Could the grade of the tumour be related to nodal involvement?

Sezai Cubuk* and Orhan Yucel
* Department of Thoracic Surgery, Gata Medical Faculty, Ankara, Turkey
* Department of Thoracic Surgery, Gata Haydarpasa Teaching Hospital, Istanbul, Turkey

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We read the article of Hattori et al. [1] with great interest. We thank the authors for this well-designed study.

Tumour node metastasis (TNM) staging is important for predicting the recurrence of the tumour and for survival. The authors mentioned that sub-centimetric pure solid nodules with high SUVmax values have a tendency toward lymph node metastasis. Also, the invasiveness of the tumour is declared to be an important determinant of recurrence and survival [2]. In this context, we think that the differentiation degree of the tumour may be a prognostic factor in lung cancer. As a result, we recommend lobectomy for high-grade sub-centimetric nodules.

Evaluation of the sub-centimetric nodules with PET scans may be misleading [3]. Too many centres do not perform a PET scan for nodules smaller than 1 cm because of high ratio of false-negative results. So, we think that the invasiveness and the grade of the tumour may be directive for whether to perform limited resection or lobectomy in these nodules. In this context, a histopathological decision is thought to be more reliable than PET scan results.

As a final comment, we think that grade of the tumour will be a component in the staging system of lung cancer over time, that is, in oesophageal cancer staging.

REFERENCES


* Corresponding author. Department of Thoracic Surgery, Gata Medical Faculty, Ankara, Turkey. Tel: +90-542-4868489; fax: +90-312-3553702; e-mail: sezaicubuk@gmail.com (S. Cubuk).

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Reply to Cubuk and Yucel

Aritoshi Hattori, Kenji Suzuki*, Kazuya Takamochi and Shiki Oh
Department of General Thoracic Surgery, Juntendo University School of Medicine, Tokyo, Japan

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We are really grateful to the letter by Cubuk and Yucel [1] regarding our recent study [2], and we are delighted by their thoughtful insights into our results.

Owing to the recent improvements in thin-section computed tomography (CT), smaller and fainter lung cancers, including sub-centimetre lung cancers, are being discovered in recent practice. Of these, lung adenocarcinomas showing a wide area of ground-grass opacity (GGO) are considered to have a good prognosis and, in most cases, their pathological features are minimally invasive [3]. Traditionally, however, postoperative nodal involvement is found in 15–20% of cases even in patients with clinical stage IA NSCLC showing a radiologically solid appearance [4, 5]. Therefore, radiologically determined solid lung cancer was considered to have more malignant potential compared with a tumour with GGO component, regardless of how small it is. These observations clearly indicated that ‘tumour size less than 1 cm’ does not indicate the absence of tumour spread, and limited resection should not necessarily be indicated even for solid sub-centimetre lesions, especially in patients with high SUVmax and a radiological pure-solid appearance on thin-section CT [2].

As mentioned by the authors, the invasiveness of the tumour is declared to be an important determinant of recurrence and survival. In this context, the differentiation degree of the tumour could be a prognostic factor in lung cancer, and the authors recommended lobectomy for pathologically high-grade tumours in sub-centimetre nodules. However, the intraoperative evaluation of pathological tumour differentiation appears to be difficult to be routinely performed in clinical practice. Our study focuses on analyses that predict pathological invasiveness based on the nodal metastases. This is because only clinical predictors can determine the proper surgical modes. In these contexts, we believe that radiological findings and SUVmax level are the useful clinical predictors of pathological nodal involvement. From this result, a thorough intraoperative evaluation of lymph nodes is needed to prevent loco-regional failure, if limited surgery is indicated for solid sub-centimetre lung cancer.

The role of FDG-PET in the evaluation of sub-centimetre lesions remains unclear [6]. Based on our study, however, FDG-PET is expected to be effective for predicting postoperative lymph node involvement and loco-regional recurrence in some selected patients with sub-centimetre lung cancer showing a pure-solid appearance on thin-section CT, because of the possibility that they are sensitive to FDG due to their invasive nature [2].

Finally, even in cases of sub-centimetre lung cancer, lymph node metastasis is frequently observed in patients with radiologically pure-solid nodule, especially for tumours that show a high SUVmax. Hopefully, our study will pave the way for a more refined treatment strategy in dealing with sub-centimetre lung cancer.

REFERENCES

**Is limited surgery recommended if nodal involvement cannot be ruled out?**

Alessandro Baisi*, Federico Raveglia, Matilde De Simone and Ugo Ciof

* Thoracic Surgery Unit, Azienda Ospedaliera San Paolo, University of Milan, Milan, Italy
b Department of Surgery, University of Milan, Milan, Italy

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We have read with interest the paper by Hattori et al. [1] about appropriate surgical strategy for sub-centimetre solid lung cancer. Indications for limited surgery of <1 cm tumours have become of greater concern in thoracic surgery, but, to date, there has been no definitive answer on the proper parenchymal resection extension (lobar, sub-lobar, non-anatomical) and on the correct nodal management (single biopsy, sampling, complete dissection). The authors have correctly distinguished <1 cm tumours in solid and non-solid nodules, and focused their attention on solid tumours (both part-solid and pure-solid). Their results are interesting since they have statistically determined that, even in case of <1 cm nodules, nodal metastases are frequently observed if the tumour has a pure-solid appearance and $SUV_{max} > 2.5$. These two factors also predicted survival. However, we have many concerns regarding the material and methods and, the conclusions.

Patients in both pure-solid and part-solid nodule groups underwent different kinds of surgical resection (lobectomy, segmentectomy or wedge resection) but the criteria adopted to determine surgical strategy are not reported. The authors only report that all patients had cN0 lung cancer. We think that such a dishomogeneous population could be a relevant bias in determining survival.

Also regarding nodal staging management, patients enrolled underwent very different procedures. In fact, some of those underwent complete dissection or nodal sampling, and, more surprisingly, 31% of candidates did not receive any nodal biopsy at all. The authors reported that, in some cases, this surgical strategy was determined by the patients’ poor general conditions. In our opinion, these criteria affect parenchymal resection extension, and not nodal dissection.

As for the conclusions, the authors do not explain if limited surgery is recommended for <1 cm solid nodules, and the only suggestion is intraoperative nodal evaluation to prevent loco-regional failure in pure-solid, $SUV_{max} > 2.5$ tumours. We think that two considerations are mandatory. First of all, nodal involvement could probably be excluded only in selected pure-ground-glass opacity (GGO) [2], therefore, we always perform and suggest nodal sampling in every other type of neoplastic pulmonary nodule. Secondly, if nodal involvement is suspected, oncological radicality is not guaranteed by limited parenchymal resection because of incomplete intraparenchymal lymphatic pathway resection [3].

We conclude that limited surgery should be considered as a second choice when lobar resection is not feasible, and nodal sampling should be performed in every patient affected by non-small-cell lung cancer.

**References**

