

ORIGINAL ARTICLE

F18-fluorodeoxyglucose-positron emission tomography and computed tomography is not accurate in preoperative staging of gastric cancer

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Purpose: To investigate the clinical benefits of F18-fluorodeoxyglucose-positron emission tomography and computed tomography (¹⁸F-FDG-PET/CT) over multi-detector row CT (MDCT) in preoperative staging of gastric cancer. **Methods:** FDG-PET/CT and MDCT were performed on 78 patients with gastric cancer pathologically diagnosed by endoscopy. The accuracy of radiologic staging retrospectively was compared to pathologic result after curative resection. **Results:** Primary tumors were detected in 51 (65.4%) patients with ¹⁸F-FDG-PET/CT, and 47 (60.3%) patients with MDCT. Regarding detection of lymph node metastasis, the sensitivity of FDG-PET/CT was 51.5% with an accuracy of 71.8%, whereas those of MDCT were 69.7% and 69.2%, respectively. The sensitivity of ¹⁸F-FDG-PET/CT for a primary tumor with signet ring cell carcinoma was lower than that of ¹⁸F-FDG-PET/CT for a primary tumor with non-signet ring cell carcinoma (35.3% vs. 73.8%, $P < 0.01$). **Conclusion:** Due to its low sensitivity, ¹⁸F-FDG-PET/CT alone shows no definite clinical benefit for prediction of lymph node metastasis in preoperative staging of gastric cancer.

Key Words: Gastric cancer, ¹⁸F-FDG-PET/CT, MDCT, Preoperative staging

INTRODUCTION

Gastric cancer remains the second most common cancer diagnosed in the world. It accounts for 9.9% of all new cases of cancer diagnosed and is responsible for 12.1% of all cancer deaths [1]. Although the number of overall cancer deaths has declined, gastric cancer is still the leading cause of cancer death in Korea [2]. An essential step in managing gastric cancer is accurately assessing the preoperative stage and deciding on the adequate surgery including endoscopic treatment, minimal invasive surgery, and pallia-

tive operation.

However, managing gastric cancer is challenging because problems in determining treatment strategy remain as the prognosis has a wide range according to TNM classification [3]. There are limitations in the treatment of advanced gastric cancer (AGC) with surgery, whereas early gastric cancer (EGC) can be treated using minimal invasive surgery including endoscopy and laparoscopy with the limitation of lymphadenectomy [4,5]. Traditionally, computed tomography (CT) has been used for preoperative staging of gastric cancer. CT provides useful in-

Received February 24, 2011, Accepted April 27, 2011

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formation on tumors based on anatomical structure, but there is a limitation in the accuracy of detection of EGC [6]. It was reported that the diagnostic accuracy in T staging can be increased using multi-detector row CT (MDCT), but N staging which is one of the most important prognostic factor as deciding treatment strategy for EGC remain unsatisfactory [7,8].

Recently, Positron emission tomography (PET) using ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) is being widely used to determine status of many different cancers, considered a new perspective on staging approach in malignancy. This advanced technology more accurately displays functional image of cancer with altered glucose metabolism, but lacks precision in localizing the tumor. A combined image of ¹⁸F-FDG-PET and CT (¹⁸F-FDG-PET/CT) can provide additional information by using the characteristics of both modalities. Improved staging accuracy has been demonstrated with the use of ¹⁸F-FDG-PET/CT in patients with lung and colon cancers [9-11].

¹⁸F-FDG-PET/CT has being widely used in Korea after the National Health Insurance Program decided to reimburse ¹⁸F-FDG-PET/CT cost in 2006 [12]. There is a paucity of data on the role of ¹⁸F-FDG-PET/CT in the preoperative diagnosis of gastric cancer. The purpose of this study is to compare the effectiveness of ¹⁸F-FDG-PET/CT to MDCT in terms of preoperative T and N staging of gastric cancer.

METHODS

Patients

A retrospective analysis of 78 preoperative ¹⁸F-FDG-PET/CT and MDCT in patients with gastric cancer who had undergone curative gastrectomy between February 2007 and October 2008 was performed. Informed consent for ¹⁸F-FDG-PET/CT and MDCT for the purpose of preoperative staging of gastric cancer was obtained from all patients. The patients comprised 53 men and 25 women with a median age of 61 years (range, 32 to 85 years). All of these patients underwent a preoperative staging procedure, including past history, physical examination, blood chemistry, abdominal MDCT, and esophagogastroduo-

denoscopy. ¹⁸F-FDG-PET/CT was performed within 4 weeks before gastrectomy.

MDCT technique

With MDCT unit, abdominal MDCT images were obtained. The MDCT scanner used was a 64-detector row scanner (Brilliance CT 64, Philips Medical System, Cleveland, OH, USA). All patients were given 4 g of effervescent granules (Top, Taejoon Pharmaceuticals, Seoul, Korea) to distend the stomach wall. The patients were placed in a supine position on the CT table. The acquisition volume included the whole abdomen from the dome of the diaphragm to lower margin of the symphysis pubis. An 18-gauge intravenous cannula was inserted into a vein in the antecubital fossa, forearm or wrist. Scanning of the abdomen was performed after intravenous injection with automatic power injector of 2 mL/kg of contrast medium (Ultravist 300, Schering, Berlin, Germany) at a flow rate of 2 to 3.5 mL/sec, total 120 mL. The scan delay time was determined by automatic bolus tracking method. The region of interest (ROI) was positioned at the descending aorta, at the level of the diaphragm. The hepatic arterial phase image was started 7 seconds after the attenuation reached 200 HU. Additional CT scan for portal phase images was started 60 seconds after the start of the contrast injection. The respective scanning parameters used for 16- and 64-MDCT scanners were 16 × 1.5 mm and 64 × 0.625 mm collimation, table feed of 24 and 46 mm per gantry rotation. X-ray tube voltage was 120 or 140 kVp, and amperage was determined by automatic dose reduction protocol. Volume data of MDCT scan were reconstructed as 5 mm thickness at 5 mm intervals. Coronal reformative images were reconstructed on a workstation, with a thickness of 3 mm at 3 mm intervals. All reconstructed images were sent to picture archiving and communication system (PACS) for evaluation.

¹⁸F-FDG-PET/CT technique

Patients were advised to fast for at least 6 hours prior to the intravenous injection of 5 to 6 MBq/kg of ¹⁸F-FDG. The ¹⁸F-FDG-PET/CT scan was obtained approximately 1 hour after administration of the FDG, using Biograph 6 system (Siemens, Knoxville, TN, USA). Seven or eight bed positions were imaged from the skull base to the mid thigh

level. Patients were advised not to speak, chew, or move during scanning.

CT acquisition used the following parameters: 100 mA, 130 kVp tube voltage, helical thickness of 5 mm, and a helical pitch of 1.5:1. Using these parameters, the CT scan from the skull base to the mid thighs was obtained in 20 seconds. Immediately following the CT scan, a PET emission scan was acquired from the mid thigh to the base of skull with an acquisition time of 2.3 minutes per bed position based on body weight.

¹⁸F-FDG-PET/CT and MDCT image interpretation

An experienced gastrointestinal radiologist interpreted the MDCT images. Transverse and coronal MDCT images were evaluated with PACS monitors in random order. A le-

sion was determined to be cancerous when the gastric wall showed a focal thickening of at least 6 mm or greater or when focal enhancement was seen in the gastric wall. Lymph nodes were considered metastatic if they were large than 8 mm in the short-axis diameter and oval [13-15].

FDG uptake lesions of gastric wall and of lymph node bearing areas, regardless of size detected on PET/CT were regarded as malignancy, and the maximum standardized uptake value (SUV_{max}) was obtained using volume ROI.

Operation

All patients underwent total gastrectomy (n = 19, 24.3%) or subtotal gastrectomy (n = 59, 75.7%) and standard lymphadenectomy (at least D2 lymphadenectomy). The advanced gastric cancer in 41 patients and EGC in 37 patients

Table 1. Characteristics of 78 patients with gastric cancer according to PET/CT results for primary tumor and LNM

Characteristics	PET/CT (-) (n = 27)	PET/CT (+) (n = 51)	P-value	PET/CT LN (-) (n = 55)	PET/CT LN (+) (n = 23)	P-value
Age (yr)			0.477			0.624
≤60	15 (39.5)	23 (60.5)		28 (73.7)	10 (26.3)	
>60	12 (30.0)	28 (70.0)		27 (67.5)	13 (32.5)	
Gender			0.308			1.000
Male	16 (30.2)	37 (69.8)		37 (69.8)	16 (30.2)	
Female	11 (44.0)	14 (56.0)		18 (72.0)	7 (28.0)	
Tumor location			0.080			0.067
Upper	2 (25.0)	6 (75.0)		3 (37.5)	5 (62.5)	
Middle	15 (50.0)	15 (50.0)		21 (70.0)	9 (30.0)	
Lower	10 (25.0)	30 (75.0)		31 (77.5)	9 (22.5)	
Tumor size			0.002			0.330
≤3.5	21 (51.2)	20 (48.8)		31 (75.6)	10 (24.4)	
>3.5	6 (16.2)	31 (83.8)		24 (64.9)	13 (35.1)	
Depth of tumor			0.005			<0.001
T1	20 (54.1)	17 (45.9)		34 (91.9)	3 (8.1)	
T2	6 (22.2)	21 (77.8)		14 (51.9)	13 (48.1)	
T3	1 (9.1)	10 (90.9)		6 (54.5)	5 (45.5)	
T4	0 (0.0)	3 (100.0)		1 (33.3)	2 (66.7)	
LNM			0.003			0.001
N0	23 (51.1)	22 (48.9)		39 (86.7)	6 (13.3)	
N1	3 (18.8)	13 (81.3)		9 (56.3)	7 (43.8)	
N2	0 (0.0)	4 (100.0)		2 (50.0)	2 (50.0)	
N3	1 (7.7)	12 (92.3)		5 (38.5)	8 (61.5)	
Histology			0.005			0.016
Non-SRC ^{a)}	16 (26.2)	45 (73.8)		39 (63.9)	22 (36.1)	
SRC	11 (64.7)	6 (35.3)		16 (94.1)	1 (5.9)	

Values are presented as number (%).

PET/CT, positron emission tomography and computed tomography; LN, lymph node; LNM, lymph node metastasis; SRC, signet ring carcinoma.

^{a)}Papillary adenocarcinoma, well differentiated adenocarcinoma, moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, and mucinous adenocarcinoma.

were revealed by pathologic diagnosis. According to the World Health Organization classification with Japanese modification [16], histopathological type of primary tumor was categorized as papillary adenocarcinoma (n = 1, 1.3%), well-differentiated adenocarcinoma (n = 4, 5.1%), moderately differentiated adenocarcinoma (n = 31, 39.7%), poorly differentiated adenocarcinoma (n = 22, 28.3%), mucinous adenocarcinoma (n = 3, 3.8%), and signet ring cell carcinoma (SRC) (n = 17, 21.8%).

Statistical analysis

We conducted Fisher's exact test for comparing the difference of respective categorical variables. The relation between SUV_{max} and pTNM stage was determined using Kruskal-Wallis test. The sensitivity and specificity of ¹⁸F-FDG-PET/CT and MDCT were calculated and compared using McNemar's chi-square test. The correlation analysis was performed to determine the relationship between tumor SUV_{max} and lymph node SUV_{max}, and also between tumor SUV_{max} and tumor size. P-values less than 0.05 were considered to be significant. The statistical analysis was carried out by the SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Fifty one primary tumors were detected by pre-

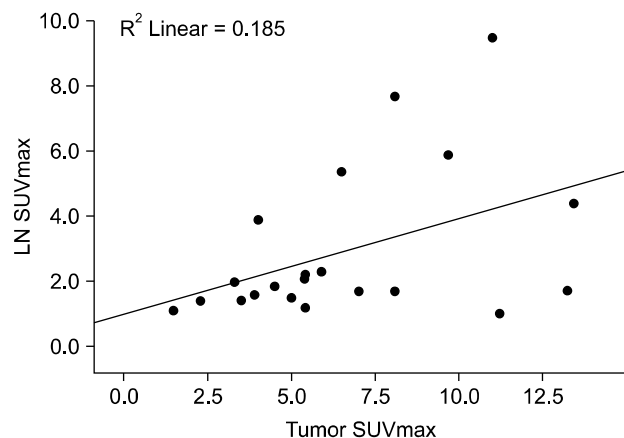


Fig. 1. Correlation analysis curve between primary tumor maximum standardized uptake value (SUV_{max}) and lymph node (LN) SUV_{max}.

operative ¹⁸F-FDG-PET/CT, and 27 patients had no noticeable results in ¹⁸F-FDG-PET/CT. Tumor size, depth of tumor, and lymph node metastasis (LNM) significantly affected the detection of primary tumor by ¹⁸F-FDG-PET/CT. As tumor size, depth of tumor, and LNM increased, the primary tumor was revealed more frequently by ¹⁸F-FDG-PET/CT. The detection rate of ¹⁸F-FDG-PET/CT for SRC was relatively lower than that for non-SRC (35.3% vs. 73.8%, P = 0.005). ¹⁸F-FDG-PET/CT detected LNM in 23 patients, and 55 patients showed no significant SUV_{max} of lymph node which was considered as metastasis. The results of ¹⁸F-FDG-PET/CT in detecting LNM were similar to the results of ¹⁸F-FDG-PET/CT in detecting primary tumor; however, tumor size had no association with detection of LNM on ¹⁸F-FDG-PET/CT (Table 1).

The correlation analysis showed a positive correlation exist between SUV_{max} of primary tumor and that of metastatic lymph node (P = 0.05, R = 0.43) (Fig. 1). However, there was no significant correlation between SUV_{max} of primary tumor and tumor size.

When assessed using the Kruskal-Wallis test, the mean SUV_{max} of primary tumor showed no significant difference between p_{T1}, p_{T2}, p_{T3}, and p_{T4} (6.0 ± 1.4, 6.3 ± 0.6, 6.2 ± 0.8, and 5.4 ± 1.7). In addition, there was no statistical difference of the mean SUV_{max} of metastatic lymph node between p_{N0}, p_{N1}, p_{N2}, and p_{N3} (1.8 ± 0.5, 3.1 ± 0.9, 5.6 ± 3.8, and 2.4 ± 0.5).

The detection rate of primary tumor by ¹⁸F-FDG-PET/CT and MDCT showed no significant difference. Among the 37 patients with EGC, ¹⁸F-FDG-PET/CT preoperatively detected 17 patients who were suspected to have gastric

Table 2. Detection rate of primary tumor and lymph node metastasis in ¹⁸F-FDG-PET/CT and MDCT

Variable	¹⁸ F-FDG-PET/CT	MDCT	P-value ^{a)}
Primary tumor in EGC	17/37 (45.9)	10/37 (27.0)	0.039
Primary tumor in AGC	34/41 (82.9)	37/41 (90.2)	0.508
LNM in EGC	0/37 (0.0)	1/37 (2.7)	NA
LNM in AGC	17/41 (41.5)	22/41 (53.7)	0.125

Values are presented as number/total number (%).

¹⁸F-FDG-PET/CT, F18-fluorodeoxyglucose-positron emission tomography and computed tomography; MDCT, multi-detector row CT; EGC, early gastric cancer; AGC, advanced gastric cancer; LNM, lymph node metastasis; NA, not available.

^{a)}Chi-square McNemar test.

cancers. However, MDCT detected only 10 patients out of 37. The other 10 gastric cancer patients had no measurable lesions on both ^{18}F -FDG-PET/CT and MDCT. A statistical difference between the detection rate of ^{18}F -FDG-PET/CT and that of MDCT in patients with EGC was found (45.9% vs. 27.0%, $P = 0.039$). However, there was no significant difference between the detection rate of ^{18}F -FDG-PET/CT (34/41 patients) and that of MDCT (37/41 patients) in AGC (Table 2). The SUV_{max} of primary tumor between EGC and AGC displayed similar result (6.0 ± 6.1 , range 1.5 to 27.0 vs. 6.2 ± 2.9 , range 2.2 to 13.2). However, the result of ^{18}F -FDG-PET/CT (17 of 78 patients) for LNM confirmed pathologically was not significantly different from that of MDCT (23 of 78 patients) with respect to the detection of LNM (21.8% vs. 29.5%, $P = 0.07$). In 41 patients with AGC, MDCT revealed 22 LNM com-

pared to 17 LNM on FDG-PET/CT (53.7% vs. 39.0%, $P = 0.125$). In EGC, detection rate of ^{18}F -FDG-PET/CT (0 of 37 patients) for LNM did not show significant difference from that of MDCT (1 of 37 patients).

Overall, the accuracy of ^{18}F -FDG-PET/CT was similar to that of MDCT in the diagnosis of LNM in gastric cancer (71.8% vs. 69.2%). However, the sensitivity of MDCT was superior to that of ^{18}F -FDG-PET/CT (69.7% vs. 51.5%, $P = 0.035$). ^{18}F -FDG-PET/CT was also superior to MDCT in terms of the specificity (86.7% vs. 75.6%, $P = 0.029$) (Table 3).

DISCUSSION

MDCT has also been widely used in the preoperative di-

Table 3. The sensitivity, specificity, PPV, NPV, and accuracy of PET/CT and CT for LNM in gastric cancer

	Sensitivity		Specificity		PPV		NPV		Accuracy	
	CT	PET/CT	CT	PET/CT	CT	PET/CT	CT	PET/CT	CT	PET/CT
EGC	20.0 (1/5)	0.0 (0/5)	78.1 (25/32)	85.3 (29/32)	12.5 (1/8)	0.0 (0/3)	86.2 (25/29)	85.3 (29/34)	70.2 (26/37)	78.4 (29/37)
AGC	78.6 (22/28)	60.7 (17/28)	46.2 (6/13)	76.9 (10/13)	75.9 (22/29)	85.0 (17/20)	50.0 (6/12)	47.6 (10/21)	70.2 (26/37)	65.9 (27/41)
Total	69.7 (23/33)	51.5 (17/33)	75.6 (31/45)	86.7 (39/45)	62.2 (23/37)	73.9 (17/23)	75.6 (31/41)	70.9 (39/55)	69.2 (54/78)	71.8 (56/78)

Values are presented as % (number/total number).

PPV, positive predictive value; NPV, negative predictive value; PET/CT, positron emission tomography and computed tomography; LNM, lymph node metastasis; EGC, early gastric cancer; AGC, advanced gastric cancer.

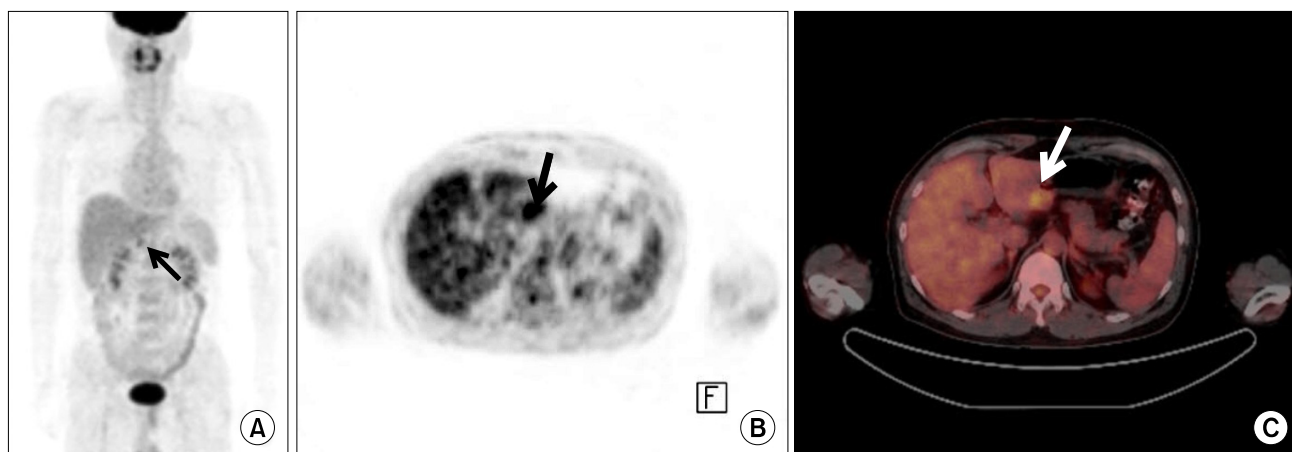


Fig. 2. Early gastric cancer in a 47-year-old man. Maximum intensity projection image of (A) positron emission tomography (PET) and (B) axial PET scan demonstrate focal hypermetabolic lesion in gastric antrum (black arrow) with maximum standardized uptake value (SUV_{max}) of 4.3. (C) PET/CT scan shows focal hypermetabolic intraluminal mass in posterior wall of gastric antrum (white arrow).

agnosis of gastric cancer, providing high-resolution anatomic details about staging, but is limited by the use of size criteria [17]. FDG-PET lacks accurate anatomical orientation when displaying metabolic information of malignancy [18]. The combination of PET and CT has emerged as the most accurate technology and provides good anatomical localization of functional data [19].

^{18}F -FDG-PET/CT is increasingly used in the preoperative diagnosis of various cancers to determine staging, as well as in the detection of recurrence after curative surgery [9]. And recently, for the purpose of the detection of recurrence for gastric cancer after curative gastrectomy, ^{18}F -FDG-PET/CT has been introduced and shown comparable results to CT [20]. As shown in this study, the performance of ^{18}F -FDG-PET/CT was comparable to that of MDCT with a similar 71.8% accuracy. The interesting result of ^{18}F -FDG-PET/CT over MDCT in this study was an improvement in the detection of EGC (45.9% vs. 27.0%), while there was no significant difference of SUV_{max} between EGC and AGC (6.0 ± 6.1 vs. 6.2 ± 2.9). The metabolic alteration of tumor allowed ^{18}F -FDG-PET/CT to detect lesion regardless of tumor advancement (Fig. 2).

In the present study, the detection rate of primary tumor and LNM in ^{18}F -FDG-PET/CT was significantly higher as the T and N stage increased, while the tumor size was not significantly associated with the detection of LNM in ^{18}F -FDG-PET/CT. The histological subtype had a strong influence on the detection of primary tumor and LNM. The detection rate of SRC in ^{18}F -FDG-PET/CT was lower than that of non-SRC in terms of detection of primary tumor and LNM. The FDG uptake in primary tumor and LNM in cases of signet ring cell carcinoma was less pronounced than that in non-SRC [21,22]. The results suggest that ^{18}F -FDG-PET/CT appears to play a less useful diagnostic role in such cases.

The evaluation of ^{18}F -FDG-PET/CT compared to MDCT in the diagnostic accuracy of EGC has not achieved consistent levels of accuracy. Previous reports have shown low detection rates for EGC in CT, with a range of 26 to 53% [23,24]. In one study, the detection rate of mucosal cancer was very low (16.7%) in comparison to that for submucosal cancer (68.8%) in MDCT [25]. In the present study, the detection rate of mucosal cancer and sub-

mucosal cancer in ^{18}F -FDG-PET/CT was 35.0% (7/20) and 58.8% (10/17), respectively, which is considerably higher detection rate for cases of mucosal cancer. From this result, ^{18}F -FDG-PET/CT displays greater superiority with respect to the detection of mucosal gastric cancer compared to MDCT, but has a limited role compared to other modalities [26].

We found a borderline statistical significant positive correlation in SUV_{max} between the primary tumor and lymph node. The high SUV_{max} of primary tumor is associated with better detection rate for LNM. High SUV_{max} in the primary tumor had a positive impact on the accuracy of ^{18}F -FDG-PET/CT assessment of LNM. Gastric cancer with SRC tended to be associated with a lower detection rate in both the primary tumor and LNM in ^{18}F -FDG-PET/CT, and ^{18}F -FDG-PET/CT may not be sufficient for preoperative staging in gastric cancer with SRC.

FDG-PET has a low to moderate sensitivity of LNM due to its limited resolution; FDG-PET have a 4- to 5-mm resolution [27], but 14.5% of metastatic lymph node in gastric cancer has the largest diameter of less than 3 mm [28]. Another reason for the low sensitivity of FDG-PET is the masking of perigastric lymph node by the FDG uptake of the adjacent primary tumor. ^{18}F -FDG-PET/CT provides both anatomical and functional information and displays more accurate localization of both the primary tumor and lymph node with increased SUV than FDG-PET alone. We found that the sensitivity and specificity of ^{18}F -FDG-PET/CT in this study was comparable to a previous report in assessing lymph node status in gastric cancer (51.5% and 86.7% vs. 54.7% and 92.2%) [29].

The interesting finding from the present study was that both techniques had important informative role in preoperative staging of gastric cancer. ^{18}F -FDG-PET/CT was superior to MDCT in terms of the detection of the primary tumor in EGC, while MDCT provided more accuracy of LNM than ^{18}F -FDG-PET/CT in AGC.

In conclusion, ^{18}F -FDG-PET/CT has a better diagnostic performance than MDCT in detecting a primary tumor in EGC and comparable accuracy of detecting LNM. However, ^{18}F -FDG-PET/CT shows no definite improvement over MDCT in detecting primary tumors and LNM in patients with gastric cancer. Moreover, ^{18}F -FDG-PET/CT has clear

limitations in preoperative staging in case of patients with SRC. This limitation must be taken into consideration when assessing gastric cancer. Therefore, randomized controlled trial on the application of ¹⁸F-FDG-PET/CT in the diagnosis of EGC and AGC, respectively, is advocated.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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