Positron Emission Tomography for Predicting Pathologic Response After Neoadjuvant Chemoradiotherapy for Locally Advanced Rectal Cancer

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Purpose: To investigate whether before and after chemoradiotherapy (CRT) positron emission tomography (PET) predict for pathologic response after preoperative CRT in patients with locally advanced rectal adenocarcinoma.

Methods: Thirty-five patients who underwent pre-CRT and post-CRT PET scans before surgery were included. All patients were staged with endoscopic ultrasound or high resolution CT. CRT was given with 50.4 Gy at 1.8 Gy per fraction and concurrent 5-fluorouracil-based chemotherapy. Surgery occurred at a median of 46 days (range, 27 to 112 d) after completing CRT. The maximum standardized uptake value (SUV_{max}) and the metabolic tumor volume (MTV) using various minimum SUV thresholds (2, 2.5, 3) on the PET scans ($MTV_{2.0}$, $MTV_{2.5}$, $MTV_{3.0}$) were determined. Post-CRT PET scans were done 3 to 5 weeks after completion of CRT. Pathologic response was assessed using the tumor regression grade (TRG) scale. Patients with complete or near-complete response (TRG = 0 to 1) were considered pathologic responders. The pre-CRT and post-CRT PET scan SUV_{max} and MTV values were correlated with TRG. The ΔSUV_{max} and ΔMTV were correlated with TRG.

Results: No correlation was seen with SUV_{max} ($P = 0.99$), $MTV_{2.0}$ ($P = 0.73$), $MTV_{2.5}$ ($P = 0.73$), or $MTV_{3.0}$ ($P = 0.31$) on the pre-CRT PET between pathologic responders versus nonresponders. No correlation was noted between SUV_{max} ($P = 0.49$), $MTV_{2.0}$ ($P = 0.73$), $MTV_{2.5}$ ($P = 0.49$), or $MTV_{3.0}$ ($P = 0.31$) on the post-CRT PET scan and pathologic response. Finally, the ΔSUV_{max} ($P = 0.32$), $\Delta MTV_{2.0}$ ($P = 0.99$), $\Delta MTV_{2.5}$ ($P = 0.31$), $\Delta MTV_{3.0}$ ($P = 0.31$) did not correlate with pathologic response.

Conclusions: Changes seen on PET have limited value in predicting for pathologic response of rectal cancer after preoperative neoadjuvant therapy.

Key Words: rectal cancer, PET response, neoadjuvant chemoradiation, pathologic response

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Large advances in the treatment of locally advanced rectal cancer have been made using multimodality treatment. The addition of preoperative radiotherapy, has been shown to improve local control,[1,2] even in the modern surgical era of total mesorectal excision (TME).[3] Preoperative chemoradiotherapy (CRT) has become the standard approach in the United States because of improved local control and reduced perioperative morbidity compared with postoperative treatment.[4] The well-known advantages of preoperative treatment include improved oxygenation of surgically undisturbed tissue, smaller treatment volumes, generally lower doses of radiation needed, potential downstaging to facilitate complete resection and less extensive operations, and the ability to monitor tumor response to therapy. The use of this treatment approach has allowed the study of radiologic predictors of pathologic response and nonresponse with the goal of modifying subsequent treatment.

As a result of the morbidity of TME and the possibility of requiring a permanent colostomy, investigators have studied the use of local excision in patients with a good clinical response to neoadjuvant therapy. This approach has been shown to have similar rates of local control when compared with radical surgery when used with T1 and T2 tumors.[5] For T3N0 lesions, preoperative CRT in conjunction with local excision has been studied with some success,[4,6–10] but some series suggest an increase in local failures.[10–13]

It has been documented that response to preoperative CRT is a predictor of disease-free survival after TME.[10,14,15] Bonnen et al[6] reported 5-year actuarial pelvic control rates of 94% in a group of 26 patients (25 T3N0, 1 T3N1) treated with local excision after CRT. However, those patients with pT3 disease after CRT had a recurrence rate of 67%.[6] Similar recurrence rates in patients with pT3 disease were reported by Mohiuddin et al.[8] This high rate of local recurrence in tumors that are unresponsive to CRT underlies the importance of correctly identifying patients that have responded for local excision.

The use of positron emission tomography (PET) or computed tomography (CT) to evaluate response to CRT has been studied to determine its utility in predicting pathologic response. Should it be a reliable method of prediction, it could serve as a useful tool to guide surgical management of patients. Those with a good response could potentially be converted from an abdominoperineal resection (APR) to a low anterior resection (LAR) or local excision. However, the results with PET/CT have had mixed results. The specificity of these studies for detecting response to CRT has ranged between 60% and 100%,[16–20] largely due variations in methodologies in defining pathologic and radiographic response.

This study was undertaken to examine how pretreatment PET characteristics and the changes on PET scanning after preoperative CRT correlate with pathologic response. In

addition, the metabolic tumor volume (MTV), which is a measure of the volume of tumor that is metabolically active, was also examined as a potential predictive parameter.

METHODS

Patient Selection and Treatment

Institutional review board approved this study; patients from January, 1998 to June, 2009 with adenocarcinoma of the rectum treated with preoperative CRT at Stanford University were identified. Patients were included if they had biopsy-proven rectal adenocarcinoma, CRT before radical surgical resection consisting of LAR or APR, and serial PET/CTs performed before and after CRT at our institution. Patients that had previously received chemotherapy, radiation, had evidence of distant metastasis, or had had earlier surgical interventions for local disease were excluded. Patients were clinically staged (uTNM) with endoscopic ultrasound (EUS; 19 patients) or high-resolution rectal protocol CT scans (2 patients), which used thin cut slices for high-resolution imaging of the primary tumor and lymph nodes. 5-fluorouracil-based chemotherapy was given concurrently.

All patients underwent treatment planning PET/CT scans in the radiation oncology department. All patients were positioned prone in a belly board. Scans were performed on a GE Discovery LS PET/CT scanner (GE Medical Systems, Milwaukee, WI). Each patient fasted for at least 8 hours before imaging. After ensuring that blood glucose levels were <180 mg/dL, patients were injected with 10 to 18 mCi of fluorodeoxyglucose (FDG). Patients then underwent PET/CT imaging after a tracer uptake time of 45 to 60 minutes. PET data covering the area of interest were acquired in 2-dimensional mode, for 3 to 5 minutes of acquisition time per bed position. The PET data were then reconstructed with an ordered set expectation maximization algorithm, using the CT images for attenuation correction. In patients who did not have previous staging PET scans, the axial field of view included the top of the head to mid-thighs, spanning 6 to 7 bed positions, for the purpose of whole body staging. Patients who had previous staging PET scans documenting lack of distant metastases had limited field of view scans including the lower lumbar region to the mid-thighs, spanning 2 to 4 bed positions, for the purpose of aiding radiation treatment planning. At the conclusion of the examination, all reconstructed image data were transferred to a radiation treatment planning workstation and also to a research workstation for tumor volume analysis. The complete PET/CT examination required approximately 90 minutes, including patient setup, tracer uptake, and CT and PET image acquisition.

Radiotherapy was given with standard whole pelvis fields with a posterior and 2 lateral fields. An anterior field was used when needed to supplement the dose anteriorly. The appropriate beam energies were used to optimize target coverage and minimize hotspots. The whole pelvis was treated to 4500 cGy at 180 cGy per fraction and a boost of 540 cGy in 3 fractions was given to the tumor and presacral space in all patients.

After the completion of CRT, patients underwent a restaging diagnostic PET/CT scan before proceeding to surgical resection in the diagnostic radiology department. PET scans were done mostly 3 to 5 weeks after completion of CRT. For these scans, 12 to 15 mCi (444 to 555 MBq) of FDG was injected intravenously with scanning performed 45 to 90 minutes later. All patients were scanned with a PET/CT unit (Discovery LS; GE Medical Systems, Waukesha, WI). The parameters for CT image acquisition were as follows: an initial scout view was obtained with 30 mAs and 120 kVp, followed by spiral CT at 0.8 second per rotation with 100 mAs, 149 kVp, section thickness of 5 mm, and a 4.25-mm interval. Intravenous contrast material was not administered. PET emission images were obtained with a weight-based protocol, with 4 to 6 minutes of acquisition time per bed position. All PET images were reconstructed by using an iterative algorithm, with CT-based attenuation correction applied.

Imaging/Interpretation

Computer-aided MTV and standardized uptake value (SUV) measurements for all FDG-PET scans were performed using commercial imaging software (MIMcontouring Advanced 4.1; MIMVista Corp., Cleveland, OH). The FDG-PET scan and coregistered CT scan could be viewed separately and as a single overlay to aide in contouring the primary site. Diagnostic nuclear medicine reports and final radiation treatment planning volumes were used as references when identifying the lesions. For pretreatment PET/CT scans, a gross tumor volume was delineated around the FDG-avid lesion. Areas of FDG-avidity from normal bowel and the bladder were carefully excluded. Automated segmentation based on SUV on the FDG-PET scan could then generate different subregions based on SUV by setting the minimum SUV thresholds. In this way, different minimum thresholds could be examined to determine which one would yield the most predictive value for MTV. The measured volume of a subregion was recorded as the MTV. Use of 3 different minimum SUV thresholds, 2.0, 2.5, and 3.0, yielded MTV_{2Pre}, $MTV_{2.5Pre}$, and $MTV_{3.0Pre}$, respectively. The maximum SUV (SUV_{max}) was also recorded. The same process was again done on the posttreatment PET-CT scans. Areas of residual FDG activity at the site of the primary tumor were included in a posttreatment gross tumor volume. As the primary site often had significantly decreased FDG-avidity due to treatment response, careful comparison of the pretreatment PET-CT scan was done to ensure that the same area of the rectum was included. This process yielded MTV_{2Post}, $MTV_{2.5Post}$, and $MTV_{3.0Post}$, respectively. Figure 1 shows pre-CRT and post-CRT PET scans of a patient.

Definitions of Pathologic and PET Response

All resection specimens were examined by single pathologist (R.K.P.) according to a standardized protocol that included pathologic staging using (yTNM stage) according to the American Joint Committee on Cancer seventh edition.[21] For obvious residual primary tumor identified on gross macroscopic evaluation, a minimum of 4 paraffin blocks of tumor were processed. If no tumor was visible, the entire fibrotic area suggestive of disease was sliced into 5-μm thick sections and were embedded in paraffin. Tumor regression of the primary tumor was semiquantitatively determined by the amount of viable tumor, according to a modified published tumor regression grading scheme (TRG)[22] advocated by the AJCC Cancer Staging Manual seventh edition.[21] The following were characteristics of each grade: TRG 0, no viable tumor cells (complete response); TRG 1, single cells or small groups of tumor cells (near-complete response); TRG 2, residual tumor outgrown by fibrosis (minimal response); TRG 3, extensive residual cancer with minimal or no tumor kill (poor response). A pathologic response was defined as having a TRG of 0 (complete response) or 1 (near-complete response).
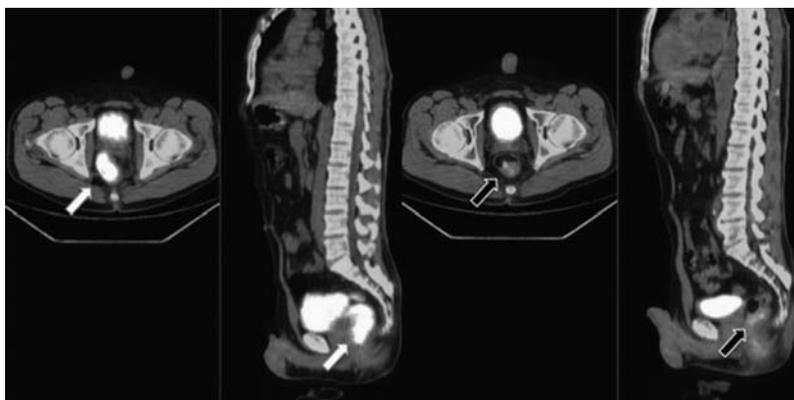
FIGURE 1. A, Left panels: prechemoradiotherapy positron emission tomography (PET) showing the metabolically active tumor (white arrow) and (B) right panels: postchemoradiotherapy PET scan showing significant metabolic response with no residual PET activity in the area of the tumor (black arrow).

Statistics

All statistical computations were accomplished with SAS and JMP software (SAS Institute, Cary, NC). Continuous variables (pre-CRT SUV_{max}, $MTV_{2.0Pre}$, $MTV_{2.5Pre}$, $MTV_{3.0Pre}$, post-CRT SUV_{max}, $MTV_{2.0Post}$, $MTV_{2.5Post}$, $MTV_{3.0Post}$) were dichotomized based on their respective medians. These reformatted variables were assessed with regard to their prognostic significance for TRG (0 to 1 vs. 2 to 3) using Fisher exact test. In addition, the changes in these PET parameters were defined as followed and correlated with TRG:

$\Delta SUV_{max} = (post\text{-}CRT\ SUV_{max})/(pre\text{-}CRT\ SUV_{max})$
$\Delta MTV_{2.0} = (MTV_{2.0Post})/(MTV_{2.0Pre})$
$\Delta MTV_{2.5} = (MTV_{2.5Post})/(MTV_{2.5Pre})$
$\Delta MTV_{3.0} = (MTV_{3.0Post})/(MTV_{3.0Pre})$

Using receiver operating characteristic curves, we further examined these variables for alternative cutoffs that might create maximum prognostic significance while preserving both sensitivity and specificity. Any area under the curve of 0.80 or higher was considered to be good evidence that a given prognostic factor had the ability to significantly discriminate TRG.

RESULTS

From January, 1998 to January, 2008, 35 patients with rectal adenocarcinoma met inclusion criteria. Thirteen patients were staged uT3N0 (37%), 2 patients were T4M0 (6%), and 20 patients were T3N1 (57%). The median time from completing CRT to the posttreatment PET scan was 29 days (range, 12 to 44 d). Thirty-two of 35 patients (91%) had scans done within 3 to 5 weeks. One patient had a PET scan before 3 weeks and 3 patients had a PET scan after 5 weeks. Patients underwent LAR or APR at a median of 47 days (range, 26 to 115 d) after completing CRT, and after a median of 18 days (range, 3 to 75 d) after the restaging PET/CT scan.

Overall, there were 6 patients (17%) with complete pathologic response (TRG = 0) and 8 patients (23%) with a near-complete pathologic response (TRG = 1). Therefore, a total of 14 patients (40%) were classified as having pathologic response. There was no association between the interval of completing CRT to the time of surgery and TRG ($P = 0.74$).

The pretreatment and posttreatment PET parameters are shown in Table 1. The median SUV_{max} decreased from 14.8 (range, 8.1 to 30.7) to 4.8 (range, 2.0 to 11.6) after the therapy. The median $\Delta MTV_{2.0}$ was 0.38 (range, 0 to 5.9), the median

$\Delta MTV_{2.5}$ was 0.15 (range, 0 to 5.8), and the median $\Delta MTV_{3.0}$ was 0.09 (range, 0 to 5.6). One patient outlier had a very high ΔMTV (ie, increase in MTV) for all 3 thresholds due to a very small but FDG-avid lesion on the pretreatment PET. The SUV_{max} was 11.9, but the $MTV_{2.0Pre}$ was 2.1 cc while the $MTV_{2.0Post}$ was 12.4 cc, presumably because of postradiation inflammatory changes. If this patient is excluded, the maximum $\Delta MTV_{2.0}$, $\Delta MTV_{2.5}$, $\Delta MTV_{3.0}$ would be 1.25, 1.08, and 0.89, respectively. There was no association between time interval from completing radiotherapy to post-CRT PET and ΔSUV_{max} ($P = 0.73$), $\Delta MTV_{2.0}$ ($P = 0.5$), $\Delta MTV_{2.5}$ (0.99), or $\Delta MTV_{3.0}$ ($P = 0.99$).

On the pretreatment PET scan, SUV_{max} ($P = 0.99$), $MTV_{2.0}$ ($P = 0.73$), $MTV_{2.5}$ ($P = 0.73$), or $MTV_{3.0}$ ($P = 0.31$) did not correlate with pathologic response. On posttreatment PET scan, again, SUV_{max} ($P = 0.49$), $MTV_{2.0}$ ($P = 0.73$), $MTV_{2.5}$ ($P = 0.49$), or $MTV_{3.0}$ ($P = 0.31$) did not correlate with pathologic response. Finally, the ΔSUV_{max} ($P = 0.32$), $\Delta MTV_{2.0}$ ($P = 0.99$), $\Delta MTV_{2.5}$ ($P = 0.31$), and $\Delta MTV_{3.0}$ ($P = 0.31$) did not have any correlation with pathologic response.

Multiple studies have reported various SUV response thresholds and corresponding sensitivity, specificity, positive predictive value, and negative predictive value. Table 2 shows these parameters for this series when applying these various cutoff values. Using receiver operating characteristic analysis, ΔSUV_{max}, $\Delta MTV_{2.0}$, $\Delta MTV_{2.5}$, and $\Delta MTV_{3.0}$ were all shown to be poor for sensitivity and specificity, with area under the curve <0.6 for all parameters.

TABLE 1. Pretreatment and Posttreatment PET Parameters

Pretreatment	
SUV_{max}	14.8 (8.1-30.7)
$MTV_{2.0Pre}$	38.5 (2.1-138.1)
$MTV_{2.5Pre}$	34.1 (1.4-125.1)
$MTV_{3.0Pre}$	29.0 (0.9-117.1)
Posttreatment	
SUV_{max}	4.8 (2.0-11.6)
$MTV_{2.0Post}$	15.0 (0-46.8)
$MTV_{2.5Post}$	8.5 (0-35.2)
$MTV_{3.0Post}$	3.8 (0-25.6)

MTV indicates metabolic tumor volume; PET, positron emission tomography; SUV_{max}, maximum standardized uptake value.

TABLE 2. Sensitivity, Specificity, PPV, and NPV of Various Definitions of PET Response

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
ΔSUV_{max} cutoff				
≤20% vs. >20%	40	95	80	67
≤34% vs. >34%	43	38	32	50
≤30% vs. >30%	36	52	31	53
≤64% vs. >64%	93	19	43	80

ΔSUV_{max} indicates percent residual maximum standardized uptake value; NPV, negative predictive value; PET, positron emission tomography; PPV, positive predictive value.

DISCUSSION

Earlier studies examining the efficacy of local excision for T3 rectal adenocarcinoma after CRT have shown that those patients that did not respond pathologically to treatment were more likely to have a local recurrence of disease.[6–10] The ability to predict for pathologic response would be an important tool in identifying those who may be good candidates for less extensive and less morbid resection, and just as important, identifying those in whom conservative surgery should not be attempted. In addition, the German rectal trial showed that preoperative CRT can increase the rate of sphincter preservation,[4] and identifying pathologic response could lead to increased used of sphincter-sparing radical resection.

This study was undertaken to address the value of PET in predicting response in the context of 2 questions: (1) what is the relationship between the initial metabolic tumor activity and pathologic response to CRT and (2) how does the change in FDG-PET after neoadjuvant CRT correlate with pathologic response? Unfortunately, comparing these types of studies with each other is plagued by the heterogeneity in definitions of pathologic and radiologic response, as each investigator reports different criteria for both.

With regard to the first question, we found no difference in the initial tumor FDG activity as measured by the SUV_{max} or MTV between those who had a pathology response to

neoadjuvant CRT and those who did not. Others have found similar results.[16,17] We, therefore, conclude that these parameters are not useful in predicting tumor response. Other studies have suggested that larger metabolic tumor burden in other disease sites such as lung, head, and neck cancer, as measured by MTV, predicts for poorer response to therapy and worse outcome.[23] However, our data did not find any relationship between MTV and pathologic response. We, therefore, conclude that pre-CRT PET alone is not sufficient to predict response to therapy.

With regard to the second question, although we found a high degree of response as measured by PET, the posttreatment PET parameters, SUV_{max}, and MTV values, were not predictive of pathologic response. In addition, the ΔSUV_{max} and ΔMTVs also did not correlate with pathologic response.

Data on the use of the predictive value of PET response are difficult to interpret because of the heterogeneity in definitions of response, both on PET scan and on pathology. These data are summarized in Table 3.

Most studies seem to show a high sensitivity, specificity, and positive and negative predictive value of post-CRT PET scans.

Contrary to these studies, however, Kristiansen et al[18] performed a study on 30 patients with locally advanced rectal cancer (T3 or T4) with PET scans done 7 weeks after preoperative CRT. Patients received 60 Gy in 30 fractions to the tumor followed by an additional 5.6 Gy with brachytherapy. The PET scans were categorized as "positive" or "negative" based on the amount of FDG uptake, but no quantitative results using SUV were analyzed. Pathologic response was determined by TRG, with complete or near-complete response defined as response. The authors found that using this classification scheme, the sensitivity was 44%, specificity was 64%, positive predictive value was 58%, and negative predictive value was 50%.

Janssen et al[20] reported on 30 patients with locally advanced rectal cancer treated with preoperative CRT. Unique to this study, PET scans were performed on days 8 and 15 during CRT. Pathologic response was assessed using the TRG scale. The investigators found that the day 15 PET scan correlated better with histologic response, and a response index (defined as percentage of reduction from pretreatment value)

TABLE 3. Comparison of Postchemoradiation PET Data

	N	Timing of PET	RI* (%)	Pathologic Response	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Melton et al[24]	21	4-6 wk after CRT	75	VRS	78.6	85.7	—	—
Amthauer et al[16]	22	2-4 wk after CRT	36.1	yT stage, tumor size	100	85.7	92.9	100
Denecke et al[25]	23	2-4 wk after CRT	36	yT stage	100	60	77	100
Guillem et al[26]	15	4-5 wk after CRT	62.5	VRS	—	—	—	—
Kristiansen et al[18]	30	7 wk after CRT	None	Positive or negative	44	64	58	50
Capirci et al[17]	87	5-6 wk after CRT	65	TRG	84.5	80	81.4	84.2
Janssen et al[20]	30	Day 15 of CRT	43	TRG	77	93	—	—
Rosenberg et al[19]	30	Day 14 of CRT	35	Becker Grade	74	70	82	58
		4 wk after CRT	57.5	Becker Grade	79	70	83	64
Cascini et al[27]	33	Day 14 of CRT	42	TRG	100	87	—	—
	17	7-8 wk after CRT	—	TRG	No correlation			

RI = [SUV (pretreatment) − SUV (posttreatment)]/SUV (pretreatment).
VRS: 0, no response/disease progression; 1, <33% response; 2, 34% to 66% response; 3, >66% response; 4, complete response.
TRG: 0, no viable cancer cells; 1, single cells or small groups of cells; 3, residual cancer outgrown by fibrosis; 4, minimal or no tumor kill, extensive residual cancer.
Becker grade[29]: grade Ia, 0% residual cells; grade Ib, <10% residual tumor per tumor bed; grade II, 10% to 50% residual tumor; grade III, >50% residual tumor.
*Note that RI = 1 − ΔSUV_{max}.
CRT indicates chemoradiation; NPV, negative predictive value; PET, positron emission tomography; PPV, positive predictive value; RI, response index; TRG, tumor regression grade; VRS, visual response score.

of >43% for SUV_{max} showed a sensitivity of 77% and a specificity of 93%. This study raises the possibility that early response by PET may be able to predict the degree of pathologic response.

A study by Cascini et al[28] interestingly compared early versus late PET scan changes in predicting histologic response. In 33 patients with locally advanced rectal cancer, patients underwent a PET scan at day 14 of CRT, and 17 of these patients underwent a repeat PET scan a few days before surgical resection, which occurred 8 weeks after the completion of CRT. Using TRG and classifying histologic response as complete or near complete, the investigators found that using a response index of ≥42% was associated with a sensitivity of 100%, a specificity of 87%, and an overall accuracy of 94%. However, the late PET scan performed after CRT showed no correlation with histologic response. This study indicates that perhaps early PET scans are better predictors of response than posttreatment scans.

Finally, a study by Melton et al[24] with 21 patients showed that the SUV and MTV were useful in predicting any tumor downstaging. They also found that the change in MTV was not useful in predicting near-complete or complete responses, but the change in the average SUV was useful.

Placing the current series in context with these other studies, our results seem to show that post-CRT PET scans may not be as predictive as these studies suggest. In addition, it is very difficult to apply these data given the wide range of SUV cutoffs, the variation in measuring pathologic tumor response, and the lack of clear consensus on the optimal timing of PET. Certainly, the results of many of these studies are likely to be drastically different if different cutoffs and response definitions are applied, a point that further obfuscates their interpretations. Table 2 shows how wide-ranging the predictive value of PET can be simply by applying some of the published SUV cutoffs to our data. Although having a single quantitative threshold would be convenient and easily integrated into clinical practice, there is still much uncertainty surrounding the best use of PET. The next generation of studies should use anatomic imaging, such as magnetic resonance imaging and/or EUS to evaluate tumor size, PET response, and pathologic response. It is likely that the histologic response of tumor to CRT is more complicated than what can be captured by SUV alone or any other single parameter. Most importantly, however, is whether these radiographic responses can be correlated with clinical outcome.

Although response by PET/CT to therapy has been useful in other disease sites in predicting disease outcome, including lymphoma,[28] esophagus,[29] and head and neck,[30] it is unclear why it was not useful for rectal cancer. One reason could be that our endpoint was simply pathologic response and not disease outcome, which was used in studies in other sites. In addition, the residual inflammation caused by radiation likely produces metabolic uptake that obscures the tumor response. Data in head and neck cancer seem to suggest that the optimal time to perform a PET/CT after radiation that allows for resolution of radiation inflammation exceeds 3 months,[31] which is much longer than was done in this study.

All PET scans were done at our institution, and all scans were retrospectively processed and analyzed using a single software package (MIMcontouring). Although this point is a relative strength of this study, there are several limitations that should be noted. Those include small sample size (although our study population is comparable to most published series), variation in imaging intervals, and lack of clinical outcome data. As our clinical experience grows and our follow-up of these patients continues, we hope to be able to study the ability of PET response to predict prognosis.

In conclusion, our findings seem to suggest that changes seen on post-CRT PET scans have limited value in predicting pathologic response. Well-designed, prospective studies are needed that incorporate PET with other imaging modalities including magnetic resonance imaging and EUS to compare predictive value. Ultimately, clinical correlation with PET response is needed to determine the true value of the metabolic imaging response.

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