

REVIEW ARTICLE

Resection of colorectal liver metastases and extra-hepatic disease: a systematic review and proportional meta-analysis of survival outcomes

William J. Hadden¹, Philip R. de Reuver², Kai Brown^{1,2}, Anubhav Mittal^{1,2}, Jaswinder S. Samra^{1,2} & Thomas J. Hugh^{1,2}

¹Northern Clinical School, University of Sydney, and ²Upper GI Surgical Unit, Royal North Shore Hospital and North Shore Private Hospital, Sydney, New South Wales, Australia

Abstract

Background: Colorectal cancer (CRC) accounts for 9.7% of all cancers with 1.4 million new cases diagnosed each year. 19–31% of CRC patients develop colorectal liver metastases (CRLM), and 23–38% develop extra-hepatic disease (EHD). The aim of this systematic review was to determine overall survival (OS) in patients resected for CRLM and known EHD.

Methods: A systematic review was undertaken to identify studies reporting OS after resection for CRLM in the presence of EHD. Proportional meta-analyses and relative risk of death before five years were assessed between patient groups.

Results: A total of 15,144 patients with CRLM (2308 with EHD) from 52 studies were included. Three and 5-year OS were 58% and 26% for lung, 37% and 17% for peritoneum, and 35% and 15% for lymph nodes, respectively. The combined relative risk of death by five years was 1.49 (95% CI = 1.34–1.66) for lung, 1.59 (95% CI = 1.16–2.17) for peritoneal and 1.70 (95% CI = 1.57–1.84) for lymph node EHD, in favour of resection in the absence of EHD.

Conclusion: This review supports attempts at R0 resection in selected patients and rejects the notion that EHD is an absolute contraindication to resection.

Received 11 December 2015; accepted 16 December 2015

Correspondence

Thomas J. Hugh, Northern Upper GI Surgical Unit, Royal North Shore Hospital, St. Leonards NSW 2065, Australia. Tel: +61 2 9463 2899. Fax: +61 2 9463 2080. E-mail: tom.hugh@sydney.edu.au

Introduction

Colorectal cancer (CRC) is a major health burden with a world-wide estimate of 1.4 million new cases annually resulting in approximately 694,000 deaths.¹ Approximately 19–31% of all patients with CRC present with, or subsequently develop, liver metastases (CRLM). These are defined as either synchronous if found at the time of presentation of the primary tumour or metachronous if identified at a later date. At diagnosis, a further 23–38% of patients already have, or will develop extra-hepatic disease (EHD).^{2–4} EHD is defined as either synchronous or metachronous to the primary CRC and/or the CRLM.

Over the past 10 years widespread use of modern chemotherapeutic and biological agents, combined with careful case selection and improved surgical techniques, have markedly

improved outcomes in patients with metastatic CRC.^{5–8} The presence of limited EHD is no longer considered an absolute contra-indication to liver resection as long as the future remnant liver is of sufficient volume, the patient is fit for a major operation, and there is potential for an R0 resection at both sites.^{9–18}

The current literature is difficult to interpret in relation to the benefit of removing EHD due to selection variability, multimodal treatment regimens and the inherent subjectivity of the term ‘resectable’. Compounding this difficulty are the numerous permutations of possible presentations regarding the timing of both the CRLM and EHD. This ambiguity is reflected in numerous inconsistencies in consensus statements and guidelines regarding the value of resection of CRLM in the presence of EHD.^{19,20}

The aim of this systematic review was to determine overall survival (OS) in patients who underwent resection of CRLM and known EHD (synchronous or prior to the CRLM). Patients were stratified by site of EHD and then comparisons made between outcomes in this group and those who underwent resection of CRLM in the absence of EHD.

Materials and methods

The study protocol for this systematic review followed the PRISMA checklist (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and consulted the MOOSE checklist (Meta-analysis of Observational Studies in Epidemiology) for relevant additions.^{21,22}

Eligibility criteria

Full-text English language studies of adult human patients published between December 2004 and December 2014 were considered for this review. Case reports, systematic reviews, meta-analyses and studies of recurrence were excluded.

Search

A systematic search was applied to PubMed, Embase, Cinahl and Medline databases up to December 2014 to identify studies reporting resection of CRLM in the presence of known EHD with the terms referenced in Fig. 1. All articles were vetted by title then abstract, with the full text of the remaining articles examined for inclusion. Reference lists of all included articles were searched for further studies also meeting inclusion criteria.

Study selection

Selection criteria were predefined and applied to results of the search strategy. Original studies reporting OS in patients undergoing first-time curative liver resection for CRLM with known EHD were included in the systematic review. Studies were excluded if follow-up was less than three years, resection was undertaken for palliative purposes or if the study population was exclusive. All included patients had undergone prior curative resection of the primary tumour. Only patients undergoing resection of both CRLM and synchronous or previous EHD were included in these analyses; outcomes in patients whose EHD was detected after resection for CRLM were excluded.

Data collection

Reported survival, mortality, morbidity, demographic, peri-operative and chemotherapy (no stratification) data specific to patients resected for CRLM with EHD were extracted.

Level of evidence/risk of bias

Level of evidence for each study was assessed using the Oxford Centre for Evidence-Based Medicine (CEBM) Levels of Evidence.²³ The methodological tool described by Downs and Black

was modified for non-randomized studies by excluding the power calculation and applied to all included studies.²⁴

Outcomes

Primary outcome measures were proportionally-weighted OS by EHD site (lung, peritoneum and lymph nodes) for those patients undergoing both CRLM and EHD resection and relative risk (RR) of death before five years comparing those resected for CRLM and EHD to those resected for CRLM without EHD.

Statistical analysis

Freeman–Tukey transformations were used to obtain proportional OS, while the X^2 test with $k-1$ degrees of freedom was used to assess RR of death by five years.²⁵ Survival data were expressed as pooled OS or RR and because significant heterogeneity (I^2) was found, more conservative random-effects methods were used.²⁶ P values were calculated with the X^2 test or Freeman–Tukey transformation as appropriate; $P < 0.05$ was considered statistically significant. Data analysis was performed using Review Manager 5.0 software (Cochrane Collaboration, Oxford, UK) and MedCalc for Windows, version 12.5 (Ostend, Belgium).^{25–27}

Results

Selection

Constrained by year, language, study type and population this search returned 1470 unique articles. Vetting as per Appendix 1 yielded 45 studies whose reference lists were searched manually, identifying six further studies whose references were also manually examined. One study was identified while background-researching other reviews in this field. This process yielded 52 articles for inclusion in the systematic review, from which data were extracted.

Study characteristics

The 52 studies included in this review examined a total of 15,144 patients who had hepatic resection for CRLM. Of these 15,144 patients, 2308 presented with EHD known at hepatic resection. Three-hundred seventy-two of these patients with EHD did not progress to resection of both CRLM and EHD and were therefore excluded from further analysis. The remaining 1936 patients underwent hepatic resection plus resection of the EHD and comprise the population in the following analyses (Table 1).

Level of evidence/risk of bias

The studies in this review are comprised of level 2b (observational cohort) and 3b (case–control) as per the Oxford CEBM guideline.²³ Median modified Downs and Black methodology score for included studies is 15/26 (IQR = 14–17) (Supplementary Fig. 1).

Download English Version:

<https://daneshyari.com/en/article/3268482>

Download Persian Version:

<https://daneshyari.com/article/3268482>

[Daneshyari.com](https://daneshyari.com)