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Original Research Article

Is ^{18}F-fluorodeoxyglucose-positron emission tomography or computed tomography scan a triaging technique for axillary dissection in breast cancer?

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ABSTRACT

Background: To determine if fluorodeoxyglucose-positron emission tomography/ computed tomography (FDG PET/CT) scan identifies axillary nodal disease in conjunction with ultrasound (US) guided fine needle aspiration cytology (FNAC) of suspicious axillary nodes in breast cancer. To determine if this will enable axillary node dissection upfront, avoiding sentinel lymph node biopsy (SLNB).
Methods: Study was performed in Apollo main hospital, Off Greams-lane, Greams road, Chennai IRB approval was obtained from institutional ethical committee-bio medical research-Apollo hospitals, (IEC application number: AMH-C-S-029/04-23). Informed consent was obtained from all the patients who met the inclusion criteria. The 61 patients with cT1-T3, N0-N1, and M0 disease underwent ^{18}F-FDG-PET/CT scans after mammographic evaluation and an US guided FNAC of nodes which were seen to be suspicious in the mammogram and correlated US of the Axilla. All patients underwent axillary lymph node dissection (ALND levels 1 and 2) without a SLNB.
Results: Out of 61 patients, 40 (65.6%) had axillary node uptake on PET/CT scan. But, after ALND, only 32 patients were found to have metastatic nodes on the histopathological examination (HPE) of the operative specimen. Out of these 32 patients, results for axillary metastasis had been noted on PET/CT, US, and guided FNAC in 18 patients (56.3%). Discordant results were noted in 14 (43.8%) patients, 29 patients had no metastasis on HPE. Negative results for axillary metastasis were noted on PET/CT, US and guided FNAC in 26 patients (89.7%). The results were discordant in 3 (10.3%) patients.
Conclusions: An expanded preoperative axillary assessment does not have sufficient reliability to serve as a reliable triaging technique in axillary management. Concordant positive results may permit directly proceeding to ALND without resorting to SLNB. Concordant negative results may similarly permit avoiding axillary surgery. But discordant results warrant SLNB for assessment of axilla.

Keywords: PET CT, Breast cancer, Axillary lymph node, US guided FNAC, ALND, SLNB

INTRODUCTION

The ^{18}F- FDG - PET/CT scanning for the staging of clinical stage 1, 11 and operable stage 111 breast cancer is not recommended.[1-3] This is due to its unreliability in the detection of axillary nodal metastases.

But, when a positive PET/CT scan is concordant with US and US guided FNAC of suspicious axillary nodes, it may allow the surgeon to proceed directly to ALND avoiding a SLNB. This is due to the high specificity of US guided FNAC.[4]

The primary objective of this retrospective study was to evaluate the status of axillary nodes by a combination of the above preoperative investigations in our institution. Whether concordant results for metastasis (by US and US guided FNAC coupled with PET/CT scan) will allow undertaking ALND up front, without resorting to SLNB. And if pre-op results are negative for metastasis, whether ALND can be avoided all together or should SLNB be undertaken. This will have the double benefit of avoiding the long term morbidity of ALND, as well as saving time and the expense of SLNB particularly with enhanced pathological assessment by IHC staining and multi-step sectioning to improve the detection of micro metastasis.

METHODS

This study was performed in Apollo Main hospital, Off Greams lane, Greams road, Chennai. After IRB approval was obtained from institutional ethical committee-bio medical research-apollo hospitals (IEC Application Number: AMH-C-S-029/04-23). Informed consent was obtained from all the patients who met the inclusion criteria. This study was undertaken of primary breast cancer patients presenting to our unit as outpatients from January 2020 to December 2022. Patients with T1-T3, N0-N1, M0 were included in the study.

Patients with Tis, inoperable T3-T4, multifocal and multicentric cancer, inflammatory breast cancer, pregnancy associated breast cancer, bilateral breast cancer, patients who had undergone neo adjuvant chemotherapy/endocrine therapy for down staging, those with severe co morbidities, history of previous breast and axillary surgery, and appropriate patients opting for SLNB were excluded. Also, patients who had undergone PET/CT scans outside our Institution were excluded.

All 61 patients underwent clinical examination of the breast and axilla, mammography with correlated US and core needle biopsy of the primary tumour. Those with suspicious axillary nodes on imaging underwent an US guided FNAC by a single dedicated interventional radiologist. A ^{18}F FDG-PET/CT scan was undertaken and the status of uptake by the axillary nodes was recorded and reported by seven dedicated radiologists. Patients with no abnormal nodes on mammography with correlated US or those who were FNAC negative despite the imaging of suspicious nodes were offered SLNB. Those who refused SLNB and opted for direct ALND were included in the study.

All patients underwent surgery for the primary tumour (Mastectomy) and ALND levels 1 and 2, and HPE report of axillary node status was studied. Outcome studied was to determine if the status of axillary nodes as determined by a combination of PET/CT with US and Image guided FNAC of axillary nodes correlated with histopathological status of ALND specimens, thus justifying direct ALND. And if expanded axillary assessment negative for metastases, if HPE status of axillary nodes negative too.

Statistical analysis

Statistical analysis was by SPSS (IBM® SPSS® software, version 29.0.

RESULTS

A total of 61 patients were studied. (Table 1 and 2). Their age ranged from 30-72 years. (Mean age 49.62 years, median age 48 years). Mammography with correlated US revealed suspicious nodes in the ipsilateral axilla in 22 patients. On guided FNAC, 18 (81.8% of the 22 patients or 29.5% of the 61 patients) of these patients were found to have metastasis. The sensitivity, specificity, PPV, NPV and accuracy of FNAC in the context of image guided FNAC of suspicious axillary nodes was: 53.12%, 96.55%, 94.44%, 65.12% and 73.77% respectively.

A PET/CT scan indicated the presence of metastatic axillary nodes in 40 patients (65.6%). When the standardised uptake values were analysed, SUVs ranged from a minimum of 0.0 to a maximum of 20.5 for metastatic nodes proven to be so on later on HPE (Mean 5.02, SD 4.82, median 3.55 and IQR of 4.3). For non-metastatic Nodes, the SUVs ranged from a minimum of 0.0 to a maximum of 12.7. (Mean 1.50, SD 2.60, median 0.00 and IQR 2.3). This difference in SUV uptake was statistically significant ($p<0.001$).

After ALND, pathological examination revealed that there were thirty-two patients (52.5%) with metastasis and the rest were non metastatic (29 patients, 47.5%). Of the thirty-two patients, twenty seven patients (84.4%), had been reported as node positive on PET/CT (True positive). In five patients (15.6%), the PET/CT had shown no significant nodal disease (False negative). Of the twenty-nine non metastatic patients, 13 (44.8%) had been reported to be positive by PET/CT (False positive). Sixteen patients (55.2%) as negative for nodal metastasis (True negative). The performance of PET/CT as an individual modality to assess axillary node status against HPE of nodes which is the gold standard is set out in Table 3 and 4.

Further analysis was done pooling together the results of the PET/CT scans with U/S and guided FNAC of suspicious nodes. 18 (56.3%) of the 32 patients were reported as metastatic on PET/CT with US + FNAC (True positive). Fourteen of them (43.8%) were reported as not having metastatic disease (False negative).

Similarly, of the 29 patients who had no metastatic disease on HPE, 26 patients (89.7%) were reported as having no metastasis (True negative) and only 3 patients were reported as metastasis (False positive). The sensitivity, specificity, and other parameters of PET/CT in conjunction with the expanded assessment provided by Imaging (U/S) and FNAC against the gold standard of HPE is set out in Table 5 and 6.

Table 1: Demographic and investigation characteristics, (n=61).

Variables	N	Percentage (%)
Age (in years)		
30-40	12	19.7
41-50	24	39.3
51-60	12	19.7
>60	13	21.3
U/S axillary nodes		
Suspicious nodes	22	36.1
Normal nodes	39	63.9
FNAC axillary nodes		
Metastatic nodes	18	29.5
Non-metastatic nodes	43	70.5
PET/CT axilla		
Metastatic nodes	40	65.6
Non-metastatic nodes	21	34.4

Table 2: Tumour stage and type.

Variables	N	Percentage (%)
pT stage		
T1	13	21.3
T2	44	72.1
T3	4	6.5
pN stage		
N0	29	47.5
Nmic	1	1.6
N1	17	27.9
N2	11	18.0
N3	3	4.9
Histological type		
Infiltrating duct carcinoma	54	88.5
Infiltrating duct carcinoma + infiltrating lobular carcinoma	3	4.9
Infiltrating lobular carcinoma	2	3.2
Other	2	3.2
Grades		
Grade1	6	9.8
Grade 2	33	54.1
Grade 3	22	36.1

Table 3: Comparison of PET/CT axilla (alone) against HPE of axillary nodes.

PET/CT axilla	HPE nodes			
	Metastatic nodes		Non-metastatic nodes	
	N	%	N	%
Metastatic nodes	27	84.4	13	44.8
Non-metastatic nodes	5	15.6	16	55.2
Total	32	100	29	100.0

Kappa value=0.4; p=0.001.

Table 4: Concurrence of PET/CT axilla with HPE.

Statistic	Value (%)	95% CI
Sensitivity	84.38	67.21 to 94.72
Specificity	55.17	35.69 to 73.55
PPV	67.50	57.46 to 76.16
NPV	76.19	57.29 to 88.42
Accuracy	70.49	57.43 to 81.48

Table 5: Comparison of PET/CT with U/S and FNAC against HPE of axillary nodes.

PET/CT axilla with U/S + FNAC	HPE nodes			
	Metastatic nodes		Non-metastatic nodes	
	N	%	N	%
Metastatic nodes	18	56.3	3	10.3
Non-metastatic nodes	14	43.8	26	89.7
Total	32	100.0	29	100.0

Kappa value=0.45; p=0.001.

Table 6: Concurrence of PET/CT axilla and U/S + FNAC with HPE of axillary nodes.

Statistic	Value (%)	95% CI
Sensitivity	56.25	37.66 to 73.64
Specificity	89.66	72.65 to 97.81
PPV	85.71	66.32 to 94.81
NPV	65.00	55.16 to 73.71
Accuracy	72.13	59.17 to 82.85

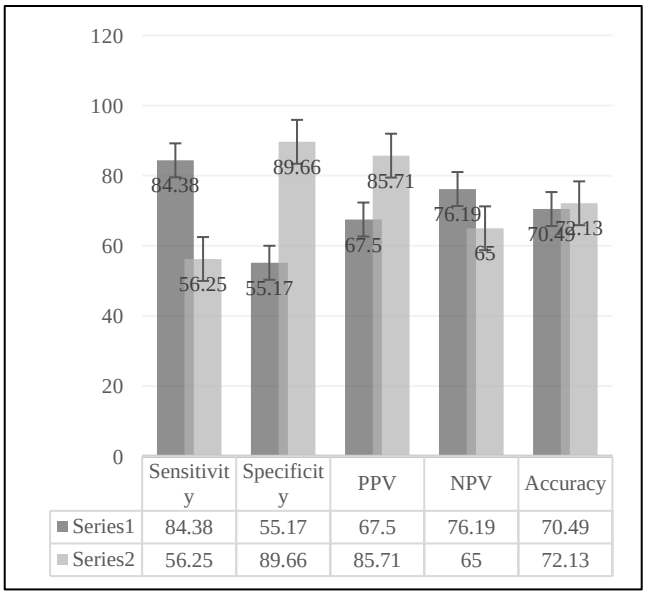

Figure 1: Concurrence of PET/CT with HPE versus concurrence of PET/CT axilla and U/S + FNAC with HPE.

Series 1: Concurrence of PET/CT with HPE (+ Error bars).
Series 2: Concurrence of PET/CT axilla and U/S+FNAC with HPE (+ Error bars).

DICUSSION

ALND and HPE remains the gold standard for the assessment of the axilla in breast cancer. The long-term morbidity of ALND is well known. SLNB has been established in the last two decades as a reliable substitute for axillary assessment. However, this too is invasive and carries its own morbidity and rising costs. The latter particularly with the advances in multistep sectioning and IHC staining. It is also time consuming when performed intra operatively.

To find a totally non-invasive method of axillary assessment ^{18} F-FDG PET/CT scans have been explored. Different authors have noted wide variations in sensitivities and specificities.[5-7] In our institution, the sensitivity, specificity and accuracy of PET/CT scans in the evaluation of the axilla was less than optimal at 84.38%, 55.17% and 70.49%. This precludes it's use in dictating a non-invasive management pathway for the axilla.

By combining U/S guided FNAC of the suspicious nodes in the axilla, which has high specificity (96.55%) with PET/CT scans, some authors found a reasonably reliable pathway for the preoperative planning of axillary management.[8]

In our institution, we too found that combining ^{18} F-FDG PET/CT with US guided FNAC of nodes gave a sensitivity, specificity, PPV, NPV and accuracy of 56.25%, 89.66%, 85.71%, 65% and 72.13% respectively. The Kappa value rose from 0.4 to 0.45 for PET/CT as a single modality of assessment as against a combination of US, guided FNAC and PET/CT.

However, this improvement was too small to open an alternative non-invasive pathway for axillary node assessment. When all the investigative modalities are concordant for metastasis, proceeding directly to ALND without the intermediate step of SLNB is acceptable. When all the results are concordant for no metastasis, skipping ALND is not acceptable as we had false negative rate of 43.8%. But when the results are discordant, one must beware of both false negative and false positive assessments of the Axilla. This makes SLNB vital in such instances.

We had a false negative rate of 43.8%. This is usually attributed to a low tumour burden and micro metastasis in the axillary nodes. It may also reflect insufficient spatial resolution on PET/CT. Moreover, some authors have noted that tumour types such as lobular breast cancers, very small size primary cancers or low-grade tumours may also result in false negative results.[9] We are unable to comment on this as these were very few in our series. We encountered a false positive rate of 10.3%. This may be attributed to inflammation and reactive lymphadenitis following FNAC as all our patients had their FNAC prior to the PET/CT scan.[10]

Limitations

The main limitations of our study are that it was observational and retrospective, conducted in a tertiary care centre with possible centripetal bias. It may be thought that most our patients had high risk breast cancer which may have led to a high pretest for axillary node metastasis. (T2-T3>T1). However, this was not borne out as N0, Nmic, and N1 patients outnumbered N2 and N3 patients as indicated by lymph node HPE. All our patients underwent PET/CT scans only after FNAC of suspicious nodes in the axilla. This may have led to false positives in the PET/CT scans.

The strength of our study lies in the fact that a single interventional radiologist performed and read the mammograms and US and performed the guided FNAC of suspicious axillary nodes. A single team of seven radiologists reported the PET/CT scan and a single Surgeon operated on all the patients avoiding bias due to variations in expertise and technique.

CONCLUSION

To summarize, the primary outcome of the study demonstrates that an expanded preoperative and minimally invasive assessment of the axilla is not reliable enough to dictate axillary management. When the results are concordant for metastasis, proceeding to direct ALND is acceptable. Conversely if the expanded assessment is concordantly negative, a case may be made for no ALND. But where the results are discordant, a SLNB is mandatory for decision making.

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