Improving Patient Selection for ^{18}F-FDG PET Scanning in the Staging of Gastric Cancer

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Standard pretreatment staging for gastric cancer includes CT of the chest, abdomen, and pelvis; gastroscopy; and laparoscopy. Although ^{18}F-PET combined with CT has proven to be a useful staging tool in many cancers, some gastric cancers are not ^{18}F-FDG–avid and its clinical value is still debatable. **Methods:** Gastric cancer patients who underwent staging ^{18}F-FDG PET scans from 2002 to 2013 at the Peter MacCallum Cancer Center were retrospectively analyzed, and a systematic review was also conducted using PubMed between 2000 to March 2014 to investigate clinicopathologic parameters associated with ^{18}F-FDG avidity. A pretreatment PET scoring system was developed from predictors of ^{18}F-FDG avidity. **Results:** Both the retrospective analysis of the patients and the systematic literature review showed similar significant predictors of ^{18}F-FDG avidity, including large tumor size, non–signet ring cell carcinoma type, and glucose transporter 1–positive expression on immunohistochemistry. A PET scoring system was developed from these clinicopathologic parameters that allowed ^{18}F-FDG–avid tumors to be detected with a sensitivity of 85% and a specificity of 71%. **Conclusion:** A pretreatment PET scoring system can assist in the selection of patients with gastric adenocarcinoma when staging ^{18}F-FDG PET is being considered.

Key Words: FDG-PET; gastric cancer; staging

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Gastric cancer is the fourth most common cancer and the second leading cause of cancer death worldwide (*1*). Despite the decline in the incidence of gastric cancer over the past 50 y, the 5-y survival rate still remains low because of the asymptomatic or nonspecific clinical presentation, resulting in advanced disease at the time of diagnosis (*1*).

Surgery remains the only curative treatment, and thus accurate preoperative staging is essential to select the most effective treatment modality for patients. Current standard staging for gastric cancer includes CT of the chest, abdomen, and pelvis; gastroscopy; and laparoscopy.

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^{18}F-FDG PET, now routinely combined with CT as a hybrid imaging modality, is a noninvasive functional imaging modality that has proven to be a useful staging tool in many cancers, including esophageal and lung cancer (*2,3*). However, its clinical value in gastric cancer remains controversial, as reports indicate that gastric cancer is not ^{18}F-FDG–avid in up to 53% of cases (*4–10*). This lack of avidity can result in a relatively low sensitivity for the detection of the primary tumor, nodal disease, and, consequently, distant metastatic disease. Such false-negative results decrease confidence in the utility of this technique, and accordingly, it is not currently used as a routine staging tool in gastric cancer.

The recent literature suggests that ^{18}F-FDG avidity correlates with certain clinicopathologic parameters in gastric cancer. The intestinal subtype has appeared to have higher ^{18}F-FDG uptake than the diffuse subtype of gastric cancer (*11–13*).

We conducted a systematic literature review, as well as a retrospective analysis on gastric cancer patients who underwent staging ^{18}F-FDG PET or ^{18}F-FDG PET/CT at our institution, to evaluate preoperative clinicopathologic parameters associated with high ^{18}F-FDG avidity. Significant predictors of ^{18}F-FDG avidity were used to develop a pretreatment PET scoring system for the selection of gastric cancer patients who may benefit from staging ^{18}F-FDG PET.

MATERIALS AND METHODS

Systematic Literature Review

Selection of Articles. An electronic literature search was conducted using PubMed to select articles from January 2000 to March 2014 evaluating patients who underwent preoperative ^{18}F-FDG PET in the staging of gastric cancer. The search terms were "PET" and "gastric cancer." Additional database searches of the Cochrane Database of Systematic Reviews, PROSPERO, DARE, and Embase were also performed.

Articles were restricted to those in English with full-text article and detailing clinicopathologic characteristics of the primary tumor with the detection rate of ^{18}F-FDG avidity, which was defined as focally increased ^{18}F-FDG uptake compared with surrounding tissue. Because of the discordance of standardized uptake values among studies, articles were excluded if the study had looked at only the standardized uptake value of the primary tumor. Attempts were made to contact the authors to obtain the detection rate of ^{18}F-FDG avidity from these studies, but these attempts were unsuccessful and these studies were excluded.

Articles were excluded if ^{18}F-FDG PET had been performed for restaging, assessment of treatment response, and detection of recurrence of the disease. Gastroesophageal junction tumors and other gastric malignancies, including gastrointestinal stromal tumor and gastric lymphoma, were also excluded.

Data Extraction and Analysis. The primary investigator reviewed all articles independently and met with the other investigator to arrive at a consensus on the final selected articles. In total, 504 articles were identified from the PubMed database, and after application of our inclusion and exclusion criteria, 18 articles were selected.

The clinicopathologic parameters in these studies were dichotomized into the following: tumor stage (early gastric cancer [EGC] or advanced gastric cancer [AGC]), site of the tumor (proximal one third or distal two thirds), size of the tumor (small [<3 cm] or large [>3 cm]), Lauren classification (intestinal or diffuse), World Health Organization (WHO) classification (signet ring cell [SRC] carcinoma or non-SRC), and glucose transporter 1 (GLUT1) status (GLUT1-positive or GLUT1-negative).

The proportion of ^{18}F-FDG–avid tumors for each clinicopathologic parameter was extracted from the selected studies and combined to obtain the total detection rate of ^{18}F-FDG avidity. Odds ratios with 95% confidence intervals and *P* values were estimated with a random effects model using the Mantel–Haenszel method to identify parameters significantly associated with ^{18}F-FDG avidity. The level of significance was a *P* value of less than 0.05.

Retrospective Analysis

Patients. Forty patients with histologically proven gastric adenocarcinoma who underwent pretreatment staging ^{18}F-FDG PET or ^{18}F-FDG PET/CT at Peter MacCallum Cancer Center (PMCC) from January 2002 to December 2013 were examined retrospectively from the PMCC PET database to assess predictors of the ^{18}F-FDG avidity of the primary tumor. Only patients who had undergone gastroscopy or surgery at PMCC were included, so that we could perform immunohistochemistry for GLUT1. This study was approved by the Peter MacCallum Cancer Centre Ethics Committee.

Data Collection. A standard protocol for ^{18}F-FDG PET/CT, including patient preparation and the processing method, has been used and described previously (*14*). ^{18}F-FDG PET or ^{18}F-FDG PET/CT reports were reviewed to identify whether the primary tumors were ^{18}F-FDG–avid or not. A primary tumor was considered ^{18}F-FDG–avid if the PET report described intensely or moderately increased radiotracer uptake in the stomach relative to the rest of the gastric wall; a primary tumor was considered not ^{18}F-FDG–avid if the PET report did not indicate any evidence of significant metabolic uptake in the stomach. Representative images of an avid and nonavid gastric adenocarcinoma are shown in Figure 1.

Pretreatment clinicopathologic parameters were obtained from the patient's electronic medical records and included stage, site, and size of the primary tumor and histologic subtype according to the Lauren and WHO classifications. AGC was defined as a bulky or large mass detected on gastroscopy, along with a CT report of a thickened or irregular gastric wall. EGC was defined as slight elevation, no mass, or mucosal abnormality detected on gastroscopy and no evidence of mass on CT.

GLUT1 Immunohistochemistry and Semiquantitative Analysis. GLUT1 staining is not routinely performed on biopsy or resection specimens of gastric cancer in our institute unless requested. Archived formalin-fixed paraffin-embedded tissue blocks from biopsy or resection specimens were retrieved from pathology storage. Tissue blocks were not available for 3 patients, leaving 37 evaluable specimens. Three-micrometer sections were prepared and mounted on positively charged microscope slides. Immunostaining was performed using antihuman GLUT1 antibody (Thermo Fisher Scientific) at 1:200 dilution (v/v) on the automated BenchMark Ultra system (Ventana Medical Systems) using the UltraView detection reagents. The slides were then counterstained using Mayer hematoxylin before scoring. Erythrocytes were used as an internal positive control. Semiquantitative analysis was done by an experienced pathologist who was masked to all clinical data. Previous studies have considered more than 30% GLUT1-positive cells as high GLUT1 expression (*15–17*) in gastric cancer. In our study, we applied immunoreactive score as described previously, with modification (*18*).

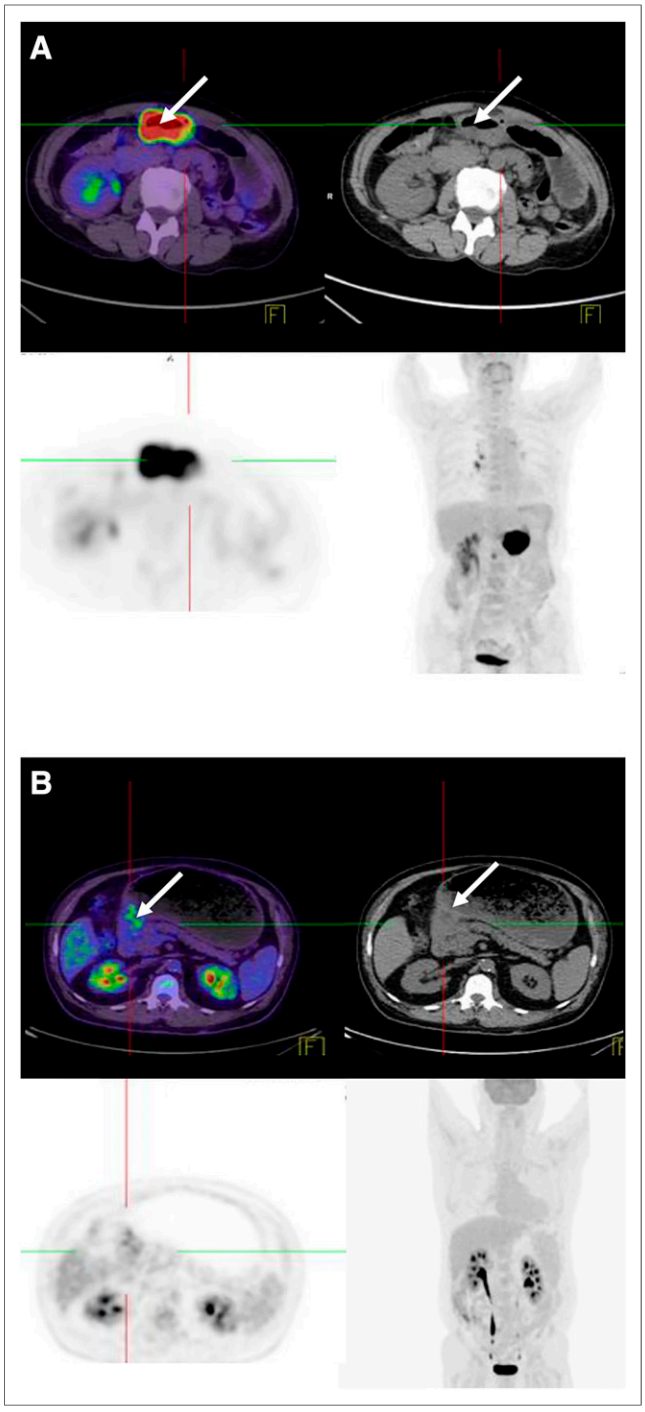


FIGURE 1. ^{18}F-FDG PET/CT image of avid and nonavid gastric adenocarcinoma. (A) Avid gastric adenocarcinoma shows intense uptake in gastric antrum, and corresponding CT image demonstrates thickening of gastric antrum wall (arrow). Nonavid gastric adenocarcinoma (B) shows minimal uptake in pylorus (considered to be physiologic), with marked focal thickening on corresponding CT image consistent with site of known primary tumor (arrow).

GLUT1 expression was categorized by percentage of positive staining: 0% (0), less than 10% (1), 11%–30% (2), or more than 31% (3). The intensity of staining was categorized as no staining (0), weak staining (1), moderate staining (2), or strong staining (3). The immunoreactive score was obtained by multiplying the level of staining intensity by the

percentage of positive tumor cells, resulting in a scale ranging from 0 to 9 and scored accordingly: negative GLUT1 expression (score 0), positive weak GLUT1 expression (1–3 = score 1), positive moderate GLUT1 expression (4–5 = score 2), and positive strong GLUT1 expression (6–9 = score 3). An immunoreactive score above 1 was considered GLUT1-positive expression.

Data and Statistical Analysis. Similar to the systematic literature review, the proportion of ^{18}F-FDG–avid tumors for each clinicopathologic parameter was calculated followed by univariate and multivariate analysis using logistic regression. The multivariate model was determined using backward selection methods. Statistical analysis was conducted using SAS software (SAS Institute). The level of significance was a P value of less than 0.05.

Pretreatment PET Scoring System

Clinicopathologic parameters significantly associated with ^{18}F-FDG avidity were assigned a score obtained from the systematic literature review odds ratio. This scoring system was developed in reference to a similar scoring method described previously (*19*). Odds ratio was rescaled using a logarithmic scale. The PET scoring model was tested on our retrospective cohort, and the total score was compared between tumors that were ^{18}F-FDG–avid and those that were not. To evaluate the performance of this scoring system, a receiver-operating-characteristic (ROC) curve analysis was performed.

To ascertain the best possible PET scoring model in our study, we developed multiple models with different combinations of clinicopathologic parameters and selected the model that the authors agreed produced the highest area under the ROC curve. The ROC curve was created using SPSS software (IBM Corp.).

RESULTS

Systematic Literature Review

Eighteen articles were selected: 10 retrospective studies and 8 prospective studies, with most (16/18 articles) being from non-Western data. ^{18}F-FDG avidity ranged from 42% to 96%, with a mean of 73%, as summarized in Table 1. The studies are outlined in Supplemental Table 1, and the clinicopathologic parameters and ^{18}F-FDG avidity for each study are described in Supplemental Table 2 (supplemental materials are available at http://jnm.snmjournals.org).

Five clinicopathologic parameters—tumor stage, size, site, WHO classification, and GLUT1 status—were significantly associated with ^{18}F-FDG avidity. AGC had significantly higher avidity (85.6%, 752/878) than EGC (26.8%, 99/370). Similarly, large tumors (70.8%, 209/295), non-SRC tumors (64.5%, 487/755), proximal tumors (75.7%, 134/177), and GLUT1-positive tumors (70.8%, 17/24) were also associated with high avidity. Table 2 summarizes the clinicopathologic parameters and ^{18}F-FDG avidity from the systematic literature review.

Retrospective Analysis of PMCC Cohort

The mean age of the 40 PMCC gastric cancer patients for whom staging ^{18}F-FDG PET or ^{18}F-FDG PET/CT scans were available was 65.7 y (range, 35–89 y). There were 25 men and 15 women. Twenty-six patients (65%) had tumors avid for ^{18}F-FDG, and the remaining 14 had nonavid tumors.

Most GLUT1-positive tumors were ^{18}F-FDG–avid (89%, 16/18 cases). Tumors with a GLUT1 score of 3 were more likely to be avid than those with scores of 0 to 2 (score 3 odds ratio, 5.87; 95% confidence interval [CI], 1.26–27.45; P = 0.0004). Furthermore, higher rates of GLUT1 positivity were observed among patients with non-SRC tumors than among patients with SRC tumors (63% compared with 23%, respectively: P = 0.04).

Most patients had advanced disease (34/40) at the time that imaging was performed. Univariate analysis demonstrated that large tumors (75%, 24/32), non-SRC tumors (84%, 21/25), intestinal tumors (82%, 14/17), and GLUT1-positive tumors (89%, 16/18) had significantly higher ^{18}F-FDG avidity than did small tumors (25%, 2/8), SRC tumors (33%, 5/15), diffuse tumors

TABLE 1
^{18}F-FDG Avidity of Studies Included in Systematic Review

Study	No. of patients	Study period	^{18}F-FDG avidity (%)
Chen et al., 2005 (*5*)	68	Aug 2000–June 2003	94.1
Chung et al., 2013 (*24*)	131	April 2006–Oct 2010	77.9
Ha et al., 2011 (*9*)	78	Feb 2007–Oct 2008	65.4
Herrmann et al., 2007 (*4*)	45	Not stated	68.9
Hur et al., 2010 (*28*)	142	Jan 2007–Nov 2008	88.7
Kameyama et al., 2009 (*29*)	20	Not stated	95
Kim et al., 2006 (*7*)	73	Oct 2002–Dec 2004	95.9
Kim et al., 2011 (*26*)	78	Oct 2003–Oct 2007	93
Lee et al., 2013 (*32*)	44	Feb 2009–Dec 2011	50
Li et al., 2012 (*27*)	124	March 2007–Sept 2011	90.3
Mochiki et al., 2004 (*6*)	85	Jan 2000–June 2002	75.3
Mukai et al., 2006 (*13*)	62	July 2004–June 2005	58.1
Namikawa et al., 2014 (*30*)	90	Jan 2009–Dec 2011	78.9
Oh et al., 2011 (*10*)	136	Dec 2007–March 2010	52.9
Stahl et al., 2003 (*12*)	40	Not stated	60
Yamada et al., 2006 (*17*)	35	April–Dec 2003	47.5
Youn et al., 2012 (*23*)	396	Jan 2009–Dec 2009	42.2
Yun et al., 2005 (*8*)	81	Not stated	87.7

TABLE 2
Systematic Literature Review Univariate Analysis

Clinicopathologic parameter	No. of studies combined	No. of patients	Patients with ^{18}F-FDG–avid tumor	Odds ratio	*P*
Tumor site					
Proximal third	9	177	134 (75.7%)	1.62 [1.05–2.50]	0.03*
Distal two thirds	9	612	424 (69.3%)	1	
Tumor size					
Small (<3 cm)	5	288	75 (26%)	1	<0.00001*
Large (>3 cm)	5	295	209 (70.8%)	7.01 [4.78–10.27]	
WHO classification					
SRC	8	205	93 (45.4%)	1	0.02*
Non-SRC	8	755	487 (64.5%)	2.24 [1.12–4.50]	
Lauren classification					
Diffuse	8	391	212 (54.2%)	1	0.14
Intestinal	8	479	284 (59.3%)	1.04 [0.90–2.19]	
Stage					
EGC	7	370	99 (26.8%)	1	<0.00001*
AGC	13	878	752 (85.6%)	11.74 [8.19–16.82]	
GLUT1					
Positive	1	24	17 (70.8%)	17 [3.03–95.3]	<0.0003*
Negative	1	16	2 (12.5%)	1	

*Statistically significant.
Data in brackets are 95% confidence interval.

(50%, 11/22), and GLUT1-negative tumors (42%, 8/19), respectively (Table 3). A non-SRC tumor type and GLUT1 positivity were the only independent predictors for ^{18}F-FDG avidity according to the multivariate analysis (Table 4).

Pretreatment PET Scoring System

To obtain the best pretreatment PET scoring system, we developed several scoring models using different combinations of clinicopathologic parameters (tumor stage, tumor size, WHO classification, and GLUT1 status) that the systematic literature review indicated were significantly associated with ^{18}F-FDG avidity. The selected model yielded a total of 16 different combinations of parameters with a combined score ranging from 0 to 8.05 (Table 5). When this PET scoring system was tested on our retrospective cohort, the mean total score was significantly higher for ^{18}F-FDG–avid patients than for nonavid patients (6.67 and 3.56, respectively; $P < 0.00001$). A score above 4.41 could distinguish between avid and nonavid tumors with a sensitivity of 85% and a specificity of 71% ($P < 0.001$) (Fig. 2).

As a result, we propose a checklist containing key prestaging clinicopathologic parameters associated with ^{18}F-FDG avidity in gastric cancer (Fig. 3). This checklist can be used as a guide in selecting which patients should undergo staging ^{18}F-FDG PET.

DISCUSSION

For ^{18}F-FDG–avid gastric tumors, ^{18}F-FDG PET has been shown to have high clinical value in assessing chemotherapy response (*20*) and in detecting recurrent disease (*21*). However, the routine use of ^{18}F-FDG PET in preoperative staging has been suggested to be of limited value because of its low sensitivity for the detection of the primary gastric cancer and lymph node metastases (*9,22*).

The incidence of ^{18}F-FDG avidity in gastric adenocarcinomas varies greatly in the literature (47%–96%) (*4*). Selection bias is likely to have contributed to the higher rates of ^{18}F-FDG–avid stomach cancer seen in the systematic review (mean, 73%) and in our own retrospective cohort (65%). At our institution, patients with bulkier tumors and a greater likelihood of having nodal and distant metastases were more likely to have undergone PET.

Differences in cellularity, mucinous content, and GLUT1 expression in the 2 main histologic subtypes of gastric adenocarcinoma can influence cellular ^{18}F-FDG uptake (*12,15*). Several studies reported that the Lauren intestinal type of gastric cancer had higher ^{18}F-FDG uptake than the diffuse type (*12,13,23,24*). Low ^{18}F-FDG uptake in some gastric cancers may be explained by high extracellular mucin content and more dispersed and diluted tumor cells. Consistent with the published literature, intestinal gastric cancers were more ^{18}F-FDG–avid in our retrospective-cohort patients. However, in the systematic review, there was no significant difference in ^{18}F-FDG avidity between the 2 subtypes of gastric adenocarcinoma, possibly because most patients in the systematic review were Asian. Previous studies have shown ethnic disparity in etiology and overall survival of gastric cancer (*25*). Non-SRC gastric tumors were significantly associated with high ^{18}F-FDG uptake in both the systematic literature review and our retrospective cohort analysis. This observation is consistent with reports by Mukai et al. and Yamada et al. that lack of ^{18}F-FDG avidity in gastric cancer is associated with SRC morphology (*13,17*).

TABLE 3
Retrospective Univariate Analysis

Clinicopathologic parameter	No. of patients	Patients with ^{18}F-FDG–avid tumor	Odds ratio	*P*
Tumor site				
Proximal third	7	5 (71%)	1.62 [0.27–9.85]	0.64
Distal two thirds	28	17 (61%)	1	
Whole/diffuse	5	4 (80%)	2.59 [0.25–26.31]	
Tumor size				
Small (<3 cm)	8	2 (25%)	1	0.009*
Large (>3 cm)	32	24 (75%)	9 [1.5–53.86]	
WHO classification				
SRC	15	5 (33%)	1	0.001*
Non-SRC	25	21 (84%)	10.5 [2.31–47.77]	
Lauren classification				
Diffuse	22	11 (50%)	1	0.03*
Intestinal	17	14 (82%)	4.67 [1.04–20.94]	
Missing	1	1	1	
Mucinous content				
Mucinous	6	5 (83%)	3.1 [0.32–29.53]	0.28
Nonmucinous	34	21 (62%)	1	
Stage				
EGC	6	2 (33%)	1	0.09
AGC	34	24 (71%)	4.8 [0.75–30.55]	
GLUT1 status				
Positive	18	16 (89%)	11 [1.95–62]	0.002*
Negative	19	8 (42%)	1	
Missing	3	2	1	

*Statistically significant.
For 1 patient, Lauren classification was not known; for 3 patients, GLUT1 results were unavailable. Data in brackets are 95% confidence interval.

AGC had significantly higher ^{18}F-FDG avidity than EGC. ^{18}F-FDG avidity above 90% in AGC was observed in more than half the studies included in the systematic literature review (*5,7,8,26–29*). The low spatial resolution of PET and the physiologic uptake of ^{18}F-FDG by benign processes such as gastritis, or simply physiologic uptake in the muscularis mucosae, make it difficult to detect early small-volume gastric cancer through a combination of partial-volume effects and high adjacent background activity. Similarly, greater depth of tumor invasion and the presence of nodal disease have been correlated with tumoral ^{18}F-FDG uptake (*13,23,30*).

TABLE 4
Retrospective Multivariate Analysis

Clinicopathologic parameter	Odds ratio	*P*
WHO classification	1	0.02*
SRC	7.7 [1.4–43.3]	
Non-SRC		
GLUT1 status	1	0.04*
Negative	7.4 [1.1–48.0]	
Positive		

*Statistically significant.
Data in brackets are 95% confidence interval.

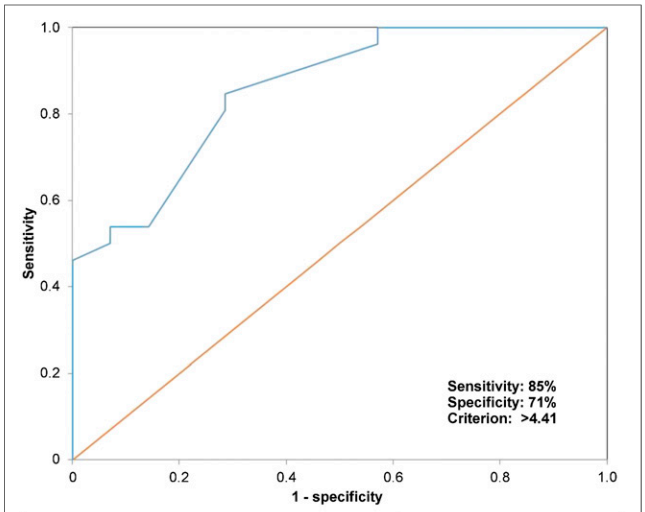
GLUT1 overexpression has been shown to be associated with increased cellular metabolism and glucose utilization (*16*). Hence, overexpression of GLUT1 may be a marker for higher ^{18}F-FDG uptake by malignant cells. In gastric cancer, the frequency of GLUT1 expression has been reported to vary between 16.9% and 60% (*15–17,31*). There have been only a few studies on GLUT1 expression and ^{18}F-FDG avidity in gastric cancer (*15,17,32*). Consistent with our current study, Yamada et al. reported that GLUT1-positive tumor cells were significantly associated with ^{18}F-FDG avidity (*17*). Similarly, gastric tumors with a high standardized uptake value on PET were shown to correlate with GLUT1 overexpression (*15*). However, Takebayashi et al. did not find any correlation between the standardized uptake value of primary gastric cancer and GLUT1 expression. Those authors reported hypoxia-inducible factor 1α to be another potential clinicopathologic parameter for ^{18}F-FDG avidity in gastric adenocarcinomas (*32*).

Currently, there are no clear guidelines on the use of ^{18}F-FDG PET for the staging of gastric cancer. Our study demonstrated that

TABLE 5
Clinicopathologic Predictors for Preoperative PET Scoring System

Parameter	Score
GLUT1-positive	2.83*
GLUT1-negative	0*
Small tumor	0*
Large tumor	1.95*
SRC	0*
Non-SRC	0.81*
EGC	0*
AGC	2.46*
AGC, GLUT+ve, large, non-SRC	8.05†
AGC, GLUT–ve, large, non-SRC	5.22†
AGC, GLUT+ve, large, SRC	7.24†
AGC, GLUT–ve l, large, SRC	4.41†
AGC, GLUT+ve, small, non-SRC	6.1†
AGC, GLUT–ve, small, non-SRC	3.27†
EGC, GLUT+ve, large, non-SRC	5.59†
AGC, GLUT+ve, small, SRC	5.29†
EGC, GLUT–ve, large, non-SRC	2.76†
AGC, GLUT–ve, small, SRC	2.46†
EGC, GLUT+ve, large, SRC	4.78†
EGC, GLUT–ve, large, SRC	1.95†
EGC, GLUT+ve, small, non-SRC	3.64†
EGC, GLUT–ve, small, non-SRC	0.81†
EGC, GLUT+ve, small, SRC	2.83†
EGC, GLUT–ve, small, SRC	0†

*Log (odds ratio).
†Total score.
+ve = positive; –ve = negative.
Score was obtained from odds ratio of clinicopathologic parameters significantly associated with ^{18}F-FDG avidity from systematic literature review. Sixteen different combinations of parameters including GLUT1 status with combined score ranging from 0 to 8.05 were used.



Area under the ROC curve (AUC)	0.870
Standard Error[a]	0.059
95% Confidence interval	0.755 to 0.985
Significance level P (Area = 0.5)	<0.001

FIGURE 2. Preoperative ^{18}F-FDG PET scoring system. ROC curve was used to evaluate performance of preoperative PET scoring system. Score above 4.41 distinguished between avid and nonavid tumor with sensitivity of 85% and specificity of 71% with GLUT1 status included ($P < 0.001$). [a]Under nonparametric assumption.

certain clinicopathologic factors such as large tumor size, advanced tumor stage, non-SRC histologic subtype, and GLUT1-positive expression were high predictors of ^{18}F-FDG avidity in gastric cancer. Identifying ^{18}F-FDG–avid predictors in gastric cancer would enable ^{18}F-FDG PET/CT to be used with greater confidence for assessing the extent of disease before planned surgical resection. Given the poor prognosis of gastric cancer, the ability to identify macroscopic distant metastases would have significant management implications by sparing patients futile surgery and allowing earlier initiation of systemic therapy. Conversely, being able to prospectively predict patients with a low likelihood of ^{18}F-FDG avidity could spare the expense of ^{18}F-FDG PET/CT. This is particularly relevant in jurisdictions such as Australia, where ^{18}F-FDG PET/CT for the staging of gastric cancer is not currently reimbursed. In such settings, a low-cost GLUT1 test could be performed rather than outlaying the high cost of a PET scan that may provide no diagnostic benefit. In an era of increasing scrutiny on the costs of imaging and the risks of unwarranted radiation exposure, our data may also provide an economic case for funding of GLUT1 staining in settings where it is not currently reimbursed. Thus, our proposed PET scoring system can be useful in supporting clinical decision making and in selecting patients who may benefit from staging ^{18}F-FDG PET/CT.

The limitations of the current study are the heterogeneity of patient groups in the systematic literature review, as well as the relatively small sample size in our retrospective analysis. Some patients had external CT scans without optimal gastric distension, making assessment of abnormal gastric wall thickening more difficult.

Interobserver variation among pathologists was not formally assessed, because GLUT1 expression scoring was determined by

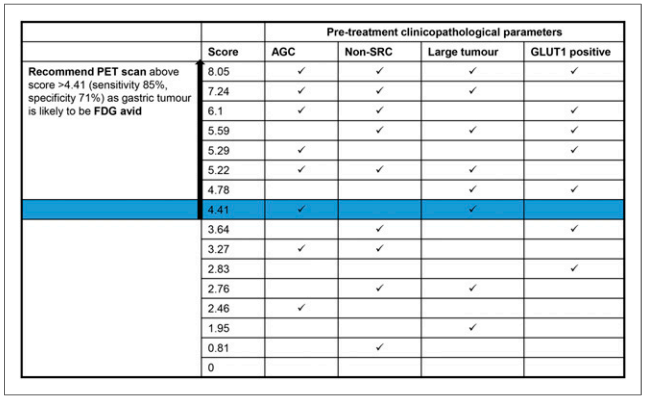


FIGURE 3. Proposed checklist to determine whether ^{18}F-FDG PET scanning should be recommended for gastric cancer patient.

a single experienced pathologist. We plan to assess the reproducibility of the GLUT1 scoring system and to validate our proposed PET scoring system on a larger independent patient cohort from other collaborating institutions.

CONCLUSION

In our study, certain clinicopathologic parameters of gastric cancer could be used to predict tumoral ^{18}F-FDG avidity, and the proposed PET scoring system may aid in the selection of patients who may benefit from staging ^{18}F-FDG PET.

DISCLOSURE

The costs of publication of this article were defrayed in part by the payment of page charges. Therefore, and solely to indicate this fact, this article is hereby marked "advertisement" in accordance with 18 USC section 1734. No potential conflict of interest relevant to this article was reported.

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