

REVIEW

Resection of pulmonary metastases: a growth industry

T. Treasure^a, E. Internullo^b and M. Utley^a

^aClinical Operational Research Unit, University College London, Gower Street, London, WC1E 6BT, UK

^bThoracic Surgery Unit, University Hospital Parma, via Gramsci 14, 43100 Parma, Italy

Corresponding address: Tom Treasure, Clinical Operational Research Unit, University College London, Gower Street, London, WC1E 6BT, UK. Email: tom.treasure@gmail.com

Date accepted for publication 17 March 2008

Abstract

Surgical metastasectomy is increasing both in the numbers of operations performed and the extensiveness of surgery that is being undertaken. Radiologists play a central role in this work. It is they who first detect metastases on cancer staging scans and it is they who detect recurrence of cancer on surveillance scans performed in the course of follow-up. Radiologists then play a key role in characterising and diagnosing any lung nodules thus discovered. For colorectal and lung cancer the clinical teams are typically quite separate, but radiologists have a role in both multidisciplinary team meetings. Thus it may well be that the radiologist is party to discussions about the same patient and the same imaging information in quite separate multidisciplinary team meetings and needs to understand the imaging needs and clinical objectives of both. As surgery is becoming more extensive, the inescapable harm done as a consequence of lung resection is increasing. Good quality evidence for benefit is lacking. The purpose of this article is to provide an update on the practice of metastasectomy, the selection of patients, the objectives of surgery, and uncertainties about its effectiveness.

Keywords: Colorectal cancer; metastasectomy.

Introduction

Over 5000 operations (all cancer types) were included in the report of the International Registry of Lung Metastases (IRLM) published over ten years ago^[1]. In the UK pulmonary metastasectomy has become an increasingly common operation. The European Society of Thoracic Surgeons (ESTS) has recently performed a web-based survey showing a wide range of beliefs and variation in practice^[2]. It appears that many surgeons will operate on bilateral lung metastases, place no upper limit on the number of metastases, and will do repeat operations. The potential number of patients is thus very large indeed as a result of widening applications and more general acceptance of this form of surgery.

Colorectal cancer represents the commonest cancer type in clinical reports of surgical metastasectomy of which there are hundreds in the literature; there are over 70 clinical case series reporting results for colorectal cancer alone. The larger and better reported of these are included in a systematic review^[3]. This surgery has

entered accepted practice and the referral of patients to thoracic surgeons for consideration of metastasectomy has been advocated by the British body providing guidance for clinical practice, the National Institute for Health and Clinical Excellence (NICE)^[4]. Radiologists not already familiar with this practice will be encountering it increasingly.

The purpose of this article is to provide an update on the practice of pulmonary metastasectomy for colorectal cancer, the selection of patients, and the objectives of surgery. There are uncertainties about the clinical effectiveness of this surgery and the authors are engaged in a programme of research to address these.

The role of the radiologist in the increase in pulmonary metastasectomy

The routine use of surveillance computed tomography (CT) scanning in the follow up of colorectal cancer patients has revealed an increasing number of clinically

well patients, deemed clear of disease at the primary site, but with evident pulmonary metastases. There is a parallel to be drawn with CT screening for lung cancer^[5]. The process reveals disease that was previously subclinical and presents an opportunity to take action. It also presents new problems. Discovery of pulmonary metastases comes as a crashing disappointment to all but because the disease is caught at an early stage, while it is low volume, it can be resected at low risk in a selected population of patients. The pervading contemporary attitude to cancer is to act early and if anything the recent trend is to be more radical. Resection, where possible, is often the favoured course of action.

The patient population selected

There are three aspects to patient selection:

- (1) Distinguishing between metastatic cancer and a separate lung primary.
- (2) Deciding on the suitability of the patient for metastasectomy.
- (3) Establishing whether all metastatic disease can be completely resected.

Distinguishing between metastatic cancer and a lung primary

If there are multiple pulmonary nodules in the context of known colorectal cancer, the diagnosis of metastatic cancer is likely. If the nodule is solitary the probability that this is a lung cancer is substantial, even if there has been proven cancer at another primary site. The age of the patient, a smoking history and the nature of the known primary cancer influence the prior probability that a solitary nodule is lung cancer^[6] but cannot clinch it and the uncertainty often remains. Fluorodeoxyglucose (FDG)-positron emission tomography (PET) should be performed, more to reveal any other occult disease than to help in characterising the solitary pulmonary nodule itself. Then the multidisciplinary team usually requires tissue diagnosis of the lung lesion so that they can inform the patient and make a management plan. The options for tissue diagnosis include CT-guided biopsy or local excision using video-assisted thoracic surgery (VATS). Some teams will go straight to thoracotomy and make a frozen section diagnosis. If so the patient should be fully staged and clinically assessed so that definitive lung cancer surgery, usually lobectomy, can follow at the same operation.

Deciding on the suitability of the patient for metastasectomy

If metastases are diagnosed, there are agreed principles which guide decisions concerning metastasectomy, loosely referred to still as Thomford's criteria^[7] despite

the criteria having been substantially widened and modified since they were first proposed.

- The patient must be fit for the necessary pulmonary resection. With minimally invasive techniques including video-assisted thoracic surgery (VATS) and the use of smaller and muscle sparing incisions, and the parenchymal sparing effects of the laser metastasectomy techniques^[8], this may be a less restrictive criterion.
- Control of cancer at the primary site was in the original criteria. However, synchronous surgery of the bowel primary and the liver metastases is now undertaken in some cases, obviating this as a requirement. For lung metastases it probably remains a basic tenet of practice for now.
- The metastatic disease must all be removable. Originally this tended to restrict surgery to single metastases but now multiple and bilateral disease can be considered feasible with modern techniques. There are patients with liver and lung metastases. Sometimes this leads to a discussion about tackling first the site where clearance of the metastatic disease is less assured.

Establishing whether all metastatic disease can be completely resected

In multivariable analyses of clinical case series (of which there are many^[9]), there are various factors associated with length of survival. One that is fairly consistent is the completeness of resection. Residual disease presence or absence (staged as R1 or R0) is associated with length of survival. In terms of a hope for 'cure', R0 is the objective. It is therefore important in the selection of patients for surgery to determine if resection with no residual disease can be achieved.

Questions and uncertainties concerning pulmonary metastasectomy

Thus far we have outlined current practice but the clinical need to detect all disease to achieve the objective of genuine R0 resection must raise a question in the minds of radiologists about the possibility of detection of all disease. This is the first of several uncertainties which we will now explore.

Can the radiologist detect all the lung metastases?

There is an argument put by surgeons that when they palpate the lung at thoracotomy they discover metastases not evident on CT scans. This hypothesis has been explored in a prospective study^[10]. An initial VATS was performed to remove all metastases revealed by CT and then the chest was opened by thoracotomy.

In 10 of the first 18 patients, additional malignant lesions were found and the study was abandoned. It should be noted that only two of the scans were helical and it is reported that 20% more nodules can be detected with helical scanning in a paper as long ago as 1993^[11]. A systematic review has concluded that there is insufficient evidence to recommend either thoracotomy or the less invasive VATS^[12].

There is a corollary to this argument: if you cannot trust the CT to identify all the lesions on the one side, what about the other side? To achieve the objective of complete removal, must we do bilateral open surgery as a routine? The options are sequential thoracotomy, or (if all are to be removed at the same operation) median sternotomy or bilateral anterior thoracotomy with transverse sternotomy, a very radical surgical approach popularly known as the 'clam shell' incision. Removing one or two metastases by VATS in the hope of benefit, at small degree of harm, may be tolerable but a commitment to routinely opening the chest on both sides sufficiently to palpate all of both lungs escalates the harm done to a point where it might exceed any benefit. The authors of a systematic review were unable to conclude that there was a proven difference in outcome for these very divergent practices^[13].

Even when lesions have been shown on CT they can be deep-seated and very hard to locate with VATS. Even with the king in the surgeon's hands, some metastases cannot be found. The surgical study faulting the ability of CT to show all the nodules that surgeons can feel is only one side's view. In the IRLM data in 25% of cases more metastases were found at the time of surgery but in 14% there were fewer found than predicted by CT^[11].

This whole debate may simply illustrate some naïve and simplistic views of how cancers metastasise. If all cancer emboli contained the same number of cells and were trapped in the lung at the same time, then there might be a crop of metastases of the same size. We might then as it were, harvest the crop. In fact there must be distribution of sizes for metastases and whatever the limits of detection for CT or the surgeon's fingers it is always possible that there will be metastases we can neither see nor feel. As a consequence surgeons who believe strongly in this practice will offer a second or third operation as more metastases become evident. This is not necessarily made explicit to the patient at the outset.

A consideration perhaps, underestimated until recently, is that the lung metastases themselves metastasise to mediastinal nodes^[14] and in these patients survival times are shorter. This means that candidates for pulmonary metastasectomy should ideally be put through mediastinal staging as in lung cancer and excluded from surgery if the mediastinal nodes are involved.

Uncertainties about effectiveness

Surgery for cancer is usually aimed at cure, or at least prolongation of life. The justification for pulmonary

metastasectomy is based on survival analysis of retrospective case series analysis. There are no randomised trials. There are no comparable survival data presented but a blithe assumption that any survivors beyond three or five years can be attributed to the beneficial effects of surgical extirpation of disease. This ignores the fact that these patients are highly selected for surgery and if their survival is to be compared with those selected out of the surgical group, any difference is possibly attributable to the selection rather than the surgery^[15,16].

The analysis of case series of pulmonary metastasectomy for colorectal cancer typically includes multivariable analysis for factors that are associated with survival time. Two of the strongest associations (apart from R0 resection mentioned above) are the number of metastases and the level of carcinoma embryonic antigen (CEA). These are both measures of the biological aggressiveness of the cancer and are again not evidence that surgery is beneficial.

Apart from survival, important measures of outcome for cancer patients include symptom control and quality of life. Neither are referred to in any of the clinical series. Psychological benefit is used as justification in clinical discussions but there are no measures of mental well being amongst the outcomes or psychologists amongst the authors.

Finding evidence for practice

The best evidence would be a randomised trial broad enough in its inclusion to define the balance of harm and benefit. We have outlined a pragmatic design for consideration^[17-19]. Radiologists are involved in both the colorectal and lung multidisciplinary teams and would be involved in any research protocol. There seems to be sufficient uncertainty to merit attention.

Conclusions

Pulmonary metastasectomy has come to be regarded as established practice in the management of colorectal cancer. This work involves radiologists in the detection of pulmonary nodules and in their characterisation. However, there are no randomised trials to support metastasectomy in the management of colorectal cancer and great emphasis is placed on case selection. Radiologists within both lung and colorectal cancer multidisciplinary teams need to know the basis of current practice and its objectives. We are engaged in formal evaluation of the effectiveness of pulmonary metastasectomy and this too will require expert collaboration with radiologists.

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