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Review

Rectal cancer with synchronous liver metastases: Do we have a clear direction?

S. Pathak [a,*], Q.M. Nunes [b], I.R. Daniels [a], N.J. Smart [a], G.J. Poston [b], L. Påhlman [c]

[a] Exeter Surgical Health Services Research Unit (HESRU), Royal Devon and Exeter NHS Foundation Trust, Barrack Road, Exeter, EX2 5DW, UK

[b] Department of HpB Surgery, University Hospital Aintree, Longmoor Lane, Liverpool, L9 7AL, UK

[c] Department of Surgical Science, University Hospital, 751 85, Uppsala, Sweden

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Abstract

Rectal cancer is a common entity and often presents with synchronous liver metastases. There are discrepancies in management guidelines throughout the world regarding the treatment of advanced rectal cancer, which are further compounded when it presents with synchronous liver metastases. The following article examines the evidence regarding treatment options for patients with synchronous rectal liver metastases and suggests potential treatment algorithms.

Keywords: Rectal cancer; Liver metastases; Synchronous rectal liver metastases; Management

What this paper adds to the literature

This paper highlights management discrepancies in patients presenting with synchronous liver metastases from rectal cancers and suggests possible algorithms in guiding treatment strategies and informing future research.

Introduction

Colorectal cancer (CRC) is the second most common cause of cancer related mortality in the UK [1] and approximately 25% of these arise in the rectum.[2] A further 25% of patients have synchronous liver metastases (SRLM) at presentation.[3] Surgical resection of both primary disease and distant metastases offers the only potential chance of long term cure.

Total mesorectal excision (TME) and restoration of the bowel continuity or removal of the rectum and anus through an extralevator abdominoperineal excision (elAPE) is now recognized as the standard of care in rectal cancer surgery.[4] The staging process today is based upon high quality MRI examination to disclose patients who need complimentary treatment. In stage I and II but also in early (TIII a/b) rectal cancer, meticulous surgery is enough to remove all cancer from the pelvis. Decisions regarding the use of neoadjuvant radiotherapy with or without chemotherapy are based upon the likelihood of not only the complete surgical excision but also a risk adjustment of having a local recurrence.[5–7] In patients presenting with locally advanced mid- and lower-rectal cancer, there is a clear benefit from long course neoadjuvant chemoradiotherapy (CRT) or short-course irradiation (SRT) to reduce local recurrence if the mesorectal fascia (MRF) is either threatened or involved.[8–10] An issue that may arise in SRLM is that CRT employed does not

* Corresponding author. Tel.: +44 1392 411 611.
E-mail address: drsamirpathak@gmail.com (S. Pathak).

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potentially treat systemic disease and hence the liver-limited metastatic disease may progress. However, SRT will not interfere with a more aggressive chemotherapy schedule supporting such an option.

Better staging of primary CRC has led to enhanced identification of liver-limited stage IV disease[11] and concurrent advances in surgical and anaesthetic technique have resulted in improved outcomes in these patients. Synchronous liver metastases and advanced primary stage worsens prognosis although long term cure is still achievable.[12–14] However, the optimum strategy for managing patients with SRLM has not been defined. Options include a staged approach where either liver or rectum are operated on separately or a synchronous surgical approach. The use of neoadjuvant therapies in this setting also remains unclear.

The data looking at synchronous presentation and subsequent management of colorectal liver metastases (CRLM) are heterogeneous as both colonic and rectal cancers are included as one entity.[15–19] The difference in treatment options locally for colonic and rectal tumours may have a major impact on the liver-limited disease. Whilst synchronous colonic and liver surgery is feasible, the real challenge lies in managing patients with SRLM due to the complexities of treatment. Furthermore, there is a discrepancy between the guidelines for management of advanced rectal tumours in North America, Europe and the United Kingdom highlighting the lack of high-level evidence and need for well-designed trials going forward.

Patients presenting with advanced rectal tumours (T3/T4) and synchronous liver metastases provide a challenge to all clinicians in the multi-disciplinary team. We provide an overview of issues and strategies to be considered in the management of patients presenting with SRLM, based on the limited evidence base and views of experienced clinicians.

Definitions

a) There is considerable variation anatomically, radiologically and surgically in how the rectum is defined.[20] We define the rectum radiologically and anatomically to begin at the level of the third sacral vertebrae.[20,21]
b) A major hepatectomy is defined as a resection of three or more Couinaud segments
c) A minor hepatectomy is defined as resection of less than Couinaud segments
d) Currently for CRLM to be considered resectable, it must be removable with a negative margin and allow for the preservation of at least two Couinaud segments with intact portal and arterial inflow, venous outflow and biliary drainage. The future liver remnant depends on the functioning liver parenchyma so can be 20% in an otherwise healthy liver, 30% in a post chemotherapy liver and 40% in a fibrotic/cirrhotic liver.[22]
e) An "easy" liver resection is defined as a major or minor resection with >1 cm tumour free surgical margin, with at least two contiguous liver segments having an independent inflow, outflow and biliary drainage, with a functional liver remnant (FLR) of 20–30%.[23]
f) A "borderline" liver resection is defined as a major or minor resection where either the resection margin or FLR is threatened.[23] There may be considerable variation between liver surgeons regarding this.[24]
g) An easy rectal resection was defined as a T1/T2 lesion where the CRM was unthreatened.

There is considerable variety in the literature as to what constitutes difficulty of surgical excision. We define borderline primary rectal resections as having any of the following features: male pelvis, BMI > 30, low rectal tumours, T3/T4 lesions, anterior tumour location.[25–27]

h) Neoadjuvant chemotherapy is defined as the first chemotherapy regime given to patients as an induction therapy, in an effort to decrease overall tumour burden.

Rectal cancer

Colorectal cancers demonstrate heterogeneity in tumourigenic pathways based on their relationship to the splenic flexure and are therefore embryologically different tumours with varying prognosis.[28,29] Tumours of the rectum do have different biology to those of the right colon with a higher rate of p53 mutations, loss of heterozygosity, a higher frequency of DNA aneuploidy, and a lower rate of microsatellite instability with less k-ras dependence.[30] Rectal cancers can therefore be considered as a different genetic entity to colon cancer and it is not appropriate for studies to consider them as one entity.[28]

Differences in staging and prognosis

In non-metastatic locally advanced rectal cancers, several trials have demonstrated the benefit of long-course chemoradiotherapy (CRT) in terms of decreased local recurrence rates.[8,10] High resolution MRI accurately predicts whether the margins will be free of tumour post-operatively[31] and therefore facilitates selection of patients with advanced rectal tumours who would benefit from preoperative irradiation. There is emerging evidence suggesting that short course radiotherapy (SRT) is as effective as CRT.[32] In T1, T2 or T3a/b rectal cancers, surgery alone will suffice as treatment. The treatment dilemma therefore occurs in patients with advanced rectal cancers (T3cd/T4, N+) who have concurrent metastatic disease in the liver.

Treatment options for locally advanced rectal cancers

North America

In locally advanced rectal cancer (T4) CRT is advocated followed by resection with possible adjunctive therapy with either single agent intravenous 5FU ± leucovorin or oral