Reply to the Letter to the Editor

Reply to Riquet et al.

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Received 23 October 2006; accepted 25 October 2006

Keywords: Lung resections; Octogenarians

Riquet et al. [1] have described their experience with pulmonary resections for malignancy in 66 octogenarians. About 35% of the patients in this series had pneumonectomies. They report an overall 5-year survival of 29.1% and an operative mortality of 7.6%. This is in contrast to a 57% 5-year survival in the Matsuoka et al.’s [2] series, which however, had no pneumonectomies.

Twenty percent of the patients had N2 disease. This series confirms the poor survival [no survivors at 5 years and median survival of 11 months] in patients with N2 disease. It would be interesting to know, if this group of patients had any neoadjuvant chemotherapy, and the extent of the resections in these patients.

It is important to carefully assess octogenarians for lung resection and try and define those factors, which would increase operative risk. Unfortunately most series have a small number of octogenarians and it is difficult to identify risk factors in these patients.

Cerfolio and Bryant [3] recently reported the results of lung resection in 51 octogenarians. Patients who received neoadjuvant therapy had three times the risk of developing major morbidity.

Dominguez-Ventura et al. [4] defined the adverse outcome predictors in 379 octogenarians. Predictors of morbidity were male sex, hemoptysis and previous stroke. Operative mortality was 6.3% and significant predictors included congestive heart failure and prior myocardial infarction.

Although elderly patients should not be denied pulmonary resection based on chronologic age, it would appear that neoadjuvant therapy, stage of the disease, extent of the resection and comorbidities (cardiovascular morbidity in particular) predict increased operative risk in this patient population.

References


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doi:10.1016/j.ejcts.2006.10.030

Letter to the Editor

Is radical mediastinal dissection mandatory for curative resection of NSCLC?

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Received 23 August 2006; accepted 12 October 2006; Available online 7 November 2006

Keywords: Lung cancer; Resection; Lymph node dissection; Systematic nodal dissection; Intrathoracic staging

We read with interest the article by Massard et al. [1] comparing nodal ‘sampling’ and ‘formal nodal dissection’ sequentially at thoracotomy, in which they found that sampling underestimated mediastinal nodal involvement that would have lead to inaccurate staging and more incomplete resections had nodal dissection not been performed. However, to fully understand the significance of their findings it would be useful to clarify the definitions of each of these terms, to be given more details of the protocol and to be provided with more raw data.

‘Sampling’ may refer to the removal of part of one node, removal of one node from a nodal station or the removal of selected stations. The ACOSOG study provided one such definition [2]. Similarly there is no universally accepted standard for ‘the usual formal lymph node dissection’ used in this study. The IASLC International Workshop on Intrathoracic Staging, held in London in 1996 [3] provided an internationally agreed term, systematic nodal dissection (SND), which avoided imprecise terms such as ‘sampling’, recommended the labelling of excised nodes according to one of the internationally agreed nodal charts, extended the evaluation of nodal disease into the hilum and other N1 stations and set a standard for adequate mediastinal nodal evaluation of three nodal stations. This was subsequently clarified in a discussion document on the definition of complete resection [4], which recommended an additional three N1 stations should also be removed for complete nodal assessment.

Would Dr Massard and his colleagues tell us the number and site of N2 nodes or stations specified in the protocol for ‘sampling’ and ‘formal dissection’ and the actual number removed in the study patients? Did such evaluations include those N1 nodes/stations not included in the ‘intrapulmonary nodes’, which were dissected by the surgeon during resection and the pathologist subsequently?

From the data provided we can only identify 44 patients who had N2 disease identified on nodal dissection in whom this would have been missed or under-estimated on sampling, and hence cannot understand why ‘resection based on sampling would have been incomplete in 53 (88%)’ of those with pN2 disease’. The discussion document by Rami-Porta et al. [4] emphasises that ‘complete resection’ entails much more than a thorough nodal evaluation and one assumes that these other features, such as negative margins, were also considered in this protocol.

We are assured that the ‘stations were adequately labelled’. In view of the multicentre, international nature of this study it is clearly important to know if this was in...
accordance with an internationally accepted nodal chart. Such a study is prone to inter-observer variability. Discordance between observers in distinguishing between stations #10 and #4 and between stations #10 and #5 occurs in one third of patients with resulting distortion of the reported stage [5]. We would ask the authors to tell us which nodal map or definitions were utilised and whether inter-observer variability was assessed between participating surgeons.

We hope that this additional information will reinforce and clarify the conclusions suggested by the authors.

References


Reply to the Letter to the Editor

Reply to Belcher and Goldstraw

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Received 11 October 2006; accepted 12 October 2006; Available online 13 November 2006

Keywords: Lung cancer; Surgery; Staging; Lymph node metastases

We thank Mrs Belcher and Mr Goldstraw [1] for their interest in our work and their expert comments.

Our colleagues ask for some more details about sampling and dissection in our experimental design [2]. Sampling was performed after mediastinal inspection and palpation, by randomly dissecting out a whole but single node. We routinely explored the following lymph node areas, as described in our article: on the right side, paratracheal nodes, subcarinal nodes and pulmonary ligament; on the left side, paraaortic nodes, left tracheo-bronchial angle, subcarinal nodes and pulmonary ligaments [2]. Lymph node dissection was made by en-bloc dissection of the above-mentioned compartments; we avoided fragmentation into sub-entities as defined by the Naruke or ATS map, and rather followed the physiology of lymphatic stream. Therefore, the paratracheal dissection for instance included stations 10, 4 and 2; the subcarinal dissection stations 7 and bilateral 8; paraaortic nodes included levels 5 and 6: the subaortic nodes included 10L and 4L. By this way, we always achieved a complete mediastinal clearance on the side of operation.

Interlobar nodes were of course dissected out when lobectomy was performed, and also routinely inspected by our pathologists in the event of pneumonectomy. However, comparison of sampling to dissection was limited to the mediastinal nodes [2].

We willingly did not consider the number of nodes harvested, because the number of nodes in a given area may considerably vary; fragmentation during dissection may further falsify the count of nodes! To our opinion, the only adequate definition of node dissection is ‘total clearance of an anatomic compartment’.

Our colleagues adequately underline that definition of a complete resection does not only implicate complete lymph node dissection, but also tumor-free resection margins on the verge of bronchus, vessels, and pleura. However, the remarkable observation of this study was that there were only 7 patients out of 60 with N2 disease, in whom the disease was limited to the sampled lymph node [2]. For all other 53, sampling would have left diseased nodes within the mediastinum. That is why we qualified these resections as incomplete. Our study adds a strong argument to include a thorough lymph node dissection into the definition of complete resection.

We are aware that a munticenter studies like the present may be subjected to inter-observer variability. To limit this bias as much as possible, we undertook some common operations between senior surgeons before starting the trial. As stated in the manuscript, we tested the hypothesis of inter-observer differences in the results, which did not exist. However, there is another potential major bias in our study, which has not been addressed to by Mrs Belcher and Mr Goldstraw: the interobserver variability of pathologists. Clear-set quality criteria for pathological evaluation of lymph nodes are lacking. Obviously, detection of small tumor foci, measuring less than 4 mm, i.e., those who typically are PET negative, requires a dedicated and time-consuming work-up [3]. Further, it is well known that a considerable amount of nodes considered as normal by optic microscopy, reveal to contain isolated tumor cells with immuno-enzymatic stainings [4].

Our study fills a lacking link in the chain of arguments in favor of lymph node dissection. Some recent studies have indirectly shown the effect of lymph node dissection on staging, by demonstrating an improved survival in stage 1 disease when more lymph nodes were resected [5]. The present study provides a direct demonstration, because each patient has been his own control; it enables us to conclude that node dissection is required to warrant a complete tumor clearance and an adequate staging. Some studies raise the hope that it could also improve survival, but this is still matter of debate and investigation [6].