Biomedicine & Healthcare Research

Biomedicine & Healthcare Research 2024 January;2:29-34

https://doi.org/10.5281/zenodo.10570015

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Original article

Role of FDG-PET/CT in the diagnosis of recurrent breast cancer

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Abstract

In patients with recurrent breast cancer, FDG PET/CT has demonstrated superior efficacy compared to conventional imaging (CI) in identifying loco-regional or distant recurrence. This holds true regardless of whether recurrence is suspected based on clinical examination, CI, or an increase in tumor markers (TM) such as CA 15.3 or CEA, and even if tumor markers are within normal ranges. PET/CT is also a powerful imaging modality for conducting a whole-body workup of a known recurrence aiding in the determination of whether the recurrence is isolated. To investigate our experience with the concordance of FDG-PET/CT and CI, we studied cases of breast carcinoma retrospectively collected between 2022 and 2023 from our institution's archive. PET images were analyzed by at least two nuclear medicine specialists. We then compared them with the findings of CI and analyzed their accuracy based on patients' follow-up. A total of 25 patients was selected. PET-CT was effective in clarifying uncertain findings from CT scans. It ruled out bone metastasis in two out of nine equivocal cases and confirmed seven out of nine. It excluded three out of seven pulmonary lesions while confirming three. It also confirmed other uncertain lesions in CT, such as muscular and parietal ones. Moreover, PET/CT detected additional lesions not seen in CT [bone (n=4) and liver (n=1)]. In conclusion, this study supported the findings of prior studies, highlighting the valuable contribution of PET/CT in the detection of recurrent breast cancer and its superiority to CI.

Keywords: Breast carcinoma, FDG-PET/CT, recurrence

Received: December 18, 2023; Accepted: January 20, 2024

1. Introduction

Breast cancer is the most frequently diagnosed malignancy, predominantly affecting women worldwide, constituting 11.7% of all cancers. Approximately 2,261,419 new cases were diagnosed in 2020, with an estimated number of cases reaching 4,074,871 by 2024, as reported by the International Agency for Research on Cancer [1].

While advancements in screening and treatment options have contributed to a decline in breast cancer mortality, it is noteworthy that 25–30% of patients still experience disease recurrence during their follow-up period, significantly impacting prognosis, especially if detected at an advanced stage [2]. Consequently, the timely identification and accurate staging of recurrence are crucial for achieving optimal therapeutic management in breast cancer cases. This, however, remains a challenge that necessitates a comprehensive diagnostic workup.

For years now, recurrence staging has been the additive value of the computed tomography scan (CT). Nevertheless, recent studies have demonstrated the increasing significance of 18F-fluorodeoxyglucose positron emission tomography coupled with computed tomography (FDG PET/CT) in identifying breast cancer recurrence [3], outperforming CI.

In this study, we described the experience of The Department of Nuclear Medicine of Habib Bourguiba University Hospital of Sfax, Tunisia, regarding the diagnosis of recurrent breast cancer by FDG PET/CT and its contribution in the establishment of precise metastatic lesion mapping when compared to CI.

2. Material and methods

We conducted a retrospective study of cases with suspected breast cancer recurrence collected from the files of Nuclear Medicine Department of Habib Bourguiba University Hospital of Sfax (Tunisia) from January 2022 to July 2023.

Cancer recurrence was described as the reappearance of the disease after a period of undetectable disease. Recurrence was suspected based either on clinical signs, morphological arguments on CI or by detecting an elevation of TMs. All patients had undergone thoraco-abdomino-pelvic CT scan prior to FDG PET/CT interpreted initially by at least two medical radiology specialists. We then compared our results to those of CT scans and eventually to the outcomes in patients' follow-up. Sensitivity, specificity, negative predictive value and positive predictive value were thus determined.

The inclusion criteria were as follows: all patients had a history of histopathologically proven and treated breast cancer, patients with confirmed recurrence or highly suspected one in order to realize a precise mapping of metastatic lesions and finally, patients with complete files. Exclusion criteria were patients who received chemotherapy in less than one month, who had breast cancer with low SBR score and whose files were incomplete.

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Statistical analysis

This is a descriptive study. The data were analyzed using Social Science Statistical Software Package (SPSS) version 22. Compared to the results of CI, FDG PET/CT is a diagnostic test to be estimated by determining its sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV).

3. Results

Throughout our study period, a total of 43 cases of suspected recurrence of breast cancer were recorded. However, only 26 met our inclusion criteria and were thus selected to be included in this descriptive study. The remaining 17 cases were excluded for the following reasons: one recently underwent chemotherapy, eight did not undergo a recent thoraco-abdomino-pelvic scan and eight had incomplete files especially histopathological reports. The median age of patients was 48.5 years (37-72 years). A family history of breast cancer was documented in only 38% of the patients.

The majority presented initially with invasive ductal carcinoma except in three patients: two patients had lobular invasive carcinoma and one patient had a mixed histologic type ductal and lobular carcinoma. For the SBR grade, 57% of carcinomas were SBR II and the remaining were SBR III. Recurrence during follow-up was suspected on the basis of clinical arguments in 30.8% of the cases, on morphological suspicious lesions in 46.2%, on positive bone scan 7.7%, on elevated TMs in 3.8% and all of the above arguments in the rest 11.5% of the cases.

PET/CT was indicated mainly in the case of equivocal lesions on CT (57.7%), in 23.1% of the cases as a whole-body workup of a known recurrence to determine whether or not it is isolated and in the rest 15.4% patients as a tool for recurrence diagnosis suspected on elevated TMs but with negative CT results.

PET results

PET/CT has shown recurrence in 73.1% of patients affecting: bone (n=11), lung (n=3), liver (n=1), axillary homo-lateral lymph nodes (n=11), distant lymph nodes (n=5) and other Out of the patients with equivocal lesions on CT, PET/CT proved effective in ruling out metastatic lesions in 53.34%. Among these cases, 37.5% comprised pulmonary nodal equivocal lesions, 25% were suggestive of distant lymph node involvement, 12.5% were indicative of nonspecific bone lesions, 12.5% exhibited nonspecific suspicious pericardial thickening, and 12.5% presented a contentious contralateral mammary glandular nodule.

It has also effectively confirmed metastasis in 33.34% of these patients; 60% of them were bone metastasis, 20% of them were pulmonary cancerous lesions and the 20% pericardial metastasis. For the rest 13.32%; PET has failed to detect cancerous spreading to the bone in one case and to the lung in one other case.

Of the PET exams conducted as a whole-body workup for a known recurrence (23.1%), PET demonstrated superiority over CT in 50% of these cases. Among them, 66.67% were related to bone metastasis and in one patient, PET aided in the detection of local recurrence, in addition to identifying bone, liver, and distant lymph node involvement, none of which were detected on CT. PET did not detect additional metastatic sites and its results were concordant to those of CT in 33.34% of these cases. In the rest 16.66%, PET helped infirm distant lymph node involvement without detecting additional lesions other than those already detected by CT.

In the portion of patients addressed to our department in order to diagnose recurrence suspected on the basis of the elevation of TMs, with negative CT results, PET actually helped detecting recurrence in all of those patients; sites of recurrence were mainly osseous, axillary and distant lymph nodes. In the light of our study results, the sensitivity, specificity, PPV and PNV of FDG PET/CT were 88.23%, 100%, 100% and 81.81%, respectively.

4. Discussion

Breast cancer mortality has witnessed a decline due to advancements in screening methods and treatment diversity. However, a recurrence rate of approximately 25–30% of disease recurrence is still recorded, thus worsening the prognosis [2,4]. Treatment strategy depends on metastatic sites, so a precise mapping of metastatic lesions is fundamental.

In many studies, it has been demonstrated that PET/CT is highly effective in detecting recurrence [5-11]. In a meta-analysis comprising 26 studies and 1752 subjects, Xiao et al. reported a combined sensitivity of 90% and specificity of 81% for the detection of recurrent breast cancer using PET/CT [12]. Across various studies, the sensitivity of FDG PET/CT ranges from 81 to 100%, specificity from 52 to 100%, and diagnostic accuracy from 60 to 96%. Notably, Vogsen et al. found an accuracy of 91% in their recent study [13].

These findings align with the results of our study, in which FDG PET/CT has shown sensitivity of 88.23% and specificity of 100%, with no known false positive and few false negative. These false negatives consisted of cases of suspected non-specific small infra-centimetric lung nodules, in which FDG uptake was insignificant or even absent (Fig.1). Subsequent follow-up revealed an increase in the size of these lesions, and the diagnosis of cancerous lung spreading was then admitted. It is well recognized that the partial volume effect phenomenon affects the quantitative measurement of FDG uptake, particularly in the case of small lesions [14]. This explains well why metastatic lesions from high-grade neoplasia did not exhibit intense FDG uptake (Fig.2).

Other false negative were cases with osteocondensing lesions, suspected to be bone site of breast cancer recurrence on CI (Fig.2). Subsequent bone scans revealed increased uptake, confirming their metastatic nature. However, it has been demonstrated that FDG PET/CT is superior to bone scans in the detection of osteolytic skeletal metastases in patients with breast cancer. The bone scan was noted to outperform PET in the identification of osteoblastic metastatic lesions, primarily due to their typically lower metabolic activity, making them often undetectable by PET

[15]. This may be linked to the relatively acellular nature of these lesions. Consequently, the extent of 18F-FDG uptake could be influenced by the reduced volume of viable tumor tissue within the lesion (16). Furthermore, many studies have shown that FDG PET/CT surpasses conventional imaging [17]. A recent study, that included 100 women, prospectively evaluated the accuracy of FDG PET/CT, contrast-enhanced CT, and bone scans, in diagnosing breast cancer recurrence. FDG PET/CT exhibited superior diagnostic accuracy compared to contrast-enhanced CT alone or a combination of contrast-enhanced CT and bone scan, notably, there were no reported false negatives, and the incidence of false positives was lower in comparison to the alternative imaging techniques [18].

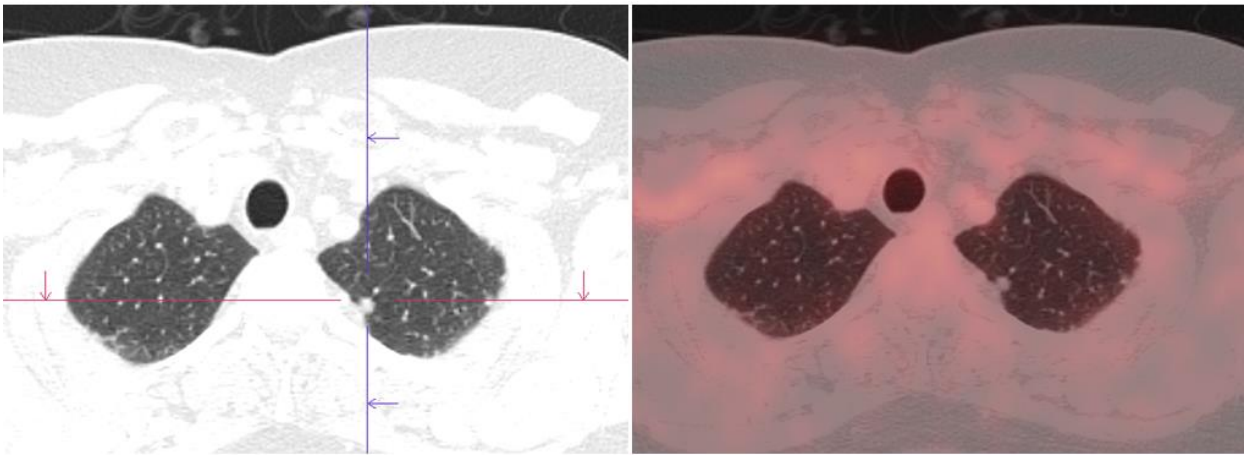

Fig.1. A 67 year-old woman with a history of bilateral ductal carcinoma, who was referred for PET/CT because of suspected recurrence of the disease based on the detection of litigious lung nodules on CT. TMs were slightly elevated. PET/CT showed no FDG uptake in these lesions, because of their small size.

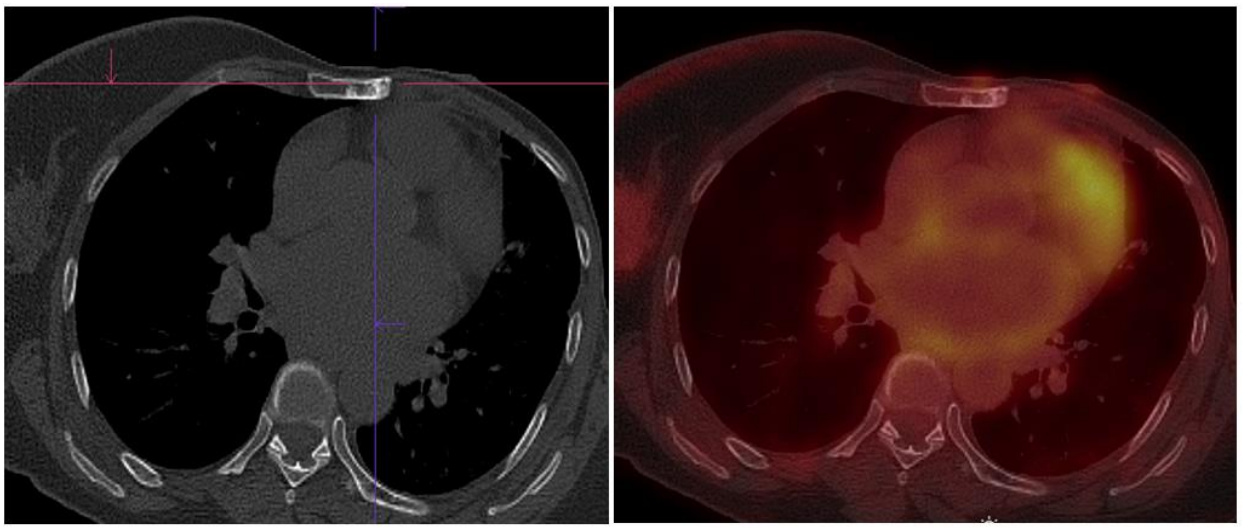

Fig.2. A 57-year-old female with a history of left mammary ductal carcinoma is currently under suspicion of recurrence based on clinical loco-regional evidence, notably the presence of an inflammatory left parasternal nodule. PET has failed to diagnose osseous extension of the cancerous disease. Bone scan has shown afterwards an increased Tc-MDP uptake in the sternum.

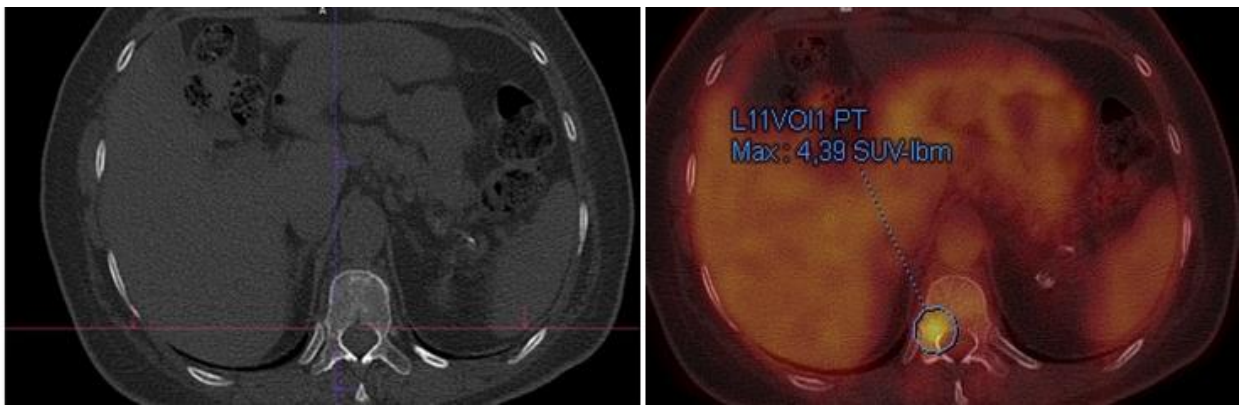

Fig.3. A 38 year-old woman with history of treated mammary ductal carcinoma, was addressed for a whole body workup by PET for a known loco-regional recurrence of her disease. PET showed osseous involvement that was not detected on CI.

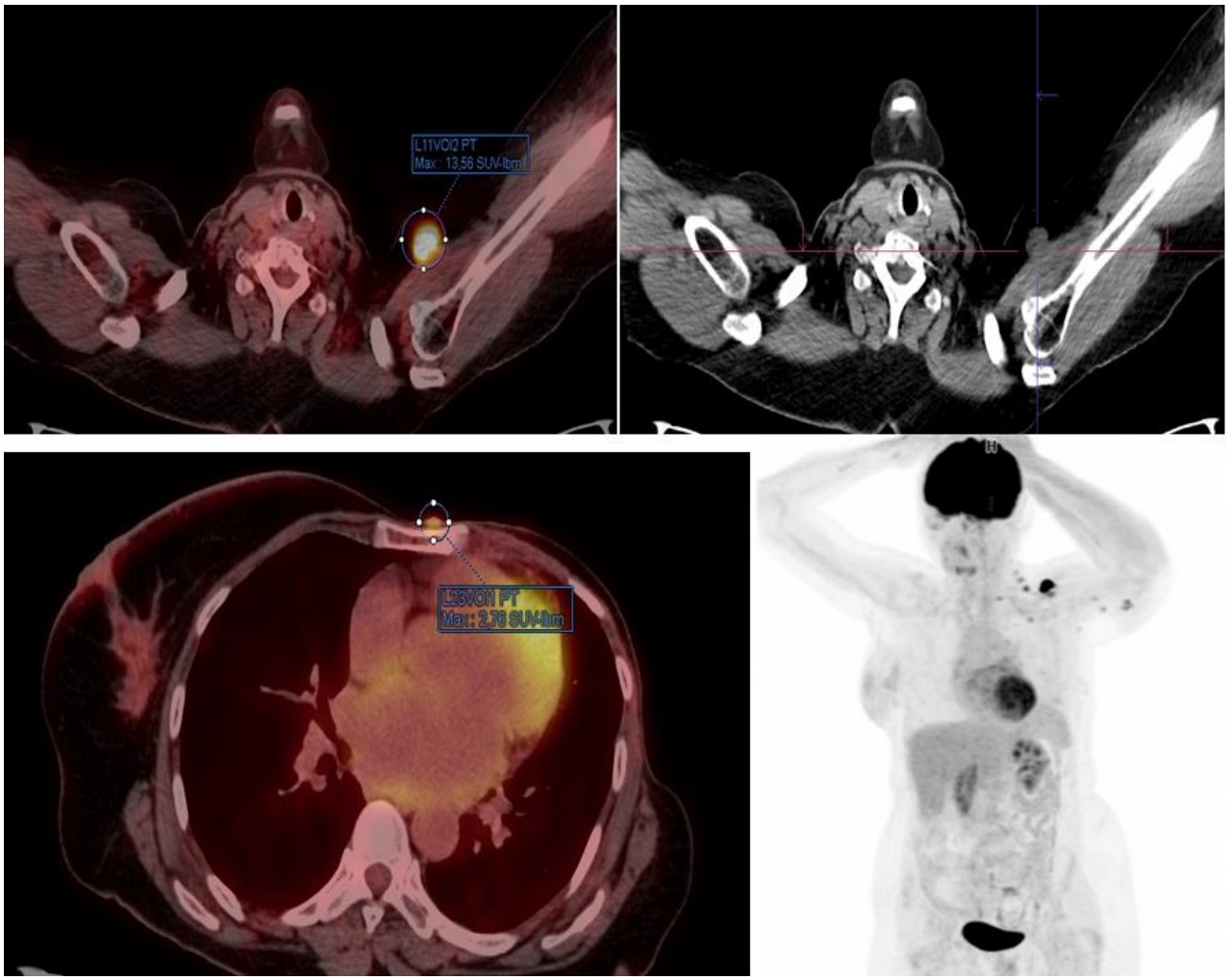

Fig.4. PET helped highlight muscular and sub-cutaneous metastatic involvement. Those lesions were equivocal on CI.

Moreover, PET/CT has demonstrated efficacy in identifying distant metastases and highlighting loco-regional recurrence, particularly in areas such as the chest wall, axillary region, and extra-axillary lymph nodes. Additionally, PET imaging can aid in distinguishing radiation plexitis from loco-regional recurrence [19]. Many study findings indicate that PET/CT demonstrates superior effectiveness compared to CT or even MRI in the identification of lymph node recurrences [20,21].

In our population, PET CT has shown its additive value compared to CT, especially in diagnosing locoregional recurrence, lymph node involvement and osseous metastasis (Fig.3) and even in the detection of muscular and sub-cutaneous involvement (Fig.4), yet our study suffers from several limitations, among which the limited number of cases an its retrospective character.

Moreover, in cases where breast cancer recurrence is documented or suspected through conventional imaging, PET/CT plays a pivotal role in determining whether the recurrence is isolated and in confirming the suspicious nature of the lesion. Consequently, conducting FDG PET/CT for the assessment of a documented recurrence significantly impacts patient management, leading to change of treatment approach in almost half of the cases [22-24], and when compared to conventional imaging methods, PET/CT provides superior prognostic stratification by distinguishing patients with isolated locoregional recurrence from those with distant metastases [7,10].

In conclusion, FDG PET/CT emerges as a valuable imaging tool for detecting recurrence in breast cancer. Its effectiveness surpasses that of conventional imaging methods in identifying both locoregional and distant recurrence in patients with recurrent breast cancer, regardless of whether suspicion arises from clinical examination, traditional imaging, or elevated tumor markers (CA 15.3 or CEA). Furthermore, PET/CT serves as a robust imaging modality for conducting a thorough whole-body assessment in confirmed recurrence cases, aiding in the determination of whether the recurrence is isolated or not.

Funding

None.

Conflict of Interest Disclosures

All authors declare that they have no conflict of interest.

Authors' contributions

Study concept and design were done by NB and FC. Data were

acquired by NB and FC. The data were analyzed and interpreted by NB, FC, TB, IJ and KC. Drafting of the manuscript was done by KC and FG. All authors read and approved the final manuscript.

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Cite this article as: Ben Fkih N, Chaltout F, Bint Mohamed T, Ben Ahmed K, Jardak I, Chtourou K, Guermazi F. Role of FDG-PET/CT in the diagnosis of recurrent breast cancer. Biomedicine Healthcare Res. 2024;2:29-34. https://doi.org/10.5281/zenodo.10570015