] Criteria of the CHEC checklist will be modified to fit this systematic review. All disagreements between review authors will be resolved through discussion, in which three additional authors were involved, all with expertise in minimal invasive techniques for treatment of rectal cancer (TAB, ECJC, and KH).

Statistical analysis

Statistical analysis will be performed using R statistical software. Categorical variables reported as numbers and percentages will be analysed using the χ^2 test. Continuous data will be analysed using the Analysis of Variance/Kruskal-Wallis test. Statistical significance will be defined as $p<0.050$ (two sided). Overall effects will be determined using the Z score. In case of a meta-analysis, the following will be done. For continuous outcome measures, standardised mean differences with basic descriptive statistics will be used to summarise patients and outcome data. Heterogeneity will be assessed by the I^2 statistics. I^2 values of 25%, 50% and 75% will be considered as low, moderate and high, respectively. In case of moderate or high heterogeneity, the pooled estimates of mean differences will be calculated using random effects models to consider potential interstudy heterogeneity and to adopt a more conservative approach. In case a random effects model is used, the robustness of the results and the potential sources of heterogeneity will be assessed by performing sensitivity analyses. Sensitivity analyses will consist of, but not limited to, comparison of RCTs versus non-randomised studies, in-hospital versus total costs and government versus private healthcare systems.

Data synthesis

A narrative synthesis will be provided presenting the findings of the included studies in text and tables, structured around the type of intervention and outcome. Data presented within and between the included studies will be assessed. Findings of studies comparing different minimal invasive techniques head-to-head will be prioritised. A meta-analysis will be performed if more than three studies use the same type of intervention with the same outcome measure. We do not expect to perform a meta-analysis due to expected high heterogeneity of studies caused by differences in range of cost components included, primary effect measures and statistical methods used across the small number of existing studies.

Meta-bias(es)

Reporting bias among studies will be assessed. Study protocols will be assessed for publication before the start of patient inclusion. Studies will be assessed for outcome reporting bias through comparing outcomes reported in the published protocol with those reported in the published journal article. Small sample bias will be assessed through comparing the fixed effect estimate against the random effects model.

Confidence in cumulative evidence

The Grading of Recommendations Assessment, Development and Evaluation working group approach (GRADE) will be used to assess the quality of evidence for the cost outcomes. The cost outcomes will be assessed using the GRADE tool. The quality of evidence will be reported as high, moderate, low or very low.

Patient and public involvement

The protocol for this systematic review was written in accordance with the Guidance for reporting Involvement of Patients and the Public 2 reporting guidelines.[15] Patients and patient organisations were involved as research partners throughout the development of this study protocol and actively contributed to identifying the lack of insight into total costs of the different techniques. Patients will remain involved and provide feedback during the systematic review. Results of this study will be dissemination adjusted for a non-specialist audience through collaboration with respective patient organisations.

Ethics and dissemination

This study is considered, according to Dutch law, a non-WMO (Medical Research Involving Human Subjects Act) study. No ethical approval is required, as this is a systematic review without collection of patient data at an individual level. Findings will be disseminated widely, through peer-reviewed publication and presentation at relevant conferences.

Study planning

Studies will be assessed and selected from 1 April 2022 till 1 May 2022. Data will be collected, analysed and risk of bias assessed from 1 May 2022 till 1 June 2022. Writing of the manuscript will be performed from 1 June 2022 till 1 July 2022.

Amendments

In the event of protocol amendments, the date of amendment and rationale for deviation will be provided.

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Contributors Substantial contributions to the conception and design of the work: RTJG, TAB, MB, BPAS, TGFL, RH, KH, MP, ECJC. Drafting the article: RTJG, TAB, MB, BPAS, TGFL. Revising the article critically for important intellectual content: RH, KH, MP, ECJC. Final approval of the version to be published: RTJG, TAB, MB, BPAS, TGFL, RH, KH, MP, ECJC. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

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