Cancer Epidemiology 51 (2017) 23–29

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Original Research Article

Meta-analysis of the clinicopathological characteristics and peri-operative outcomes of colorectal cancer in obese patients

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ARTICLE INFO

Keywords:
Obesity
Body-mass index
Stage
Colorectal cancer
Lymph node yield
Anastomotic leak

ABSTRACT

Background: The effect of obesity on the clinicopathological characteristics of colorectal cancer (CRC) has not been clearly characterized. This meta-analysis assesses the pathological and perioperative outcomes of obese patients undergoing surgical resection for CRC.
Methods: Meta-analysis was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Databases were searched for studies reporting outcomes for obese and non-obese patients undergoing primary CRC resection, based on body-mass index measurement. Results were reported as mean differences or pooled odds ratios (OR) with 95% confidence intervals (95% CI).
Results: A total of 2183 citations were reviewed; 29 studies comprising 56,293 patients were ultimately included in the analysis, with an obesity rate of 19.3%. Obese patients with colorectal cancer were more often female (OR 1.2, 95% CI 1.1–1.2, $p < 0.001$) but there was no difference in the proportion of rectal cancers, T4 tumours, tumour differentiation or margin positivity. Obese patients were significantly more likely to have lymph node metastases (OR 1.2, 95% CI 1.1–1.2, $p < 0.001$), have a lower nodal yield, were associated with a longer duration of surgery, more blood loss and conversions to open surgery (OR 2.6, 95% CI 1.6–4.0, $p < 0.001$) but with no difference in length of stay or post-operative mortality.
Conclusion: This meta-analysis demonstrates that obese patients undergoing resection for CRC are more likely to have node positive disease, longer surgery and higher failure rates of minimally invasive approaches. The challenges of colorectal cancer resection in obese patients are emphasized.

1. Introduction

One of the greatest challenges to global health in the 21st century is obesity, with its associated effects on physiology, quality of life, co-morbidity and life expectancy. Increased body-mass index (BMI) is an independent etiological factor in many cancers, including colorectal cancer (CRC) − currently the third leading cause of cancer death [1]. This epidemic has led to obesity in the United States doubling to 36% since the 1980's, with those in Class III (BMI $> 40\ kg/m^2$) now comprising over 5% of the American population [2,3].

Obesity is associated with a 33% increased risk of CRC [4] − thus as world obesity rates soar, CRC will concomitantly increase. This will pose specific challenges for surgeons, who must address the physical, technical and physiological problems associated with abdominopelvic surgery in the obese patient.

Obesity is associated with increased colorectal cancer-specific mortality and all-cause mortality [5]. However, it remains unclear whether these negative long-term outcomes are reflective of insufficient oncological resection, failure to respond to neoadjuvant or adjuvant treatment, or a more advanced TNM stage at presentation than their non-obese counterparts. The body morphology of the obese patient incurs technical difficulty for surgeons. Omental fat accumulation can make organ manipulation cumbersome, difficulty in retraction, and can hinder vision of the operative field. For laparoscopic approaches, increased abdominal wall thickness leads to difficulty with peritoneal access and impairs manipulation of laparoscopic instruments. These difficulties combined may explain the longer operative duration seen in obese patients [6], as well as the higher risk of conversion to open surgery [7,8]. Furthermore, excess visceral fat may render the plane of dissection for total mesorectal or mesocolic excision (TME) unclear, yielding an incomplete resection specimen or reducing the lymph node yield within the specimen. With this in mind, this study hypothesized

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http://dx.doi.org/10.1016/j.canep.2017.09.004
Received 17 July 2017; Received in revised form 18 September 2017; Accepted 24 September 2017
1877-7821/

Inclusion Criteria

Original publication (reviews, opinions, letters, protocols and conference proceedings excluded)

Patients with colorectal adenocarcinoma undergoing curative treatment (surgical resection +/- nCRT +/- adjuvant therapy) where BMI was reported

Reported outcome measures studied

- Pathological outcomes
  - Sex, tumour location, T4 tumours, lymph node positivity, poorly differentiated tumours, lymph node yield, margin positivity, pathological complete response
- Perioperative outcomes
  - Operative duration, operative blood loss, conversion to open surgery, anastomotic leak, length of hospital stay, post-operative mortality

Exclusion criteria

Papers in languages other than English.

Papers where data was unavailable or uninterpretable and authors uncontactable

Non-human studies

Fig. 1. Study inclusion and exclusion criteria.

that surgery for CRC in obese patients is more technically challenging, and may be linked with worse outcomes as a consequence. This aim of this meta-analysis is to compare the clinicopathological and perioperative outcomes of obese and non-obese patients undergoing surgical resection for colorectal cancer.

2. Methods

2.1. Literature search

The meta-analysis was conducted in accordance with PRISMA guidelines [9]. Embase, Medline, Pubmed, Pubmed Central, and Cochrane databases were searched using a Boolean search algorithm (Appendix 1) for articles published up to November 2016. Original studies were included which documented patients undergoing surgical resection for primary colorectal adenocarcinoma, with outcomes stratified depending on BMI status. Studies were included if one or more of the chosen outcome measures were reported (Fig. 1). All search results were combined in a reference manager database (Endnote™, Version X7, Thompson Reuters, New York, USA) and duplicates were removed by hand. Reference lists of included studies were screened for additional relevant studies.

2.2. Data extraction

Three independent reviewers applied inclusion and exclusion criteria to retrieve citations, the abstracts reviewed and full papers selected for analysis. Reviewers extracted data from full text papers and applied exclusion criteria; discrepancies were agreed by consensus. Where two publications reported results in the same population, the most complete dataset was chosen. For each study, data on baseline characteristics (author institution, country, study period, total number of patients, sex, site of cancer, BMI definition, obesity rates and study methodology) were extracted. Where data was presented in BMI groups, obesity was chosen to be defined as a BMI ≥ 30 kg/m^2, as per World Health Organization (WHO) reporting criteria [10]. If studies were designed to case-match for certain variables, these studies were excluded from analysis of that variable. Pathological variables studied were T4 tumours, rates of lymph node metastases and yield, and tumour differentiation. Perioperative outcomes included operative duration, blood loss, anastomotic leak rate and length of stay (LOS). For anastomotic leak rate, patients were only included for analysis where a primary anastomosis was formed (i.e. abdominoperineal resections were excluded depending on data availability). Authors were contacted if data were not available or interpretable. Where median and range were presented, methods described by Hozo and colleagues [11,12] were followed to derive mean and standard deviation. Where means were presented without standard deviation (SD) but p values available, the average of the two SDs were imputed [13]. Study methodological quality and risk of bias was assessed by applying the MINORS criteria for observational studies [14].

2.3. Statistical analysis

Analyses were performed using RevMan software (Review Manager, version 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). The I^2 statistic was calculated from Cochran's Q test to provide an objective measure of heterogeneity for each of the outcome measures; an I^2 value greater than 50% was taken to denote significant heterogeneity between studies. A fixed-effects meta-analysis was performed for each variable, and where there was appreciable heterogeneity (I^2 > 50%) a random-effects model was used for meta-analysis. For continuous variables, the weighted mean differences are presented. For categorical variables Mantel–Haenszel odds ratios (ORs) were calculated and described with 95% confidence intervals (CI). Sensitivity analysis excluded studies if they had data which was