according 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


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Reply to the Letter to the Editor

Reply to Belcher and Goldstraw

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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 multicenter 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].
References


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