Clinics of Surgery

Research Article ISSN: 2638-1451 | Volume 10

Relationship Between Metabolic Response and Histology in Squamous Esophageal Cancer: Response to Neoadjuvant Therapy

Saad HA[1*], Baz A[2], Riad M[1], Eraky ME[1], El-Taher A[1], Farid MI[1], Sharaf K[1] and Said HEM[3]

[1]Surgical Department, Faculty of Medicine, Zagazig University, Zagazig City, Egypt

[2]Surgical Department, Alahrar Teaching Hospital, Zagazig University, Zagazig City, Egypt

[3]Clinical Pathology Department, Faculty of Medicine, Zagazig University, Zagazig City, Egypt

[*]Corresponding author:

Hassan A Saad,
Surgical Department, Faculty of Medicine,
Zagazig University, Zagazig City, Egypt
ORCID:0000-0002-6242-7823

Received: 18 Sep 2023
Accepted: 24 Oct 2023
Published: 30 Oct 2023
J Short Name: COS

Copyright:

©2023 Saad HA, This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially.

Citation:

Saad HA. Relationship Between Metabolic Response and Histology in Squamous Esophageal Cancer: Response to Neoadjuvant Therapy. Clin Surg. 2023; 10(2): 1-7

Keywords:

Gastric cancer; Multimodality; Oversightneoadjuvant medicine

1. Abstract

1.1. Summary Objective: The incidence of esophageal squamous cell carcinoma is increasing in India in the modern period. Conventional staging modalities involve contrast-enhanced computed tomography (CECT) and positron emission tomography (PET). Therefore, we need to determine whether the effect of neoadjuvant therapy can be seen on imaging, specifically the standardized uptake value (SUV) on a PET scan used to measure response, and whether this can be linked to histopathological response and survival. Multimodal treatment has achieved evaluable tumor responses, including pathological complete response (pCR), assesses the first section of the identical research question.

1.2. Methods: This retrospective investigation was conducted at our facilities. Patients with esophageal squamous cell carcinoma who underwent surgery between 2011 and 2021 were included in the study. A total of 1369 patients were assessed. Of these, 44 underwent NACTRT, and 1325 underwent NACT with curative surgery. After post-neoadjuvant therapy (NAT), positron emission tomography (PET) was used to measure the standardized uptake value (SUV) of 18-fluorodeoxyglucose. Using a subjective response method, the histology of the final resected specimen was assessed. There are three different states of the tumor: no residual tumor (NRT), sparse residual tumor (SRT), residual tumor, and objective response. Mandard group tumor regression grade (TRG) 0–5. We sought a cut-off point for the primary tumor site's post-neoadjuvant SUV associated with an improved histological response.

1.3. Results: Of the 1325 patients with esophageal SCC who underwent surgery at our Zagazig University Hospital, 943 had TRG data available. These patients were divided into two categories: those with 0–2 had 325 patients (34.5%), and those with 3-5 had 618 patients (65.5%). One hundred and eighty-six patients, 151 from the NACT group and 35 from the NACTRT group, had access to the SUV, which was removed from the institution's PET scan. The NACT cohort's SUV cutoff, determined using the ROC approach and showing a significant difference in the result, was 5.05. Of these, 58 had SUVs > 5.05. And 93 patients who received NACT had an SUV >5.05.

The subjective and objective histopathological scores were correlated, with a p-value of less than 0.0001. To be more precise, most SRT instances fell into the 3-5 TRG category, while most NRT cases fell into the 0-2 TRG category. There were 76 SUVs in the >=5.05 category that had SRT. There were 26 instances of SRT and 32 cases of NRT in the NACT cohort, with an SUV <5.05 category. Of the SRT instances, 25.5% had SUV <5.05, while 74.5% had SUV ≥ 5.05. 34.7 Of the NRT cases, 34.7% had an SUV ≥ 5.05, whereas 65.3% had an SUV <5.05. (P = 0.007), respectively. In the NACTRT group, there was no discernible link in the radiopathology.

1.4. Conclusions: With a cutoff SUV of 5.05 in our group, our investigation validated the relationship between histopathological

response and post-neoadjuvant chemotherapy PET SUV. This validates the predictive value presented in previous research. Moreover, numerous studies have confirmed its predictive relevance in terms of survival. Larger-scale randomized trials could help identify the subset of patients who are morphologically and physiologically borderline operable, for which alternative treatment plans might be recommended to enhance results.

2. Introduction

Cancers of the esophagus and gastroesophageal junction (GEJ) are serious health issues in low- and middle-income nations, with a high prevalence in the Indian subcontinent of central Asia. The results are subpar despite improvements in the methods and technical aspects of both surgery and non-surgical care. Multimodal management has gained momentum as a result, because of a high body mass index and decreased nicotine use. Esophageal adenocarcinoma, or AdenoCa, is the most common cancer in the Western world, and squamous cell carcinoma (SCC) is more prevalent elsewhere. Despite having comparable survival rates, SCC and AdenoCa differ biologically, with SCC being more sensitive to neoadjuvant therapy. [1], **2**60% of cases of SCC esophagus occur in the mid-esophagus, 30% in the lower esophagus, and the remaining cases occur in the upper part of the intrathoracic esophagus. It spreads locally through the submucosa, regionally through the lymphatics and nearby structures, and far away through hidden and obvious metastasis because there is no serosal cover. Approximately 90 percent of the bone marrow samples contain disseminated tumor cells [3]. Neoadjuvant therapy can downstage tumors, improve dysphagia, and predict the response to additional adjuvant treatment. It is also thought to lower micrometastasis and improve tumor penetration because of the intact blood supply. Neoadjuvant radiation aids in R0 resection by sterilizing the margins. Neoadjuvant chemotherapy (NACT) and neoadjuvant chemoradiation (NACTRT) are two treatments for esophageal SCC that have been shown to improve the overall survival and disease-free outcomes. On the other hand, neoadjuvant therapy hurts nutrition and may postpone curative resection, increasing the chance of distant spread in non-responders. This study examined patients with esophageal SCC treated with NACT or NACTRT at our institute between 2009 and 2019. The aim of this study was to determine how much response there was, both histopathologic and metabolic, to survival. They did this by examining the relationship between the histology after surgery and the metabolic response to neoadjuvant treatment, which FDG PET measured. We performed positron emission tomography (PET) after neoadjuvant therapy to determine their association with tumor regression grade and pathological complete response (pCR).

3. Patients and Methods

Presented a retrospective analysis of prospectively maintained data on esophageal SCC patients treated at a single institute between 2011and 20121 1967 and saw the operation of patients with esophageal carcinoma (Ca). Of these, 222 underwent upfront surgery and 1743 underwent neoadjuvant therapy. A total of 1369 patients with SCC, 353 patients with AdenoCa, and others with uncommon histology received NAT. Neoadjuvant treatment was administered to 1369 patients with squamous cancer. All patients with esophageal SCC who underwent curative surgery after NACT/NACTRT were included in our analysis. Post-neoadjuvant therapy (NAT) PET scans were analyzed using the electronic medical data of these patients. The histological findings were further correlated with their matching absolute SUV after the SUV of the PET scan was established. Patients who had non-curative surgery removed, including 160 patients who were inoperable during surgery and whose imaging deteriorated to the point where surgical resection was not possible, and the residual disease on the final histology specimen as well as the Tumor Regression Grade (TRG) were further associated with the previously mentioned variables.

4. Results

Demographic factors: Our study included 546 female patients (41.2%) and 779 male patients (58.8%). There were 433 patients (32.7%) who did not smoke and 325 (24.5%) who smoked. Six hundred ninety-five patients (52.5%) did not drink alcohol, while 62 (4.7%) did. Based on staging according to the AJCC 8th edition, most patients were classified as stage T3. Most of the patients underwent routine two-field lymphadenectomy and were classified as ASA grade 1. These are the demographic details summarized in Table demographic Elements (Table 1).

TRG stands for tumor response grade in the Mandard system; SUV stands for standardized uptake value; VATS stands for video-assisted thoracoscopic surgery; and T staging, according to the AJCC 8th edition final variables:The pathologist's subjective report of SRT was made when sparse tumor cells appeared in the specimen. The Mandard group proposed the tumor regression grade (TRG) as an objective scoring system for tumor regression as an institutional protocol. The histopathological report recorded the histopathological response as NRT, SRT, and residual viable tumor. TRG1 suggested total remission, fibrosis, and no histologically detectable malignancy. TRG2 suggested that fibrosis was dotted, with a few remaining cancer cells. TRG 3 suggests that there were more cancer cells in the fibrosis pool. TRG 4 suggests a higher degree of residual malignancy than fibrosis. No regressive adjustments were suggested by the TRG 5. Because of the large difference in survival rates, this score, which has been confirmed by other studies, was split into two groups: TRG (1 + 2), which stands for "histological responders" [5], and TRG (3 + 4 + 5], which stands for "histological non-responders" [6]. Evaluation:Frequencies and percentages were used to summarize the categorical data related to surgical features, demographics, and imaging. In contrast, standard deviation (SD) and mean (average) were used to characterize

continuous data. A receiver operating characteristic (ROC) curve was used to determine the best threshold for the maximum standardized uptake value (SUV) for detecting residual tumors. Metrics such as sensitivity, specificity, and area under the curve (AUC) were then presented. A significant p-value indicated that the AUC differed significantly from the null value of 0.5. The Chi-square test was used to evaluate the association between SUV and TRG (classified as 0-2, 3–5) and the existence of residual tumors. of less than 0.05 to be statistically significant.Of the 1369 patients with esophageal SCC who underwent surgery, 943 had TRG data available. The patients were divided into two categories:0–2 (325 patients, 34.5%) and 3–5 (618 patients, 65.5%). The SUV was obtained from the institution's PET scan and was available for 186 patients (151 in the NACT group and 35 in the NACTRT group). Histopathological scores were found to be associated with a p-value < 0.0001. More specifically, patients with SRT typically fall into the 3–5 TRG category, whereas cases with NRT typically fall into the 0–2 category. There were 76 cases of SRT and 17 occurrences of NRT in the SUV >= 5.05 group. There were 26 instances of SRT and 32 cases of NRT in the NACT cohort, which fell into the SUV <5.05 category. Of the SRT cases, 74.5% had an SUV >= 5.05, and 25.5% had an SUV < 5.05. Of the NRT instances, 34.7% had an SUV >= 5.05, and 65.3% had an SUV < 5.05 (p-value = 0.007). In the NACTRT group, there was no discernible link in the radiopathology (Table 1).

Relationship between SUV and remaining tumor on histology in the NACT arm: Of the 102 patients with SUV<5.05 group, 26 (25.5%) had residual disease, and 32 (65.3%) had no residual disease. There were 58 patients in this study. Of the 102 patients with an SUV > 5.05 group, 76 (74.5%) had residual disease and 17 (34.7%) had no residual disease. Ninety-three patients were included in this group. The association between the SUV and response had a p-value of less than 0.001, which suggests a statistically significant association. This implies that, in comparison to patients with higher SUV values (>5.05), patients with SUV<5.05 are considerably more likely to have no residual disease following treatment (as described in Table 2).

SUV and TRG correlation in the NACT arm: Of the patients in the Chemotherapy SUV< 5.05 group, 35 (59.3%) had a TRG between 0 and 2, and 20 (23%) had a TRG between 3 and 5. Fifty-five patients were included in this study. 24 out of 59 patients (40.7%) in the chemotherapy SUV > 5.05 group had a TRG of 0–2, and 67 out of 87 patients (77%) had a TRG of 3–5. There were ninety-one patients in this study. There was a statistically significant correlation between the SUV and TRG, as indicated by a p-value of 0.001. According to this, patients who have an SUV < 5.05 are substantially more likely than those who have an SUV > 5.05 to have a TRG of 0–2 (as indicated by Table 2). SUV correlation with residual tumor and TRG in the NACTRT arm:44 patients were in the NACTRT group. With an AUC of 0.655 and a p-value of 0.126, the ideal cut-off (SUV-7.95 using the ROC technique) in this group was not statistically significant. To evaluate the correlation, we considered the 5.05 cut-off obtained from the NACT group. Six of 21 patients (28.6%) in the SUV < 5.05 group had residual disease, while seven of 14 patients (50%) had no residual illness. Thirteen patients were included in this study. Of the 21 patients (71.4%) with an SUV > 5.05 group, seven patients (50%) had no residual disease, and 15 (71.4%) had residual disease. There were 22 patients in this study. As shown in Table 2, the p-value for the correlation between SUV and response was 0.199. This implies that, in this subgroup, there was no statistically significant correlation between the SUV and CTRT response. The decrease in the number of patients in this category was most likely the cause. Table 2 Outcome factors. The format for each column was as follows: Number of patients (valid percentage).

Table 1: Demographic elements. (taxol: taxanes; SUV: standardised uptake value; VATS: video aided thoracoscopic surgery; T staging according to AJCC 8th edition; Tumor response grade (TRG) in the Mandard system

Variables	Categories	Chemotherapy	NACTRT
1. Demographic characteristics			
Sex	Male	779 (58.8)	32 (72.7)
	Female	546 (41.2)	12 (27.3)
Smoking	Yes	325 (42.9)	12 (44.4)
	No	433 (57.1)	15 (55.6)
	Total	758 (100)	27 (100)
Alcohol	Yes	62 (8.2)	1 (3.7)
	No	695 (91.8)	26 (96.3)
	Total	757 (100)	27 (100)
Weight	< 54	656 (49.8)	15 (34.1)
	>=54	660 (50.2)	29 (65.9)
	Total	1316 (100)	44 (100)
2. Stage			

CT T stage	T1	2 (0.2)	39 (88.6)
	T2	33 (2.5)	5 (11.4)
	T3	1242 (93.9)	44 (100)
	T4	45 (3.4)	0
	Total	1322 (100)	0
3. Neoadjuvant treatment			
Regimen	Taxol-Carbo	512 (43)	19 (51.4)
	Taxol-Cis	550 (46.2)	2 (5.4)
	Cisplat-5FU	75 (6.3)	3 (8.1)
	Weekly Tax-Carbo	53 (4.5)	13 (35.1)
	Total	1190 (100)	37 (100)
4. PET response post neoadjuvant therapy			
SUV	>=5.05	93 (0)	22 (0)
	<5.05	58 (0)	13 (0)
5. Surgical details- approach and LN fields			
Level	Upper third	7 (0.5)	3 (6.8)
	Middle third	642 (48.5)	26 (59.1)
	Lower third	676 (51)	15 (34.1)
Thoracic approach	Transhiatal Esophagectomy	174 (13.2)	4 (9.3)
	Open (Right thoracotomy)	722 (54.8)	27 (62.8)
	VATS	333 (25.3)	6 (14)
	VATS converted to open	18 (1.4)	1 (2.3)
	Left thoracotomy	22 (1.7)	2 (4.7)
	VATS Semiprone	2 (0.2)	0
	Robotic	44 (3.3)	3 (7)
	Robotic converted to open	2 (0.2)	0
	Total	1317 (100)	43 (100)
Abdomen approach	Left thoracoabdominal	90 (6.8)	2 (4.7)
	Open	1033 (78.3)	33 (76.7)
	Laparoscopy+minilaparotomy	97 (7.3)	3 (7)
	Laparoscopy	76 (5.8)	4 (9.3)
	Laparoscopic converted to open	9 (0.7)	0
	Robotic+minilaparotomy	14 (1.1)	1 (2.3)
	Robotic	1 (0.1)	0
	Total	1320 (100)	43 (100)
Lymphadenectomy Fields	2	719 (69.8)	33 (97.1)
	3	311 (30.2)	1 (2.9)
	Total	1030 (100)	34 (100)
6. HPR response			
TRG	0–2	325 (34.5)	8 (40)
	3–5	618 (65.5)	12 (60)
	Total	943 (100)	20 (100)
Response	Scanty Residual Tumor (SRT)	871 (76)	25 (59.5)
	No Residual Tumor(NRT)	275 (24)	17 (40.5)
	Total	1146 (100)	42 (100)
Total		1325 (0)	44 (0)

Table 2: Outcome factors. (The format for each column is as follows: number of patients (valid percent.

			Response		Total	P	TRG		Total	P
			Residual Disease	No residual disease			0–2	3–5		
Overall	SUV	<5.05	32 (26)	39 (61.9)	71 (38.2)	<0.001	38 (58.5)	23 (23.5)	61 (37.4)	<0.001
		>5.05	91 (74)	24 (38.1)	115 (61.8)		27 (41.5)	75 (76.5)	102 (62.6)	
	Total		123 (100)	63 (100)	186 (100)		65 (100)	98 (100)	163 (100)	
NACT	SUV	<5.05	26 (25.5)	32 (65.3)	58 (38.4)	<0.001	35 (59.3)	20 (23)	55 (37.7)	<0.001
		>5.05	76 (74.5)	17 (34.7)	93 (61.6)		24 (40.7)	67 (77)	91 (62.3)	
	Total		102 (100)	49 (100)	151 (100)		59 (100)	87 (100)	146 (100)	
NACTRT	SUV	<5.05	6 (28.6)	7 (50)	13 (37.1)	0.199	3 (50)	3 (27.3)	6 (35.3)	0.6
		>5.05	15 (71.4)	7 (50)	22 (62.9)		3 (50)	8 (72.7)	11 (64.7)	
	Total		21 (100)	14 (100)	35 (100)		6 (100)	11 (100)	17 (100)	

5. Discussion

NAT is the standard of care for esophageal SCC. Our findings emphasize the importance of PET SUVs in post-NAT settings. Using NACT, our findings demonstrated a correlation between SUV, histopathological response, and TRG in the final histopathological specimen. Among the patients who underwent NACT, we found that patients with SUV values greater than or equal to 5.05 on the response assessment PET scan typically had a lower histopathological response to neoadjuvant chemotherapy, and patients with SUV values less than or equal to 5.05 had a better response to therapy ($p < 0.001$). Similar to this, but to a lesser extent (p-value < 0.19 for tumor response and < 0.6 for TRG), SUV also correlates with histological response in the NACTRT group. This validates the results of numerous other studies. Because there were fewer cases in the NACTRT group, the correlation strength was lower, and numerous retrospective studies have examined the impact of neoadjuvant therapy. A shorter total survival was associated with residual tumor in the specimen. Retrospective investigations have shown that increased survival and decline in FDG SUV are indicative of pathological responses [2], [6]–[9]. According to Cerfolio et al., the median SUV of esophageal Ca decreased by 37% in minimal responders, 58% in partial responders, and 72% in pCR ($p = 0.003$) [8]. Smith et al. showed a link between improved 12-month DFS and an SUV decline of > 50% [10]. A few prospective studies have reported similar effects. After 2.3 years of follow-up, Munich II found a survival advantage with a >35% decline in SUVs [11]. The respondents' EFS was 29.7 months, whereas that of the non-respondents was only 14 months. In surgical studies, the PET response has been utilized to switch from one regimen to another, as in the CALGB 80803 trial, or to stop chemotherapy and proceed with surgery, as in the MUNICON 1 trial [12], [13]. Because RT-induced inflammation frequently results in false-positive results, guidelines advise that PET CECT should be performed 5-8 weeks following NAT [6, 9, 14]. What is the relationship between the PET response and pCR? Studies have shown that pCR at resection is related to the baseline PET SUV, response PET SUV absolute value, percent fall in SUV, and absolute fall in SUV. In the study by Levine et al., a baseline SUV > 15 was associated with an observed 77.8% significant response, compared to 24.2% for a pretreatment SUV < 15 ($P = 0.005$). In [15]. A significant response was observed in 71.4% of patients when the SUV decreased by > 10, compared to 33.3% when the SUV decreased by less than 10 ($P = 0.004$). Compared to only 33% of the specimens from patients who had a higher PET uptake, 53% of the esophagectomy specimens from patients who had a PET response showed a significant pathological reaction ($P = .18$). The pathogenic reactivity and outcomes were unrelated [2]. When the SUV decreased by 64%, the patient was probably a complete responder [8]. Song et al. reported a pCR rate of 66 percent pCR in 32 patients undergoing NACTRT. They also found that metabolic and pathologic responses were related; however, this was limited to cancers whose primary tumors had a high initial metabolic rate (i.e., > 4.0 SUV). Although a correlation has been shown between pCR and survival in certain cancers, this pattern is absent in other tumors, including breast cancer. At most, pCR can be used as a stand-in for survival because trials that show an OS benefit of pCR were never meant or designed to support this finding. Nonetheless, several studies have shown that PCR and survival are correlated. Brucher (2001) prospectively evaluated 37 patients with T2-4 squamous cell cancer who had received chemoradiation; 24 of these patients underwent surgery. (5). After NACTRT, patients who had reacted and whose histology revealed fewer than 10% viable tumor cells, which closely corresponded with TRG 1 and 2, were identified using PET. FDG uptake decreased by 42.722% in responders compared with non-responders, and a significant decrease (P140.002) was associated with a lower overall survival rate. Respondent PET

SUV > 4 had a significantly lower 2-year survival rate than SUV 4 (P 0.01), per Swisher et al. (6). In fact, post-CRT FDG-PET was the only preoperative variable in that trial that showed a correlation with survival and could predict early response to CRT, providing a strong foundation for surgery or definitive chemoradiotherapy as a subsequent course of treatment. Two weeks after the initiation of polychemotherapy, a pilot study by Weber et al. using PET in esophageal cancer demonstrated a strong connection between PET SUV and histological responses (P = 0.001). When a patient's disease is non-responsive, FDG-PET can predict the prognosis early in the clinical radiation treatment (CRT) process through response assessment. This provides a strong basis for moving quickly to either urgent surgery or definitive chemoradiotherapy, or for continuing non-adjuvant chemotherapy if there is a PET response [16]. The mean tumor FDG uptake in the Weider et al. trial was 9.3 SUV before therapy, and it decreased to 5.7 SUV after that. Fourteen days after radiation and chemotherapy were initiated (38% + -18%; P _.0001). On the preoperative scan, there was a drop in metabolic activity to 3.3 SUV (P _.0001). In histopathologic responders (10% viable cells in the resected material), the SUV decreased from baseline to day 14 by 44% ± 15%, whereas in non-responders, it decreased by only 21% ± 14% (P _.0055). Metabolic changes during this period were associated with survival (P _.011) [17]. Benefits of PET in the management of patients with unacceptable risks: Since local treatment is the main goal of surgery after NAT, patients who show improvement in PET following NACTRT may not benefit much from resection because their local control is good (71% at two years) and similar to that of the trimodality group. Due to the elimination of FDG-PET residual disease, patients undergoing trimodality therapy showed no improvement in PET response. Patients receiving final chemoradiotherapy with a full PET response showed remarkable outcomes similar to those of trimodality therapy, although their baseline characteristics were worse. In summary, patients who show a positive PET response may not be candidates for surgery because of their excellent results without resection [2]. A meta-analysis by Kroese et al. indicated that to prevent a possibly ineffective esophagectomy, 12 scans are needed (95% CI:5–13). A further 5% of patients experience a false-positive result after restaging, leading to unnecessary harm (i.e., more testing) and patient anxiety [18]. These numbers support the need for more tailored applications of PET restaging. Similarly, in patients receiving NACT, an intermediate radiological examination may help decide when to discontinue treatment [19]. Finally, the currently accepted standard of care for esophageal reflux after NAT PET response does not include active surveillance.

The limitations of our concept include the possibility of false-positive responses in responders due to radiation-induced inflammation and confounding changes in tumor glucose metabolism linked to treatment effects. The time delay between the last PET scan and surgery was another confounding factor. In diagnostic investigations, it is advised to have a brief lag between the previous PET and surgery [20] to avoid falsely negative results that are unavoidable owing to logistics. The time of the second scan after the end of NAT is another element that complicates PET interpretation. The effects of NAT on tumor metabolism might not be at their peak if the scan is performed before it, and if it is done too late, post-radiation inflammation might disguise the results. The time needed for FDG absorption, blood glucose levels, the reconstruction technique utilized, and the pixels collected are only a few variables that affect SUV measurement errors, which further calls into question the validity of our findings [21]. Constraints on our research:The SUV value for the NACT group is substantially connected to low TRG and pCR. Regarding the NACTRT, the numbers were insufficient to determine any importance; therefore, the same cannot be said. The significant discrepancy in the number of NACT and NACTRT candidates can be attributed to our organization's implementation of the NACTRT methodology in 2019, following a gradual shift. Similarly, our pathology department's lack of standardization in TRG reporting contributed to the vast majority of missing data on tumors from patients who underwent surgery before 2016, and the study did not include patients without a PET scan at our facility. While this aids in consistency and interpretation reliability, it weakens the study's power by lowering the sample size. The dependability of data is further diminished by data loss resulting from insufficient recording, particularly for patients treated before 2015 when our institute did not widely use electronic data documentation. Because fewer patients were in the NACTRT group, our analysis revealed a weaker association between the SUV and response in that group.

6. Conclusions

Our research validated the relationship between PET and PCR using a 5.05. SUV cutoff. This is consistent with recent research on this topic. Even with such a significant connection, the evidence is only at Level 3. Therefore, further research is needed to fully rely on PET characteristics to guide clinical decisions. The ongoing randomized SANO study [22] examines this matter by contrasting surgery and observation in clinically complete responders 12 weeks after NACTRT [23]. PET can be integrated with liquid biopsy and other response assessment biomarkers, such as esophageal brush cytology, appearance on endoscopy, and narrow-band imaging, to improve patient selection for observation, particularly in patients whose surgical risks are too significant.

References

1. Smithers BM. Positron emission tomography and pathological evidence of response to neoadjuvant therapy in adenocarcinoma of the esophagus. Dis. Esophagus Off. J. Int. Soc. Dis. Esophagus. 2008; 21(2): 151–158.
2. Monjazeb AM. Outcomes of Patients With Esophageal Cancer Staged With [18F] Fluorodeoxyglucose Positron Emission Tomography (FDG-PET): Can Postchemoradiotherapy FDG-PET Predict the Utility of Resection?. J. Clin. Oncol. 2010; 28(31): 4714–4721.
3. Napier KJ, Scheerer M, Misra S. Esophageal cancer: A Review of epidemiology, pathogenesis, staging workup and treatment modalities. World J. Gastrointest. Oncol. 2014; 6(5): 112–120.
4. Mandard AM. Pathologic assessment of tumor regression after preoperative chemoradiotherapy of esophageal carcinoma. Clinicopathologic correlations. Cancer. 1994; 73(11): 2680–2686.
5. Brücher BLDM. Neoadjuvant Therapy of Esophageal Squamous Cell Carcinoma: Response Evaluation by Positron Emission Tomography. Ann. Surg. 2001; 233(3): 300–309.
6. Swisher SG. 2-Fluoro-2-deoxy-D-glucose positron emission tomography imaging is predictive of pathologic response and survival after preoperative chemoradiation in patients with esophageal carcinoma. Cancer. 2004; 101(8): 1776–1785.
7. Westerterp M. Monitoring of response to pre-operative chemoradiation in combination with hyperthermia in oesophageal cancer by FDG-PET. Int. J. Hyperth. Off. J. Eur. Soc. Hyperthermic Oncol. North Am. Hyperth. Group. 2006; 22(2): 149–160.
8. Cerfolio RJ, Bryant AS, Talati AA, Eloubeidi MA, Cerfolio RM, Winokur TS. Change in maximum standardized uptake value on repeat positron emission tomography after chemoradiotherapy in patients with esophageal cancer identifies complete responders. J. Thorac. Cardiovasc. Surg. 2009; 137(3): 605–609.
9. Konski AA. Correlation of molecular response as measured by 18-FDG positron emission tomography with outcome after chemoradiotherapy in patients with esophageal carcinoma. Int. J. Radiat. Oncol. Biol. Phys. 2007; 69(2): 358–363.
10. Long NM, Smith CS. Causes and imaging features of false positives and false negatives on 18F-PET/CT in oncologic imaging. Insights Imaging. 2011; 2(6): 679–698.
11. PET to assess early metabolic response and to guide treatment of adenocarcinoma of the oesophagogastric junction: the MUNICON phase II trial - The Lancet Oncology. 2023.
12. Ott K, Herrmann K, Krause BJ, Lordick F. The Value of PET Imaging in Patients with Localized Gastroesophageal Cancer. Gastrointest. Cancer Res. GCR. 2008; 2(6): 287–294.
13. Goodman KA, OU FS, Hall NC. Randomized Phase II Study of PET Response-Adapted Combined Modality Therapy for Esophageal Cancer: Mature Results of the CALGB 80803 (Alliance) Trial - 2023.
14. McLoughlin JM. Are patients with esophageal cancer who become PET negative after neoadjuvant chemoradiation free of cancer?. J. Am. Coll. Surg. 2008; 206(5): 879–886.
15. Levine EA. Predictive value of 18-fluoro-deoxy-glucose-positron emission tomography (18F-FDG-PET) in the identification of responders to chemoradiation therapy for the treatment of locally advanced esophageal cancer. Ann. Surg. 2006; 243(4): 472–478.
16. Flamen P. Positron emission tomography for assessment of the response to induction radiochemotherapy in locally advanced oesophageal cancer. Ann. Oncol. 2002; 13(3): 361–368.
17. Wider HA, Brucher BLDM. Time course of tumor metabolic activity during chemoradiotherapy of esophageal squamous cell carcinoma and response to treatment. J Clin Oncol.2023.
18. Kroese TE. Detection of distant interval metastases after neoadjuvant therapy for esophageal cancer with 18F-FDG PET(/CT): a systematic review and meta-analysis. Dis. Esophagus Off. J. Int. Soc. Dis. Esophagus. 2018; 31(12).
19. Motoori M. Early response to neoadjuvant chemotherapy in advanced esophageal cancer evaluated by computed tomography predicts the utility of a second cycle of chemotherapy. Mol. Clin. Oncol. 2013; 1(3): 521–526.
20. Bhargava P, Rahman S, Wendt J. Atlas of confounding factors in head and neck PET/CT imaging. Clin. Nucl. Med. 2011; 36(5): e20-29.
21. Benveniste MF. Recognizing Radiation Therapy–related Complications in the Chest. Radio Graphics. 2019; 39(2): 344–366.
22. Eyck BM. Updated protocol of the SANO trial: a stepped-wedge cluster randomised trial comparing surgery with active surveillance after neoadjuvant chemoradiotherapy for oesophageal cancer. Trials. 2021; 22(1): 345.
23. Valkema MJ. Accuracy of 18F-FDG PET/CT in Predicting Residual Disease After Neoadjuvant Chemoradiotherapy for Esophageal Cancer. J. Nucl. Med. Off. Publ. Soc. Nucl. Med. 2019; 60(11): 1553–1559.