

Comment on: Synchronous resection of primary colorectal cancer with liver metastases: Two birds with one stone?

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Dear Editor

I read with interest the needlepoint article arguing that there is no *clinical equipoise* between simultaneous or staged resection for synchronous limited liver-only colorectal metastases¹. Based on one randomized trial (METASYNC) and a prospective cohort study (CoSMIC), the author finds it unethical to randomize to two operative procedures given the equivalent outcomes in these two studies. On the contrary, a large international, multi-institution, retrospective study describing trends and outcomes of simultaneous surgery², concluded that the mortality and morbidity rates associated with synchronous resections increased incrementally based on the extent of liver and colorectal resections. The authors suggest that both the extent of hepatectomy as well as the type of colectomy should be considered when deciding the appropriate treatment strategy for patients with synchronous colorectal liver metastases.

Unfortunately, there are several limitations in the METASYNC randomized trial which makes it worrisome to draw the conclusion that we have adequate high-level evidence to not pursue future randomized trials on this topic. Firstly, although 10 centres in France were involved in the trial, the overall recruitment time was a decade. Even this was not enough time to reach the calculated sample size (estimated sample size 222

patients; included 105 patients of whom 48 synchronous and 52 staged resections, and assessed for primary endpoint 39 and 38 patients, respectively). This was in spite of broad inclusion criteria, accepting major hepatectomy, bi-lobar liver metastases, and patients with rectal cancer. As the trial was underpowered to answer the primary outcome, the question still stands: for whom is simultaneous resection beneficial?

Although simultaneous resection of both primary tumour and liver-only limited liver metastases sounds appealing and reasonable, there is still *clinical equipoise*. High-quality trials are needed to evaluate the role of systemic therapy, oncological outcomes, and healthcare system implications before we can recommend simultaneous resections for synchronous colorectal liver metastases.

References

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2. Tsilimigras DI, Sahara K, Hyer JM, Diaz A, Moris D, Bagante F *et al*. Trends and outcomes of simultaneous versus staged resection of synchronous colorectal cancer and colorectal liver metastases. *Surgery* 2021;**170**:160–166