Based on the present evidence: what patients with lung metastases are candidates for metastasectomy?
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It must be stated at the outset that the quality of the present evidence is low.\cite{1} None of the systematic reviewers searching the literature from 1971 to 2011 found a randomised trial (RCT).\cite{2-5} The evidence available is predominately in observational studies, typically surgical-follow reports; there are about 100 of them. In the most inclusive of the systematic reviews, data were aggregated on 3504 patients from 51 studies published between 1971 and 2007.\cite{3} The most recent and most methodologically rigorous includes 2925 patients from 25 studies between 2000 and 2011.\cite{5}

Surgical follow up studies are inherently prone to a whole series of erroneous interpretations.\cite{6} The patients who are recorded in these follow up studies were selected to have lung metastasectomy by skilled, knowledgeable and experienced clinicians typically in multidisciplinary teams. Many patients are discounted at the outset because of the extent of their disease. During the necessary time taken to assess patients those with progressive disease are not rushed through to surgery but are more likely to be advised against it. Those progressing while on chemotherapy are usually excluded. Only a highly selected few have lung metastasectomy. We know from the Spanish study by Grupo Español de Cirugía Metástasis Pulmonares de Carcinoma Colo-Rectal (GECMP-CCR)\cite{7} that patients having metastasectomy are fewer than one in twenty of all patients with lung metastases so the selection is extreme.

Over the years surgeons and their analysts have worked hard with the data, performing repeated multivariate analyses. A cohesive story has emerged. There are three factors, identifiable before surgery, associated with poorer five year survival: multiple metastases, a short interval between primary surgery and metastasectomy, and elevated carcinoembryonic antigen (CEA). These are all prognostic factors which will identify those more or less likely to survive, whatever treatments they are given.\cite{8} Whether patients with favourable disease survive because of metastasectomy, of their inherent characteristics, cannot be derived from these analyses; we need a control group to establish that.

The belief in effectiveness of lung metastasectomy was based on clinical experience from 1960s up to about 2000. Amongst 3504 patients 60\% had a solitary metastasis, 36 months was the median inter-operative interval, and 60\% had normal CEA. Overall, two patients out of five were alive at five years.\cite{3} In the most favourable groups who have none of the adverse features three out of five live beyond five years.\cite{9;10} In the recent meta-analysis the survival is approximately
halved if there is more than one metastasis or a shorter interval or elevation of CEA. [5] If all three apply only on or two out of ten survive five years.

If one chance in five seems a chance worth taking we must remember that belief in effectiveness is premised on the assumption that there would be no survivors amongst patients with metastases were it not for metastasectomy. Cancer registry data shows this is not the case: there are more than 5% of patients with metastases alive at five years in cancer registry data sets. [11] A very simple arithmetical model demonstrates the possibility of 40% survival in a selected group of patients by selection alone. More sophisticated mathematical models of cancer registry data to find groups comparable with reported metastasectomy series raise greater doubts about beliefs based on uncontrolled data. [12]

Based on the present evidence we cannot identify any group of patients for whom there is evidence of cure by metastasectomy because we cannot distinguish between the effect of selection for surgery and the effect of the surgery itself. That is the purpose of a trial Pulmonary Metastasectomy in Colorectal Cancer (PulMiCC). [13] This RCT is supported by the National Cancer Research Institute in England and is also open in centres in Serbia and Italy. Any patient in whom the clinical team are uncertain about benefit from lung metastasectomy is eligible for inclusion in this trial.
Reference List


