

Use and Abuse of PET Imaging in Hodgkin Lymphoma

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The use of PET scanning in the management of Hodgkin lymphoma is in several places. It is firstly in the staging of the disease. It is secondly in the intermediate assessment of response, and it is thirdly at the end of treatment, and we have emerging data that it is increasingly valuable in these three settings. For the staging of Hodgkin lymphoma, we now have evidence to suggest that if you have a FDG PET scan at the baseline as well as the conventional CT evaluation, this really is enough staging information to determine the anatomical extent of the disease, and the new guidelines which will be coming out in the *Journal of Clinical Oncology* shortly tell us that bone marrow biopsies as a routine in the evaluation of Hodgkin lymphoma are no longer required. So we can use PET scanning to substitute for bone marrow biopsies in order to determine the extent of the disease, and what we will find with that is a few patients will be upstaged, a few patients indeed will be down staged with PET scanning because you pick up things which are PET negative although they appear like a mass on the CT scan, for example, small pulmonary nodules. But in practice, it makes little difference to the management of Hodgkin lymphoma to do bone marrow as a matter of routine, so that is good for patients because it means we are going to do a lot less bone marrow biopsies both in clinical trials and in routine practice.

Interim PET scanning is increasingly being tested as a means of determining the response to treatment usually after the first 2 cycles. Using the five-point scale, the so-called Deauville score is a very reliable and reproducible method of determining how well the chemotherapy is working. So patients who have metabolically negative disease, reduced FDG uptake to below the level of the mediastinal blood pool have an extremely good prognosis both in retrospective series and in the prospective trials which have been carried out, so we can confidently say that patients who have a negative PET scan after the initial 2 cycles of treatment can safely carry on with the same treatment, and in many cases can avoid the need for consolidation radiotherapy. Those who have a positive PET scan, we know from historic series, have a much less favorable outlook, and there are now good arguments for escalating therapy so if a patient has been having ABVD, they may go on to BEACOPP or one of the more intensive regimens in order to produce a better response.

PET scanning at the end of therapy is increasingly used in order to evaluate the residual masses that we frequently see, particularly in patients who present with bulky disease, so the German

Hodgkin Study Group HD15 examined the use of PET scanning in patients with residual masses on the CT of more than 2.5 cm. What they found was that the PET negative masses could safely be left without consolidation radiotherapy while the PET-positive masses treated with involved-field radiation had a really very good outlook and certainly much better than we would have expected historically. So, the message there is that PET scanning at the end of treatment is a highly effective means to evaluate residual masses, and if it is clearly negative, we think that it is a good case for omitting consolidation radiotherapy in those.

In early Hodgkin lymphoma, interim PET scanning is increasingly used also to look at whether or not radiotherapy is required. And there are two studies which have completed recently—the U.K. rapid study and the EORTC Intergroup Study, both of which examined the idea of whether or not you could use a negative PET scan to rule out the need for consolidation radiotherapy at the end of treatment. What both of these showed was that although there was a small increase in the risk of recurrence if you do not do irradiate patients who are PET negative after 2 or 3 cycles of ABVD, in practice this has no impact on the overall survival figures, so patients can make a choice, and this is something which doctors will want to discuss with patients if they have a negative PET scan in early Hodgkin lymphoma whether they wish to receive the consolidation radiotherapy and absolutely minimize their chance of progression or whether they would rather omit the radiation therapy and avoid the chances of long-term toxicity. And of course, this will depend on the particular circumstances of the patient, so a man with a mass in the neck at the age of 40 may well opt to have consolidation radiotherapy because of the risks in the long term from treating that particular field will be very low, whereas the young woman with a mediastinal mass may much prefer to avoid consolidation radiotherapy because of the risks of breast cancer or of accelerated coronary disease, so what we are increasingly seeing is a much more personal approach to the determination of treatment algorithms in this setting.

One of the areas in which PET is unfortunately abused these days is in the surveillance of patients after the end of treatments, and we have really good data now to suggest that there is no value in repeated PET scanning for patients who have achieved a complete remission. It does not really increase the rate of pickup of recurrent disease which in general is something which the patient tells us about rather than the other way around, and there is really no evidence of any survival benefit from the exposure to quite substantial doses of radiation which people can be subjected to if PET scans are used in surveillance post-treatment.

Previously, there have been a lot of concerns about the reproducibility and standardization of FDG PET scanning. One of the things where I think we have made a lot of progresses is in the implementation of the five-point Deauville scale in order to be able to really compare results between trials. So the trials that have been conducted, in particularly the U.K. studies, have used a very strict quality control system where we standardize and calibrate the scanners that are being used with dummies to make sure that the absorption coefficients and so forth are

absolutely reproducible. But provided you do this and provided you use the five-point scale to report PET scans, what we find is a very high rate of concordance between observers in Hodgkin lymphoma. I am not sure it is quite the same for non-Hodgkin lymphoma, but in Hodgkin lymphoma certainly, we are comfortable with the idea that we can reliably read PET scans across a broad body of international observers and specialists in nuclear medicine and be confident that the results that we are getting will be reproducible and can be applied in routine practice, not just in specialist centers.