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Solid to ground-glass opacity ratio in lung adenocarcinomas: is it a new criterion for limited pulmonary resection?

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Early diagnosis of lung cancer is possible with low-dose computed tomography (CT) scan screening [1]. The collateral result of CT screening is frequent detection of ground-glass opacities (GGOs). Colleagues from the Far East have been contributing articles on GGOs for several decades.

Current paper by Huang *et al.* [2] from Taiwan on 789 patients is another such contribution to the literature. The article focuses on the ratio between solid and ground-glass components of lung adenocarcinomas using CT scans. The lesion is measured based on tomographic appearance, and clinical T stage is determined. GGO to solid tumour ratio ≥ 0.75 was found to have a positive prognostic impact upon univariate and multivariate analyses. Patients with a ratio ≥ 0.75 ($n = 267$) were found to have no lymph node involvement, very low recurrence rate (2.2%) and a 5-year survival rate of 95.5%, despite undergoing sublobar resections more frequently (wedge resection in 129, segmentectomy in 40, 63.3% in total). A similar study from Korea had shown that patients with clinical Stage Ia GGO-dominant adenocarcinomas (same ratio of ≥ 0.75) had an excellent prognosis, even though all of them underwent wedge resections [3].

The current study raises 3 questions:

1. Does GGO component of the tumour contribute to the prognosis of the patient or is it only the solid part that is the determinant of survival?

In the current study, the average diameter of the tumour in the GGO ≥ 0.75 group was 1 ± 0.57 cm, which means the average size of the solid part was 3 mm [2]. Even for tumours > 2 cm, the solid component would be 5 mm. The current paper also shows that survival was 100% for subcentimetre tumours. In a study by Sakurai *et al.* [4], 4 groups were formed from subcentimetre lung cancers. Pure GGO and $\geq 50\%$ GGO tumours had a 5-year survival of 100%, while tumours with $< 50\%$ GGO had 98% and pure solid tumours had 88%. It was recommended that tumour size staging should only be applied to completely solid tumours and pure or partly solid tumours should have a different stage group. In that

study, pure GGO tumours were recommended to be included in clinical Tis, and partly solid tumours in clinical T1a categories [4]. Several other studies also recommended the elimination of GGO components from T assessment, as those tumours have excellent overall and recurrence-free survival [5–7].

2. Is it acceptable to perform a sublobar resection in a patient with a solid component?

The current study shows that wedge resections were not associated with high loco-regional recurrence rate in the GGO ratio ≥ 0.75 group even if the size was > 2 cm. However, this data should be approached with caution, as the average solid component of the tumours is 0.17 ± 0.67 mm in the GGO ratio ≥ 0.75 group, whereas it is 21.8 ± 15.61 mm in the GGO ratio < 0.75 group. Thus, wedge resections were applied to tumours with very small solid components. In a long-term follow-up study, recurrence rates were 1.4% in pure GGO patients, whereas 15% in patients with GGO ratio < 0.75 [3]. In pure solid subcentimetre tumours that were treated with lobectomy, segmentectomy or wedge resection, 12 (13%) of the 90 patients recurred; 6 of them loco-regionally, 4 in distant site and 2 in both [4]. Thus, the decision for a limited resection should depend on the solid component of the tumour rather than the radiological size of the whole lesion.

3. What should we expect from these patients in terms of second primary lung cancers?

The current study also includes important data that would affect decision-making in terms of the magnitude of lung resection. Over a period of 10 years, 954 patients were operated on and 14 (1.5%) patients developed second primary lung cancers. When patients with pathological Stages 2–4 and those with early recurrence are excluded, the incidence of second primary cancers is higher, which means that we should think about a possible second lung cancer developing several years later, which may need additional lung resection. Thus, in pure GGO tumours or tumours

with GGO ratio ≥ 0.75 , it would be reasonable to proceed with a limited resection, given the risk of second primary lung cancer in the following years.

The current study strengthens the view that pure GGO or GGO-dominant tumours should be classified in a different clinical T category, regardless of their radiological size. Our surgical resection decision will certainly rely on this new classification which is being and will be validated with good quality studies in large number of patients.

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