Letter to the Editor

PET/CT in Locally Advanced Breast Cancer: Time for a Guideline Change?


We read with interest the article by Hyland et al,1 in which 564 complete records of breast cancer patients with clinical stage II–III disease, who initiated screening for the I-SPY2 trial at 4 institutions, were reviewed to compare staging with FDG-PET/CT versus standard of care (SoC). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Breast Cancer recommend considering CT of the chest, abdomen ± pelvis, and bone scan in appropriate patients.2 At this time, the NCCN Guidelines do not recommend FDG-PET/CT, but state that “FDG-PET/CT may … be helpful in identifying unsuspected regional nodal disease and/or distant metastases when used in addition to standard imaging studies.”3 In the multicenter study by Hyland et al,1 PET/CT reduced false-positive risk by half and decreased workup for incidental findings, allowing for earlier treatment start. PET/CT was cost-effective, and at one institution was shown to be cost-saving. The de novo metastatic disease rate was 4.6%. However, the authors offer no results by stage or tumor/node combination to help clinical decisions. In another recent study published in JNCCN,4 among 196 patients with breast cancer, the overall upstaging rate to stage IV based on findings of unsuspected distant metastases was 14% (n=27), including 0% for stage IIA, 13% for stage IIB (10/79), 22% for stage IIIA (9/41), 17% for stage IIIB (5/30), and 37% for stage IIC (3/8). PET/CT had comparable costs than SoC and had lower radiation dose exposure.3 In another recent retrospective study, PET/CT demonstrated distant disease in 4.9% of 303 patients with stage I or II breast cancer, including 0.8% in stage IIA and 9.8% in stage IIB breast cancer.4 In a prospective study of 254 patients with breast cancer, we detected distant metastases with PET/CT in 2.3% of patients with stage IIA disease, and in 10.7% with clinical stage IIB disease.5 PET/CT had similar performances whatever the breast cancer subtype. Other studies also showed that PET/CT reveals distant metastases in 10% to 15% of patients with stage IIB disease, whatever the breast cancer subtype.5 Nodal metastases outside Berg-I/II levels should also be taken into account, identified with PET/CT, with impact on management.5,6 The 2 recent manuscripts in JNCCN add financial and radiation protection data to support the assertion that FDG-PET/CT should be used in patients with IIB–IIC breast cancer. We hope this growing evidence will lead consensus guidelines to include FDG-PET/CT for the systemic staging of IIB–IIC breast cancer at initial diagnosis.

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References


Authors’ Reply

To the Letter to the Editor by Groheux et al

The recent articles by Ko et al1 and our group2 contribute to the growing consensus that 18F-FDG PET/CT adds value to the care of locally advanced breast cancer. Retrospective and prospective evidence suggests that 18F-FDG PET/CT detects unsuspected axillary and distant metastases in a sizable proportion of patients, with detection rate increasing by stage.1–3 18F-FDG PET/CT is both more sensitive and specific than conventional imaging (CT + bone scan) in this patient population.2,5–7 Identification of distant metastatic disease directly affects management, potentially preventing costs, morbidity, and emotional burden associated with inappropriate treatments. In the ECOG-ACRIN E2108 trial, no survival benefit was observed in patients with de novo stage IV breast cancer randomized to surgery for locoregional control after a course of systemic therapy.8 Although some patients still opt to proceed with surgery in the setting of stage IV disease, recognition of distant metastases may lead some to revise their surgical preferences. Furthermore, in known stage IV disease, oncologists may opt to refrain from recommending chemotherapy with the goal of cure and are more likely to recommend a hormone-based therapy regimen, particularly for older patients or those with minimal visceral disease. Conversely, data from the phase II SABR-COMET trial...
suggest that stereotactic ablative radiotherapy in patients with solid tumors and 1 to 5 known metastatic sites improves overall survival.9 Although the number of patients with breast cancer in this study was small, the potential of “cure” in patients with oligometastatic disease has resonated, driving a rationale for the most sensitive imaging study to ascertain stage and sites of disease, not only at diagnosis but also along the trajectory of care.

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Breast Cancer as well as other guidelines do not yet recommend 18F-FDG PET/CT for first-line imaging in locally advanced breast cancer.10 This is at least partly related to concerns regarding higher up-front cost of 18F-FDG PET/CT. As physicians, we have a duty to balance individual patient well-being with prudent stewardship of limited healthcare resources. For staging locally advanced breast cancer, there is mounting evidence that 18F-FDG PET/CT is not just diagnostically superior but also cost-effective. In the Ko et al1 study, overall costs of 18F-FDG PET/CT and CT plus bone scan were comparable. In the Hyland et al2 study, costs were comparable or in some cases less for 18F-FDG PET/CT, driven by decreased biopsies and follow-up imaging to resolve equivocal or suspicious findings on CT and/or bone scan. Neither study evaluated cost savings associated with avoidance of futile surgery and/or radiation in accurately upstaged patients, which may further increase the cost-effectiveness of 18F-FDG PET/CT. Further study is needed to determine overall cost effectiveness of 18F-FDG PET/CT across different practice systems and patient populations. Additionally, we must determine the impact of more sensitive up-front staging on outcomes such as disease-specific and overall survival in patients with locally advanced breast cancer. Given the increasing evidence supporting the improved accuracy of 18F-FDG PET/CT, it is time to include this imaging modality in the guidance for metastatic workup for stage II and III breast cancer, given that it is the more patient-centered option.

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References

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