In the recent issue of Annals of Thoracic Surgery, Hattori et al. reported the impact of the maximum tumor size and solid component size on the prognosis of patients with non-small cell lung cancer (NSCLC) (1). They evaluated 1,181 surgically resected cases of clinical N0 M0 NSCLC. The patients were divided into three groups according to the radiologically determined consolidation tumor ratio (CTR): the pure ground-glass opacity (GGO) group (CTR =0; n=168), the part-solid (0<CTR<1; n=448) group and the solid (CTR =1; n=565) group. The authors reported that the tumor size had a significantly impact on the 5-year overall survival (OS) of patients with radiologically solid tumors (≤20 mm, 83%; 21–30 mm, 75.4%; 31–50 mm, 56.2%; ≥51 mm, 45.3%; P<0.0001). In contrast, the tumor size did not influence the 5-year OS of patients with radiologically pure GGOs (100%, regardless of the tumor size) or part-solid tumors (≤20 mm, 97.7%; 21–30 mm, 94.6%; 31–50 mm, 93.4%; P=0.1028). In addition, the size of the solid component and CTR were not associated with OS in patients with part-solid tumor. They therefore concluded that the impact of maximum tumor size should only be applied to radiologically solid lung cancer (1).

It has been demonstrated that lung adenocarcinomas that exhibit part-solid nodules with a proportion of GGOs tend to be less invasive than solid tumors of the same size (2,3). Several authors have also demonstrated that the solid-area diameter without GGOs on HRCT is a more effective measurement of tumor nodules for predicting the prognosis of patients with NSCLC (4-8). Tsutani et al. reported that the solid tumor size on high-resolution CT had greater value for predicting high-grade malignancy and the prognosis in clinical stage IA lung adenocarcinoma (6,7). Kudo et al. reported that the CTR and consolidation size were important for predicting the pathological invasion factor and for diagnosing invasive adenocarcinoma in part-solid tumors (8). Recently, Takenaka et al. reported a retrospective study that drew attention to the tumor volume in NSCLC (9). According to the report, the whole tumor volume and the solid part volume were correlated with DFS in patients with surgically resected clinical stage IA NSCLC. In addition, the solid part volume was much better for predicting the prognosis than the tumor size, the whole tumor size and CTR. As mentioned above, many previous reports have suggested the adverse impact of the solid part of tumors on the prognosis in solid or part solid lung cancer (2-9). On the other hand, most previous studies evaluated the impact of the whole tumor size, consolidation size and CTR on the prognosis together with all types of CT findings (2-7,9).

In this study, the authors divided the patients into three groups based on the radiological findings and then calculated the OS separately for each of the groups. This was the strong point of the study. In addition, the number of enrolled patients was relatively larger and analyses were more detailed in comparison to previous studies. On the other hand, the surprising conclusions that were drawn in this study raise some concerns. First, while there were no statistically significant correlations among the CTR, tumor size and OS in part-solid tumors, the 5-year OS were decreased with an increase in the tumor size (≤20 mm, 97.7%; 21–30 mm, 94.6%; 31–50 mm, 93.4%) or CTR (0<CTR≤0.50, 98.4%; 0.50<CTR<1.0, 95.0%), respectively. Furthermore, lymphatic or vascular invasion was observed significantly more frequently in solid-dominant tumors.
(0.50<CTR<1.0) which were more frequently pathologically up-staged than the GGO-dominant tumors (0<CTR≤0.50). Only 7 (3.7%) patients in the GGO-dominant groups were pathologically up-staged. In contrast, 87 patients (31.4%) in the solid-dominant group were up-staged. In addition, post operative chemotherapy was administered to 12.8% of the GGO-dominant patients and 24.5% of the solid-dominant patients. Based on these results, there were significant correlations between recurrence-free survival and whole tumor size or CTR (1). According to the results, the authors should not easily conclude that neither maximum tumor size nor the solid component size is prognostic in patients with part-solid lung cancer.

One reason for the difference between recurrence-free survival and OS may be derived from the follow-up in this study. According to the report, the study population included patients who were treated from January 2008 to April 2013; the median follow up time was 43 months. Less than 3 years have passed since the last patient was followed in this study. Advances in chemotherapy have greatly improved post-recurrent survival. The median duration of post-recurrence survival has been reported to be 22.5–43.6 months (10-12). In particular, the median duration of post-recurrence survival in EGFR-mutation positive patients who receive EGFR-TKI therapy is reported to be 49 months (10). Moreover, more than 25% of the patients with part-solid GGO can receive the benefits of EGFR-TKI therapy after recurrence (13). Thus, when considering the OS among patients with surgically resected NSCLC, a much longer follow-up period may be necessary to clarify the actual relationships.

Another concern is how to handle tumors that cannot easily be classified according to the CT findings (such as consolidation and GGO) due to inflammation of the background lung or a scattered distribution, or other reasons. Actually, the authors previously reported that it was difficult to measure GGOs due to a scattered distribution in 12.4% of lung cancer patients (14). The authors evaluated scattered consolidation tumors as a new category of lung cancer according to the thin-section CT findings and reported outcome of those tumors was favorable (14). On the other hand, the authors did not mention such tumors in the present study (1).

In conclusion, Hattori et al. offered new insight into the diagnosis and prognosis of lung cancer. Further clinical studies using large cohorts, such as a national database are warranted to establish a new T category of lung cancer that more accurately reflects the prognosis than the whole tumor size.

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