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Letter

Lung metastasectomy for colorectal cancer in the PulMiCC randomised controlled trial – Authors' reply

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We are grateful for Tom Treasure's and Norman R Williams' interest in our publication "Repeated centralized multidisciplinary team assessment of resectability, clinical behavior, and outcomes in 1086 Finnish metastatic colorectal cancer patients (RAXO): A nationwide prospective intervention study" [1], and especially resection of lung metastases [2].

The iterative selection of patients with favourable prognostic features is a relevant issue with metastasectomy in metastatic colorectal cancer (mCRC), but lung, liver, peritoneal, and other resections provide the best median overall survival (mOS) rates noted in this disease and, in all probability, the only chance for cure.

For most multidisciplinary teams, the time for randomised trials of metastasectomy versus non-metastasectomy, especially in mCRC patients with good prognostic features, has passed [3], as worded by D'Angelica "Would you perform a randomized trial of whether to deploy a parachute when jumping out of an airplane at high altitudes?" [4] This was also seen in the PulMiCC study where 263 (51%) patients were not randomised, but were resected upfront [5]. In contrast, 128 were selected not to have metastasectomy, and were not randomized either, for reasons unknown. Only 93 of 512 (18%) patients were randomized over a period of seven years and these clearly had more negative prognostic features (impaired ECOG, multiple metastases, higher CEA, etc.) [6], explaining the poor outcome in PulMiCC with an mOS of only 42 months in the metastasectomy arm. This in contrast with 72–102 months for recently published population-based series [7,8]. The results for the non-randomised patients need to be fully published before the PulMiCC study can be put into perspective. We therefore believe it is premature to question the value of lung resections, especially in patients with favourable prognostic features. As always, patients must be selected for interventions where it is believed that sufficient benefit will be seen.

Treasure and Williams refer to a meta-analysis of randomised follow-up studies after resection of primary colorectal cancer that showed that more intensive monitoring advanced the diagnosis of recurrence by a median of 10 (interquartile range 5–24) months [9]. The seven studies (patient recruitment 1982–2009) showed no significant survival difference in all-cause mortality, without reporting outcomes in the small subgroup of patients having had a metastasectomy. Salvage surgery frequency was doubled in intensive follow-up according to the Cochrane review, but this intervention is still not sufficiently common in the cohort studied, to result in an overall survival gain. Many interventions in oncology result in intermediate gains insufficient in magnitude to reveal a survival difference. Again, outcomes are not presented for those with salvage surgery [10]. Thus, these meta-analyses do not support the decision of whether to remove resectable metastases in mCRC or not, especially as diagnostics, metastasectomies, ablations, radiotherapy, and oncologic treatments have significantly developed since these inclusion periods.

The few randomised metastasectomy studies have failed due to accrual difficulties. Our results are in line with the abundant evidence from population-based series that have consistently demonstrated impressive survival for resected good prognosis patients, and with a non-negligible chance for cure. We show a high resectability rate with good survival, and potential cure in 38% (5-year RFS-rate from first resection/LAT with one or multiple resections), even if we have stretched the boundaries for metastasectomies outside the best prognosis groups.

Contributors

Pia Osterlund and Helena Isoniemi contributed equally. They have reviewed the letter by Treasure and Norman R Williams, performed the literature search and written the response.

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Declaration of interest

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References

[1] Osterlund P, Salminen T, Soveri Ll-M, et al. Repeated centralized multidisciplinary team assessment of resectability, clinical behavior, and outcomes in 1086 Finnish metastatic colorectal cancer patients (RAXO): a nationwide prospective intervention study. The Lancet Region Health - Eur 2021;3:100049.
[2] Treasure T, Williams NR. Lung metastasectomy for colorectal cancer in the PulMiCC randomised controlled trial. Lancet Region Health - Eur 2021;3:100080.
[3] Wei AC, Jarnagin WR. Questioning why more patients with colorectal liver metastases are not referred for metastasectomy. JAMA Surg 2020.
[4] D'Angelica M. Metastatic Liver Tumors: the Path to Disease-Free Survival. Surg Oncol Clin N Am 2021;30(1):xv–xvi.
[5] Milosevic M, Edwards J, Tsang D, et al. Pulmonary metastasectomy in colorectal cancer: updated analysis of 93 randomized patients - control survival is much better than previously assumed. Colorectal Dis 2020;22(10):1314–24.
[6] Gonzalez M, Poncet A, Combescure C, Robert J, Ris HB, Gervaz P. Risk factors for survival after lung metastasectomy in colorectal cancer patients: a systematic review and meta-analysis. Ann Surg Oncol 2013;20(2):572–9.
[7] Rumpold H, Kirchweger P, Niedersüß-Beke D, et al. Prognostic value of metastatic pattern in colorectal cancer: a multicenter retrospective analysis in a real-life cohort. Acta Oncol 2021;60(2):180–6.
[8] Tampellini M, Di Maio M, Baratelli C, et al. Treatment of patients with metastatic colorectal cancer in a real-world scenario: probability of receiving second and further lines of therapy and description of clinical benefit. Clin Colorectal Cancer 2017;16(4):372–6.
[9] Mokhles S, Macbeth F, Farewell V, et al. Meta-analysis of colorectal cancer follow-up after potentially curative resection. Br J Surg 2016;103(10):1259–68.
[10] Jeffery M, Hickey BE, Hider PN. Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev 2019;9(9):Cd002200.