



# Simultaneous resection of synchronous colorectal liver metastases: a promising alternative to staged resections

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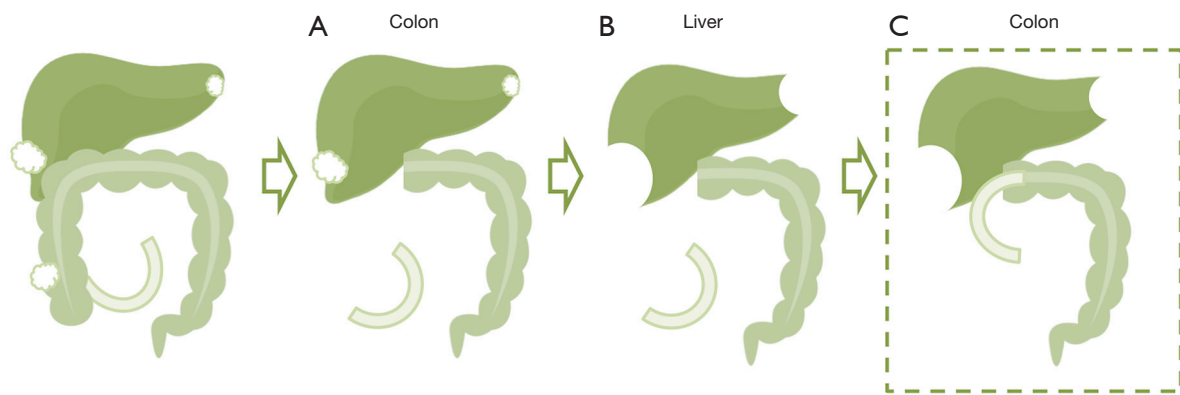
Management of patients with synchronous colorectal liver metastases (SCRLM) has transformed dramatically over the past 2 decades (1-3). A step-by-step, patient tailored approach as orchestrated by a multidisciplinary tumor board (MDT), combined with advances in surgical techniques, perioperative care and the evolution of systemic therapies have led to remarkable long-term outcomes (2,4). In particular, selected patients with resectable SCRLM undergoing surgery have been reported to enjoy 5-year survival rates as high as 76% (1). However, the optimal surgical strategy for these patients remains elusive with multiple retrospective studies presenting conflicting outcomes (4). In their up-to-date review of the literature Lillemoe and Vauthey sought to evaluate and critically appraise currently available surgical treatment strategies for patients presenting with SCRLM.

Synchronous disease poses a complex treatment scenario, due to the large tumor burden and its impact on patient survival. Therefore, there is consensus for preoperative chemotherapy treatment, which allows for better patient selection, increased resectability rates, improved systemic control of the disease and the ability to prevent further progression. Furthermore, metastases originating from right-sided primary colorectal cancer (CRC) are associated with dismal prognosis and have a worse response to conversion chemotherapy than metastases from left-sided CRC. In addition to the biologic aspects of the location

of the primary tumor, rectal cancer surgery is more challenging than colonic surgery, due to more complex anatomy, higher complication rates and many neoadjuvant treatment options (i.e., chemoradiotherapy, radiotherapy or chemotherapy alone), for which it is difficult to establish therapeutic guidelines.

To date the only published randomized trial, which compared outcomes among the simultaneous and the primary-first approaches is the METASYNC trial (5). The study demonstrated no difference in postoperative complications within 60 days of surgery between the two approaches. Interestingly, the simultaneous resection group had superior 2-year overall survival compared to the staged resections group (87.2% and 69.6%;  $P < 0.05$ ). Despite these findings, drawing robust conclusions from this study is difficult, due to the small number of included patients and significant heterogeneity in terms of tumor characteristics. Other limitations of the trial included changes in administration of neoadjuvant and adjuvant chemotherapy over time and no evaluation of tumor biology (6).

The sequence of resections during the simultaneous approach is a critical aspect of this strategy. Indeed, despite thorough preoperative planning, unexpected intraoperative events may influence the course of such complex procedures. We favor the COLon-Liver-COLon (COLICO) approach (*Figure 1*), which was also used during the METASYNC trial (5). Simultaneous resections commence



**Figure 1** Schematic illustration of the COLICO approach; Simultaneous resection begins with resection of the primary colonic/rectal tumor without formation of anastomosis (A) then followed by the liver resection (B). Digestive anastomosis is formed as the last step (C).

with resection of the primary colorectal tumor (CO) without formation of an anastomosis, followed by the liver resection (LI). Formation of the colonic/rectal anastomosis (CO) is the last step of the procedure with the aim of avoiding congestion of the anastomosis due to any potential Pringle maneuvers during liver resection. Formation of defunctioning stomas could be considered in rare cases with elevated blood loss during liver resection or need for high doses of vasoconstrictors, which could affect the integrity of the digestive anastomosis.

We fully agree with the authors that the extent of both colorectal and liver resections is undeniably a major determinant of perioperative morbidity and mortality. Notably a consensus from the Expert Group of Onco-Surgery management of Liver Metastases (EGOSLM) group cautions against combined major liver and colorectal resection (4). Nevertheless, a number of retrospective series have reported that concurrent major liver resection, including even associating liver partition and portal vein ligation for staged hepatectomy (ALPPS), can be performed simultaneously with colorectal resections safely and efficiently (3,7,8). Of note, using the ACS-NSQIP database and analyzing outcomes from 922 patients who underwent simultaneous resections, Shubert *et al.* showed major morbidity and mortality for low-risk colorectal with minor liver resection were 25.9% and 1.5%, respectively; whilst the same rates for high-risk colorectal resection combined with major hepatectomy increased significantly to 55% and 5%, respectively (9). In a similar analysis from an international multicenter study, Tsilimigras *et al.* showed severe morbidity (Clavien-Dindo Classification  $\geq 3$ ) and mortality for low-risk colorectal and minor liver resection

were 15.7% and 2%, respectively; whilst the same rates for high-risk colorectal resection combined with major hepatectomy increased significantly to 50% and 25%, respectively (2). Thus, major liver resections are technically feasible when combined with colorectal resection, but strict patient selection is paramount in order to minimize postoperative morbidity and mortality.

Lillemoe and Vauthey have highlighted that close collaboration between all involved specialties and subspecialties is essential for optimal management of these patients (10). Indeed, one critical aspect which needs to be clarified by future studies is whether these simultaneous resections are routinely undertaken by both individual colorectal and hepatobiliary surgical teams. To date, this information has not been adequately provided by published series, and most likely varies based on institutional and national guidelines and policies. We firmly believe that presence and active contribution of both teams is indispensable, regardless of the complexity of the colorectal resection.

Minimally invasive liver resections (MILR) for both primary and metastatic lesions are increasingly being performed during the past decade and are currently standard of care in multiple centers worldwide (11-13). MILR are acknowledged as safe procedures, with oncological outcomes equivalent to those of open liver resections for CRLM. Furthermore, multiple studies have shown that simultaneous resections can be performed via minimally invasive surgical approaches with low morbidity and mortality rates, whilst maintaining oncological adequacy (8,14). A recently published systematic review focusing on laparoscopic simultaneous resections showed a cumulative morbidity of

19.9% and a mortality of 1%, with no difference in long-term outcomes when compared to open resection studies (8). Similarly, low morbidity and mortality rates were shown in another systematic review focusing in robotic-assisted simultaneous resections (14), with major morbidity and mortality at 7% and 0%, respectively. All these reported outcomes however should be interpreted cautiously, as these patients were well selected and undertaken by surgeons with significant experience in both colorectal and hepatobiliary minimally invasive surgery.

Simultaneous resection of SCRLM is an emerging alternative to the traditional staged approach and has been shown to be safe and efficient, with promising long-term outcomes for well-selected patients. Patients with SCRLM are in fact a heterogeneous group with a variable location of primary tumor, metastatic load, and most importantly tumor biology. We believe that the simultaneous or staged approaches should not be a one-way decision and that an optimal treatment strategy should be individualized with a MDT taking into account patient, tumor and biology characteristics. Further well-designed prospective studies are necessary to decipher which patients benefit most from a simultaneous rather than a staged approach for metastatic colorectal disease.

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