

Potential impact of ^{18}F FDG-PET/CT on surgical approach for operable squamous cell cancer of middle-to-lower esophagus

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Background: Fluorodeoxyglucose-positron emission tomography (PET)/computed tomography (CT) is reported to have a significant advantage over CT for staging esophageal cancer (EC). However, whether PET/CT may play a useful role in guiding surgical approach remains undetermined.

Methods: Patients with potentially resectable squamous cell EC were randomized into either PET/CT group or CT group. The surgical data and survival outcomes were compared.

Results: Compared to the CT group, the right-sided approach was more frequently used (42.6% versus 25.5%, $P=0.065$) in the PET/CT group in order to allow surgical access to radiographically suspicious lymph nodes inaccessible from the left, thus enabling the removal of more involved lymph nodes (2.83 versus 1.76; $P=0.039$) as well as their stations (1.65 versus 1.08; $P=0.042$). Although the overall survival between the two groups was similar, the PET/CT group had a longer disease-free survival (DFS) than the CT group (27.1 months versus 18.9 months; $P=0.019$), especially in the subgroup of node-positive patients (22.5 months versus 13.5 months; $P=0.02$). Preoperative imaging arm was the only prognostic factor found to independently influence DFS.

Conclusion: For patients with middle-to-lower EC, surgical approaches directed by PET/CT may increase the likelihood of complete resection and affect DFS.

Keywords: esophagectomy, surgical approach, survival, esophageal cancer, PET/CT

Introduction

Most patients with esophageal cancer (EC) exhibit an advanced stage of disease at the time of diagnosis. Surgery remains the therapy of choice, provided a complete resection can be achieved (R0 resection). However, the high incidence of nodal involvement, present in approximately half of the patients, results in a 5-year survival rate of only 15%–25% even after apparently curative surgery.^{1–4}

Controversy remains regarding the optimal extent of lymph node (LN) resection during esophagectomy and whether systemic or extensive removal of LNs provides a survival benefit.^{2,5} An extensive lymphadenectomy may offer a better chance of cure, but it is technically demanding and increases the risk of postoperative complications substantially.^{4,6} Conversely, as in the People's Republic of China and most western countries, esophagectomy with LN sampling or less extensive lymphadenectomy via less invasive approaches still remains the mainstay of treatment and may reduce morbidity; the therapeutic outcomes appear to be comparable to operations via thoracotomy when combined with adjuvant therapy.^{7–10}

Since there is no accepted standard to date as to the appropriate extent of LN resection,⁴ most surgeons take a compromise position, or a selective resection of LNs, to balance

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the potential benefit of resecting all diseases with the potential downside of three-field, complete lymphadenectomy.^{7,8,10}

Meanwhile, more and more patients with EC in the People's Republic of China are aged, and many of them have poor cardiac or pulmonary function; the reduced injury seems to be important for them to recover from the surgery. If selective resection of LNs is undertaken, presurgical means of precisely localizing metastatic LNs would likely be quite important, as these studies could be used to determine the proper focus and extent of LN removal.^{4,11}

A number of radiologic modalities, including computed tomography (CT), endoscopic ultrasonography, and magnetic resonance imaging, have been used in defining metastatic spread of EC, but the diagnostic value is often limited,^{12–15} hampering the utility of these techniques in guiding the surgical approach. Positron emission tomography (PET) with fluorine-18 fluorodeoxyglucose (¹⁸FDG) has generally been found to be more accurate than CT in

detecting cancerous lesions. Several reports have been especially encouraging on the utility of PET in the direction of surgery for EC.^{12–19}

Unlike other studies that mainly evaluate the diagnostic value of PET for EC, the current investigation is specifically focused on the practical application of PET/CT to surgery in comparison to that of CT. The aim of this study is to evaluate the impact of preoperative PET/CT (and CT) on surgical approaches for squamous cell cancer of the middle and lower esophagus. We also sought to determine whether surgical treatment based on the two imaging modalities yields different survival outcomes.

Materials and methods

Patients

Between April 2009 and September 2012, 210 patients with squamous cell cancer of the esophagus were evaluated for surgery (Figure 1). Exclusion criteria for this study included

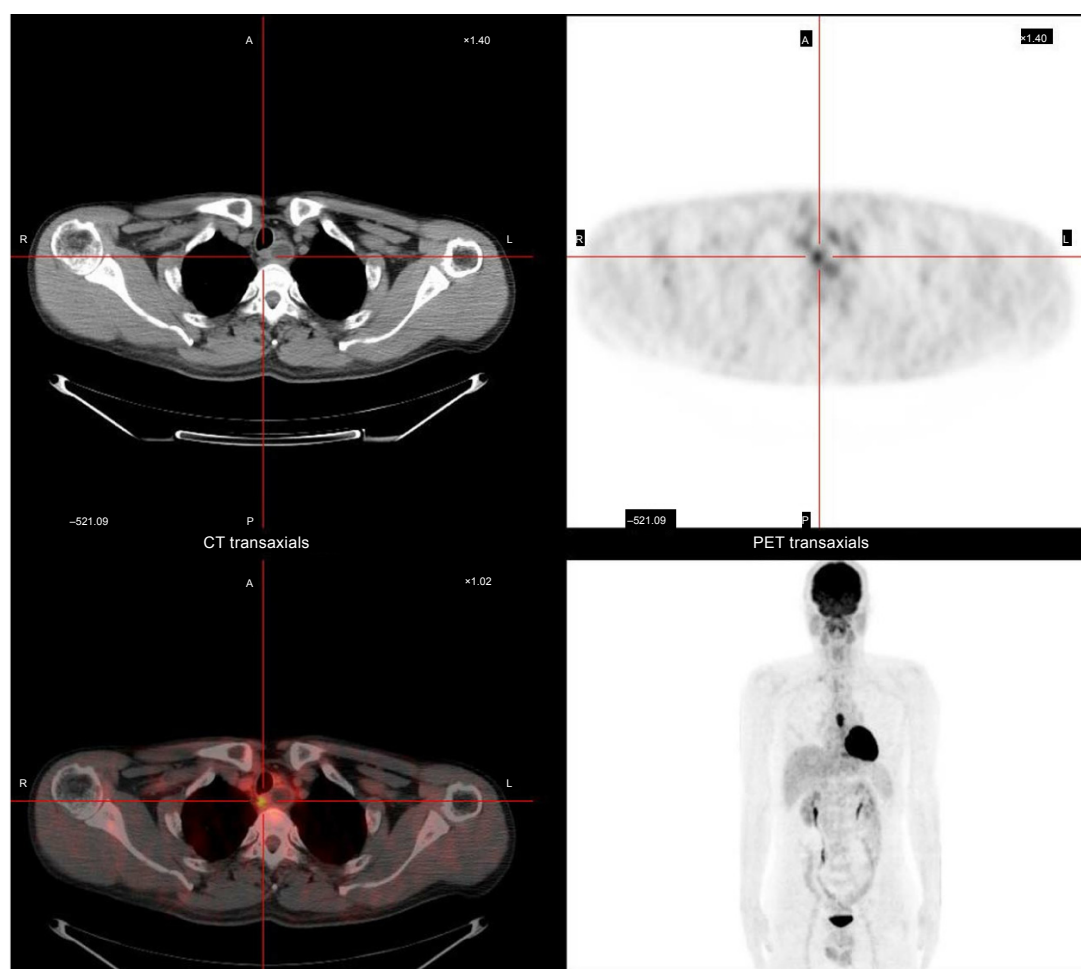


Figure 1 Whole-body fusion PET/CT imaging for a 58-year-old male with squamous carcinoma of the lower thoracic esophagus at biopsy.

Notes: Increased FDG accumulation exhibited at the esophagus with a SUVmax of 11.9; a positive lymph node adjacent to trachea, measuring 0.6 cm in short-axis diameter (SUV = 5.6), was confirmed as malignant on pathology. Since PET/CT showed the positive node at the right-upper mediastinum, a right thoracotomy, instead of left transthoracic approach which was routinely used for the lower EC, was performed.

Abbreviations: SUV, standardized uptake value; PET, positron emission tomography; CT, computed tomography; FDG, fluorine-18 fluorodeoxyglucose.

upper EC, prior treatment, uncontrolled diabetes mellitus, and inoperability due to medical reasons (eg, severe pulmonary or cardiac disease). Before surgery, all patients underwent history and physical examination, blood studies, electrocardiograms, abdominal ultrasonography, pulmonary function analyses, barium meals, magnetic resonance imaging, and other conventional workups (eg, bronchoscopy and endoscopic ultrasonography when indicated). Patients felt to be operable at that point (n=157) were then randomly divided into two groups: a PET/CT group and a CT group. According to the comprehensive evaluation of PET/CT or CT (including the above examinations), an additional 47 patients were considered unresectable after these studies based on M1 disease (including celiac and cervical LN involvement) or T4 disease, and the remaining 110 patients were taken to surgery. The study was approved by the local Shandong Cancer Hospital and Institute, and all patients signed the informed consent to participate.

PET/CT imaging

All patients fasted and rested for at least 6 hours before undergoing PET/CT (Discovery LS; GE Healthcare, Milwaukee, WI, USA). Serum glucose levels were measured to ensure that the results were <6.6 mmol/L. Sixty minutes after intravenous injection of 370 MBq (10 mCi) of ¹⁸FDG, PET emission images were acquired from the level of the mid-skull to that of the proximal thigh for 5 minutes per field of view, each covering 14.5 cm, at an axial sampling thickness of 4.25 mm per slice. The spiral CT component was performed with an X-ray tube voltage peak of 120 kV, 90 mA, a 6:1 pitch, 0.8 seconds per rotation, and a slice thickness of 4.25 mm. A full-ring dedicated PET scan of the same axial range was acquired. Both PET and CT scans were obtained during normal tidal breathing. PET images were reconstructed with CT-derived attenuation correction using the ordered-subset expectation maximization algorithm. The attenuation-corrected PET images, CT images, and fused PET/CT images, subsequently displayed as coronal, sagittal, and transaxial slices, were viewed on a Xeleris workstation. The standardized uptake value (SUV) was calculated using the standard commercial software delivered with the PET/CT scanner.

All studies were interpreted jointly and in consensus by two experienced nuclear medicine physicians. Initially, the attenuation-corrected PET images were analyzed visually, and lesions with abnormal FDG uptake were considered indicative of malignancy. The CT and fused PET/CT images were reviewed together to amend the initial findings. When SUVs were ≥ 2.5 , the LNs were considered

abnormal. There was no specific maximum SUV value that can be used to outstandingly represent benign or malignant disease.

Computed tomography

Spiral CT scans were obtained with Sensation 16 (Siemens Limited Company, Forchheim, Germany). After intravenous injection of 30 g of iodinated contrast (Ultravist 300, 300 mgI/mL; Bayer AG, Leverkusen, Germany), CT scanning was performed from the neck to the middle portion of both kidneys with 0.75 mm collimation, a pitch of 1.75, for 5 minutes per field of view, each covering 14.5 cm, at an axial sampling thickness of 4.25 mm per slice. All CT images were analyzed and in consensus by two radiologists. Nodal enlargement >1 cm in the maximum short-axis diameter was considered indicative of tumor involvement.

Surgical therapy

Surgery was usually performed within 1 week after imaging. Eligible patients underwent either a left- or right-sided approach for esophagectomy with lymphadenectomy. The choice of approach was left at the surgeon's discretion based on the locations of tumor and suspicious LNs by imaging. On the left, thoracotomy without laparotomy was used, and the anastomosis was placed either just below the aortic arch if the tumor is below the inferior pulmonary vein or in the cervix if the tumor is above the inferior pulmonary vein. On the right, the standard Ivor Lewis operation (laparotomy followed by repositioning and right thoracotomy) was used, the anastomosis was placed either at the apex of the thorax or in the neck. A circular stapler was routinely used for intrathoracic anastomosis, whereas a hand-sewn anastomosis was performed in case of cervicotomy. Enteral nutrition support through nasojejun tube was initiated on the third day after operation.

The left-sided approach was the preferred approach since it was felt to be more straightforward and perhaps less morbid than the Ivor Lewis.⁷ However, LNs in the upper right mediastinal compartment, along recurrent nerves or bilaterally and adjacent to the celiac trunk, cannot be removed via the left-sided approach.⁷ Therefore, if CT or PET/CT suggested LN involvement in any of these areas, the Ivor Lewis approach was used.

All LNs were grouped according to their stations at pathology. Cervical nodes were scarce in this study since we excluded patients having cervical M1 LN disease preoperatively. The accuracy of detecting the involvement of nodal stations with each modality (PET/CT and CT, independently) was determined and compared with the

pathological results. Patients with advanced pathological stages were further treated with chemotherapy (cisplatin and fluorouracil for four to six cycles; $n=24$) or chemoradiation (55–65 Gy during 6–7 weeks for radiation; $n=49$).

Statistical analysis

All patients were monitored through clinical visits or telephone interview up to a closeout date of December 1, 2014. Overall survival (OS) was measured from the date of surgery to that of death from any cause or to the time of the last follow-up. Disease-free survival (DFS) was measured from the date of surgery to that of a first relapse or death from any cause or to the time of the last visit without a developed recurrence. Survivals were estimated using the Kaplan–Meier method (log-rank test). The Cox regression model was used to evaluate independent predictors affecting the survival. Only significant variables after univariate analysis ($P<0.1$) were included in multivariate analysis. Continuous and categorical variables were analyzed by independent sample *t*-test and chi-square test, respectively. $P<0.05$ was considered as significant.

Results

A total of 210 consecutive patients with EC were evaluated for possible participation in the study. Fifty-three were excluded, including 17 with a carcinoma above the level of carina, 6 with uncontrolled cardiac ($n=4$) or pulmonary disease ($n=2$), 21 who were felt to be unresectable, and nine who were surgically operable but refused surgery. The remaining 157 patients were randomized into two groups: PET/CT group ($n=83$) and CT group ($n=74$).

All patients in the PET/CT group displayed significant FDG uptake in their primary tumors, with a mean SUV of 12.3 (range, 3.8–22.1). Twenty-seven patients were denied operation based on the PET/CT findings. The PET/CT of six patients suggested direct invasion to adjacent organs (T4), one detected a synchronous tumor at the hypopharynx, and 20 patients had distant metastatic lesions discovered in non-regional LNs (12), liver (4), lung (3), and adrenal (1). Among these lesions, eight LNs (biopsy in five and fine needle aspiration in three), two liver mass and two lung nodules were confirmed as a malignancy by histopathology, and others were all considered to be malignant on the tumor board and the patients were referred to palliative treatment.

In the CT group, 20 patients were denied surgery based on the CT findings. T4 tumors were detected in eight patients, and 12 patients had distant metastatic disease in nonregional LNs (7), liver (3), and lung (2). Among these lesions, all of

the LNs were confirmed as a malignancy by biopsy, two liver mass and one lung nodule were confirmed by fine needle aspiration, and others were all considered to be malignant on the tumor board.

The remaining 110 patients were treated with surgery with curative intent. Among them, three patients (two in the PET/CT group and one in the CT group) were identified with unresectable disease at exploration, and two patients (1.8%) in the CT group died within 1 month after surgery. One patient died of a gastric leak in the thorax, and the other suffered from a sudden death that might be caused by pulmonary embolism. Thus, 105 patients (54 patients in the PET/CT group and 51 patients in the CT group) were suitable for analysis (Table 1).

There were 86 men and 19 women, aged 37–79 years (median 59 years). Among them, 68 patients had middle EC and 37 had a lower third tumor. There were no differences in case distributions between the PET/CT and CT groups (Table 1).

Histology confirmed all primary tumors to be squamous cell carcinoma: 20 well-differentiated, 60 moderately differentiated, and 25 poorly differentiated tumors. Radical esophagectomy was performed in 51 (94.4%) patients of the PET/CT group and 47 (92.2%) patients of the CT group. A total of 69 patients underwent esophagectomy through left-sided transthoracic approach and 36 patients underwent right-sided thoracotomy, which consisted of Ivor Lewis procedure in 28 patients and Mckeown procedure in eight patients. Right-sided thoractomy tended to be more frequently used (42.6% versus 25.5%) in the PET/CT group compared to the CT group ($P=0.065$; Table 2). Pathological stage was not significantly different between the PET/CT and the CT groups ($P=0.834$ for stage IIa, $P=0.989$ for stage IIb, $P=0.118$ for stage III, and $P=0.471$ for stage IV).

After surgery, recurrent laryngeal nerve injury occurred in seven patients, but the symptom of hoarseness resolved spontaneously within a few months in all the patients. Cervical anastomotic leak occurred in three cases. There were no intrathoracic anastomotic leaks. Chylothorax occurred in one patient. As previously stated, two postoperative deaths were already reported.

Results of the nodal resection

A total of 1058 LNs at 373 nodal stations were resected in the PET/CT group versus 896 LNs at 358 stations in the CT group ($P=0.430$ and $P=0.831$, respectively). Sixty-one patients (58.1%) had pathological LN involvement. Among these, 33 patients (61.1% of total 54) in the PET/

Table 1 Characteristics of patients and results of survival analysis for predicting DFS

Characteristics	N		Univariate analysis		P-value	Multivariate analysis		P-value
	PET	CT	HR	95% CI		HR	95% CI	
Age ^a			0.998	0.972–1.024	0.842			
Sex								
Male	46	40	1.133	0.578–2.223	0.716			
Female ^b	8	11						
Tumor location								
Lower	18	19	0.954	0.574–1.587	0.857			
Middle ^b	36	32						
Tumor differentiation								
Well	11	9	0.744	0.404–1.371	0.343			
Moderate	28	32	0.87	0.456–1.663	0.674			
Poor ^b	15	10						
Therapeutic modality								
Surgery alone	14	18	1.857	0.869–3.968	0.110	1.630	0.737–3.603	0.228
Plus chemoradiation	27	22	2.207	1.177–4.138	0.014	1.852	0.949–3.614	0.071
Plus chemotherapy ^b	13	11						
Surgery								
Curative surgery	51	47	0.440	0.2–0.969	0.042	0.523	0.208–1.315	0.168
Palliative surgery ^b	3	4						
Pathological stages								
IIa	11	9	0.272	0.101–0.732	0.01	0.378	0.138–1.030	0.057
IIb	4	5	0.060	0.007–0.502	0.009	0.089	0.317–1.373	0.088
III	36	32	0.459	0.194–1.087	0.077	0.563	0.236–1.342	0.195
IV ^b	3	5						
Thoractomy								
Right thoractomy	23	13	1.280	0.777–2.107	0.332			
Left thoractomy ^b	31	38						
Preoperative imaging								
PET/CT	54		0.566	0.347–0.923	0.023	0.568	0.355–0.970	0.038
CT ^b		51						

Notes: ^aContinuous variable. ^bReference.

Abbreviations: CT, computed tomography; DFS, disease-free survival; HR, hazard ratio; PET, positron emission tomography.

CT group had 153 metastatic LNs at 89 nodal stations (two cervical, 62 mediastinal, and 25 abdominal), whereas 28 patients (54.9% of total 51) in the CT group had 90 involved LNs at 55 stations (one cervical, 39 mediastinal, and 15 abdominal) ($P=0.007$ for individual nodes and $P=0.004$ for stations). It appears that more invaded LNs and their stations were removed in the PET/CT group. The involved cervical nodes were occasionally found and removed when cervicotomy was performed for a cervical anastomosis.

The total number of LNs removed during surgery averaged 19.59 (6.91 stations) and 17.57 (7.02 stations) in the PET/CT and CT groups, respectively. Statistical analysis showed no significant difference between the groups ($P=0.088$ and $P=0.724$, respectively). However, PET/CT allowed a dissection of more positive LNs (mean 2.83 versus 1.76; $P=0.039$) as well as positive LN stations (average 1.65 versus 1.08; $P=0.042$) than CT. For node-positive patients, the percentage of invaded nodal stations that were totally removed in the

Table 2 Comparison of operative procedures between the two groups

Tumor location	Operative procedures	PET/CT group (n)	CT group (n)	Total (n)
Middle segment	Left thoracotomy	22 ^a	24	46
	Ivor Lewis procedure	11	6	17
	McKeown procedure	3	2	5
Lower segment	Left thoracotomy	9	14	23
	Ivor Lewis procedure	7	4	11
	McKeown procedure	2	1	3
Total		54	51	105

Note: ^aOne patient underwent left thoracotomy instead of right thoracic approach because of low pulmonary function.

Abbreviations: CT, computed tomography; PET, positron emission tomography.

Table 3 Comparison of results of nodal resection between the two groups

	Number of resected nodes			Number of nodal stations removed		
	PET/CT	CT	P-value	PET/CT	CT	P-value
Total LNs	19.59	17.57	0.088	6.91	7.02	0.724
Mediastinal	11.37	10.2	0.114	4.09	4.16	0.788
Abdominal	8.17	7.35	0.239	2.78	2.84	0.737
Involved LNs	2.83	1.76	0.039	1.65	1.08	0.042
Mediastinal	2.06	1.31	0.078	1.15	0.76	0.083
Abdominal	0.72	0.43	0.129	0.46	0.29	0.168
Invaded nodes ^a	21.5%	18.1%	0.148	36.3%	27.9%	0.038

Note: ^aPercentage of invaded lymph nodes among totally removed from positive lymph nodes patients.

Abbreviations: CT, computed tomography; LNs, lymph nodes; PET, positron emission tomography.

PET/CT group (36.3%) was significantly higher than that in the CT group (27.9%) ($P=0.038$; Table 3).

Assessment of nodal metastasis by imaging

On a station-based analysis, PET/CT displayed an overall sensitivity of 86.5% and an accuracy of 92.2% in the detection of the metastasis. CT showed a lower sensitivity of 67.3% ($P=0.006$) and an accuracy of 87.2% ($P=0.024$). Comparison of specificity between the two modalities (94% versus 90.8%; $P=0.139$) showed no statistically significant difference (Table 4).

Survival outcome

Up to the closeout date, five patients were lost to follow-up. The mean follow-up period was 23 months, ranging from 5 months to 51.5 months. The estimated mean OS for the PET/CT group (28.4 months; 95% CI: 24.1–32.7 months) was slightly higher than that for the CT group (25.7 months; 95% CI: 21.7–29.6 months) but did not achieve statistical significance ($P=0.38$). However, the estimated mean DFS for the PET/CT group (27.1 months; 95% CI: 21.9–32.3 months) was markedly higher than that for the CT group (18.9 months; 95% CI: 14.7–23.1 months) ($P=0.019$). The

Table 4 Comparison of PET/CT and CT by different methods

	PET/CT	CT	P-value
Total resected LNs, n	1,058	896	0.430
True positive, n	153	90	0.007
Sensitivity	86.5%	76.3%	0.006
Accuracy	92.2%	87.2%	0.024
Specificity	94.0%	90.8%	0.139

Abbreviations: CT, computed tomography; LNs, lymph nodes; PET, positron emission tomography.

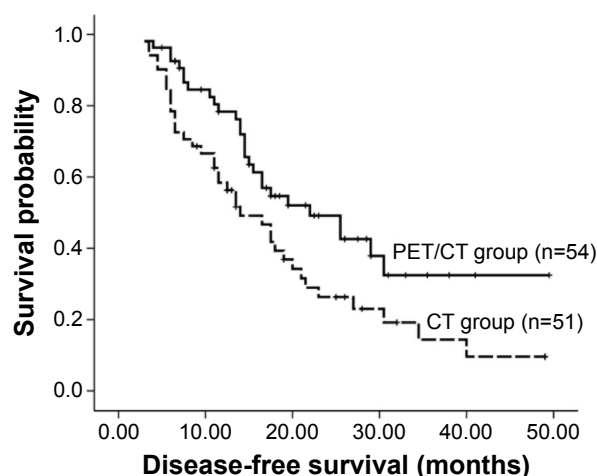


Figure 2 Kaplan-Meier curves of DFS for the two groups (PET/CT and CT group). **Abbreviations:** CT, computed tomography; PET, positron emission tomography; DFS, disease-free survival.

cumulative 1-year, 2-year, and 3-year DFS rates were 78.3%, 49.2%, and 32.5% in the PET/CT group versus 62.6%, 26.3%, and 14.4% in the CT group, respectively (Figure 2). Subgroup analysis of node-positive patients indicates that the PET/CT group again demonstrates longer mean DFS (22.5 months; 95% CI: 17.4–27.6 months versus 13.5 months; 95% CI: 9.6–17.5 months) ($P=0.02$; Figure 3).

Among the factors influencing DFS, pathological staging, therapeutic modality, operative features (curative or palliative), and preoperative imaging (the grouping factor) showed P -values <0.1 on univariate analysis (Table 1). The multivariate analysis with Cox regression model revealed that preoperative imaging modality was the only independent significant predictor for DFS.

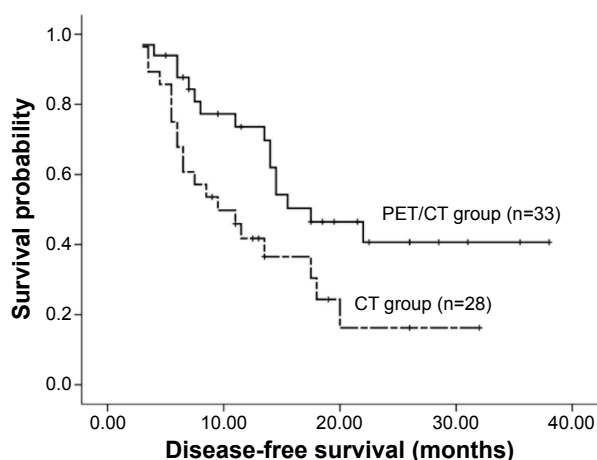


Figure 3 Kaplan-Meier curves of DFS for the subgroup of positive lymph nodes patients (PET/CT and CT group). **Abbreviations:** CT, computed tomography; PET, positron emission tomography; DFS, disease-free survival.

Discussion

Lymphatic metastasis is relatively frequent in EC, especially once the tumor involves the submucosal layer, and evaluation of nodal status is quite important before surgery.^{12,18} CT suggests clinical nodal status based only on size criteria, and, as a result, the accuracy is limited.^{3,15,20,21} FDG-PET detects alterations in tissue metabolism.²² Therefore, FDG-PET appears to be more accurate than CT, especially when PET images are fused with CT images.^{23–26}

This study confirms both the greater sensitivity and accuracy of PET/CT than CT in detecting LN metastasis in patients with EC. The specificity of the two modalities was similar. Several other reports have also confirmed the advantage of PET/CT in the detection of LN metastasis for patients with EC.^{13–15,18,19,27,28} One prospective study revealed that the sensitivity, specificity, and accuracy of PET/CT were 76.19%, 95.93%, and 93.06%, respectively, whereas those of CT were 33.33%, 94.31%, and 85.42%, respectively (*P*-values: 0.0117, 0.7539, and 0.0266, respectively).²⁹ Furthermore, it would appear from our results that the improved detection of nodal metastasis with PET/CT resulted in our surgeons removing more involved nodal groups in the PET/CT group.

We performed the Ivor Lewis procedure, instead of left thoracotomy, only when imaging findings suggested the presence of LNs that would not be removable by the left-sided approach. Owing to the additional detection of metastatic nodes within the right mediastinum, 42.6% of the patients in the PET/CT group versus 25.5% of the patients in the CT group underwent the right-sided operation.

The increased number of involved LNs and LN stations dissected in the PET/CT group may have important therapeutic implications. The DFS was significantly improved in the PET/CT group. This may have resulted from the fact that the PET/CT-directed operation increased the likelihood of proper staging and thereby directed appropriate postoperative therapy more accurately.^{28,30,31} Alternatively, the improved DFS may have resulted from more complete excision of involved LNs in the PET/CT group. In >40% of cases with EC, the first recurrence after surgery occurs within the regional LNs,³² and consequently, complete nodal resection may affect postoperative survival. Adjuvant therapy and pathological staging can also pose an impact on survival. However, as demonstrated in Table 1, there were no differences in case distributions between the PET/CT and CT group. It is reasonable to conclude that the DFS advantage in the PET/CT group was due to a relatively complete resection guided by PET/CT imaging.

Basing more extensive (right-sided) resection of LNs upon preoperative PET/CT imaging was an independent prognostic

factor in DFS. Therefore, it is quite likely that the improved DFS observed in the PET/CT group was due to the increase in the removal of positive LNs. Further subgroup analysis of N+ patients also confirmed this point (Figure 3).

It is generally acknowledged that the increased number of invaded LNs indicates a poorer prognosis.³² However, our data interestingly revealed that patients with more invaded nodes through PET/CT-based nodal resection had an equivalent OS and improved DFS.

It may appear possibly on the first glance that our study shows improved LN yield and DFS in the PET/CT group only by virtue of the fact that the PET/CT group had a greater percentage of patients undergoing right- versus left-sided approaches. In other words, one might argue that perhaps all we have demonstrated is that the Ivor Lewis approach is superior from an oncological point of view to the left-sided thoracotomy alone approach. However, the results of the multivariate analysis of factors influencing DFS, which identified imaging modality and not thoracotomy (transthoracic approach; Table 1) as a significant factor, do not support this line of reasoning. Additionally, the left-sided thoracotomy alone approach is both simpler to carry out (no repositioning) and (we believe) less morbid. Therefore, we believe that it is ideal to reserve the right-sided approach and more extensive lymphadenectomy for patients in whom this is indicated by imaging-demonstrated nodal involvement. Our low complication and mortality rates bear out the reasonableness of this approach.

Conclusion

We confirm the increased accuracy of PET/CT versus CT for LN involvement in EC. Furthermore, we find that PET/CT is useful in determining those patients who will benefit from a right-sided approach with more extensive LN resection. Patients who underwent preoperative PET/CT evaluation and consequent image-directed surgical approach had an improved DFS versus those having CT alone, while still allowing many patients to undergo a less morbid approach with a less radical lymphadenectomy. Surgery directed by PET/CT, as described here, appears to represent a reasonable compromise between routine, extensive LN dissection (eg, three-field lymphadenectomy) and minimally invasive surgical procedures with lesser lymphadenectomy (eg, transhiatal approach).

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Disclosure

The authors have no conflicts of interest in this work.

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