First, in our experimental animal model, in which steroids were not administered, DXR dose-dependently increased myocardial ^{18}F-FDG accumulation. Second, as suggested by Finessi et al. in their previous study (*6*), the extra-steroid administration might be a strong, independent thought "transient" variable able to affect myocardial ^{18}F-FDG accumulation. However, in our retrospective analysis, left-ventricular (LV) SUV was significantly increased in DXR-treated patients with respect to controls at the third PET study but remained persistently elevated 6 mo after chemotherapy (and eventually extra-steroid) discontinuation. Finally, and more importantly, when we focused on adriamycin, bleomycin, vincristine, dacarbazine–treated patients who accepted to undergo a later clinical evaluation, the occurrence of DXR-induced cardiotoxicity was significantly related to lower values of LV-SUV at baseline, in which patients did not received any therapy.

Altogether these observations seem to indicate that whatever its degree, the effect of cortisone therapy should have been transient and independent from baseline condition.

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Staging, Restaging, and Treatment Response Assessment in Lymphomas: What We Should Know

TO THE EDITOR: We read with interest the review published by Jadvar and colleagues (*1*) who highlight the main indications of ^{18}F-FDG PET/CT for restaging and treatment response assessment in oncology. They point out its clinical impact in 7 of the most commons cancers. However, we think it is necessary to give additional information on the role of ^{18}F-FDG PET/CT in lymphomas and to draw the attention of the readers to the most relevant papers in the field. Indeed, on the basis of the results of important studies, PET/CT has changed the management of many subtypes of lymphoma and we would like herein to address some key points.

Lymphomas are a heterogeneous group of tumors encompassing numerous entities with different prognosis and treatment. Lymphomas were usually classified as ^{18}F-FDG–avid or nonavid, depending of their subtypes. The role of ^{18}F-FDG PET/CT, initially limited to some of the ^{18}F-FDG–avid subtypes (Hodgkin lymphoma [HL], diffuse large B cell [DLBCL], and follicular lymphomas), is now recognized for the clear majority of lymphomas and has been recently demonstrated for T cell lymphoma, mantle cell lymphoma, and plasmablastic lymphomas. It should be emphasized that, among the main roles of ^{18}F-FDG PET/CT at staging, PET is now recommended as a noninvasive technique for the detection of bone marrow involvement in HL and DLBCL and has replaced the invasive bone marrow biopsy in HL and in some cases in DLBCL (*2*). This recommendation has improved the quality of a patient's life. The second point is the role of ^{18}F-FDG PET/CT in follicular lymphoma, where it has shown capabilities (*3*) in identifying the tumor site of transformation and guiding biopsy for diagnosis. For staging, it is important to underline that for the ^{18}F-FDG–avid lymphoma there is no more proven advantage than to perform separate contrast-enhanced CT because ^{18}F-FDG PET/CT has a much better sensitivity.

Excellent general reviews and consensus papers have documented the indications of ^{18}F-FDG PET/CT according to each clinical challenge for each subtype of lymphoma. Therefore, we will mainly focus on the response assessment to treatment and will report on the main studies demonstrating the usefulness of interim PET–guided therapy.

Lymphomas are certainly the oncologic application for which ^{18}F-FDG PET/CT provided the most significant improvement compared with conventional imaging. ^{18}F-FDG PET/CT allows a better identification of treatment failure and identifies patients who are deemed to benefit from salvage therapy. This evaluation at the end of the first line of treatment has been standardized on the basis of a Deauville 5-point scale and more recently reshaped in the Lugano classification (*2*). Compared with conventional imaging, ^{18}F-FDG PET/CT provides a more reliable evaluation (removing the CT unconfirmed responses) and a better specificity in response evaluation, and leads to a more accurate identification of nonresponder patients with a strong prognostic impact. This high clinical value has been documented in large series for the main common lymphomas such as HL, DLBCL, and follicular lymphoma and was also validated in cost-effectiveness studies (*4–6*).

Large prospective trials, especially in HL, have shown that an early evaluation of treatment response using interim PET/CT after 2 cycles of chemotherapy (PET2) could be used to adapt treatment strategy. The H10 trial for early-stage HLs has shown that PET-driven chemointensification (adriamycin, bleomycin, vincristine, dacarbazine [ABVD] to BEACOPP regimen) of PET2-positive patients significantly enhances the progression-free survival (*7*). Similar data have been shown for advanced HL in several trials in which interim PET2–negative patients followed the initial ABVD treatment whereas the therapy regimen for PET2-positive patients was intensified with BEACOPP (*8*). This interim PET–personalized

strategy is now used by several groups. A major advantage of this strategy is that PET-negative patients (>80% of the total population) can be spared from the adverse effects of BEACOPP.

Interim PET/CT has been also successfully evaluated to reduce long-term toxicity with treatment deescalation of advanced-stage HL (BEACOPP to ABVD) in the case of metabolic complete response after 2 cycles (*9*). In young high-risk patients with DLBCL, it has been shown that, when using the quantitative ΔSUV approach, interim PET was a good predictor of outcome and if the result was negative thus decreased the need for intensive treatment such as autologous stem-cell transplantation (ASCT) (*10*).

Beyond the first line of treatment, ^{18}F-FDG PET/CT has also a strong predictive value for relapsed or refractory HL and DLBCL patients. Especially, ^{18}F-FDG PET/CT positivity before ASCT is strongly predictive of treatment failure and allows patient selection for ASCT or other alternative therapy (*4*). Regarding classic MRI, it is not part of international recommendations, and diffusion-weighted MRI suffers from the lack of intercenter reproducibility.

If personalized medicine based on ^{18}F-FDG PET/CT performed early in the course of therapy is becoming a reality, it is mainly due to the amazing work done by the various national lymphoma groups and international meetings addressing specifically these topics (http://www.lymphomapet.com). This work has led to a significant improvement of disease control or toxicity reduction in several clinical situations.

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REPLY: We appreciate the letter to the editor written by Kanoun et al. from France. They address 2 important issues related to ^{18}F-FDG PET/CT in lymphoma, one is initial staging and the other is interim ^{18}F-FDG PET/CT for early evaluation of response to therapy. Regarding the first point, our review was solely focused on the utility of ^{18}F-FDG PET/CT in restaging and treatment response assessment (*1*). For initial staging, ^{18}F-FDG PET/CT has demonstrated high efficacy in many cancers including lymphoma (*2*). However, this will be a topic for another appropriate use criteria document. Kanoun et al. summarize some of the diagnostic value that ^{18}F-FDG PET/CT can offer in initial staging of lymphomas.

With regards to the role of ^{18}F-FDG PET/CT in the interim evaluation of response to therapy before completion of therapy, we did not include it in our analysis, as there is still no consensus based on the relatively limited available evidence (*3–7*), even if some groups have incorporated interim ^{18}F-FDG PET/CT in their clinical practice. However, we do agree that there is increasing literature on this specific topic (*8–15*). We feel that at this point the use of interim ^{18}F-FDG PET/CT for the early assessment of response to therapy in lymphoma should probably remain limited to clinical trials and not as routine clinical procedure; the only exception could be for those expert groups with experience in this setting within controlled environments (e.g., standardized protocols, homogeneous population, and double-blind reading) (*16*).

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