

Is Surgery Warranted for Oligometastatic Disease?



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KEYWORDS

- Lung metastasectomy • Colorectal cancer • Clinical effectiveness • Citation network analysis • Ablation

KEY POINTS

- The removal or ablation of pulmonary metastases for carcinoma (especially colorectal) is being increasingly carried out with the aim of improving survival.
- Lung metastases from carcinoma are rarely the primary cause of death.
- Observational studies cannot reliably show the long term effectiveness of pulmonary metastasectomy; there have been no randomised trials.
- There have been randomised trials of monitoring strategies to detect and treat metastatic disease earlier: they have shown no survival benefit.
- Pulmonary metastasectomy with curative intent is not justifiable on the currently available evidence.

It is now widely believed that the resection of metastases from the lung of a patient with cancer is a useful procedure and one that improves survival. That there is an issue of *Thoracic Surgery Clinics* devoted to the topic is a testament to this belief. The new less-invasive techniques of ablating metastases and the increased use of videothoracoscopy seem to be making this approach even more popular. This article strongly challenges the belief in clinical effectiveness and demonstrates that metastasectomy is supported neither by a sound biological rationale nor by any good evidence. Reasons are suggested why this unfounded belief has become so prevalent.

The authors are not dogmatic nihilists. The noted British economist John Maynard Keynes once wrote, "When my information changes, I alter my conclusions. What do you do, sir?" The authors' current position is based on a careful consideration of the current evidence and if this evidence changes the authors are prepared to change their minds.

Colorectal cancer is currently the most common histology for lung metastasectomy. For most of this article, unless otherwise stated, colorectal cancer

is used to make generalizable points that apply to the management of other carcinomas that have similar overall behavior. Sarcoma and germ cell tumors may be different¹ and are discussed in Chapter 7 by Duykhanh Ceppa. Metastases are rarely symptomatic and usually remains so even in later stages of colorectal cancer. Policies of surveillance are specifically designed to detect asymptomatic metastatic disease. Furthermore, the practice of metastasectomy is selective and the rare metastases that cause symptoms generally fall outside the criteria for lung metastasectomy performed with intent to cure.

THE PARADIGM OF CANCER SURGERY WITH INTENT TO CURE

The paradigm of curative cancer surgery used to be simple. The cancer had to be localized so that the surgeon could perform an operation that successfully removed it with clear margins, confirming by microscopy that the intent to leave no residual primary disease was achieved. Local lymph nodes could be included in what was intended to be an en bloc

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curative resection. This might also include regional nodes taken with the intervening tissue in continuity, but the presence of more remote lymph nodes and blood-borne metastases (M1 disease) was believed to make surgery futile or unavailing. Of the two, the authors prefer to use the word unavailing which retains a sense of a well-intentioned operation even if surgeons' efforts may have not been effective.

The Halsted operation for breast cancer followed this paradigm of taking the whole breast, with the primary cancer within it, and the draining lymph nodes, in continuity. The operation held sway for 80 years and any less radical surgery was regarded as undertreatment, which compromised the chance of cure. The Halsted paradigm was en bloc clearance of all disease and extending the operation to remove as many lymph nodes as possible gave the best chance of cure. Radical mastectomy was challenged by Bernard Fisher in 1970 in a 50-page treatise.²

The abbreviated version of the history³ is that radical mastectomy was definitively overturned by the results of a randomized trial published in 1981 the *New England Journal of Medicine*.⁴ Even prior to that study, however, many surgeons had already desisted from performing radical mastectomy. When invited to write a state-of-the-art article published in 1978 in the *British Medical Journal*, Harold Ellis, a highly regarded surgical teacher, never mentioned radical mastectomy.⁵ Radical mastectomy was already on the wane. This illustrates a corollary that unless and until there is sufficient uncertainty to allow a balance of opposing views, now known as group equipoise, controlled trials with treatment assignment by randomization are not ethically possible.

The implication of all this is that breast cancer (and probably many other common cancers) may well be a systemic condition earlier than was previously considered and that extensive, often mutilating, surgery does not achieve the hoped-for cure and is not in patients' interests. So it is unlikely that removing a few radiologically visible metastases from the lung changes the course of the disease. Removing as many as 124 metastases from the lungs, as has been reported, seems to the authors to be beyond reason.⁶

The paradigm of resection of the primary and locoregional disease en bloc now seems to be abandoned and replaced by a sincerely held belief that resecting a few liver or lung metastases can result in durable disease-free survival. From basic principles, it seems implausible that survival can be substantially altered by piecemeal removal of blood-borne metastases from a destination organ such as the lung. It is not clear to the authors that there is any substantial evidence to justify

this change. Doubts about effectiveness of lung metastasectomy were published in a well-reasoned but rarely cited article 35 years ago.^{7,8}

DEFINING TERMS: OLIGOMETASTASIS

Oligometastatic disease is now a popular term but what exactly does it mean? As argued in this article, it means nothing more than what the word itself says: few metastases. The authors conclude that the oligometastatic state is a therapeutic opportunity where there are few enough metastases to consider ablating or removing them all in turn. There is nothing wrong in itself with defining a disease by the treatment available. There is an excellent precedent in the case of end-stage renal disease (ESRD), which is a diagnostic label, or perhaps better, a frame,⁹ for a disease that, once diagnosed, attracts federal funding for renal replacement therapy (**Box 1**).¹⁰

The term *oligometastasis* seems to have appeared for the first time in the literature in 1995.¹¹ The article's authors, Hellman and Weichselbaum, introduce their exposition of the metastatic state with reference to Halsted and breast cancer. The Halsted theory, according to their account, proposed that cancer spread is orderly, extending in a contiguous fashion from the primary tumor through the lymphatics to the lymph nodes and then to distant sites.¹¹ The investigators use the words, "theory" and "hypothesis", in their introduction before proposing the existence of a clinically significant state of oligometastases.

Box 1 Framing disease

History of renal failure from dropsy to ESRD¹³

- From ancient times to the eighteenth century, dropsy was a clinical diagnosis for a body overloaded with water.
- From the 1820s, Richard Bright of Guy's Hospital in London recognized that some patients with dropsy had albumen in their urine and shriveled kidneys, which distinguished them from those with heart disease as the cause of what is now called edema, and this was known as Bright disease.
- People who have kidney disease necessitating renal replacement therapy now receive the diagnosis of ESRD, which since 1972 entitles them to centrally funded renal replacement therapy.¹⁰

Data from Rosenberg CE, Golden J. Framing disease: studies in cultural history. New Brunswick (NJ): Rutgers University Press; 1992.

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