Original Research Paper

Volume-8 | Issue-2 | February-2018 | PRINT ISSN No 2249-555X

Surgery

A PROSPECTIVE CROSS SECTIONAL STUDY TO EVALUATE THE RELATIONSHIP BETWEEN MAXIMUM STANDARDIZED UPTAKE VALUE OF [18F]-FLUORO-2-DEOXY-GLUCOSE PET AND STANDARD PROGNOSTIC MARKERS IN PATIENTS WITH BREAST CANCER.

Richa Joshi — Surgical Oncologist MDTC Command Hospital Pune - 411040

Ramakrishnan Shankaran* — Associate Professor Department of Surgery Armed Forces Medical College Pune - 411040 *Corresponding Author

ABSTRACT **Background:** Studies have demonstrated the prognostic value of FDG Maximum Standardized Uptake (SUV) uptake in various tumours, including head and neck cancer, lung cancer and cervical cancer but the same has not been validated for breast cancer. Method: 120 patients with breast cancer were evaluated and correlated with FDG PET SUV score and various prognostic markers of tumour size, lymph node status, grade, ER/PR and Her 2 neu status. Results: SUV correlated significantly with histopathological prognostic markers of tumor size, grade and, triple negativity. There was also correlation with ER and PR status though statistical significance was not reached. Conclusion: PET CT has the potential to emerge as a preoperative prognostic marker and can emerge as a useful adjunctive imaging modality to diagnose as well as prognosticate breast cancer.

KEYWORDS : Breast cancer, Prognostic markers, FDG PET SUV Maximum value

Introduction

Breast cancer is the commonest cancer in women worldwide with a widely variable incidence between countries and regions [1]. Factors that determine the rate of cancer progression include tumour size (T) and lymph node metastasis (N). Prognosis also include ER/PR, Her-2/neu, Ki-67 labelling index, and nuclear grade status. While [18F]-fluoro-2-deoxy-glucose Positron Emission Tomography (FDG PET) is valuable for detecting distant metastasis, identifying recurrence and evaluating response to chemotherapy, the role of FDG PET/CT for initial staging of breast cancer has not yet been well-defined in clinical practice. FDG PET/CT is not recommended as a routine imaging modality for initial staging of early breast cancer [2]. Reports have demonstrated the prognostic value of FDG Maximum Standardized Uptake (SUV) uptake in various tumours, including head and neck cancer, lung cancer and cervical cancer[3-5]. Correlation between FDG uptake in breast tumour or axillary lymph node and known various clinical or pathologic markers of prognosis was noted in multiple other studies[6], but the data appear insufficient to form a conclusion on the association between FDG uptake and prognosis in breast cancer[7].

In this study, we investigated the relationship between the maximum SUV of the primary tumour and known prognostic parameters of breast cancer.

Materials and methods

A Cross-sectional, single centre study, with prospective data collection, involving patients with histo-pathologically confirmed breast carcinomas was done after approval by the Ethics Committee of the institution. The study was conducted over a period of 24 months. A total of 120 female patients with primary breast cancer diagnosed with core-needle biopsy were enrolled in this study.

All the patients underwent F-18 FDG PET/CT before any anticancer treatment was instituted. Exclusion criteria were patients with excisional biopsy of breast lump, patients with active tuberculosis/ or on anti-tubercular treatment, immune-compromised patients and patients with blood sugar (random) >150 mg%. Acquisition protocol PET-CT scans were performed with a dedicated PET-CT scanner (SEIMENS, BIOGRAPH 2) and the maximum SUV (SUV max) was calculated by the inbuilt software of the PET scanner. The histological data was obtained from reports provided by the Pathology Department of the hospital. The following parameters were observed; T stage, N stage, tumour grade and Immunohistochemistry. The tumour tissue was analysed for ER, PR, and HER-2/neu status using standardized immunohistochemical techniques.

The results obtained were statistically compared and analysed using appropriate statistical tests (Student's T test and Pearson x2 tests) using SPSS software (version 22, SPSS Inc, Chicago, IL,USA). The p value less than 0.05 was considered significant.

Results

This study was carried out at a tertiary care centre over 2 years. A total of 120 consecutive patients were enrolled. Patients ranged from 29 to 74 years of age, maximum being between age groups 51 to 60 years (31.7%). Histologically 117 patients had invasive ductal carcinomas with only 03 being invasive lobular variety. Tumours were staged as per AJCC 7th edition TNM classification. 12 patients had clinically T1 (</=2 cm), 74 had T2 (2.1cm -5cm) and 34 had T3(>5cm) lesions. Clinical lymph node status was N0 in 36 patients (30%) and N1 in 84 (70%). The Scarff Bloom Richardson grade was Gd I in 4 (3.3%), Gd II in 22(18.3%), Gd III in 94 (78.4%) patients. The ER status was positive in 58 of 120 patients (48.3%), PR status was positive in 44 of 120 patients (36.6%). 38 out of 120 patients were triple negative.

Table 1. SUV values with various prognostic markers in breast cancer

Criterion	Number	Percentage (%)	SUV (max)	Std deviation	P value
Tumour size					
<2cm	12	10.0	6.02	3.80	
2-5cm	74	61.7	11.19	7.16	
>5 cm	34	28.3	15.44	7.66	0.012
Lymph node status					
No	36	30.0	5.6	3.20	
N1	84	70.0	6.6	3.53	0.43
Tumour grade					
I + II	26	21.6	6.15	3.43	
III	94	78.4	13.46	7.51	0.007
ER					
Positive	58	48.3	10.39	6.35	
Negative	62	51.7	12.27	8.25	0.137
PR					
Positive	44	36.7	11.16	6.94	
Negative	76	63.3	12.29	7.83	0.58
Her-2 neu					
Positive	62	51.7	9.79	5.10	
Negative	58	48.3	14.11	8.94	0.024
Triple negative	38	31.7	14.70	9.24	
Others	82	68.3	10.57	6.20	0.046

Comparing with SUV max of tumour with various histopathological parameters, significant correlation was found with tumour size < 2cm compared to T2 and T3 tumours. SUV max of tumour did not appear to be much influenced by nodal status with mean SUV in N0 being 5.6 and in N1 being 6.6, with p value 0.43. Tumours with higher grade showed a trend towards higher SUV max values and the results were statistically significant (p value = 0.007). 62 estrogen receptors negative patients had a mean SUV max of 12.27 ± 8.25, and the 58 patients who were positive for the receptor status had a mean SUV max of 10.39 ± 6.35 respectively but there was no significant difference in SUV max of these groups (p value = 0.137). Similar findings were found with progesterone positive cases also (p value = 0.58). 58 patients whose tumour was negative for the Her 2/ neu receptors had a mean SUV max of 14.11 ± 8.94, and the 62 patients who were positive

for the receptor status had a mean SUV max of 9.79 ± 5.10 respectively and patients with negative receptor status had statistically significant higher SUV max values compared to those who were receptor positive (p value = 0.024). 38 patients who were negative for PR / ER and Her 2 neu receptor status (triple negative) were compared with 82 patients with positive receptor status and it was seen that patients with negative receptor status had significantly higher mean SUV max values (14.70 ± 9.24 vs 10.57 ± 6.20, p value = 0.046).

Discussion

Various prognostic factors have been proposed for the risk stratification of patients with breast cancer, such as involvement of axillary LNs, presence of distant metastases, hormone receptor status, and HER2/neu receptor status. However, these pathological predictors can only be obtained after surgery or with invasive diagnostic procedures. On the other hand, F-18 FDG PET can provide quantitative information about tumour glucose metabolism, which represents tumour aggressiveness which can be evaluated noninvasively and be measured with good inter-test reproducibility, at the time of diagnosis, before starting any treatment. Therefore, quantitative FDG-PET can be a valuable adjunct to conventional preoperative clinical assessment and may allow for identification of more aggressive tumours at histologic analysis. In this prospective study we measured tumour uptake of FDG in 120 proven cases of breast cancer prior to any neoadjuvant chemotherapy.

We found SUV max level significantly correlating with tumour size, grade and triple negative status, which has also been proven in earlier studies [8,9]. The tumour size findings are in agreement with Kumar et al. who found a lower SUV value in small tumours [10]. Our findings did not match with those of Berriolo-Riedinger et al who found no influence of tumour size on baseline SUV [11]. As regard lymph nodal status and SUV, no correlation could be established in our study which is in agreement with results of other studies like Berriolo-Riedinger et al.

Tumours with positive receptor status for estrogen receptors had lower SUV values than their negative counterparts (10.39 ± 6.35 vs 12.27 ± 8.25, p = 0.137) on PET scan. However the same was statistically insignificant. There have been contradictory reports on steroid hormone receptor status and 18F-FDG uptake. Some studies showed no correlation between hormone receptor status and SUV values (10).However others showed higher SUV in ER negative tumours [12]. When we analysed the FDG uptake with progesterone receptor status, it was found that PR positive tumours had lower SUV values than PR negative tumours but it was statistically insignificant (11.16 ± 6.94 vs 12.29 ± 7.83, p = 0.58). The results from this study were concordant with the one done by Osborne and colleagues who, in a study of 36 patients, found no significant association with SUV and PR status [13]. The study by David Groheux et al [6] could document a significantly higher 18F-FDG uptake in PR negative tumours than in PR positive tumours (p=0.003) which does not match with our results.

Her 2/ neu negative patients had statistically significant higher SUV max values compared to those who were receptor positive (p = 0.024). This finding is in contrast with the fact that Her 2 neu overexpression is a well-known factor of tumour aggressiveness and poor prognosis. The results from this study were discordant with the one done by Ueda et al, who found a significant relationship between 18F-FDG uptake and HER-2/neu over expression [14]. In the study by David Groheux [6] no significant influence of HER-2/neu overexpression on SUV was found. Our findings suggest that HER-2/neu has major influence on glycolytic pathways hence affecting FDG uptake and SUV. Based on receptor status when the SUV max of the group with triple negative receptor status (ER-/PR-/Her2 neu -) was compared to rest of the patient group, it was seen that patients with negative receptor status had significantly higher mean (14.70 ± 9.24 vs 10.57 ± 6.20 p value = 0.046) SUV max values. The results from this study were concordant with the one done by M. Ohara et al. [15].

Conclusion

SUV correlated significantly with histopathological prognostic markers of tumor size, grade and, triple negativity. There was also correlation with ER and PR status though statistical significance was not reached. This data indicates that PET CT has the potential to emerge as a preoperative prognostic marker and can emerge as a useful adjunctive imaging modality to diagnose as well as prognosticate breast cancer. A limitation of this study was its small size and short follow up. Therefore, large-scale prospective studies are warranted to confirm the utility of SUV max for predicting clinical outcomes in patients with breast cancer.

References

1. Youlden DR, Cramb SM, Dunn NA, Muller JM, Pyke CM, Baade PD: The descriptive epidemiology of female breast cancer: an international comparison of screening, incidence, survival and mortality. Cancer Epidemiol 2012, 36(3):237–248.
2. Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, Coleman RE, Wahl R, Paschold JC, Avril N, Einhorn LH, Suh WW, Samson D, Delbeke D, Gorman M, Shields AF. Recommendations on the use of 18F-FDG PET in oncology. J Nucl Med 2008; 49: 480-508
3. Liao C, Chang JT,Wang H, Ng S, Hsueh C, Lee L, et al. Pretreatment primary tumor SUVmax measured by FDG-PET and pathologic tumor depth predict for poor outcomes in patients with oral cavity squamous cell carcinoma and pathologically positive lymph nodes. Int J Radiat Oncol Biol Phys. 2009; 73(3):764–71.
4. Casali C, CuccaM, Rossi G, Barbieri F, Iacuzio L, Bagni B, et al. The variation of prognostic significance of Maximum Standardized Uptake Value of [18F]-fluoro-2-deoxy-glucose positron emission tomography in different histological subtypes and pathological stages of surgically resected Non-Small Cell Lung Carcinoma. Lung Cancer. 2010; 69(2):187–93.
5. Kidd EA, Siegel BA, Dehdashti F, Grigsby PW. Pelvic lymph node F-18 fluorodeoxyglucose uptake as a prognostic biomarker in newly diagnosed patients with locally advanced cervical cancer. Cancer.2010;116(6):1469–75.
6. Groheux D, Giacchetti S, Moretti J, Porcher R, Espi M, Lehmann Che J, et al. Correlation of high 18F-FDG uptake to clinical, pathological and biological prognostic factors in breast cancer. Eur J Nucl Med Mol Imaging. 2011;38(3):426–35.
7. Robertson IJ, Hand F, Kell MR. FDG-PET/CT in the staging of local/regional metastases in breast cancer. Breast 2011; 20:491-494
8. Ikenaga N, Otomo N, Toyofuku A, Ueda Y, Toyoda K, Hayashi T,et al. Standardized uptake values for breast carcinomas assessed by fluorodeoxyglucose-positron emission tomography correlate with prognostic factors. Am Surg. 2007;73:1151–7.
9. Ueda S, Tsuda H, Asakawa H, Shigekawa T, Fukatsu K, Kondo N, et al. Clinicopathological and prognostic relevance of uptake level using 18F-fluorodeoxyglucose positron emission tomography/computed tomography fusion imaging (18 F-FDG PET/CT)in primary breast cancer. Jpn J Clin Oncol. 2008;38:250–8.
10 Kumar R, Chauhan A, Zhuang H, Chandra P, Schnall M, Alavi A. Clinicopathologic factors associated with false negative FDG-PET in primary breast cancer. Breast Cancer Res Treat 2006;98:267– 74.
11. Berriolo-Riedinger A, Touzery C, Riedinger J, et al. [18F]FDG-PET predicts complete pathological response of breast cancer to neoadjuvant chemotherapy. Eur J Nucl Med Mol Imaging. 2007;34:1915–1924.
12. Mavi A, Cermik TF, Urhan M, Puskulcu H, Basu S, Yu JQ, et al. The effects of estrogen, progesterone, and HER-2/neu receptor states on 18F-FDG uptake of primary breast cancer lesions. J Nucl Med 2007;48:1266–72
13. Osborne JR, Port E, Gonen M, Doane A, Yeung H, Gerald W, et al. 18F-FDG PET of locally invasive breast cancer and association of estrogen receptor status with standardized uptake value: microarray and immunohistochemical analysis. J Nucl Med 2010;51:543–50
14. Ueda S, Tsuda H, Asakawa H, Shigekawa T, Fukatsu K, Kondo N, et al. Clinicopathological and prognostic relevance of uptake level using 18F-fluorodeoxyglucose positron emission tomography/ computed tomography fusion imaging (18F-FDG PET/CT) in primary breast cancer. Jpn J Clin Oncol 2008; 38: 250–8.
15. Masahiro Ohara, Hideo Shigematsu, Yasuhiro Tsutani, Akiko Emi, Norio Masumoto, Shinji Ozaki et al. Role of FDG-PET/CT in evaluating surgical outcomes of operable breast cancer and Usefulness for malignant grade of triple-negative breast cancer The Breast xxx (2013) 1-6.