

Thoracic intervention & surgery to cure lung cancer

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Lung cancer survival in the UK has changed little in the last 40 years. Overall 90% of people with lung cancer are dead within five years of diagnosis. A further 5% die from their lung cancer by 10 years. As the prevalence of smoking has declined lung cancer has become less common and is seen in aging cohorts who typically are socially deprived and afflicted by the other effects of smoking. The inclusion of the paper from Papworth Hospital's intensivists is a reminder that good recovery from treatments calls for great care and special measures[1] but the mortality statistics indicate that our attempts at 'cure' generally fail.

The only treatment associated with long survival has been surgical resection of the primary lung cancer. With current selection, 98% of patients having lobectomy survive to leave hospital but the operation reduces lung capacity and well-being. The theme running through the collection of articles is lessening the burden of treatment of lung cancer. Ablative techniques may begin to replace lung resection[2;3] and when surgery is the chosen treatment, collateral damage can be reduced by using videothoracoscopy and by minimising the volume of functioning lung parenchyma that is resected.[4] David Waller reminds us that Russell Brock defined the anatomy of the bronchopulmonary segments but its relevance then was in septic lung disease, lung abscess and bronchiectasis, not lung cancer. Brock advocated 'block dissection pneumonectomy'. [5] It was Jack Belcher and colleagues who worked to reduce the sacrifice of functioning lung parenchyma by anatomical lobectomy which became the standard of care.[6] Waller in his article moves the 'less is more' theme on by emphasising the margin of clearance of the primary rather than the radicality of the resection. It shifts our attention to the cancer rather than the organ – more of that later.

Since Belcher's report on lobectomy, the five year survival rate after lung cancer resection has doubled from 25% to 50% but this has provided no net gain in survival from lung cancer. Higher surgical rates were the result of operating on more rigorously selected and hence relatively fewer patients. It was achieved by the successive introduction of the means of diagnosing lymphatic spread and thus excluding patients who could not be cured by removal of the primary cancer. In Brock and Belcher's time the plain chest radiograph and rigid bronchoscope were all they had. CT scanning, mediastinoscopy and transbronchial lymph node biopsy, and PET scans allowed the multidisciplinary lung cancer teams to narrow down surgical referrals to those in whom an operation to remove the primary cancer could potentially remove all the disease. This change was in the same direction as the retreat from radical mastectomy for breast cancer - towards less mutilating but no less effective surgery for those curable by resection of the primary cancer.[7] Waller's title 'margin ... is the new standard' reminds us to reconsider what exactly we are trying to achieve with local surgery: it is first and foremost, control of the primary cancer. The focus of the surgeon will be, as with ablation, the cancer not the organ. We rely on systemic treatments to treat systemic disease.

In what to me is a curious reversal, the case for surgery is being bolstered by the opportunity presented at operation (but not during ablation) to do systematic mediastinal lymphadenectomy. This is essentially what Brock called 'block dissection'. This seems to move the cancer operation back to Halsted's concept, not just resection of the primary but of all the lymphatics within reach. It is variously argued that lymphadenectomy provides more thorough staging to guide treatment strategies, cancer tissue to guide targeted therapies, and as a bonus, the chance removal of unseen residual disease and thus 'cure' some patient who otherwise would have been left with cancer in their lymph nodes. The practice of systematic lymphadenectomy is written into thoracic surgical consensus statements. Working as an international multidisciplinary team we performed a meta-analysis of five randomised controlled trials found on systematic review.[8] These trials compared radical

lymphadenectomy to sampling. There was a non-significant marginal difference but there were many opportunities for bias in the hands of those doing the studies, and there was clear evidence of the exercise of bias. But the practice is entrenched. Belief in the value of lymphadenectomy has become an obstacle to adoption of SABR or IGTA for other than inoperable patients.

As far as primary resection is concerned, if the less invasive ablative treatments can be proven to achieve equivalent local control, they should be preferred to thoracotomy and lung resection. Stereotactic ablative radiotherapy (SABR) described by Chia and Conibear[2] and image guided thermal ablation (IGTA) described by Smith and Jennings[3] might, and indeed should have a role. That is if they can be shown objectively to achieve the clearance margin that Waller calls for. But observational studies of clearance are difficult when the cancer is ablated – there is nothing to offer the pathologist on which to examine clearance margins. And to ensure, it is a fair test, and that like is being compared with like, will require controlled trials. Uncontrolled studies of survival tend to overlook the fact that not all survival is attributable to what the doctors did. Operation is offered to the prognostically most favoured 10-20%. Some of the survivors would have made five years without surgery. Conversely, if ablation is only offered to those unlikely to survive not all deaths are failures of treatment. All the authors point to the paucity of trials and indeed, they are difficult to do for interventions.[9] There have been trials intended to compare SABR with surgery but recruitment was dismally slow. We have to bear in mind that while SABR is attractive to patients and lucrative for therapists,[10] thoracic surgeons stand to ‘lose market share’ and random assignment met with resistance, probably on both sides. A laudable effort to salvage data from two such trials suggested that SABR might have similar results to surgery.[11] The response of the leading cardiothoracic surgical journal was four editorial pages setting out all the possible flaws.[12] Pushing for bigger and better trials to answer the question would seem to be better use of the journal’s pages.

The articles on SABR and IGTA include the treatment of metastases which seems to me to stretch the remit of writing about ‘cure’.[2;3] In 1995 radiotherapists in Chicago proposed a concept of an oligometastatic state.[13] The idea lay dormant for 10 years but is now in the argot of cancer teams.[14] Treating a specific metastasis to relieve symptoms may be justified on the merits of the case but it seems to be unlikely that a policy of ablating a few metastases will ‘cure’ lung cancer. An observed association between additional treatments and longer survival is as likely to be reverse causation: longer survival provides opportunities for piecemeal ablation rather than the ablation of metastases lengthening survival. But as the authors write there are no controlled trials address. There are many trials of systemic treatments and treatment combinations. For treatments given ‘with curative intent’ there is little high quality evidence. The authors of the collected articles have provided us with excellent updates on current practice and some food for thought.

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