



Hot Topic

Managing synchronous liver metastases from colorectal cancer: A multidisciplinary international consensus



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ABSTRACT

An international panel of multidisciplinary experts convened to develop recommendations for managing patients with colorectal cancer (CRC) and synchronous liver metastases (CRCLM). A modified Delphi method was used. CRCLM is defined as liver metastases detected at or before diagnosis of the primary CRC. Early and late metachronous metastases are defined as those detected ≤ 12 months and > 12 months after surgery, respectively. To provide information on potential curability, use of high-quality contrast-enhanced computed tomography (CT) before chemotherapy is recommended. Magnetic resonance imaging is increasingly being used preoperatively to aid detection of subcentimetric metastases,

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Multidisciplinary team management
Surgery
Synchronous colorectal liver metastases
Systemic therapy

and alongside CT in difficult situations. To evaluate operability, radiology should provide information on: nodule size and number, segmental localization and relationship with major vessels, response after neoadjuvant chemotherapy, non-tumoral liver condition and anticipated remnant liver volume. Pathological evaluation should assess response to preoperative chemotherapy for both the primary tumour and metastases, and provide information on the tumour, margin size and micrometastases. Although the treatment strategy depends on the clinical scenario, the consensus was for chemotherapy before surgery in most cases. When the primary CRC is asymptomatic, liver surgery may be performed first (reverse approach). When CRCLM are unresectable, the goal of preoperative chemotherapy is to downsize tumours to allow resection. Hepatic resection should not be denied to patients with stable disease after optimal chemotherapy, provided an adequate liver remnant with inflow and outflow preservation remains. All patients with synchronous CRCLM should be evaluated by a hepatobiliary multidisciplinary team.

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Introduction

Colorectal cancer (CRC) has become the third most common malignancy worldwide in terms of incidence and fourth for cancer mortality [1]. At CRC diagnosis, 20–25% of patients have stage IV disease [2–5], in which synchronous CRC liver metastases (CRCLM) are present in 15–25% of cases [6] and metastases are confined to the liver in 70–80% of these cases [7]. Surgical resection is the most effective treatment approach for CRCLM, but only a minority of patients are suitable for upfront surgery [8]. Although data from the population-based Burgundy registry have to be interpreted with caution as they are from the period 1976 to 2000, they show that resection for cure of CRCLM is performed significantly less often in cases of synchronous metastases than for metachronous metastases (6.3% vs 16.9%, respectively) [7]. The prognosis for patients with untreated CRCLM is poor; in the Burgundy registry, fewer than 30% of patients with untreated disease were alive after 1 year and fewer than 5% survived 5 years after diagnosis [7]. Data from this registry also showed that 5-year survival rates were shorter with synchronous than with metachronous CRCLM (3.3% vs 6.1%, respectively) [7], although some studies have shown no significant difference [9]. The reported percentage of synchronous CRCLM is increasing compared with metachronous metastases [10], probably due to improved imaging techniques leading to earlier diagnosis. However, different definitions of synchronous metastases can be found in the literature and adoption of a standardized definition is needed to clarify future reporting.

An international multidisciplinary group of experts in managing liver metastases (LM) from CRC (the EGOSLIM group) convened to discuss synchronous metastases and their management. In the absence of data from randomized controlled trials (RCTs) to guide decisions, the aims of the meeting were to agree: a definition for synchronous CRCLM; imaging for their detection; pathological evaluation and reporting; resectability of CRCLM; timing for surgery of the primary tumour and CRCLM; chemotherapy and treatment regimens; postoperative management; and the multidisciplinary approach to management. Through dissemination of the consensus decisions reached, it is hoped that the management of patients with synchronous CRCLM will be optimized.

Methods

The international consensus panel comprised experts from the USA, Europe and Asia in the treatment of patients with CRCLM and included one coordinator, five medical oncologists (including two gastroenterologists), five hepatic surgeons, one colorectal surgeon, two radiologists, one pathologist and one molecular gastrointestinal oncologist. All important aspects of multidisciplinary team (MDT) management of synchronous CRCLM were identified before

the meeting by the coordinator and referred to experts for presentation at the meeting. Meta-analyses, RCTs and studies evaluating clinical practice in the management of synchronous CRCLM were identified and reviewed before, and discussed during, the meeting. A modified Delphi method was used to aid achievement of a consensus (see Appendix 1) [11]. Recommendations were formulated when approved by all or a large majority of the panel members and are summarized in Table 1. Strength of recommendations was attributed based on the Strength of Recommendation Taxonomy [12]. For all recommendations, there is an assumption that all imaging, surgery and therapy are optimal. Some panel members were not present for the whole meeting and some members chose to abstain from voting on some questions not in their area of expertise.

Definition and prognosis of synchronous LM

Different definitions of synchronous CRCLM exist. Although, by definition, all metastases are synchronous (occult or detectable at diagnosis), most definitions include detection at or before diagnosis or surgery of the primary tumour [13], whilst some also include metastases detected up to 3 [14,15], 4 [16] or 6 months [17,18] following diagnosis.

With regard to prognosis of resected synchronous LM, a disease-free interval from the primary to discovery of the LM of less than 12 months has been associated with a hazard ratio of 1.3 for disease recurrence [19]. The majority of the panel (14/15, 93%) agreed that synchronicity is a sign of poor prognosis, irrespective of the treatment. In the ongoing LiverMetSurvey international registry, an international registry of patients undergoing surgery for CRCLM, [20], available current data show a significant difference in survival when metastases are detected at or 1 month before diagnosis vs 0–3 months after diagnosis ($p < 0.0001$); 5-year survival is 39% vs 44%, respectively (Fig. 1). Survival rates are not significantly different between patients in whom metastases are detected at or 1 month before vs up to 6 months or 6–12 months after diagnosis (Fig. 1). However, survival rates are significantly different between patient groups when metastases are detected at or within 1 month before diagnosis vs more than 12 months after the primary diagnosis ($p < 0.0001$). Although lacking confirmatory molecular biological information, these data support the division of LM into those diagnosed at the following time points: at or before the time of diagnosis; 0–12 months following diagnosis; and more than 12 months following diagnosis.

Consensus recommendations

- Synchronous CRCLM have less favorable cancer biology and expected survival than metachronous, particularly late metachronous, metastases.

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