Comparison of ^{68}Ga-FAPI-04 and ^{18}F-FDG for the Detection of Primary Gastric Cancers and Metastasis

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Research Article

Keywords: Gastric adenocarcinoma, Signet ring cell carcinoma, Fibroblast activation protein, Cancer-associated fibroblasts, 68Ga-FAPI-04

Posted Date: March 22nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-326617/v1

Version of Record: A version of this preprint was published at European Journal of Nuclear Medicine and Molecular Imaging on July 23rd, 2021. See the published version at https://doi.org/10.1007/s00259-021-05441-w.

Abstract

Introduction Early and precise diagnosis and staging of gastric cancer are important for its treatment and management. However, the low sensitivity of ^{18}F-fluorodeoxyglucose (^{18}F-FDG) for gastric cancer diagnosis limits its application. Currently, the tracer ^{68}Ga-FAPI, which targets fibroblast activation protein (FAP), is widely used to diagnose various cancers. However, the diagnostic value of ^{68}Ga-FAPI in gastric cancer is still unclear. In this study, we aimed to investigate the potential advantage of ^{68}Ga-FAPI-04 over ^{18}F-FDG in the evaluation of gastric cancer.

Methods: Thirty-eight patients with gastric cancer (31 with adenocarcinoma and 7 with signet ring cell carcinoma) were recruited for this study. All of the participants underwent ^{68}Ga-FAPI-04 and ^{18}F-FDG imaging by positron emission tomography (PET)/computed tomography (CT) or PET/magnetic resonance (MR). The results were interpreted by two experienced nuclear medicine physicians, and the maximum standardized uptake value (SUV_{max}) was calculated.

Results: For the detection of primary gastric cancer, the sensitivities of ^{68}Ga-FAPI-04 PET and ^{18}F-FDG PET were 100% (38/38) and 81.6% (31/38), respectively. Four cases of adenocarcinoma and three cases of signet ring cell carcinoma were missed by ^{18}F-FDG PET. The SUV_{max} of ^{68}Ga-FAPI-04 in tumors greater than 4 cm (11.0 ± 4.5) was higher than tumors less than 4 cm (4.5 ± 3.2) (P = 0.0015). The SUV_{max} of ^{68}Ga-FAPI-04 was higher in T2-4 tumors (9.7 ± 4.4) than in T1 tumors (3.1 ± 1.5) (P = 0.0002). For the detection of metastatic lesions, the sensitivities of ^{68}Ga-FAPI-04 PET and ^{18}F-FDG PET in 10 patients with regional lymph node metastasis and distant metastasis were 6/10 and 5/10, respectively.

Conclusion: Compared to ^{18}F-FDG PET, ^{68}Ga-FAPI-04 PET had superior potential in detecting primary gastric cancers and metastatic lymph nodes, ^{68}Ga-FAPI-04 PET also had a better performance on small gastric cancer detection. ^{68}Ga-FAPI-04 PET could provide better performance for gastric cancer diagnosis and staging.

Introduction

Gastric cancer is one of the most common malignant tumors, with a poor prognosis in East Asia and the USA [1, 2]. Although the diagnosis and treatment of gastric cancer have improved, the prognostic outcome remains suboptimal. Early diagnosis, accurate staging and quantitative evaluation of gastric cancer are important for its treatment, management, and prognosis. In the clinic, gastroscopy and imaging examinations are the main diagnostic methods for gastric cancer. Computed tomography (CT) and magnetic resonance imaging (MRI) have been used for the primary staging of gastric cancer. However, CT and MRI are anatomy-based imaging techniques that have been inadequate in staging, such as lymph node involvement and distant metastasis [3].

Positron emission tomography (PET) using ^{18}F-fluorodeoxyglucose (^{18}F-FDG) has been used in various cancer diagnoses and in gastric cancer detection [4, 5]. However, up to 53% of primary tumors in gastric cancer are not avid for ^{18}F-FDG [6, 7]. Furthermore, low sensitivity in detecting lymph node metastasis limits the use of ^{18}F-FDG in gastric cancer diagnosis [7]. Signet ring cell carcinoma and mucinous carcinoma also show lower ^{18}F-FDG uptake and sensitivity than conventional adenocarcinoma [8-10]. Therefore, new tracers such as 3'-deoxy-3'-^{18}F-fluorothymidine (^{18}F-FLT) have been developed for gastric cancer [7, 11]. Since the lower uptake of ^{18}F-FLT in gastric cancer, this tracer is not applied in clinical practice.

Currently, fibroblast activation protein (FAP), which is highly expressed in the cancer-associated fibroblasts (CAFs) of many malignant tumors, is used as a new target for tumor tracer development since CAFs are one of the most abundant stromal components in the tumor microenvironment [12]. Several tracers targeting FAP have been developed, among which ^{68}Ga-FAPI-04 is the most promising, with high affinity towards FAP and suitable kinetics [13-15]. ^{68}Ga-FAPI-04 PET has achieved good outcomes for the diagnosis and staging of several tumor types [12, 16-18]. Moreover, previous studies have shown that FAP is overexpressed in the CAFs of gastric cancer and plays an important role in the invasion and migration of gastric carcinomas [19, 20]. ^{68}Ga-FAPI-04 PET was used to image primary gastric carcinoma and metastatic lesions in one patient [21]. However, no research has reported the potential advantage of ^{68}Ga-FAPI-04 in gastric cancer diagnosis and the difference between ^{68}Ga-FAPI-04 and ^{18}F-FDG.

The aim of this study was to assess the potential advantage of ^{68}Ga-FAPI-04 PET over ^{18}F-FDG in the diagnosis of gastric cancer and to investigate the performance of ^{68}Ga-FAPI-04 in detecting lymph node metastasis in patients with gastric cancer.

Materials And Methods

Patients

Forty patients with gastric cancer were enrolled in this study. Two patients with gastric cancer recurrence were excluded. The rest 38 patients were confirmed by pathological biopsy under gastroscopy (Fig. 1). All patients received both ^{18}F-FDG and ^{68}Ga-FAPI-04 PET/CT or PET/MR for tumor staging on separate days and had no antitumor treatment prior to PET scans. Twenty-nine patients received both ^{18}F-FDG and ^{68}Ga-FAPI-04 PET/MR, and 9 patients received PET/CT. Patients with recurrent tumors, aged less than 18 years, or pregnant women were excluded from the study. This project was approved by the ethics committee in Huashan Hospital, Fudan University and Shanghai East Hospital, Tongji University School of Medicine, and all enrolled patients signed informed consent forms.

Radiopharmaceuticals and imaging protocols

^{18}F-FDG and ^{68}Ga-FAPI-04 were prepared as described previously [16, 22, 23], and both tracers were synthesized in the Radiochemistry Facility of the PET Center, Huashan Hospital, Fudan University, under a

GMP environment.

PET/MR (uPMR790 TOF, United Imaging, China) or PET/CT (Biograph mCT, Siemens Healthineers, Germany; Ingenuity TF, Philips Healthcare, USA; uMI510, United Imaging, China) scanners were used in this study. Since different scanners were applied in this study, standardized uptake value (SUV) measurements generated by different devices were normalized after data collection. A NEMA IEC body phantom (Data Spectrum Corporation, Durham, NC, USA) with 6 simulated lesion spheres (diameters: 10 mm, 13 mm, 17 mm, 22 mm, 28 mm, and 37 mm) was applied for SUV normalization with 2, 4, 8, and 16 times the background activity (background activity concentration equal to 2 kBq/ml). The CT template of the NEMA IEC body phantom was prepared for the attenuation correction of PET/MR. Images of the phantom were acquired in each scanner with its own routine protocols. Correlation coefficients for the SUV were obtained through this phantom study and used to standardize the SUV measurements to those measured with Siemens Biograph mCT.

^{18}F-FDG PET/CT or PET/MR was performed based on routine procedures for ^{18}F-FDG PET tumor imaging [24]. Whole-body ^{68}Ga-FAPI-04 PET scans were obtained by PET/MR or PET/CT at 60 min after the intravenous injection of 111~ 185 MBq (3~5 mCi) of ^{68}Ga-FAPI-04 [12, 25]. A low-dose CT scan (120 keV, 100-120 mA) or an MR scan was collected for attenuation correction and image fusion. PET images were acquired in 3D mode and were reconstructed by the ordered subset expectation maximization 3D (OSEM 3D) method. The two PET scans were performed within 48 hours apart (1.6 ± 0.8 days, range: 1-2 days).

Data analysis

For calculation of the maximum SUV (SUV_{max}), circular regions of interest were drawn around the tumors on transaxial slices and automatically adapted to a three-dimensional VOI with Syngo.via software (Siemens Molecular Imaging, Hoffman Estates, Illinois, USA) at a 60% isocontour. The results of ^{68}Ga-FAPI-04 PET and ^{18}F-FDG PET scans were independently evaluated by 2 experienced nuclear medicine physicians (JZ and FH) who were blinded to the clinical data and pathologic findings. Any difference of opinion between these two physicians was resolved by a consensus. For primary tumors and metastatic lesions, positive uptake was identified as areas of focal increase compared to surrounding normal tissue by a visual assessment supported by the ratio of suspicious lesions to surrounding normal tissue [16, 26].

Immunohistochemistry of FAP expression

Immunohistochemical staining of FAP was performed on the tumor tissue obtained after surgical resection in one patient with adenocarcinoma. An antibody against FAP (ab207178, Abcam) was used.

Statistical analysis

Statistical analysis was performed using Prism 7 (GraphPad Software, CA, USA) and STATA (version 15.1 StataCorp LLC) software. The comparisons of sensitivity, specificity, and accuracy for detection of gastric cancer between ^{18}F-FDG and ^{68}Ga-FAPI-04 were using the McNemar's test. Categorical variables are

described as frequencies and percentages. Continuous variables are described as the mean ± standard deviation (SD). The Mann-Whitney U test was used to compare the SUV_{max} between different categorized groups. A *P* value less than 0.05 was considered statistically significant.

Results

Patients

The clinical characteristics of the 38 patients are shown in Table 1 and Supplementary Table 1. Among 38 patients with gastric cancer (29 men and 9 women; age 63.7 ± 15.3 years; age range, 25–86 years) whose diagnosis was confirmed by pathological biopsy under gastroscopy, 31 had adenocarcinoma and 7 had signet ring cell carcinoma. After the PET evaluation, 24 patients (19 with adenocarcinoma and 5 with signet ring cell carcinoma) received surgical treatment, while the other patients received chemotherapy. Among 24 patients treated with surgery, 10 (9 with adenocarcinoma and 1 with signet ring cell carcinoma) were confirmed pathologically with regional lymph node metastasis after surgical resection. According to the depth of tumor invasion based on examination of the surgical specimen after resection, 12 patients were classified as T1 (tumor invading the lamina propria, muscularis mucosae, or submucosa), 3 patient was classified as T2 (tumor invading the muscularis propria), and 9 patients were classified as T4 (tumor invading the visceral peritoneum or adjacent structures). According to the maximum tumor diameter, 17 patients had a small tumor (≤ 4 cm in diameter), and 7 patients had a large tumor (> 4 cm in diameter). According to the histologic grade, 1 patient had a well-differentiated tumor, 15 patients had a moderately differentiated tumor, and 8 patients had a poorly differentiated tumor (4 adenocarcinomas and 4 signet ring cell carcinomas).

Diagnostic performance of ^{68}Ga-FAPI-04 and ^{18}F-FDG PET

For the detection of primary gastric cancer, the sensitivities of ^{68}Ga-FAPI-04 PET and ^{18}F-FDG PET were 100% and 82% (38/38 vs. 31/38, $P = 0.016$), respectively. The sensitivity of ^{68}Ga-FAPI-04 PET and ^{18}F-FDG for detection of tumors less than 4 cm were 100% and 70% (17/17 vs. 12/17, $P = 0.062$). ^{68}Ga-FAPI-04 PET also exhibited a sensitivity of 100% in detecting both adenocarcinoma and signet ring cell carcinoma. In contrast, four cases of adenocarcinoma and three cases of signet ring cell carcinoma were missed by ^{18}F-FDG PET.

Regional lymph node metastasis was confirmed by postsurgical pathology in 10 patients (10/24, 42%). With ^{68}Ga-FAPI-04 PET examination, 6 patients were diagnosed true positive, 13 patients true negative, 1 patient false positive and 4 false negative. And 5 patients were diagnosed true positive, 13 patients true negative, 1 patient false positive and 5 false negative with ^{18}F-FDG. For the detection of regional lymph node metastatic lesions, the sensitivity, specificity and accuracy were 60% (6/10), 93% (13/14), and 79% (19/24) for ^{68}Ga-FAPI-04, respectively, and 50% (5/10), 93% (13/14), and 75% (18/24) for ^{18}F-FDG. Comparison of the sensitivity, specificity and accuracy and of the two tracers yielded no significant difference ($P > 0.05$).

Furthermore, 3 patients showed high ^{68}Ga-FAPI-04 uptake in distant lymph nodes (2 patients with retroperitoneal lymph nodes and another patient with clavicle and mediastinal lymph nodes) and 2 patients showed focal ^{68}Ga-FAPI-04 hypermetabolism in the liver, which were considered metastases by imaging techniques, while ^{18}F-FDG uptake was neglected.

Comparison of ^{68}Ga-FAPI-04 and ^{18}F-FDG uptake

The SUV_{max} measurements of ^{68}Ga-FAPI-04 and ^{18}F-FDG in positive lesions are shown in Table 2. The SUV_{max} of ^{68}Ga-FAPI-04 in the primary tumor was similar to that of ^{18}F-FDG (7.4 ± 5.0 vs. 6.5 ± 5.7, P = 0.3536). But the tumor-to background ratio of ^{68}Ga-FAPI-04, such as SUV_{max} tumor/blood pool, in the primary tumor was significantly higher than that of ^{18}F-FDG (9.2 ± 5.9 vs. 5.9 ± 4.2, P = 0.0073). In the subgroup analysis of ^{68}Ga-FAPI-04, there was no difference of the SUV_{max} on different histologic type (P = 0.599) or tumor differentiation (P = 0.1575). The SUV_{max} of ^{68}Ga-FAPI-04 in tumors greater than 4 cm was higher than tumors less than 4 cm (11.0 ± 4.5 vs. 4.5 ± 3.2, P = 0.0015). The SUV_{max} of ^{68}Ga-FAPI-04 was higher in T2-4 tumors than in T1 tumors (9.7 ± 4.4 vs 3.1 ± 1.5, P = 0.0002). In the subgroup analysis of ^{18}F-FDG, there was no significant difference of the SUV_{max} on different histologic type (P = 0.3523). The SUV_{max} of ^{18}F-FDG in tumors greater than 4 cm was higher than tumors less than 4 cm (6.3 ± 1.8 vs. 3.6 ± 1.7, P = 0.0064). The SUV_{max} was higher in T2-4 tumors than in T1 tumors (5.6 ± 1.9 vs. 2.7 ± 0.9, P = 0.0021). The SUV_{max} in poorly differentiated tumors () was significantly higher than in well and moderately differentiated tumours (6.2 ± 2.0 vs. 3.8 ± 1.9, P = 0.032).

Immunohistochemistry

One primary tumor sample obtained from one patient with gastric adenocarcinoma was assessed for FAP expression by immunohistochemistry. Stromal cells around the tumor presented prominent FAP expression, while tumor cells showed weak FAP expression (Fig. 2). ^{68}Ga-FAPI-04 PET showed high uptake (SUV_{max} = 10.2) in the primary gastric tumor of this patient.

Discussion

Gastric cancer is one of the most common cancers and the third leading cause of cancer-related death worldwide [27]. Early and accurate diagnosis is extremely important for its treatment and prognosis. ^{68}Ga-FAPI-04 PET has achieved good outcomes for diagnosis in various tumors [12, 16-18]. These include high expression across a wide range of cancer types including several with typically low FDG-avidity, low uptake in almost all normal tissues, where high physiological uptake can obscure primary or metastatic disease [28]. However, the usefulness of ^{68}Ga-FAPI-04 for the detection of primary gastric cancer remains unclear. In this study, we aimed to evaluate the usefulness of ^{68}Ga-FAPI-04 PET for the detection of gastric cancer compared with that of ^{18}F-FDG PET.

Our results demonstrated the potential advantage of ^{68}Ga-FAPI-04 PET over ^{18}F-FDG PET for the detection of primary gastric cancer. In all 38 patients with gastric cancer, all primary tumors were detected by ^{68}Ga-FAPI-04 PET. ^{68}Ga-FAPI-04 PET (100%, 38/38) provided better sensitivity than ^{18}F-FDG PET (82%, 31/38), consistent with a previous study reporting that more positive lesions on other type of tumors were discovered with ^{68}Ga-FAPI-04 than with ^{18}F-FDG, especially in gastric cancer [29]. In the present study, ^{68}Ga-FAPI-04 PET detected signet ring cell carcinoma of the stomach in one case that was missed by ^{18}F-FDG PET (Fig. 3). Furthermore, in another patient with gastric adenocarcinoma, ^{68}Ga-FAPI-04 displayed focal uptake in the primary tumor, whereas ^{18}F-FDG showed slightly and diffusely elevated uptake in the gastric wall (Fig. 4). As a result, ^{68}Ga-FAPI-04 could provide better surgery determination for gastric cancer. Moreover, the background activity of ^{68}Ga-FAPI-04 was low, resulting in a higher tumor-to-background contrast than ^{18}F-FDG.

Previous studies have shown that the sensitivity of ^{18}F-FDG PET in the detection of gastric cancer ranges from 47% to 96% [7]. One of the reasons for this disparity may be the different histologic types of gastric cancer. ^{18}F-FDG showed lower sensitivity and uptake in signet ring cell carcinoma and mucinous carcinoma than in conventional adenocarcinoma [8-10]. This is due to the relatively low expression level of glucose transporter 1 (GLUT-1) in signet ring cell and mucinous carcinomas [30]. These results are consistent with our finding that signet ring cell carcinoma had lower ^{18}F-FDG uptake than adenocarcinoma, although the difference was not statistically significant. In our study, ^{68}Ga-FAPI-04 detected 3 cases of signet ring cell carcinoma that were negative in ^{18}F-FDG, resulting in a sensitivity of 100% (7/7) in detecting signet ring cell carcinoma and outperforming ^{18}F-FDG (57%, 4/7). Therefore, ^{68}Ga-FAPI-04 PET has an obvious advantage for the detection of signet ring cell carcinoma, especially when negative with ^{18}F-FDG. But the sensitivity of ^{68}Ga-FAPI-04 on signet ring cell carcinoma need larger samples to evaluate.

Tumor size is also an important factor influencing the detection rate of gastric cancer in PET scans. Nakajo et al. [31] examined the relationship between the SUV_{max} of primary gastric cancers and the size of visible tumors and found that the ^{18}F-FDG uptake of primary tumors was significantly associated with tumor size. In another study, small gastric cancers were reported to be difficult to detect by ^{18}F-FDG PET [32]. Interestingly, for detection of tumors less than 4 cm, ^{68}Ga-FAPI-04 PET also provided a better sensitivity than (100% vs. 70%, $P = 0.062$) ^{18}F-FDG, although the difference is not significant. All 17 tumors ≤ 4 cm in size, including 5 with negative ^{18}F-FDG uptake, were detected by ^{68}Ga-FAPI-04 PET in our study. The uptake of ^{68}Ga-FAPI-04 in small gastric cancers (≤ 4 cm in diameter) was lower than that in large gastric cancers (> 4 cm in diameter), it needs to be further confirmed whether ^{68}Ga-FAPI-04 PET has advantages in detecting small gastric cancers.

The depth of invasion in primary gastric cancer is essential for prognosis and therapy. The results from previous studies have shown that the SUV_{max} of ^{18}F-FDG does not correlate with the degree of infiltration [31, 33, 34]. In addition, other tracers used to detect gastric cancer, such as ^{18}F-FLT, are not suitable for

evaluating the degree of infiltration in gastric cancers [31]. In our study, the SUV_{max} of ^{68}Ga-FAPI-04 in pathologically T4 tumors was significantly higher than that in T1 and T2 tumors (10.9 ± 4.3 vs. 3.8 ± 2.1, P = 0.0002). Thus, ^{68}Ga-FAPI-04 PET could provide insight into the degree of tumor invasion in gastric cancer.

In our patient-based analysis, the sensitivity of ^{18}F-FDG PET for detecting regional metastatic lymph nodes was 50% (5/10), which is in line with previous studies of ^{18}F-FDG PET for detecting lymph node metastasis (mean sensitivity: 45%) [7]. The sensitivity of ^{68}Ga-FAPI-04 PET for the detection of regional metastatic lymph nodes was 60% (6/10). As shown in Fig. 5, lymph node metastasis at the lesser curvature of the stomach in one patient with moderately differentiated adenocarcinoma presented elevated uptake of ^{68}Ga-FAPI-04 but negative uptake of ^{18}F-FDG. Chen et al. [16] reported 12 cases of gastric cancer (4 signet ring cell carcinomas and 8 adenocarcinomas) and found that ^{68}Ga-FAPI-04 PET/CT showed higher sensitivity than ^{18}F-FDG PET/CT for the detection of lymph node metastases of gastric cancer from their lesion-based analysis.

In addition, in contrast to ^{18}F-FDG PET, ^{68}Ga-FAPI-04 PET has an advantage in detecting distant metastasis in gastric cancer. Although pathological analysis of a biopsy serves as the gold standard for the diagnosis of metastases in gastric cancer, the noninvasive imaging technique has become a standard modality for staging before treatment. In this study, distant lymph nodes in 3 patients showed high ^{68}Ga-FAPI-04 uptake but negative ^{18}F-FDG uptake. These distant lymph nodes, which included the posterior peritoneum lymph nodes and supraclavicular lymph nodes, are prevalent metastatic sites of gastric cancer. As shown in Fig. 6, one patient displayed discernible ^{68}Ga-FAPI-04 uptake in the peritoneum that was not detected by ^{18}F-FDG PET. It is known that distant metastasis has an important impact on treatment and prognosis. In gastric cancer, peritoneal metastasis is associated with a poor prognosis [35]. According to previous studies, the sensitivity of ^{18}F-FDG PET for the detection of metastatic peritoneal disease is low [36, 37]. Overall, ^{68}Ga-FAPI-04 PET may play an important role in detecting metastases of gastric cancer with or without confirmation by pathological biopsy.

There were several limitations to our study. The small sample size limited the power of the analysis, and not all histological types of gastric cancer were analyzed. Moreover, as there was no histological verification available for some cases of highly suspicious distant metastases, latent bias may be present. We also intended to investigate the advantage of PET/MR in the detection of gastric cancer metastases, but it seems infeasible due to the lack of contrast-enhanced MRI data in this study. Nevertheless, the usefulness of ^{68}Ga-FAPI-04 PET for the detection of distant metastases of gastric cancer needs to be further investigated on a larger cohort.

Conclusion

In summary, ^{68}Ga-FAPI-04 PET presents superior potential in detecting primary gastric cancers and metastatic lymph nodes than ^{18}F-FDG PET. And for tumor size less than 4 cm, ^{68}Ga-FAPI-04 PET can also

provide a better sensitivity. The SUV_{max} of ^{68}Ga-FAPI-04 was higher in T2-4 gastric cancers than in T1 gastric cancers, indicating its potential role in the assessment of the degree of gastric cancer invasion. ^{68}Ga-FAPI-04 PET could be a better method for gastric cancer diagnosis and staging. Nonetheless, it is still necessary to evaluate the potential role of ^{68}Ga-FAPI-04 in gastric cancer in a larger cohort.

Declarations

Author contribution

FX, JZ, YG, FH designed this study and organized the data collection, FX, DJ, XC, ZY, HW, XZ, XL, SR, QH collected the data, DJ, HW, QH processed and analyzed the data, FX and DJ lead the manuscript writing, all authors reviewed and revised the manuscript.

Acknowledgments

The authors appreciate the excellent technical assistance of the staff at the PET Center, Huashan Hospital, Fudan University, and the staff at the Department of Nuclear Medicine, Shanghai East Hospital, Tongji University School of Medicine.

Funding information

This work was supported by the National Natural Science Foundation of China (81801752), Shanghai Sailing Program (20YF1404400), Startup Fund of Huashan Hospital, Fudan University (2017QD081), Shanghai Municipal Key Clinical Specialty (shslczdzk03402), Shanghai Municipal Science and Technology Major Project (No. 2018SHZDZX01), and Shanghai Municipal Health Commission Fund (202040420).

Compliance with ethical standards

Disclosure/Conflict of Interest

None.

Research involving human participants

All procedures performed in this study involving human participants were n accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent to participate

Informed consent was obtained from all participants.

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Tables

Table 1: Clinical and pathological characteristics of patients

N = 38	**Overall**
Age (years)	
Mean (SD)	63.7 (15.3)
Median [min, max]	67.5 [25.0, 86.0]
Sex	
Male	29
Female	9
Type	
Adenocarcinoma	31
Signet ring cell carcinoma	7
Treatment	
Surgery	24
Chemotherapy	5
None	5

Table 2: Relationships between pathological factors and the uptake of ^{68}Ga-FAPI-04 or ^{18}F-FDG in positive lesions

	^{68}Ga-FAPI-04			^{18}F-FDG		
	No.	SUV_{max}	*P*	No.	SUV_{max}	*P*
All	38	7.4 ± 5.0		31	6.5 ± 5.7	
Histologic type						
AC	31	7.5 ± 5.0	0.599	27	6.9 ± 5.9	0.3523
SRCC	7	6.7 ± 5.1		4	3.8 ± 2.3	
Tumor size (cm)						
≤ 4	17	4.5 ± 3.2	0.0015	12	3.6 ± 1.7	0.0064
> 4	7	11.0 ± 4.5		6	6.3 ± 1.8	
Depth of invasion						
T1	12	3.1 ± 1.5	0.0002	7	2.7 ± 0.9	0.0021
T2, T3 and T4	12	9.7 ± 4.4		11	5.6 ± 1.9	
Degree of differentiation						
Well and moderately	16	5.2 ± 3.4	0.1575	13	3.8 ± 1.9	0.032
Poorly	8	9.0 ± 6.0		5	6.2 ± 2.0	

Twenty-four patients (19 with adenocarcinoma and 5 with signet ring cell carcinoma) who received surgical treatment had detailed pathology results.

Figures

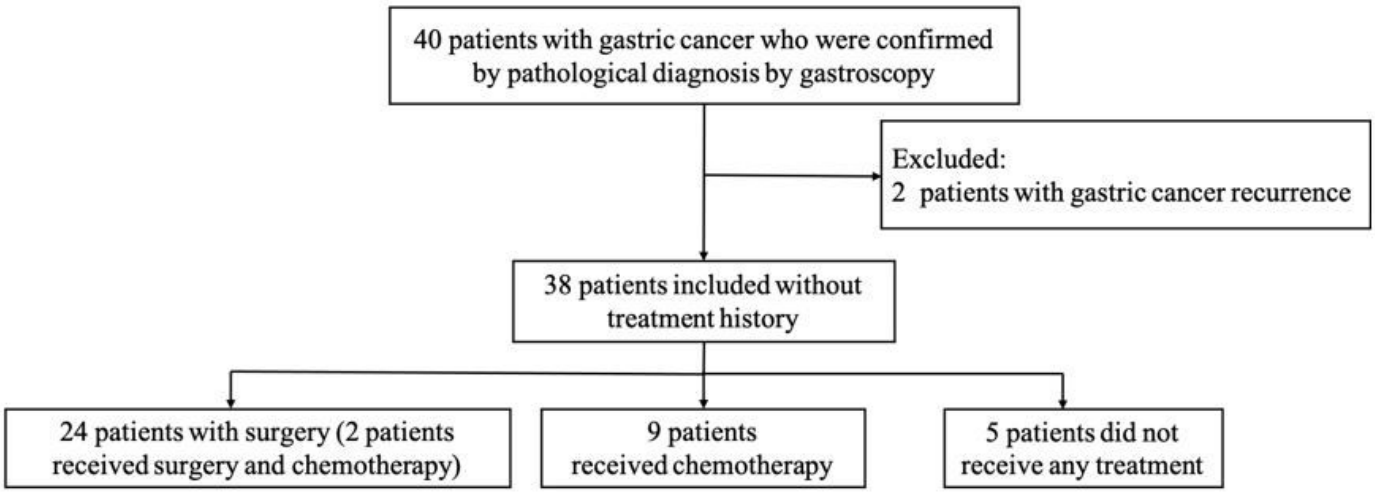

Figure 1

Flowchart with excluded patients and reasons for exclusion.

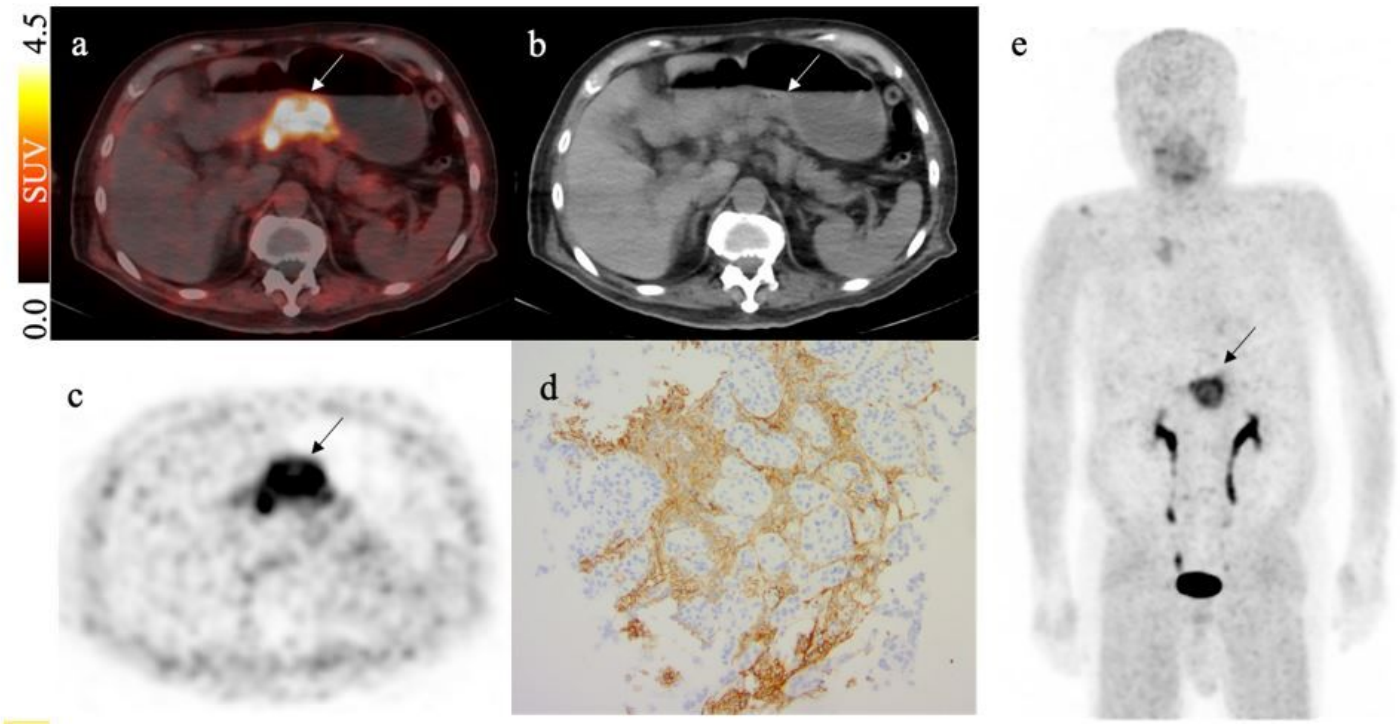

Figure 2

An 86-year-old male patient with gastric adenocarcinoma confirmed by pathological biopsy under gastroscopy. a, b, c, e 68Ga-FAPI-04 PET/CT showed high uptake (SUVmax = 10.2) in the primary tumor (arrows). d Immunohistochemical staining showed strong FAP expression in stromal cells.

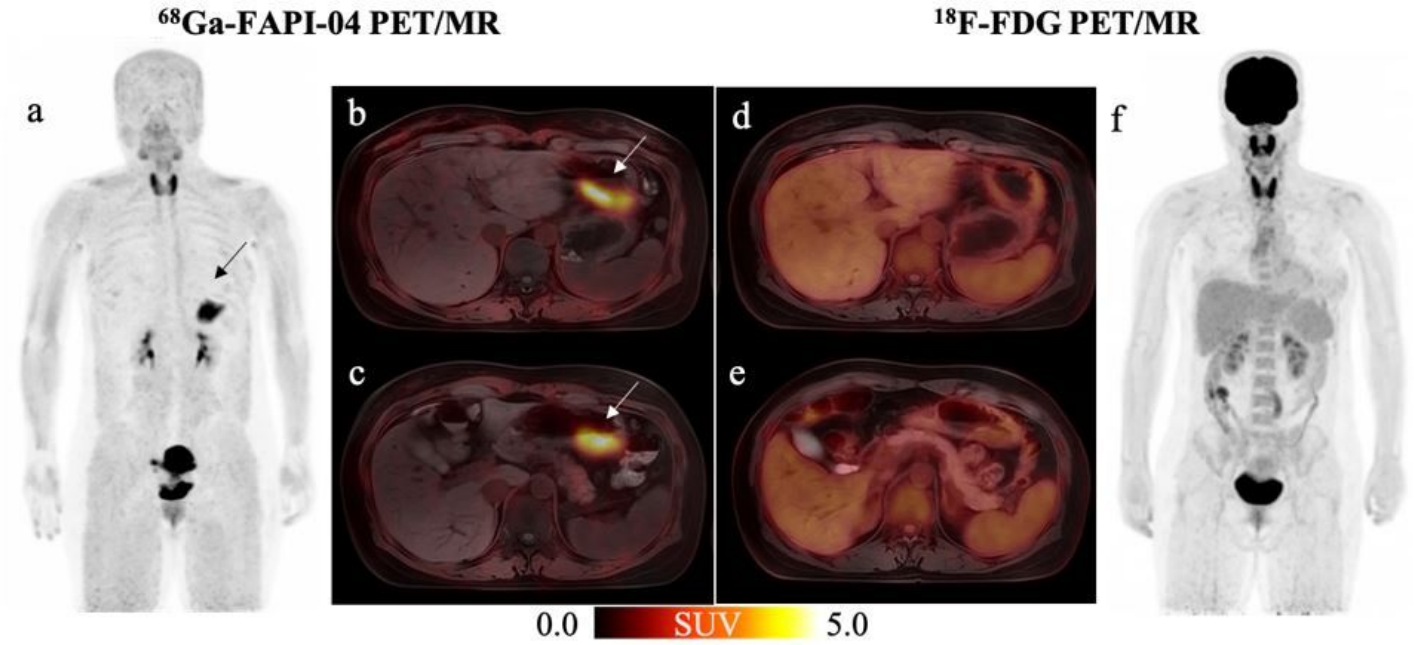

Figure 3

A 30-year-old female patient with gastric signet ring cell carcinoma confirmed by pathology postoperatively. a, b, c 68Ga-FAPI-04 PET/MR displayed high uptake (SUVmax = 11.1) in the primary lesion (arrows). Diffuse 68Ga-FAPI-04 uptake (SUVmax = 9.3) in the thyroid gland was found. d, e, f 18F-FDG PET/MR showed negative uptake in this lesion.

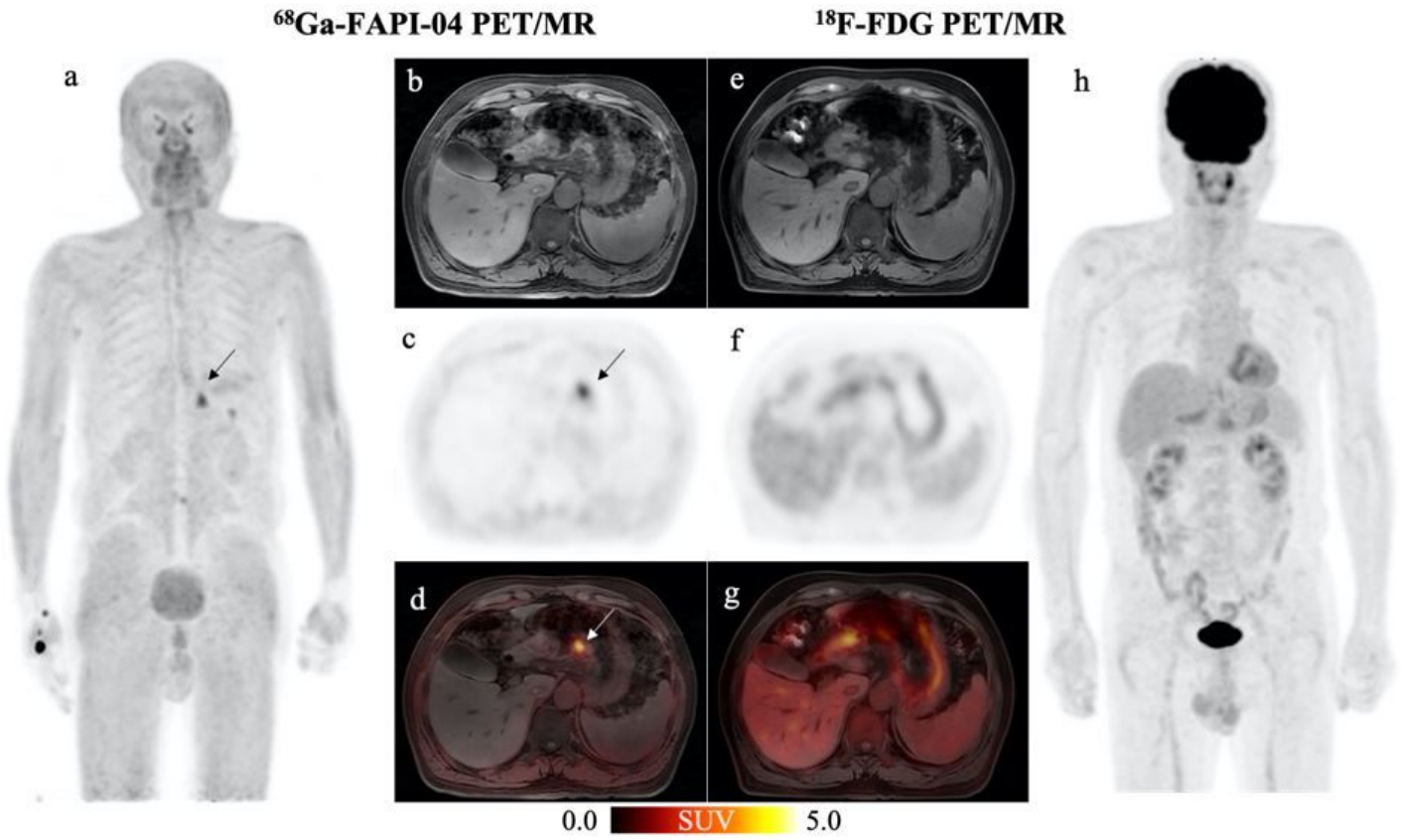

Figure 4

A 67-year-old male patient with gastric adenocarcinoma confirmed by pathology postoperatively. a, b, c, d 68Ga-FAPI-04 PET/MR displayed focal strong uptake (SUVmax = 4.7) in the primary lesion (arrows). e, f, g, h 18F-FDG PET/MR showed slightly and diffusely elevated uptake (SUVmax = 2.6) in the gastric wall.

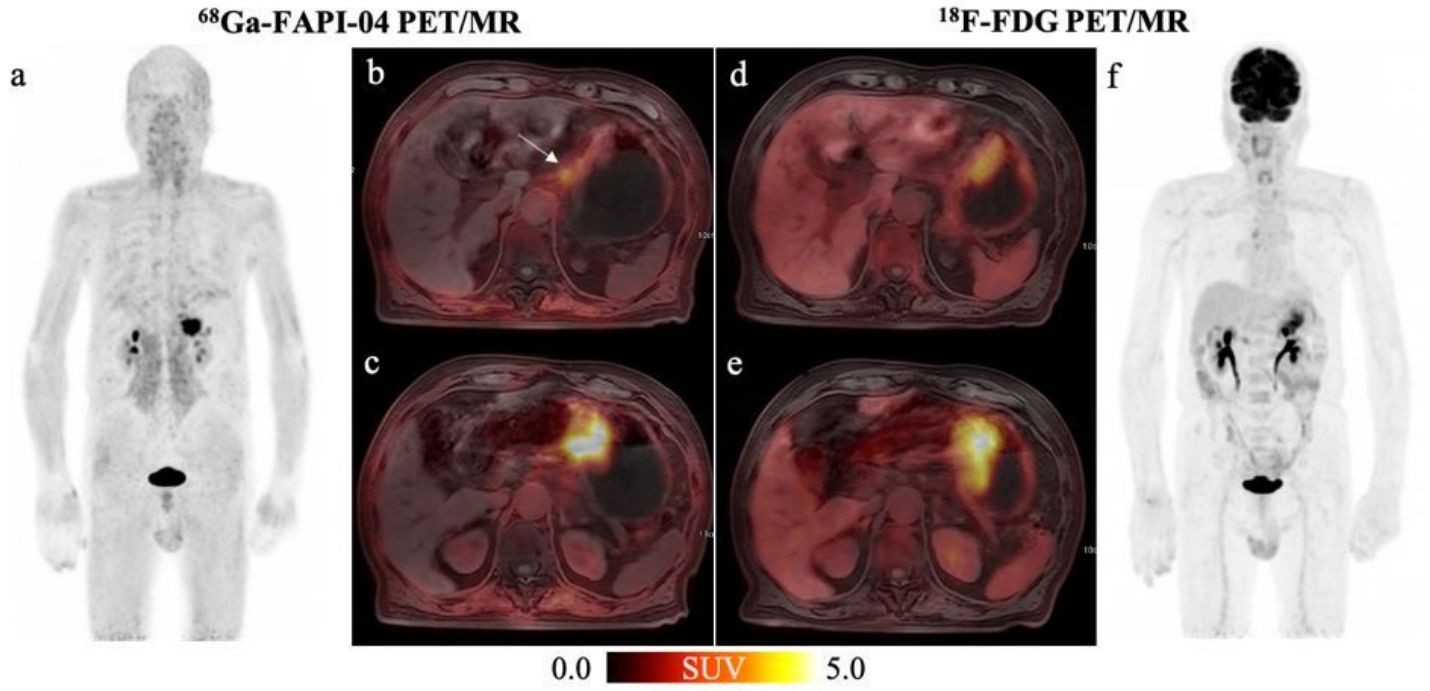

Figure 5

A 65-year-old male patient with gastric adenocarcinoma and regional lymph node metastasis confirmed by pathology postoperatively. a, b, c 68Ga-FAPI-04 PET/MR displayed increased uptake in the primary lesion (SUVmax = 9.7) and lymph nodes (SUVmax = 3.3) at the lesser curvature of the stomach (arrow). d, e, f 18F-FDG PET/MR showed high uptake in the primary tumor (SUVmax = 6.9) but no uptake in the regional lymph nodes.

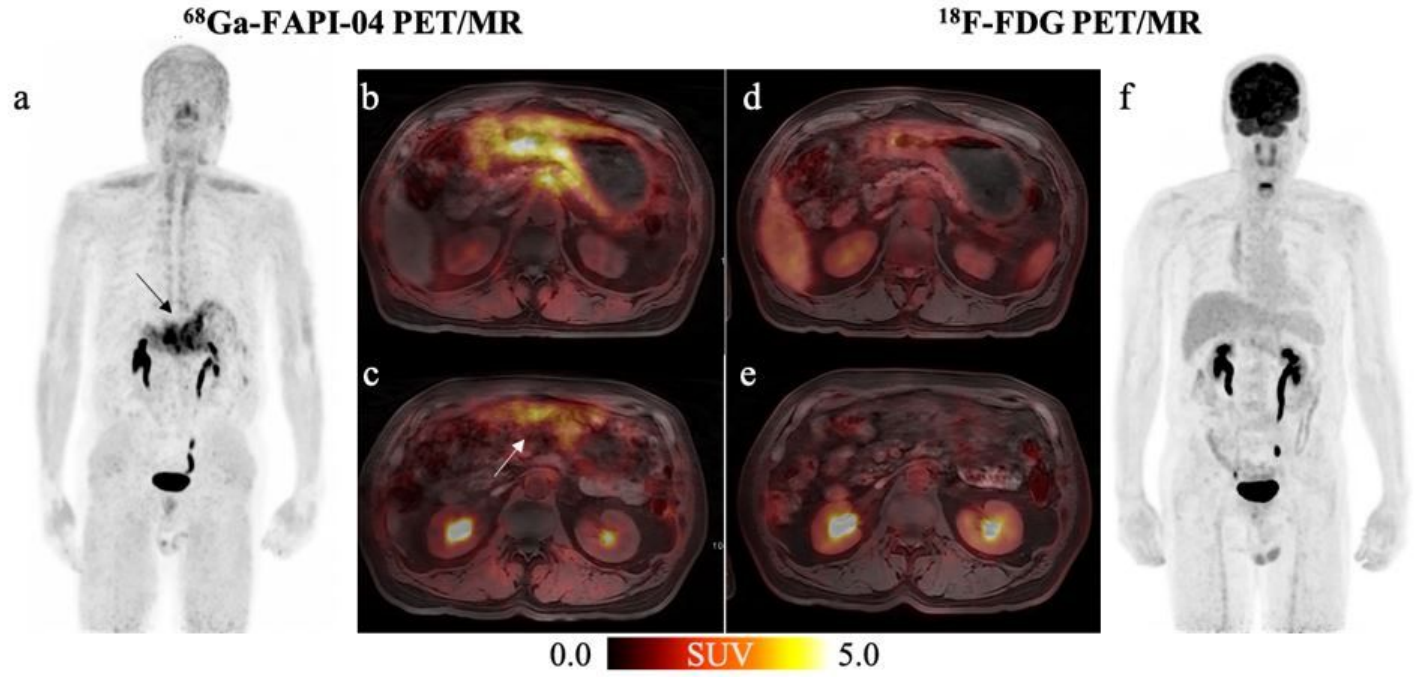

Figure 6

A 65-year-old male patient with gastric adenocarcinoma confirmed by pathological biopsy under gastroscopy. a, b, c 68Ga-FAPI-04 PET/CT showed high uptake in the primary tumor (SUVmax = 9.2) and peritoneum (SUVmax = 7.3) (arrows). d, e, f 18F-FDG PET/MR showed increased uptake in the primary tumor (SUVmax = 2.8) but negative uptake in the peritoneum.

Supplementary Files

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- SupplementaryInformation.docx