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Prognostic Significance of Baseline Positron Emission Tomography And Importance of Clinical Complete Response In Patients With Esophageal or Gastroesophageal Junction Cancer Treated With Definitive Chemoradiotherapy

Akihiro Suzuki, **Lianchun Xiao**, **Yuki Hayashi**, **Homer A. Macapinlac**, **James Welsh**, **Steven H. Lin**, **Jeffrey H. Lee**, **Manoop S. Bhutani**, **Dipen M. Maru**, **Wayne L. Hofstetter**, **Stephen G. Swisher**, and **Jaffer A. Ajani**
Departments of Gastrointestinal Medical Oncology (AS, YH, JAA) and Gastroenterology, Hepatology, and Nutrition (JHL, MSB), and Thoracic and Cardiovascular Surgery (WLH, SGW), Pathology (DMM), and Radiation Oncology (JW, SHL), Radiology (HAM), Biostatistics (LX) at the University of Texas M. D. Anderson Cancer Center, Houston, Texas

Abstract

Background—Metabolic imaging is of interest in esophageal cancer, however, the usefulness of initial standardized uptake value (iSUV) of positron emission tomography (PET) is unknown in patients with esophageal or gastroesophageal carcinoma (E-GEC) treated with definitive chemoradiotherapy. We hypothesized that iSUV would correlate with patient outcome.

Methods—We retrospectively analyzed E-GEC patients who had a baseline PET and endoscopic ultrasonography (EUS) in addition to other routine staging. All patients received definitive chemoradiotherapy. Multiple statistical methods were employed.

Results—We analyzed 209 consecutive E-GEC patients treated with definitive chemoradiation for outcome; of these 179 had baseline PET for additional analyses. The median overall survival (OS) for all patients was 20.7 months (95% confidence interval; 18.8, 26.3 months). Patients with clinical complete response (cCR) lived longer than those with <cCR (p=<0.0001). The median iSUV was 12.7 (range, 0–51). Higher iSUV was associated with longer tumors (p=0.0001), higher T stage (p=<0.0001), positive N (p=0.0001), higher overall stage (P=<0.0001), lack of cCR (p=0.0002), and squamous cell histology (p=<0.0001). In the univariate analysis, iSUV was associated with OS (Cox model, P=0.016; log-rank test, P=0.002). In the multivariate analysis, iSUV dichotomized by the median value (P=0.024) and tumor grade (p=0.016) were independent OS prognosticators. Median iSUV for cCR patients was 10.2 compared to 15.3 for <cCR patients (p=0.0058).

Conclusions—Our data indicate that a higher iSUV is associated with poorer OS in patients with E-GEC receiving definitive chemoradiation. Upon validation, baseline PET may become a useful stratification factor in randomized trials and for individualizing therapy.

Introduction

Esophageal and gastroesophageal carcinomas (E-GEC) are highly aggressive malignancies. Approximately 482,000 new cases and 407,000 deaths were estimated in the world in 2008[1]. The incidence of E-GEC adenocarcinoma has been increasing on a consistent basis for more

Address Correspondence to: Jaffer A. Ajani, MD, Department of GI Medical Oncology, UT M. D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030, 713-792-2828, Jajani@mdanderson.org.

than 30 years in the western countries[2, 3]. Obesity, gastroesophageal reflux disease, and Barrett's metaplasia are associated with the rapid increase in the incidence of adenocarcinoma of the E-GEC[4]. Surgery is still a commonly recommended primary therapy, however, prognosis following resection is poor.[5] In North America, the use of preoperative chemoradiotherapy (trimodality therapy) is common and preferred over preoperative chemotherapy to improve patients' prognosis[6, 7]. This approach has been substantiated by the positive results reported by a recent and the largest trial in its class.[8]

Definitive chemoradiotherapy (bimodality therapy) has also been established as an important approach for patients with locally advanced esophageal carcinoma[9]. Bimodality therapy is appropriate for patients who do not want surgery or in whom surgery is not possible as a result of technical or medical reasons. Recent studies reported that in those patients with high thoracic squamous cell carcinoma, bimodality therapy might be a preferred option[10, 11].

Heterogeneity in patient's outcome is frequently noted even if similarly staged patients receive same therapy. This heterogeneity in patient outcome could be related to differing molecular biology of individual esophageal cancer responsible for various levels of sensitivity to chemotherapy and radiotherapy and its metastatic potential[12]. The challenge is to identify patients who can benefit from a specific therapy and also identify those who will not benefit. Some advances have been made in metabolic imaging through positron emission tomography (PET).[13-23]

Interesting results have been reported with initial SUV (iSUV) and its correlation with overall survival (OS) in surgically managed E-GEC patients who did not receive any preoperative therapy. Lower iSUV was associated with longer OS.[24, 25] In patients who received trimodality therapy, iSUV did not correlate with OS[13, 26, 27]. In one of our studies,[19] higher iSUV tended to be associated with improved OS in patients who received trimodality therapy. The association between iSUV and prognosis of patients treated with bimodality therapy has not been reported.

In this paper, we report our retrospective experience in patients with E-GEC treated with BM therapy. We hypothesized that iSUV would correlate with outcome of bimodality patients. We also reviewed the importance of clinical complete response after chemoradiation.

Materials and Methods

Patient Selection

We studied 209 consecutive patients with biopsy-proven E-GEC who were treated with bimodality therapy between 2002 and early 2008. iSUV was available for analysis in 179 patients. Bimodality therapy was recommended based on the evaluation of patient's cancer staging and other appropriate evaluations by the multidisciplinary team that included medical oncologists, gastroenterologists, radiation oncologists, pathologist, radiologists, and thoracic oncologic surgeons. There were some patients who were recommended trimodality therapy but did not want surgery (reasons are given below).

Pretreatment investigations included a complete blood count, measurement of serum electrolytes, chest radiograph, computed tomography scan of the chest and abdomen, barium swallow radiography, upper gastroesophageal endoscopy with endoscopic ultrasound (EUS) and a PET (when feasible).

Study Design

Our objective was to perform two analyses: 1) to assess the effectiveness of the bimodality therapy at our institution in consecutive patients (n=209) and 2) to correlate iSUV (n=179) with clinical parameters including OS and relapse-free survival (RFS).

Definitive chemoradiotherapy (BM therapy)

All patients received concurrent chemotherapy with radiotherapy. Before definitive chemoradiotherapy, 84 patients (40.2%) received up to 8 weeks of induction chemotherapy. The total radiation dose delivered was either 45 grays (Gy) in 25 fractions or 50.4 Gy in 28 fractions, at 1.8 Gy per fraction delivered once a day, 5 days a week. All patients received a fluoropyrimidine (iv or oral) and either a taxane or a platinum compound as the second cytotoxic agent during radiation. Five to six weeks after the completion of chemoradiation, all patients underwent comprehensive re-staging that included complete blood count, measurement of serum electrolytes, upper gastroesophageal endoscopy with biopsies, and imaging studies of the chest and abdomen including a PET.

SUV Calculations

The maximum SUV was calculated with the following equation: SUV = A/(ID/BW), in which A is the decay-corrected mean activity in tissue (measured in millicuries per milliliter), ID is the injected dose of FDG (measured in millicuries), and BW is the patient's body weight (measured in grams). At our institution, we follow the National Cancer Institute guidelines for image preparation, acquisition, and analysis.[28]

Imaging

PET-CT in 179 patients was performed before any therapy as a baseline study in all patients. PET-CT images were acquired with an integrated PET-CT device (Discovery ST-8; GE Medical System, Milwaukee, Wisconsin), and the whole-body mode was implemented as the standard software. Before PET-CT, patients fasted for at least 6 hours. All patients were tested to confirm that their glucose level was within the normal range (80-120 mg/dl) before FDG administration. Before PET, unenhanced CT was performed from the base of the skull to the upper thigh according to a standardized protocol performed with the following settings: transverse 3.75 mm section thickness, 140-kilovolt peak, 120 mA, and 13.5-mm table speed. Emission scans were obtained 60 minutes after the intravenous administration of FDG (15 to 20 milliCuries or 555 to 740 megabecquerels [MBq]). The acquisition time was 3 minutes per bed position in the 2-dimensional mode. Images were reconstructed with attenuation-weighted ordered-subset expectation maximization with and without attenuation correction. These have been described in detail elsewhere.[19-22]

Assessments after chemoradiation—Upon completion of all post-chemoradiation staging, each patient was assigned to one of two categories: (1) clinical complete response (cCR) or (2) less than cCR. cCR was defined as having no cancer cells in the post-chemoradiation biopsy in all patients. This was coupled with having a physiologic level of SUV max on post-chemoradiation PET (Figures 1a and 1b) or when SUV max was higher than normal but was distributed in the esophagitis pattern (Figures 2a and 2b). This is a working definition at our institution and we acknowledge that there is no agreed upon standard definition for cCR.

Follow-up and Survival

Patients were followed periodically until 5 years or until death. Follow-up data were obtained from MDACC tumor registry and the hospital records or social security database.

Statistical Methods

Continuous variables were summarized using descriptive statistics such as mean, standard deviation, median and range. Categorical variables were tabulated by frequency and percentage.

Kaplan-Meier method was used to estimate the probability of OS and RFS, Log rank test, and Cox proportional hazards regression analysis were employed to determine the association of OS and RFS with clinical and demographic parameters including iSUV values. Multivariate analysis was applied to determine the association of iSUV with OS after adjusting the effects of other covariates. First a base Cox proportional hazards model for OS was established. To build the base model, initially a full model was fitted, including all variables with p value less than 0.15 in the univariate analysis. Then a backward selection procedure was used to remove one variable at a time, until all variables retained in the model were at the 0.05 significance level. After that a model including iSUV and variables in the base model was fit in order to evaluate the prognostic effect of iSUV or its changes on OS after adjusting the effects of the covariates in the base model. iSUV was dichotomized based the median value for assessment but we also performed the recursive partitioning and regression tree analyses[29] for OS and RFS to identify an optimum cut-point for iSUV.

Fisher's exact test and Wilcoxon rank sum test were employed to compare the patient characteristics.

Results

Patient Characteristics

Characteristics of the 209 patients who received definitive chemoradiotherapy (without surgery) are shown in Table 1. White men and adenocarcinoma histology dominated. Among these 209 patients, 73 (34.9%) had significant co-morbid conditions, 69 (33.0%) patients had technically unresectable tumor, and 45 patients (21.5%) elected not to undergo surgery (but were recommended surgery). During chemoradiotherapy, 24 patients (11.5%) had severe adverse events and they were considered too high-risk (estimated mortality >10%) for surgery.

Survival and Relapse (n=209)

The median follow up time is 38.1 months (95 % confidence interval [CI]; 30, 43.1 months). The estimated median survival time for all 209 patients was 20.7 months (95% CI; 18.8, 26.3 months) and median RFS time was 11.15 months (95 % CI; 9.44, 14.34). The estimated OS and RFS rates at 3 years were 35.7 % (95 % CI; 29.0, 43.9%) and 24.8% (95 % CI; 19.1, 32.1%), respectively.

Following definitive chemoradiotherapy, 130 patients (62.2%) had a cCR. The median OS of patients with cCR was 37.47 months (95% CI; 27.14, not reached in months) and that for patients with <cCR was 12.6 months (95% CI; 12.27, 23.78 months); this difference was highly significant ($p<0.0001$; Figure 3). Similarly, RFS for patients with cCR was 20.07 months (95% CI; 15.48, 36.94 months) compared to 4.84 months (95% CI; 4.54, 5.49 months); this difference was highly significant ($p<0.0001$; Figure 4).

Cancer recurrence or persistence cancer was documented in 151 of 209 patients (72.2%). In addition, 125 patients (59.8%) had died at the time of this analysis.

iSUV and OS (all iSUV data are in 179 patients)

Table 2 presents the results of fitting univariate Cox for continuous variables. The results suggested that higher iSUV was associated a higher chance of death (HR=1.02, p=0.016). In Table 3, the Log rank test shows that OS was significantly associated with T-stage status (p=0.001), N-stage status (p=0.007), overall stage (p=0.006), tumor grade (p=<0.0001), iSUV (dichotomized by the median value; p=0.002), and if the patients had cCR or not (p=<0.0001). Location of the primary[30], tumor histology, induction chemotherapy, and type of cytotoxics administered were not associated with OS.

Table 4 shows the multivariate analysis using dichotomized iSUV (by the median as the cut off), after adjusting for the effect of lymph node status and tumor grade, iSUV was significantly associated with OS (p=0.024) and the grade of the tumor was also an independent prognosticator (p=0.016). Patients with a higher iSUV (>/=12.7) had a higher risk death (HR=1.61; p=0.024). Patients with lower than the median value of SUV had a longer OS (Figure 5; p=0.002) and improved RFS (Figure 6, p<0.001) compared with those with a higher iSUV.

Table 5 lists the results of Wilcoxon rank sum test for continuous variables, and Table 6 summarizes the Fisher's exact test result to compare categorical patient characteristics between the iSUV low and high groups. Wilcoxon rank sum test indicated that longer tumors were associated with higher iSUV (p=0.0001). Fisher's exact test indicated that iSUV was significantly associated with primary site (p<0.0001), T-stage status (p<0.0001), N-status status (p=0.0001), overall stage (p<0.0001), and tumor histology (p<0.0001). For example, 80.5% of squamous cell carcinoma patients had iSUV >/=12.7, while only 40.9% of adenocarcinoma patients had iSUV >/=12.7.

Recursive Partitioning and Regression Tree Analysis (iSUV)—Recursive partitioning and regression tree analyses were carried out to find optimal cut-point for iSUV. We identified cut-point of 6 and when this cut-point was used to dichotomize the iSUV results, it correlated similarly to the median cut-point for OS (p=<0.0001; Figure 7) and RFS (p=<0.0001; Figure 8). The cut-point of 6 was also an independent prognosticator in the multivariate analysis for OS (p=0.0013) and RFS (p=0.007). Approximately, 20% of patients had iSUV <6.

Patients who achieved a cCR had a median iSUV of 10.2 (range, 0-43.8) compared to those with <cCR had a median iSUV of 15.3 (range, 0-51); this difference was statistically significant (p=0.0058).

Discussion

Patients who receive bimodality therapy usually have the following features: (1) unresectable tumor because of unresectable T4 stage or distribution or size of the enlarged nodes, (2) severe co-morbid conditions resulting prohibitive risk of death from surgery, and or (3) patients personal choice to decline surgery. In 209 patients treated at our institution, 164 patients (77.8 %) had inoperable conditions and 45 patients (21.5 %) could undergo surgery but declined. Definitive chemoradiotherapy is the best alternative therapy for such patients and this approach has been systematically studied in controlled trials[9, 31, 32]. One issue remains that patients undergoing BM therapy have variable outcomes but currently we are not able to discriminate between the groups of patients who are likely to do well and those whose prognosis is likely to be extremely poor. Imaging with PET has shown some promise but has not been applied to baseline PET. We elected to study the value of baseline PET and also combine post-chemoradiation PET results with post-chemoradiation biopsy to determine if the subgroups can emerge.

Our data indicate that pretreatment PET scan results correlate with OS and RFS. 18[F]-FDG PET is an assessment of glucose consumption by various normal and abnormal tissues. The well-known Warburg effect suggests that most tumors are hypermetabolic and switch from oxidative to glucose metabolism as the main substrate for energy even in the presence of oxygen. The FDG PET has a number of shortcomings but most importantly it is not a direct measure of cell proliferation.[33, 34] Energy produced by glycolysis creates an acidic microenvironment. It has been proposed that increased extracellular acid production may be the underlying the basis for cancer cell survival and progression in the context of the 6 hallmarks of cancer; self-sufficiency in growth signals, insensitivity to antigrowth signals, evasion of apoptosis, limitless replicative potential, sustained angiogenesis, and tissue invasion and metastasis[35]. For these reasons, iSUV measured by PET may be associated with aggressive clinical behavior and shorter OS.

This is the first study in bimodality patients to demonstrate that iSUV as an independent prognostic variable for OS in a multivariate analysis. Patients with low iSUV had better prognosis than those with high iSUV. In 1998, Fukunaga et al. reported 48 Japanese patients' data in that iSUV was associated with OS in patients with esophageal squamous cell carcinoma who were treated with surgery alone[24]. From Memorial Slone-Kettering Cancer Center, Rizk et al. reported similar results in 50 esophageal adenocarcinoma patients[25]. Those two sets of data suggest that high iSUV is associated with poor prognosis in patients treated with surgery alone. Those two studies also suggest, in conjuction with this report, that when single modality (such as surgery) or bimodality (definitive chemoradiation) is used, high iSUV leads to poor patient outcome and most likely reflects aggressive tumor behavior. In contrast, we previously observed that 161 patients who received trimodality therapy, high iSUV was associated with prolonged OS.[19] A clear explanation for these intriguing and contradicting observations is lacking but we speculate that surgery plays an important role following chemoradiation and overcomes the adverse influence of high iSUV as a manifestation of tumor's aggressive behavior. Additional investigations are clearly warranted and should include prospective strategies.

In this report, we analyzed clinical staging after chemoradiation and its influence of patient outcome. We were interested in assessing critical determinants (post-chemoradiation PET results and post-chemoradiation endoscopic biopsies) that seem to segregate patients in a good or poor prognostic group. In addition, we analyzed the influence of iSUV (n=179) to assess if it alone can correlate with cCR or lack of it. Our findings suggest that iSUV max value (by either median value as the cut-point or identified optimal cut-point) correlates significantly with the achievement of cCR, OS, and RFS. We also found that the combination of post-chemoradiation PET and endoscopic biopsy is useful in separating “cCR” patients from “<cCR” patients and the OS rates of these two groups are dramatically different. This observation may be of considerable value in patients who decline surgery but have high iSUV and achieve <cCR following chemorardiation; these variables can be discussed with patients to further persuade them to undergo surgery. Our data can form a basis for developing novel therapeutic strategies for patients who have chemoradiation resistant (<cCR) tumors.

Our data demonstrate considerable differences in the emerging variables between the univariate and multivariate analyses. Multivariate analysis variables are more robust than the univariate variables because multivariate analysis selects for variables that are not totally interdependent.

We acknowledge several weaknesses in our analyses and these include: (1) it is a retrospective analysis, (2) single institution experience and may not be representative of all practices in North America, (3) although most investigators are reporting on SUV max, the

ideal measure is still not known and it may be that the global tumor glycolysis[36] might represent the biology more accurately than SUVmax, and (4) these results are not confirmed by others. In addition, all the weaknesses ingrained in the PET assessments of individual patient (example, those with diabetes) apply. The strengths of our results include: (1) first report in BM therapy patients, (2) large series, (3) novel findings regarding iSUV's ability to classify patients and establishment of the post-chemoradiation cCR category that combines biopsy with PET results.

In conclusion, our data suggest that iSUV has a prognostic value in patients with E-GEC patients treated with BM therapy. The results also suggest that following BM therapy, patients can be classified in two groups: (1) those with good prognosis after having achieved a cCR and (2) those with poor prognosis after having a chemoradition resistant cancer (<cCR). Further studies are warranted to validate these observations.

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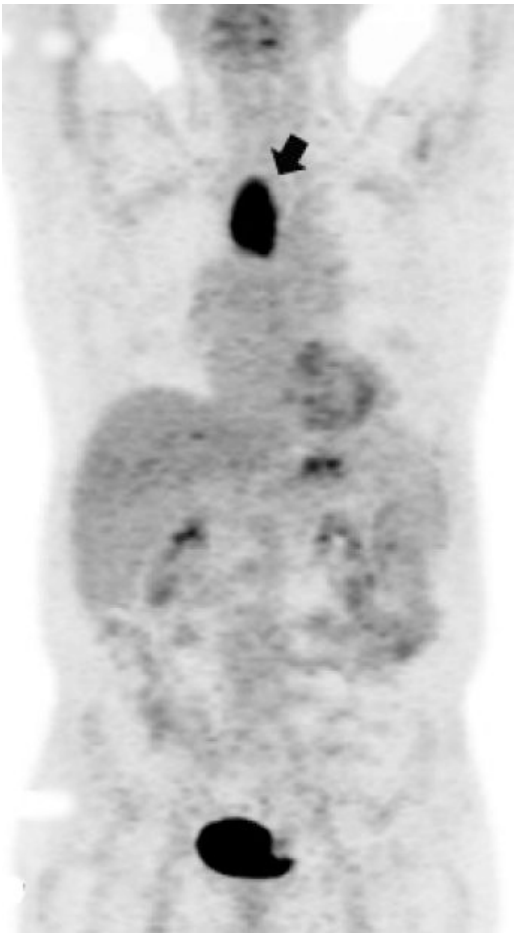


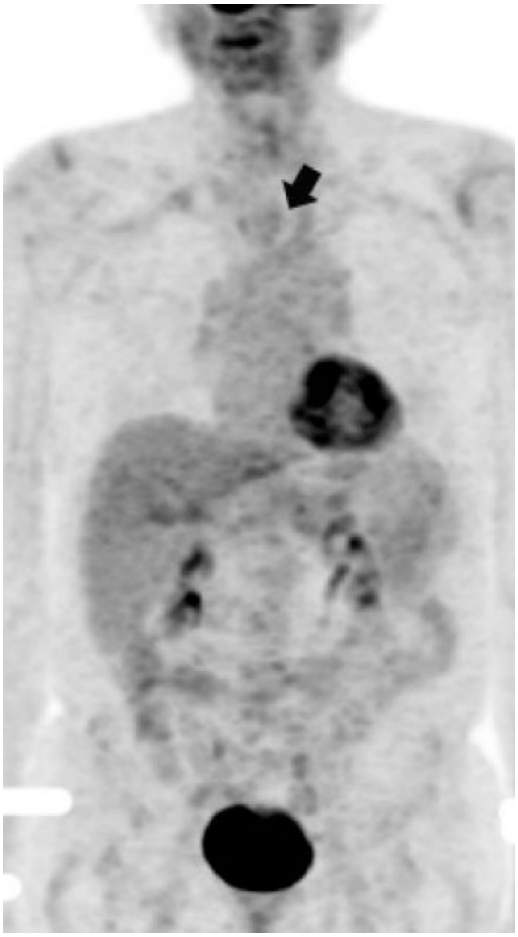
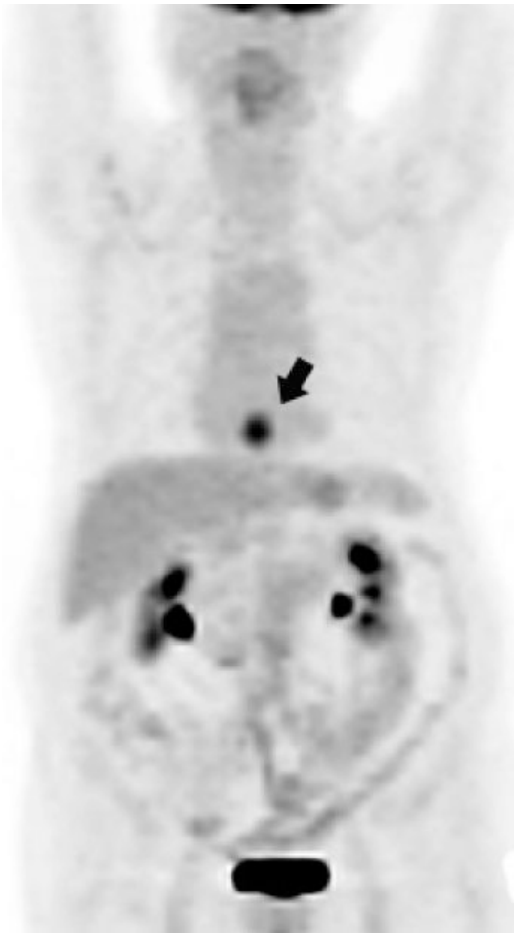


Figure 1.

Figure 1a. Upper thoracic esophageal cancer with an FDG glucose uptake on a PET portion of the PET-CT examination.

Figure 1b. Upper thoracic esophageal cancer with evidence of complete resolution of FDG glucose uptake on a PET portion of the PET-CT examination after chemoradiation.



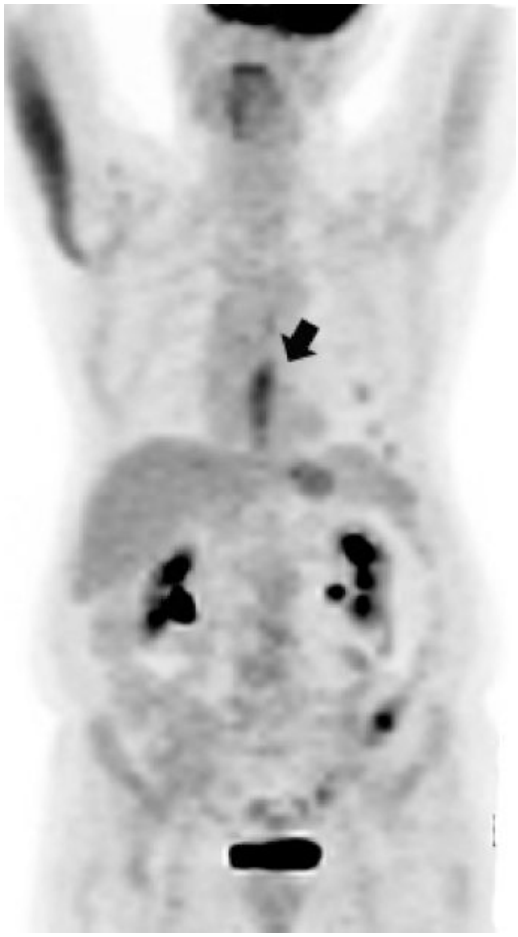


Figure 2.

Figure 2a. Lower thoracic esophageal cancer with evidence of FDG glucose uptake on a PET portion of the PET-CT examination.

Figure 2b. Lower thoracic esophageal cancer with FDG glucose uptake on a PET portion of the PET-CT examination that is indicative of esophagitis after chemoradiation (since post-chemoradiation biopsy was negative, this patient was classified as having achieved a cCR)

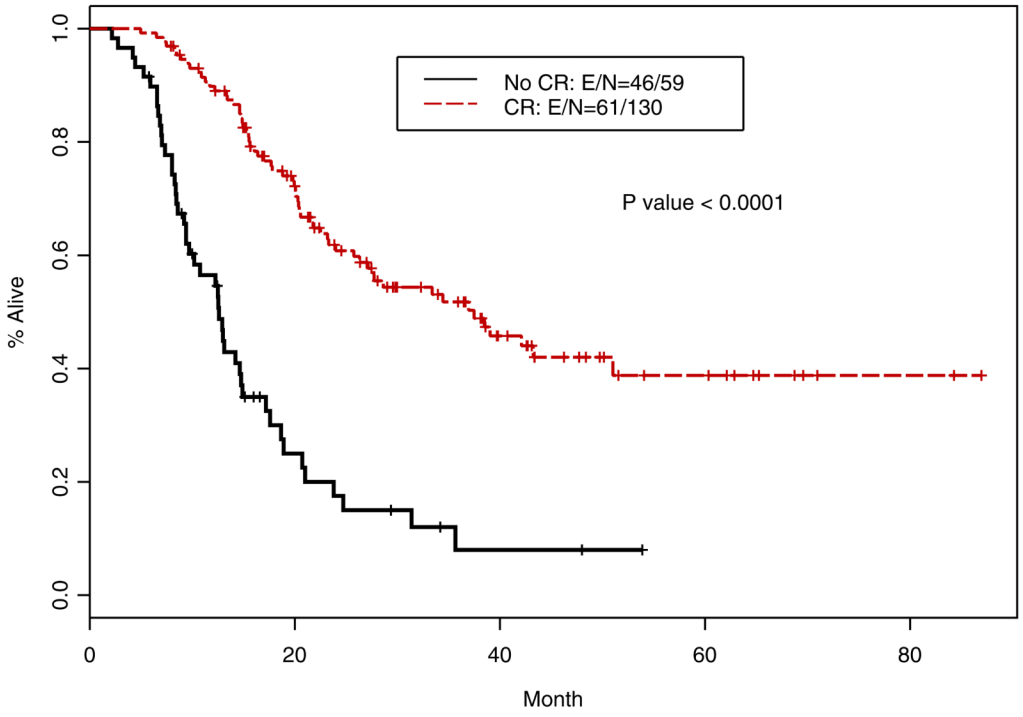


Figure 3.
Kaplan-Meier overall survival curves for patients with cCR and <cCR (n=209)

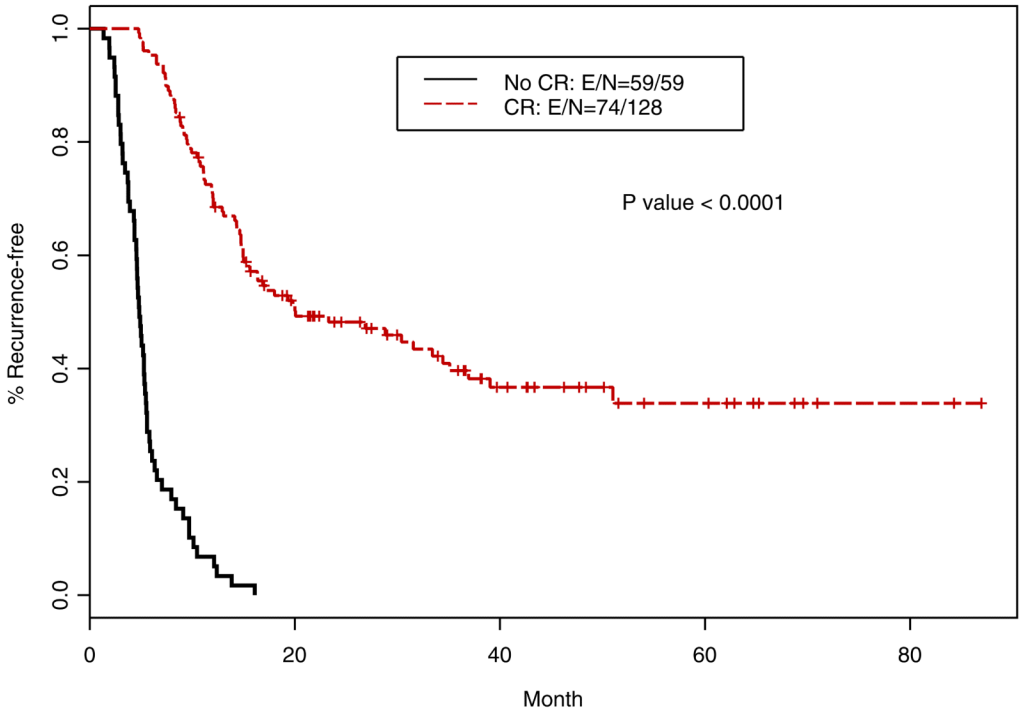


Figure 4.
Kaplan-Meier relapse-free survival curves for patients with cCR and <cCR (n=209)

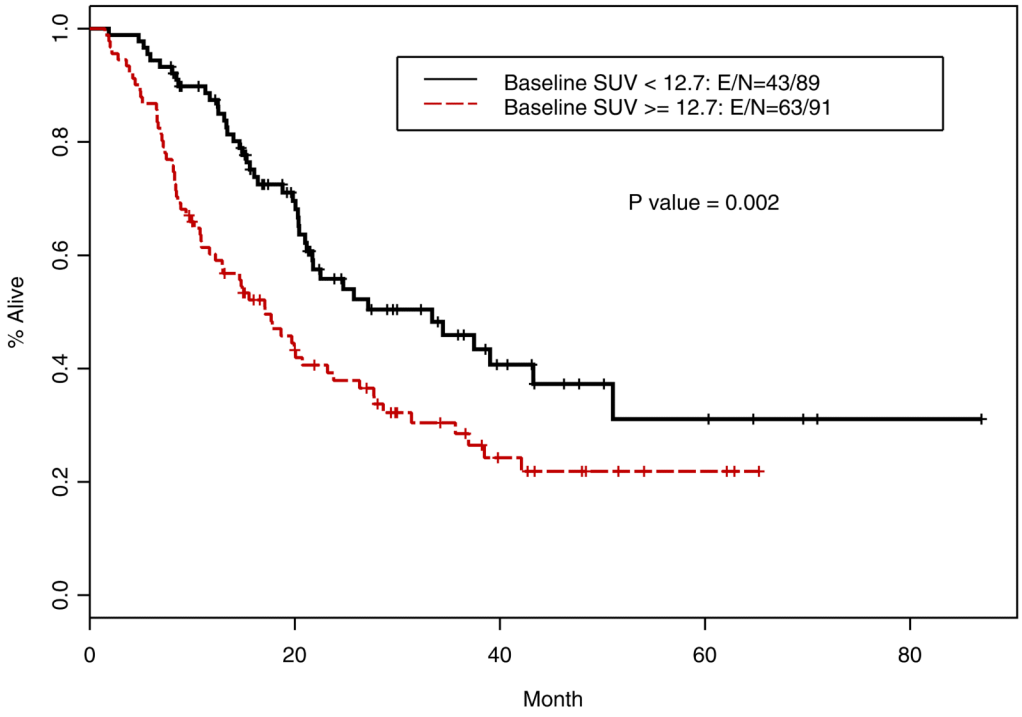


Figure 5.
Kaplan-Meier overall survival curves for patients with high iSUV vs low iSUV (n=179)

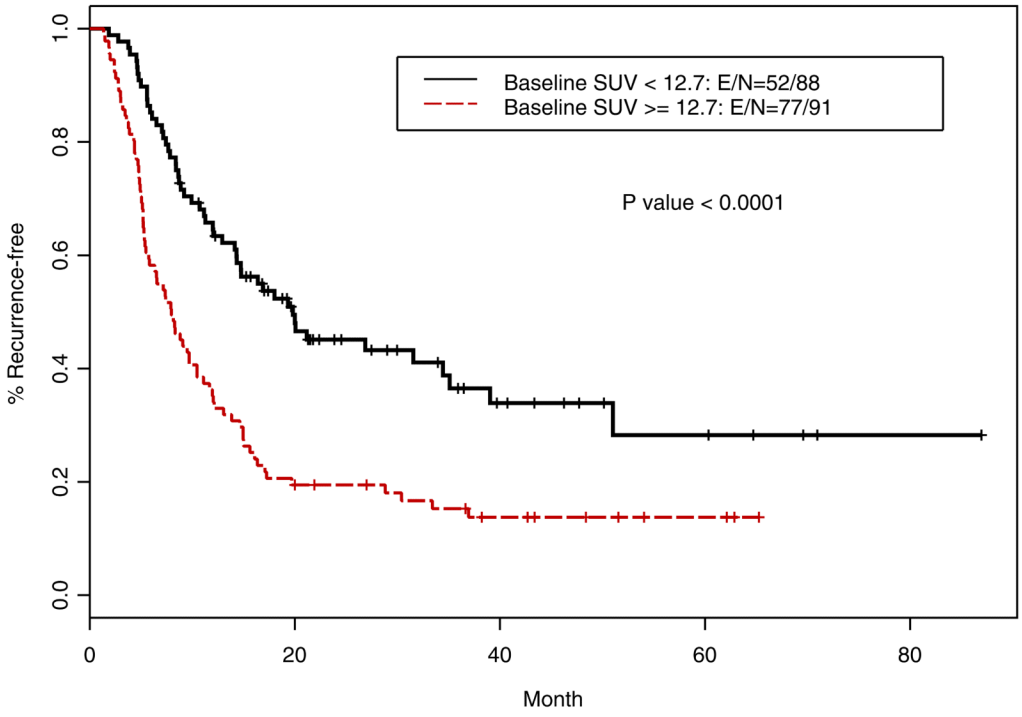


Figure 6.
Kaplan-Meier relapse-free survival curves for patients with high iSUV vs low iSUV (n=179)

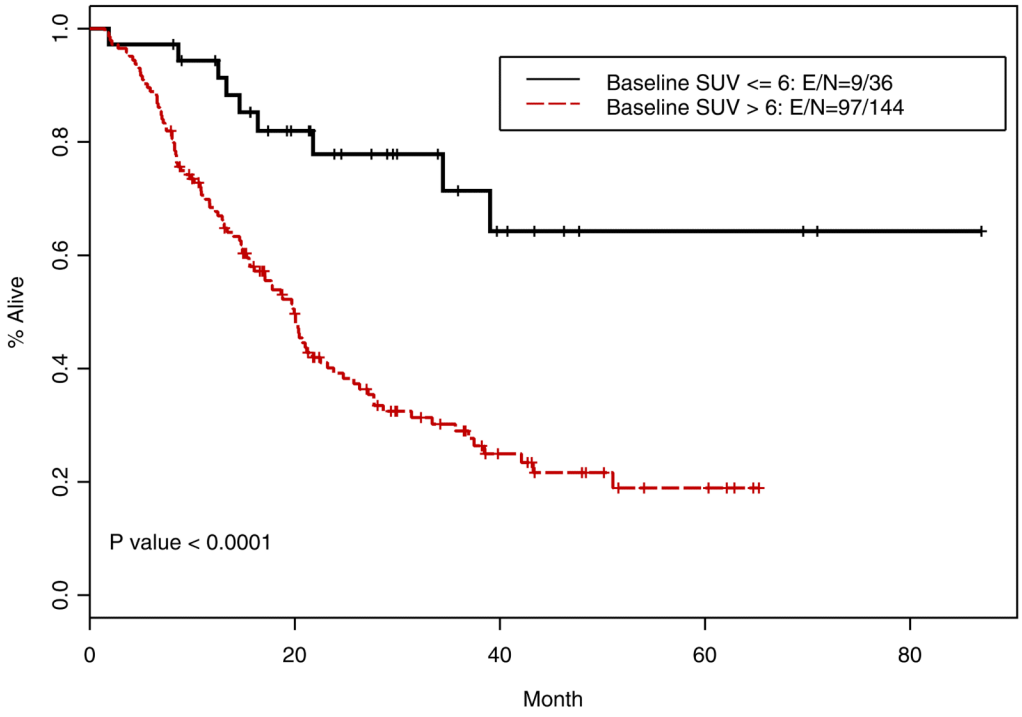


Figure 7.
Kaplan-Meier overall survival curves for patients with iSUV cut-point of 6 identified by recursive partitioning and regression tree analysis (n=179)

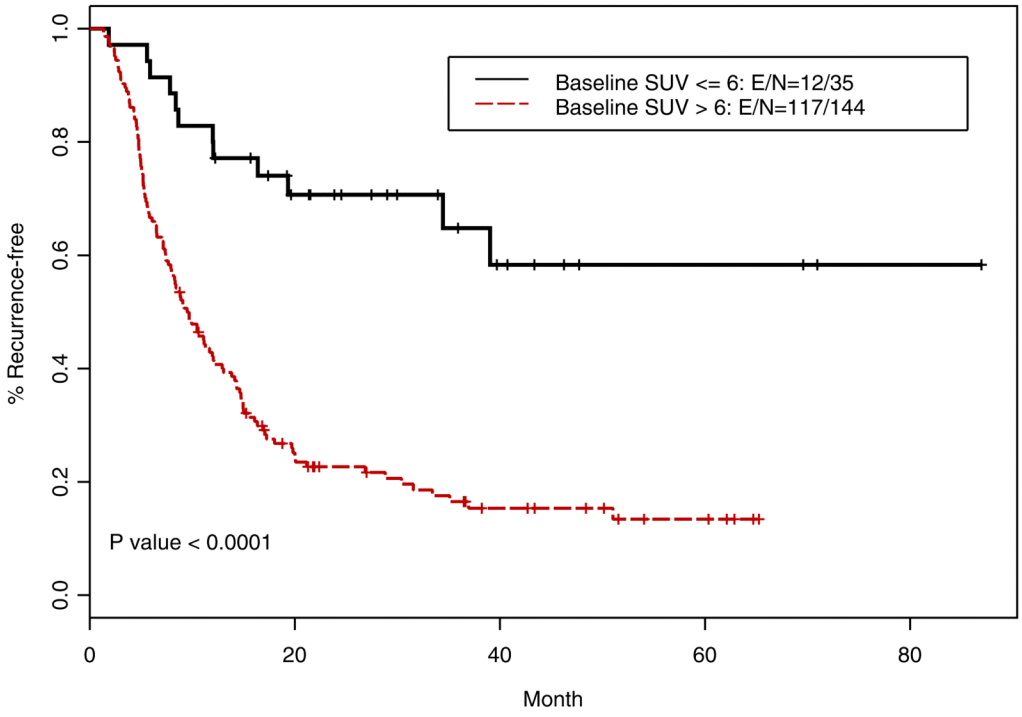


Figure 8.
Kaplan-Meier relapse-free survival curves are shown for patients with high initial standardized uptake value (SUV) versus low initial SUV. E/N indicates event (death or relapse)/number.

Table 1

Patient characteristics (n=209)

Covariate	Frequency (%)
Gender	
Male	181 (86.6)
Female	28 (13.4)
Age	
Average	66.6
SD	10.3
Race	
Asian	6 (2.9)
Black	11 (5.3)
Hispanic	10 (4.8)
White	182 (87.1)
Tumor Length	
Average (cm)	5.3
SD	2.5
Histology	
Adenocarcinoma	158 (75.6)
Squamous cell carcinoma	51 (24.4)
Tumor Grade	
G1 well diff.	2 (1.0)
G2 moderately diff.	96 (45.9)
G3 poorly diff.	110 (52.6)
GX undetermined	1 (0.5)
Reasons for no surgery	
Poor medical condition	73 (34.9)
Technically unresectable	69 (33.0)
Patient's choice	45 (21.5)
Deterioration after chemoradiation	22 (10.5)

SD denotes standard devition;

Table 2

Univariate Cox proportional hazards model to determine the association of OS with iSUV used as a continuous variable (iSUV data on 179 patients)

Variable	HR (95 % CI)	P-value
Age	0.993 (0.977, 1.01)	0.44
Length of tumor (cm)	1.07 (0.993, 1.14)	0.077
Baseline BMI	0.984 (0.952, 1.02)	0.35
iSUV (continuous)	1.02 (1, 1.04)	0.016

CI denotes confidence interval; BMI denotes body mass index; iSUV denotes initial standardized uptake value.

Table 3

Log rank test on OS for categorical variables (n=209) (CI denotes confidence interval; *primary site by Siewert's classification[30]; staging by AJCC 6th Edition[37].

Level	Frequency (%)	Median OS time (95 % CI) (month)	P-value
Primary Site*			
Esophagus	50 (23.9)	20.36 (16.05, NA)	0.173
AEG 1	93 (44.5)	18.82 (15.3, 23.78)	
AEG 2	61 (29.2)	33.39 (20.07, NA)	
AEG 3	5 (2.4)	20.43 (6.51, NA)	
Tumor Status			
T1	10 (4.8)	39.05 (39.05, NA)	0.001
T2	17 (8.1)	NA (34.44, NA)	
T3	166 (79.4)	20.30 (17.11, 23.78)	
T4	14 (6.7)	15.53 (12.27, NA)	
TX	2 (1.0)	7.73 (6.58, NA)	
Lymph Node Status			
N0	61 (29.2)	37.47 (25.76, NA)	0.007
N+	146 (69.9)	18.91 (15.53, 21.71)	
NX	2 (1.0)	11.10 (9.7, NA)	
Metastatic Status			
M0	161 (77.0)	21.02 (17.17, 27.7)	0.773
M1A	22 (10.5)	23.98 (18.82, NA)	
M1B	26 (12.4)	17.80 (14.74, NA)	
Stage			
I	8 (3.8)	39.05 (39.05, NA)	0.006
IIA	48 (23.0)	37.47 (25.76, NA)	
IIB	9 (4.3)	43.26 (34.44, NA)	
III	96 (45.9)	14.90 (13.12, 20.3)	
IVA	22 (10.5)	23.98 (18.82, NA)	
IVB	26 (12.4)	17.80 (14.74, NA)	
Tumor Histology			
Adenocarcinoma	158 (75.6)	21.02 (18.82, 27.73)	0.744
Squamous cell carcinoma	51 (24.4)	19.70 (15.53, NA)	
Tumor Grade			
G1 well diff.	2 (1.0)	3.37 (1.48, NA)	<0.0001
G2 moderately diff.	96 (45.9)	34.44 (21.78, NA)	
G3 poorly diff.	110 (52.6)	19.93 (14.87, 21.71)	
GX undetermined	1 (0.5)	23.78 (NA, NA)	
Induction chemotherapy			
Yes	84 (40.2)	18.82 (16.05, 27.7)	0.984
No	125 (59.8)	21.78 (19.8, 34.44)	
Chemoradiotherapy Agents			

Level	Frequency (%)	Median OS time (95 % CI) (month)	P-value
Platinum + Fluoropyrimidine	56 (26.8)	21.02 (17.17, 43.26)	0.197
Taxane + Fluoropyrimidine	115 (55.0)	22.50 (19.93, 35.66)	
Others	34 (16.3)	17.07 (14.01, NA)	
Unknown	4 (1.9)	8.29 (7.34, NA)	
Clinical CR after chemoradiation			
Achieved	130 (68.8)	37.47 (27.14, NA)	<0.0001
Not achieved	59 (31.2)	12.6 (9.7, 17.17)	
iSUV (dichotomized)			
< 12.7 (median)	89 (49.4)	33.39 (21.71, NA)	0.002
>= 12.7 (median)	91 (50.6)	17.11 (12.27, 23.78)	

Table 4

Multivariate analysis for iSUV (dichotomized by the median value) and OS after adjusting the effect of initial N and tumor grade

variable		HR (95% CI)	P-value
Lymph Node Status	N+/NX vs. N0	1.53 (0.918, 2.54)	0.1
Tumor Grade	G3/GX vs. G1/G2	1.65 (1.100, 2.45)	0.016
iSUV	>= 12.7 vs. < 12.7	1.61 (1.065, 2.41)	0.024
iSUV (by optimal cut-point)	>6 vs. <=6	3.19 (1.57, 6.46)	0.0013

CI denotes confidence interval; iSUV denotes initial standardized uptake value.

Table 5

Wilcoxon rank sum test to determine the association between iSUV (dichotomized by the median value [12.7]) and clinical parameters (n=179)

Covariate and iSUV	N	Mean +/- std, median (range)	P-value
Age			
Low (<12.7)	89	66.3 +/- 10.2, 68 (30 - 84)	0.8336
High (>=12.7)	91	66.4 +/- 10.3, 68 (34 - 85)	
Length of Tumor (cm)			
Low (<12.7)	83	4.5 +/- 2.4, 4 (0 - 11)	0.0001
High (>=12.7)	89	6.1 +/- 2.3, 6 (2 - 13)	
Baseline BMI			
Low (<12.7)	89	27.9 +/- 6.3, 26.6 (19 - 63.9)	0.6725
High (>=12.7)	91	27.7 +/- 5.6, 27.6 (15 - 43.4)	

iSUV denotes standardized unit value; std denotes standard; BMI denotes body mass index

Table 6

Fisher's exact test result to compare categorical patient characteristics between iSUV low and high groups (n=179)

	iSUV		
	Low (<12.7)	**High (>=12.7)**	**P-value**
Primary Site			
Esophagus	9(21.4%)	33(78.6%)	<0.0001
AEG1	40(50.6%)	39(49.4%)	
AEG2	39(70.9%)	16(29.1%)	
AEG3	1(25%)	3(75%)	
Baseline Tumor Status			
T1	9(100%)	0(0%)	<0.0001
T2	14(93.3%)	1(6.7%)	
T3	63(44.4%)	79(55.6%)	
T4	3(25%)	9(75%)	
TX	0(0%)	2(100%)	
Baseline Lymph node Status			
N0	38(71.7%)	15(28.3%)	0.0001
N+	50(39.7%)	76(60.3%)	
NX	1(100%)	0(0%)	
Metastatic Status			
M0	75(54.3%)	63(45.7%)	0.0590
M1a	6(31.6%)	13(68.4%)	
M1b	8(34.8%)	15(65.2%)	
Baseline Stage			
I	7(100%)	0(0%)	<0.0001
IIA	29(69%)	13(31%)	
IIB	7(87.5%)	1(12.5%)	
III	32(39.5%)	49(60.5%)	
IVA	6(31.6%)	13(68.4%)	
IVB	8(34.8%)	15(65.2%)	
Tumor Histology			
Adenocarcinoma	80(58%)	58(42%)	<0.0001
Squamous cell carcinoma	9(21.4%)	33(78.6%)	
Tumor Grade			
G1 well diff.	1(50%)	1(50%)	0.8249
G2 moderately diff.	38(47.5%)	42(52.5%)	
G3 poorly diff.	50(51.5%)	47(48.5%)	
GX undetermined	0(0%)	1(100%)	
Induction Chemotherapy			
Yes	36(50%)	36(50%)	1.0
No	53(49.1%)	55(50.9%)	
Chemoradiotherapy Agents			

	iSUV		
	Low (<12.7)	**High (>=12.7)**	**P-value**
Platinum + Fluoropyrimidine	23(51.1%)	22(48.9%)	0.9133
Taxane + Fluoropyrimidine	51(50.5%)	50(49.5%)	
Others	14(45.2%)	17(54.8%)	
Unknown	1(33.3%)	2(66.7%)	
Clinical CR after chemoradiation			
Achieved	70 (60.3%)	46 (39.7%)	0.0002
Not achieved	13 (27.7%)	34 (72.3%)	

iSUV denotes standardized uptake value;