https://doi.org/10.33472/AFJBS.6.2.2024.829-837

African Journal of Biological Sciences

Research Paper Open Access

Comparison between RECIST and PERCIST criteria in assessment of response to neoadjuvant therapy in patients with locally advanced rectal cancer

Sherin Wagieh [1], *Dina Deif [2], Ahmed Said Abdelmaksoud [2], Abeer Ali El-Sharawy [3] and Esraa EL-Kholy [2]

[1] Department of Oncology and Nuclear Medicine, Faculty of Medicine, Cairo University.
[2] Department of Radiation Oncology and Nuclear Medicine , National Cancer institute, Cairo University.
[3] Department of Radiology, National Cancer Institute, Cairo University.
*Corresponding author: Dina Deif

Email: deenadeif@gmail.com

Article History

Volume 6, Issue 2, April 2024

Received:19 April 2024

Accepted: 27 May 2024

Published: 27 May 2024

doi: 10.33472/AFJBS.6.2.2024.829-837

Abstract: Response to neoadjuvant therapy (NAT) in patients with locally advanced rectal cancer (LARC) has a great impact on further management strategy. MRI and FDG- PET/CT using RECIST and PERCIST response criteria respectively play an important role in response assessment.
Aim: To detect the value of MRI and PET/CT using RCIST and PERECIST criteria in assessment of response to NAT in patients with LARC with comparison between diagnostic performance of both diagnostic modalities.
Patients and methods: A total of 30 patients with LARC were included, PET/CT and Pelvic MRI were performed pre and post NAT followed by surgical resection. Imaging studies were analyzed and response was evaluated with RCIST and PERECIST response criteria and subsequently correlated with post-operative pathological results.
Results: Assessment response criteria for MRI (RECIST) and for PET/CT (PERCIST) showed statistically significant correlation with pathological response. Discordance response results between both studies were found in 7 patients (23.3%). MRI using RECIST response criteria has better specificity (78.3 % vs 47.8 %), positive predictive value (58.3 %vs 36.8%) and overall accuracy (83.3% vs 60%) in comparison to PET/CT using PERCIST response criteria.
Conclusion: MRI and PET/CT using RECIST and PERCIST response criteria have significant value for assessment of response to NAT in patients with LARC with relatively more superior diagnostic performance figures for the former.

Keywords: *PETCT, MRI, PERCIST, RECIST, assessment of response*

Introduction

The standard treatment strategy of locally advanced rectal cancer (LARC) is in the form of neoadjuvant chemoradiotherapy (NAT), total mesorectal excision, and postoperative chemotherapy. Response to NAT ranged from sustained tumor progression to complete pathological response, the latter was reported to occur in up to 42% of patients in some reports. Those patients can benefit from less invasive treatment options with previous evidence indicated that surgery could be omitted in those patients, applying the watch-and-wait strategy. Therefore, accurate assessment of response to NAT using proper diagnostic modalities as MRI and

FDG-PET/CT becomes mandatory for more therapy optimization aiming at personalized treatment strategy. (1)

In 2000, the Response Evaluation Criteria in Solid Tumors working Group proposed RECIST guidelines version 1.0 as response evaluating criteria, and in 2009 RECIST 1.1 has been developed. In RECIST criteria a single (unidimensional) measurement is used for tumor response evaluation depending on degree of tumor shrinkage overtime. Despite the fact that it is widely used as an anatomic tumor response metric, yet, this morphological assessment has some limitations that raised the need for a diagnostic modality that can evaluate metabolic tumor response. Many authors stated that the latter can be used as a predictor of response to therapy before occurrence of any tumor shrinkage.(2, 3; 4)

FDG- PET/CT is a hybrid imaging modality that is widely used for evaluating metabolic activity in various tumors. It is believed to be more informative for the evaluation of early treatment response to NAT in different malignancies. Wahl et al in 2009, published the PET Response Criteria in Solid Tumors (PERCIST) as a new standardized method for quantitative assessment of metabolic tumor response that becomes one of the most popular PET/CT criteria used to assess response to traditional and novel anticancer therapy. (5, 6)

Many studies are there comparing the diagnostic performance of RECIST and PERCIST criteria in assessment of response to preoperative NAT in locally advanced various malignancies including rectal cancer, part of the literature is in favor of PET/CT and part highlights MRI as superior in this setting (2, 7, 8).

The aim of the current study is to assess the diagnostic value of MRI and PET/CT using RECIST and PERCIST criteria in assessment of response to NAT in patients with LARC with comparison between their diagnostic performance.

Patients and methods:

-This is a prospective follow up study done in National Cancer Institute in Egypt in the period from June 2021 and August 2022. All enrolled patients had locally advanced colorectal cancer, they underwent both pre and post neoadjuvant treatment FDG PET/CT and Pelvic MRI. Both diagnostic modalities were interpreted and analysed using PERCIST and RECIST response criteria and results were subsequently correlated with post-operative pathological results. Patients were enrolled in the current study according to the following criteria.

Inclusion criteria:

a) Adult patients (>18 years) with pathologically proven colorectal cancer.
b) Locally advanced non metastatic tumors.
c) Patients who agree to perform both MRI and FDG-PET/CT scans prior and post NAT for initial staging and for assessment of response to therapy respectively.
d) Patients who perform surgery post adjuvant therapy and diagnostic imaging with full pathological report.
e) Patients who provided consent.
f) No comorbid disease.

Exclusion criteria:

a) Pregnancy
b) Patients with double primary
c) Presence of metastatic lesions
d) Patients who received any form of previous anti-cancer therapy.

MRI technique:

-DWMRI

In all patients a 1.5 Tesla MRI machine with the following MR sequences:

-Multiplanar MRI sequences; including T1 and T2 weighted images.

-The axial T2 weighted and diffusion weighted image sequences are angled in identical planes perpendicular to the rectal lumen at the site of the tumor.

-Contrast-enhanced T1 & fat-suppressed T1-weighted sequences.

FDG-PET/CT technique

Patients were given the instruction to fast at least 6 hours before tracer injection and avoid rigorous activity and high carbohydrate meals the day before PET/CT scan.

The 18 F FDG PET/CT was done by the following technique on GE hybrid PET/CT:

- Patient was injected intravenously by a dose of F18 FDG dose of 5 MBq/Kg after confirming adequate blood glucose level.
- Image acquisition was done approximately 45-60 minute after IV injection.
-Low dose non contrast CT was acquired first for the purpose of anatomic localization and attenuation correction.
-PET is acquired from skull to knees (6-8 beds) and reconstructed using ordered subset expectations maximization algorithm and attenuation correction data from CT.
-Data were processed and displayed and fused images are displayed in trans-axial, sagittal and coronal projections.

Management strategy:

According to guidelines for management of patients with LARC in National Cancer Institute in Egypt, included patients are managed as follow:

a) Neo-adjuvant therapy (NAT): long course of chemo-radiotherapy, consists of 25 to 28 fractions of localized radiotherapy with alongside fluorouracil-based chemotherapy.

b) Diagnostic imaging in the form of MRI and PET/CT for assessment of response to NAT.

c) Surgical excision and histopathological assessment: surgery is done mainly by either abdominal perineal excision or lower abdominal resection depending on the involvement and proximity to sphincters.

Imaging analysis

Image analysis:

DW MRI Images were read on PACS system by a radiology consultant, structural data and measurements were obtained and tabulated for analysis and RECIST 1.1 criteria for response was used.

FDG - PE/ CT:

PET/CT images were analyzed both qualitatively and quantitatively on GE workstation, whole body images were analyzed and 3D ROI (region of interest) were placed over entire lesion to obtain quantitative data, the ROI was placed using a semi quantitative software with calculation of SUV. FDG uptake corrected to lean body mass (SULpeak) was quantitatively calculated.

Images were analyzed by nuclear medicine consultant through visual inspection, comparison of PET and CT data, and viewing of fused PET/CT images and quantitative data were all used in the analysis of the PET/CT study. For PET/CT interpretation, PERCIST 1.0 criterion were applied.

Response evaluation method

Objective therapeutic responses in MRI according to RECIST 1.1 are as follows (1): complete remission (CR) is disappearance of target lesion, partial remission (PR) is a decline of at least 30% in tumor diameter; stable disease (SD) is neither PR nor progressive disease (PD); and PD is at least a 20% increase in tumor diameter.(Aykan & Özatlı, 2020). We considered those who achieved CR and PR responders to NAT and those with SD or PD are non-responders.

The objective therapeutic responses based on PERCIST 1.0 (1) Complete resolution of 18F-FDG uptake inside the quantifiable target lesion, with no additional new 18F-FDG-avid lesions, to the point where it is less than mean liver activity and indistinguishable from background blood-pool levels in the surrounding area is known as complete metabolic response or CMR. (2) At least 30% decrease in the target tumor's 18F-FDG SUL peak is known as a partial metabolic response, or PMR (3) Diseases other than CMR, PMR, or progressive metabolic disease (PMD) are referred to as stable metabolic diseases (SMD); (4) PMD is defined as a 30% increase in 18F-

FDG SULpeak or the emergence of new lesions that are 18F-FDG-avid and are indicative of malignancy.(16) . Responders to NAT are those who achieved CMR and PMR, while non-responders are those with SMD and PMD.

Histopathological analysis

Pathological response served as the gold standard and pathology derived TRG (tumor regression grading system) was established by a pathologist; 0, 1 were categorized as major responders and 2 and 3 were considered as non-responders.

Statistical analysis: Data were analyzed using software package for the Social Sciences (SPSS) version 28. For categorical data, Chi square ($\chi 2$) test was performed. (Chan, 2003). Standard diagnostic indices including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic efficacy were calculated as described by (Galen, 1980). P-values less than 0.05 were considered as statistically significant.

Results:

PERCIST Versus RECIST in Relation to Response to Therapy:

There was difference in response to NAT in PET/CT and MRI using PERCIST and RECIST response criteria, 11 patients were non responders on PERCIST as compared to 18 according to RECIST criteria (table 1, Fig1). Using pathological response as the gold standard, only seven patients (23.3%) were responders (0,1 TRG), and the remaining 23 were non-responders (2,3TRG). Those 7 responders were also responders in PET/CT and MRI using PERCIST and RECIST response criteria (table 2, Fig 2). Both PET/CT and MRI using their corresponding response criteria showed a statistical significance in assessment of tumour response to NAT compared to gold standard (post-operative pathology) , with a p value of 0.029 and <0.001 respectively (table2).The use of RECIST response criteria in MRI study exhibits relatively better diagnostic performance figures with more specificity, positive predictive value and overall accuracy compared to employment of PERCIST response criteria in PET/CT (Table3).

Table 1 Response according to PERCIST & RECIST (n=30)

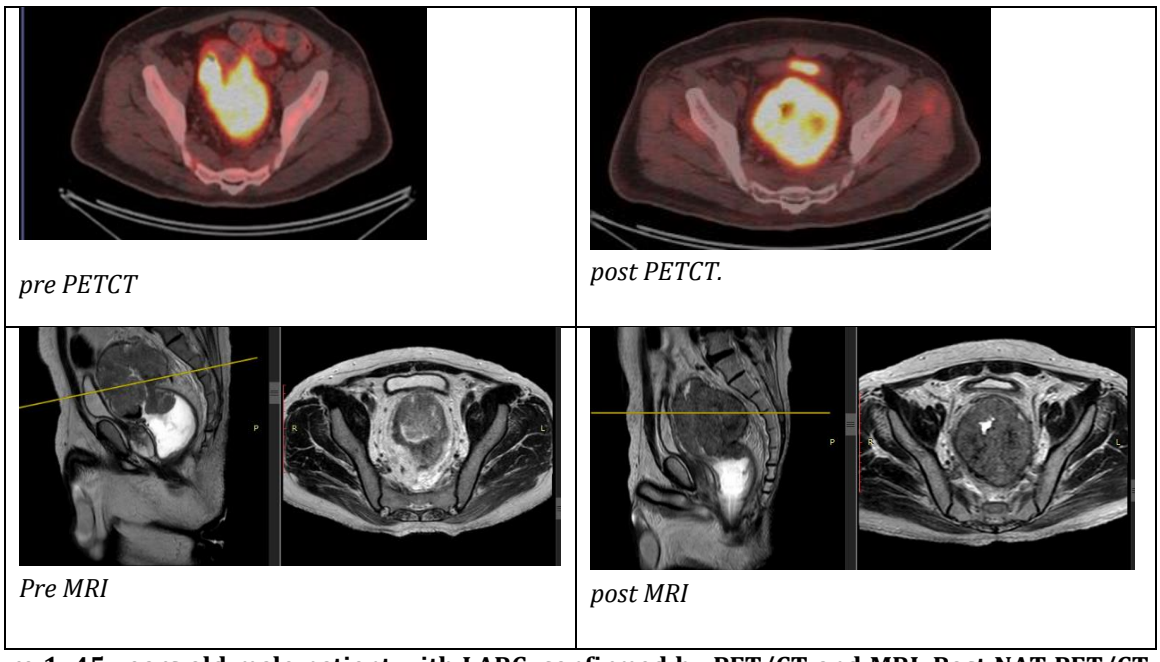
	(n=30)	
PERCIST response		
	N	**(%)**
Non responders	**11**	**36.7**
SMD (stable metabolic disease)	**10**	**33.3**
PMD (progressive metabolic disease)	**1**	**3.3**
Responders	**19**	**63.3**
CMR (complete metabolic remission)	**1**	**3.3**
PMR (partial metabolic remission)	**18**	**60**
RECIST response		
Non responders	**18**	**60**
SD (stable disease)	**17**	**56.6**
PD (progressive disease)	**1**	**3.36**
Responders	**12**	**40**
CR (complete response)	**1**	**3.3**
PR (partial response)	**11**	**36.6**

Table 2: Correlation between response according to PERCIST & RECIST to pathological response

		Pathological response				
		Non responder (n=23)		**Responder (n=7)**		
		n	**(%)**	**n**	**(%)**	p-value
PERCIST	Non responders (n=11)	11	(100)	0	(0.0)	0.029
	Responders (n=19)	12	(63.2)	7	(36.8)	
RECIST	Non responders (n=18)	18	(100)	0	(0.0)	<0.001
	Responders (n=12)	5	(41.7)	7	(58.3)	

Table 3: Diagnostic performance of PERCIST/RECIST for prediction of response to neoadjuvant therapy

Parameter	PERCIST	RECIST
Sensitivity	100%	100.00%
Specificity	47.8%	78.26%
Positive predictive value	36.8%	58.33%
Negative predictive value	100%	100.00%
Overall accuracy	60.0%	83.33%



pre PETCT

post PETCT.

Pre MRI

post MRI

Figure 1: 45 years old male patient with LARC, confirmed by PET/CT and MRI. Post NAT PET/CT and MRI showed PMD and PD using PERCIST and RECIST criteria respectively. Post operative pathology revealed extensive residual tumour

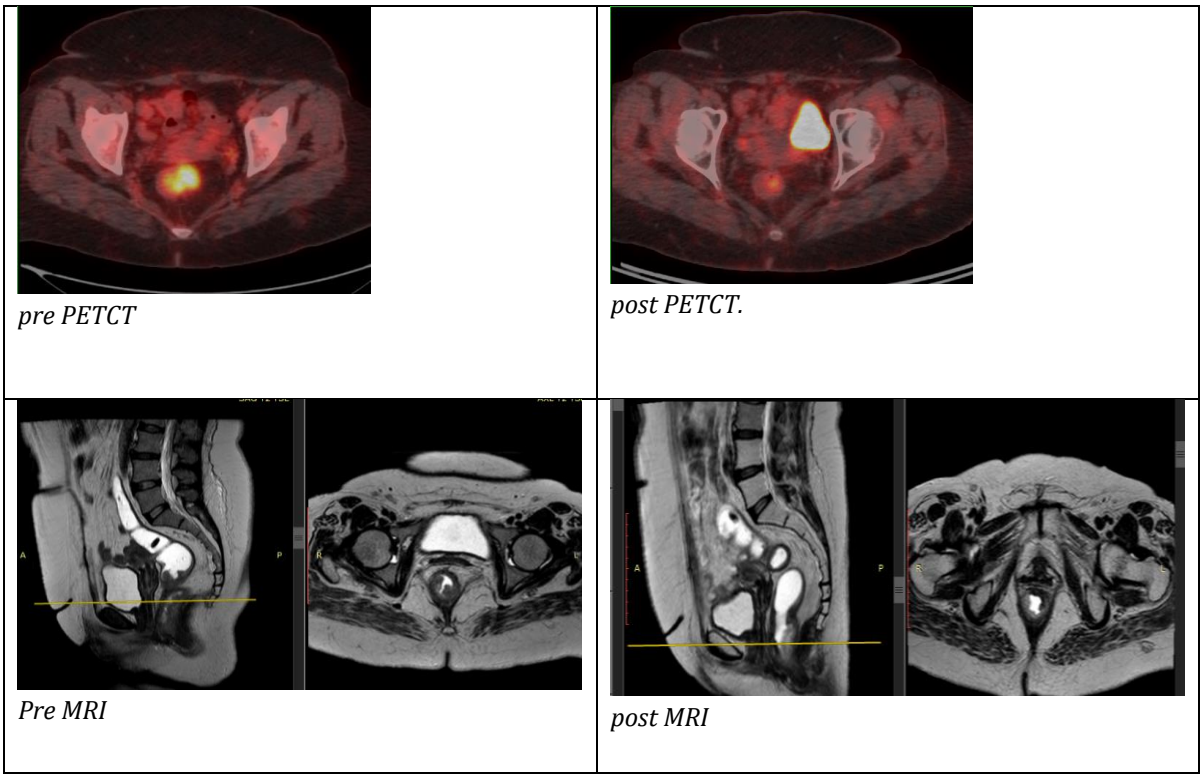


Figure 2: 44 years old female Patient with LARC confirmed by PET/CT and MRI. Post NAT, PET/CT and MRI showed CMR and CR using PERCIST and RECIST criteria respectively. Post operative pathology revealed complete pathological response

Discussion

Assessment of regional tumor response of LARC to NAT is currently mainly performed with MRI, being considered the accepted standard of care. Ramos et al. (10), reported that MRI is a crucial tool for staging and assessing clinical response to NAT in patients with LARC. It has a great value in estimating the degree of tumor response, in detecting mesorectal and extra-mesorectal lymph node status and tumor relationship to the mesorectal fascia post NAT. (9, 10). Liu et al. (11) stated that MRI is useful in assessment of response to NAT with 51% of patients experienced a reduction in T stage and 60% in N stage when evaluated with MRI. Ramos et al. (10) reported that MRI accuracy is 59.4% for stage T, 65.1% for stage N, and 77% for circumferential resection margin involvement.

Though it was reported that MRI is essential for evaluation response to NAT, yet, Ramos et al. (10) stated that it should not be the sole basis for therapeutic decisions as its concordance with anatomopathological study is limited (10). This is due to the fact that morphological assessment can be limited by several issues such as ill-defined margins, complex lesions with partially cystic areas, post therapeutic scar tissue or fibrosis and more importantly inability to detect an ongoing tumor metabolic change in response to early effective therapy.(4)

In the last few decades, PET/CT has gained a continuously emerging role in staging and restaging of malignant lesions. With the appearance of its different quantitative parameters, it becomes a greatly valuable metabolic diagnostic modality for tumor imaging. It rapidly acquires a pivotal role in assessment of tumor response to therapy aiming to overcome the limitations of other imaging modalities depending solely on morphological changes and tumor shrinkage. (7).

Caruso et al, (12), in a study using FDG PET/CT on 137 patients with LARC found an optimal cut-off to distinguish responders from the non-responders to NAT at 70% of the Δ%SUV. Furthermore, they stated that Δ%SUV was a strong discriminator between responders and non-responders with an accuracy of 81%, a

sensitivity of 84.4%, a specificity of 80%, a positive predictive value of 81.4%, and a negative predictive value of 84.2%. They concluded that 18F-FDG PET-CT may be an indicator to evaluate pathological response to NAT in patients with LARC.

In our study both PERCIST and RECIST response criteria in PET/ CT and MRI diagnostic performance for assessment of response to NAT in patients with LARC was analysed. A difference in response to NAT regarding both PERCIST and RECIST was found, 11 patient (36.7%) were non responders with 19 responders (63.3%) on PECIST as compared to 18 non responders (60%) and 12 responders (40%) according to RECIST response criteria. Discordance between PERCIST and RECIST was found in 7 patients (23.3%), diagnosed as responders in PERCIST and non-responders in RECIST. Applying both PERCIST and RECIST response criteria showed a statistical significance ($P<0.05$) when compared with pathological response. For assessment of response to NAT in patients with LARC, the use of RECIST criteria in MRI study has better specificity (78.3% *vs* 47.8%), positive predictive value (58.33% *vs* 36.8%) and accuracy (83.3% *vs* 60%) in comparison with the application of PERCIST criteria in PET/CT study.

Min et al (4) in a study for comparison of PET /CT's PERCIST and MRI's RECIST criteria in assessment of response of various solid tumors to NAT, reported that discordant results between the two criteria was seen in 37.7% of patients. They estimated significantly different overall response rates between the two criteria in favor of PET/CT's PERCIST (35.1% by RECIST vs. 54.1% by PERCIST, $P < 0.0001$). They concluded that PERCIST might be more suitable for assessing tumor response than the RECIST criteria. Kim et al (13), in another similar report on patients with different malignancies confirmed these results, with higher discordance in the assessment of tumor response between the two response criteria of 44.5%. They also stated that on adopting the metabolic criteria instead of RECIST criteria, there is significant increase in detected overall response rate(13). The results from those two reports are different from the finding in the current study as the discordance in the results of the two response criteria in our study is 23.3%. Besides, we found that the use of RESICT criteria was more accurate with more specificity in response assessment of LARC to NAT, in discordance to results from the two aforementioned studies. This may be due to evidently smaller number of patients in our study and more importantly the inclusion of different types of malignancy receiving different NAT regimens in their reports compared to inclusion of one type of malignancy in the current study. Kim et al, (13) recommended the need for further assessment of the metabolic response criteria to be investigated in larger studies with homogeneous patient cohorts for assessment of the value of both response criteria in single malignancy as done in our study.

Few reports are there comparing the two response criteria in assessment of response of LARC to NAT. Lee et al (14), in a report based on a systematic review and meta-analyses of studies conducted for direct comparison of the diagnostic performance of F-18 FDG PET/CT and MRI for the prediction of pathologic response to NAT in patients with LARC reported a pooled sensitivity and specificity of F-18 FDG PET/CT of 0.79 and 0.74 respectively. Those figures for MRI were 0.89 and 0.66. They concluded that F-18 FDG PET/CT and MRI showed similar diagnostic performances for the prediction of pathologic responses to NAT in patients with LARC. They concluded that each modality can be a complement to the other rather than being used singly.

Gao et al in (15), in another meta-analysis based on published studies and investigated the predictive value of MRI and FDG-PET for the response to NAT of patients with LARC. They concluded that MRI and FDG-PET have a moderate diagnostic ability for assessment of response of patients with LARC to NAT. The results of their analyses suggested that MRI was associated with elevated specificity and positive likelihood ratio than FDG-PET in predicting response to NAT in patients with LARC. This goes with the higher specificity, positive predictive value and accuracy of MRI using RECIST response criteria reported in our study. Their final conclusion was that MRI might be superior than FGD-PET for the prediction of the response of patients with LARC to NAT.

Conclusion:

-Using RECIST response criteria, imaging using MRI owes a sensitivity, specificity, positive predictive value, negative predictive value and accuracy 100%, of 78.3% ,58.3%, 100%and 83.3% in assessment of response to NAT in patients with LARC. Those figures for PET/CT using PERCIST response criteria are100%, 47.8% ,36.8% and 100% and 60%.

-The discordance between both criteria in assessment of response to therapy is seen in 23.3% of patients.

- MRI and PET/ CT derived RECIST and PERCIST response criteria have a significant value for assessment of response to NAT in patients with LARC with relatively more superior diagnostic performance figures for the former.

References:

1. Lopes-Ramos, C. M., Habr-Gama, A., De Souza Quevedo, B., Felcio, N. M., Bettoni, F., Koyama, F. C., Asprino, P. F., Galante, P. A., Gama-Rodrigues, J., Camargo, A. A., Perez, R. O., & Parmigiani, R. B. (2014). Overexpression of miR-21-5p as a predictive marker for complete tumor regression to neoadjuvant chemoradiotherapy in rectal cancer patients. *BMC Medical Genomics*, *7*(1).
2. Yanagawa, M., Tatsumi, M., Miyata, H., Morii, E., Tomiyama, N., Watabe, T., Isohashi, K., Kato, H., Shimosegawa, E., Yamasaki, M., Mori, M., Doki, Y., & Hatazawa, J. (2012). Evaluation of response to neoadjuvant chemotherapy for esophageal cancer: PET response criteria in solid tumors versus response evaluation criteria in solid tumors. *Journal of Nuclear Medicine : Official Publication, Society of Nuclear Medicine*, *53*(6), 872–880.
3. Kim, J. H. (2016). Comparison of the RECIST 1.0 and RECIST 1.1 in patients treated with targeted agents: A pooled analysis and review. *Oncotarget*, *7*(12), 13680–13687.
4. Min, S. J., Jang, H. J., & Kim, J. H. (2016). Comparison of the RECIST and PERCIST criteria in solid tumors: A pooled analysis and review. *Oncotarget*, *7*(19), 27848–27854.
5. Skougaard, K., Nielsen, D., Jensen, B. V., & Hendel, H. W. (2013). Comparison of EORTC criteria and PERCIST for PET/CT response evaluation of patients with metastatic colorectal cancer treated with irinotecan and cetuximab. *Journal of Nuclear Medicine*, *54*(7), 1026–1031.
6. Ding, Q., Cheng, X., Yang, L., Zhang, Q., Chen, J., Li, T., & Shi, H. (2014). PET/CT evaluation of response to chemotherapy in non-small cell lung cancer: PET response criteria in solid tumors (PERCIST) versus response evaluation criteria in solid tumors (RECIST). *Journal of Thoracic Disease*, *6*(6), 677–683.
7. Tawfik, M. M. H., Monib, A. M., Yassin, A., & Ali, S. A. (2020). Comparison between RECIST and PERCIST criteria in therapeutic response assessment in cases of lymphoma. *Egyptian Journal of Radiology and Nuclear Medicine*, *51*(1), 82.
8. Caracciolo, M., Castello, A., Urso, L., Borgia, F., Marzola, M. C., Uccelli, L., Cittanti, C., Bartolomei, M., Castellani, M., & Lopci, E. (2023). Comparison of MRI vs. [18F]FDG PET/CT for Treatment Response Evaluation of Primary Breast Cancer after Neoadjuvant Chemotherapy: Literature Review and Future Perspectives. *Journal of Clinical Medicine 2023, Vol. 12, Page 5355*, *12*(16), 5355.
9. Stefanou, A. J., Dessureault, S., Sanchez, J., & Felder, S. (2023). Clinical Tools for Rectal Cancer Response Assessment following Neoadjuvant Treatment in the Era of Organ Preservation. *Cancers*, *15*(23).
10. Ramos, S., Simoes, S., Amorim, M., Silva, P., Calcada, C., & S. Costa, P. (2024). Assessment of Response to Neoadjuvant Therapy using Magnetic Rresonance Imaging in Rectal Cancer: Comparison with Anatomopathological Study. *Surgery, Gastroenterology and Oncology*, *29*(1), 05.
11. Liu, W., Li, Y., Zhang, X., Li, J., Sun, J., Lv, H., & Wang, Z. (2022). Preoperative T and N Restaging of Rectal Cancer After Neoadjuvant Chemoradiotherapy: An Accuracy Comparison Between MSCT and MRI. *Frontiers in Oncology*, *11*.
12. Caruso, R., Vicente, E., Quijano, Y., Duran, H., Fabra, I., Diaz, E., Malave, L., Agresott, R., Cañamaque, L. G., Ielpo, B., & Ferri, V. (2021). Role of 18F-PET-CT to predict pathological response after neoadjuvant treatment of rectal cancer. *Discover Oncology*, *12*(1).
13. Kim, H. D., Kim, B. J., Kim, H. S., & Kim, J. H. (2019). Comparison of the morphologic criteria (RECIST) and metabolic criteria (EORTC and PERCIST) in tumor response assessments: A pooled analysis. *Korean Journal of Internal Medicine*, *34*(3), 608–617.

14. Lee, S. W., Jeong, S. Y., Kim, K., & Kim, S. J. (2021). Direct comparison of F-18 FDG PET/CT and MRI to predict pathologic response to neoadjuvant treatment in locally advanced rectal cancer: a meta-analysis. *Annals of Nuclear Medicine*, *35*(9), 1038–1047.
15. Gao, P. F., Lu, N., & Liu, W. (2023). MRI VS. FDG-PET for diagnosis of response to neoadjuvant therapy in patients with locally advanced rectal cancer. *Frontiers in Oncology*, *13*, 1031581.
16. Joo Hyun, O., Lodge, M. A., & Wahl, R. L. (2016). Practical percist: A simplified guide to PET response criteria in solid tumors 1.0. *Radiology*, *280*(2), 576–584.