Prognostic Value of FDG Uptake in Stage I Non–Small-Cell Lung Cancer

Fact or Bias?

To the Editor:

I read with interest the elegant study by Kwon et al[1] in which the authors demonstrated a significant correlation between survival and fluorodeoxyglucose (FDG) uptake on positron emission tomography in stage I non–small-cell lung cancer (NSCLC) patients. However, I found it surprising that tumor size, as reflected in the "T" classification (e.g., T1 versus T2a, or T1a versus T1b versus T2a), was not taken into account in the multivariate analysis of potential prognostic factors.

In the Discussion section,[1] among their study limitations, the authors correctly mention the fact that FDG uptake can be underestimated in small tumors (e.g., <2 cm) because of "volume averaging effects inherent in positron emission tomography." However, they fail to infer that this limitation could explain in part (if not all) their findings. I note that 36% of the study population (122 out of 336 patients) had T1aN0 tumors, and 40% of the study population (134 patients) had T2aN0 tumors.

Therefore, I wonder if the prognostic value attributed to FDG uptake could be in fact a mere tumor size effect as, by definition, tumor size reflected in the T classification is a strong and well-characterized prognostic factor in early-stage NSCLC.[2] Could the authors provide their study results after introducing the T classification in the multivariate analysis, and/or explain why they chose not to do so? Without such an analysis and positive results, I would remain reluctant to accept FDG uptake as an "independent" (statistically speaking) prognostic factor for survival in stage I NSCLC patients from this study.

Philippe Girard, MD
Département Thoracique, L'Institut Mutualiste Montsouris
Paris, France

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Address for correspondence: Philippe Girard, MD, Département Thoracique, L'Institut Mutualiste Montsouris, 42 boulevard Jourdan, 75014 Paris, France. E-mail: philippe.girard@imm.fr

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Reply to "Prognostic Value of Fluorodeoxyglucose-Positron Emission Tomography"

In Response

We appreciate Dr. Girard's comments about our recent study in the Journal of Thoracic Oncology on fluorodeoxyglucose-positron emission tomography in patients with early-stage lung cancer.[1] We recognize the importance of the T-stage and have reanalyzed our primary data. By analysis of variance and the Wilcoxon rank sum test, we show that the distribution of maximum standardized uptake value (SUV_{max}) within the three "T" groups (T1a/T1b/T2a) is significantly different ($p < 0.0001$).

Cox proportional hazards model was then used to assess the relationship between T-stage and survival with and without adjustment for SUV_{max} (uncategorized). After adjustment for T-stage, the effect of SUV_{max} remains statistically significant ($p = 0.003$). In our study, the effect of T-stage was not a statistically significant predictor of survival with or without adjustment for SUV_{max}. The lack of statistical significance for T-stage does not necessarily imply that the variable does not have prognostic importance. Rather, the power of this statistical analysis may be limited by there being only 134 deaths, which in general drives the power of a study to detect a clinically meaningful effect.

As we suggested, prospective treatment trials in early-stage disease could incorporate SUV_{max} to stratify patients for therapy, although we acknowledge that other features including T-stage need to be considered.

Woocheol Kwon, MD
Department of Radiology Wonju Severance Christian Hospital
Yonsei University Wonju College of Medicine Wonju,
Republic of Korea

Brandon A. Howard, MD, PhD
James E. Herndon, PhD
Edward F. Patz, Jr, MD
Duke University Medical Center
Durham, North Carolina

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Disclosure: The authors received a recent DOD grant on lung cancer. Duke University has a patent pending for a new therapeutic for lung cancer developed in the laboratory of Dr. Patz. Dr. Patz is the founder of Cue Biologics.

Address for correspondence: Edward F. Patz, MD, Department of Radiology, Duke University Medical Center, Box 3808, Durham, NC 27710. E-mail: patz0002@mc.duke.edu

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