^{18}F-FDG PET/CT in Staging Patients with Locally Advanced or Inflammatory Breast Cancer: Comparison to Conventional Staging

David Groheux[1,2], Sylvie Giacchetti[3], Marc Delord[4], Elif Hindié[2,5], Laetitia Vercellino[1], Caroline Cuvier[3], Marie-Elisabeth Toubert[1], Pascal Merlet[1,6], Christophe Hennequin[7], and Marc Espié[3]

[1]Department of Nuclear Medicine, Saint-Louis Hospital, Paris, France; [2]B2T, Doctoral School, IUH, University of Paris VII, France; [3]Breast Diseases Unit, Department of Medical Oncology, Saint-Louis Hospital, Paris, France; [4]Department of Biostatistics and Bioinformatics, Institut Universitaire d'Hématologie, Paris, France; [5]Department of Nuclear Medicine, Haut-Lévêque Hospital, CHU Bordeaux, University Bordeaux-Segalen, Bordeaux, France; [6]Service Hospitalier Frédéric Joliot, SHFJ/I2BM/DSVCEA, Orsay, France; and [7]Department of Radiation Oncology, Saint-Louis Hospital, Paris, France

The prognosis of patients with locally advanced breast cancer (LABC) remains poor. We prospectively investigated the impact of ^{18}F-FDG PET/CT at initial staging in this clinical setting and compared PET/CT performance with that of conventional distant work-up. **Methods:** During 60 mo, consecutive patients with LABC (clinical T4 or N2–N3 disease) underwent ^{18}F-FDG PET/CT. The yield was assessed in the whole group and separately for noninflammatory and inflammatory cancer. The performance of PET/CT was compared with that of a conventional staging approach including bone scanning, chest radiography, or dedicated CT and abdominopelvic sonography or contrast-enhanced CT. **Results:** 117 patients with inflammatory (n = 35) or noninflammatory (n = 82) LABC were included. ^{18}F-FDG PET/CT confirmed N3 nodal involvement in stage IIIC patients and revealed unsuspected N3 nodes (infraclavicular, supraclavicular, or internal mammary) in 32 additional patients. Distant metastases were visualized on PET/CT in 43 patients (46% of patients with inflammatory carcinoma and 33% of those with noninflammatory LABC). Overall, ^{18}F-FDG PET/CT changed the clinical stage in 61 patients (52%). Unguided conventional imaging detected metastases in only 28 of the 43 patients classified M1 with PET/CT (65%). ^{18}F-FDG PET/CT outperformed conventional imaging for bone metastases, distant lymph nodes, and liver metastases, whereas CT was more sensitive for lung metastases. The accuracy in diagnosing bone lesions was 89.7% for planar bone scanning versus 98.3% for ^{18}F-FDG PET/CT. The accuracy in diagnosing lung metastases was 98.3% for dedicated CT versus 97.4% for ^{18}F-FDG PET/CT. **Conclusion:** ^{18}F-FDG PET/CT had the advantage of allowing chest, abdomen and bone to be examined in a single session. Almost all distant lesions detected by conventional imaging were depicted with PET/CT, which also showed additional lesions.

Key Words: ^{18}F-FDG-PET/CT; locally advanced breast cancer; inflammatory breast cancer; work-up; initial staging

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The prognosis of patients with locally advanced breast cancer (LABC) remains poor (*1*). LABC includes breast cancer in clinical stages IIIA (excluding T3N1), IIIB, and IIIC, according to the staging system of the American Joint Committee on Cancer (*2,3*). These patients had clinical N2, N3, or T4 disease. Within this entity, a distinction is made between inflammatory carcinoma (T4d) and noninflammatory LABC (*1*).

Guidelines from the National Comprehensive Cancer Network (NCCN) recommend a systematic locoregional work-up including physical examination, bilateral mammogram, sonography, or breast MR imaging (*3*). Systematic distant staging including chest diagnostic CT, abdominal or pelvic diagnostic CT or MR imaging, and bone scanning is also recommended for LABC (*3*). The use of ^{18}F-FDG PET/CT is optional (category 2B) (*3*). Experts of the NCCN consider that "FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious." It is, however, stated that "FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in LABC when used in addition to standard staging studies" (*3*).

In this prospective study, we aimed to investigate the role of ^{18}F-FDG PET/CT in LABC breast cancer patients. We examined the yield in the overall group, as well as separately in inflammatory carcinoma and noninflammatory LABC. We compared the performance of PET/CT with that of conventional distant work-up with the understanding that if ^{18}F-FDG PET/CT is helpful it should be a substitute rather than an additional imaging procedure. Finally, we examined the

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For correspondence or reprints contact: David Groheux, Service de Médecine Nucléaire, Hôpital Saint-Louis, Assistance Publique Hôpitaux de Paris, 1 Avenue Claude Vellefaux, 75475 Paris Cedex 10, France.
E-mail: dgroheux@yahoo.fr.
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prognosis for inflammatory and noninflammatory LABC and the impact of PET/CT results on prognosis.

MATERIALS AND METHODS

Patient Inclusion, Clinical Initial Staging, Treatment, and Follow-up

One hundred seventeen patients with LABC (based on clinical examination, mammography, sonography of the breast and axilla, and breast MR imaging) were prospectively included during a 60-mo period. Invasive breast cancer was biopsy-proven for each patient.

LABC was defined as a T4 primary tumor or N2 or N3 lymph node disease according to the classification of the American Joint Committee on Cancer (*2*): T4, tumor of any size with direct extension to the chest wall or to the skin (T4a/b/c) or inflammatory breast cancer (T4d); N2, metastases in ipsilateral level I/II axillary lymph nodes that are clinically fixed or matted or in ipsilateral internal mammary nodes in the absence of axillary lymph node metastases; N3, metastases in ipsilateral infraclavicular (level III axillary) or supraclavicular lymph nodes or in clinically detected ipsilateral internal mammary lymph nodes with clinically evident axillary lymph node metastases.

Inflammatory carcinoma (T4d) was defined as LABC with diffuse erythema and edema (peau d'orange) involving a third or more of the skin of the breast (*2*).

Exclusion criteria were a previous history of breast or other cancer, uncontrolled diabetes mellitus, pregnancy, and age younger than 18 y. The study followed the guidelines of the institutional ethical committee.

All patients had a conventional imaging work-up to search for distant metastases, as well as ^{18}F-FDG PET/CT before any treatment (Fig. 1). Conventional imaging and PET/CT were performed within a time interval of less than 10 d.

Treatment consisted of neoadjuvant chemotherapy, followed by surgery, locoregional radiotherapy, and adjuvant treatment tailored to breast cancer subtype. After initial treatment, patients had follow-up visits every 4 mo for 2 y and then twice yearly with clinical examination, as well as biologic and imaging follow-up as deemed appropriate (tumor marker, breast sonography, chest radiography, abdominal sonography).

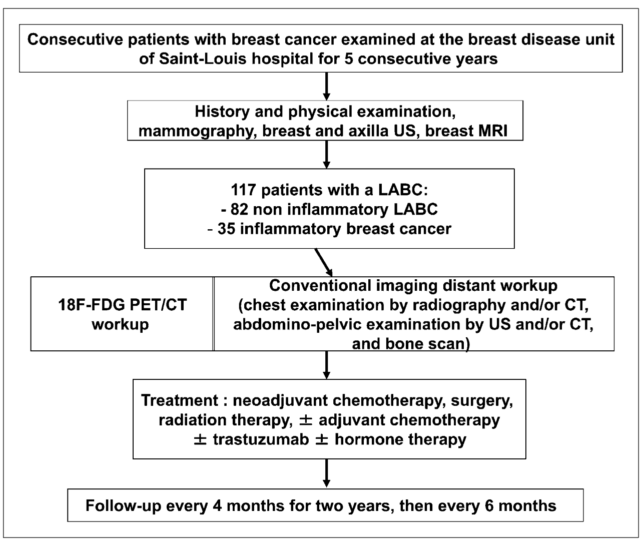

FIGURE 1. Study flow diagram. US = ultrasonography.

Conventional Distant Work-up

A conventional work-up, to rule out distant involvement, was performed according to routine practice in our institution (and current practice in France) and comprised bone scanning, chest examination by radiography or dedicated CT, and abdominopelvic examination by sonography or contrast-enhanced CT (Fig. 1). The choice between liver sonography and abdominal CT was left to the discretion of the oncologist, with some women receiving both examinations.

Planar whole-body bone scanning was performed on a Symbia camera (Siemens), 3 h after injection of 12 MBq of ^{99m}Tc-methylene diphosphate per kilogram of body weight. Most of the chest or abdominal CT procedures were performed on a Brilliance 16-MDCT scanner (Philips Healthcare), using routine clinical protocols with dose modulation, and contrast enhancement for abdominal imaging. A few patients underwent part of their conventional imaging outside Saint Louis Hospital. In those cases, the examinations that were already performed were not repeated.

^{18}F-FDG PET/CT Acquisition, Interpretation, and Modification in Staging and Management

The patients fasted for 6 h. Their blood glucose level had to be less than 7 mmol/L. ^{18}F-FDG (5 MBq/kg) was injected intravenously in the arm contralateral to the tumor using a venous line to prevent extravasation. Sixty minutes after injection, imaging was performed on a Gemini XL PET/CT device (Philips) combining germanium oxyorthosilicate–based PET and 16-slice Brilliance CT. The patients were allowed to breathe normally. No oral or intravenous contrast medium was used for the CT part. CT and PET data was acquired from the mid-thigh level to the base of the skull, with the arms raised. PET emission counts were collected over 2 min per table position, were acquired in 3-dimensional mode, and then were reconstructed using a 3-dimensional row-action maximum-likelihood algorithm.

PET/CT findings were interpreted by 2 nuclear medicine specialists who had no knowledge of the results of conventional imaging. If the interpretation of the 2 specialists differed, consensus was reached with the help of a third reader. Lymph node evaluation and interpretation of distant foci were performed as previously described (*4*). ^{18}F-FDG uptake was interpreted together with CT findings (*4*).

^{18}F-FDG PET/CT findings (regional lymph nodes and distant metastases) considered suggestive of malignancy were compared with biopsy results, further work-up, or patient follow-up. For bone foci, MR imaging was performed instead of biopsy.

^{18}F-FDG PET/CT was not used for the local evaluation of the breast tumor or multifocality, because previous reports demonstrated that whole-body PET/CT is suboptimal, in comparison to breast MR imaging (*5,6*).

We based stage modifications on findings of distant metastasis or lymph node involvement outside classic areas of axillary dissection with an impact on treatment management. N3 (infraclavicular, supraclavicular, or internal mammary lymph nodes) depicted by PET/CT changed the initial stage from IIIA or IIIB to IIIC. The stage of patients with distant metastasis was modified from IIIA–IIIC to IV.

Statistical Analysis

Modifications resulting from ^{18}F-FDG PET/CT in comparison to the initial clinical staging were evaluated in the whole population and then separately for inflammatory carcinoma and noninflammatory LABC. A χ^2 test for trends in proportions was performed to determine whether modifications in initial staging differed between noninflammatory LABC and inflammatory carcinoma.

The performance of staging using PET/CT was compared with that of the conventional staging approach. A Fisher exact test was used to compare ^{18}F-FDG PET/CT findings with bone scan findings for the number misclassified in each approach.

Disease-specific survival was measured in patients with inflammatory carcinoma and in those with noninflammatory LABC. Disease-specific survival was also measured in patients with and without distant metastases discovered on ^{18}F-FDG PET/CT, and comparisons between the 2 groups were assessed with a log-rank test.

A Cox model was used to explore a possible relationship between the intensity of ^{18}F-FDG uptake by the primary breast cancer (maximal standardized uptake value) and survival.

A P value of less than 0.05 was considered significant. Analyses were performed using R 2.12.0 statistical software (R Foundation for Statistical Computing).

RESULTS

One hundred seventeen patients were included in the study, 35 with inflammatory and 82 with noninflammatory LABC. Patient and tumor characteristics are outlined in Table 1.

Yield of PET/CT

All primary tumors showed ^{18}F-FDG uptake (mean maximal standardized uptake value, 8.7; range, 1.2–27.6). However, in 6 of the 117 patients, only weak uptake was seen, with standardized uptake values of less than 2.5. Of the 103 patients with clinical N+ disease, 100 had positive ^{18}F-FDG PET/CT findings at the axillary level.

^{18}F-FDG PET/CT confirmed N3 nodal involvement in stage IIIC patients and revealed unsuspected N3 nodes (infra- or supraclavicular or internal mammary) in 32 additional patients. In most patients, lymph node dissection and radiation fields were adapted on the basis of the PET/CT results.

Distant metastases were visualized on PET/CT in 43 patients (37%) (Table 2). Sites of distant involvement in the 43 patients included bone (n = 30), distant lymph nodes (n = 19), liver (n = 10), lung (n = 6), and pleura (n = 2). Chemotherapy was adapted to metastatic disease, some liver metastases were operated on or treated by radiofrequency, and some bone lesions were treated by radiation therapy.

Overall, ^{18}F-FDG PET/CT changed the stage in 61 of 117 patients (52%) (Table 2).

Considering ancillary findings, ^{18}F-FDG PET/CT allowed the depiction of another primary carcinoma in 2 patients (1 differentiated thyroid carcinoma and 1 colorectal carcinoma).

We separately evaluated the yield of PET/CT in inflammatory and noninflammatory groups. Thirty-five women had inflammatory carcinoma (29 stage IIIB and 6 stage IIIC). The stage was modified more frequently in patients with inflammatory carcinoma (22/35 [63%]) than in patients with noninflammatory LABC (39/82 [48%]), but this difference was not statistically significant (P = 0.12). ^{18}F-FDG uptake suggestive of distant metastases was seen in 16 of 35 patients (46%) with inflammatory carcinoma and in 27 of 82 patients (33%) with noninflammatory LABC (P = 0.18) (Table 2).

TABLE 1
Patients and Tumor Characteristics

Characteristic	No. of patients (of 117 total)
Noninflammatory LABC*	82 (70)
T1 N2 M0	1 (1)
T1 N3 M0	2 (2)
T2 N2 M0	11 (9)
T2 N3 M0	1 (1)
T3 N2 M0	14 (12)
T3 N3 M0	5 (4)
T4a/b/c N0 M0	13 (11)
T4a/b/c N1 M0	20 (18)
T4a/b/c N2 M0	12 (10)
T4a/b/c N3 M0	3 (3)
Inflammatory breast cancer*	35 (30)
T4d N0 M0	1 (1)
T4d N1 M0	16 (14)
T4d N2 M0	12 (10)
T4d N3 M0	6 (5)
Tumor type	
Invasive ductal carcinoma	98 (84)
Invasive lobular carcinoma	12 (10)
Other	7 (6)
Grade	
Grade 1	2 (2)
Grade 2	49 (42)
Grade 3	58 (49)
Unspecified	8 (7)
Estrogen receptor status†	
Positive	59 (50)
Negative	57 (49)
Unspecified	1 (1)
Progesterone receptor status†	
Positive	28 (24)
Negative	87 (75)
Unspecified	1 (1)
HER2 status‡	
Positive	22 (19)
Negative	94 (80)
Unspecified	1 (1)

*Clinical classification before PET/CT and conventional distant work-up.

†Tumors were considered positive for ER or for PR if >10% of cells showed staining by immunohistochemistry.

‡Tumors were considered to overexpress c-erbB-2 oncoprotein (HER2-positive) if >30% of invasive tumor cells showed definite membrane staining resulting in so-called fishnet appearance.

Data in parentheses are percentages.

Comparison Between ^{18}F-FDG PET/CT and Conventional Imaging Distant Work-up

For bone lesions, the performance of ^{18}F-FDG PET/CT was compared with that of bone scanning. ^{18}F-FDG PET/CT depicted bone metastases in 30 of 117 patients. Bone scanning revealed metastases in 19 of these women, was equivocal in 4 others (these cases were considered true-positive for the present analysis), and was falsely negative in 7 (Table 3). MR imaging or follow-up confirmed the

TABLE 2
Findings with ^{18}F-FDG PET/CT in 3 Different Groups

Results expressed on per-patient basis	Noninflammatory LABC	Inflammatory breast cancer	Whole population
Patients	82 (70)	35 (30)	117 (100)
Overall stage modifications*	39 (48)	22 (63)	61 (52)
Lymph nodes† outside level I and level II axillary levels	27 (33)	22 (63)	49 (42)
Internal mammary node involvement	12 (15)	10 (28)	22 (19)
Infraclavicular	19 (23)	15 (43)	34 (29)
Supraclavicular	13 (16)	13 (37)	26 (22)
Distant metastases‡	27 (33)	16 (46)	43 (37)
Bone	20 (24)	10 (29)	30 (26)
Lung	3 (4)	3 (9)	6 (5)
Pleura	2 (2)	0	2 (2)
Distant lymph nodes§	11 (13)	8 (23)	19 (16)
Liver	6 (7)	4 (11)	10 (8)
Second cancer	0	2 (6)	2 (2)

*Some women had extraaxillary lymph nodes as well as distant metastases.
†Some women had lymph node metastases in different areas.
‡Some women had distant metastases in different viscera.
§Distant lymph nodes were cervical, mediastinal, hilar, contralateral axillary, or abdominopelvic.
Data are *n,* with percentages in parentheses.

presence of bone metastases in the 11 patients who were positive on ^{18}F-FDG PET/CT, whereas their bone scan results were negative or equivocal.

PET/CT was falsely positive in 2 patients. Bone scanning was falsely positive in 5 patients with benign osteoarticular lesions.

The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in diagnosing bone lesions were, respectively, 76.7%, 94.2%, 82.1%, 92.1%, and 89.7% for planar bone scanning and 100%, 97.7%, 93.7%, 100%, and 98.3% for ^{18}F-FDG PET/CT. MR imaging was performed in cases of doubtful PET/CT and bone scan findings but not for each patient. The sensitivity of ^{18}F-FDG PET/CT would probably be lower if all patients had undergone MR imaging. Overall, PET/CT led to 2 misclassifications whereas bone scanning led to 12 misclassifications ($P = 0.013$). Figs. 2 and 3 show examples of bone metastases detected by PET/CT.

For lung and pleura evaluation, the performance of ^{18}F-FDG PET/CT was compared with that of dedicated CT and chest radiography. Six of the 117 patients had lung nodules detected by dedicated CT as well as by PET/CT. In 2 of these patients, pulmonary nodules had no ^{18}F-FDG uptake and were detected by the CT part of PET/CT. Additional distant lesions that were ^{18}F-FDG–avid were present in these 2 patients (1 patient had mediastinal lymph nodes and the other had bone metastases). Chest radiography was positive in only 2 of the 6 patients.

TABLE 3
Performance of PET/CT Versus Conventional Imaging Work-up to Depict Distant Metastases in Overall Series

Site	PET/CT	Bone scanning	Chest imaging (radiography or dedicated CT)	Abdominal imaging (sonography or enhanced CT)	Total*
Bone metastases	30	23†	—	—	30
Lung metastases	6‡	—	7	—	7
Pleura	2	—	1	—	2
Distant lymph node metastases	19	—	10§	1	19
Liver metastases	10	—	—	9‖	10

†19 positive bone scans and 4 suggestive nonequivocal bone scans.
*In total, 43 patients had distant metastases. Some women had metastases in different viscera.
‡Two women with lung metastases had no ^{18}F-FDG uptake; metastases were detected only on CT part of PET/CT imaging.
§Among 19 patients with lymph node metastases detected by PET/CT, 18 were positive in supradiaphragmatic area. All these patients had chest radiography, and 13 had dedicated chest CT.
‖Among 10 patients with liver metastases, 7 had liver sonography and 8 had abdominal enhanced CT.
Data are expressed per patient (not per lesion).

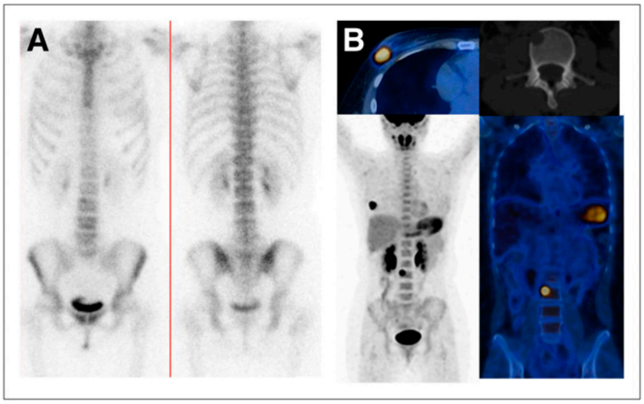

FIGURE 2. Bone scan (A) and PET/CT (B) findings in patient with clinical T4bN0 (stage IIIB), estrogen receptor–positive, progesterone receptor–positive, HER2-negative, grade 3 invasive ductal carcinoma of right breast. PET/CT showed primary tumor and depicted lytic metastasis of vertebral body of L3. MR imaging confirmed bone metastasis (not shown). Bone scanning was falsely negative (slight heterogeneity of upper border of L3 was considered suggestive of arthrosis).

^{18}F-FDG PET/CT was falsely negative at the lung level in 1 patient with lymphangitis. High-resolution dedicated CT showed evidence of septal thickening that was missed by the CT part of PET/CT recorded during free breathing. However, this patient was classified as stage IV with PET/CT because of ^{18}F-FDG–avid bone and liver metastases. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in diagnosing lung metastases were, respectively, 100%, 98.2%, 77.8%, 100%, and 98.3% for dedicated CT and 85.7%, 98.2%, 75%, 99.1%, and 97.4% for ^{18}F-FDG PET/CT.

^{18}F-FDG PET/CT showed pleural metastases in 2 patients. In 1 case, conventional imaging was also positive (pleural effusion with a lytic lesion of a rib), and in the other case, enhanced CT showed a tiny pleural effusion that was interpreted as benign (false-negative). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in diagnosing pleural metastases were, respectively, 50%, 100%, 100%, 99.1%, and 99.1% for dedicated CT and 100%, 99.1%, 66.7%, 100%, and 99.1% for ^{18}F-FDG PET/CT.

The performance of ^{18}F-FDG PET/CT and conventional imaging in detecting distant lymph node metastases was evaluated separately at the supradiaphragmatic and infradiaphragmatic levels. Of the 117 women, 18 showed supradiaphragmatic (cervical, mediastinal, hilar, or contralateral axillary) lymph node involvement on ^{18}F-FDG PET/CT. Dedicated CT missed mediastinal lymph nodes in 3 patients. Chest radiography did not detect involved lymph nodes in any patient.

Four patients had ^{18}F-FDG PET/CT findings suggestive of abdominal or pelvic lymph node involvement (3 were also N+ at the supradiaphragmatic level). One woman had a limited follow-up, and no biopsy could be performed. Among the 3 others, 2 were true-positive and 1 was false-positive (^{18}F-FDG uptake in pelvic lymph nodes due to cryptosporidiosis in an HIV-positive patient). Among these 3 patients, conventional imaging was true-positive in the first, false-negative in the second, and true-negative in the third.

For the detection of liver metastases, the performance of ^{18}F-FDG PET/CT was compared with that of abdominal enhanced CT and liver sonography. Of the 117 patients, 9 had liver metastases on abdominal enhanced CT or ultrasound. PET/CT depicted liver metastases in all 9 patients and showed a metastasis in an additional patient in whom sonography was negative, and the case was confirmed by MR imaging and follow-up (Table 3). In 3 cases, PET/CT helped to settle doubtful findings on conventional imaging. In 1 patient, liver sonography was suggestive of metastasis (false-positive) but PET/CT and MR imaging were negative. A second patient had a biliary cyst, and the last patient had a liver angioma; these lesions were not ^{18}F-FDG–avid.

In total, in this series of 117 patients with LABC, ^{18}F-FDG PET/CT detected all distant lesions evidenced by the combination of conventional imaging, except in 1 case (of pulmonary lymphangitis). Also PET/CT showed additional unknown lesions in bone, pleura, distant lymph nodes, and liver (Table 3). Distant metastases were visualized on PET/CT in 43 patients. Only 28 of these 43 patients (65%) had distant metastases reported on unguided conventional imaging.

Relationship Between ^{18}F-FDG PET/CT Findings and Survival

Among the 104 evaluable patients with adequate follow-up, disease-specific survival was significantly shorter in inflammatory cancer than in noninflammatory LABC (log-rank $P = 0.02$). PET/CT at initial staging showed metastases in 40. Disease-specific survival was significantly shorter in the 40 M1-PET/CT women than in the 64 M0-PET/CT women (log-rank $P = 0.002$), with a 3-y disease-specific survival of 53% versus 78% (Fig. 4).

No correlation was found between maximal standardized uptake value of the primary breast tumor and survival in

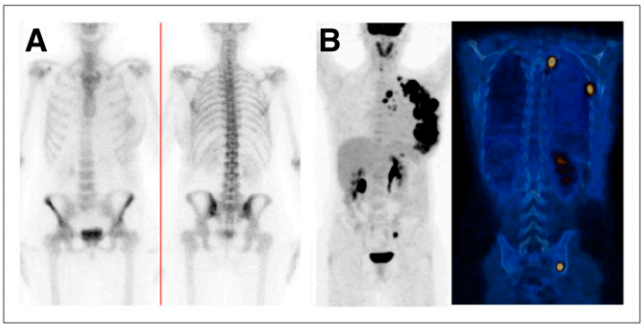

FIGURE 3. Bone scan (A) and PET/CT (B) findings in patient with clinical T4bN3 (stage IIIC) estrogen receptor–positive, progesterone receptor–negative, HER2-negative, grade 3 invasive ductal carcinoma of left breast. PET/CT showed locally advanced primary breast cancer with axillary and supraclavicular lymph nodes, as well as numerous distant metastases to bones and pleura. Bone scanning was true-positive, showing faint uptake at lower part of left sacroiliac joint.

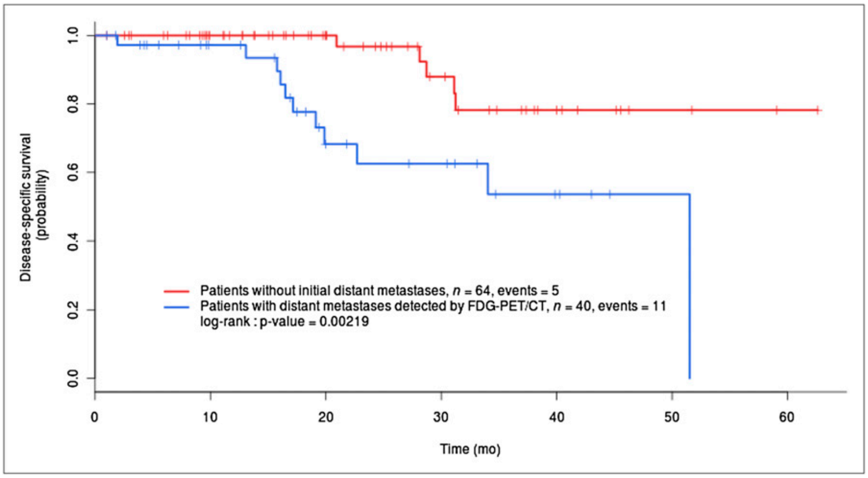

FIGURE 4. Kaplan–Meier disease-specific survival for 104 patients with adequate follow-up.

inflammatory LABC (P = 0.35), in noninflammatory LABC (P = 0.88), or in the overall population (P = 0.98).

DISCUSSION

In this prospective study, ^{18}F-FDG PET/CT provided powerful information that had a potential impact on management in 61 of 117 patients with locally advanced or inflammatory breast cancer (52%). PET/CT revealed unsuspected N3 lymph nodes (infra- or supraclavicular or internal mammary) in 32 patients and depicted distant metastases in 43 patients. Detection of extraaxillary lymph nodes may have a major impact on locoregional treatment by, for example, defining the target volume for radiotherapy or the extent of the surgical clearance (*7,8*). Early detection of distant metastases has an impact on systemic treatment and can lead to local treatment (e.g., liver surgery or radiofrequency ablation, radiotherapy for bone metastases).

^{18}F-FDG PET/CT identified more distant metastases in patients with inflammatory carcinoma than in patients with noninflammatory LABC (46% vs. 33%), although the difference did not reach significance levels.

Bone is the most frequent site of distant involvement in breast cancer (*9*). In our study, all patients with metastases detected by bone scanning were also positive on PET/CT. Seven additional cases (essentially bone marrow involvement or lytic metastases; Fig. 2) were detected only by PET/CT. Some teams noted that osteoblastic metastases showed lower metabolic activity and were frequently undetectable by ^{18}F-FDG PET when performed on a PET-alone instrument; they advised performing bone scanning in addition to ^{18}F-FDG imaging. Yet, these osteoblastic metastases are usually visible on the CT part of PET/CT (even in the absence of ^{18}F-FDG uptake) and should not escape detection when current hybrid PET/CT is used. In agreement with other recent studies (*10–12*), our data showed that PET/CT outperformed bone scanning. However, most of the examinations were performed with planar bone scanning (not with SPECT/CT). It is expected that the use of routine SPECT/CT (over the spine and pelvis) would increase the sensitivity and specificity of bone scanning. Further improvement can also be expected with bone scanning with ^{18}FNa PET/CT.

In the present study, similar to the practice in most PET/CT centers, data were acquired from the mid-thigh level to the base of the skull, with the arms raised. Most of the skull, upper extremities, and lower extremities would not be included in the imaged field of view. On the other hand, whole-body bone scanning is a true whole-body method. When ^{18}F-FDG PET/CT is used in lieu of bone scanning, this point should be taken into consideration.

Brain metastases can be missed by ^{18}F-FDG PET/CT examinations. Dedicated brain imaging is probably useful as an adjunct to PET/CT in some categories of patients at high risk of brain metastases (patients with an HER2-overexpressing breast tumor or with a triple-negative tumor).

Whole-body PET/MR imaging is a potential future possibility to further improve sensitivity in staging breast cancer patients in a single examination (*13*).

Regarding pulmonary parenchyma, PET efficiently detected supracentimetric pulmonary nodules. However, because of the partial-volume effect and respiratory movements, PET lacked sensitivity for smaller nodules. In our series, multiple small nodules were considered metastases even in the absence of ^{18}F-FDG uptake. Reporting of the CT part of the PET/CT examination obviously improved the sensitivity of PET/CT in comparison to stand-alone PET. However, free-breathing CT remains less efficient than standard diagnostic thoracic CT. Lymphangitis in 1 patient was detected only by enhanced diagnostic CT.

^{18}F-FDG–avid mediastinal lymph node metastases are not rare in cases of LABC or inflammatory carcinoma (*8,10,14,15*). In 2 studies (*14,15*), PET/CT depicted mediastinal lymph nodes in about 20% of women with inflammatory carcinoma. In the present series, 18 of 117 patients (15%) had distant lymph node involvement in the thorax. Lymph nodes larger than 1 cm were easily detected by enhanced CT in our study, as they were in others (*14,16*), although overall sensitivity was lower than for ^{18}F-FDG PET/CT, with 3 falsely negative patients. In agreement with the recent report of

Koolen et al. (*10*), chest radiography did not detect mediastinal lymph node metastases in any patient. Distant lymph nodes in the abdomen were rare and were usually concomitant with thoracic lymph node involvement.

^{18}F-FDG PET/CT had a sensitivity for liver metastases similar to that of conventional imaging. PET/CT helped to classify doubtful findings on conventional imaging (angiomas and cysts), as also reported by Fuster et al. (*17*).

We used the CT part of PET/CT not only for lesion localization but also for diagnosis. Without the CT part, specificity and sensitivity would have been lower, with a higher risk of missing lung nodules and bone lesions not avid for ^{18}F-FDG. Many PET sites are still using PET-only scanners. In this setting, conventional imaging is complementary to stand-alone PET.

In the present study, we did not use CT contrast agents during PET/CT. There is now a progressive shift toward the use of contrast enhancement, which is expected to further improve PET/CT performance (*6,18*).

At the moment, NCCN experts leave the use of PET or PET/CT in LABC as an option, suggesting its use when findings on conventional imaging are equivocal (*3*). One reason for the current reticence to recommend use of PET/CT in LABC staging is that although studies showed PET/CT to be highly efficient in depicting distant metastases, the impact on survival remains unclear. PET/CT is a fairly recent technique, and the relationship between initial staging with PET/CT and survival has not yet been extensively studied. Alberini et al. followed a group of 42 patients with inflammatory carcinoma (median follow-up, 44 mo) (*14*). They found a trend toward longer survival for M0 than for M1 patients—a trend that nearly reached significance ($P = 0.06$). Among the 104 evaluable patients in our series, we found a significantly longer disease-specific survival in the 64 M0-patients than in the 40 women with distant metastases evidenced by PET/CT (log-rank $P = 0.002$). The 3-y survival in these groups was, respectively, 78% and 53%.

CONCLUSION

In this series of 117 LABC patients, almost all lesions detected by conventional imaging were also depicted with ^{18}F-FDG PET/CT, which also showed additional lesions. PET/CT had the clear advantage of examining the chest, abdomen, and bones in a single session. ^{18}F-FDG PET/CT offered powerful prognostic stratification at initial staging.

DISCLOSURE

The costs of publication of this article were defrayed in part by the payment of page charges. Therefore, and solely to indicate this fact, this article is hereby marked "advertisement" in accordance with 18 USC section 1734. No potential conflict of interest relevant to this article was reported.

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