^{68}Ga -DOTA-FAPI-04 PET/MR in the evaluation of gastric carcinomas: comparison with ^{18}F -FDG PET/CT

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ABSTRACT

We sought to evaluate the performance of ^{68}Ga -DOTA-FAPI-04 (^{68}Ga -FAPI) PET/MR for the diagnosis of primary tumor and metastatic lesions in patients with gastric carcinomas and to compare the results with those of ^{18}F -FDG PET/CT.

Methods: Twenty patients with histologically proven gastric carcinomas were recruited, and each patient underwent both ^{18}F -FDG PET/CT and ^{68}Ga -FAPI PET/MR. A visual scoring system was established to compare the detectability of primary tumors and metastases in different organs/regions (the peritoneum, abdominal lymph nodes, supradiaphragmatic lymph nodes, liver, ovary, bone, and other tissues). The original maximum standardized uptake value (SUV_{max}) and normalized SUV_{max} (calculated by dividing a lesion's original SUV_{max} with the mean SUV of the descending aorta) of selected lesions on both ^{18}F -FDG PET/CT and ^{68}Ga -FAPI PET/MR were measured. Original/normalized $\text{SUV}_{\text{max-FAPI}}$ and $\text{SUV}_{\text{max-FDG}}$ were compared for patient-based (including a single lesion with the highest activity uptake in each organ/region) and lesion-based (including all lesions $[\leq 5]$ or the 5 lesions with highest activity $[> 5]$) analyses, respectively.

Results: The 20 recruited patients (median age: 56.0 y; range: 29–70 y) included 9 men and 11 women, 14 patients for initial staging and 6 for recurrence detection. ^{68}Ga -FAPI PET was superior to ^{18}F -FDG PET for primary tumor detection (100.00% [14/14] vs 71.43% [10/14], $p = 0.034$), and the former had higher tracer uptake levels ($p < 0.05$). ^{68}Ga -FAPI PET was superior to ^{18}F -FDG PET in both patient-based and lesion-based

evaluation except for the metastatic lesions in supradiaphragmatic lymph nodes and ovaries. Additionally, multiple sequences of MR images were beneficial for the interpretation of hepatic metastases in 3 patients, uterine and rectal metastases in 1 patient, ovarian lesions in 7 patients, and osseous metastases in 2 patients.

Conclusion: ^{68}Ga -FAPI PET/MR outperformed ^{18}F -FDG PET/CT in visualizing the primary and most metastatic lesions of gastric cancer, and might be a promising method with the potential of replacing ^{18}F -FDG PET/CT.

Key Words: fibroblast activation protein; ^{68}Ga -FAPI; PET/MR; gastric cancer; ^{18}F -FDG

INTRODUCTION

Gastric cancer is the fifth most common malignant tumor and the third most common cause of cancer death in the world (1). It has typical characteristics of high incidence, high metastasis rate, high mortality rate, low early diagnosis rate, low radical resection rate, and low 5-year survival rate (2). Many gastric cancer patients present with advanced-stage disease because of the lack of specific early signs and symptoms. Early diagnosis and accurate staging are crucial for choosing appropriate therapy strategy (3).

^{18}F -FDG PET/CT is extensively used in the diagnosis, staging, and preoperative evaluation of gastric cancer. However, ^{18}F -FDG PET/CT has been reported to have a low detection rate for primary gastric cancer (approximately 55%), especially in the early stage, as well as signet-ring cell, mucinous, and poorly differentiated adenocarcinomas, which are typically less metabolically active (4). Moreover, variable and occasionally intense physiological uptake exist within the gastric wall, which can cover ^{18}F -FDG uptake by the primary tumor, and the presence of gastritis may cause false positive results (5). In addition, Stahl et al. showed that the intensity of tumor ^{18}F -FDG uptake is not predictive of survival (6). Therefore, other more sensitive PET probes are needed for the diagnosis and staging of gastric cancer.

Fibroblast activation protein (FAP) is overexpressed in cancer-associated fibroblasts (CAFs) of several tumor entities (7). FAP inhibitors (FAPIs) can specifically target and bind to FAP. FAPIs have been radiolabeled and used as probes to visualize FAP-expressing tumors. The probes including ^{68}Ga -FAPIs have been demonstrated promising results in various cancers, including lung cancer, breast cancer, prostate cancer, sarcoma, head and neck cancer, and so on (8,9). Different from ^{18}F -FDG PET which reflects the glucose metabolism of tumor cells, radiolabeled FAPIs imaging may show

the CAFs and extracellular fibrosis in tumor stroma. Recent studies indicated that primary tumors and most sites of metastases in patients with different cancers are well visualized using ^{68}Ga -FAPI PET/CT (10,11). However, the effect of FAPI imaging in gastric cancer has only been described in scattered case reports (12,13) or in comprehensive studies involving many malignancies (10,11). Additionally, as previous researches on FAPI mainly focused on PET/CT, the performance of PET/MR with FAPI needs to be clarified. In this study, we aimed to further evaluate the performance of ^{68}Ga -DOTA-FAPI-04 (abbreviated as ^{68}Ga -FAPI) PET/MR in gastric cancer and to compare with ^{18}F -FDG PET/CT.

MATERIALS AND METHODS

Patients

This prospective study was approved by the institutional review board of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (IRB 20200290) and all subjects signed a written informed consent. Twenty patients with gastric cancer were enrolled from June 2020 to July 2020. The key eligibility criteria were as follows: (i) histologically proven gastric carcinomas for initial staging or recurrence detection after therapy, (ii) no prior treatment within 4 weeks before PET imaging, (iii) no contraindications to MRI, (iv) agreement to perform both ^{18}F -FDG PET/CT and ^{68}Ga -FAPI PET/MR, (v) performance of 2 scans with an interval of less than 1 week.

^{18}F -FDG PET/CT

^{18}F -FDG was synthesized with ^{18}F produced by a cyclotron (MINItrace®, GE Healthcare), with radiochemical purity > 95%. ^{18}F -FDG (3.70–5.55 MBq/kg) was administrated after fasting for at least 6 h with normal blood glucose level. Imaging was

performed approximately 60 min after administration using an integrated PET/CT scanner (Discovery VCT®, GE Healthcare) from the top of the head to the upper thighs with the following parameters: 120 kV, 110 mAs, thickness of 3.75 mm. PET was acquired with 3 min per bed position.

⁶⁸Ga-FAPI PET/MR

The radiolabeling of ⁶⁸Ga-FAPI was performed according to a previously described method (11). Briefly, ⁶⁸GaCl₃ eluted from ⁶⁸Ge/⁶⁸Ga generator (ITG) was reacted with 20 µg (20 nmol) FAPI-04 ligand (C S Bio Company) using a manual synthesis module (ITG) in 1 mL of 0.25M sodium acetate buffer for 5 min at 100 °C and purified before use.

Imaging was performed approximately 30-60 min after ⁶⁸Ga-FAPI intravenously administration with a dose of 1.85-3.7MBq/kg by an integrated PET/MR scanner (SIGNA PET/MR; GE Healthcare). MR images (a high-resolution axial T1-weighted LAVA-Flex sequence and a coronal T2-weighted fast recovery fast spin echo [FRFSE]) from brain to upper thigh were acquired during the PET scan (3 min/bed position). Next, dedicated multiple-sequence MR images (T1- and T2-weighted images (T1WI, T2WI) and diffusion-weighted images (DWI) of the abdominal and pelvic cavity were acquired. All PET data were reconstructed using time of flight information with 3D ordered subsets expectation maximization protocol iterative reconstruction algorithms.

Image Interpretation

All images were registered on the AW workstation (Version 4.6, GE Healthcare). To avoid bias, 2 groups of experienced nuclear medicine physicians independently analyzed the ¹⁸F-FDG PET/CT and ⁶⁸Ga-FAPI PET/MR images. Image interpretation included visual analysis and quantitative assessment, and the results were discussed to reach a consensus.

VISUAL ANALYSIS. Abnormally elevated ^{18}F -FDG/ ^{68}Ga -FAPI uptake, accompanied by the abnormal density/signal in the corresponding sites on CT/MRI, was interpreted as positive if the possibility of physiological uptake, trauma, infection, and inflammation could be excluded. According to the location, lesions were divided into primary tumor and extra-gastric organs/regions, including the peritoneum, abdominal lymph nodes, liver, ovary, supradiaphragmatic lymph nodes, bone, and other tissues. Additionally, the lesions which were missed or insufficient for diagnosis by ^{18}F -FDG PET/CT and ^{68}Ga -FAPI PET whereas MR provided additional value for the interpretation, were also recorded.

A visual scoring system was established to compare the lesion detection capabilities of ^{18}F -FDG PET and ^{68}Ga -FAPI PET, which was based on the lesion area (primary tumor and peritoneal metastases) or number (positive lymph nodes, liver, bone, and other tissues metastases) or the obviousness (ovaries) detected in the same patient by the two imaging studies. If the area/number/obviousness of lesions detected by ^{68}Ga -FAPI PET was > 1 & < 3 , $3-5$ and > 5 times more than that of ^{18}F -FDG PET, ^{68}Ga -FAPI PET gets 1', 2', and 3', respectively, and vice versa. If the area/number of lesions detected by the 2 imaging modalities was the same, the score was 0'.

QUANTITATIVE ASSESSMENT. Quantitative assessment mainly involved the comparison of ^{18}F -FDG and ^{68}Ga -FAPI uptake in the same lesion. Regions of interest were drawn around foci with increased uptake in the transaxial slices, and an original maximum standardized uptake value (SUV_{max}) was automatically obtained. To ensure SUV_{max} relatively comparable, the original SUV_{max} was normalized by the following formula:

$$\text{Normalized SUV}_{\max} = \text{Original SUV}_{\max} / \text{SUV}_{\text{bkgd}}. \quad (1)$$

SUV_{bkgd} refers to average SUV of the descending aorta.

Quantitative assessment was also divided into patient-based and lesion-based investigations. The former included the primary tumor or a single lesion with the highest uptake in each organ/region, while the latter referred to the analysis including all lesions (≤ 5) or the 5 lesions with highest activity (> 5) if multiple metastases exist.

Statistical Analysis

Statistical analysis was performed on SPSS software (22.0, IBM Inc.). Continuous variables are expressed as mean $\pm$ SD. Categorical variables are expressed as number and percentage. The number of positive lesions was compared using the chi-squared test, and Student's *t*-test was used to assess the differences of $\text{SUV}_{\max}$ between two groups. A *p*-value of < 0.05 was defined as statistically significant.

RESULTS

Patient Characteristics

The median age of the cohort (9 men and 11 women) was 56.0 y (range: 29–70 y). The imaging studies were performed in 14 patients for initial staging and in 6 patients for recurrence detection. Patient characteristics are listed in Table 1.

Of the 14 patients for initial staging, 4 patients with earlier imaging stages underwent surgery, 1 underwent omental biopsy, and the remaining 9 received anti-tumor treatment without surgery due to advanced staging. Notably, for the 4 patients underwent surgery, pathology confirmed 3 patients had abdominal lymph nodes metastases, which were completely/partially missed by PETs. ^{68}Ga -FAPI PET altered 2 patients' staging (patient No. 6 and 14) compared to that by ^{18}F -FDG PET/CT. Positive findings revealed by the

two imaging methods are listed in the supplement data (Supplemental Table 1).

Comparison of Detection Rates

For the patient-based analysis, ^{68}Ga -FAPI PET were superior to ^{18}F -FDG PET in visualizing primary tumor (100.00% [14/14] vs 71.43% [10/14]) and peritoneal metastases (100% [10/10] vs 4/10 [40%]). They were equivalent in exploring metastases in the abdominal lymph nodes (11/11 vs 10/11), liver (3/3 vs 3/3), bone (3/3 vs 3/3), ovarian lesions (7/7 vs 7/7) and positive supradiaphragmatic lymph nodes (6/7 vs 6/7) (Table 2).

Comparison of Visual Assessment

In comparison to ^{18}F -FDG PET, ^{68}Ga -FAPI PET provide excellent contrast with low background throughout the body (Fig. 1). Moreover, whether it was the primary tumor or metastasis, the lesion detectability of ^{68}Ga -FAPI PET was superior to that of ^{18}F -FDG PET, and the former got much higher total score (Fig. 2, 87' vs 13'). In particularly, ^{68}Ga -FAPI PET detected significantly more/larger lesions than ^{18}F -FDG PET in primary tumor (23' vs 1'), metastases in the peritoneum (23' vs 0'), abdominal lymph nodes (18' vs 1'), liver (5' vs 0') (typical case shown in Fig. 3), and the bones (7' vs 0'). Additionally, 4 metastases at uncommon sites in 3 patients (uterus metastasis and rectum involvement in 1 patient [Fig. 4], soft tissue metastasis in the abdominal wall, and left ureteral metastasis) were revealed. However, for the detection of ovarian lesions (5' vs 3') (Fig. 5) and positive lymph nodes above the diaphragm (4' vs 8'), ^{68}Ga -FAPI PET has no obvious advantage compared with ^{18}F -FDG.

Comparison of Quantitative Assessment

Table 2 exhibits the comparison of metabolic parameters (including original and normalized SUV_{max}) between ^{68}Ga -FAPI and ^{18}F -FDG. Both the original and normalized

SUV_{max} of primary tumor on ⁶⁸Ga-FAPI PET were higher than those on ¹⁸F-FDG PET. For patient-based analysis, there was no statistically significant difference between original SUV_{max-FAPI} and SUV_{max-FDG} of the metastasis with highest activity in each organ/region, and the normalized indicators only affected the results in the abdominal lymph nodes ($p = 0.086$ changed to $p = 0.003$) and hepatic metastases ($p = 0.741$ changed to $p = 0.037$). For lesion-based analysis, the number of lesions in the peritoneum, abdominal lymph nodes, liver and bone on ⁶⁸Ga-FAPI PET was greater than that of ¹⁸F-FDG PET. Remarkably, the normalized values of SUV_{max-FAPI} were significantly higher than that of ¹⁸F-FDG for all lesions.

Additional Value of MR

Multiple sequences of MR enhanced the interpretation confidence in hepatic metastases in 3 patients (Fig.3), uterine and rectal metastases in 1 patient (Fig.4), ovarian lesions in 7 patients (6 metastases [Fig.5] and 1 corpus luteum as a false positive finding [Fig.6]), and osseous metastases in 2 patients.

DISCUSSION

In this preliminary study, we found that ⁶⁸Ga-FAPI PET imaging is superior to ¹⁸F-FDG PET in detecting primary lesions and metastases in patients with gastric cancer at the initial diagnosis and recurrence detection, which embodied on the former detected more/larger lesions and higher tracer uptake. The low background of ⁶⁸Ga-FAPI can show small metastatic lesions of gastric cancer in the peritoneum, abdominal lymph nodes, liver, and bone, which are more difficult to detect with ¹⁸F-FDG. However, ⁶⁸Ga-FAPI has physiological uptake in the uterus and ovaries, which may affect the observation of the corresponding regional lesions. MR has higher soft tissue contrast and affords multiple sequences, which is conducive to the observation of abdominal and pelvic organs that assists diagnosis. Therefore, ⁶⁸Ga-FAPI PET/MR exhibited good value in

visualizing primary and metastatic gastric cancer.

Previous studies have shown that preoperative ^{18}F -FDG PET/CT has a low detection rate for primary gastric cancer (14,15). In our study, ^{18}F -FDG PET has a relatively high detection rate of 71.4% (10/14) for primary tumor detection. This might be because most of these patients were at an advanced stage, with relatively large tumor size/higher malignancy degree. In fact, the uptake of ^{68}Ga -FAPI by the primary tumors was significantly higher than that of ^{18}F -FDG (approximately 2-4 $\times$), as shown in our results (Fig. 1). Especially when set against the low background of the gastric area, ^{68}Ga -FAPI-avid lesions will be particularly obvious and easily visualized. A recent comparative study demonstrated much higher sensitivity of ^{68}Ga -FAPI PET/CT than that of ^{18}F -FDG PET/CT in the detection of primary gastric tumors (100.00 % [11/11] vs 36.36 % [4/11]), and the former had higher tracer uptake (SUV_{max} : 12.7 vs 3.7 $p=0.03$) (15). These findings are consistent with our results. Notably, because most patients in this cohort had distant metastases, the evaluation of the degree of invasion and involvement of the primary tumor was of little significance to staging. Therefore, we only compared the involved area of the primary tumor visualized by the 2 imaging modalities; assessment associated with T staging was not performed. In addition, ^{68}Ga -FAPI PET imaging only changed 2 patients' staging (2/14, 14.3%), which is attributed to the staging proportion of patients. Most of the enrolled patients are in stage IV (11/14, 78.5%). Although our results show that ^{68}Ga -FAPI PET can display more lesions than ^{18}F -FDG PET, for patients with multiple distant metastases, however, it does not change the clinical staging and further affect treatment decisions.

Our results showed that although ^{18}F -FDG PET and ^{68}Ga -FAPI PET were equally effective in visualizing and determining whether metastases existed in a given region, in terms of the lesions' number/area, ^{68}Ga -FAPI had significantly better detectability. Because there were too many, even countless metastatic lesions in some regions (such as

the peritoneum and the abdominal lymph nodes), establishing a visual scoring system simplified the comparison. Our scoring system intuitively displayed that ^{68}Ga -FAPI PET outperformed ^{18}F -FDG PET in identifying lesions, especially the peritoneal, abdominal lymph node, hepatic, and osseous metastases, which was consistent with the results of previous publications (11,16). This can be attributed to the higher sensitivity and the lower gastrointestinal background of ^{68}Ga -FAPI. The latter was an important factor limiting ^{18}F -FDG PET, especially with peristaltic activity, the heterogeneous uptake in the intestinal wall would increase the difficulty of interpretation by ^{18}F -FDG PET/CT (17). Although the superiority of ^{68}Ga -FAPI PET in detecting peritoneal metastases did not significantly change the staging of gastric cancer, it can more accurately determine the involvement extent, which can be used for evaluation of the response to treatment.

The usefulness of ^{18}F -FDG PET-CT in gastric cancer with lymph node metastasis also remains controversial (14,18). We found that ^{68}Ga -FAPI PET was indeed superior to ^{18}F -FDG PET in visualizing abdominal lymph node metastases, which was similar to the conclusions of other studies (8,10,11). Whereas ^{18}F -FDG PET had higher scores than ^{68}Ga -FAPI PET in detecting supradiaphragmatic lymph nodes. However, due to lack of pathological proof and the common presence of false positive on ^{18}F -FDG PET imaging (19), whether the ^{18}F -FDG+/ ^{68}Ga -FAPI- lesions were truly metastases remained to be determined.

According to our results, both ^{18}F -FDG PET/CT and ^{68}Ga -FAPI PET were ambiguous for the interpretation of ovarian lesions due to the physiological uptake of ^{18}F -FDG (20) or ^{68}Ga -FAPI (Fig. 6) in the ovaries in premenopausal women. MR has been playing an increasing role in the evaluation of gastrointestinal diseases (21). Therefore, we introduced PET/MR to explore the additional value of MR, which assisted to interpret some lesions in the ovary, uterus, liver, or bone owing to the excellent soft tissue

resolution and more valuable information provided by multiple sequences (22).

The present study had several limitations. First, the limited number of patients and pathological types might cause bias. Second, T staging–related assessments were not conducted because most enrolled patients were in advanced stage. Whether ^{68}Ga -FAPI PET/MR can be beneficial for the staging of patients with gastric cancer in earlier stage needs further assessment. Third, most (9/14) patients did not undergo surgery or biopsy for metastatic lesions. For some patients, although surgery was performed, not all lesions were removed for pathological examination, especially the supradiaphragmatic lymph nodes. These may result in lack of gold standard for the positive lesions. Therefore, we should conduct a clinical trial involving a larger number of gastric cancer patients with comprehensive pathological types and earlier stage to remedy these limitations and further confirm our results.

CONCLUSION

Compared with ^{18}F -FDG PET/CT, ^{68}Ga -FAPI PET/MR had superior detection capabilities for primary tumors and metastases in the peritoneum, abdominal lymph nodes, liver, and bones in patients with gastric cancer. The detection ability of ^{68}Ga -FAPI PET for ovarian metastases was not better than that of ^{18}F -FDG PET, however, combining with hybrid MR imaging could be helpful for avoiding misdiagnosis. In general, ^{68}Ga -FAPI PET/MR outperformed ^{18}F -FDG PET/CT in visualizing primary and metastatic lesions of gastric cancer and may potentially replace ^{18}F -FDG PET/CT.

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DISCLOSURE

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

KEY POINTS

QUESTION:

Is ^{68}Ga -FAPI PET/MR superior to ^{18}F -FDG PET/CT in detecting primary tumor and metastases of gastric cancer?

PERTINENT FINDINGS:

In a cohort of 20 patients with gastric cancer, ^{68}Ga -FAPI PET/MR showed a higher detection rate, more lesions and higher uptake than ^{18}F -FDG PET/CT in both primary lesions and most metastatic organs/tissues.

IMPLICATIONS FOR PATIENT CARE:

^{68}Ga -FAPI PET/MR outperformed ^{18}F -FDG PET/CT in visualizing primary and metastatic lesions of gastric cancer and may potentially replace ^{18}F -FDG PET/CT.

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Fig. 1 Representative images of ^{68}Ga -FAPI PET (**A**) and ^{18}F -FDG PET (**B**) in patients with gastric cancer for initial staging (patient #1, #2, #3, #10) and recurrence detection (patient #18, #19) from left to right. The ^{68}Ga -FAPI images are superior to ^{18}F -FDG images in the visualization of primary tumors and metastases. ^{68}Ga -FAPI total scores were 8', 7', 6', 5', 3' and 2', respectively, and all of the ^{18}F -FDG total scores were 0'.

Fig. 2 Comparison of visual assessment between ^{68}Ga -FAPI PET and ^{18}F -FDG PET.

Note: n (n') in each bar refers to patient number (scores'); M = metastases.

Fig. 3 A 61-year-old man (Patient #7) with moderately differentiated gastric adenocarcinoma. In addition to the primary tumor (A, white arrow, $\text{SUV}_{\text{max}} = 11.0$), 2 foci of elevated activity in the liver were noted on the ^{18}F -FDG PET/CT images (A, yellow arrows, $\text{SUV}_{\text{max}} = 5.8$). On the ^{68}Ga -FAPI PET/MR images, the primary tumor had more intense uptake (B-C, white arrows, $\text{SUV}_{\text{max}} = 14.2$), and the 2 hepatic lesions had more prominent ^{68}Ga -FAPI accumulation (B, yellow arrows, $\text{SUV}_{\text{max}} = 7.6$). Additionally, multiple foci of increased ^{68}Ga -FAPI activity were also revealed in the liver (C, red outline, yellow arrows), which corresponded to multiple high signals on DWI (yellow arrows), suggesting multiple hepatic metastases.

Fig. 4 A 45-year-old woman (patient #20) with a surgical history of gastric cancer 4 years previously. ^{18}F -FDG PET/CT (**A**) showed a mass in uterus with heterogeneous density and intense ^{18}F -FDG activity (yellow arrows, $\text{SUV}_{\text{max}} = 9.1$), which involved the adjacent rectum (white arrows, $\text{SUV}_{\text{max}} = 5.7$). On the ^{68}Ga -FAPI PET/MR (**B**), there was intense ^{68}Ga -FAPI uptake throughout the uterus ($\text{SUV}_{\text{max}} = 12.7$), which may be physiological uptake. By interpreting the signal changes on multiple sequences of MR, uterine masses (yellow arrows), disappearance of the fat space, and rectal involvement (white arrows) can be observed and diagnosed as metastases.

Fig. 5 Comparison between ^{18}F -FDG PET/CT (A) and ^{68}Ga -FAPI PET/MR (B) for ovarian metastases in a 38-year-old woman (patient #1). The ovaries had slightly increased ^{18}F -FDG accumulation ($\text{SUV}_{\text{max}} = 2.6$) (A, arrows), which was difficult to determine whether physiological uptake or metastases. On ^{68}Ga -FAPI PET/MR imaging, increased uptake ($\text{SUV}_{\text{max}} = 4.1$) was observed in enlarged ovaries with significant MR signal changes (heterogeneous signal on T2WI, high signal on DWI, and low signal on ADC), which enhanced the confidence in making a diagnosis of metastases.

Fig. 6 Corpus luteum as false positive on ^{18}F -FDG PET/CT and ^{68}Ga -FAPI PET/MR in a 35-year-old woman (patient #12). Two foci of increased ^{18}F -FDG activity (**A**, arrows, $\text{SUV}_{\text{max}} = 5.0$ [right], 5.7 [left]) and ^{68}Ga -FAPI activity (**B**, arrows, $\text{SUV}_{\text{max}} = 4.3$ [right], 3.3 [left]) were observed in ovaries, but without obvious abnormal morphology and signal changes on MR images (**B**). Operative exploration confirmed these “lesions” as corpus luteum.

Graphical Abstract

Table 1. Clinical characteristics of patients with gastric cancer

No.	Sex	Age	Role of PET	Pathology	Primary tumor	Confirmed metastases*	Clinical stage /final diagnosis
1	Female	38	IS	PDAC	whole Stomach	PM, LNM, OM	IV
2	Female	36	IS	SRCC	greater curvature of gastric body	PM, LNM, OM	IV
3	Male	66	IS	Nonkeratinizing squamous cell carcinoma	esophagus-Stomach cardia	LNM, LM, BM	IV
4	Male	56	IS	Adenocarcinoma	gastric body	LNM, LM	IV
5	Male	58	IS	PDAC, partial SRCC	gastric antrum, angular notch	LNM	IIIA
6	Female	70	IS	PDAC, partial SRCC	whole stomach	PM, LNM	IV
7	Male	61	IS	Moderately differentiated adenocarcinoma	whole stomach	LNM, LM, Abdominal wall#	IV
8	Male	61	IS	Low-adhesion carcinoma, partial SRCC	stomach pylorus	PM, LNM	IV
9	Female	59	IS	PDAC	gastric antrum, angular notch	LNM, BM	IV
10	Male	66	IS	PDAC	greater curvature of gastric body	PM, LNM, BM	IV
11	Male	58	IS	SRCC	angular notch	LNM	IV
12	Female	35	IS	PDAC, partial SRCC	gastric body	LNM	IIIB
13	Male	50	IS	SRCC	stomach pylorus-duodenal bulb	None	II
14	Male	63	IS	Adenocarcinoma	remnant stomach	PM, LNM	IV
15	Female	54	RD	PDAC		PM, OM	PD
16	Female	33	RD	Low adhesion carcinoma		PM, LNM, OM, left ureter#	PD
17	Female	29	RD	PDAC		PM, OM	PD
18	Female	50	RD	PDAC		PM, OM	PD
19	Female	56	RD	SRCC		LNM	PD
20	Female	45	RD	PDAC, partial SRCC		LN, uterus#, rectum#	PD

IS: Initial staging; RD: Recurrence detection; PDAC: Poorly differentiated adenocarcinoma; SRCC: Signet ring cell carcinoma; PM: peritoneal metastasis; LNM: lymph node metastasis; LM: liver metastasis; OM: ovarian metastasis; BM: bone metastasis; GC: Gastric cancer; PD: Progression of disease

* Metastases were confirmed by the comprehensive consideration of imaging findings and pathological results.

Metastases at uncommon sites.

Table 2. Comparison of semiquantitative parameters between ⁶⁸Ga-FAPI PET and ¹⁸F-FDG PET

		Primary tumor	Peritoneal metastases	Lymph node (abdominal)	Ovarian	Liver metastases	Bone metastases	Lymph node (supradiaphragm)
Patient based analysis		14	10	12	7	3	3	7*
Patient number	¹⁸ F-FDG/PET/CT	10	4	10	7	3	3	6
	⁶⁸ Ga-FAPI PET/MR	14	10	12	7	3	3	6
	P Value	0.034	0.011	1	—	—	—	—
Original SUVmax	¹⁸ F-FDG/PET/CT	6.18±2.46	7.60±5.85	6.58±2.78	4.19±1.72	5.63±1.96	5.8±5.39	8.42±6.14
	⁶⁸ Ga-FAPI PET/MR	11.31±3.96	8.43±3.46	9.93±5.58	4.63±2.17	6.30±2.61	12.33±5.70	6.93±5.60
	P Value	0.002	0.743	0.086	0.680	0.741	0.223	0.671
Normalized SUVmax	¹⁸ F-FDG/PET/CT	3.99±1.53	4.97±2.43	4.04±1.76	3.00±1.35	3.45±0.48	3.16±2.77	5.07±2.78
	⁶⁸ Ga-FAPI PET/MR	12.40±5.17	9.58±4.26	10.90±6.17	4.88±2.06	6.54±1.67	11.76±4.71	7.70±4.80
	P Value	0.000	0.068	0.003	0.067	0.037	0.053	0.273
Lesion based analysis								
Lesion number	¹⁸ F-FDG/PET/CT		14	33	12	6	4	24
	⁶⁸ Ga-FAPI PET/MR		42	45	12	13	12	18
	P Value		0.000	0.000	—	0.011	0.001	0.022
Original SUVmax	¹⁸ F-FDG/PET/CT		5.74±3.28	6.13±2.79	3.74±1.53	5.72±1.33	5.2±4.56	6.77±4.83
	⁶⁸ Ga-FAPI PET/MR		7.61±2.98	8.65±4.38	4.19±1.76	5.81±2.03	10.05±6.18	6.41±4.51
	P Value		0.052	0.003	0.511	0.915	0.167	0.807
Normalized SUVmax	¹⁸ F-FDG/PET/CT		3.71±1.53	3.73±1.66	2.73±1.08	3.30±0.40	2.90±2.32	3.96±1.93
	⁶⁸ Ga-FAPI PET/MR		8.74±3.82	9.43±5.01	4.38±1.81	5.84±1.44	9.48±5.42	7.41±4.06
	P Value		0.000	0.000	0.013	0.000	0.004	0.003

* Among the 7 patients with supradiaphragmatic lymph nodes, 5 patients were both positive on ^{68}Ga -FAPI and ^{18}F -FDG PETs, and the remaining 2 patients were FAPI⁺/FDG⁻ and FAPI⁻/FDG⁺ respectively. “-” means no need to compare.

⁶⁸Ga-DOTA-FAPI-04 PET/MR in the evaluation of gastric carcinomas: comparison with ¹⁸F-FDG PET/CT

SUPPLEMENTAL TABLE 1. Positive findings revealed by ¹⁸F-FDG PET and ⁶⁸Ga-FAPI PET (+, positive; -, negative)

Patient No.	Primary tumor		Peritoneal metastases		Lymph nodes (abdominal)		Ovaries		Liver metastases		Bone metastases		Lymph nodes (supradiaphragm)		Other tissues	
	FDG	FAPI	FDG	FAPI	FDG	FAPI	FDG	FAPI	FDG	FAPI	FDG	FAPI	FDG	FAPI	FDG	FAPI
1	+	+	-	+	-	-	+	+	-	-	-	-	-	+	-	-
2	+	+	+	+	+	+	+	+	-	-	-	-	+	+	-	-
3	+	+	-	-	+	+	-	-	+	+	+	+	-	-	-	-
4	-	+	-	-	+	+	-	-	+	+	-	-	-	-	-	-
5&	-	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-
6&§	-	+	-	+	-	+	-	-	-	-	-	-	-	-	-	-
7	+	+	-	-	+	+	-	-	+	+	-	-	+	+	-	+
8	+	+	+	+	-	-	-	-	-	-	-	-	+	+	-	-
9	+	+	-	-	+	+	-	-	-	-	+	+	-	-	-	-
10	+	+	+	+	+	+	-	-	-	-	+	+	-	-	-	-
11	+	+	-	-	+	+	-	-	-	-	-	-	+	+	-	-
12&	+	+	-	-	-	-	+	+	-	-	-	-	-	-	-	-
13	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
14§	+	+	-	+	-	+	-	-	-	-	-	-	-	-	-	-
15			-	+	-	-	+	+	-	-	-	-	-	-	-	-
16			-	+	+	+	+	+	-	-	-	-	+	+	-	+
17			+	+	-	-	+	+	-	-	-	-	-	-	-	-
18			-	+	-	-	+	+	-	-	-	-	-	-	-	-
19			-	-	+	+	-	-	-	-	-	-	-	-	-	-
20			-	-	+	+	-	-	-	-	-	-	-	-	+	+
Total + No.	10	14	4	10	10	12	7	7	3	3	3	3	6	6	1	3

& False negative abdominal lymph nodes in patient 5 (metastatic LN number/total dissected LN number: 5/50), patient 6 (9/24, only 1 LN was positive on ⁶⁸Ga-FAPI PET), patient 12 (19/25). § ⁶⁸Ga-FAPI PET leads to upstage to stage IV in patient 6 and 14.