^{18}F-FDG PET Response After Induction Chemotherapy Can Predict Who Will Benefit from Subsequent Esophagectomy After Chemoradiotherapy for Esophageal Adenocarcinoma

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This study aimed to determine whether ^{18}F-FDG PET response after induction chemotherapy before concurrent chemoradiotherapy can identify patients with esophageal adenocarcinoma who may benefit from subsequent esophagectomy. **Methods:** We identified and analyzed 220 patients with esophageal adenocarcinoma who had received induction chemotherapy before chemoradiotherapy, with or without surgery, with curative intent; all underwent ^{18}F-FDG PET scanning before and after induction chemotherapy. ^{18}F-FDG PET responders were defined as patients who achieved complete response (CR) after induction chemotherapy (maximum SUV $\leq$ 3.0). The predictive value of ^{18}F-FDG PET response for patient outcomes was evaluated. **Results:** Overall, 86 patients had bimodality therapy (BMT; induction chemotherapy + chemoradiotherapy) and 134 had trimodality therapy (TMT; induction chemotherapy + chemoradiotherapy with surgery). Forty-eight patients (21.8%) achieved an ^{18}F-FDG PET CR after induction chemotherapy. ^{18}F-FDG PET CR was found to correlate with overall survival (OS) and progression-free survival (PFS) in BMT patients. For TMT patients, ^{18}F-FDG PET CR predicted pathologic response ($P = 0.003$) but not survival. Among ^{18}F-FDG PET nonresponders, TMT patients had significantly better survival than did BMT patients ($P < 0.001$). However, among ^{18}F-FDG PET responders, BMT patients had OS ($P = 0.201$) and PFS ($P = 0.269$) similar to that of TMT patients. After propensity score-matched analysis, ^{18}F-FDG PET responders treated with BMT versus TMT still had comparable OS and PFS, but TMT was associated with better locoregional control. **Conclusion:** ^{18}F-FDG PET response to induction chemotherapy could be a useful imaging biomarker to identify patients with esophageal adenocarcinoma who could benefit from subsequent esophagectomy after chemoradiotherapy. Compared with BMT, TMT can significantly improve survival in ^{18}F-FDG PET nonresponders. However, outcomes for ^{18}F-FDG PET responders were similar after either treatment (BMT or TMT). Prospective validation of these findings is warranted.

Key Words: esophageal cancer; induction chemotherapy; chemoradiotherapy; FDG-PET response; prognosis

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Locally advanced esophageal cancer is typically treated with combined modalities, as the 5-y survival rates after surgery alone rarely exceed 20% (*1*). Trimodality therapy (TMT), consisting of neoadjuvant chemoradiotherapy followed by surgery, is generally recommended as a standard care option for advanced esophageal cancer because of its positive effects on resectability, locoregional control, and long-term overall survival (OS) compared with surgery alone (*2–4*). However, whether chemoradiotherapy and subsequent esophagectomy have an obvious advantage over definitive chemoradiotherapy is still debated. Two prospective randomized studies have challenged the role of surgery after chemoradiotherapy because of the equivalent OS rates after these two approaches (chemoradiotherapy vs. chemoradiotherapy followed by surgery), especially in patients who showed a clinical response after chemoradiotherapy (*5,6*). Notably, chemoradiotherapy followed by surgery was associated with significantly higher treatment-related mortality rates than chemoradiotherapy only, but the latter was associated with higher locoregional recurrence rates. The RTOG 0246 trial recently demonstrated that an organ-preserving selective-resection strategy for patients treated with definitive chemoradiotherapy had promising efficacy, with a 7-y OS rate of 31.7% (*7*). Therefore, interest is growing in defining reliable criteria with which to identify which patients treated with chemoradiotherapy can safely defer or avoid surgery after chemoradiotherapy.

^{18}F-FDG PET scanning is now commonly used in both the initial workup and the treatment response assessment in esophageal cancer (*8*). However, the prognostic value of ^{18}F-FDG PET response after chemoradiotherapy has not been definitively established, most likely because of the confounding effects of radiation-induced esophagitis (*9,10*). On the other hand, ^{18}F-FDG PET response after induction chemotherapy seems to be a more dependable imaging marker for predicting survival (*11–13*). Previous studies have suggested that ^{18}F-FDG PET response after induction chemotherapy could predict pathologic complete response (pCR) and was associated with survival outcomes in esophageal cancer

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patients treated with induction chemotherapy followed by neoadjuvant or definitive chemoradiotherapy (*11–13*). Moreover, an early ^{18}F-FDG PET response could provide useful information for choosing a chemotherapy regimen to be used during radiation for those who do not show an ^{18}F-FDG PET response (*14*). However, the value of ^{18}F-FDG PET response after induction chemotherapy in terms of identifying which patients will benefit from subsequent surgery after chemoradiotherapy has never, to our knowledge, been investigated. The aim of this study was to determine whether ^{18}F-FDG PET response after induction chemotherapy could identify patients with esophageal adenocarcinoma who may not benefit from esophagectomy after chemoradiotherapy.

MATERIALS AND METHODS

Patient Selection

We reviewed all consecutive patients with esophageal cancer seen at the University of Texas M.D. Anderson Cancer Center between January 2003 and June 2015 using a prospectively maintained database. Patients who met the following criteria were included: histologic documentation of esophageal adenocarcinoma; disease stage I–III according to the seventh TNM staging system of the American Joint Committee on Cancer (*15*); thoracic or gastroesophageal junction carcinoma; induction chemotherapy before concurrent chemoradiotherapy (radiation dose $\geq$ 40 Gy); baseline ^{18}F-FDG PET/CT showing ^{18}F-FDG–avid tumors and ^{18}F-FDG PET rescanning obtained after induction chemotherapy at M.D. Anderson; multidisciplinary evaluation before initiation of treatment; and complete and retrievable clinical records. On the basis of baseline characteristics, whether the patient underwent esophagectomy was at the discretion of the multidisciplinary team and the patient's intent. Patients with stage T1N0 or non–^{18}F-FDG-avid tumors at baseline were excluded. The institutional review board approved this retrospective study, and the requirement to obtain informed consent was waived.

Treatment

All patients received induction chemotherapy followed by concurrent chemoradiotherapy, with or without subsequent surgery, with curative intent. The most common induction chemotherapy regimens included a fluoropyrimidine (5-fluorouracil or capecitabine), a platinum compound (oxaliplatin, cisplatin, or carboplatin), and a taxane (docetaxel or paclitaxel). Two-drug combinations were also given to some patients (fluoropyrimidine/platinum, fluoropyrimidine/taxane, or platinum/taxane). The typical radiation dose was 50.4 Gy in 28 fractions 5 d per week, given by 3-dimensional conformal radiotherapy, intensity-modulated radiotherapy, or proton beam therapy. The chemotherapy regimen given during radiation generally consisted of a fluoropyrimidine with either a platinum or a taxane.

Four to 6 wk after completion of chemoradiotherapy, all patients underwent restaging procedures. Some patients then underwent esophagectomy by transthoracic (Ivor Lewis), transhiatal, minimally invasive, or 3-field technique, with the choice of technique at the discretion of the treating surgeon. Resection specimens were examined histopathologically, and pCR was defined as the complete absence of residual tumor in esophagus and lymph nodes. For patients who received chemoradiotherapy without surgery, clinical CR was defined as ^{18}F-FDG PET with only physiologic uptake and endoscopic biopsies without cancer cells, as well as no evidence of distant metastasis.

PET Imaging

Whole-body PET/CT scans were obtained before and after the completion of induction chemotherapy using an integrated PET/CT device (Discovery RX, ST, or STE; GE Healthcare). All patients were required to fast for at least 6 h before being injected with ^{18}F-FDG. A noncontrast CT scan was obtained before PET for attenuation correction. PET scans were acquired 60–90 min after the intravenous administration of ^{18}F-FDG (dose, 555–740 MBq). The SUV_{max} was calculated as described previously (*13*). An ^{18}F-FDG PET CR was defined as an SUV_{max} of no more than 3.0 after induction chemotherapy (*16*). Patients were assigned to 1 of 2 groups: ^{18}F-FDG PET responders (^{18}F-FDG PET CR) or ^{18}F-FDG PET nonresponders (^{18}F-FDG PET non-CR).

Statistical Analysis

Categoric variables were compared using χ^2 or Fisher exact tests. The relationship between independent variables and ^{18}F-FDG PET response was quantified by logistic regression analysis. Propensity score matching analysis was used to reduce the effects of potentially confounding factors in the comparison of survival between treatment groups at a ratio of 1:1. Locoregional recurrence was defined as the persistence or recurrence of tumor at the primary tumor or regional lymph nodes, and distant recurrence was defined as systemic metastasis or nonregional lymph node recurrence. Recurrences were established on histologic, cytologic, or explicit radiologic proof.

Survival outcomes were defined from the date of diagnosis. All data were updated in August 2016 for censored data analysis. OS, progression-free survival (PFS), locoregional failure–free survival (LRFFS), and distant metastasis–free survival (DMFS) were analyzed using the Kaplan–Meier method. Log-rank tests were used to examine the differences between groups, and a Cox proportional hazards regression model was applied in multivariate analysis. Variables with *P* values of less than 0.2 in the univariate analysis were included in the multivariate analysis. Statistical analyses were done with Stata 12.0 and SPSS 22.0 software (SPSS Inc.). *P* values of less than 0.05 were considered statistically significant.

RESULTS

Patient Characteristics

Patient and treatment characteristics are shown in Table 1. A total of 220 patients with esophageal adenocarcinoma who met the inclusion criteria were selected for analysis, including 86 patients (39.1%) who received definitive chemoradiotherapy (bimodality therapy [BMT]) and 134 patients (60.9%) who received TMT. The median age of the entire group was 61 y (range, 26–87 y), and the median length of the primary tumor was 6.0 cm (range, 0.4–13.0 cm). Compared with patients treated with TMT, Patients who received BMT tended to be older, had worse performance status, had greater weight loss at baseline, had squamous cell carcinoma at the proximal esophagus, and had more advanced disease.

All patients received induction chemotherapy; most patients (62.3%) received 1–2 cycles before chemoradiotherapy, and 37.7% received 3–8 cycles. The induction chemotherapy regimen comprised 3 drugs for 133 patients (60.5%) and 2 drugs for 87 (39.5%). The median radiation dose was 50.4 Gy (range, 43.2–63.0 Gy), delivered by conformal techniques. After chemoradiotherapy, 127 of the 134 patients in the TMT group (94.8%) achieved R0 resection and 33 patients (24.6%) achieved a pCR.

Follow-up and Survival

Median follow-up times were 34.1 mo (range, 3.9–145.5 mo) for the entire group and 63.9 mo (range, 9.3–145.5 mo) for patients who were alive at the time of this analysis. When these data were analyzed, 115 patients (52.3%) had recurrences and 124 patients (56.4%) had died in the whole cohort. A total of 59 patients (68.6%) in the BMT group experienced recurrences, versus 66 patients (41.8%) in the TMT group ($P < 0.001$). The TMT

TABLE 1
Patient Characteristics

Characteristic	All patients, $n = 220$	BMT patients, $n = 86$	TMT patients, $n = 134$	P
Age (y)				0.002
<61	98 (44.5)	27 (31.4)	71 (53.0)	
≥61	122 (55.5)	59 (68.6)	63 (47.0)	
Sex				0.206
Male	201 (91.4)	76 (88.4)	125 (93.3)	
Female	19 (8.6)	10 (11.6)	9 (6.7)	
ECOG performance status				0.128
0	88 (40.0)	29 (33.7)	59 (44.0)	
1–2	132 (60.0)	57 (66.3)	75 (56.0)	
Weight loss				0.010
0%	157 (71.4)	53 (61.6)	104 (77.6)	
≥10%	63 (28.6)	33 (38.4)	30 (22.4)	
Histologic subtype				0.381
Signet ring cell	35 (15.9)	16 (18.6)	19 (14.2)	
None	185 (84.1)	70 (81.4)	115 (85.8)	
Histologic grade				0.223
G1/G2	93 (42.3)	32 (37.2)	61 (45.5)	
G3	127 (57.7)	54 (62.8)	73 (54.5)	
Tumor location				0.645
Upper/middle	4 (1.8)	2 (2.3)	2 (1.5)	
Distal/GEJ	216 (98.2)	84 (97.7)	132 (98.5)	
Primary tumor length				0.874
≤6 cm	137 (62.3)	53 (61.6)	84 (62.7)	
6 cm	83 (37.7)	33 (38.4)	50 (37.3)	
Clinical T stage				0.415
T1–T2	15 (6.8)	4 (4.7)	11 (8.2)	
T3–T4	205 (93.2)	82 (95.3)	123 (91.8)	
Clinical N stage				0.528
N0	43 (19.5)	15 (17.4)	28 (20.9)	
N1–3	177 (80.5)	71 (82.6)	106 (79.1)	
Clinical TNM stage				0.242
IB/II	50 (22.7)	16 (18.6)	34 (25.4)	
III	170 (77.3)	70 (81.4)	100 (74.6)	
Induction chemotherapy regimen				0.002
Fluoropyrimidine/platinum/taxane	133 (60.5)	63 (73.3)	70 (52.2)	
Two-drug combination*	87 (39.5)	23 (26.7)	64 (47.8)	
No. of induction chemotherapy cycles				<0.001
≤2	137 (62.3)	41 (47.7)	96 (71.6)	
>2	83 (37.7)	45 (52.3)	38 (28.4)	
Radiotherapy modality				0.111
3DCRT	28 (12.7)	16 (18.6)	12 (9.0)	
IMRT	138 (62.7)	50 (58.1)	88 (65.7)	
Proton therapy	54 (24.5)	20 (23.3)	34 (25.4)	

*Fluoropyrimidine/platinum or fluoropyrimidine/taxane or platinum/taxane.

ECOG = Eastern Cooperative Oncology Group; GEJ = gastroesophageal junction; 3DCRT = 3-dimensional conformal radiation therapy; IMRT = intensity-modulated radiation therapy.

Data are *n* followed by percentage in parentheses.

group demonstrated a significantly lower locoregional recurrence rate (16.4% vs. 39.5%, $P < 0.001$) and distant failure rate (41.0% vs. 60.5%, $P = 0.005$) than did the BMT group. As anticipated, patients in TMT group had significantly better 5-y OS rates (54.7% vs. 28.1%, $P < 0.001$) and 5-y PFS rates (51.4% vs. 20.6%, $P < 0.001$) than did patients in the BMT group.

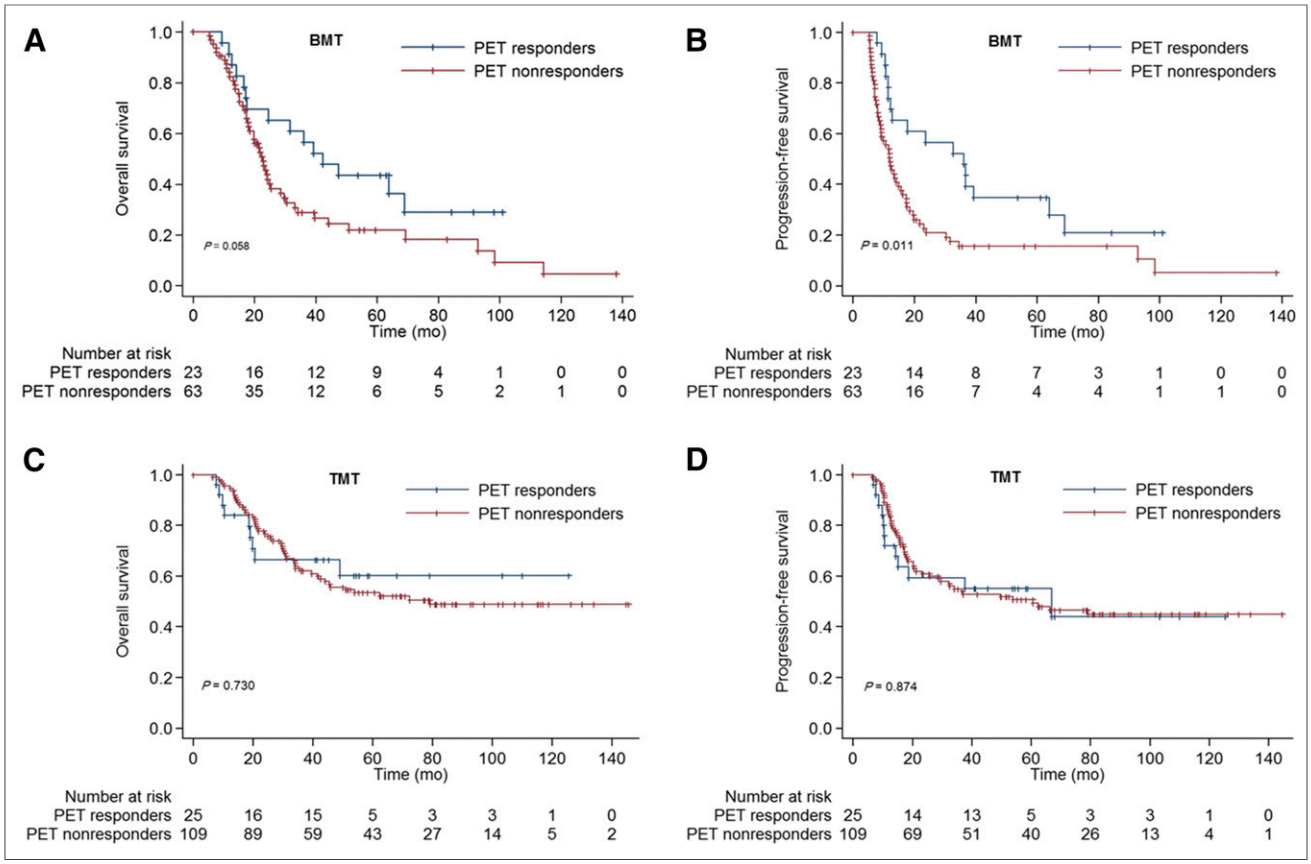

FIGURE 1. OS (A and C) and PFS (B and D) according to response or no response on ^{18}F-FDG PET after induction chemotherapy in patients receiving BMT or TMT.

^{18}F-FDG PET Response After Induction Chemotherapy

The median time from the completion of induction chemotherapy to the repeated ^{18}F-FDG PET scans was 17 d (range, 9–27 d). The median baseline ^{18}F-FDG PET SUV_{max} for the entire group was 11.4 (range, 3.1–60.3), and the median SUV_{max} for the entire group after induction chemotherapy was 5.1 (range, 0.0–27.0). Of the 220 patients, 48 (21.8%) achieved an ^{18}F-FDG PET CR after induction chemotherapy.

Among the BMT group, ^{18}F-FDG PET responders demonstrated a significantly higher clinical CR rate than did ^{18}F-FDG PET nonresponders (89.6% vs. 69.8%, $P = 0.006$). The OS and PFS were also better among ^{18}F-FDG PET responders than ^{18}F-FDG PET nonresponders (5-y OS rates, 43.5% vs. 21.9%, $P = 0.058$; 5-y PFS rates, 34.8% vs. 15.7%, $P = 0.011$; Fig. 1). Similarly, among the TMT group, ^{18}F-FDG PET responders had a higher pCR rate (48.0% vs. 19.3% for nonresponders; $P = 0.003$). However, ^{18}F-FDG PET response was not associated with OS or PFS in patients who received TMT (Fig. 1).

Univariate and multivariate logistic regression analysis to determine the relationships, if any, between prognostic variables and the probability of ^{18}F-FDG PET CR revealed that primary tumor length was the only independent predictor of ^{18}F-FDG PET CR (Table 2). Patients with tumors no more than 6.0 cm long were more likely to achieve an ^{18}F-FDG PET CR than those with tumors longer than 6.0 cm (odds ratio, 0.426; $P = 0.023$).

Survival Analysis in ^{18}F-FDG PET Responders

Among the 48 ^{18}F-FDG PET responders, 23 patients had BMT and 25 patients had TMT. As shown in Figure 2, no significant differences were found between the BMT and TMT groups in terms of 5-y OS rates (43.5% vs. 60.3%, $P = 0.201$), 5-y PFS rates (34.8% vs. 55.1%, $P = 0.269$), or 5-y DMFS rates (52.4% vs. 66.2%, $P = 0.606$). However, LRFFS was better in the TMT group than in the BMT group ($P = 0.01$). Multivariate analysis revealed that age was the only independent predictor of OS in this cohort ($P = 0.004$; Supplemental Table 1; supplemental materials are available at http://jnm.snmjournals.org).

Several pretreatment characteristics were not balanced between the BMT and TMT groups in ^{18}F-FDG PET responders, and propensity score matching analysis was used to reduce this bias (Supplemental Table 2). After adjustment, the comparison demonstrated that OS ($P = 0.533$), PFS ($P = 0.428$), and DMFS ($P = 0.731$) were still comparable between the two groups. Moreover, the TMT group still had significantly better LRFFS than did the BMT group ($P = 0.014$; Supplemental Fig. 1).

Survival Analysis in ^{18}F-FDG PET Nonresponders

Among the 172 ^{18}F-FDG PET nonresponders, 63 patients had BMT and 109 patients had TMT. Patients receiving TMT had remarkably better OS, PFS, LRFFS, and DMFS than did the BMT group ($P < 0.001$ for all; Fig. 3). Multivariate analysis identified sex and surgery to be independent prognostic factors for OS (Supplemental Table 3).

For propensity score matching analysis in this cohort, 57 patients who received BMT were matched with 57 patients who received TMT (Supplemental Table 4). With comparable pretreatment characteristics after adjustment, the TMT group still had

TABLE 2
Influence of Baseline and Treatment Characteristics on ^{18}F-FDG PET CR After Induction Chemotherapy

Characteristic	*n*	Univariate analysis		Multivariate analysis	
		Odds ratio	*P*	Odds ratio	*P*
Age (y)			0.435		
<61	98	Ref.			
≥61	122	1.297 (0.676–2.488)			
Sex			0.508		
Male	201	Ref.			
Female	19	0.65 (0.181–2.331)			
ECOG performance status			0.947		
0	88	Ref.			
1–2	132	0.978 (0.509–1.881)			
Weight loss			0.651		
10%	157	Ref.			
≥10%	63	1.174 (0.586–2.354)			
Histologic subtype			0.467		
Signet ring cell	35	Ref.			
None	185	1.420 (0.552–3.648)			
Histologic grade			0.450		
G1/G2	93	Ref.			
G3	127	1.289 (0.668–2.487)			
Tumor location			0.877		
Upper/middle	4	Ref.			
Distal/GEJ	216	0.834 (0.085–8.207)			
Primary tumor length			0.042		0.023
≤6 cm	137	Ref.		Ref.	
6 cm	83	0.474 (0.231–0.975)		0.426 (0.204–0.890)	
Clinical T stage			0.639		
T1–T2	15	Ref.			
T3–T4	205	0.752 (0.228–2.475)			
Clinical N stage			0.283		
N0	43	Ref.			
N1–N3	177	0.66 (0.308–1.411)			
Induction chemotherapy regimen			0.048		0.059
Fluoropyrimidine/platinum/taxane	133	Ref.		Ref.	
Two-drug combination*	87	0.492 (0.243–0.995)		0.501 (0.244–1.026)	
No. of induction chemotherapy cycles			0.102		0.082
≤2	137	Ref.		Ref.	
>2	83	1.717 (0.899–3.281)		1.814 (0.927–3.547)	

*Fluoropyrimidine/platinum, fluoropyrimidine/taxane, or platinum/taxane.
ECOG = Eastern Cooperative Oncology Group; GEJ = gastroesophageal junction.
Odds ratios are followed by 95% confidence intervals in parentheses.

better OS, PFS, LRFFS, and DMFS survival than did the BMT group ($P < 0.05$ for all; Supplemental Fig. 2).

DISCUSSION

We investigated the value of ^{18}F-FDG PET response after induction chemotherapy for identifying who would benefit (or not benefit) from subsequent esophagectomy after chemoradiotherapy in patients with esophageal adenocarcinoma. Our results demonstrated that among patients who did not show an ^{18}F-FDG PET response after induction chemotherapy, TMT could significantly improve survival compared with BMT. In addition, ^{18}F-FDG PET responders had similar outcomes regardless of whether the treatment was BMT or TMT after induction chemotherapy. Therefore,

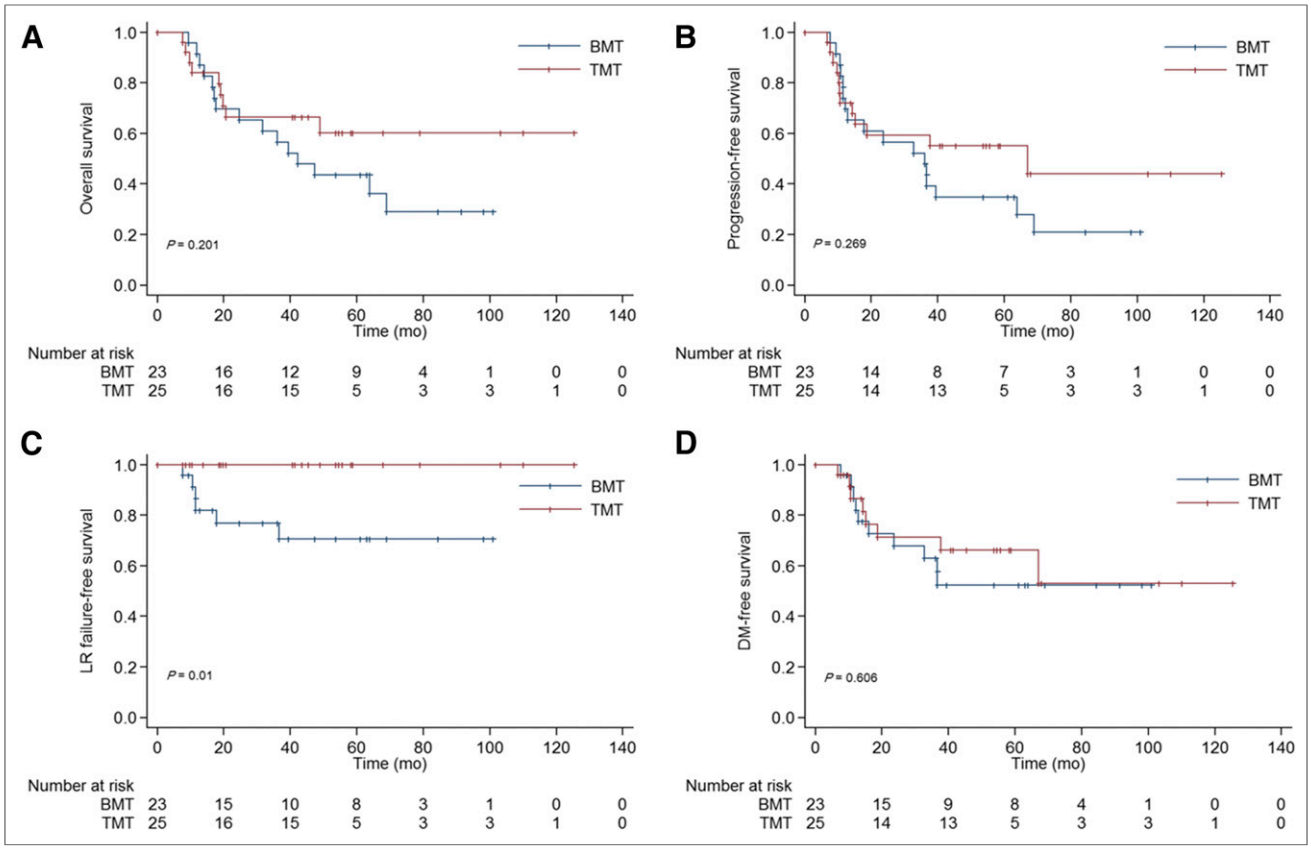

FIGURE 2. OS (A), PFS (B), LRFFS (C), and DMFS (D) according to type of therapy (BMT vs. TMT) among 48 ^{18}F-FDG PET responders.

a ^{18}F-FDG PET response to induction chemotherapy could be useful as an early imaging biomarker for helping guide clinical decision-making for the treatment of esophageal adenocarcinoma.

Because 40%–50% of patients with esophageal cancer experience recurrence after either BMT or TMT (*4,17*), the addition of induction chemotherapy before chemoradiotherapy is common in clinical practice as an attempt to eliminate occult micrometastases. Several retrospective studies and single-arm phase II trials suggested that induction chemotherapy before chemoradiotherapy could improve treatment response and survival, but the 2 prospective, randomized trials conducted to date failed to show a benefit from induction chemotherapy (*11,18–20*). Despite these inconclusive results, several studies have demonstrated the predictive value of ^{18}F-FDG PET response after induction chemotherapy (*11–13*). Unlike response after chemoradiotherapy, the ^{18}F-FDG PET response after induction chemotherapy can be assessed earlier and would avoid the confounding influence of radiation-induced inflammation. Chhabra et al. investigated the prognostic significance of ^{18}F-FDG PET response in 52 esophageal cancer patients treated with definitive chemoradiotherapy (*12*). They found that a prespecified decrease in SUV_{max} of 35% after induction chemotherapy predicted both OS and DMFS. In our study, survival was also significantly better among ^{18}F-FDG PET responders than among nonresponders in the BMT group, which confirmed the prognostic value of early ^{18}F-FDG PET response for this group of patients. Regarding patients treated with TMT, investigators from Memorial Sloan Kettering Cancer Center reported that ^{18}F-FDG PET response to induction chemotherapy was associated with pCR, R0 resection, and PFS (*11*). This result was verified by van Rossum et al. (*13*). However, the Swiss Group for Clinical Cancer Research 75/02 trial revealed that survival among patients with an ^{18}F-FDG PET response to induction chemotherapy was similar to that of nonresponders among patients who received TMT (*21*). The differences in survival among the TMT group were also not statistically significant in our study. The lack of association between ^{18}F-FDG PET response and survival for patients undergoing TMT could have several explanations. First, the prognostic value of ^{18}F-FDG PET response could be affected by the subsequent esophagectomy. Compared with patients receiving no surgery, the presence of residual disease after chemoradiotherapy was less important for patients treated with TMT (*16*). Second, although ^{18}F-FDG PET response after induction chemotherapy did correlate with pCR, some ^{18}F-FDG PET nonresponders could turn into pathologic responders after chemoradiotherapy, potentially influencing the accuracy of ^{18}F-FDG PET response to predict survival. Lastly, patients with distant recurrences after chemoradiotherapy (i.e., before surgery) did not receive esophagectomy. Therefore, a subset of patients with poor prognosis were excluded from the TMT group, and this exclusion may further limit the significance of ^{18}F-FDG PET response with regard to survival outcomes.

The predictive value of early ^{18}F-FDG PET response has prompted interest in using it to direct the choice of subsequent treatments in esophageal cancer. For ^{18}F-FDG PET responders in our study, patients who had BMT had promising and similar survival relative to the patients who had TMT, despite having worse baseline characteristics. The propensity score-matched analysis confirmed this result, suggesting that ^{18}F-FDG PET responders could be considered candidates for organ preservation without

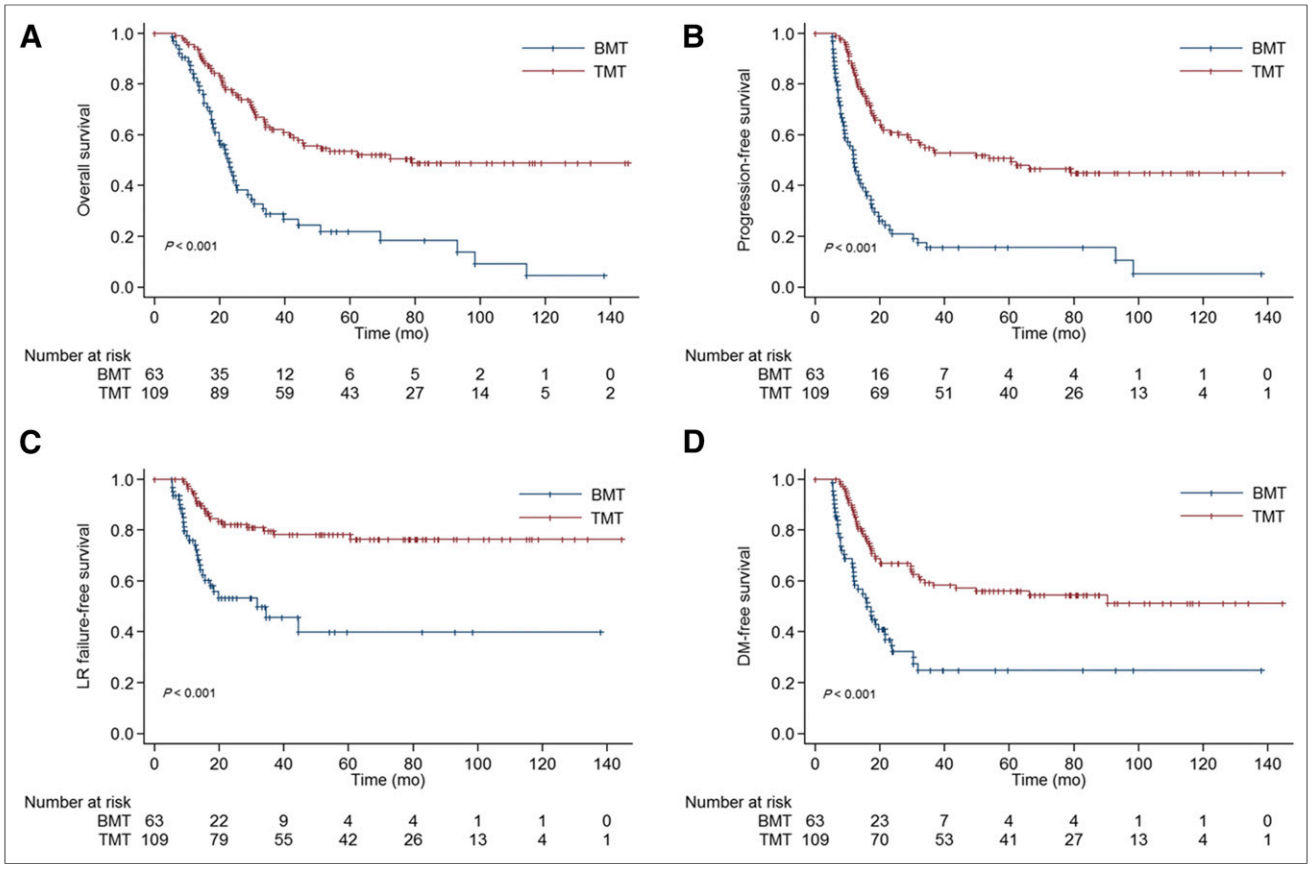

FIGURE 3. OS (A), PFS (B), LRFFS (C), and DMFS (D) according to type of therapy (BMT vs. TMT) among 172 ^{18}F-FDG PET nonresponders.

surgery. However, given the higher rate of locoregional recurrence among those given BMT, vigilant surveillance is indicated, especially during the first 2 y after chemoradiotherapy (*17*). For patients who experience locoregional recurrence only after BMT, selective salvage surgery should be considered, because its long-term outcomes are comparable to those for patients undergoing planned esophagectomy after chemoradiotherapy (*22*).

The current study also suggested that ^{18}F-FDG PET nonresponders should be encouraged to receive esophagectomy because of the significant advantage in survival among those who receive TMT. Changing the chemotherapy regimen during radiation for ^{18}F-FDG PET nonresponders might also be effective. Ku et al. reported that patients who did not respond on ^{18}F-FDG PET after induction chemotherapy and whose chemotherapy was changed during the chemoradiotherapy had significantly better PFS than did patients whose chemotherapy regimen was not changed (*14*). On the other hand, whether nonresponders can proceed directly to surgery is unclear. The RTOG 8911 trial compared receipt of induction chemotherapy plus surgery versus surgery alone for esophageal cancer and showed no difference in survival for ^{18}F-FDG PET nonresponders after induction chemotherapy compared with the surgery-only group (*23*). Therefore, prospective studies are needed to address the question of whether ^{18}F-FDG PET nonresponders after induction chemotherapy should proceed to surgery directly or continue with chemoradiotherapy and subsequent surgery.

This study had several limitations. The number of patients was large, but the number of patients who achieved ^{18}F-FDG PET CR was relatively small, which limited the number of patients in the propensity score–matched analysis. Another potential bias was the diversity of induction chemotherapy regimens and numbers of cycles among patients. However, this bias should have only minor effects on the results, as the type of induction agents and the number of cycles were not associated with the probability of ^{18}F-FDG PET CR in logistic regression analysis. Finally, the timing at which ^{18}F-FDG PET scans were obtained after induction chemotherapy was not uniform among patients in this retrospective study.

CONCLUSION

^{18}F-FDG PET response to induction chemotherapy could be a useful imaging biomarker to identify patients with esophageal adenocarcinoma who could benefit from subsequent esophagectomy after chemoradiotherapy. In fact, compared with BMT, TMT can significantly improve survival in ^{18}F-FDG PET nonresponders. However, outcomes for ^{18}F-FDG PET responders could be similar regardless of whether they receive BMT or TMT after induction chemotherapy. Therefore, esophageal preservation strategies could be considered for this subset of patients. Prospective validation of using ^{18}F-FDG PET findings to guide the choice of therapy is needed.

DISCLOSURE

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