Does [18F] fluorodeoxyglucose–positron emission tomography/computed tomography have a role in cervical nodal staging for esophageal squamous cell carcinoma?

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Bin Li, MD,[a,b] Nan Li, MD,[b,c] Shuoyan Liu, MD,[d] Yin Li, MD,[e] Bin Qian, MD,[f] Yawei Zhang, MD,[a,b] Hao He, MD,[d] Xiankai Chen, MD,[e] Yihua Sun, MD,[a,b] Jiaqing Xiang, MD,[a,b] Hong Hu, MD,[a,b] and Haiquan Chen, MD[a,b]

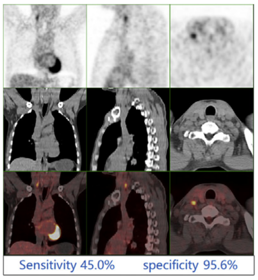
ABSTRACT

Objective: Accurate nodal staging is crucial for esophageal cancer. A prospective study was performed to assess the value of [18F] fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) for diagnosing cervical lymph node metastasis (LNM) of esophageal squamous cell carcinoma.

Methods: From June 2018 to November 2018, 110 patients with resectable esophageal cancer were prospectively enrolled. Esophagectomy with 3-field lymphadenectomy was performed after FDG-PET/CT scanning. The primary end point was cervical LNM determined via postoperative histologic examination. The sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and accuracy (AC) of FDG-PET/CT for the assessment of LNM were determined using histologic results as reference standards.

Results: Positive lymph nodes as determined via FDG-PET/CT were detected in 61 patients (55.5%), of whom 13 (11.8%) had positive cervical lymph nodes. After surgery, 59 patients (53.6%) exhibited pathologic LNM, of whom 20 (18.2%) had cervical LNM. SE, SP, PPV, NPV, and AC were 65.6%, 61.2%, 67.8%, 58.8%, and 63.6%, respectively, with regards to diagnosing overall LNM, and were 45.0%, 95.6%, 69.2%, 88.7%, and 86.4%, respectively, for diagnosing cervical LNM. Of the 110 patients, 90 underwent both FDG-PET/CT scanning and ultrasonography in the neck, and there were no significant differences in SE, SP, PPV, NPV, or AC with respect to cervical LNM diagnosis between FDG-PET/CT and ultrasonography.

Conclusions: For cervical LNM of esophageal squamous cell carcinoma, FDG-PET/CT scanning exhibited high specificity but low sensitivity, suggesting that it is of limited value for this purpose. (J Thorac Cardiovasc Surg 2020;160:544-50)



FDG-PET/CT in diagnosing cervical lymph nodes metastases of esophageal cancer.

CENTRAL MESSAGE

FDG-PET/CT scanning exhibited high specificity but low sensitivity in diagnosing cervical lymph node metastases of esophageal cancer, indicating its limited value for this purpose.

PERSPECTIVE

This prospective study evaluated the role of FDG-PET/CT in diagnosing cervical LNM of esophageal cancer using pathologic LNM as standard. The results indicated that FDG-PET/CT was of limited value in diagnosing cervical LNM for esophageal squamous cell carcinoma.

See Commentaries on pages 551 and 553.

Esophageal cancer is notorious for early and distant lymph node metastasis (LNM). Primary surgery can be applied to patients at an early stage without LNM. However, if LNM is detected, extended lymphadenectomy and/or neoadjuvant chemo/radiotherapy is usually indicated.[1-3] Of note, thoracic–abdominal 2-field lymphadenectomy is widely

From the Departments of [a]Thoracic Surgery and [c]Nuclear Medicine, Fudan University Shanghai Cancer Center, Shanghai; [b]Department of Oncology, Shanghai Medical College, Fudan University, Shanghai; [d]Department of Thoracic Surgery, Fujian Medical University Cancer Hospital, Fuzhou; [e]Department of Thoracic Surgery, National Cancer Center/Cancer Hospital, Beijing; and [f]Department of Thoracic Surgery, Jiangdu People's Hospital of Yangzhou, Jiangdu, China.

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Drs B. Li, N. Li, Liu, Y. Li, and Qian contributed equally to this article.

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Address for reprints: Haiquan Chen, MD or Hong Hu, MD, 270 Dong'an Rd, Shanghai 20032, China (E-mail: hqchen1@yahoo.com or huhong0997@163.com).

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Abbreviations and Acronyms

3-FLD = 3-field lymphadenectomy
CI = confidence interval
CT = computed tomography
FDG = fluorodeoxyglucose
LNM = lymph node metastasis
PET = positron emission tomography
TNM = Tumor–Node–Metastasis

Scanning this QR code will take you to the article title page to access supplementary information.

accepted for esophageal surgery; however, cervical LNM is common, with an incidence of approximately 20%.[4,5] Thus, accurate nodal staging is crucial for patients with esophageal cancer.

Recent studies showed [18F] fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) scanning was useful for the initial staging of esophageal carcinoma, particularly for distant metastases.[6-8] However, the cost of the examination is expensive, and the efficacy of FDG-PET/CT scanning for evaluating LNM of esophageal cancer, specifically for cervical LNM, has not been thoroughly investigated. Based on the theoretical possibility that treatment decisions could be determined based on FDG-PET/CT scanning, a multicenter prospective study was performed to evaluate the potential role of FDG-PET/CT scanning in cervical nodal staging of esophageal squamous cell carcinoma.

PATIENTS AND METHODS

From June 2018 to November 2018, 4 medical centers in China were involved in this prospective clinical research, and each routinely performs more than 100 esophagectomy procedures per year. The study protocol was individually approved by the institutional review boards of all 4 participating centers. All patients enrolled provided written informed consent. All surgeries were performed by senior thoracic surgeons who had performed at least 100 esophagectomies with cervical–thoracic–abdominal 3-field lymphadenectomy (3-FLD). Senior surgeons in the 4 participating centers (C.-H.Q., L.-S.Y., L.Y., and Q.B.) maintained the standardization of the operation following protocol. The study was registered in Clinicaltrial.gov (NCT03244566). All authors had access to the study data and reviewed and approved the final manuscript.

The preoperative workup for assessing patient operability entailed a panel of oncologic evaluations, including histologic confirmation of squamous cell carcinoma of the thoracic esophagus via upper gastrointestinal endoscopy, CT of the chest, and ultrasonography of the neck. Pulmonary and cardiac function tests were also performed.

The inclusion criteria were age <80 years, resectable esophageal cancer in the thoracic esophagus (20 cm to incisor and 3 cm superior to the cardia), and no evidence of distant metastasis (including unresectable celiac lymph nodes, and enlarged lymph nodes with the diameter of short axis greater than 1.5 cm by CT scan). Because cervical lymph node dissection was performed in the trial, patients with resectable cervical lymph nodes were also included. The exclusion criteria were a history of other malignant diseases, previous gastric or esophageal surgery, severe major organ dysfunction, and a Karnofsky index of <80. Currently, surgery plus postoperative chemo/radiotherapy is still the mainstream treatment strategy for advanced esophageal cancer in China. Moreover, this study was to evaluate the role of PET/CT in guiding treatment decision-making. Thus, patients who received neoadjuvant chemo/radiotherapy were also excluded.

FDG-PET/CT Procedure

Patients eligible for surgery after routine preoperative workup underwent FDG-PET/CT scanning. Imaging acquisitions at the Fudan University Shanghai Cancer Center were performed via the protocol described to follow, and very similar protocols were used at the other 3 institutions that participated in the current study. Patients fasted for at least 6 hours before tracer administration. Serum glucose levels were routinely checked and confirmed to be <10 mmol/L. The standard dosage of intravenous FDG administration was 7.4 MBq/kg body weight. A Siemens Biograph 16HR PET/CT scanner (Knoxville, Tenn) with a transaxial intrinsic spatial resolution of 4 mm (full width at half maximum) and 16.2-cm axial field width was used for image scanning.

PET/CT data acquisition began with low-dose CT from the inguinal region to the head, with 120 kV, 80- to 250-mA automatic modulation, a pitch of 3.6, and a rotation time of 0.5 seconds, followed by PET emission scanning in 3-dimensional mode with 2 to 3 minutes per bed position. PET data were reconstructed using the ordered subset expectation maximization technique selecting 8 subsets and 4 iterations, a 168×168 matrix. CT data were used for attenuation correction of the PET images, and coregistered images were displayed on a workstation. Analysis of FDG-PET/CT images was performed using a multimodality computer platform (Syngo; Siemens). The maximum standardized uptake value of the primary tumor and metastasis were measured via a region-of-interest technique and calculated using dedicated software in accordance with standard formulas. All PET/CT images were evaluated by 2 experienced nuclear medicine physicians, and the diagnoses were made by consensus. Nodes were classified as "involved" via PET/CT if the nodes were implicated via CT and the relevant component exhibited FDG uptake that was greater than background.

Esophagectomy and Lymphadenectomy

Esophagectomies were scheduled based on tumor location; specifically, with reference to the McKeown procedure with cervical anastomoses for upper thoracic tumors and the Ivor–Lewis procedure with thoracic anastomoses for middle and lower thoracic tumors. With regards to the surgical techniques used, the surgeons in charge decided between open and minimally invasive esophagectomy. All surgeries were performed within 2 weeks after whole-body PET/CT scanning.

All lymph nodes in the lower neck, chest, and upper abdomen were resected via 3-FLD. Cervical lymphadenectomies were performed via a collar incision as previously described.[9] Lymph node sites were classified based on the Japanese Classification of Esophageal Cancer, 11th edition.[10] In cases of cervical lymphadenectomy, cervical paraesophageal lymph nodes (no. 101, including lymph nodes along the recurrent nerve in the neck) were resected, whereas deep cervical lymph nodes (no. 102) and supraclavicular nodes (no. 104) were resected together (Video 1). Total mediastinal lymphadenectomy was performed and the lymph nodes included the upper paraesophageal nodes (no. 105), thoracic paratracheal lymph nodes (no. 106), subcarinal nodes (no. 107), middle paraesophageal nodes (no. 108), main bronchus lymph nodes (no. 109), lower paraesophageal nodes

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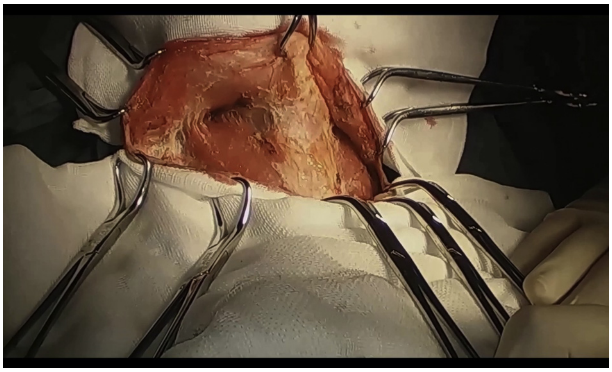

VIDEO 1. Cervical lymph nodes dissection by Dr Jiaqing Xiang. Video available at: https://www.jtcvs.org/article/S0022-5223(19)33960-1/fulltext.

(no. 110), diaphragmatic nodes (no. 111), and posterior mediastinal lymph nodes (no. 112). The upper abdominal lymph nodes included the paracardial, lesser curvature, greater curvature, left gastric, common hepatic, and celiac lymph nodes. Lymph nodes were labeled for pathologic examination according to anatomic locations and submitted entirely for staining. It was recorded if the actual number of nodes submitted could not be ascertained as the pieces of tissue submitted may represent multiple fragments of a single node. All patients were staged according to the Tumor-Node-Metastasis (TNM) classification in the American Joint Committee for Cancer Staging Manual, 8th edition.

Outcomes

The primary end point was cervical LNM determined via postoperative histologic examination. Secondary end points were mediastinal and abdominal LNM determined via postoperative histologic examination.

Cervical LNM in this study referred to lymphatic metastases of cervical paraesophageal lymph nodes (no. 101), deep cervical lymph nodes (no. 102), and/or supraclavicular nodes (no. 104). LNM along the bilateral recurrent nerve (from neck to the chest) referred to positive cervical paraesophageal lymph nodes (no. 101) and thoracic paratracheal lymph nodes (no. 106).

Statistical Analysis

The minimum sample size required for sensitivity and specificity testing was calculated using the "Tests for One-Sample Sensitivity and Specificity" component of PASS software (PASS 15; NCSS, LLC, Kaysville, Utah). The predetermined (assumed) incidence of cervical LNM was 20% based on published studies.[4] Null sensitivity and specificity were respectively set at 50% and 80%,[11-13] and alternative sensitivity and specificity values were respectively set at 85% and 95%. A total of 110 patients was required to achieve a power of 90% and an alpha value of 2.5%. Prescribed power calculation was done to ensure the reported data had a sufficiently narrow 95% confidence interval (CI).

The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FDG-PET/CT for the assessment of LNM were determined using histologic results as reference standards. FDG-PET/CT and ultrasound in the neck were also compared to assess the efficacy of the 2 examinations in diagnosing cervical LNM in terms of sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. The diagnosis of cervical LNM by ultrasound was made by the shape of the lymph nodes (long axis, short axis, and short-to-long axis ratio), and the physicians' experience. No fine-needle aspiration was performed during ultrasound examination, as all patients in this study were scheduled to have radical cervical lymph nodes dissection.

The data were collated as numbers and percentages, means and standard deviations, and medians and interquartile ranges. The χ^2 test or Fisher exact test was used to compare categorical data. All statistical analyses were performed using the SPSS statistical package (version 16.0, Chicago, Ill). Two-sided P values < .05 were considered statistically significant.

RESULTS

A total of 110 patients were scheduled to undergo esophagectomy with 3-FLD under protocol (Figure 1). Patient characteristics are shown in Table 1. The mean patient age was 67 ± 7 years, and 62 of 110 patients (56.4%) had the tumor located in the middle thoracic esophagus. The primary cancer exhibited FDG uptake in 107 of 110 patients (97.3%), and the mean tumor-maximum standardized uptake value was 9.9 ± 6.3. Potential distant metastasis was identified in 4 of 110 patients (3.6%). One lung metastasis was confirmed to be benign after surgery. The other 3 of these 4 patients had potential but unconfirmed metastases due to difficult biopsy, one in the left lung, one in a rib, and one in the eighth thoracic vertebra. Postoperative data are shown in Table 2. Of the 110 patients, 101 (91.8%) had open esophagectomy. There were 108 patients (98.2%) who had squamous cell carcinoma, and 2 (1.2%) who had adenosquamous carcinoma. All patients

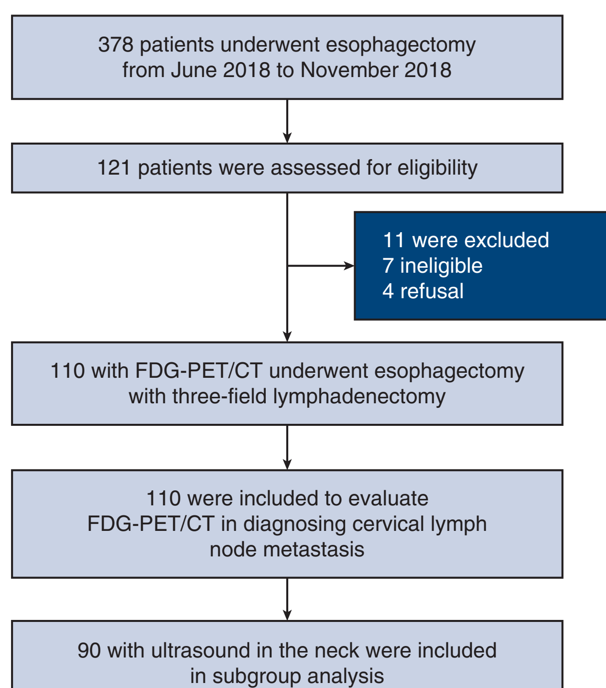

FIGURE 1. Flow diagram of the study. *FDG-PET/CT*, Fluorodeoxyglucose–positron emission tomography/computed tomography.

TABLE 1. Patient characteristics (n = 110)

	n (%, 95% CI)
Age, y*	63 ± 7
Sex	
Male	88 (80.0, 71.3-87.0)
Female	22 (20.0, 13.0-28.7)
Body mass index*	23.1 ± 2.9
Hypertension	30 (27.2, 19.2-36.6)
Diabetes	1 (0.9%, 0.0-0.05)
Tumor location	
Upper	9 (8.2, 3.8-15.0)
Middle	62 (56.4, 46.6-65.8)
Lower	39 (35.5, 26.6-45.1)
Tumor, SUV_{max}*	9.9 ± 6.3
Cervical lymph nodes, SUV_{max}*	4.6 ± 2.4
Mediastinal lymph nodes, SUV_{max}*	4.6 ± 1.9
Abdominal lymph nodes, SUV_{max}*	5.2 ± 2.6
LNM diagnosed by FDG-PET/CT	61 (55.5, 45.7-64.9)
Neck	13 (11.8, 6.4-19.4)
Mediastinum	47 (42.7, 33.3-52.5)
Upper abdomen	18 (16.4, 10.0-24.6)
Specific region	
Lymph nodes along recurrent nerve (no. 101 and 106)	40 (36.4, 27.4-46.1)
Supraclavicular lymph nodes (no. 102 and 104)	10 (9.1, 4,4-16.1)

CI, Confidence interval; SUV_{max}, maximum standardized uptake value; *LNM*, lymph node metastases; *FDG-PET/CT*, fluorodeoxyglucose–positron emission tomography/computed tomography. *Data are shown as mean ± standard error.

TABLE 2. Postoperative complications and pathologic data (n = 110)

	n (%, 95% CI)
Surgery type	
Open	101 (91.8, 85.0-96.2)
Minimally invasive	9 (8.2, 3.8-15.0)
Hospital stay, d*	7 (6-11)
Anastomotic leak	4 (3.6, 1.0-9.0)
Reoperation	4 (3.6, 1.0-9.0)
Pathologic type	
Squamous cell carcinoma	108 (98.2, 93.6-99.8)
Adenosquamous carcinoma	2 (1.8, 0.2-6.4)
Number of lymph nodes resected*	39 (31-46)
Number of cervical lymph nodes resected*	15 (10-20)
No. 101 nodes (left)	2 (1-4)
No. 101 nodes (right)	3 (2-4)
No. 102/104 nodes (left)	6 (4-10)
No. 102/104 nodes (right)	6 (3-9)
Pathologic LNM	59 (53.6, 43.9-63.2)
Neck	20 (18.2, 11.5-26.7)
Mediastinum	40 (36.4, 27.4-46.1)
Upper abdomen	34 (30.9, 22.4-40.4)
Specific region	
Lymph nodes along recurrent nerve (no. 101 and 106)	29 (26.4, 18.4-35.6)
Supraclavicular lymph nodes (no. 102 and 104)	10 (9.1, 4.4-16.1)
Pathologic T category	
T1	39 (35.5, 26.6-45.1)
T2	16 (14.5, 8.5-22.5)
T3	54 (49.1, 39.4-58.8)
T4	1 (0.9, 0.0-5.0)
Pathologic N category	
N0	51 (46.4, 36.8-56.1)
N1	34 (30.9, 22.4-40.4)
N2	16 (14.5, 8.5-22.5)
N3	9 (8.2, 3.8-15.0)

CI, Confidence interval; *LNM*, lymph node metastases. *Data are shown as median (interquartile range).

underwent esophagectomy with 3-FLD, and the median number of lymph nodes resected was 39.

FDG-PET/CT Scanning

PET/CT scanning indicated positive lymph nodes in 61 of 110 patients (55.5%). Based on PET/CT scanning, 13 of 10 patients (11.8%) had positive cervical lymph nodes, and 40 of 110 (36.4%) had positive nodes along the bilateral cervical (no. 101) and thoracic recurrent nerve (no. 106). A total of 59 of 110 patients (53.6%) exhibited LNM after surgery. Based on pathologic examination, 20 of 110 patients (18.2%) had metastasis in the neck, and 29 of 110 (26.4%) had positive nodes along the bilateral cervical and thoracic recurrent nerve.

With regards to diagnosing overall LNM, the parameter values associated with PET/CT were sensitivity 65.6%, specificity 61.2%, positive predictive value 67.8%, negative predictive value 58.8%, and accuracy 63.6%. With regards to diagnosing cervical LNM, the parameter values associated with PET/CT were sensitivity 45.0%, specificity 95.6%, positive predictive value 69.2%, negative predictive value 88.7%, and accuracy 86.4%. With regards to diagnosing LNM along the bilateral cervical and thoracic recurrent nerve, the parameter values associated with PET/CT were sensitivity 72.6%, specificity 76.5%, positive predictive value 52.5%, negative predictive value 88.6%, and accuracy 75.5% (Table 3).

Comparison of FDG-PET/CT and Ultrasound

Of the 110 patients in the current study, 90 underwent ultrasonographic examination of the neck. In comparisons of ultrasonography and FDG-PET/CT scanning for diagnosing LNM, there were no significant differences in sensitivity, specificity, positive predictive value, negative predictive value, or accuracy (Table 4). Of the 90 patients, 7 of 8 (87.5%) had cervical LNM when both FDG-PET/CT and

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TABLE 3. Overview of FDG-PET/CT in diagnosing LNM (n = 110)

	Sensitivity % (n) [95% CI]	Specificity % (n) [95% CI]	Positive predictive value % (n) [95% CI]	Negative predictive value % (n) [95% CI]	Accuracy % (n) [95% CI]
Cervical LNM	45.0 (9/20) [23.1-68.5]	95.6 (86/90) [89.0-98.8]	69.2 (9/13) [38.6-90.1]	88.7 (86/97) [80.6-94.2]	86.4 (95/110) [78.5-92.2]
Mediastinal LNM	60.0 (24/40) [43.3-75.1]	67.1 (47/70) [54.9-77.9]	51.1 (24/47) [36.1-65.9]	74.6 (47/63) [62.1-84.7]	64.5 (71/110) [54.9-73.4]
Upper abdominal LNM	38.2 (13/34) [22.2-56.4]	93.4 (71/76) [85.3-97.8]	72.2 (13/18) [46.5-90.3]	77.2 (71/92) [67.2-85.3]	76.4 (84/110) [67.3-83.9]
Overall LNM	67.8 (40/59) [54.4-79.4]	58.8 (30/51) [44.2-72.4]	65.6 (40/61) [52.3-77.3]	61.2 (30/49) [46.2-74.8]	63.6 (70/110) [53.9-72.6]
Specific region					
LNM along the recurrent nerve (no. 101 and 106)	72.4 (21/29) [52.8-87.3]	76.5 (62/81) [65.8-85.2]	52.5 (21/40) [36.1-68.5]	88.6 (62/70) [78.7-94.9]	75.5 (83/110) [66.3-83.2]
Supraclavicular LNM (no. 102 and 104)	40.0 (4/10) [12.2-73.8]	94.0 (94/100) [87.4-97.8]	40.0 (4/10) [12.2-73.8]	94.0 (94/100) [87.4-97.8]	89.1 (98/110) [81.7-94.2]

CI, Confidence interval; *LNM*, lymph node metastases.

ultrasonography were positive in the neck, compared with 8 of 70 (11.4%) when both FDG-PET/CT and ultrasonography were negative in the neck (Table 5). The sensitivity and specificity were 38.9% (7/18; 95% CI, 17.2%-64.3%) and 98.6% (71/72; 95% CI, 92.5%-100.0%) when FDG-PET/CT and ultrasonography were positive in the neck and 55.6% (10/18; 95% CI, 30.8%-78.5%) and 86.1% (62/72; 95% CI, 75.9%-93.1%) when FDG-PET/CT and ultrasonography were negative.

In patients with suspicious cervical LNM by ultrasonography, the sensitivity and specificity of FDG-PET/CT in diagnosing LNM were 77.8% (7/9; 95% CI, 40.0%-97.2%) and 85.7% (6/7; 95% CI, 42.1%-99.6%), respectively. In those without suspicious cervical LNM by ultrasonography, the sensitivity and specificity were 11.1% (1/9; 95% CI, 0.3%-48.2%) and 95.4% (62/65; 95% CI, 87.1%-99.0%), respectively.

DISCUSSION

Accurate disease staging of esophageal cancer is important for the determination of treatment, particularly with regards to the extent of lymphadenectomy and the application of neoadjuvant therapy. Unforeseen cervical LNM is common after traditional pretreatment examinations.[4] In recent years, FDG-PET/CT has been used as a component of the initial routine evaluation of patients with esophageal cancer to detect the presence of metastasis, particularly for distant metastases. In the Z0060 trial conducted by the American College of Surgeons Oncology Group, 18 of 189 patients with esophageal cancer were upstaged from M0 to M1b after PET.[8] Of the 18 M1b patients in that trial, 16 had hilar, cervical, supraclavicular, or other lymphadenopathies that met the criteria for M1b disease.

In the present study, FDG-PET/CT scanning exhibited low sensitivity and low specificity in diagnosing lymphatic metastases. With regards to cervical LNM, although FDG-PET/CT exhibited high specificity of 95.6%, sensitivity was only 45.0%. Of the 13 patients who exhibited potentially cervical LNM, positive lymph nodes in the neck were only detected in 9 via postoperative examination. Accuracy was greatest in the neck, followed by the upper abdomen and chest. One major reason is that detection via PET/CT is associated with the size and metastatic foci of the lymph nodes. Kato and colleauges[14] reported that the smallest LNM that was detected by FDG-PET imaging was 6 mm. Lymph nodes are always small, however, particularly in the neck. Of the 110 patients in the study, 97 exhibited no FDG uptake in the neck lymph nodes. Another reason is the presence of inflammation in the tissue, leading

TABLE 4. Comparison of FDG-PET/CT and cervical ultrasonography in diagnosing cervical LNM (n = 90)

	FDG-PET/CT % (n) [95% CI]	Ultrasound % (n) [95% CI]	*P* value
Sensitivity	44.4 (8/18) [21.5-69.2]	50.0 (9/18) [26.0-74.0]	.738
Specificity	94.4 (68/72) [86.4-98.5]	90.3 (65/72) [81.0-96.0]	.347
Positive predictive value	66.7 (8/12) [34.9-90.1]	56.3 (9/16) [29.9-80.2]	.705
Negative predictive value	87.2 (68/78) [77.7-93.7]	87.8 (65/74) [78.2-94.3]	.902
Accuracy	84.4 (76/90) [75.3-91.2]	82.2 (74/90) [72.7-89.4]	.689

FDG-PET/CT, Fluorodeoxyglucose–positron emission tomography/computed tomography; *CI*, confidence interval.

TABLE 5. Cervical lymph node metastasis based on FDG-PET/CT and ultrasound (n = 90)

		Metastasis	
		Yes (%, 95% CI)	No (%, 95% CI)
PET/CT (positive)	Ultrasound (positive)	7 (87.5, 47.3-99.7)	1 (12.5, 0.3-52.7)
	Ultrasound (negative)	1 (25.0, 0.6-80.6)	3 (75.0, 19.4-99.4)
PET/CT (negative)	Ultrasound (positive)	2 (25.0, 3.2-65.1)	6 (75.0, 34.9-96.8)
	Ultrasound (negative)	8 (11.4, 5.1-21.3)	62 (88.6, 78.7-94.9)

CI, Confidence interval; *PET/CT*, positron emission tomography/computed tomography.

to a false-positive diagnosis via PET/CT, which is much more common in the hilar and subcarinal regions. The present study suggests that due to its low sensitivity, the results of PET/CT scanning should be interpreted carefully when there is no abnormal FDG uptake by lymph node.

External ultrasonography is the modality that has traditionally been used to diagnose LNM in the neck—mostly based on the shape of lymph nodes—but the accuracy of the method is operator-dependent, with reported variating ranging from 72% to 87.6%.[15-17] In conjunction with the increasing use of FDG-PET/CT scanning, several studies have indicated that cervical ultrasonography has no additional value over negative FDG-PET/CT scanning for diagnosing cervical LNM. In 1 report, of 133 patients with negative FDG-PET/CT results 12 had suspicious nodes on cervical ultrasonography, but the nodes were confirmed to be benign in all 12 patients.[18] Notably, however, fine-needle aspiration was used to confirm metastasis in that study. In the current trial, all patients underwent radical 3-FLD. Ninety patients had both FDG-PET/CT and cervical ultrasonography, and only 4 of these patients (4.4%) had negative ultrasonography but positive FDG-PET/CT. Of these 4 patients, only 1 had metastasis. Given the difference in cost between the 2 examination modalities (eg, 7000 RMB for PET/CT and 100 RMB for ultrasonography at the Shanghai Cancer Center), ultrasonography remains our modality of choice for detecting cervical LNM, and 3-FLD is recommended for those with suspicious cervical LNM.

The results of the present study using FDG-PET/CT scanning are consistent with those of previous studies. In previous studies the sensitivity of FDG-PET for diagnosing locoregional LNM ranges from 30% to 82%, its specificity ranges from 60% to 97%, and its accuracy ranges from 70% to 86%.[11-13] Clinical initial staging using PET/CT scanning should be interpreted carefully and combined with other examinations. PET/CT is only of limited value when the primary esophageal cancer lesions exhibit low FDG uptake due to low sensitivity.[19] Moreover, in patients

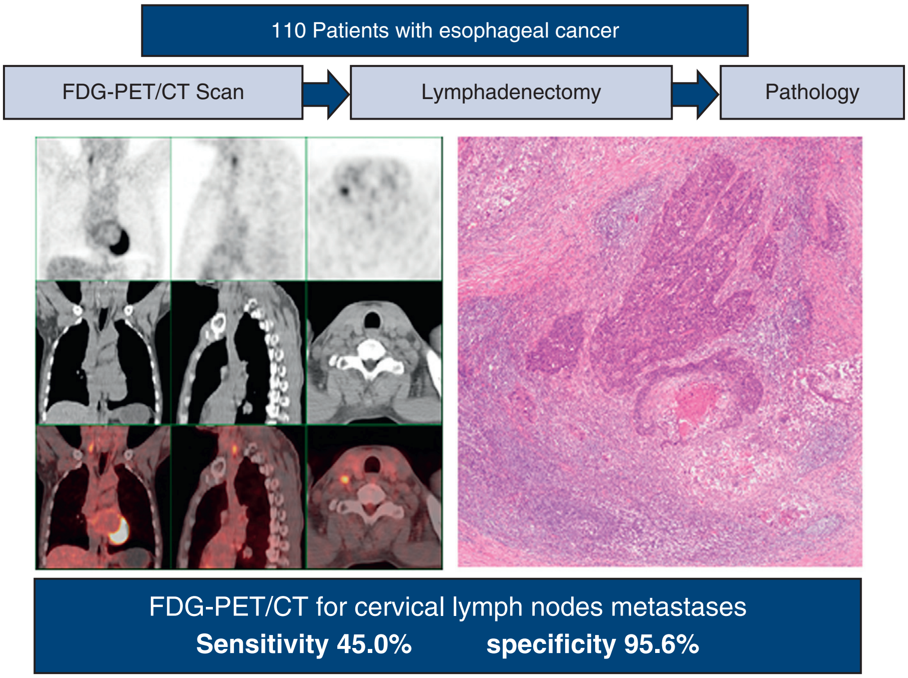

FIGURE 2. FDG-PET/CT in diagnosing cervical lymph nodes metastases of esophageal cancer. *FDG-PET/CT*, Fluorodeoxyglucose–positron emission tomography/computed tomography.

with early-stage esophageal cancer determined when endoscopy and biopsy indicate cTis and cT1, FDG-PET/CT is not useful for clinical TNM staging because regional nodal metastases are reportedly uncommon and distant metastases are rare.[20] It has been reported that PET using new imaging probes exhibited advantages over PET using FDG in the assessment of metastatic lymph nodes, but further studies are needed.[21]

One of the main strengths of the current study is that all patients underwent 3-FLD with all lymph nodes examined, rather than fine-needle aspiration confirmation. However, the study has several limitations. First, all patients included in the trial were potential candidates for surgical resection as determined via routine CT and ultrasound examinations. FDG-PET/CT sensitivity and accuracy may therefore have been underestimated. Patients with advanced disease who required neoadjuvant therapy were excluded, thus extrapolation of the results of the study to such patients is not warranted. Second, there is currently no established consensus on the criteria to use to diagnose tumor positive lymph nodes via FDG-PET/CT imaging. Diagnosis of cervical LNM in the present study was based on FDG-FDG uptake being greater than background values. The results may have been different using different diagnostic criteria. Moreover, clinical TNM staging was not assessed, as endoscopy ultrasonography was not routinely performed in this study, and FDG-PET/CT could perform differently in different clinical stages of the disease.

In conclusion, FDG-PET/CT scanning exhibited low specificity and sensitivity in the diagnosing LNM of esophageal squamous cell carcinoma. Although FDG-PET/CT exhibited high specificity in diagnosing cervical LNM, sensitivity was low, suggesting that it is of limited value for this purpose. A graphical depiction of methods, results, and implications of this study is shown in Figure 2.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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