



Review

Colorectal cancer with synchronous hepatic metastases: Systematic review of reports comparing synchronous surgery with sequential bowel-first or liver-first approaches

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Accepted 8 November 2015

Available online ■ ■ ■

Abstract

Background: The management of colorectal cancer with synchronous liver-limited metastases currently lacks randomised trial evidence to inform case selection for any of the bowel-first, liver-first or synchronous surgery routes. We examine the literature to report outcome data from reports utilising all three approaches.

Methods: A systematic review was conducted using OvidSP (including Embase, EBM Reviews and MEDLINE databases) to find articles reporting discrete peri-operative and long-term outcomes for patients undergoing sequential bowel-first, liver-first surgery or synchronous liver and bowel surgery.

Results: Of 223 unique citations, 3 cohort studies were identified comprising a pooled population of 1203 patients who completed treatment protocols between 1982 and 2011. Patients were allocated to bowel-first surgery (748 patients, 62.2%), liver-first surgery (75, 6.2%) or synchronous liver/bowel surgery (380, 31.6%). Minor complications were similar between procedures. Major complications were consistent with a pooled fixed estimate of 9.1% (95%CI: 7.6%–10.8%, $I^2 = 48\%$). Post-operative death was rare and consistent with a pooled fixed effect estimate of 3.1% (95%CI: 2.2%–4.3%, $I^2 = 0\%$). Median follow-up ranged from 25.1 to 40.0 months, with a pooled underlying 5-year survival fixed effect estimate of 44% ($I^2 = 39\%$).

Conclusion: This review assesses outcomes of patients with colorectal cancer with synchronous liver metastases managed by either synchronous, sequential liver-first or bowel-first surgery. Overall treatment-related mortality is low and survival is similar among the three groups. These findings provide support for the continued use of all three pathways until better evidence to guide selection of an individual treatment option is available.

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Keywords: Colorectal cancer; Liver metastases; Synchronous; Surgery

Introduction

Up to a fifth of patients with colorectal cancer have synchronous hepatic metastases at their index presentation.^{1,2} Management is influenced by the mode of presentation

and the extent and distribution of the disease.³ There are four main treatment options for patients who present electively with colorectal cancer and in whom comprehensive high-resolution cross-sectional imaging has confirmed synchronous liver-limited hepatic metastases.³ First, chemotherapy with palliative intent is advocated by current guidelines for those with severe comorbidity and/or where disease is not amenable to resection such as extensive multi-segment liver involvement, unfavourable hepatic location of tumours or a locally advanced unresectable

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colorectal primary tumour.⁴ In some of these patients, chemotherapy may downsize the tumour burden making subsequent surgical resection feasible.⁵ Chemotherapy may also be delivered with neoadjuvant intent to patients who are suitable for surgery.⁶

Where surgical resection is an option there are currently three potential pathways: synchronous resection of liver and bowel tumours, bowel-first resection or liver-first surgery.^{7–9} Criteria that influence selection of a particular pathway such as anatomic location of disease, patient comorbidity, requirement for non-surgical treatment prior to surgery (such as chemoradiotherapy in patients with a rectal primary tumour) are complex and are typically treatment decisions are made by a multidisciplinary board on an individual patient basis.

There is evidential equipoise around these three surgical treatment options. Although there are reports comparing synchronous to staged resection, the majority are case cohort series comparing synchronous liver and bowel resection at a single operation to the traditional staged bowel-first surgery.^{10–12} These comparisons of synchronous to staged surgery no longer take account of the complexity of current treatment pathways where staged treatment may refer either to the bowel-first approach or the liver-first option.

This study undertakes a systematic review of reports of the management of colorectal cancer with synchronous liver-limited hepatic metastases and focuses on reports where all three surgical treatment pathways have been available. Thus the aim of this review is to assess whether there are preferential outcomes associated with a given treatment option for patients with synchronous disease or alternatively to provide continued support for the use of all three pathways (with individual case-based selection) pending the generation of more definitive evidence.

Methods

Design

A systematic review of published articles reporting outcomes of patients with colorectal cancer and synchronous liver metastases. The review focuses on reports with individual patient-level data on those receiving synchronous (combined liver and bowel) surgery, classical sequential bowel-first surgery, or the sequential liver-first approach within study cohorts. All three surgical pathways must be available for patients with synchronous disease within the same cohort.

Literature search strategy

The OvidSP online database (encompassing Embase, EBM Reviews and MEDLINE) was searched from January

1994 to January 2014. MESH index and text search terms included: colorectal cancer, liver metastasis, surgery and synchronous. Terms were combined using Boolean operators, and results were restricted to full-text human studies published in English. The search strategy was designed and refined before being applied to select references. The titles of the articles and their abstracts were then reviewed independently by two reviewers; when inclusion was uncertain the full article was retrieved for further scrutiny. Reviewers independently assessed each full study report to see whether or not it met the inclusion criteria. If there was disagreement regarding inclusion, the senior authors (AKS and JMM) would compare findings and arbitrate a decision.

Data extraction

Data were extracted independently by two reviewers using a data extraction form designed and agreed by the review team. Disagreements were resolved by consensus or consultation with the senior reviewers.

Evaluation of the quality of reports

Two authors assessed and scored the methodological quality of studies using the modified methodological index for non-randomized studies criteria (MINORS criteria).¹³ Although the studies in this review compare groups of patients thus meeting the criteria for comparative studies, the criterion of “adequate control group” is not applicable and thus the maximum score was set at 22 instead of 24.

Analysis

Rates of complications and survival are reported. Statistical pooling of proportion estimates was explored using fixed effect models within StatsDirect[®] Version 3 (StatsDirect Ltd, Altrincham, Cheshire, UK).

Results

Searches identified 223 unique citations of which 23 provided comparative outcome data for alternative treatments for synchronous disease. The majority of these (n = 20) compared data between simultaneous and staged approaches without parallel information on all three surgical options and thus were excluded. Only 3 cohort studies met the inclusion criteria by reporting outcomes separately for the three treatment modalities.^{14–16} The MINORS score was 14/22 for the study by van der Pool and colleagues, 14/22 for that of Brouquet et al. and 13/22 for that of Mayo and colleagues. A CONSORT flowchart of the data search is provided in Fig. 1 and the search strategy in the Appendix.

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