with cause-specific mortalities (2). More sophisticated statistical methods have been newly presented to efficiently assess the relationship of exposure with multiple outcomes such as cause-specific mortalities (3).

Second, the authors used the Cox proportional-hazards model to compare the hazard of diabetes mellitus among 3 treatment modalities. However, the proportional-hazards assumption—one of the most important assumptions in the Cox model—has been violated in their study, as shown in their Figure 3C (1). Hence, variants of this model, such as the stratified or extended Cox regression model, must be applied to avoid any misleading findings (4).

REFERENCES

1. Umlauft M, Radojewski P, Spanjol PM, et al. Diabetes mellitus and its effects on all-cause mortality after radiopeptide therapy for neuroendocrine tumors. *J Nucl Med.* 2017;58:97–102.
2. Sashasai SR, Kaptoge S, Thompson A, et al. Diabetes mellitus, fasting glucose, and risk of cause-specific death. *N Engl J Med.* 2011;364:829–841.
3. Richardson DB, Hamra GB, MacLehose RF, Cole SR, Chu H. Hierarchical regression for analyses of multiple outcomes. *Am J Epidemiol.* 2015;182:459–467.
4. Kleinbaum DG, Klein M. *Survival Analysis: A Self-Learning Text.* New York, NY: Springer; 2006:161–200.

Reza Pakzad
Saeid Safiri*
Maragheh University of Medical Sciences
N. Moallem St.
Maragheh, Iran
E-mail: saeidsafiri@gmail.com

REPLY: We thank Drs. Pakzad and Safiri for their interest in our paper (1). We agree that there are a variety of methodologic questions to potentially be discussed (2–4), but we disagree with their criticism of our paper.

First, they prefer an analysis of cause-specific survival over overall survival. Understanding causes of death is an important aim but is, perhaps, less pressing a question in oncology. We considered a cohort of patients with locally advanced, metastatic neuroendocrine tumors, for whom death would likely be related to this diagnosis and the subsequent disease course. Consequently, overall survival is the single most important time-to-event outcome in oncology. Pakzad and Safiri also argue that a cause-specific analysis would have required "newly presented" methodology, whereas, in fact, the required methodology falls within the realm of the well-established statistics of competing risks (5). We used such competing-risks methodology in our analysis of the incidence of diabetes after DOTATOC.

Second, they express concern about a possible misspecification of the Cox model. This is, in fact, a common concern in the analysis of time-to-event data. Cox regression is commonly used to study not only overall survival but composites such as progression-free survival and competing risks—that is, the single components of a composite outcome. It is impossible to correctly specify the Cox model for all these endpoints (6), and analyses must consequently be interpreted as time-averaged hazard ratios (7). We believe that the great usefulness of the Cox model is partly due to the meaningful summaries of effect that such time-averaged hazard ratios provide. Pakzad and Safiri refer to our Figure 3C, illustrating no incident diabetes event in the ^{177}Lu-DOTATOC group, which theoretically corresponds to an infinite regression coefficient or a zero hazard ratio. In our analysis, we followed the advice of Therneau and Grambsch (section 3.4.1 (8)) in interpreting this result as representing a very pronounced reduction in the diabetes hazard.

REFERENCES

1. Umlauft M, Radojewski P, Spanjol PM, et al. Diabetes mellitus and its effects on all-cause mortality after radiopeptide therapy for neuroendocrine tumors. *J Nucl Med.* 2017;58:97–102.
2. Pakzad R, Safiri S. Prevalence and predictors of depression among general surgery residents: methodological issues to avoid misinterpretations. *Am J Surg.* January 25, 2017 [Epub ahead of print].
3. Pakzad R, Safiri S. Predictors of weight regain in patients who underwent Roux-en-Y gastric bypass surgery: methodological issues. *Surg Obes Relat Dis.* January 2, 2017 [Epub ahead of print].
4. Pakzad R, Safiri S. Poor sleep quality predicts hypogonadal symptoms and sexual dysfunction in male non-standard shift workers: methodological issues to avoid prediction fallacy [letter]. *Urology.* 2017;103:277–278.
5. Beyersmann J, Scheike TH. Classical regression models for competing risks. In: Klein JP, van Houwelingen HC, Ibrahim JG, Scheike TH, eds. *Handbook of Survival Analysis.* New York, NY: CRC Press; 2014:157–178.
6. Klein JP. Modelling competing risks in cancer studies. *Stat Med.* 2006;25:1015–1034.
7. Hjort NL. On inference in parametric survival data models. *Int Stat Rev.* 1992;12:355–387.
8. Therneau TM, Grambsch PM. *Modeling Survival Data: Extending the Cox Model.* New York, NY: Springer; 2013:57–58.

Maria Umlauft
Piotr Radojewski
Petar-Marko Spanjol
Rebecca Dumont
Nicolas Marincek
Attila Kollar
Philippe Brunner
Jan Beyersmann
Jan Müller-Brand
Helmut R. Maecke
Markus Laimer
Martin A. Walter*
The University Hospital of Bern
Freiburgstrasse 4
CH-3010 Bern, Switzerland
E-mail: m.a.walter@gmx.net

Brain ^{18}F-FDG PET Metabolic Abnormalities in Macrophagic Myofasciitis: Are They Stable?

TO THE EDITOR: We are writing this letter as an addition to our recently published study (1). Our aim is to add some insight to the evolution of the brain abnormalities that are observed with macrophagic myofasciitis (MMF). MMF is a chronic disease whose evolution is slow and whose symptoms may first occur

months to years after a vaccination containing aluminum hydroxide adjuvant particles (2). Nevertheless, the evolution of MMF is not fully understood or known. MMF-associated cognitive dysfunction is based on a tripod combining dysexecutive syndrome, memory impairment, and interhemispheric disconnection. One pilot study suggested that MMF-associated cognitive dysfunction appears to be clinically stable over time (3), and a recent study evaluating a support vector machine classifier suggested that the abnormalities observed with ^{18}F-FDG PET may be sensitive and can be used to monitor patients.

In order to evaluate the evolution of ^{18}F-FDG PET brain metabolic abnormalities, we retrospectively included 18 patients on whom an additional follow-up ^{18}F-FDG PET brain scan was performed because of persisting cognitive complaints (median age, 56.9 y [range, 22.3–66.2 y]). ^{18}F-FDG PET was performed following the same brain protocol acquisition as previously described (1). The Institutional Review Board (Comité de Protection des Personnes Ile-de-France VI), taking into account the retrospective nature of the study, approved the protocol (December 18, 2013) without requiring informed consent by the patients. The median time between the two examinations was 32.9 mo (range, 6.4–48.6 mo). Using analysis of covariance and negative or positive contrast in SPM12, we generated a t test mask by comparing the mean of the first cerebral ^{18}F-FDG PET acquisition with that of the second. The results of the comparison were collected at a P value of less than 0.005 at the voxel level, for clusters of at least 200 voxels (corrected for cluster volume).

Brain abnormality maps did not show any statistically significant negative or positive metabolic difference between the two examinations, confirming the idea that MMF is a slowly progressive or nonprogressive disease, in concordance with the fact that neurologic symptoms—even if they fluctuate—do not worsen or improve over time.

REFERENCES

1. Van Der Gucht A, Aoun Sebaiti M, Guedj E, et al. Brain ^{18}F-FDG PET metabolic abnormalities in patients with long-lasting macrophagic myofasciitis. *J Nucl Med.* 2017;58:492–498.
2. Gherardi RK, Coquet M, Chérin P, et al. Macrophagic myofasciitis: an emerging entity. Groupe d'Etudes et Recherche sur les Maladies Musculaires Acquises et Dysimmunitaires (GERMMAD) de l' Association Française contre les Myopathies (AFM). *Lancet.* 1998;352:347–352.
3. Passeri E, Villa C, Couette M, et al. Long-term follow-up of cognitive dysfunction in patients with aluminum hydroxide-induced macrophagic myofasciitis (MMF). *J Inorg Biochem.* 2011;105:1457–1463.

Paul Blanc-Durand*
Axel Van Der Gucht
Mehdi Aoun Sebaiti
Mukedaisi Abulizi
François-Jérôme Authier
Emmanuel Itti
*Hôpital Henri Mondor AP-HP
51 Ave. du Mal de Lattre de Tassigny
F-94010 Créteil, France
E-mail: paul.blancdurand@gmail.com