controversy II: has PET changed the approach to lymphoma patients?

120 HAS PET CHANGED THE APPROACH TO LYMPHOMA PATIENTS? (PROS)

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Positron emission tomography (PET) using the glucose analogue F-18-
fluorodeoxyglucose (FDG) is now widely used for staging and treatment monitoring in
patients with Hodgkin’s disease (HD) and non-Hodgkin’s lymphoma (NHL). In
contrast to many solid tumors, lymphomas are highly sensitive to chemotherapy or
radiotherapy and substantial long-term cure-rates of 90% for HD and 50% for
aggressive NHL are expected with the current treatment options. However, the
magnitude of late treatment-related morbidity and mortality especially in young HD
patients treated with combination chemo-radiotherapy as well as the fact that still
a considerable amount of NHL patients cannot be cured with standard induction
therapy, has tempered the initial enthusiasm. Accordingly, tailoring the intensity of the
treatment to individual patient basis has become very important and FDG-PET is
coming a valuable tool in this context.

PET can obtain complementary information in addition to conventional staging
procedures. A modification of disease stage and subsequent management is observed in
20% of patients but the impact on outcome remains unknown. The data today do not
support the use of PET as the only imaging modality for staging lymphoma because of
the potential for PET-negative tumor lesions that are detectable by conventional
imaging. PET findings not seen by CT should be confirmed by histopathology or
additional imaging before any change in management is contemplated. The most
important reason to perform a baseline PET is the fact that it facilitates the evaluation
of residual disease after therapy, currently the most established indication for PET in
lymphoma.

At the end of treatment, lymphoma patients often present with a residual mass but
only a minority of them will eventually relapse. Structural imaging can not reliably
discriminate fibrotic from viable tumor masses. Numerous studies have shown the
effectiveness of FDG-PET in the detection of residual disease at the end of therapy. The
increased use of combined PET-CT scanners resulted in the formulation of new
response criteria including both PET and CT results which were recently reported by
Cheson et al and are recommended for the evaluation of response at the end of
therapy in potentially curable and routinely FDG-avid lymphoma types (e.g. HL,
DLBCL). These criteria are based on a consensus reached by experts in the field, instead
of deducted from large clinical studies and it is therefore essential to check these criteria
for their validity.

PET and PET/CT after a few cycles of chemotherapy is now recognized as an
important prognostic factor in aggressive lymphoma. Dann et al. was the first to
demonstrate that risk-adapted treatment based on early PET-results in Hodgkin’s
lymphoma (HL) can reduce the cumulative dose of chemotherapy without impairment of
outcome. Although it was not shown that PET-adapted therapy improves outcome
yet, most clinicians tend to start salvage treatment when there is evidence of persistent
lymphoma on PET after few cycles of chemotherapy, and we may ask whether it is still
ethical to administer chemotherapy when it is unlikely that this will lead to a complete
remission. Recently, several large randomized controlled studies have started to
compare clinical outcome in patients with a positive interim FDG-PET who either
continue to receive the installed induction therapy or change to a more aggressive one.

121 HAS PET CHANGED THE APPROACH TO LYMPHOMA PATIENTS? (CONS)

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FDG-PET is increasingly become a standard part of the diagnosis, staging, restaging,
surveillance, and prognosis of patients with lymphomas. However, this use has thus far
exceeded the supporting data. PET should not be used as a diagnostic test as it is not
sufficiently specific, with many inflammatory and infectious disorders resulting in false
positive findings. Although, for staging, PET has greater sensitivity and specificity and
identifies more sites of disease than CT scan, in only about 15-30% of pts is the stage
altered, and in fewer than 15% of pts does it change treatment, with no evidence for
improvement in outcome. Numerous studies show that PET performed following 1 or
more courses of therapy predicts outcome, yet no available data demonstrate that
changing treatment on the basis of that information improves survival. The strongest
evidence supporting PET is as post-treatment restaging, however, it is mostly valuable
in histologies such as diffuse large B-cell NHL and Hodgkin’s lymphoma where
persistent disease generally warrants intervention if cure is to be achieved. For incurable
lymphomas, time-dependent endpoints, such as progression-free or overall survival are
generally more important. Available data fail to support the routine use of surveillance
PET scans for detecting disease recurrence. Many issues remain to be resolved before
PET can be considered a standard part of lymphoma management, including universal
availability, variability of equipment, standardization of interpretation, potential
differences among treatment regimens, and prospective validation of its usefulness. The
International Harmonisation Project developed guidelines for PET interpretation and
published revised response criteria for clinical trials including this technology. These
guidelines recognized the differences in FDG-avidity and relevant clinical trials
endpoints among lymphoma histologies. The CALGB 50303 comparison of R-CHOP
vs R-EPOCH and other international studies are prospectively validating whether
this technology has the potential for improving the outcome of lymphoma patients.