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Key Words: ground-glass opacity, pure-solid tumor, prognosis, clinical-T classification

Discussion

Presenter: Dr Aritoshi Hattori

Dr Peter Licht *(Odense, Denmark).* Although data on GGOs are increasing, the surgical management criteria for these GGOs are not well defined, and we are looking forward to clear surgical guidelines. Dr Hattori and colleagues and other predominantly Japanese research groups have studied and published extensively on GGOs over the last decade. Your previous article showed the prognostic influence of any GGO component in early-stage lung cancer, which was read at the American Association for Thoracic Surgery meeting in Boston 2 years ago and recently published in the *Journal*. It was considered groundbreaking by many colleagues, and it certainly stirred up some debate because you are suggesting that the T descriptor of the International Association for the Study of Lung Cancer staging system should not only include the size and location of the tumor but also the behavior of the tumor, meaning that any component of a GGO should influence the T descriptor. It is a radical paradigm shift that you're suggesting. In today's presentation, you aimed to validate these retrospective single-institution retrospective study by using a multicenter prospective cohort.

I have a problem with your results, and I would caution about safely concluding that your earlier findings have now been validated. The baseline characteristics in the 2 groups of the JCOGO201 were significantly different regarding known and important prognostic indicators. Thus, there were substantially more men and more lymph node upstaging in the solid group. Likewise, there was more lymphatic and vessel infiltration in the solid group, and there were more lobar versus sublobar resections in the solid group. Pathology differed substantially, not only the histological subtypes, but also differentiation, which was lower in the solid group. Can we really rely on your conclusion? Please explain why you compared the 2 groups by simple univariate Kaplan–Meier survival analysis and why you did not use a multivariate analysis model such as a Cox proportional hazards model that would have allowed you to adjust for obvious differences in baseline characteristics?

Dr Aritoshi Hattori *(Tokyo, Japan).* In our previous report published in the *Journal*, we performed a multivariable analysis including several clinicopathological variables. But in this study, because of the prospective study data, and the study was started in 2002, there are not so many variables to assess by a multivariable analysis. Furthermore, the aim of the study was to validate whether the presence of a GGO component in itself is prognostic or not. So, we did not perform the multivariate analysis and only evaluated the survival outcomes.

Dr Licht. You certainly demonstrated that there's a difference and that GGO has an influence in your univariate analysis. I would have loved to see a multivariate model. My second question relates to the prevalence of early-stage lung cancer with a GGO component, which appears to be significantly more frequent in Japan and perhaps in all of Asia, compared with, for example, Europe or North America. What is your view on validating such data in other

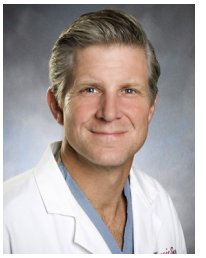
continents before we consider changing the T descriptor in the international staging system?

Dr Hattori. Yes. This result is based on the Japanese prospective study data. So, biologically, especially in Asian patients, GGO lung cancer is more common. But this feature is not always prevalent in all the regions. So, if possible, we need a further worldwide validation study.

Dr Licht. Indeed, a word of caution. My last question relates to the use of PET scan in these patients. Previous studies have shown significant differences in SUVmax values between part-solid and solid tumors. You also published on this topic earlier, and yet you decided to use the JCOG0201 cohort in which I believe none had a PET scan. Why would you choose this cohort to validate your previous findings where you did have a PET scan, and what do you think that PET could have added to the data of the JCOG0201?

Dr Hattori. The data with SUVmax are more impressive, but recently, PET scan is not always available all over the world. In contrast, T descriptor is used worldwide and must be a universal application. So, in that meaning, simply available GGO findings on CT scan is important, but for clinical research, PET scan is more effective for the treatment of lung cancer.

Unidentified Speaker. I just wanted to add that I agree with the findings. In the *Journal of Thoracic Oncology*, there will be a publication that says the same thing, that they should be divided, there should be a T descriptor for solid versus part-solid and nonsolid nodules, and we did the Cox regression, the Cox hazard, multivariate analysis, and all of them showed the same thing.



Dr Scott J. Swanson *(Boston, Mass).* Did you look at the ratio between the amount of GGO in the solid? I could imagine a millimeter of GGO might be different prognostically than 10 or 15 mm, and some people have looked at that before. Did that play into the prognosis, the ratio of the inflammation to the solid piece?

Dr Hattori. With regard to the solid and GGO relation?

Dr Swanson. Right. Of the ones that were part GGO, did it stratify out based on how much GGO relative to the solid component? Did you look at that at all?

Dr Hattori. In the study, we did not evaluate the consolidation to tumor ratio because the most focusing point was the presence or absence of GGO. There are several radiological findings in which it is difficult or impossible to measure the solid component size because of multiple, scattered, or island-shaped solid area compared with those of the single progress. But the most important finding is that regardless of the solid component size, the survival outcome was excellent if the tumor had a GGO component. So, in this study, we did not evaluate the ratio of solid or GGO component.