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RESEARCH

Impact of ^{68}Ga-FAPI positron emission tomography/computed tomography on staging and tumor management in patients with gastric cancer

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Abstract

Purpose To evaluate the added value of additional ^{68}Ga-FAPI PET/CT following CT for primary staging, detection of postoperative recurrence, and management of gastric cancer patients.

Methods We retrospectively included patients with gastric cancers who underwent contrast-enhanced computed tomography (ceCT), followed by ^{68}Ga-FAPI PET/CT within 30 days. ^{68}Ga-FAPI PET/CT was performed for initial staging or detection of postoperative recurrence. Two nuclear medicine physicians and a radiologist independently decided on imaging-based staging. Pre-^{68}Ga-FAPI PET/CT treatment decisions were made by a simulated tumor board and post-^{68}Ga-FAPI PET/CT decisions were extracted from medical records. We evaluated the impact of ^{68}Ga-FAPI PET/CT with inconsistent new findings based on the initial findings from ceCT and the resulting changes in treatment strategies.

Results We included 112 patients, 84 for initial staging and 28 for detection of postoperative recurrence. Compared to CT, 29 new findings in 24 patients were diagnosed as, or ruled out, cancer involvement on ^{68}Ga-FAPI PET/CT. Among the 112 patients, 21 patients (18.8%) experienced changes in stage or postoperative recurrence. Among patients for initial staging, 14 had stage changes, with 10 being upstaged and 4 being downstaged. Among patients for detection of postoperative recurrence, 7 more patients were diagnosed with tumor recurrence. New findings of ^{68}Ga-FAPI PET/CT led to treatment change in 20/112 (17.9%) patients, which was deemed of major change in 19 patients and minor change in 1 patient.

Conclusions ^{68}Ga-FAPI PET/CT is valuable for precise staging and detection of postoperative recurrence of gastric cancers, and has the potential to influence management.

Keywords ^{68}Ga-FAPI PET/CT · Gastric cancer · Staging · Restaging · Therapeutic management

Shunyu Zhang and Minggang Su contributed equally to the work.

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Abbreviations

PET/CT	Positron emission tomography/computed tomography
^{18}F-FDG	18 F-fluorodeoxyglucose
CAFs	Cancer-associated fibroblasts
FAP	Fibroblast activation protein
FAPIs	Fibroblast activation protein inhibitors
ceCT	Contrast-enhanced computed tomography
68Ga-FAPI PET/CT	68Ga-FAPI positron emission tomography/computed tomography
MMR	Mismatch repair
dMMR	Deficient mismatch repair
pMMR	Proficient mismatch repair
EBER-ISH	Epstein-Barr virus-encoded RNA in

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	situ hybridization
HER2	Human epidermal growth factor receptor-2

Introduction

Gastric cancer is the fifth most common cancer and the fourth leading cause of cancer-related death worldwide (Sung et al. 2021). Accurate staging of gastric cancer is crucial for the development of multidisciplinary management strategies (Joshi et al. 2021), and for guiding follow-up examinations to enable timely detection of recurrence or metastasis.

Contrast-enhanced computed tomography (ceCT) and endoscopic ultrasound are widely used for the clinical staging of gastric cancers, but they have low sensitivity for detecting lymph nodes and peritoneal metastases (Zhong et al. 2016; Gertsen et al. 2021; Kwee et al. 2015). Although ^{18}F-fluorodeoxyglucose (^{18}F-FDG)-PET/CT is recommended as an add-on test in the staging of various cancers (Ettinger et al. 2023; Bevers et al. 2023), its limitations in staging gastric cancer have been long recognized (Gertsen et al. 2021; Wang et al. 2011). Due to the low uptake of ^{18}F-FDG in certain pathological types of gastric cancer, such as signet ring cell carcinoma and mucinous adenocarcinoma, and the high physiological uptake of ^{18}F-FDG in the gastrointestinal tract, ^{18}F-FDG PET/CT has a high false-negative rate in diagnosing gastric cancer, particularly for peritoneal metastasis (Dassen et al. 2009; Shimada et al. 2011; Honma et al. 2018).

Cancer-associated fibroblasts (CAFs) are a major component of the tumor stroma that accounts for 90% of the total tumor mass in some tumors and play a crucial role in tumor growth, invasion, and metastasis (Chen et al. 2019; Fitzgerald et al. 2020; Hamson et al. 2014). Fibroblast activation protein (FAP) is a type II transmembrane serine protease, which is highly expressed in CAFs but nearly absent in healthy tissues (Fitzgerald, et al. 2020; Jacob et al. 2012). Given this unique composition of the tumor mesenchyme, radiotracers consisting of FAP inhibitors (FAPIs) have been developed to target the tumor stroma and visualize various malignancies (Fitzgerald, et al. 2020; Jacob et al. 2012; Gilardi et al. 2022; Zhao et al. 2022), with a particular advantage in detecting small lesions (Gilardi et al. 2022; Zhao et al. 2022). Recent studies found that ^{68}Ga-FAPI PET/CT has superior diagnostic capabilities than ^{18}F-FDG PET/CT for detecting primary tumors, lymph nodes, and distant metastases in gastric cancer patients based on either visual or quantitative analysis (Jiang et al. 2022; Lin et al. 2022; Miao et al. 2023; Zhang et al. 2022). These results suggest a promising value of ^{68}Ga-FAPI PET/CT in the staging and treatment management of gastric cancers. However, these studies are of small sample size, and the impact of ^{68}Ga-FAPI PET/CT on clinical staging and decision-making has not been fully explored. Thus, we aimed to examine the impact of additional ^{68}Ga-FAPI PET/CT following CT on the initial staging and postoperative recurrence detection, as well as changes in management for gastric cancer patients.

Materials and methods

Patient cohort

From our prospectively maintained gastric cancer database, we retrospectively enrolled gastric cancer or gastroesophageal junction cancer patients who underwent ^{68}Ga-FAPI PET/CT between April 2022 and September 2023. The crucial eligibility criteria were as follows: (1) histologic confirmation of gastric cancer or gastroesophageal junction cancer; (2) patients who underwent enhanced chest and abdominal CT for initial staging or detection of postoperative recurrence, followed by ^{68}Ga-FAPI PET/CT within 30 days. Patients with the following characteristics were excluded: incomplete clinical or imaging records, patients from other clinical trials, and patients who underwent antitumor therapies between enhanced CT and ^{68}Ga-FAPI PET/CT. This study was approved by the Ethics Committee of our hospital.

68Ga-FAPI PET/CT imaging protocol

The ^{68}Ga-FAPI PET/CT scans were conducted 60 min after the intravenous injection of 111–185 MBq ^{68}Ga-FAPI PET/CT. PET/CT images were acquired from the head to the upper thighs. CT scans were executed with a tube voltage of 120 kV, an effective tube current ranging from 70 to 200 mAs (utilizing dose modulation [uMI780, United-Imaging Healthcare]), and a slice thickness of 3 mm. PET scans were promptly conducted after the CT scan in 3D acquisition mode (matrix: 192 × 192) with 4–5 bed positions and 3 min per position. PET data were iteratively reconstructed (2 iterations and 20 subsets) with CT data for attenuation correction. Subsequently, PET/CT images were co-registered and presented using dedicated software (Image Fusion software, UIH).

Contrast-enhanced CT imaging protocol

For CT, the scan was performed using Siemens Somatom Definition AS + Siemens Somatom Definition in our center. Before the CT scan, patients were instructed to abstain from food for a minimum of 6 h and to consume 600–1000 mL of water orally to facilitate gastric distension before the

procedure. Patients were initially trained to hold their breath throughout the CT scanning process, which encompassed the entire abdominal region. Patients were scanned using a CT system with specific parameters as detailed in Supplementary Table 1.

Interpretation of contrast-enhanced CT imaging

A radiologist with 10 years of experience determined the ceCT-based stage. Staging was determined according to the eighth edition of the AJCC staging system for gastric cancer or gastroesophageal junction cancer(Amin et al. 2017).

Interpretation of 68Ga-FAPI PET/CT imaging

Two certified nuclear medicine physicians with 17 and 5 years of experience independently determined the ^{68}Ga-FAPI PET/CT-based imaging, blinded to the ceCT results. Primary tumors and metastatic lesions were confirmed as positive when their tracer intensity exceeded the local background level and was accompanied by a change in density at the corresponding sites on CT scans(Lin et al. 2022).

We also acquired semiquantitative data by measuring the maximum standardized uptake value (SUV_{max}) of the primary tumor. We drew a region of interest using the work station (United-Imaging Healthcare), which automatically obtained the SUV_{max}.

Confirmation of inconsistent new findings between 68Ga-FAPI PET/CT and ceCT

We defined new findings as any inconsistent findings between ^{68}Ga-FAPI PET/CT and ceCT, including new detected lesions on ^{68}Ga-FAPI PET/CT but missed by ceCT, and lesions on ceCT without ^{68}Ga-FAPI uptake. Inconsistent new findings were confirmed with histopathological data when available.

In the absence of histopathology, a multidisciplinary team consisting of experts in oncology, surgery, radiology, and nuclear medicine reached a consensus on the difference in lesion characteristics between ceCT and 68Ga-FAPI PET/CT scans, and clinical and other imaging information was also used to determine the nature of the lesions. We conducted follow-up on the lesions for a period of at least 6 months, during which follow-up imaging validated the malignant nature of the lesions by showing either the progression of metastatic disease or the response to anticancer treatment. Distant metastatic foci that were positive on ceCT but showed no significant tracer uptake on 68Ga-FAPI PET/CT were ruled out, and these lesions were confirmed through clinical follow-up, with the criterion being no significant change in the lesions within a six-month observation period.

Evaluation of the impact of 68Ga-FAPI PET/CT on patient management

We formed a simulated tumor board, consisting of experts in oncology and surgery to determine pre-^{68}Ga-FAPI PET/CT tumor management, with international guidelines as the reference. Post-^{68}Ga-FAPI PET/CT tumor management was extracted from medical records of real-world practice. Changes in management were classified into major changes and minor changes. Major changes included shifts in the type of treatment or intent, such as transitioning from curative to palliative treatment. Modifications within the same type of treatment strategy were classified as minor changes, such as adjustments to chemotherapy drugs or the incorporation of local therapies.

Statistical analysis

We conducted a descriptive analysis of the data by comparing changes in tumor stage, postoperative recurrence status, and tumor management. Statistical analyses were performed using SPSS software (26.0, IBM Inc.). Continuous variables were expressed as the mean ± SD. Categorical variables were presented as numbers and percentages. The Sankey diagram was used to visually depict the changes in tumor staging and clinical management from the pre-^{68}Ga-FAPI PET/CT phase to the post-PET/CT phase.

Results

Patient characteristics

In total, 177 gastric or gastroesophageal junction cancer patients underwent ^{68}Ga-FAPI PET/CT scan were selected. 65 patients were excluded, resulting in the inclusion of 112 patients. The flowchart in Fig. 1 showed the distribution of patient exclusion criteria.

The baseline characteristics of the patients are summarized in Table 1. Included patients comprised 38 females and 74 males, aged between 24 and 83 years (median age: 60 years). The cohort predominantly consisted of inpatients (n = 89, 79.5%). Most of the tumors were located in the gastric region (n = 80, 71.4%), with approximately one-quarter of the tumors located at the esophagogastric junction (n = 32, 28.6%). According to the histological type, 68 patients (60.7%) were classified with no signet ring cell carcinoma, while 42 patients (37.5%) exhibited signet ring

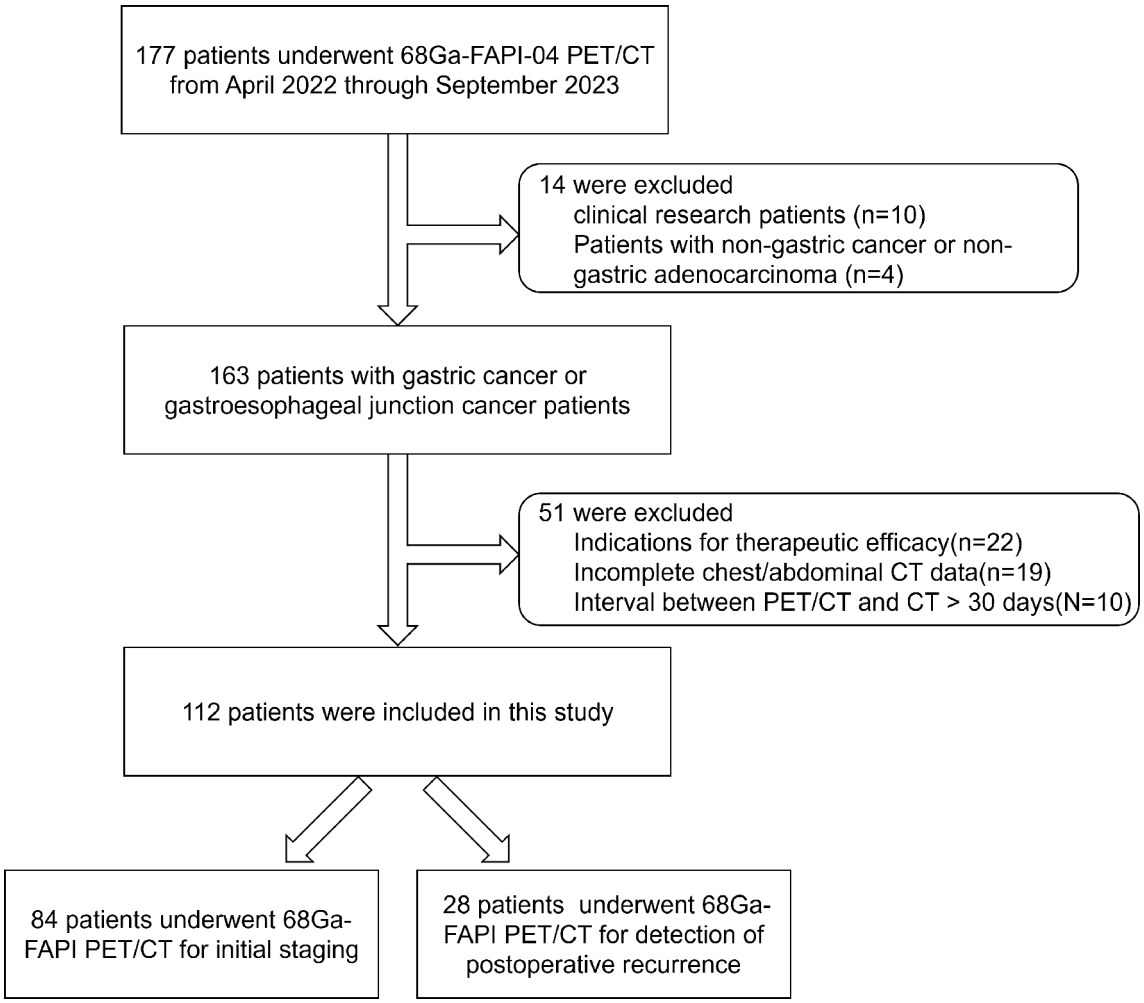

Fig. 1 Flowchart showing exclusion criteria

cell carcinoma. Further pathological features are detailed in Table 1.

Indications for 68Ga-FAPI PET/CT

84 (75%) patients underwent ^{68}Ga-FAPI PET/CT scans at the time of initial diagnosis (initial staging group), while 28 (25%) underwent scans in the postoperative setting to investigate suspected recurrence (detection of postoperative recurrence group). Most patients evaluated by ceCT had advanced T stage of the primary lesion, with 15 patients (17.9%) at T3 stage, 58 patients (69.0%) at T4a stage, and 9 patients (10.7%) at T4b stage. Only 2 patients (2.4%) were identified as T2 stage. The other group underwent ^{68}Ga-FAPI PET/CT scanning to detect postoperative recurrence in the presence of clinical symptoms, abnormal laboratory tests, and ambiguous CT findings. Further details regarding the indications for ^{68}Ga-FAPI PET/CT are provided in Supplemental Table 2.

Detection of primary tumors in initial staging group

The ability of ^{68}Ga-FAPI PET/CT to detect primary tumors was comparable with that of ceCT. Among the 84 patients who were imaged for initial staging, both techniques correctly identified all 84 primary tumors. The median SUV_{max} of the primary lesion was 13.60, with a range of 1.73 to 28.43.

New findings on 68Ga-FAPI PET/CT

Twenty-nine new findings in 24 patients were diagnosed as, or ruled out cancer involvement on ^{68}Ga-FAPI PET/CT. In patients of initial staging group, 12 new distant metastatic lesions in 12 patients were identified and 4 in 4 patients were ruled out. In postoperative patients, 13 new distant metastatic lesions in 8 patients were discovered. The new metastatic lesions located in peritoneum (10/25, 40%), distant lymph nodes (9/25, 36%), bone (2/25, 8%), adrenal (2/25, 8%) and liver (2/25, 8%). Of the newly detected distant

Table 1 Baseline characteristics of study population

Characteristics	*N* = 112	%
Age(mean ± SD)	60.47 ± 11.87	
Gender		
Male	74	66.1
Female	38	33.9
Patient origin		
Inpatient	89	79.5
Outpatient	23	20.5
Tumor location		
Esophagogastric junction	32	28.6
Gastric	80	71.4
Pathological pattern		
Signet-ring cell carcinoma	42	37.5
No signet-ring cell carcinoma	68	60.7
Unknow	2	1.8
EBER-ISH		
Positive	4	3.6
Negative	71	63.4
Unknown	37	33.0
MMR		
dMMR	9	8.0
pMMR	96	85.7
Unknown	7	6.3
HER2		
0 / 1+	92	82.1
2+	8	7.1
3+	5	4.5
Unknown	7	6.3
T Stage(*N* = 84)[a]		
T2	2	2.4
T3	15	17.9
T4a	58	69.0
T4b	9	10.7

Abbreviation: MMR, mismatch repair; dMMR, deficient mismatch repair; pMMR, proficient mismatch repair; EBER-ISH, Epstein-Barr encoding region (EBER) in situ hybridization; HER2: human epidermal growth factor receptor-2

[a] T-staging based on CT assessment in 84 patients in the initial staging group

lymph nodes, five (20%) were retroperitoneal lymph nodes, and four (16%) were nonabdominal lymph nodes. Three distant lymph nodes and 1 adrenal metastasis were ruled out by ^{68}Ga-FAPI PET/CT. In addition, ^{68}Ga-FAPI PET/CT led to a new second primary diagnosis in three cases, including a sigmoid colon cancer, a gallbladder cancer, and a prostate cancer. All of these 3 cases were in the initial staging group. Further details of the ^{68}Ga-FAPI PET/CT findings are summarized in Supplemental Table 3.

Impact of 68Ga-FAPI PET/CT on initial staging or detection of postoperative recurrence

In the overall cohort, 21 patients (18.8%) experienced changes in staging or postoperative recurrence status. Among which, 10 patients (47.7%) were upstaged and 4 (19.0%) were downstaged, and 7 (33.3%) more tumor recurrence was detected.

Among the 12 patients who were initially staged as Stage II, 1 patient (8.3%) progressed to Stage IV after ^{68}Ga-FAPI PET/CT examination, while among the 44 patients who were initially classified as Stage III, 9 (20.5%) progressed to Stage IV. Conversely, in the cohort initially staged as IV by CT (28 patients), 4 (14.3%) were downstaged: 3 to stage III and 1 to stage II. In these patients, CT had initially detected metastases in the retroperitoneal lymph nodes and the adrenal gland, whereas subsequent imaging follow-up with 68Ga-FAPI PET/CT confirmed no metastases. In the cohort for the detection of postoperative recurrence, a total of 7 patients were determined to have tumor recurrence due to the discovery of new distant lesions by ^{68}Ga-FAPI PET/CT. Recurrence or metastasis were confirmed by either histopathology or clinical follow-up. Supplemental Table 4 depicts the number of different stages stratified by subgroup of indications. Figure 2 depicts changes in clinical staging for initial staging and postoperative recurrence detection patients after ^{68}Ga-FAPI PET/CT.

Impact of 68Ga-FAPI PET/CT on patient management

In the overall study cohort, ^{68}Ga-FAPI PET/CT had an impact on tumor management in 20 out of 112 patients (17.9%), and all were from the patients whose disease stage or recurrence status changed. Among these patients,

Table 2 Summary of stage, recurrent status and treatment strategy changes

Results	Full cohort		Initial staging		Postoperative	
	Number	%	Number	%	Number	%
Number	112		84		28	
Change in staging or recurrent status	21	18.8	14	16.7	7	25.0
Upstaging or recurrence	17	15.2	10	11.9	7	25.0
Downstaging or non-recurrence	4	3.6	4	4.8	0	0.0
Changes in treatment	20	17.9	14	16.7	6	21.4
Minor change	1	0.9	1	1.2	0	0.0
Major change	19	17.0	13	15.5	6	21.4

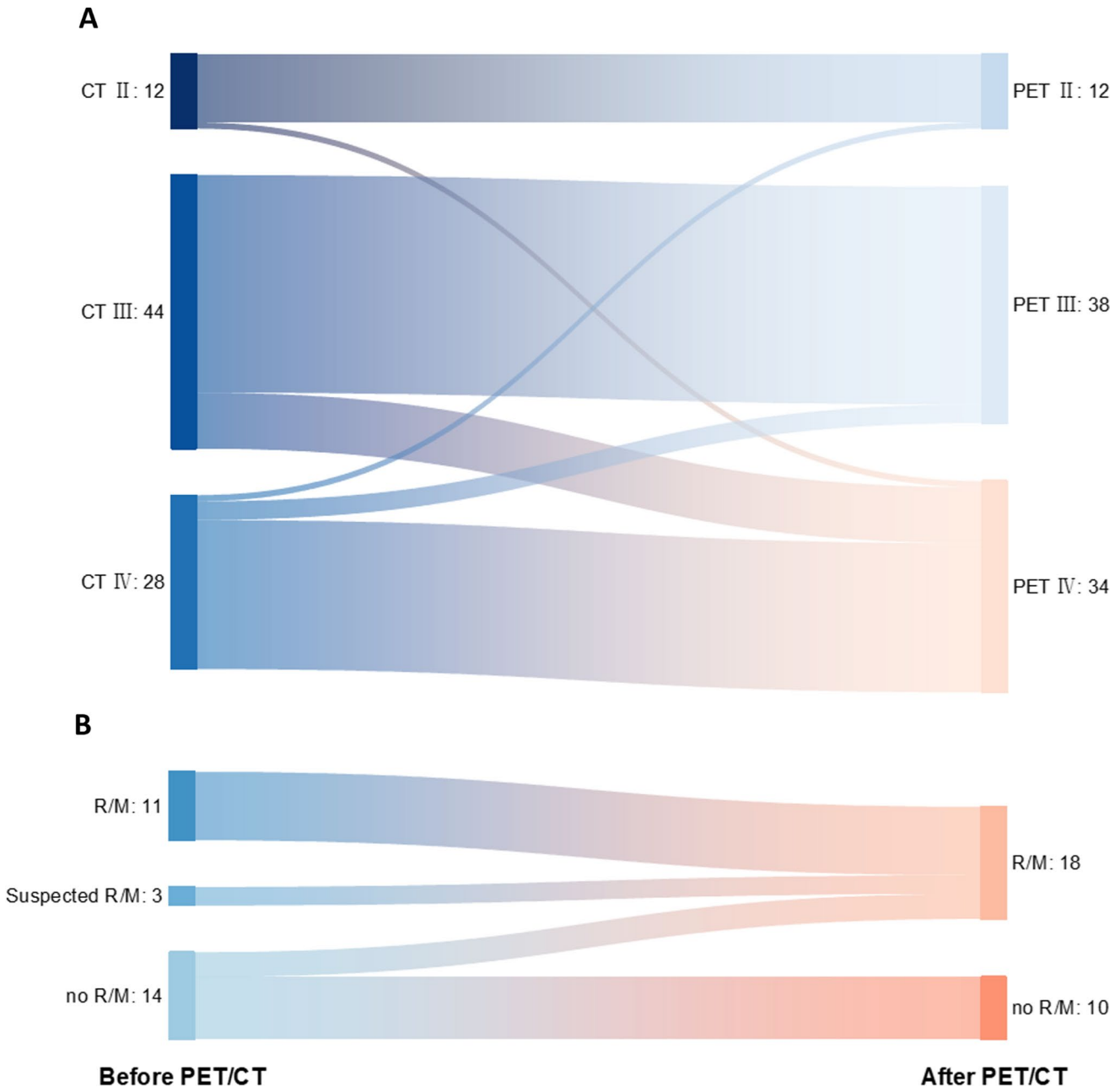

Fig. 2 Changes in clinical staging for initial staging and postoperative recurrence detection patients after ^{68}Ga-FAPI-04 PET/CT (N = 112). A, staging changes in the initial staging cohort; B, recurrence or metastasis changes in the detection of postoperative recurrence cohort. Abbreviation: R/M, recurrence or metastasis

19 patients (17.0%) experienced major changes, while 1 patient (0.9%) experienced minor changes (Table 2).

In the initial staging cohort, all 10 upstaged patients experienced changes in treatment management. Among them, 9 patients underwent major changes, including changes in treatment strategy, such as switching from radical surgery to advanced first-line therapy. One patient underwent a minor adjustment. Upon initial ceCT scan assessment, the patient was diagnosed with stage III. She refused surgical intervention, prompting the implementation of a systemic treatment protocol. After a ^{68}Ga-FAPI PET/CT scan detected peritoneal metastasis, intraperitoneal perfusion chemotherapy was added to the therapeutic regimen. Meanwhile, major changes in management occurred for all 4 patients who were down-staged, shifting their treatment from first-line to neoadjuvant chemotherapy. In the patient with second primary sigmoid colon cancer, a radical resection was performed on both the sigmoid colon and the gastric during laparoscopic exploration. In the patient with second primary gallbladder cancer, no changes were made to the treatment regimen due

to the similar treatment regime. Another patient continued to focus on gastric cancer due to the relatively favorable prognosis of prostate cancer.

In the detection of postoperative recurrence cohort, ^{68}Ga-FAPI PET/CT detected recurrences in 7 patients who were previously not identified by ceCT, leading to management changes for 6 of them. Among these patients, the management was adjusted from surveillance or adjuvant therapy to first-line treatment for the advanced stage. A patient underwent a ^{68}Ga-FAPI PET/CT scan for recurrence detection one month after surgery. Despite a transition in treatment strategy from postoperative adjuvant therapy to first-line therapy, the chemotherapy drugs remained the same. Table 2 summarizes the changes in stage, recurrent status and treatment strategy within the cohort. Figure 3 shows specific changes and distribution of staging and treatment management in patients with changes in staging and recurrent status.

Representative cases

As shown in Fig. 4, a 66-year-old man with gastric moderately differentiated adenocarcinoma was classified as T4a (long arrow) and regional node-positive (short arrow) on contrast CT (a). There was a normal-size (7 mm in short axis) node at the para-aortic region (arrow head, b), and there was no other metastasis on the contrast CT. Then he was classified as stage IIIC and arranged surgery after neoadjuvant therapy. On his staging ^{68}Ga-FAPI PET/CT, both the primary tumor and regional nodes accumulate the tracer, with SUV_{max} of 13.5 and 12.4 respectively (c). Besides, the para-aortic node also accumulated the tracer, with a SUV_{max} of 11.6 (arrow head, d). It was suspected to be metastasis. On the maximum intensity projection image of PET (e), there was no other metastasis. Then a cT4aN+M1, stage IV was assigned, and immunotherapy with Nivolumab was initiated. After six cycles of immunotherapy, another ^{68}Ga-FAPI PET/CT was performed. No tumor lesion could be identified from the PET maximum intensity projection image (f), axial PET (g), and CT (h) through the corresponding level of the para-aortic node. It supported our metastasis diagnosis of that node at initial staging. Another case (Fig. 5) shows that a 68-year-old man with poor gastric differentiated adenocarcinoma was classified as T4a (long arrow) and regional node-positive (short arrow) on contrast CT (a). He was suspected with adrenal metastasis (M1) due to an enhanced mass (arrow head, b). Then he was classified as stage IIIC and arranged palliative therapy. For accurate staging, he received a ^{68}Ga-FAPI PET/CT. On the maximum intensity projection image of PET (c), only the primary tumor could

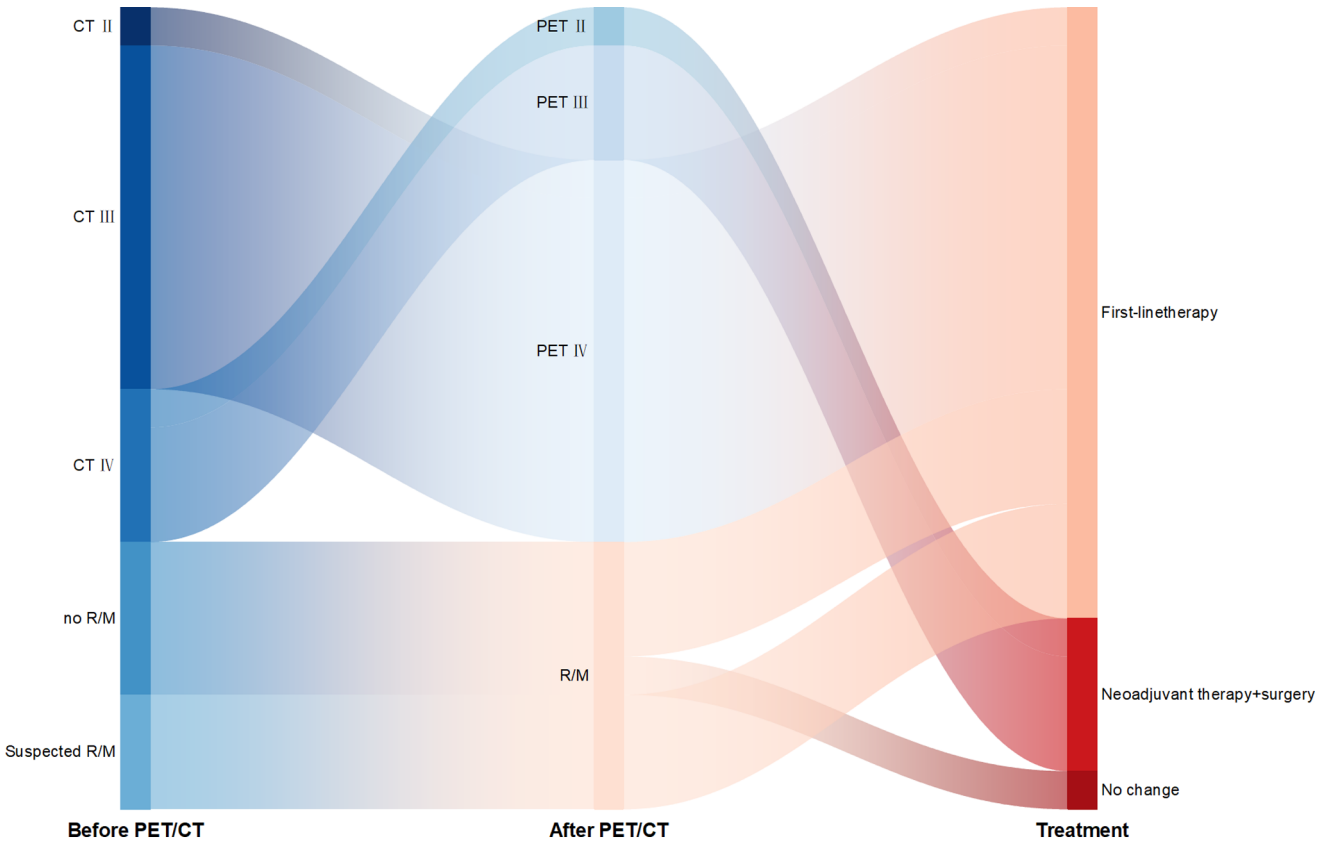

Fig. 3 Specific changes and distribution of staging and treatment management in patients with changes in staging and recurrent status. (N=21

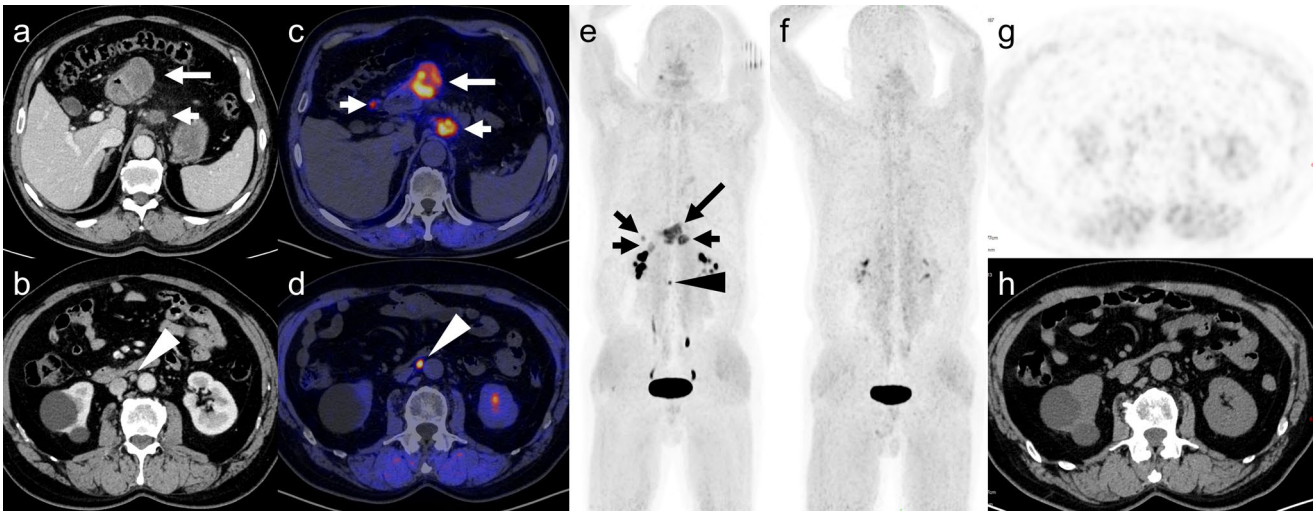

Fig. 4 Representative case 1. T4a staging of primary lesions (long arrow) and regional node positive (short arrow) on contrast CT (**a**). A normal-size (7 mm in short axis) node at the para-aortic region on contrast CT (arrow head, **b**). The primary tumor and regional nodes, showing SUV_{max} of 13.5 and 12.4 respectively, with tracer accumulation on PET (**c**). The para-aortic node, with a SUV_{max} of 11.6, indicating tracer accumulation on PET (arrow head, **d**). The maximum projection image of PET (**e**). f, g,h The results of another 68Ga-FAPI PET/CT scan after six cycles of immunotherapy. The PET maximum projection image (**f**), axial PET (**g**), and CT (**h**) at the level of the para-aortic node, with no identifiable tumor lesions

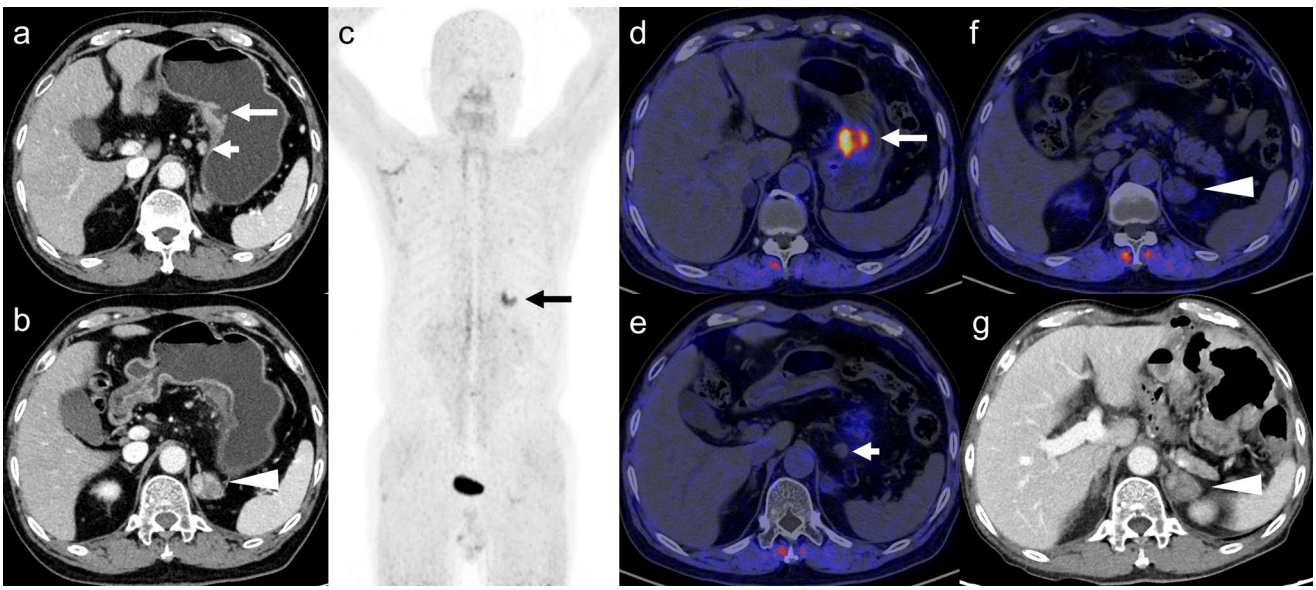

Fig. 5 Representative case 2. T4a staging of primary lesions (long arrow) and regional node positive (short arrow) on contrast CT (**a**). Suspected adrenal metastasis (M1) due to an enhanced mass (arrow head, **b**). The primary tumor identified (long arrow) on the maximum projection image of PET (**c**). The primary tumor (long arrow, **d**) with SUV_{max} of 8.4 on the PET/CT fused image. No tracer accumulation in the regional node (short arrow, **e**) or the adrenal mass (arrow head, **f**). A stable adrenal mass (arrow head, g) on the follow-up contrast CT at 15.5 months

be identified (long arrow). It had a SUV_{max} of 8.4 on PET/CT fused image (long arrow, d). But neither the regional node (short arrow, e) nor the adrenal mass (arrow head, f) accumulated the tracer. Both of them were suspected to be benign. Then a cT4aN0M0, stage IIB was assigned. The patient received surgery after neoadjuvant therapy. All of the harvested regional nodes were negative. His follow-up contrast CT after 15.5 months showed a stable adrenal mass (arrow head, g), which supported the benign diagnosis at initial staging.

Discussion

Our large retrospective cohort study investigated the impact of ^{68}Ga-FAPI PET/CT scans as a supplementary diagnostic tool following CT scans on the detection of new findings in gastric cancer patients, specifically assessing how to influence initial staging, detection of postoperative recurrence and subsequent treatment managements ^{68}Ga-FAPI PET/CT resulted in changes in clinical staging or postoperative recurrence status in approximately 18.8% of patients. The majority of patients (20/21) with staging or postoperative recurrence status change also experienced a change in tumor management, suggesting that ^{68}Ga-FAPI PET/CT-based new findings might directly affect clinical management. These results suggest that ^{68}Ga-FAPI PET/CT is a promising new imaging modality for gastric cancer staging and detection of postoperative recurrence.

PET/CT with ^{18}F-FDG plays a pivotal role in tumor staging and detection of postoperative recurrence providing reference information for guiding clinical management. However, its diagnostic performance in gastric cancer remains controversial. This controversy may stem from various factors affecting ^{18}F-FDG uptake, including tumor size, physiological uptake in the gastric wall, and specific gastric cancer types such as signet ring cell carcinoma(Seko-Nitta et al. 2021). According to a systematic review, ^{18}F-FDG PET/CT changed the management of 3–29% of gastric cancer patients by detecting additional diseases (Foley et al. 2022). Studies with larger cohort sizes often report a lower proportion of cases where ^{18}F-FDG PET/CT changes staging and management, reflecting the data heterogeneity in different studies. The largest and only prospective study reported that ^{18}F-FDG PET/CT changed the treatment plan for only 3% of patients (Gertsen et al. 2021). Findlay et al. conducted the largest retrospective analysis on the routine role of ^{18}F-FDG PET/CT for staging gastric cancer (N=279) and discovered additional metastases in 4.7% of patients (Findlay et al. 2019). These results highlight the limited additional value of ^{18}F-FDG PET/CT in gastric cancer staging and management.

Previous studies have also confirmed the superiority of ^{68}Ga-FAPI over ^{18}F-FDG in identifying primary lesions and determining distant metastasis in gastric cancer (Lin et al. 2022; Miao et al. 2023; Kuten et al. 2022). Compared with ^{18}F-FDG PET/CT, ^{68}Ga-FAPI PET/CT has demonstrated greater accuracy in staging gastrointestinal tumors, with 8.7-28% of patients experiencing increased staging due to the discovery of new distant metastases (Miao et al. 2023; Zhang et al. 2022; Wang et al. 2024; Pang et al. 2021; Chen et al. 2023). Consequently, ^{68}Ga-FAPI PET/CT could provide more reliable evidence for disease staging and enhance the credibility of staging assessments. Our study showed that ^{68}Ga-FAPI PET/CT resulted in a change in staging or detection of postoperative recurrence for 18.8% of patients, which is comparable to previous studies. It is notable that there is currently a paucity of research regarding the influence of ^{68}Ga-FAPI PET/CT on treatment strategies. Some studies have also validated the positive role of ^{68}Ga-FAPI PET/CT in the management of digestive system tumors (Koerber et al. 2020, 2023; Kosmala et al. 2023; Röhrich et al. 2021; Qin et al. 2022). However, in these studies, gastric cancer patients were analyzed only as a subgroup with small sample sizes, showing that ^{68}Ga-FAPI PET/CT led to changes in oncologic management for 20-26.7% of patients (Kosmala et al. 2023; Qin et al. 2022). Moreover, not all findings were confirmed by pathology or imaging follow-up. Zhang et al. reported that ^{68}Ga-FAPI PET/CT resulted in restaging in 7/25 patients (28.0%) with gastric cancer whose treatment management had completely changed (Zhang et al. 2022). This indicated that ^{68}Ga-FAPI PET/CT had a superior impact on clinical management compared with ^{18}F-FDG PET/CT, although the cohort size was small. Our large-sample retrospective study showed that 18.8% of patients experienced stage changes or postoperative recurrence due to new findings from ^{68}Ga-FAPI PET/CT, leading to changes in clinical management for 17.9% of patients. It is evident that ^{68}Ga-FAPI PET/CT is important for the staging, detection of postoperative recurrence, and management of gastric cancer patients.

Our study showed that ^{68}Ga-FAPI PET/CT can detect more new findings, especially distant metastases than CT. In our cohort, the most common types of distant metastasis found on ^{68}Ga-FAPI PET/CT were distant lymph node metastasis and peritoneal metastasis. Previous studies indicated that ^{68}Ga-FAPI PET/CT exhibited a significantly greater detection rate for distant lymph node metastases in the supraclavicular, mediastinal, abdominal, and pelvic regions compared with ^{18}F-FDG PET/CT (Zhang et al. 2022; Liu et al. 2023). Several studies have also validated the unique advantages of ^{68}Ga-FAPI PET/CT in diagnosing peritoneal metastasis of gastric cancer (Lin et al. 2022; Qin et al. 2022; Li et al. 2023), and our research findings paralleled these findings. There are several potential reasons for the advantage of the^{68}Ga-FAPI PET/CT in diagnosing peritoneal metastases. A robust fibrotic response might occur as tumors invade peritoneal tissue (Kurashige et al. 2015; Capobianco et al. 2017). Additionally, the intestinal uptake of ^{68}Ga-FAPI was minimal, and the high contrast of the target background aided in highlighting small peritoneal foci (Hathi et al. 2019).

We recognize the following limitations of our study. First, not all ^{68}Ga-FAPI PET/CT-positive lesions had a robust pathological biopsy as a reference standard. Thus, we compared the staging based on ^{68}Ga-FAPI PET/CT, and

avoided commenting on lesion-based accuracy and impacts. Second, ^{18}F-FDG PET/CT was not integrated into the standard screening regimen for gastric cancer. Third, this was a single-center retrospective study in which many patients who were strongly suspected of having recurrence or who presented with challenging late-stage disease (stages III-IV) underwent ^{68}Ga-FAPI PET/CT evaluation, potentially leading to selection bias. Future large-scale prospective studies are required to document the treatment management of pre- and post-PET/CT interventions, facilitate efficacy comparisons, and offer a comprehensive overview of the diagnostic utility of ^{68}Ga-FAPI PET/CT in gastrointestinal cancer. Ultimately, our retrospective analysis did not delve into the cost-effectiveness associated with the additional use of 68Ga-FAPI PET/CT based on initial ceCT findings, and further investigation is needed through prospective studies. The objective of this study was to investigate the supplementary value of ^{68}Ga-FAPI PET/CT in the diagnosis of gastric cancer compared to ceCT, rather than comparing their diagnostic efficacies. We plan to conduct research in this area in the future.

Conclusion

^{68}Ga-FAPI PET/CT is a valuable tool for precise staging and detection of postoperative recurrence of gastric cancer patients, particularly in patients initially assessed by CT as locally advanced, and in postoperative patients with abnormal laboratory tests, clinical symptoms, or equivocal CT findings. Additionally, the revised staging based on ^{68}Ga-FAPI PET/CT has the potential to alter clinical management.

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Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical approval This is a retrospective cohort study. Approval was granted by the Ethics Committee of West China Hospital, Sichuan University (Date2024/No843).

Consent to participate Not applicable.

Competing interests The authors declare no competing interests.

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