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Dual time point [18F]Flurodeoxyglucose (FDG) Positron Emission Tomography (PET)/Computed Tomography (CT) with water gastric distension in differentiation between malignant and benign gastric lesions

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ABSTRACT

Objectives: To assess diagnostic accuracy and added value of dual time point ^{18}F-FDG PET/CT after gastric distention using oral water in differentiating malignant from benign gastric lesions.

Methods: Patients (n = 30, 19 males, mean age 58.6 ± 16.4 years). All patients are known or suspected oncology patients. All patients underwent whole body ^{18}F-FDG PET/CT scan and 2 h delayed PET/CT abdominal images following oral water gastric distension. The best cut off values for early SUVmax (SUVmax1), delayed SUVmax (SUVmax2) and SUVmax2-SUVmax1 (ΔSUVmax) to differentiate benign from malignant lesions were set based on ROC analysis. Data analyzed included in addition; age, sex and ^{18}F-FDG uptake pattern in delayed images. Suspicious gastric lesions were correlated with biopsy in 18 patients (60 %) and with clinical and follow-up imaging (^{18}F-FDG PET/CT, CT or MRI) in 12 patients (40 %). Unpaired *t*-test was used to compare the mean deference in continuous variables between patients with gastric malignancy and those with benign gastric lesions. Fisher's exact test was used to analyze categorical variables. Logistic regression analysis was performed to identify the most powerful factors to predict malignant lesions.

Results: Fifteen patients (50 %) had confirmed malignant gastric lesions. Patients with confirmed gastric malignancy were older (65 ± 13 vs 52 ± 17; p = 0.023) and had significantly higher mean ΔSUVmax (1.29 ± 1.76 vs −0.89 ± 1.59; p = 0.003). The mean SUVmax1 (6.99 ± 6.66 vs 5.31 ± 2.53; p = 0.367) and SUVmax2 (8.29 ± 7.41 vs 4.44 ± 3.34; p = 0.077) although both higher in patients with malignant lesions, they did not reach statistical significance. Sensitivity, specificity, PPV, NPV, and accuracy to detect malignant gastric lesions were highest for lesions with localized uptake pattern in delayed images post water oral contrast as well as for lesions with ΔSUVmax>0. Regression analysis revealed both variables as independent predictors for malignant lesions with odd ratios of 22.9 and 9.5 respectively and final model Chi-Square of 19.9 (p < 0.0001). The model correctly identified 12/15 (80 %) malignant lesions and 13/15 (86.7 %) benign lesions with 2 false positives confirmed as chronic active gastritis with helicobacter pylori and 3 false negatives including 1 signet ring gastric cancer and 1 low grade gastrointestinal stromal tumor (GIST), both with poor 18 F-FDG uptake.

Conclusion: Localized uptake pattern in delayed PET/CT images following gastric distention with oral water contrast as well as ΔSUVmax>0 are powerful independent variables to identify malignant gastric lesions with fairly high sensitivity and reasonable accuracy. Malignancies with inherently low ^{18}F-FDG avidity are the main cause of false negatives while active gastritis is the main cause of false positives.

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1. Introduction

Physiological gastric fluorine-18-fluorodeoxyglucose (^{18}F-FDG) uptake is a common phenomenon encountered on ^{18}F-FDG positron emission tomography/computed tomography (PET/CT), especially noted at the gastroesophageal junction (GEJ), and gastric antrum (GA) [1–3]. This inhomogeneous physiological gastric mural ^{18}F-FDG uptake may influence the diagnosis of a malignant gastric tumor [4].

As in a fasting state, the stomach is collapsed and wall is thickened; ingestion of water reduces the wall thickness, and tumor involvement of the gastric wall can be visualized more accurately in CT studies [5]. In a similar way, water intake just before ^{18}F-FDG PET/CT scanning will result in gastric distention and thinning of the gastric wall, which in turn may lead to a reduction in the physiological ^{18}F-FDG uptake in the gastric wall [4,6].

In addition to the patient-to-patient variation in the physiological gastric ^{18}F-FDG uptake, the presence of mucosal inflammation, subclinical infection with Helicobacter pylori, or secondary effects of chemotherapeutic agents are potential causes of this variable gastric ^{18}F-FDG uptake [7,8].

Again, many clinicopathologic factors including the location, histopathological type, size, and depth of invasion of the primary tumor were independently related to ^{18}F-FDG uptake in gastric neoplasms [9]. Some histological subtypes of gastric cancer including signet-ring cell adenocarcinoma, mucinous adenocarcinoma, and poorly differentiated adenocarcinoma, have been shown to have significantly lower ^{18}F-FDG avidity [10,11]. Thus, the usefulness of conventional ^{18}F-FDG PET/CT imaging for evaluating and differentiating malignant and benign gastric lesions is limited [11–13].

Multiple recent studies have shown that Dual-time point (DTP) ^{18}F-FDG PET/CT may provide more help in the differentiation of malignant lesions from benign ones [14,15], but few has addressed the use of DTP ^{18}F-FDG PET/CT together with water gastric distension to assess gastric lesions.

The purpose of this study was to assess diagnostic accuracy and added value of DTP ^{18}F-FDG PET/CT after gastric distention using oral water in differentiating malignant from benign gastric lesions.

2. Materials and methods

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and its later amendments.

2.1. Patients

Following approval by the institutional ethics committee, ^{18}F-FDG PET/CT scans of 30 patients who underwent DTP ^{18}F-FDG PET/CT protocol after gastric distention using oral water due to suspicious or ^{18}F-FDG avid gastric lesions were retrospectively reviewed. All patients were known or suspected oncology patients including 19 males and 11 females; mean age was 58.6 ± 16.4 years).

2.2. Dual-phase ^{18}F-FDG PET/CT image acquisition and reconstruction

All patients underwent whole body ^{18}F-FDG PET/CT scan and 2 h delayed PET/CT abdominal images following oral water gastric distension.

Early whole body ^{18}F-FDG PET/CT (E) was acquired at 60 min (range, 45–76 min; mean, 61.7 ± 9.1 min), and delayed limited ^{18}F-FDG PET/CT (D) on the abdomen was acquired at 120 min (range, 108–153 min; mean, 126.2 ± 12.6 min) after the tracer injection after drinking 500 mL water for gastric distension. All imaging and data acquisition were performed using a Gemini TF 16 slice PET/CT scanner with patient port of 70 cm (Philips Medical Systems). The patients fasted except for water for 4−6 hours, and had blood glucose levels <165 mg immediately prior to IV administration of approximately 5.18 MBq/kg (0.14 mCi/kg) of ^{18}F-FDG, with a maximum dose of 444 MBq (12 mCi) of ^{18}F-FDG. During the subsequent 40−60 min following injection (uptake phase), patients were advised to remain seated or recumbent calmly in a quiet room, covered with a blanket to avoid uptake of the radiotracer at physiological sites as brown fat, which can result in image artifacts.

During image acquisition patients were instructed to avoid motion and were allowed to breathe normally without specific instructions. Emission data were acquired for 11–14 bed positions. Emission scans were acquired in a three-dimensional (3D) mode at 1 min/bed position and increased up to 2 or 3 min/bed position in case of obese patients according to patient's body mass index (BMI). The 3D whole body acquisition parameters consisted of a 128 × 128 matrix and an 18 cm FOV with a 50 % overlap. An imaging field of view (FOV) from the base of the skull to mid-thigh with the arms above the head whenever possible was used or otherwise the arms were positioned over the chest. Low dose CT scans were used for attenuation correction purposes and to help in anatomic localization of ^{18}F-FDG uptake.

The CT scan was performed as a single sweep adjusted to 120−140 kV, 50−100 mA (based on BMI), 0.5 s per CT rotation, pitch - 1.675:1, slice thickness of 5 mm and 512 × 512 matrix. CT acquisition was performed before the emission acquisition. CT data were used for image fusion and the generation of the CT transmission map. No intravenous contrast was used.

2.3. Image analysis and semi-quantitative evaluation

Visual and semi-quantitative analysis were performed on both early and delayed images. All ^{18}F-FDG PET/CT scans in our study population were reviewed by two nuclear medicine physicians. Any suspicious ^{18}F-FDG avid gastric lesion in ^{18}F-FDG PET/CT was evaluated and either correlated with biopsy in 18 patients (60 %) or with clinical and follow-up imaging (^{18}F-FDG PET/CT, CT or magnetic resonance imaging [MRI]) in 12 patients (40 %) and recorded and tabulated. Localized uptake pattern in delayed images post water oral contrast, early maximum standardized uptake value (SUVmax1), delayed SUVmax (SUVmax2) and interval changes in SUVmax (ΔSUVmax) between early (E) ^{18}F-FDG PET/CT at 60 min post injection and delayed (D) limited ^{18}F-FDG PET/CT of abdomen at 120 min post injection following oral water gastric distension were recorded.

In the current study the pattern of uptake in ^{18}F-FDG avid lesions was analyzed as follows:

- True Positive (TP): if the lesion show localized uptake pattern in delayed images post water oral contrast, and confirmed to be malignant on biopsy.
- False Positive (FP): if the lesion show localized uptake pattern in delayed images and there was no evidence of malignancy on biopsy or follow-up.
- True Negative (TN): if the lesion did not show localized uptake pattern in delayed images and there was no evidence of malignancy on biopsy or follow-up.
- False Negative (FN): if the lesion did not show localized uptake pattern in delayed images and confirmed to be malignant on biopsy.

2.4. Statistical analysis

All data were analyzed using SPSS software (SPSS 20.0) and MedCalc version 11 software (MedCalc, Mariakerke, Belgium). Data are presented as mean and standard deviation (SD) (mean ± SD). The best cut off values for early SUVmax (SUVmax1), delayed SUVmax (SUVmax2) and SUVmax2-SUVmax1 (ΔSUVmax) to differentiate benign from malignant lesions were set based on ROC analysis. Data analyzed included in addition; age, sex and ^{18}F-FDG uptake pattern in delayed images

(localized versus diffuse).

Suspicious gastric lesions were correlated with biopsy in 18 patients (60 %) and with clinical and follow-up imaging (^{18}F-FDG PET/CT, CT or MRI) in 12 patients (40 %). Only histopathology is accepted as a proof of malignancy.

Unpaired *t*-test was used to compare the mean deference in continuous variables between patients with gastric malignancy and those with benign gastric lesions. Fisher's exact test was used to analyze categorical variables. The sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy of localized uptake pattern in delayed images post water oral contrast, early SUVmax (SUVmax1), delayed SUVmax (SUVmax2) and (ΔSUVmax) in differentiation between malignant and benign lesions were calculated. Logistic regression analysis was performed to identify the most powerful parameters to predict malignant lesions. Forward stepwise method was performed with entry significance level set to $p < 0.05$ and removal significance level set to $p > 0.10$. A P value <0.05 was considered statistically significant.

3. Results

Fifteen patients (50 %) had confirmed malignant gastric lesions including 8 cases (26.67 %) with gastric adenocarcinoma, 4 cases (13.33 %) with gastric lymphoma, 2 cases (6.67 %) with metastatic lesions and one case (3.33 %) with gastrointestinal stromal tumor (GIST) (Fig. 1).

Patients with confirmed gastric malignancy were older (65 ± 13 vs 52 ± 17; $p = 0.023$) and had significantly higher mean ΔSUVmax (1.29 ± 1.76 vs −0.89 ± 1.59; $p = 0.003$). The mean SUVmax1 (6.99 ± 6.66 vs 5.31 ± 2.53; $p = 0.367$) and SUVmax2 (8.29 ± 7.41 vs 4.44 ± 3.34; $p = 0.077$) although both higher in patients with malignant lesions, they did not reach statistical significance.

ROC analysis yielded a ΔSUVmax >0 as an optimal cut-off to identify malignant lesions with area under the curve (AUC) of 0.8240 (95 % CI 642 to 0.938, $p = 0.0003$). The cut-off for the SUVmax2 to detect malignant lesions was 4.1 with AUC of 0.733 (95 % CI 0.560 to 0.889, $p = 0.0054$). The best cut-off for SUVmax1 to detect malignant lesions was 5.5, however was poor to discriminate between malignant and benign gastric lesions with AUC of 0.542, (95 % CI 0.352 to 0.724, $p = 0.692$). The presence of localized uptake pattern in delayed images post gastric distension was more superior in differentiating between malignant and benign lesions with AUC of 0.833, (95 % CI 0.61 to 0.92, $p = 0.0001$).

Sensitivity, specificity, PPV, NPV, and accuracy to detect malignant gastric lesions based on SUVmax1 cutoff >5.5, SUVmax2 cutoff >4.1, ΔSUVmax cutofff >0 and localized uptake pattern are shown in Table 2 with highest accuracy for lesions with localized uptake pattern in delayed images post water oral contrast followed by ΔSUVmax>0.

Comparison of ROC curves for SUVmax1 > 5.5, SUVmax2 > 4.1, ΔSUVmax cutoff >0 and presence of localized uptake pattern as binary variables in differentiating malignant from benign lesions is shown in Fig. 2. The last 3 variables revealed highly significant p-values in differentiating benign from maligant lesions with frequency of patients in each category demonstrated in Fig. 3.

Variables tested in this regression analysis model included SUVmax1 > 5.5, SUVmax2 > 4.1, ΔSUVmax >0 and presence of localized uptake pattern in delayed images post water oral contrast. The final regression model revealed both the localized uptake pattern and ΔSUVmax >0 as independent predictors for malignant lesions with odd ratios of 22.9 and 9.5 respectively and final model Chi-Square of 19.9 ($p < 0.0001$) (Table 3). The model correctly identified 12/15 (80 %) malignant lesions (Fig. 4) and 13/15 (86.7 %) benign lesions corresponding to sensitivity, specificity, PPV, NPV and an overall accuracy of 80.0 %, 86.7 %, 85.75, 81.3 % and 83.3 % respectively, with 3 false negatives including 1 signet ring gastric cancer and 1 low grade GIST tumor (Fig. 5), both known by frequent association with poor ^{18}F-FDG uptake while only 2 false positives were identified and confirmed as chronic active gastritis with helicobacter pylori (Fig. 6).

4. Discussion

A remarkable number of publications have described the added value of ^{18}F-FDG PET/CT in differentiating malignant from benign lesions in cancer patients [14–19]. However, differentiation between malignant and benign gastric lesions can represent a diagnostic challenge and is particularly difficult in cancer patients, who frequently have a history of gastritis, subclinical infection with Helicobacter pylori, or secondary effects of chemotherapeutic agents [7,8].

Difficult evaluation of the stomach especially if it is contracted on conventional ^{18}F-FDG PET/CT requires some novel modifications to the standard oncologic protocol to reduce the number of false-positive or false negative results, predominantly related to physiological gastric wall or mucosal uptake. Expanding the stomach with gas, liquids, diluted barium or foods are simple and rapid methods that had been

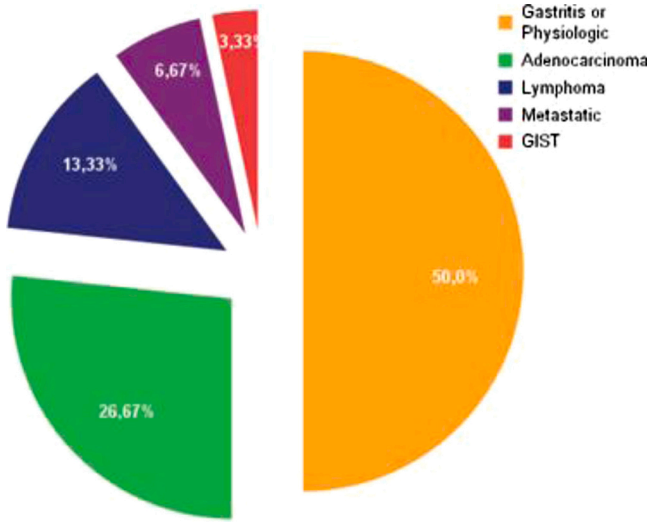

Fig. 1. Nature of Detected Gastric lesions.

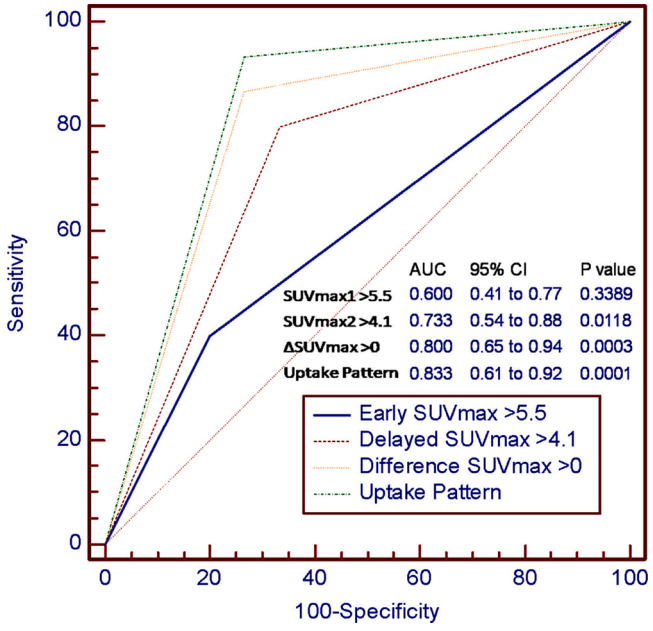

Fig. 2. Comparison of ROC curves for SUVmax1 cutoff >5.5, SUVmax2 cutoff >4.1, ΔSUVmax cutoff >0 and localized uptake pattern as binary variables in differentiating malignant from benign lesions.

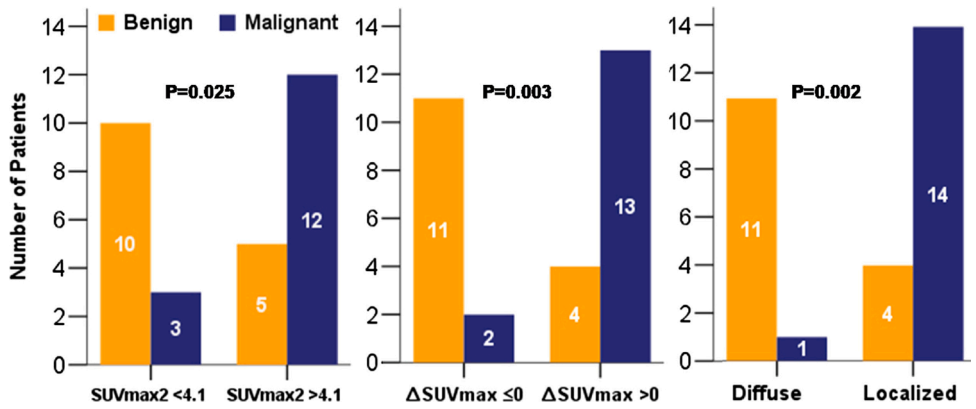

Fig. 3. Stratification of gastric lesions based on post gastric distension uptake pattern, ΔSUVmax>0 and SUVmax2 > 4.1 (p-values for Fisher's Exact test).

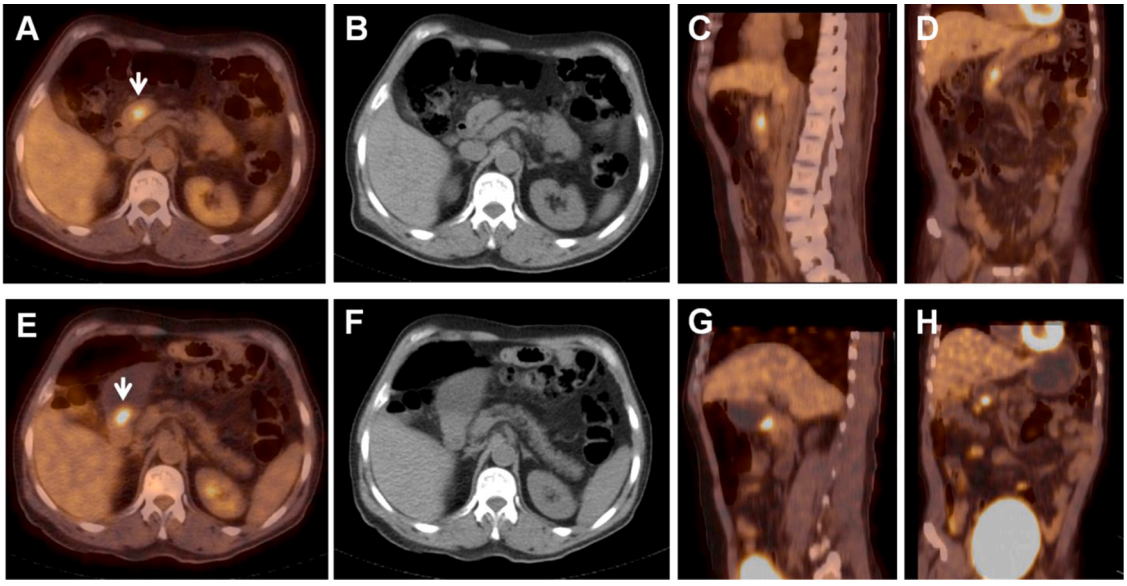

Fig. 4. 59 years old male with gastric carcinoma of distal stomach (moderately differentiated adenocarcinoma intestinal type). Early PET/CT images (upper panel) revealed a gastric pyloric FDG avid focal lesion (arrows) with SUVmax of 5.7 that increased to 6.9 in post gastric distension delayed images (lower panel).

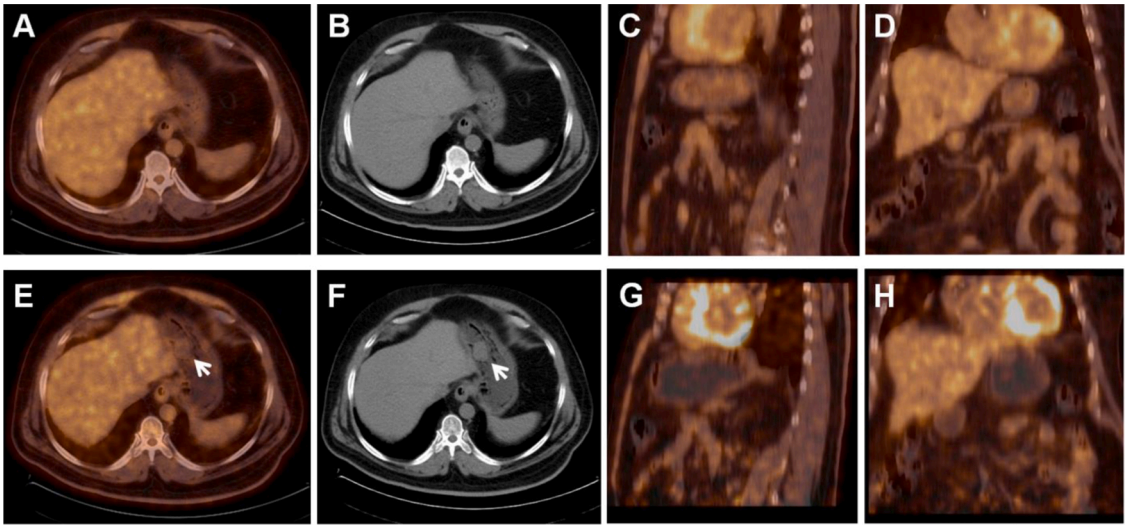

Fig. 5. 69 years old male with recently discovered gastric mass. Early PET/CT (upper panel) revealed no obvious gastric lesion. A non-FDG avid lesion (arrows) became visible at lesser curvature in gastric distension delayed images (lower panel). A well defined submucosal lesion seen on low dose CT (F). Biopsy revealed low grade GIST tumor.

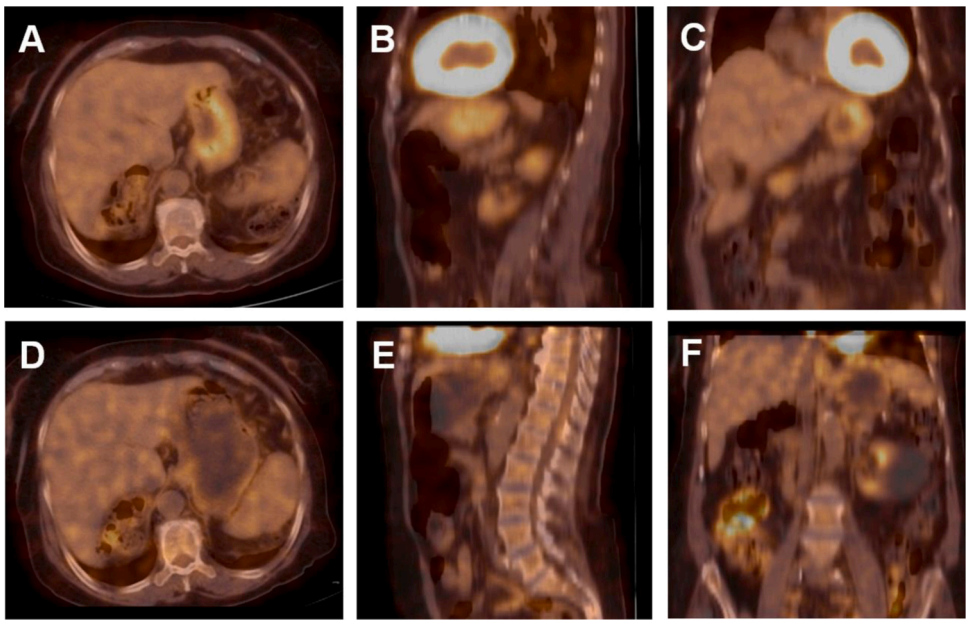

Fig. 6. 77 years old female with history of treated right heel melanoma. Early PET/CT images (A, B & C) revealed diffusely increased gastric FDG uptake that significantly decreased in post gastric distension delayed images (D, E & F). Endoscopic biopsy indicated moderate degree of chronic active gastritis with Helicobacter Pylori.

utilized to achieve gastric distention, thinning of the gastric wall and to reduce the physiological ^{18}F-FDG uptake in the gastric wall [4,6,20–23]. These maneuvers help to delineate the lesions more clearly, however the improvement in diagnostic accuracy is still controversial [23,24].

Other approaches have tried to use pharmaceutical intervention to reduce ^{18}F-FDG uptake of the gastric wall. However, the potential effects of these medications on uptake of ^{18}F-FDG by the stomach and other organs are still not well defined [25,26].

The usefulness of DTP ^{18}F-FDG PET/CT protocol in differentiation of malignant from benign lesions has been reported in some studies of certain body regions and certain cancer types [15,27–29]

In the present study we are evaluating the usefulness of both visual and quantitative parameters related to DTP ^{18}F-FDG PET/CT after gastric distention using oral water, in differentiating malignant from benign gastric lesions. Such parameters included the lesional uptake pattern, early SUVmax (SUVmax1), delayed SUVmax (SUVmax2) and difference in SUVmax between early and delayed imaging (ΔSUVmax).

The AUCs of localized uptake pattern in delayed images, ΔSUVmax, and SUVmax2 were greater than that of SUVmax1. Localized uptake pattern in delayed images, and ΔSUVmax, had the largest AUC and higher overall accuracy respectively among the four indices. Table 1 summarizes these results and shows that the localized uptake pattern in delayed images post water oral contrast followed by ΔSUVmax were the best parameters to differentiate benign from malignant lesion. As binary variables SUVmax2 > 4.1, ΔSUVmax >0 and localized uptake pattern were all statistically significant in differentiating benign from malignant lesions on the contrary to SUVmax1 > 5.5 which did not reach statistical significance (Table 2 and Fig. 2).

Table 1
Comparison of clinical characteristics and PET metabolic parameters between patients with malignant gastric lesions and benign lesions.

	Confirmed gastric malignant lesions	No gastric malignancy	p-value
Age	65 ± 13	52 ± 17	0.023
Sex			
Male	9 (47.4 %)	10 (52.6 %)	1.000
Female	6 (54.5 %)	5 (45.5 %)	
Mean SUVmax1	6.99 ± 6.66	5.31 ± 2.53	0.367
Mean SUVmax2	8.29 ± 7.41	4.44 ± 3.34	0.077
Mean ΔSUVmax	1.29 ± 1.76	0.89 ± 1.59	0.003
Localized Uptake Pattern	14 (73.7 %)	5 (26.3 %)	0.0001

According to our results, the early SUVmax as a binary variable (SUVmax1 > 5.5) had high false negative rate, poor sensitivity, PPV, NPV and overall accuracy though with relatively high specificity. This high false negative rate and poor sensitivity can be related to two main factors: First the high physiological uptake within the contracted gastric wall, probably masking low or moderately hypermetabolic neoplastic lesions and second the histopathological factors affecting the visibility of gastric cancers on ^{18}F-FDG PET/CT. The underestimated ^{18}F-FDG uptake due to a partial volume averaging effect on PET/CT as a result of small tumor size in early gastric cancer is an important reason [9]. Cancer cells have accelerated metabolism and high glucose requirements. The up-regulation of specific glucose transporters may represent a key mechanism by which malignant cells may achieve increased glucose uptake to support the high rate of glycolysis [30]. Kawamura et al. [31] reported that the expression level of glucose transporter-1 (GLUT-1) protein in stomach carcinomas was 30 %, and its expression in signet ring cell carcinoma and mucinous adenocarcinoma was especially low at 2 % and 6 %, respectively. Hence, low ^{18}F-FDG uptake is more often seen in signet ring cell and mucinous types of gastric cancer [32]. Also poorly-differentiated types of gastric cancers show low ^{18}F-FDG uptake [33] as a result of the reported lower GLUT-1 expression levels in poorly-differentiated types of gastric cancers than that in moderately and well-differentiated types [34]. Furthermore, Borrmann type IV gastric cancer often undiagnosed on ^{18}F-FDG PET/CT due to the abounding mucin content [35]. Other tumors such as low-grade neuroendocrine, lymphomas and carcinoids as well as extensive superficial lesions, such as those with central necrosis may have a low ^{18}F-FDG uptake [1,36]. Moreover, several studies reported a lower ^{18}F-FDG -avidity and a lower SUV for diffuse subtype gastric cancer than for tumors of the intestinal type [11,37–41]. A lower delectability of tumors in the proximal and middle thirds of the stomach had also been described due to the higher incidence of diffuse type tumors at these locations while more incidence of intestinal type tumors in distal third [9].

Table 2
Results of the 4 stratification methods to detect malignant gastric lesions.

	Sens.	Spec.	PPV	NPV	Acc.	TP	TN	FP	FN	p-value
Localized Uptake	93.3 %	73.3 %	77.8 %	91.7 %	80.0 %	14	10	5	1	0.002
ΔSUVmax>0	86.7 %	73.3 %	76.5 %	84.6 %	80.0 %	13	11	4	2	0.003
SUVmax2 > 4.1	80.0 %	66.7 %	70.8 %	76.9 %	73.3 %	12	10	5	3	0.025
SUVmax1 > 5.5	40.0%	80.0 %	66.7 %	57.1 %	60.0 %	6	12	3	9	0.427

Table 3
Regression model for prediction of malignant lesions.

Variable	Coefficient	Std. Error	Odds Ratio (95 % CI)	p-value	Total Model χ^2	p-value
ΔSUVmax>0	2.2565	1.1347	9.549 (1.033–88.289)	0.0468	19.889	P < 0.0001
Uptake Pattern	3.1317	1.2749	22.913 (1.883–278.779)	0.0140		
Constant	−3.4190					

In our study, the sensitivity of early ^{18}F-FDG PET/CT (SUVmax1 > 5.5) in differentiating malignant from benign gastric lesions was 40 %, and specificity was 80 % with AUC of only 0.600 (95 % CI 0.41−0.77, p = 0.3389). There has been a wide range of reported ^{18}F-FDG PET/CT sensitivities (21 %–100 %) and specificities (78 %–100 %), for detection of gastric cancer [11–14,37,42–46], probably related to variations in imaging techniques, physiological and histopathological factors affecting the visibility of gastric tumors on ^{18}F-FDG PET/CT.

Cui et al. studied the value of DTP ^{18}F-FDG PET/CT imaging following water drinking in differentiating malignancy from benign gastric disease and reported sensitivity, specificity, and AUC of 65.2 %, 64.3 % and 0.635 (95 % CI 0.507–0.764) respectively on early imaging, which is comparable to our findings, but they reported numerous benign cases had increased ^{18}F-FDG uptake indistinguishable from that of malignancy; and again they did not find an acceptable SUVmax cut-off value on early imaging [14].

Our study showed improved sensitivity, PPV, NPV, and overall accuracy to detect malignant gastric lesions on the delayed ^{18}F-FDG PET/CT images after gastric distention using oral water contrast, with the highest accuracy for lesions with localized uptake pattern in delayed images as well as for lesions with more tracer retention (ΔSUVmax>0). This is probably due to better delineation of the gastric lesions on the delayed images as a result of gastric distention and thinning of the gastric wall, reduction in the physiological ^{18}F-FDG uptake in the gastric wall and probably more ^{18}F-FDG retention by malignant lesions compared to benign lesions.

Considerable overlap between the SUVmax of malignant and benign lesions had been previously reporting, causing frequent false positive results on conventional F-^{18}F-FDG PET/CT imaging [47–49]. Fortunately, malignant and inflammatory lesions exhibit a differential ^{18}F-FDG uptake pattern over time. The high hexokinase/phosphatase ratio in malignant cells with relatively decreased expression of glucose-6-phosphatase, results in gradual ^{18}F-FDG uptake by malignant cells [50]. In contrast, mononuclear cells, which represent the major cell population in chronic inflammation and infection, express high levels of glucose-6-phosphatase [51] and therefore, ^{18}F-FDG -6-phosphate can be rapidly dephosphorylated and cleared after reaching a certain level [50]. Consequently, most malignant lesions will have increased ^{18}F-FDG uptake on delayed imaging, leading to a higher lesion-to-background ratios, and higher sensitivity in comparison to inflammatory lesions [52]. Based on these differences between malignant and inflammatory cells, the DTP ^{18}F-FDG PET/CT protocol have gained a considerable interest in the recent literature as an important approach to improve the diagnostic performance of ^{18}F-FDG PET/CT in differentiating malignant from benign lesions [53].

In our study, there was significant improvement of sensitivity, overall accuracy and AUC in the delayed ^{18}F-FDG PET/CT images after gastric distention using oral water contrast to 80 %, 73.3 % and 0.733 (95 % CI 0.54–0.88, p = 0.0118) respectively with SUVmax cut-off of 4.1 on delayed images. Further improvement of sensitivity, overall accuracy and AUC in the delayed ^{18}F-FDG PET/CT images to 86.7 %, 80 %, and 0.800 (95 % CI, 0.65–0.94, p = 0.0003) when the retention parameter ΔSUVmax>0 was used for analysis, and to 93.3 %, 80 %, and 0.833 (95 % CI, 0.61–0.92, p = 0.0001) when localized uptake pattern was used for analysis. Again, Cui et al. reported that the sensitivity and AUC had significant improvement to 86.7 % and 0.873 (95 % CI, 0.786–0.961) in delayed images; which is similar to our findings [14]. Also, our findings were concordant with those reported by Xu et al. who studied the value of DTP ^{18}F-FDG PET/CT in differentiation of malignant from benign gastrointestinal diseases and found significantly higher accuracy of DTP ^{18}F-FDG PET/CT imaging than that of single-time point ^{18}F-FDG PET/CT imaging. They also found that the SUVmax in delayed imaging was significantly higher in malignant lesions than those in early imaging, while no significant differences between early and delayed SUVmax for benign lesions. The ΔSUVmax were also significantly higher for malignant lesions than for benign ones [54]. On the other hand, it had been reported that some inflammatory, granulomatous and active infectious diseases may show higher ^{18}F-FDG uptake on delayed PET imaging, similar to malignant lesions, possibly due to ^{18}F-FDG -avidity of activated inflammatory cells involved [55].

On multivariate analysis, a regression model including both the localized uptake pattern and ΔSUVmax >0 as independent predictors, had further boosted the specificity and overall accuracy of delayed imaging to detect malignant lesions. The current study is one of few studies to assess diagnostic accuracy and added value of DTP ^{18}F-FDG PET/CT following gastric distention using oral water contrast in differentiating malignant from benign gastric lesions. Importantly, unlike previous studies that had emphasized only on evaluation of quantitative and/or visual parameters individually to assess the value of DTP ^{18}F-FDG PET/CT following gastric distension, the current study, in addition incorporated both quantitative and visual parameters into multivariate analysis in order to identify the best predictive model for gastric malignancy.

4.1. Limitations

First, the retrospective design of the study may render selection bias unavoidable. Second, this is a single-center study with a limited number of subjects, probably due to exclusive application of the current imaging technique in patients with controversial early images. Third, the degree of chronic atrophic gastritis was not separately evaluated in current study, because the endoscopic diagnosis was qualitative and operator dependent. Further prospective multi-center studies using both DTP ^{18}F-FDG PET/CT after gastric distention using oral water contrast as well as upper gastrointestinal endoscopy in a larger group of patients, may be considered to validate our findings in order to avoid unnecessary more invasive procedures.

5. Conclusion

Localized uptake pattern in delayed ^{18}F-FDG PET/CT images following gastric distention with oral water contrast as well as ΔSUVmax>0 as an indicator of tracer retention are both powerful independent predictors of malignant gastric lesions with fairly high sensitivity and reasonable accuracy, especially if combined. Malignancies with inherently low ^{18}F-FDG avidity were the main cause of false negatives while active gastritis was the main cause of false positives.

Declaration of Competing Interest

The authors report no declarations of interest.

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