Five-year survival of patients in control groups of randomised controlled trials is much higher than that assumed in observational study reports.

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Dear Editor

If longer survival and 'cure' are attributed to an operation for cancer it is fundamental to have a reliable estimate of what would have been the survival for patients with similar characteristic but who did not have the operation being reported. The results of the PulMiCC trial (Pulmonary Metastasectomy in Colorectal Cancer) have been published recently.[1] The survival for patients in the control arm (none crossed over to metastasectomy) was 29% (16–52%) much higher than the 5% given by Davini, Ricciardi and colleagues.[2]

There are now three randomised controlled trial testing effectiveness of local interventions for metastases. The CLOCC trial which tested effectiveness of radiofrequency ablation for liver metastases reported 5-year survival in the control group as 30.3% (95% CI: 19-42%) commenting that *RFA* "results in an excellent survival, which however was also achieved in the control arm."[3] SABR-COMET which tested stereotactic radiotherapy for any primary and any secondary site (except brain) reported a 25% five-year survival in the control group commenting the "better-than-expected survival in both groups suggest that oligometastatic cancers behave more indolently than previously appreciated".[4] The confidence interval of all the RCTs is several times higher than the <5% generally assumed.

In the early years of the establishment of lung metastasectomy into routine practice, forty years ago, Torel Åberg wrote "It has been assumed, implied, or claimed that the 5-year survival without operation is nil. Control material is, however, lacking."[5] The systematic review by Gonzalez which the authors cite states 5-year survival without metastasectomy is "worse than 5 %" and 5% is given by Davini, Ricciardi and colleagues[2;6] but neither provides a data based source. Misleadingly low prognostication of survival encourages patients and oncologists to hold inflated and unrealistic expectations of the actual benefit from lung metastasectomy.

Reference List

- Treasure T, Farewell V, Macbeth F, Monson K, Williams NR, Brew-Graves C, Lees B, Grigg O, Fallowfield L: Pulmonary Metastasectomy versus Continued Active Monitoring in Colorectal Cancer (PulMiCC): a multicentre randomised clinical trial. Trials 2019;20:718.
- Davini F, Ricciardi S, Zirafa CC, Romano G, Ali G, Fontanini G, Melfi FMA: Lung metastasectomy after colorectal cancer: prognostic impact of resection margin on long term survival, a retrospective cohort study. Int J Colorectal Dis 2020;35:9-18.
- Ruers T, Punt C, van Coevorden F, Pierie JP, Borel-Rinkes I, Ledermann JA, Poston G, Bechstein W, Lentz MA, Mauer M, Van Cutsem E, Lutz MP, Nordlinger B: Radiofrequency ablation combined with systemic treatment versus systemic treatment alone in patients with non-resectable colorectal liver metastases: a randomized EORTC Intergroup phase II study (EORTC 40004). Ann Oncol 2012;23:2619-2626.
- Palma DA, Olson R, Harrow S, Gaede S, Louie AV, Haasbeek C, Mulroy L, Lock M, Rodrigues GB, Yaremko BP, Schellenberg D, Ahmad B, Griffioen G, Senthi S, Swaminath A, Kopek N, Liu M, Moore K, Currie S, Bauman GS, Warner A, Senan S: Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. Lancet 2019;393:2051-2058.
- Aberg T, Malmberg KA, Nilsson B, Nou E: The effect of metastasectomy: fact or fiction? Ann Thorac Surg 1980;30:378-384.
- 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;20:572-579.