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MRI VS. FDG-PET for diagnosis of response to neoadjuvant therapy in patients with locally advanced rectal cancer

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Aim: In this study, we aimed to compare the diagnostic values of MRI and FDG-PET for the prediction of the response to neoadjuvant chemoradiotherapy (NACT) of patients with locally advanced Rectal cancer (RC).

Methods: Electronic databases, including PubMed, Embase, and the Cochrane library, were systematically searched through December 2021 for studies that investigated the diagnostic value of MRI and FDG-PET in the prediction of the response of patients with locally advanced RC to NACT. The quality of the included studies was assessed using QUADAS. The pooled sensitivity, specificity, positive and negative likelihood ratio (PLR and NLR), and the area under the ROC (AUC) of MRI and FDG-PET were calculated using a bivariate generalized linear mixed model, random-effects model, and hierarchical regression.

Results: A total number of 74 studies with recruited 4,105 locally advanced RC patients were included in this analysis. The pooled sensitivity, specificity, PLR, NLR, and AUC for MRI were 0.83 (95% CI: 0.77–0.88), 0.85 (95% CI: 0.79–0.89), 5.50 (95% CI: 4.11-7.35), 0.20 (95% CI: 0.14–0.27), and 0.91 (95% CI: 0.88–0.93), respectively. The summary sensitivity, specificity, PLR, NLR and AUC for FDG-PET were 0.81 (95% CI: 0.77-0.85), 0.75 (95% CI: 0.70–0.80), 3.29 (95% CI: 2.64–4.10), 0.25 (95% CI: 0.20–0.31), and 0.85 (95% CI: 0.82–0.88), respectively. Moreover, there were no significant differences between MRI and FDG-PET in sensitivity (P = 0.565), and NLR (P = 0.268), while the specificity (P = 0.006), PLR (P = 0.006), and AUC (P = 0.003) of MRI was higher than FDG-PET.

Conclusions: MRI might superior than FGD-PET for the prediction of the response of patients with locally advanced RC to NACT.

KEYWORDS

rectal cancer, diagnostic value, MRI, FDG-PET, FDG-PET/CT, neoadjuvant therapy, response

Introduction

Rectal cancer (RC) as is a common malignant tumor, with nearly 39,910 new cases in US annually (1, 2). Currently, surgical resection is the main curative method for patients with early-stage RC, whereas nearly 55% of RC cases are diagnosed at stage II or higher, when additional treatment strategies are needed (3, 4). Neoadjuvant chemoradiotherapy (NACT), total mesorectal excision, and postoperative chemotherapy are standard treatment strategies in patients with locally advanced RC (5, 6). Earlier studies showed that NACT improved locoregional control with significant pathologic complete response (pCR), which was defined as the absence of viable tumor cells established by pathologic examination (7–10). The tumor responses to NACT ranged from sustained tumor progression to complete remission, and adjuvant postoperative therapy could affect by the heterogeneity of patients' tumor response to NACT. Previous evidence indicated that surgery could be omitted in patients with pCR to NACT, in which the watch-and-wait strategy was associated with better prognosis (11, 12). Therefore, the accurate assessment of the response to NACT could contribute to more effective clinical care aimed at personalized treatment strategy in patients with locally advanced RC.

Recent studies established the role of imaging modalities, including fluorine-18 fluorodeoxyglucose-positron emission tomography (^{18}FDG-PET), irrespective whether combined with computed tomography (CT) or MRI in the prediction of the response to NACT (13, 14). The apparent diffusion coefficient (ADC), measured by MRI, could facilitate tumor cellularity and cell membrane integrity which are sensitive to intratumoral changes induced by NACT. MRI was found to have a relatively better predictive value for the tumor response during and after neoadjuvant therapy (15). FDG-PET has been widely used for the diagnosis of recurrent or metastatic colorectal cancer (CRC), with a detection accuracy rate for pelvic recurrence within 74%–96% (16–18). ^{18}FDG-PET combined with CT (FDG-PET/CT) showed an even higher accuracy rate for diagnosing locally recurrent and metastatic CRC (19, 20). Several studies revealed that FDG-PET predicted successfully the response to NACT, while the predictive value between MRI and FDG-PET for the response to NACT in locally advanced RC patients remains controversial. Therefore, here, we performed a meta-analysis focused on indirect comparisons between the diagnostic values of MRI and FDG-PET for the assessment of the response to NACT.

Materials and methods

Data sources, search strategy, and selection criteria

This review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement issued in 2009 (21). Studies that had investigated the diagnostic value of MRI or FDG-PET for the assessment of the response to NACT in patients with locally advanced RC were eligible for inclusion in this analysis, with no restrictions placed on the publication language and status. The PubMed, Embase, and Cochrane Library electronic databases were searched for articles published through December 2021. The following search terns were used: "Magnetic Resonance Imaging" OR "Positron-Emission Tomography" OR "computed tomography" AND "rectal cancer" AND "preoperative" OR "neoadjuvant". The details of searching strategy in PubMed are specified in Supplemental 1. We also conducted manual searches of the reference lists of all relevant original and review articles to identify additional eligible studies.

The literature search and study selection were independently performed by two authors using a standardized approach. Any inconsistencies between authors were settled by consultation and discussion with an additional author until a consensus was reached. The following inclusion criteria were applied: (1) Study design: prospective or retrospective design; (2) Participants: all patients were diagnosed with locally advanced RC by pathologic examination; (3) Diagnostic tool: MRI, FDG-PET, or FDG-PET/CT; (4) Gold reference: tumor response diagnosed using the postoperative histological results; and (5) Outcomes: true and false positive, true and false negative, or data could be transformed into the aforementioned information data.

Data collection and quality assessment

The data collection and quality assessment were conducted by two authors, and the information collected was examined and adjudicated by an additional author. The data collected included the first author's surname, publication year, country, study design, sample size, median or mean age, number of men and women included, preoperative regimen, diagnostic tool, responders and non-responders, true and false positive, and true and false negative. The quality of the included studies was assessed using QUADAS, based on 14 items; "yes", "no", or "unclear" were the possible answers to each question/item. A study that had collected 12 or more "yes" answers was regarded to have high quality, and those that received 10–12 "yes" answers for were considered to be of moderate quality.

Statistical analysis

The sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and the area under the receiver operating characteristic curves (AUC) with corresponding 95% confidence intervals (CIs) were calculated based on true positive, false positive, false negative, and true negative results in each individual study before data pooling. Then, the pooled sensitivity, specificity, PLR, NLR, and AUC for each diagnostic tool were calculated using a bivariate generalized linear mixed model, random-effects model, and hierarchical regression (22–24). Heterogeneity across the included studies was evaluated by I^2 and Q statistic; $P < 0.10$ was considered to indicate significant heterogeneity (25). Subgroup analyses for sensitivity, specificity, PLR, NLR, and AUC were conducted based on the study design (retrospective or prospective), sample size (>50 and <50), and mean age (>60.0 and <60.0). The ratio of between the MRI and FDG-PET diagnostic parameters in the subgroups were calculated for indirect comparison of between the MRI and FDG-PET diagnostic values

(26). The publication biases for CT and FDG-PET were assessed using funnel plots and Deeks' asymmetry tests (27). The P-value for all pooled analyses were two-sided; $P < 0.05$ was considered to indicate statistically significant differences. Stata software (version 10.0; Stata Corporation, College Station, TX, USA) was employed to conduct all statistical analyses.

Results

Literature search

The results of the study-selection process are depicted in Figure 1. We initially identified 2946 potentially eligible articles after the original electronic search. Of these, 2539 articles were excluded during an initial review of the titles. Abstracts assessment for 407 articles, and 278 studies were excluded due to the use of other diagnostic tools and review designs. The remaining 129 studies were subjected to further tests to identify any other potential studies eligible for inclusion, and 74 of them satisfied the inclusion criteria and were ultimately included in the quantitative analysis (28–101). A manual search of the reference lists contained within these studies did not yield any new eligible studies. The general characteristics of the included studies are presented in Table 1.

Study characteristics

Seventy-four studies with a total number of 4,105 patients with locally advanced RC were included in this analysis. Forty-five studies were designed as prospective, whereas the remaining 29 studies were designed as retrospective. The mean age of the patients was 49.5–71.5 years; 12–146 individuals were included in each of the included studies. Seventy studies employed radiochemotherapy as preoperative regimen, whereas radiotherapy or chemotherapy was used as preoperative regimen in the remaining four studies. The predictive value of MRI for the response to NACT was established in 41 studies, the predictive value of FDG-PET in 9 studies, and the predictive value of FDG-PET/CT in 29 studies. Seventeen of included studies were of high quality, whereas the remaining 57 studies were of moderate quality.

MRI

The sensitivity and specificity are presented in Figure 2. The pooled sensitivity and specificity of MRI for predicting the response to NACT were 0.83 (95% CI: 0.77–0.88) and 0.85 (95% CI: 0.79–0.89), respectively. Substantial heterogeneity in the sensitivity (I^2 =76.46%;

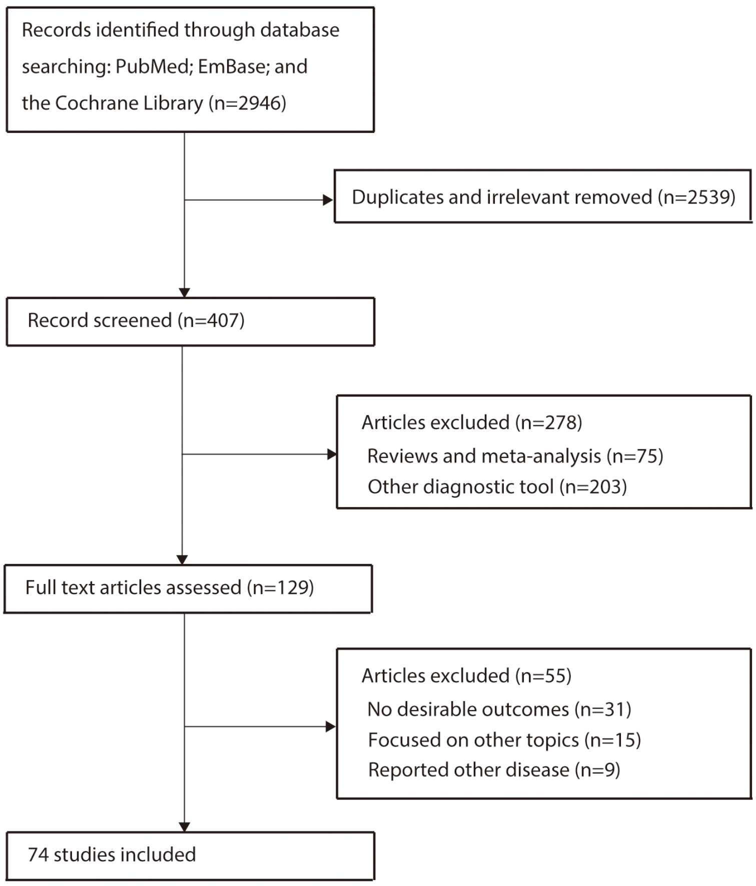

FIGURE 1
Flow diagram of the study selection process.

TABLE 1 The baseline characteristics of included studies.

Study and publication year	Country	Study design	Sample size	Age (years)	No of men and women	Preoperative regimen	Diagnostic tool	Responders and non-responders	Study quality
Amthauer 2004 (28)	Germany	Pro	20	53.1	14/6	RC	FDG-PET	Res: 13; NR: 7	Moderate
Capirci 2004 (29)	Italy	Retro	81	63.9	53/28	RC	FDG-PET	Res: 49; NR: 32	Moderate
Denecke 2005 (30)	Germany	Pro	23	53.0	16/7	RC	FDG-PET	Res: 13; NR: 10	Moderate
Cascini 2006 (31)	Italy	Pro	33	58.0	20/13	RC	FDG-PET	Res: 18; NR: 15	Moderate
Melton 2007 (32)	USA	Retro	21	61.0	13/8	RC	FDG-PET/CT	Res: 14; NR: 7	Moderate
Kristiansen 2008 (33)	Denmark	Retro	30	63.0	16/14	RC	FDG-PET/CT	Res: 14; NR: 16	Moderate
Capirci 2009 (34)	Italy	Pro	81	58.0	58/23	RC	FDG-PET/CT	Res: 40; NR: 41	High
Rosenberg 2009 (35)	Germany	Pro	30	61.0	20/10	RC	FDG-PET/CT	Res: 19; NR: 10	Moderate
Palma 2010 (36)	Spain	Pro	50	60.0	37/13	RC	FDG-PET/CT	Res: 20; NR: 30	Moderate
Lambrecht 2010 (37)	Belgium	Pro	22	59.8	17/5	RC	FDG-PET/CT	Res: 6; NR: 16	Moderate
Martoni 2011 (38)	Italy	Pro	80	65.0	55/25	RC	FDG-PET/CT	CR: 16; IR: 20; NR: 48	High
Hur 2011 (39)	Korea	Pro	37	59.0	25/12	RC	FDG-PET	Res: 25; NR: 12	Moderate
Yoon 2011 (40)	Korea	Pro	72	66.0	56/16	RC	FDG-PET/CT	Res: 43; NR: 29	Moderate
Kim 2011 (41)	Korea	Pro	34	58.1	24/10	RC	MRI	Res: 16; NR: 18	Moderate
Kim 2011 (42)	Korea	Retro	76	60.0	49/27	RC	MRI	CR: 11, nearly CR: 14; MR: 51	Moderate
Herrmann 2011 (43)	Germany	Pro	28	61.0	20/8	RC	FDG-PET/CT	Res: 20; NR: 8	Moderate
Guerra 2011 (44)	Italy	Pro	31	67.0	23/8	RC	FDG-PET/CT	Res: 22; NR: 9	Moderate
Everaert 2011 (45)	Belgium	Pro	45	65.4	34/11	R	FDG-PET	Res: 20; NR: 25	Moderate
Curvo-Semedo 2011 (46)	Netherlands	Retro	50	71.5	36/14	RC	MRI	CR: 14; IR: 36	Moderate
Song 2012 (47)	Korea	Retro	50	56.0	39/11	RC	MRI; FDG-PET/CT	CR: 6; near CR: 13; MR: 31	Moderate
Ippolito 2012 (48)	Italy	Pro	30	66.0	21/9	RC	MRI; FDG-PET/CT	Res: 21; NR: 9	Moderate
Perez 2012 (49)	Brazil	Pro	99	60.3	47/52	RC	FDG-PET/CT	CR: 18; IR: 81	High
Lambrecht 2012 (50)	Belgium	Retro	20	60.0	16/4	RC	MRI	CR: 6; NR: 14	Moderate
Jung 2012 (51)	Korea	Retro	35	62.0	29/6	RC	MRI	Res: 23; NR: 12	Moderate
Janssen 2012 (52)	Netherlands	Pro	51	NA	NA	RC	FDG-PET/CT	Res: 17; NR: 29	Moderate
Huh 2012 (53)	Korea	Pro	50	64.0	38/12	RC	FDG-PET/CT	Res: 32; NR: 18	Moderate
Chennupati 2012 (54)	USA	Retro	35	NA	NA	RC	FDG-PET/CT	CR: 6; near-CR: 8; NR: 21	Moderate
Barbaro 2012 (55)	Italy	Pro	62	64.0	43/19	RC	MRI	Res: 37; NR: 25	High
Guillem 2013 (56)	USA	Pro	121	60.0	76/45	RC	FDG-PET	CR: 26; IR: 95	High
Hatt 2013 (57)	France	Retro	28	67.0	18/10	RC	FDG-PET	Res: 12; NR: 16	Moderate
Murcia Duréndez 2013 (58)	Spain	Pro	41	66.0	25/16	RC	FDG-PET/CT	Res: 14; NR: 27	Moderate
Calvo 2013 (59)	Spain	Pro	38	62.0	27/11	RC	FDG-PET/CT	Res: 19; NR: 19	Moderate

(Continued)

TABLE 1 Continued

Study and publication year	Country	Study design	Sample size	Age (years)	No of men and women	Preoperative regimen	Diagnostic tool	Responders and non-responders	Study quality
Sun 2013 (60)	China	Pro	53	53.0	44/9	RC	FDG-PET/CT	Res: 21; NR: 32	Moderate
Genovesi 2013 (61)	Italy	Pro	28	68.3	17/11	RC	MRI	Res: 10; NR: 18	Moderate
Park 2014 (62)	Korea	Retro	88	59.2	64/24	RC	FDG-PET/CT	CR: 17; non-CR: 71	Moderate
Niccoli-Asabella 2014 (63)	Italy	Pro	56	62.3	38/18	RC	FDG-PET/CT	Res: 23; NR: 33	High
Cai 2014 (64)	China	Retro	65	56.0	52/13	RC	MRI	Res: 43; NR: 22	Moderate
Aiba 2014 (65)	Japan	Retro	40	56.0	32/8	C	MRI; FDG-PET/CT	Res: 16; NR: 24	High
Doi 2015 (66)	Japan	Pro	16	62.5	13/3	RC	MRI	Res: 9; NR: 7	Moderate
Blažić 2015 (67)	Serbia	Pro	58	61.3	38/20	RC	MRI	Res: 19; NR: 39	Moderate
Martens 2015 (68)	Netherlands	Retro	146	64.6	90/56	RC	MRI	CR: 29; non-CR: 117	High
Petrillo 2015 (69)	Italy	Pro	29	62.0	NA	RC	MRI	Res: 14; NR: 15	Moderate
Choi 2015 (70)	Korea	Retro	86	64.3	58/28	RC	MRI	CR: 16; non-CR: 70	High
Leccisotti 2015 (71)	Italy	Pro	126	65.0	79/47	RC	FDG-PET/CT	CR: 31; non-CR: 95	High
Tong 2015 (72)	China	Pro	38	52.0	25/13	RC	MRI	CR: 12; non-CR: 26	Moderate
Martens 2015 (73)	Netherlands	Pro	30	66.0	23/7	RC	MRI	Res: 13; NR: 17	Moderate
Altini 2015 (74)	Italy	Pro	68	63.0	41/27	RC	FDG-PET/CT	Res: 25; NR: 43	Moderate
Lambregts 2015 (75)	Netherlands	Retro	112	67.0	76/36	RC	MRI	CR: 20; non-CR: 92	Moderate
Koo 2016 (76)	Korea	Retro	103	66.0	78/25	RC	FDG-PET/CT	CR: 22; non-CR: 81	High
Travaini 2016 (77)	Italy	Pro	41	61.0	26/15	RC	FDG-PET/CT	Res: 23; NR: 18	Moderate
Li 2016 (78)	China	Pro	64	53.0	49/15	RC	FDG-PET/CT	Res: 31; NR: 33	Moderate
De Cecco 2016 (79)	Italy	Pro	12	63.2	4/8	RC	MRI	Res: 9; NR: 3	Moderate
Chen 2016 (80)	China	Retro	100	55.0	68/32	RC	MRI	CR: 50; non-CR: 50	Moderate
Iannicelli 2016 (81)	Italy	Pro	34	65.0	19/15	RC	MRI	Res: 11; NR: 23	Moderate
Sathyakumar 2016 (82)	India	Pro	64	49.5	48/16	RC	MRI	CR: 11; non-CR: 53	High
Jacobs 2016 (83)	Netherlands	Pro	22	62.9	16/6	RC	MRI	Res: 9; NR: 13	Moderate
Petrillo 2017 (84)	Italy	Retro	35	67.0	27/8	R	MRI	Res: 16; NR: 19	Moderate
Bassaneze 2017 (85)	Brazil	Retro	33	59.6	18/15	RC	MRI	CR: 7; non-CR: 26	Moderate
De Felice 2017 (86)	Italy	Pro	37	62.0	28/9	RC	MRI	CR: 11; non-CR: 26	Moderate
Zhu 2017 (87)	China	Pro	98	57.5	64/34	RC	MRI	CR: 19; non-CR: 79	High
Yu 2017 (88)	China	Retro	41	NA	25/16	RC	MRI	Res: 17; NR: 24	Moderate
Petrillo 2018 (89)	Italy	Pro	88	66.0	62/26	RC	MRI	Res: 52; NR: 36	Moderate
Fusco 2018 (90)	Italy	Retro	34	67.0	26/8	R	MRI	Res: 15; NR: 19	Moderate
Murata 2018 (91)	Japan	Retro	36	66.0	27/9	RC	MRI; FDG-PET/CT	CR: 10; non-CR: 26	Moderate

(Continued)

TABLE 1 Continued

Study and publication year	Country	Study design	Sample size	Age (years)	No of men and women	Preoperative regimen	Diagnostic tool	Responders and non-responders	Study quality
Liu 2018 (92)	China	Pro	124	59.0	75/49	RC	MRI	CR: 20; non-CR: 104	Moderate
Aker 2018 (93)	UK	Retro	103	NA	NA	RC	MRI	CR: 20; non-CR: 83	Moderate
Horvat 2018 (94)	Brazil	Retro	114	55.0	67/47	RC	MRI	CR: 21; non-CR: 93	High
Pizzi 2018 (95)	Italy	Pro	43	67.4	22/21	RC	MRI	CR: 21; non-CR: 22	High
Nahas 2019 (96)	Brazil	Retro	95	62.9	58/37	RC	MRI	CR: 20; non-CR: 75	Moderate
Giannini 2019 (97)	Italy	Retro	52	68.0	35/17	RC	MRI; FDG-PET	Res: 22; NR: 30	Moderate
Palmisano 2020 (98)	Italy	Pro	43	61.0	27/16	RC	MRI	Res: 33; NR: 10	High
Bae 2020 (99)	Korea	Retro	38	60.0	17/21	RC	MRI	CR: 26; non-CR: 12	Moderate
López-López 2021 (100)	Spain	Pro	68	63.4	36/32	RC	FDG-PET/CT	CR: 15; non-CR: 53	High
Uemura 2021 (101)	Japan	Retro	40	68.5	26/14	RC	MRI	Res: 17; NR: 23	Moderate

*C, chemotherapy; CR, complete responder; IR, incomplete responder; MR, moderate or minimal responder; NR, non-responder; Pro, prospective; R, radiotherapy; RC, radiochemotherapy; Res, responders; Retro, retrospective.

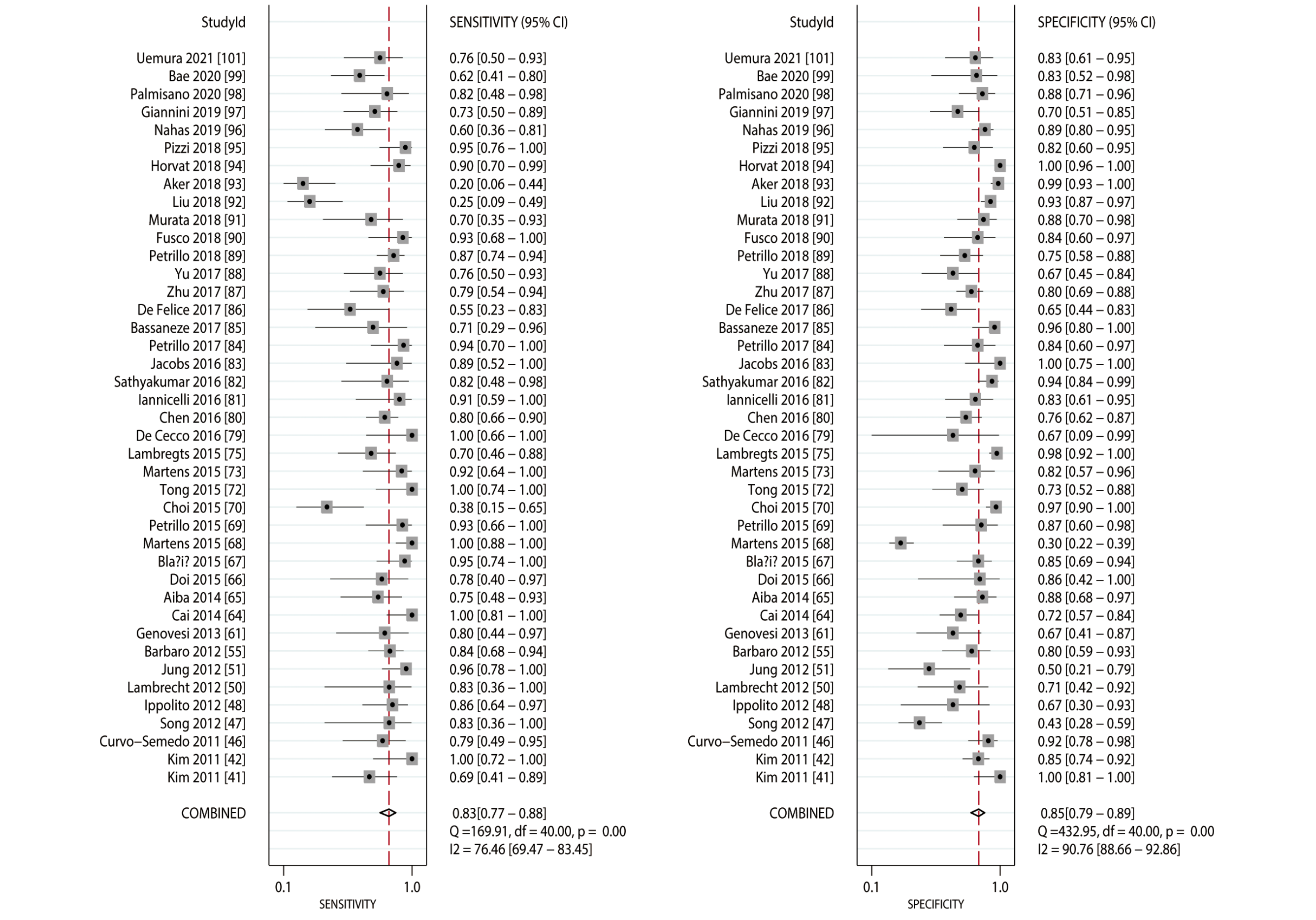

FIGURE 2
Pooled sensitivity and specificity of MRI.

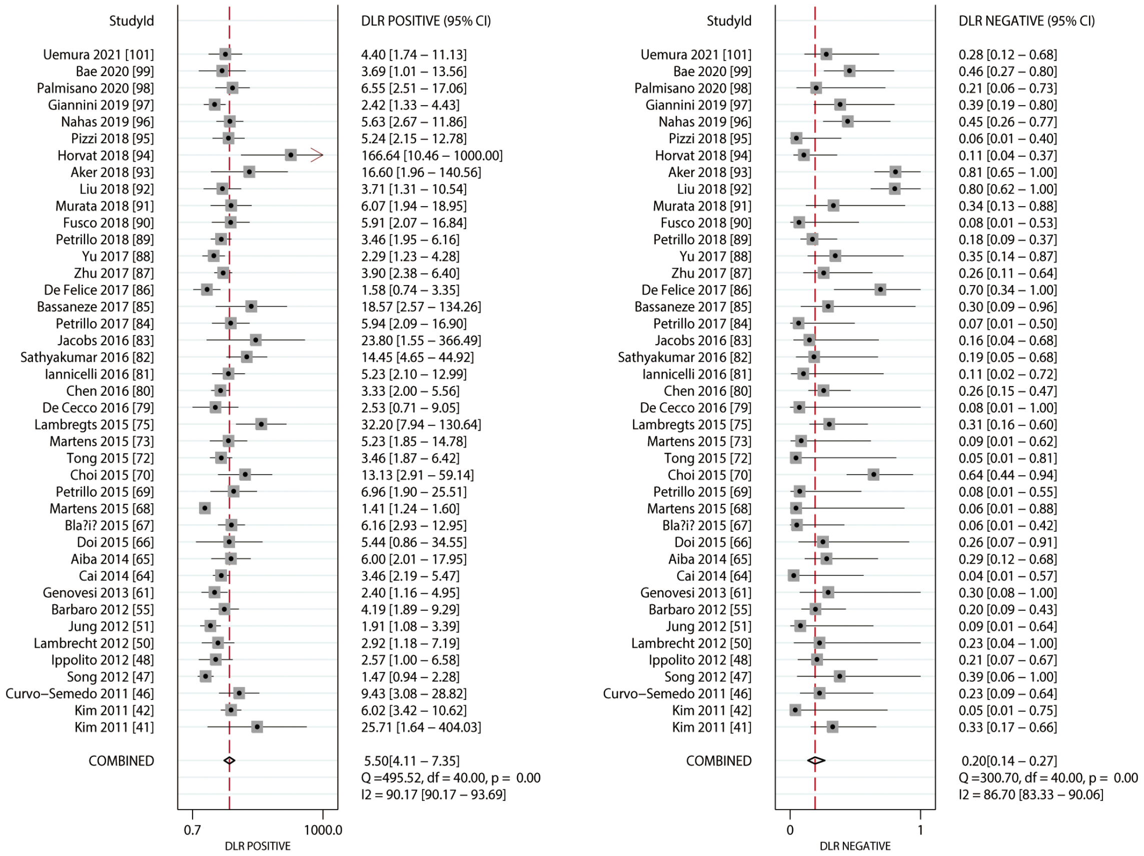

FIGURE 3
Pooled PLR and NLR of MRI.

P<0.01) and specificity (I^2 =90.76%; *P*<0.01) of the included studies was observed. Moreover, the summarized PLR and NLR of MRI for predicting the response to NACT were 5.50 (95% CI: 4.11–7.35) and 0.20 (95% CI: 0.14–0.27), respectively (Figure 3), with significant heterogeneity in PLR (I^2 =90.17%; *P*<0.01) and NLR (I^2 =86.70%; *P*<0.01) across the included studies. In addition, the summarized AUC of MRI for predicting the response to NACT was 0.91 (95% CI: 0.88–0.93; Figure 4). Finally, there was no significant publication bias for MRI (*P* = 0.89; Figure 5).

FDG-PET

The summarized sensitivity and specificity are illustrated in Figure 6. The pooled sensitivity and specificity of FDG-PET for predicting the response to NACT were 0.81 (95% CI: 0.77–0.85) and 0.75 (95% CI: 0.70–0.80), respectively. Significant heterogeneity was detected in the sensitivity (I^2 =49.40%; *P*<0.01) and specificity (I^2 =80.77%; *P*<0.01) of FDG-PET. Moreover, the pooled PLR and NLR of FDG-PET for predicting the response to NACT were 3.29 (95% CI: 2.64–4.10) and 0.25 (95% CI: 0.20–0.31) respectively, with substantial heterogeneity for PLR (I^2 =78.03%; *P*<0.01) and NLR (I^2 =51.41%; *P*<0.01) across the included studies (Figure 7). In addition, the summary AUC of FDG-PET was 0.85 (95% CI: 0.82–0.88; Figure 8). Finally, no significant publication bias was observed in FDG-PET (*P* = 0.12; Figure 9).

Indirect comparison of MRI and FDG-PET

The indirect comparison of the predictive values of MRI and FDG-PET for the response to NACT were calculated, the results of which

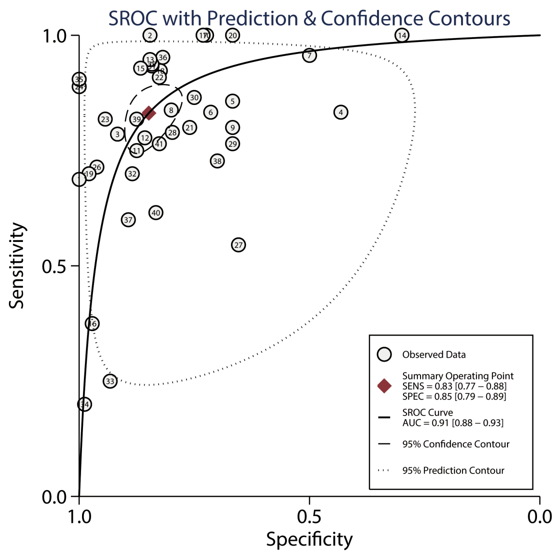

FIGURE 4
Summarized ROC curve and AUC for MRI.

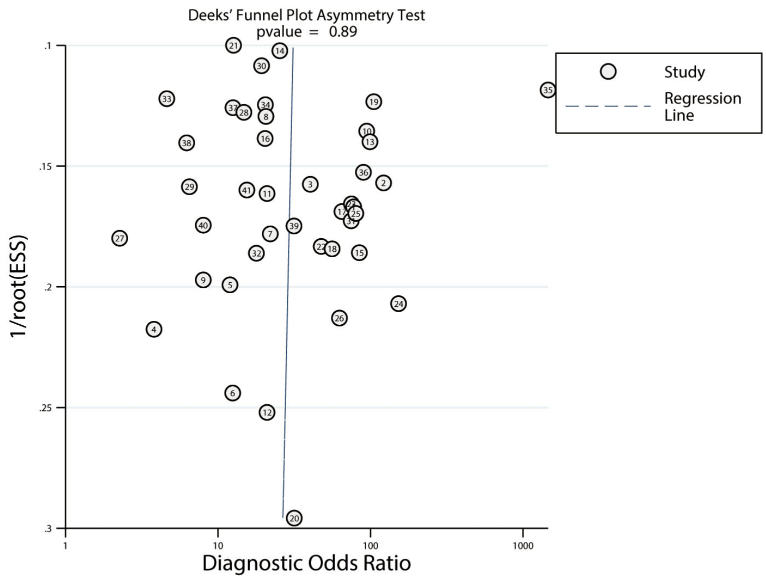

FIGURE 5
Publication biases for MRI.

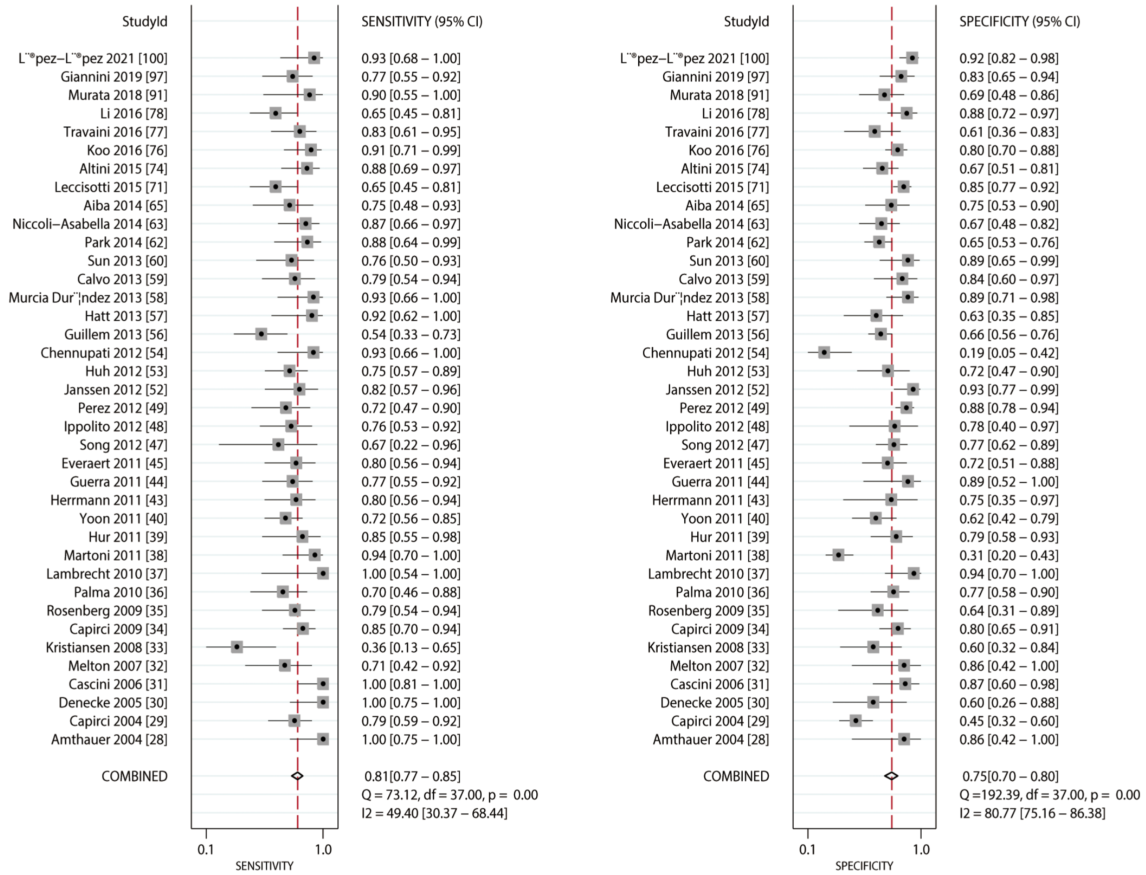

FIGURE 6
Pooled sensitivity and specificity of FDG-PET and FDG-PET/CT.

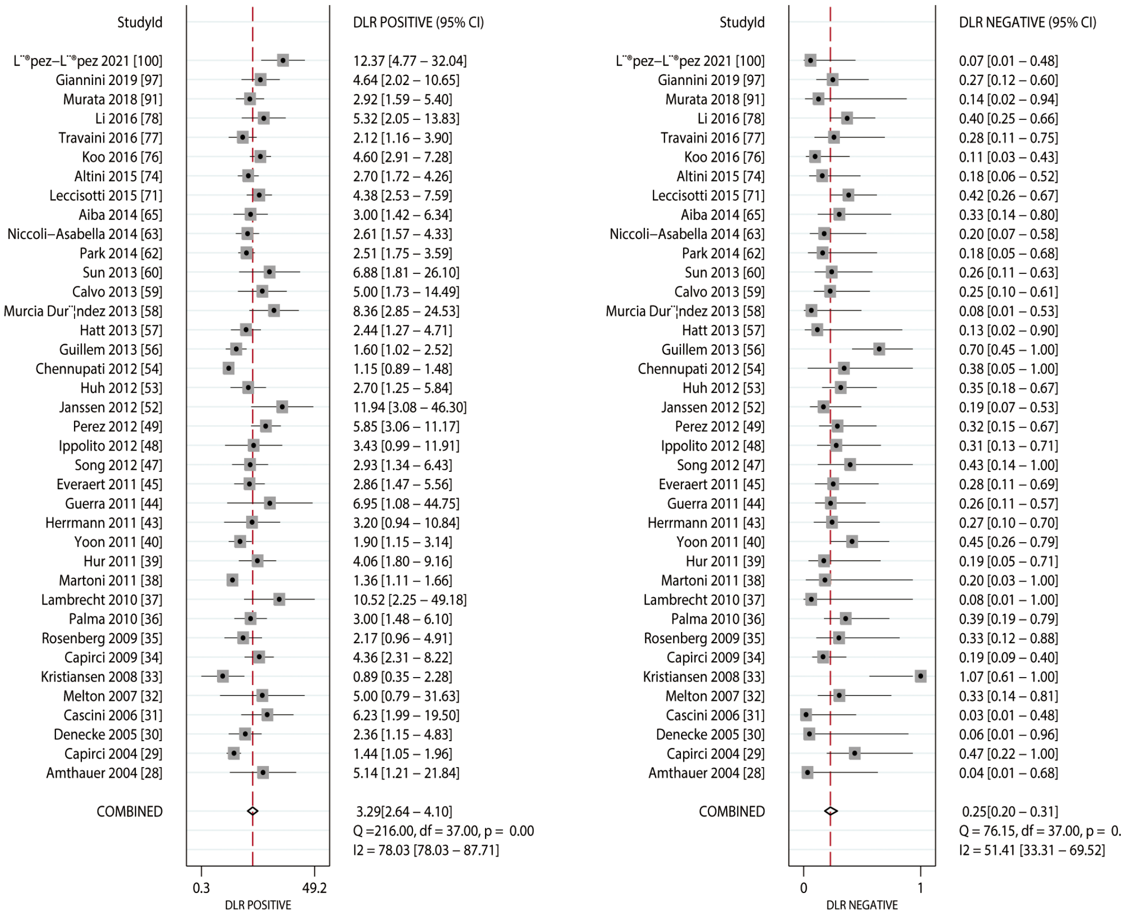

FIGURE 7
Pooled PLR and NLR of FDG-PET and FDG-PET/CT.

suggested no significant differences between MRI and FDG-PET or FDG-PET/CT for the response to neoadjuvant chemoradiotherapy in patients with locally advanced RC, in terms of sensitivity (ratio: 1.02; 95% CI: 0.94–1.11; $P = 0.565$), and NLR (ratio: 0.80; 95% CI: 0.54–1.19; $P = 0.268$). Moreover, we noted the specificity (ratio: 1.13; 95% CI: 1.04–1.24; $P = 0.006$), PLR (ratio: 1.67; 95% CI: 1.16–2.41; $P = 0.006$), and AUC (ratio: 1.07; 95% CI: 1.02–1.12; $P = 0.003$).

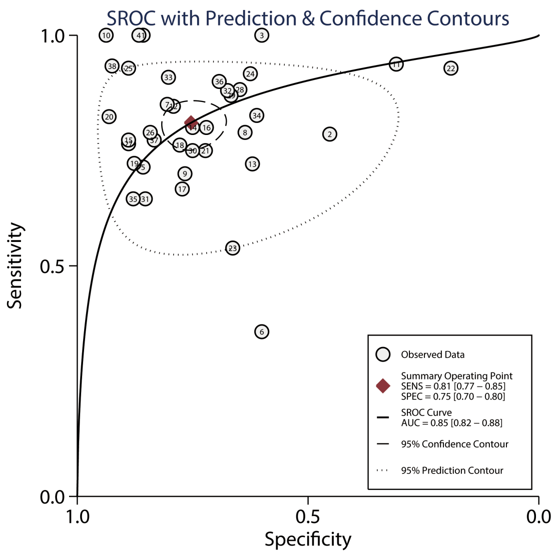

FIGURE 8
Summarized ROC curve and AUC for FDG-PET and FDG-PET/CT.

Meta-regression and subgroup analyses

The results of our meta-regression analyses showed that the sample size and mean age affected the sensitivity of MRI, whereas the study design did not affect MRI sensitivity. Moreover, the study design, sample size, and mean age did not affect the specificity of MRI. No bias was established in the sensitivity and specificity of FDG-PET exerted by study design, sample size, and mean age (Supplemental 2). The results of the subgroup analyses regarding the sensitivity, specificity, PLR, NLR, and AUC of MRI and FDG-PET are presented in Table 2. We noted a higher specificity in patients that had received MRI than in those subjected to FDG-PET if pooled retrospective studies ($P = 0.010$), at a sample size > 50 ($P = 0.046$). Furthermore, MRI had a higher PLR than FDG-PET when the pooled study was designed as retrospective ($P = 0.003$), with a sample size > 50 ($P = 0.027$) and a mean age of the patients > 60.0 years ($P = 0.013$). Finally, MRI was associated with lower NLR than FDG-PET if mean age of the patients > 60.0 years ($P = 0.033$).

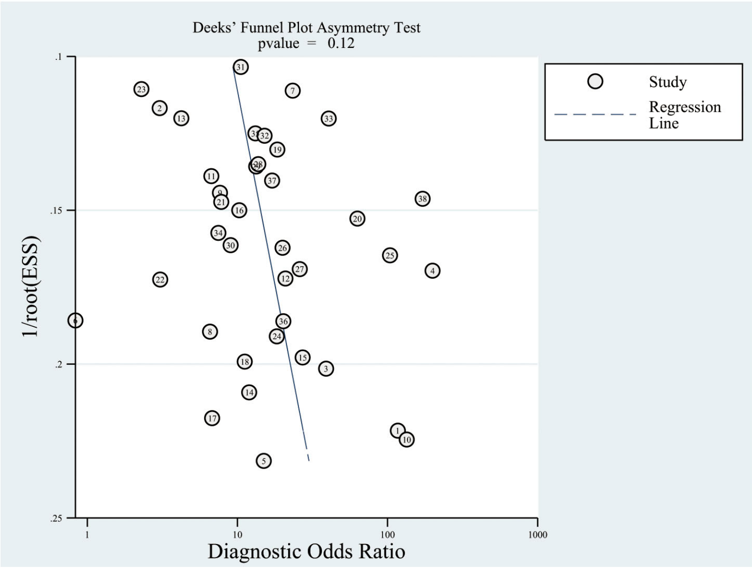

FIGURE 9
Publication biases for FDG-PET and FDG-PET/CT.

TABLE 2 Subgroup analyses for diagnostic parameters.

Parameters	Variable	Group	Diagnostic tool	Number of studies	Pooled effect estimate and 95% confidence intervals	Heterogeneity (%)	Comparisons of MRI and PET or PET/CT
Sensitivity	Study design	Prospective	MRI	19	0.85 (0.76-0.91)	72.43	1.05 (0.94-1.17); P=0.373
			PET or PET/CT	27	0.81 (0.76-0.85)	47.17	
		Retrospective	MRI	22	0.81 (0.71-0.89)	78.85	1.01 (0.86-1.19); P=0.880
			PET or PET/CT	11	0.80 (0.70-0.88)	59.43	
	Sample size	>50	MRI	18	0.81 (0.67-0.90)	85.78	1.04 (0.88-1.22); P=0.652
			PET or PET/CT	19	0.78 (0.72-0.83)	41.13	
		<50	MRI	23	0.84 (0.78-0.89)	38.70	0.99 (0.89-1.09); P=0.820
			PET or PET/CT	19	0.85 (0.77-0.90)	56.94	
	Mean age (years)	>60	MRI	28	0.85 (0.78-0.89)	67.49	1.09 (0.99-1.19); P=0.067
			PET or PET/CT	25	0.78 (0.73-0.83)	45.42	
		<60	MRI	11	0.82 (0.67-0.91)	78.05	0.94 (0.79-1.13); P=0.519
			PET or PET/CT	11	0.87 (0.77-0.93)	54.16	
Specificity	Study design	Prospective	MRI	19	0.83 (0.78-0.88)	51.97	1.05 (0.95-1.16); P=0.323
			PET or PET/CT	27	0.79 (0.72-0.84)	81.87	
		Retrospective	MRI	22	0.86 (0.77-0.92)	94.35	1.28 (1.06-1.55); P=0.010
			PET or PET/CT	11	0.67 (0.55-0.77)	78.72	
	Sample size	>50	MRI	18	0.87 (0.78-0.93)	95.85	1.14 (1.00-1.31); P=0.046
				19	0.76 (0.68-0.83)	87.26	

(Continued)

TABLE 2 Continued

Parameters	Variable	Group	Diagnostic tool	Number of studies	Pooled effect estimate and 95% confidence intervals	Heterogeneity (%)	Comparisons of MRI and PET or PET/CT
			PET or PET/CT				
		<50	MRI	23	0.82 (0.76-0.86)	38.76	1.11 (0.97-1.26); P=0.126
			PET or PET/CT	19	0.74 (0.65-0.82)	63.29	
	Mean age (years)	>60	MRI	28	0.82 (0.76-0.87)	89.81	1.11 (1.00-1.23); P=0.059
			PET or PET/CT	25	0.74 (0.67-0.79)	81.12	
		<60	MRI	11	0.89 (0.77-0.95)	91.49	1.14 (1.00-1.31); P=0.055
			PET or PET/CT	11	0.78 (0.71-0.84)	41.18	
PLR	Study design	Prospective	MRI	19	5.12 (3.90-6.71)	7.25	1.35 (0.92-1.98); P=0.124
			PET or PET/CT	27	3.79 (2.89-4.96)	76.87	
		Retrospective	MRI	22	5.80 (3.62-9.30)	93.61	2.39 (1.33-4.27); P=0.003
			PET or PET/CT	11	2.43 (1.73-3.41)	72.45	
	Sample size	>50	MRI	18	6.46 (3.82-10.93)	95.37	1.98 (1.08-3.61); P=0.027
			PET or PET/CT	19	3.27 (2.43-4.41)	80.47	
		<50	MRI	23	4.61 (3.53-6.03)	34.62	1.40 (0.92-2.15); P=0.121
			PET or PET/CT	19	3.29 (2.36-4.58)	81.15	
	Mean age (years)	>60	MRI	28	4.82 (3.60-6.47)	90.87	1.62 (1.11-2.38); P=0.013
			PET or PET/CT	25	2.97 (2.32-3.80)	71.85	
		<60	MRI	11	7.60 (3.43-16.85)	76.24	1.89 (0.80-4.44); P=0.144
			PET or PET/CT	11	4.02 (2.95-5.49)	0.00	
NLR	Study design	Prospective	MRI	19	0.18 (0.12-0.29)	85.37	0.75 (0.45-1.24); P=0.264
			PET or PET/CT	27	0.24 (0.19-0.31)	50.09	
		Retrospective	MRI	22	0.22 (0.14-0.33)	87.13	0.76 (0.41-1.42); P=0.385
			PET or PET/CT	11	0.29 (0.19-0.47)	59.87	
	Sample size	>50	MRI	18	0.22 (0.13-0.38)	92.36	0.76 (0.42-1.36); P=0.356
			PET or PET/CT	19	0.29 (0.23-0.37)	46.48	
		<50	MRI	23	0.19 (0.14-0.27)	36.22	0.95 (0.54-1.66); P=0.857
			PET or PET/CT	19	0.20 (0.13-0.32)	55.68	
	Mean age (years)	>60	MRI	28	0.19 (0.13-0.26)	91.75	0.63 (0.42-0.96); P=0.033
			PET or PET/CT	25	0.30 (0.23-0.37)	52.39	
		<60	MRI	11	0.20 (0.10-0.39)	88.41	1.18 (0.47-2.92); P=0.726
			PET or PET/CT	11	0.17 (0.09-0.30)	35.85	

Discussion

The present meta-analysis was based on published studies and investigated the predictive value of MRI and FDG-PET for the response to NACT of patients with locally advanced RC. This comprehensive, quantitative study included 74 studies with 4,105 patients with a wide range of patients' characteristics. Our findings suggest that MRI and FDG-PET had a moderate predictive value for the response to NACT. Moreover, the predictive value of MRI might be superior to that of FDG-PET, in terms of specificity, PLR, and AUC. Finally, the predictive value of MRI and FDG-PET for predicting the response to NACT of patients with locally advanced RC could affect by sample size, and mean age.

A previous meta-analysis of 33 studies was conducted to compare the predictive value of MRI and FDG-PET for the pathological response to NACT in patients with RC (102). Its authors found that MRI was superior to FDG-PET in predicting the pathological response to NACT, whereas the specificity and positive predictive value of MRI was relatively lower, especially in patients with mucinous-type rectal adenocarcinomas. However, several studies were not included in this analysis, and indirect comparisons of MRI and FDG-PET were not performed. Moreover, an important meta-analysis evaluated the diagnostic performance of MRI, endorectal ultrasonography, and CT in predicting the response to preoperative therapy for patients with locally advanced RC based on 46 studies. They suggested MRI, endorectal ultrasonography, and CT could not used to predict complete response to NACT, and the positive predictive value for above imaging techniques was low for evaluated the tumor invasion in the circumferential resection margin. Furthermore, the diagnostic accuracy of MRI, endorectal ultrasonography, and CT for the prediction of metastatic lymph node disease was low. However, the study pooled only the diagnostic parameters for each diagnostic tool, and no comparisons of these imaging techniques were conducted. In addition, no stratification of analyses based on study or patients' characteristics was conducted (103). Therefore, the current meta-analysis was performed to compare the diagnostic value of MRI and FDG-PET for the response to NACT in patients with locally advanced RC.

The summarized diagnostic parameters of MRI were higher than those of FDG-PET in terms of sensitivity, specificity, PLR, and AUC; the NLR of MRI was lower than that of FDG-PET. Moreover, the diagnostic values of MRI and FDG-PET were moderate for the response to NACT. Moreover, an indirect comparisons results indicated MRI were associated with higher specificity, PLR, and AUC than FDG-PET. Nevertheless, these results require further prospective research for a more comprehensive update of the diagnostic values of MRI and FDG-PET for the response to NACT. Several advantages of MRI should be mentioned: (1) The application of MRI in patients with locally RC without ionizing radiation prevents the stimulation of tumor progression by ionizing radiation; (2) The ancillary equipment of cyclotron is not installed nearby, which is associated with a lower cost than that of FDG-PET/CT application (104); and (3) The examination time in MRI was shorter than that in FDG-PET/CT (105). Therefore, MRI should be largely employed for preoperative evaluation in patients with RC.

To explore the sources of substantial heterogeneity, meta-regression and subgroup analyses were conducted based on the study design, sample size, and mean age of patients. The results of the meta-regression analyses indicated that the sample size and the mean age might have contributed to a significant heterogeneity in the sensitivity of MRI. Moreover, our subgroup analyses indicated that MRI was superior to FDG-PET when the pooled study was designed as retrospective, with a larger sample size, and a mean age of patients > 60.0 years. The potential reasons for this discrepancy could the evidence level, weighted based on the overall analyses and the tumor stages are affecting by mean age.

Several strengths of our study should be highlighted. First, the large sample size allowed us to quantitatively compare the predictive values of MRI and FDG-PET for the response to NACT in patients with locally advanced RC. Thus, our findings are potentially more robust than those of any other earlier individual study. Second, the consistency of the findings of this investigation and the lack of significant publication bias also support the robustness of our present findings. Third, indirect comparisons of the predictive value of MRI and FDG-PET were conducted to provide a better imaging tool for the response to NACT. Finally, the present study provides evidence for evaluation of the diagnostic values of MRI and FDG-PET in patients with specific characteristics.

The limitations of our study are as follows: (1) A study designed as retrospective was included in this analysis, which might have introduced uncontrolled bias; (2) Inconsistencies in the characteristics were present among the included studies, especially in terms of tumor properties, which were not reported in most of the included studies; (3) The heterogeneity across included studies were not fully explained by subgroup analyses; (4) Although the imaging examination were performed after NACT and before surgery, while the exact timing of the scanning might play an important role on the diagnostic ability of MRI and FDG-PET; (5) Although our results indicated no significant publication bias, this study was based on published articles, and publication bias was inevitable; and (6) Stratified analyses based on additional characteristics of patients were not conducted since this information was not available.

Conclusion

The results of this study show that MRI and FDG-PET have a moderate diagnostic ability for the response of patients with locally advanced RC to NACT. The results of our indirect analyses suggested MRI was associated with elevated specificity, PLR, and AUC than FDG-PET. Subgroup analyses indicated that the predictive value of MRI was superior to that FDG-PET when the pooled study was designed as retrospective, with a large sample size, and a mean age of the patients > 60.0 years. These results add to the existing evidence but need further prospective research that would perform direct comparisons between the predictive values of MRI and FDG-PET for the response of patients with locally advanced RC to NACT.

Author contributions

PG performed data acquisition, analysis, and interpretation, drafted the article, and obtaining the final approval. NL was responsible for data acquisition, analysis, and interpretation, drafting of the article, and obtaining the final approval. WL developed the conception and design of the study, conducted critical revision, and participated in obtaining the final approval. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2023.1031581/full#supplementary-material

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