

PulMiCC and other controlled trial data challenge the usefulness of metastasectomy

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We appreciate the acknowledgement of the PulMiCC randomised controlled trial in the paper from van Dorp and colleagues which reports the Dutch experience of lung metastasectomy. Mindful of PulMiCC's vulnerability to criticism because of its size, we draw attention to the further report on all 93 randomised patients, with 43% more participants and 18 months longer follow-up.(1) 'The median survival after metastasectomy was 3.5 years (95%CI:3.1,6.6) compared with 3.8 years (95%CI:3.1,4.6) for controls.' Median survival is easier to grasp than hazard ratios, and there it is. These survival figures challenge the perceived usefulness of lung metastasectomy for colorectal cancer.

The power calculation, referred to by van Dorp and colleagues, is important when *planning* a trial but once the analysis has been done, it is important to respect the trialists and the willingly randomised patients, and to *look at the data*. These show that the widely held assumption that without the lung metastasectomy, nearly all these patients die within a few years is false. All three RCTs of local treatments of metastases, CLOCC, SABR-COMET, and PulMiCC.(1-3) consistently show that in the control groups (N=59,33,47 respectively) survival *without* metastasectomy is better than had been assumed in the power calculation. Future power calculations will have to be based on these new data. These RCTs were not as big trials needed to show the typically small benefit for chemotherapy, but together they include 139 control patients with a 5-year survival of 30% (about 20-40% with 95% confidence). The assumption that 5-year survival is <5% is nowhere close to the truth.(4, 5) Both CLOCC and SABR-COMET had important imbalance in the number of metastases, and SABR-COMET had additional imbalance in primary cancer types. All these favoured the treatment arm over control, and so bias had crept in, all avoidable by tighter trial design. Balance was achieved by the trial design of PulMiCC.

The authors' hope of 'a large European multicentre study' will only be possible, if those caring for patients with lung metastases recognise the uncertainty about the supposed >35% gain in magnitude of 5-year survival and become less convinced of the value of metastasectomy. The reasons for not randomising were explored in PulMiCC and when the clinicians overrode the trial protocol, 99% of decisions were for surgery, while if fully-informed patients opted to choose for themselves, nearly half preferred to not have an operation.

The authors estimate that in Europe, lung metastasectomy may represent 15% of all lung resections. It is important that this large number of operations, that involve suffering, and some risk, to patients, is of proven benefit. We note that 45 centres contributed patients, many with small numbers. The practice may be out of control and clear guidelines, based on reliable evidence, are urgently needed.

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