

The evidence for surgical interventions: lung metastasectomy outcomes in the PulMiCC trial, an observational cohort study. and big data analysis.

Letter to the Editor in response to Moran and Guerra

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We enjoyed the thought provoking literary essay from Brendan Moran and Glen Guerra.(1) Gaining acceptance of innovative ideas can be an uphill struggle, but convincing practitioners to discontinue ineffective therapies can be even more difficult. And in fairness to the many PulMiCC trialists (Pulmonary Metastasectomy in Colorectal Cancer) their hard-won evidence should be considered more thoughtfully, rather than dismissed in a few words with an outdated citation.

The full PulMiCC cohort study in 512 patients is now published.(2) The known characteristics which predict longer life with CRC lung metastases were more prevalent in the 263 non-randomised patients selected for metastasectomy compared with the 128 not selected for operation. Five-year survival was commensurately better. Only a small minority of patients have lung metastasectomy indicating a high degree of selectivity.(3) In the PulMiCC controlled trial there was excellent balance between the arms and there was no survival difference at any time point.(4) A recent analysis of the Surveillance, Epidemiology and End Results (SEER) data-base also found no benefit from lung metastasectomy.(5) We can now be sure that selection is responsible for a large part of the perceived survival difference. Some small difference in long term survival cannot be excluded.

By using the quote from Swift as an introduction to their article Moran and Guerra are clearly implying that the benefits of cytoreductive surgery (CRS) of peritoneal metastases are a 'truth' that will be revealed once the 'fake news' about it has been dispelled. Clinical research does not necessarily lead to the uncovering of truths. It starts with hypotheses. These are tested against the evidence which is always imperfect and provisional, so that conclusions can be drawn. These conclusions lead to beliefs underpinning clinical practice. Some beliefs are well founded in robust evidence, others are not. Moran and Guerra seem to have at least three firm beliefs: that the oligometastatic state is a real clinical entity, that the removal of a few detectable metastases is effective and that CRS saves lives. None of these beliefs—though widely held—is currently supported by reliable evidence. They also implicitly accept that randomised controlled trials are the way to determine the true treatment effect when there are many variables at play as did ~~did~~ the world when the pandemic struck. Trials were designed, gained ethics approval and were implemented at pace.

Basingstoke influenced world practice by developing, proving, and promoting the benefits for of total mesorectal excision by direct observational study of pathological specimens and patterns of cancer recurrence. For disseminated disease, with very many more variables, controlled trials may be the only way to know what works. Instead of disregarding PulMiCC, peritoneal specialists could learn from its difficulties and limitations. While randomisation was constrained by powerful influences, the observational cohort thrived.(2, 4) With the addition of big data research, general ineffectiveness of piece meal removal of blood borne metastases is becoming evident.(3, 5) Why doesn't Basingstoke use its resource of a large clinic base and highly respected leadership to lead on bigger, better and focused trials of peritoneal disease, thus challenging falsehood with evidence?

References

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