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PERCIST 1.0 Versus RECIST 1.1 in the Evaluation of Locally Advanced and Metastatic Breast Cancer: An Observational Study

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Abstract

Background: RECIST 1.1 is widely used in treatment response evaluation of breast cancer, although it considers certain lesion as non-measurable which constitute major disease burden. FDG PETCT has the ability to quantitatively measure response in this category causing change in management.

Objectives: 1) To compare PERCIST 1.0 with RECIST 1.1 in quantifying the treatment response of the locally advanced, metastatic and recurrent breast cancer. 2) To evaluate difference in RECIST 1.1 and PERCIST 1.0 criteria in patients with non-measurable disease over measurable disease.

Methods: This retrospective study was conducted on 45 patients of locally advanced, recurrent or metastatic breast cancer patients between April 2016 to March 2017. Treatment response was evaluated on baseline and post-treatment FDG PET/CT scans and compared between RECIST 1.1 and PERCIST 1.0. Difference in response between RECIST 1.1 and PERCIST 1.0 was also compared in two groups of patients 1) non-measurable and 2) mixed disease (non-measurable and measurable) as defined by RECIST 1.1.

Results: Discordant response between RECIST 1.1 and PERCIST 1.0 was seen in 28.8% of patients and all of them belonged to stable disease with RECIST 1.1, but with PERCIST 1.0, 11.1% showed CMR, 4.4% PMR while 13.3% PMD. Based on RECIST 1.1, on further dividing the patients into two categories of non-measurable disease only and mixed disease, discordant results was seen in category of non-measurable disease only. 50% of patients in non-measurable disease only category showed change in response between RECIST 1.1 and PERCIST 1.0 and 70% of patients with bone metastases showed significant change in response with P value: 0.002.

Conclusion: PERCIST 1.0 is superior to RECIST 1.1 in quantitative response evaluation in locally advanced, recurrent and metastatic breast cancer, especially in patients with non-measurable disease mainly bony metastatic disease. All patients with non-measurable disease should be evaluated with FDG PET/CT rather than CT.

Clinical Impact: All patients with non-measurable disease on CT scan can be directed to FDG PET/CT staging and response evaluation, which would lead to adequate management of these patients with appropriate use of resources.

Key Findings: 28% of patients showed discordant results between RECIST 1.1 and PERCIST 1.0 and all of them were having non-measurable disease only. 50% of patients with non-measurable disease and 70% of patients with bone metastases showed discordant results between RECIST 1.1 and PERCIST 1.0.

Importance: Significant number of patients with non-measurable disease showed change in response from RECIST 1.1 to PERCIST 1.0 and should be evaluated with PET scan.

Keywords: RECIST 1.1; PERCIST 1.0; FDG PET/CT; Breast cancer

Introduction

Breast cancer is the most common cancer in women and the leading cause of cancer death in women. According to WHO (World Health Organization) there were over 2 million new cases in 2018 and approximately half a million death due to breast cancer/year [1]. Breast cancer is anatomically staged using TNM staging- 8th editions of Union for International Cancer Control

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(UICC) and American Joint Committee on Cancer (AJCC). Anatomical stage group- I, II and IIIA- are called early-stage breast cancer. Anatomical stage group- IIIA (T3, N2), IIIB, IIIC- are called locally advanced breast cancer. Agnomical stage group- IV- is called metastatic breast cancer [2]. Accurate staging and treatment response assessment is crucial in management of breast cancer. Patients with locally advanced breast cancers (LABC; defined as a breast cancer typically >5 cm with regional and/or metastatic involvement of those that involve the skin or chest wall including inflammatory breast cancers) are often treated with neoadjuvant chemotherapy before definite surgical intervention [3]. Various radiological imaging like Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and F18 Fluorodeoxyglucose Positron Emission Tomography/ Computed Tomography (FDG PET/CT) are frequently performed to stage and evaluate treatment response in breast cancer patients. Response evaluation of the solid tumor on imaging is performed using RECIST 1.1 (on CT or MRI scan) and PERCIST 1.0 (on 18-FDG PET/CT scan).

RECIST 1.1 (Response Evaluation Criteria in Solid Tumors version 1.1) is currently widely used to assess response to treatment in breast cancer, however RECIST 1.1 is based on anatomical changes in tumor and has a number of limitations. One major limitation with RECIST 1.1 is that it designates numerous lesions as non-measurable, which cannot be quantified for response assessment. Non-measurable lesions by RECIST 1.1 include small tumors <10 mm, lymph nodes <15 mm in short axis, leptomeningeal disease, lymphangitic spread, inflammatory breast disease, pericardial/pleural effusions, palpable abdominal masses/organomegaly not reproducible on imaging studies, lesions surrounded by scar tissue, ascites, cystic lesions and bone metastases with soft tissue masses measuring <10 mm (includes majority of bone metastases) [4]. This non-measurable disease in the locally advanced, metastatic and recurrent breast cancer group represents significant disease burden and may influence the treatment strategies and management. RECIST 1.1 is also of limited accuracy in certain cases due to delayed tumor shrinkage and poor discrimination between scar/fibrosis/viable tissue [5]. In addition; certain new targeted anticancer drugs are cytostatic and not cytocidal which causes necrosis or cystic change rather than tumor shrinkage and thus making response assessment with RECIST 1.1 difficult [6].

FDG PET/CT is being increasingly used by oncologist for treatment response assessment in breast cancer. It can assess tumor response early, before anatomical changes in the tumor [6]. It also has the potential to revolutionize the definition of non-measurable disease because of its ability to quantify metabolic disease load by PERCIST 1.0 (Positron Emission Tomography Response Criteria in Solid Tumors). Quantification of the non- measurable disease by PERCIST 1.0 criteria may upstage or downstage the disease. PERCIST 1.0 may effectively evaluate the disease burden in this selected group of patients which falls in the "non-measurable" category in RECIST 1.1 [6].

According to National Comprehensive Cancer Network (NCCN) guidelines, FDG PET is considered optional for locally advanced (clinical stage 3a), recurrent, or stage 4 disease. Currently its role in breast cancer patients is to provide additional information in selected group of patients in which results of conventional imaging are indeterminate or of limited utility [7]. Guidelines for appropriate imaging in quantification of the disease and its response to treatment are yet to be standardized in breast cancer. With the increasing work load on PET/CT and limited resources, appropriate patient selection for FDG PET/CT is also challenging.

Our primary aim is 1) To compare PERCIST 1.0 with RECIST 1.1 in quantifying the treatment response of the locally advanced, metastatic and recurrent breast cancer. 2) To evaluate difference in RECIST 1.1 and PERCIST 1.0 criteria in patients with non-measurable disease over measurable disease.

Materials and Methods

This retrospective, observational and cross-sectional study was conducted at Sultan Qaboos University Hospital, Muscat, Oman between April 2016 to March 2017 (12 months). The study was approved by the institutional review board and informed consent was waived as it was retrospective study. The study was HIPAA compliant. A computerized search of health records of FDG PET/CT performed from April 2016 to March 2017 in the institution's Radiology database (XIRIS, Philips) were done by department research coordinator. Patients' cohort consist of total 910 patients underwent FDG PET/CT including 214 patients with primary breast malignancy. Final study population was segregated by the nuclear medicine physician based on inclusion and exclusion criteria. Inclusion criteria include; 1) All breast cancer patients with locally advanced (AJCC-TNM-anatomical stage IIIA (T3, N2), IIIB, IIIC), metastatic breast cancer (AJCC-TNM- anatomical stage IV) and recurrent disease. 2) All age groups and both genders. 3) All histopathological types of breast cancer. 4) All hormone receptors types/Molecular subtypes.

Exclusion criteria include; 1) Patients without two sets of PET imaging a) baseline and b) a follow-up scan. 130 patients were excluded as did not have follow-up scan. Baseline scan performed within 1 month of the initiation of the treatment and follow up scan after at least 3 weeks of 3 cycles of chemotherapy but before next cycle of chemotherapy, was included in the study. 2) 23 patients with early stage breast cancer (stage I/II/IIIa) were excluded.

Thus, total 61 patients fell into locally advanced and metastatic breast cancer category. In addition; 16 more patients were excluded due to 3) suboptimal quality, 4) follow-up scans not full-filling time criteria and 5) patients with inflammatory disease on baseline (proven to be inflammatory on biopsy) e.g., Lung nodule, contralateral axillary lymph node etc.). Remaining 45 patients made our study population (Figure 1).

All baseline and follow up FDG PET/CT scans were performed with uniform departmental FDG PET/CT acquisition protocol on biograph mCT flow with 128 slice CT scanner, Siemens healthcare, Erlangen Germany. All patients were prepared as per standard guidelines. Patients were kept fasting for 6 h before the scan with restriction of i.v. Dextrose drip and insulin 6 h before the study. Patients were instructed to avoid strenuous exercise 24 h before the scan. Blood sugar values for all scans were <11.1 mmol/l. F18-FDG doses were administered based on body weight calculation (3.7 Mbq/kg to 5.2 Mbq/kg). Total uptake time for all scans was 60 min ± 10 min after radiotracer administration. Water was given as negative oral contrast. Intravenous contrast was not administered. Non- breath hold CT and PET images were acquired sequentially from the skull base to mid-thigh with patient's arms up. Firstly, low dose CT protocol was used for attenuation correction and anatomical localization, followed by PET acquisition using the 3-dimensional emission scan with 5 mm slice thickness. Acquisition parameters are shown in Table 1. All base and reconstruction images were transferred to SyngoVia workstation through Philips IntelliSapce

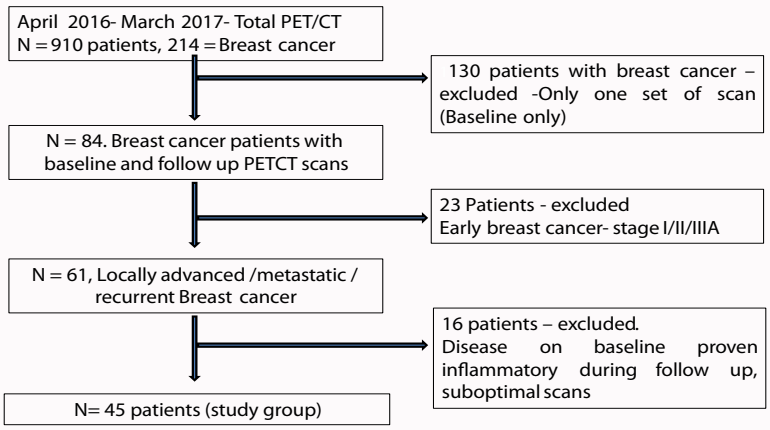

Figure 1: Patient enrolment chart.

PACS. All scans were checked for optimal image quality by nuclear medicine physician. After acquisition, images were interpretated.

In the first step; response evaluation of each set of baseline and follow-up 18-FDG PET/CT was performed by RECIST 1.1 [4]. By 2 radiologist having 15 and 10 years of experience in oncology respectively. RECIST 1.1 was calculated on the available low dose CT part of PET scans. Based on the RECIST 1.1, the lesions were categorized into measurable/non-measurable groups. Two groups of patients with a) non-measurable disease and b) Mixed disease (measurable and non-measurable) were defined. RECIST 1.1 treatment responses were categorized into 1) Complete Response (CR)- disappearance of all target lesions with reduction in lymph nodes <10 mm in short axis. 2) Partial Response (PR)- 30% or greater decrease in sum of diameter of target lesions. 3) Progressive Disease (PD)- 20% or greater increase in sum of diameter of target lesions with appearance of new lesions 4) Stable Disease (SD)- No significant shrinkage or increase of lesions, to be classified as PR or PD.

In second step; Response evaluation on each set of FDG PET/CT was performed by PERCIST 1.0 by nuclear medicine specialist with 9 years of experience [8,9]. Quantitative estimation of FDG uptake values in the form of peak standardized uptake value normalized to lean body mass (SUL peak) of the lesions was calculated using 1.0 cm diameter is contour volume Region of Interest (ROI) at the hottest tumor site. SUL peak was derived for up to 5 hottest tumor lesions (maximum of 2 per organ). The percentage of change in SUL peak of target lesions was calculated in follow-up scan using following formula:

{Baseline target lesion SUL peak - follow-up target lesion SUL peak/baseline target lesion SUL peak} × 100

Based on PERCIST 1.0, Metabolic responses were categorized as A) Complete Metabolic Response (CMR) where target lesions show complete resolution of FDG uptake with uptake indistinguishable from the surrounding background or liver, B) Partial Metabolic Response (PMR): Decrease of greater or equal to 30% and of at least 0.8 SUL units between hottest lesions on two scans with no new lesion or identifiable increase in size of tumor. C) Stable Metabolic Disease (SMD): Increase or decrease of SUL peak of less than 30%. D) Progressive Metabolic Disease (PMD): Increase of SUL peak greater than or equal to 30% with new lesions.

Statistical analysis was performed with SPSS version 23 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp). For the comparison of change in response category of bone lesions versus other non-measurable lesions, Fischer's Exact test was applied. Difference was considered significant when P value <0.05. Response differences between RECIST 1.1 and PERCIST 1.0 were noted and compared in two groups of patients having non-measurable and mixed disease pattern (non-measurable and measurable).

Results

The study population comprise of total 45 patients, including 43 females and 2 males with age ranging from 30 to 80 years (mean age: 48.71, Std Dev: 13.1). 3 patients presented with bilateral breast involvement, while 22 patients with right and 20 patients with left breast carcinoma. Histopathologically 38 patients were of invasive ductal carcinoma, 2 of invasive ductal carcinoma with focal neuroendocrine differentiation, 2 of mucinous carcinoma, 2 of invasive lobular carcinoma and 1 with keratinizing squamous cell carcinoma. 24 patients were hormone receptor positive with negative HER2, 7 patients with negative hormone receptor with positive HER2, 11 patients with both receptor and HER2 positive and 3 patients with receptor and HER2 negative.

After RECIST 1.1 evaluation: 26 patients (57.8%) were having only non-measurable disease and 19 patients (42.2%) were having mixed disease (Both measurable and non-measurable lesions) on the baseline scans. Non-measurable disease burden in total 45 patients includes; Bone metastases- 23 patients (51 %), small lymph nodes (Less than 15 mm in short axis)- 12 patients (26%), lung nodules (Less than 10 mm)/Pleural disease- 8 patients (17%), diffuse subcutaneous/ cutaneous/intramuscular lesions– 8 patients (17 %), inflammatory breast disease- 3 patients (6.7%), liver and adrenal lesion (less than 10 mm) – 1 patient (2.2 %).

Table 1: PET/CT Acquisition parameters.

CT: Topogram	KV- 120, mA-35, slice-0.6 mm, direction craniocaudal
CT; Whole body	CT: Care Dose 4D activated, Quality reference effective mA: 30, KV -120. Slice -5 mm, second reconstruction- 3 mm, Direction- Craniocaudal. Rotation time-0.5 s, Pitch: 0.9. delay 2 s, Algorithm- 30f medium smooth, window- abdomen, strength- 4, safire-on
PET: whole body	Reconstruction method: Iterative reconstruction. TOF, True x point spread function. Iterations-2. Subset 21. Image matrix- 400. Zoom-1.0. Filter- Gaussian. FWHM- 3.0. Offset: X-00, Y- 00.

Table 2: Comparison of RECIST 1.1 versus PERCIST 1.0 in total study population: Shows discordant results in 13 (28.8%) patients - showing stable disease on RECIST 1.1, while PERCIST showed CMR in 5, PMR in 2 and PMD in 6 patients.

Tumour Response by RECIST 1.1	Tumour response by PERCIST 1.0				
	CMR	PMR	SMD	PMD	Total
CR	2	0	0	0	2
PR	0	9	0	0	9
SD	5	2	5	6	18
PD	0	0	0	16	16
Total	7	11	5	22	45

Table 3: Comparison of RECIST 1.1 versus PERCIST 1.0: Mixed group (non-measurable + measurable): No discordant results in this group of 19 patients.

Tumour Response by RECIST 1.1	Tumour response by PERCIST 1.0				
	CMR	PMR	SMD	PMD	Total
CR	1	0	0	0	1
PR	0	9	0	0	9
SD	0	0	1	0	1
PD	0	0	0	8	8
Total	1	9	1	8	19

Response evaluation by RECIST 1.1 categorized into; CR in 2 (4.4 %) patients (1 in non-measurable, 1 in mixed group), PR in 9 (20%) patients (0 in non-measurable, 9 in mixed group). SD in 18 (40%) patients (17 in non-measurable, 1 in mixed group). PD in 16 (35.6%) patients (8 in non-measurable, 8 in mixed group).

Response evaluation by PERCIST 1.0 categorized into; CMR in 7 (15.6%) patients (6 in non-measurable, 1 in mixed group). PMR in 11 (24.4%) patients (2 in non-measurable, 9 in mixed group), SMD in 5 (11.1%) patients (4 in non-measurable, 1 in mixed group). PMD in 22 (48.9 %) patients (14 in non-measurable, 8 in mixed group). These results are summarized in Table 2.

Table 4: Comparison of RECIST 1.1 versus PERCIST: Non-measurable Group: shows discordant results in 13 (50%) out of 26 patients- showing stable disease on RECIST 1.1, while PERCIST showed CMR in 5, PMR in 2 and PMD in 6 patients.

Tumour Response by RECIST 1.1	Tumour response by PERCIST 1.0				
	CMR	PMR	SMD	PMD	Total
CR	1	0	0	0	1
PR	0	0	0	0	0
SD	5	2	4	6	17
PD	0	0	0	8	8
Total	6	2	4	14	26

Out of total 45 patients' discordant results between RECIST 1.1 and PERCIST 1.0 were seen in 13 patients (28.8%). All patients showing discordant results were showing stable disease by RECIST 1.1 criteria, but PERCIST 1.0 criteria showed complete metabolic response in 5 patients (11.1%), Partial metabolic response in 2 patients (44.4%) and progressive disease in 6 patients (13.3%).

These results were further grouped into 2 categories based on RECIST 1.1.

A) First category with both measurable and non-measurable disease components; According to RECIST 1.1 measurable disease was taken as target lesion and non-measurable disease as nontarget lesions and response was quantified accordingly. In total 19 patients in this group, the RECIST 1.1 and PERCIST were concordant in all the cases. No discordant results were found in this category between RECIST 1.1 and PERCIST 1.0. These results are shown in Table 3.

B) The second category was of patients with non-measurable disease component only, which included bone lesions, lung and pleural disease, diffuse cutaneous, subcutaneous, intramuscular disease, inflammatory breast cancer and lesions less than <10 mm and lymph nodes <15 mm in short axis. With RECIST 1.1 target lesion could not be defined and non-measurable component was quantified

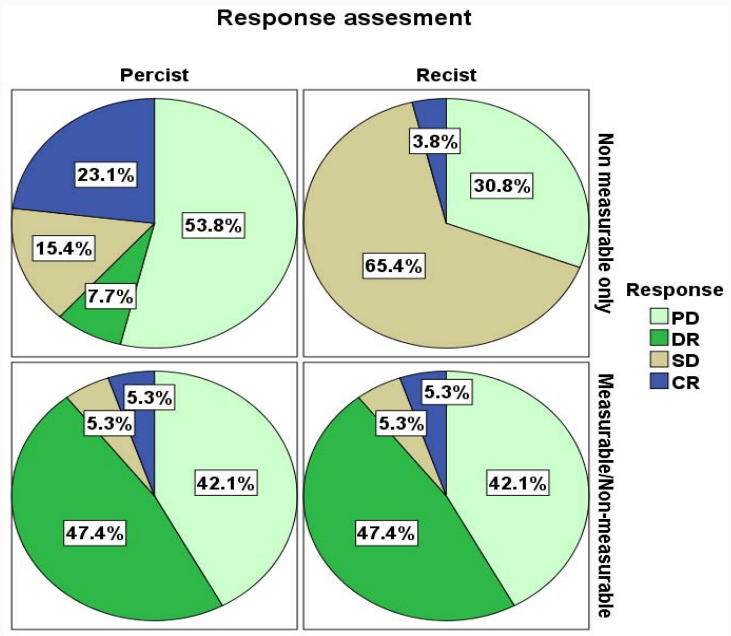

Figure 2: Pie charts comparing PERCIST versus RECIST in categories of 1) non-measurable disease and 2) mixed– Measurable with non-measurable disease shows significant change in response category in non-measurable disease group: 13 patients (50% of patients). No change in category of mixed group.

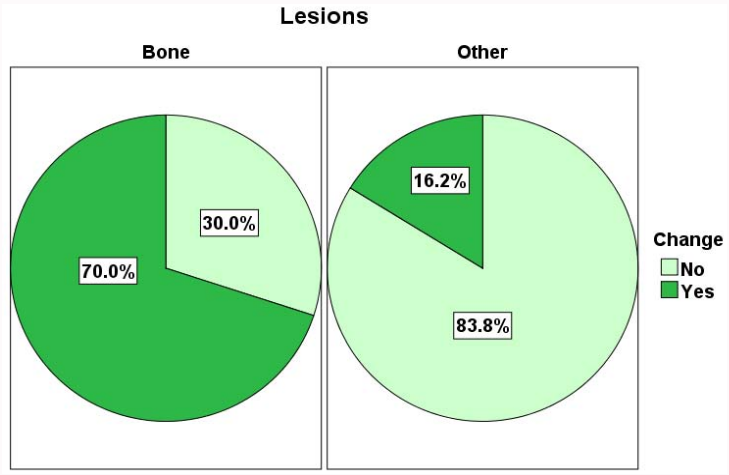

Figure 3: Pie Chart comparing change in response from RECIST to PERCIST with patients of bone metastases versus other site of metastases in non-measurable category: Shows significant change in patients with bone disease. Fishers Exact Test: P value – 0.002.

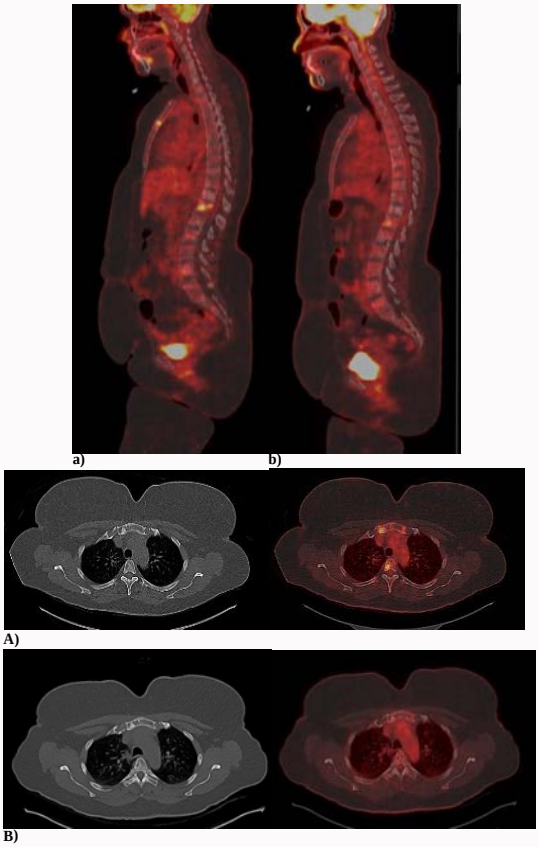

Figure 4: 52-year female with metastatic breast cancer. PET/CT images obtained at baseline (a) and after treatment (b); shows multiple FDG avid osteolytic bone metastases on baseline which on follow up shows stable disease with RECIST 1.1 and Partial Metabolic response with PERCIST 1.0.

as nontarget lesions on CT images. PERCIST 1.0 could well quantify disease in this category with SUV values. Out of 26 patients in this group, discordant results were seen in 13 patients. 50% of patients in this category showed discordant results between RECIST 1.1 and PERCIST 1.0. All the discordant category patients showed stable disease on RECIST 1.1, while PERCIST showed complete metabolic response in 5, partial metabolic response in 2 and progressive disease in 6 patients. These results are summarized in table 4 and Figure 2.

In 26 patients with non-measurable disease only category, 17 patients showed single site of metastases (10 patients bone, 3 with lymph nodes <15 mm in short axis, 1with lung nodules <10 mm, 1 patient with diffuse Cutaneous/subcutaneous and intramuscular disease and 2 with infiltrating breast disease). Rest of the 9 patients presented with multiple sites of non-measurable disease with different combinations of bone, lymph nodes, lung nodules, pleural disease, liver lesions, and adrenal gland lesion and diffuses cutaneous, subcutaneous and intramuscular disease.

Bone was the most common site of metastases as compared to

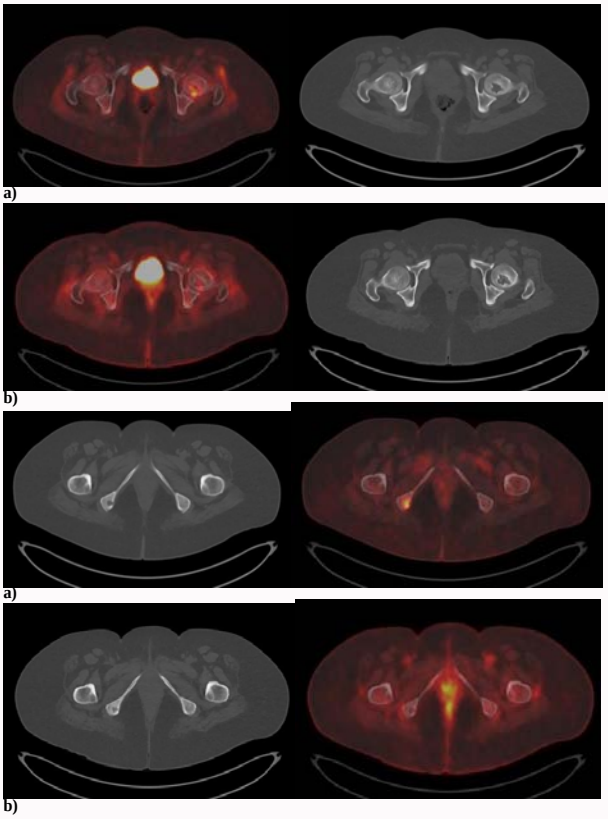

Figure 5: 49 Year female with bone metastases. PET/CT images obtained at baseline (a) and follow up after treatment (b): Shows multiple FDG avid osteolytic bone metastases on baseline. Follow up shows Stable disease by RECIST 1.1 and complete metabolic response by PERCIST 1.0.

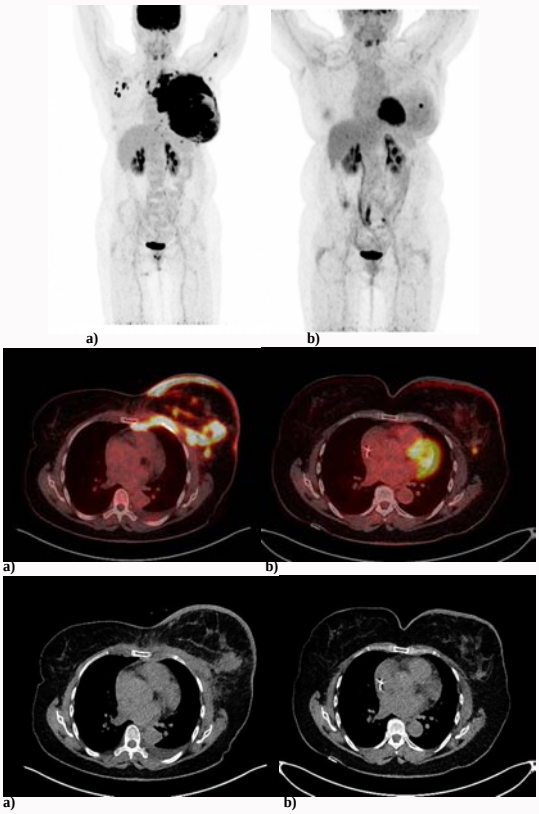

Figure 6: 65 yr/Female. Breast cancer with both measurable and non-measurable disease. PET/CT images obtained at baseline (a) and follow up after treatment (b): Shows multiple FDG avid lesion in left breast and left anterior chest wall on baseline. Follow up images show partial response on RECIST 1.1 and partial metabolic response on PERCIST 1.0

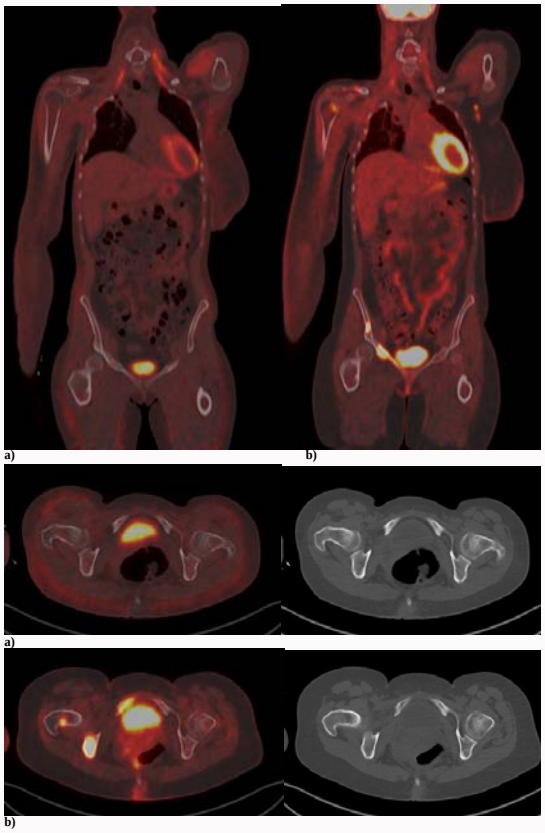

Figure 7: 38 Year female with treated breast cancer on follow up. PET/CT images obtained at baseline (a) and follow up after treatment (b): Shows an absence of FDG avid disease on baseline, which remains unchanged on CT images and RECIST 1.1, however new FDG avid skeletal lesions are seen on PET with progressive metabolic disease with PERCIST 1.0.

other lesions in non-measurable disease category. Ten patients showed only bone metastases with no other site of metastases. Out of 10 patients 7 patients (70%) showed change in response from RECIST 1.1 to PERCIST 1.0. Significant change was seen in bone lesions (70%) as compared to other lesions (16.2%) between RECIST 1.1 and PERCIST 1.0 with P value- 0.002 (Figure 3).

Both (2) patients with inflammatory breast cancer showed change in response between the two categories. None of the patients with lymph nodes in non-measurable disease category showed change from RECIST 1.1 to PERCIST 1.0. Most of the lung nodules which were non-measurable by RECIST 1.1 (those with size <10 mm) were also negative on PET scan and thus could not be quantified either by CT or FDG PET/CT. 4 out of 9 patients with multiple sites of non-measurable disease also showed change in response category from RECIST 1.1 to PERCIST 1.0 (Figure 4).

Discussion

Our study compared RECIST 1.1 and PERCIST 1.0 in locally advanced, recurrent and metastatic breast cancer and 28.8% of patients showed discordant results Between RECIST 1.1 and PERCIST 1.0. All patients with discordant results were showing stable disease by RECIST 1.1 criteria, although PERCIST 1.0 criteria showed complete metabolic response in 5 patients (11.1%), Partial metabolic response in 2 patients (4.4%) and progressive disease in 6 patients (13.3%). We also compared RECIST 1.1 and PERCIST 1.0 response in patients with a) non-measurable disease and b) Mixed disease including both measurable and non-measurable disease. Discordant results between the two criteria (RECIST 1.1 and PERCIST 1.0) were seen in only the group of non-measurable disease with significant difference in osseous metastases with p value- 0.002 (Figure 5). Discordant results were also seen in inflammatory breast cancer and in patients with multiple sites of non- measurable disease.

Various studies in literature have compared RECIST 1.1 with PERCIST 1.0 and have shown superiority of PETCT over other imaging in breast cancer patients.

Pooled analysis by Seon Jeong Min et al. in 2016 showed six articles comparing RECIST and PERCIST from 2009 till Jan 2016. Out of 268 patients, considerable disagreement of response between the two criteria was seen in 37.7% of the patients. Tumor response was upgraded in 85 patients and downgraded in 16 with PERSIST. They also observed that change in response category was seen most frequently seen in patients with SD by RECIST. If PERCIST is adopted for response assessment instead of RECIST the management plan will change in 7.8% of patients and they concluded that PERCIST might be more suitable for assessing tumor response. Their results were similar to our results. Although they included different types of solid tumors in their study and only 28 patients were of breast cancer [6].

Similarly other study has shown advantage of PERCIST over RECIST as it can overcome the limitations of RECIST. The authors have shown that PERCIST can overcome the problem of the RECIST-stable category by showing the metabolic response or progression. Since FDG uptake is determined by metabolic activity, it has been shown to correlate with tumor cell proliferation. The inhibition of tumor growth will result in reduced FDG uptake and will not remain stable. They demonstrated that PET/CT is more accurate in

identification of progressive disease from stable disease and FDG PET and PERCIST may be better suited to detect true disease stabilization in single arm studies than CT. This is also similar to our study findings where change in response category was seen only in patients with stable disease by RECIST 1.1 [10] (Figure 6).

Adequate response evaluation is critical in avoiding cost and harmful effects of ineffective chemotherapeutic drugs. PET has shown to predict early response, before the anatomical changes. PERCIST 1.0 has also shown to be superior in correlating response criteria with clinical course of disease and survival. Different authors [11,12], in their studies on different tumors showed a better correlation of PERCIST response with progression free survival as compared to RECIST. In their study PERCIST response identified two groups of patients with significantly different survival within patients classified as SD by RECIST.

Furthermore, studies have shown poor correlation between tumor response and survival by RECIST. Data from a meta-analysis of randomized phase trials including a total of 2,126 patients of metastatic breast cancer showed poor correlation between survival and tumor response according to RECIST, which led to an ongoing discussion if tumor response according to RECIST should be, used an endpoint for drug approval in breast cancer [13].

In our study in addition to comparison between RECIST 1.1 and PERCIST 1.0 we have also compared the change in these response categories in two groups of lesions defined by RECIST 1.1. A) Non-measurable disease only B) Mixed- measurable and non-measurable disease. Our results have shown that no difference in response category was seen in patients with mixed disease. All discordant results were seen in patients with non-measurable disease only. Our study is unique as there is no similar study done in the past.

In our study 50% of patients in non-measurable disease category showed change in response from RECIST 1.1 to PERCIST 1.0. Bone lesions, which is also the most common site of metastases has showed significant difference between RECIST 1.1 and PERCIST 1.0. Non-measurable lesions like inflammatory breast disease have shown difference in response category by RECIST 1.1 and PERCIST 1.0. Bone is known to be the most common metastatic site in breast cancer patients as seen in our study as well. It affects approximately 50% to 70% of patients with relapse and in 28% to 44% of patients is the only site of disease [14,15]. As mentioned in literature also there is significant difference between RECIST 1.1 and PERCIST 1.0, while assessment of bone metastases. Different authors [10,16,17,18] have shown advantage of PET CT over other imaging modalities. PETCT can better detect tumor response and progression in the skeletal disease as compared to CT. These studies have also demonstrated FDG PETCT to be superior in differentiating healing (flare-phenomenon) response from true progression in sclerotic skeletal metastases. Skeletal metastases show decline in FDG uptake similar to soft tissue metastases and are more sensitive than CT in response assessment. Further response in patients with only skeletal metastases cannot be assessed with RECIST.

According to ACR [3], PET/CT is the most appropriate imaging for staging or assessment of response to therapy in patients with locally advanced breast cancer and suspected metastatic disease. PET/CT is preferable to conventional CT chest, abdomen, and pelvis imaging in these settings if available. PET/CT is an alternative to CT and bone scan to be done routinely if greater than stage IIIA disease. It is superior in detecting internal mammary and mediastinal lymphadenopathy. It is not useful for invasive lobular carcinoma or low-grade malignancy. In our study, we have also observed that FDG PETCT can change response category from RECIST 1.1 to PERCIST 1.0 when done in selected patients with non-measurable disease. The limitations of our study were small sample size, retrospective study and selection bias as only those patients undergoing PETCT scans were included and may not represent the entire breast cancer population. Brain lesions were not assessed due to low sensitivity of PET scan. RECIST 1.1 was calculated from the non-enhanced low dose CT examination (which is a standard protocol for PET/CT) (Figure 7).

Conclusion

PERCIST 1.0 is superior to RECIST 1.1 in quantitative response evaluation in locally advanced, recurrent and metastatic breast cancer, especially in patients with non- measurable disease mainly bony metastatic disease. PERCIST 1.0 can better evaluate disease in patients with stable category by RECIST 1.1. FDG-PET/CT is preferred to CT due to presence of significant non measurable disease which can be accurately quantified on PET/CT. All patients with non-measurable disease on CT should be evaluated with FDG PET/CT rather than CT.

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