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In Response:

We thank Dr. Detterbeck for his interest and thoughtful comments about our systematic review. We agree with him that measuring fluorodeoxyglucose (FDG) uptake by using the standardized uptake value (SUV) is subject to many different sources of imprecision, as described in our discussion and further delineated in his letter.

Several working groups have recently developed guidelines for FDG positron emission tomography (PET) acquisition to help direct the research community.[1,2] These guidelines suggest that the resolution of PET scanners should be no less than half the tumor size diameter. These same guidelines suggest using a 12-mm region of interest centered around the most intense FDG uptake defined as "peak" SUV. Thus, SUV measurements for tumors smaller than 2.5 cm in size may yield important clinical information.

We agree with Dr. Detterbeck that tumor size is a potentially important confounding variable, because it is clearly associated with both the "exposure" (FDG uptake) and, arguably, with the outcome (survival). Accordingly, multivariable analysis is both necessary and sufficient to adjust for the confounding influence of tumor size.[3]

Two studies in our systematic review found that SUV was a significant predictor of survival after adjusting for tumor size.[4,5] In addition, we recently completed a study of prognosis in 75 patients with clinical stage Ia non-small cell lung cancer (NSCLC) and found that SUV was a significant predictor of survival both before and after adjustment for tumor size (hazard ratio: 1.21, 95% confidence interval 1.01–1.45 per 1 unit increment in SUVmax). There was a significant interaction between SUVmax and tumor size, such that the magnitude of the association between FDG uptake and survival was even stronger for patients with tumors larger than 18 mm (mean tumor diameter in our study).[6] Of note, only three of the nine studies in our review provided data on tumor size for patients with stage I NSCLC; in these studies, the mean diameters were 14, 24, and 31 mm, respectively.[4,7,8] We did not examine the effect of histology or attenuation characteristics because this information was not provided in the primary studies.

We continue to believe, along with others in the field, that a large, prospective, multicenter trial using standardized protocols is necessary to fully examine the potential use of PET FDG uptake as a biomarker for prognosis in NSCLC. We hope that our review stimulates additional interest in performing such a study.

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