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Value of ^{68}Ga-FAPI-04 and ^{18}F-FDG PET/CT in Early Prediction of Pathologic Response to Neoadjuvant Chemotherapy in Locally Advanced Gastric Cancer

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This prospective study investigated whether PET parameters from ^{18}F-FDG and ^{68}Ga-fibroblast activation protein inhibitor (FAPI)-04 PET/CT can predict a pathologic response to neoadjuvant chemotherapy (NAC) early in patients with locally advanced gastric cancer (LAGC). **Methods:** The study included 28 patients with LAGC who underwent ^{18}F-FDG PET/CT and ^{68}Ga-FAPI-04 PET/CT at baseline and after 1 cycle of NAC. PET parameters including SUV and tumor-to-background ratio (TBR), as well as the change rate of SUV and TBR, were recorded. Patients were classified as major or minor pathologic responders according to postoperative pathology findings. We compared the PET parameters between the 2 pathologic response groups and different treatment regimens and analyzed their predictive performance for tumor pathologic response. **Results:** Major pathologic responders had significantly lower ^{68}Ga-FAPI change rates (percentage SUV_{max} [%SUV_{max}], percentage SUV_{peak} [%SUV_{peak}], and percentage TBR [%TBR]) than minor pathologic responders. Among the PET parameters, ^{68}Ga-FAPI %SUV_{max} (area under the curve, 0.856; $P = 0.009$), %SUV_{peak} (area under the curve, 0.811; $P = 0.022$), and %TBR (area under the curve, 0.864; $P = 0.007$) were significant parameters for early prediction of pathologic response to NAC in LAGC; they had the same predictive accuracy of 89.29%, with the thresholds of decrease to at least 52.43%, 60.46%, and 52.96%, respectively. In addition, ^{68}Ga-FAPI %SUV_{max} and %TBR showed significant differences between the different treatment regimens. **Conclusion:** In this preliminary study, ^{68}Ga-FAPI-04 PET change rate parameters were preferable to ^{18}F-FDG in predicting pathologic response to NAC at an early stage in LAGC. ^{68}Ga-FAPI %SUV_{max} and %TBR may be better predictors of therapeutic response between different treatment regimens. These findings may help optimize the treatment for patients with LAGC.

Key Words: fibroblast activation protein inhibitor; PET/CT; neoadjuvant chemotherapy; locally advanced gastric cancer

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In patients with locally advanced gastric cancer (LAGC) before radical surgery, neoadjuvant chemotherapy (NAC) is increasingly being applied because it may help control focal lesions, downstage tumors, increase R0 resection rates, and improve the disease-free and overall survival of patients (*1–4*). However, the role of preoperative NAC in LAGC remains controversial (*5,6*). For patients with poor sensitivity to chemotherapy, NAC may not only increase treatment-related adverse effects but also delay the optimal timing of surgery. Tumor regression grade (TRG) is an indicator of pathologic response to NAC and an important prognostic factor after NAC in gastric cancer (*7–9*). However, TRG can be determined only by postoperative pathology after completion of NAC treatment. Therefore, early prediction of patients with a suboptimal pathologic response and timely adjustment of their treatment plan are clinically important.

^{18}F-FDG PET aids in assessing treatment response in various malignancies (*10–13*). However, the interference of physiologic or inflammatory accumulation of ^{18}F-FDG in the gastric wall, as well as the low ^{18}F-FDG uptake in signet ring cell carcinoma (SRCC), mucinous adenocarcinoma, and some poorly differentiated carcinomas with a high mucinous component, limits its use for assessing treatment response in patients with gastric cancer (*14*).

^{68}Ga-labeled fibroblast activation protein inhibitor (FAPI), an emerging PET tracer, targets fibroblast activation protein overexpressed on cancer-associated fibroblasts, which are predominant in the tumor microenvironment (*15*). The use of FAPI-based tracers has shown promise in the assessment of digestive system tumors, particularly gastric cancer (*16,17*). Our recent study has substantiated that ^{68}Ga-FAPI-04 PET/CT is better than ^{18}F-FDG in detecting primary gastric cancer lesions and peritoneal metastases, particularly in poorly cohesive carcinoma (PCC) (including SRCC) (*18*). However, the value of ^{68}Ga-FAPI PET/CT in the assessment of treatment response is still unclear.

Hence, this prospective study aimed to investigate whether PET parameters from ^{18}F-FDG and ^{68}Ga-FAPI-04 PET/CT can be used to predict pathologic response to NAC early. The results would help personalize the treatment for patients with LAGC.

MATERIALS AND METHODS

Patients

This prospective clinical study was approved by the Ruijin Hospital Ethics Committee of Shanghai Jiao Tong University School of Medicine

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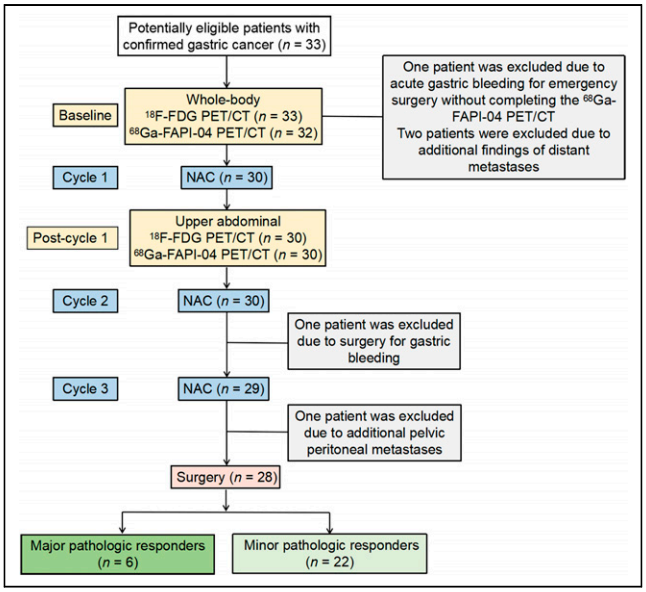

FIGURE 1. Flowchart of study.

and registered at ClinicalTrials.gov (NCT05140746). Patients were enrolled consecutively from September 2020 to October 2022, and all provided written informed consent. The inclusion criteria were as follows: age of 18–75 y; gastric adenocarcinoma histologically confirmed through gastroscopy; resectable gastric cancer; Eastern Cooperative Oncology Group performance status of 0–1; white blood count greater than 4×10^9/L; absolute neutrophil count greater than 2×10^9/L; hemoglobin greater than 90 g/L; platelets greater than 100×10^9/L; ejection fraction greater than 50%; serum bilirubin less than 1.5 times the upper level of normal; alanine-transaminase and aspartate-transaminase less than 1.5 times the upper level of normal; serum creatinine no more than 1.5 times the upper level of normal or glomerular filtration rate more than 60 mL/min; a signed informed consent form; willingness and ability to comply with the protocol throughout the study period; and no childbearing plan within 6 mo. Conversely, the exclusion criteria included the following: a second primary malignant disease in the past 5 y, except for basal cell and squamous cell carcinoma of the skin that have been cured; a known hypersensitivity reaction to chemotherapy drugs or with contraindications; severe disease or other unsuitable conditions determined by investigators and inadequate organ function; uncontrollable diabetes or a fasting blood glucose level of at least 11 mmol/L on the test day; severe mental symptoms, unconsciousness, or inability to complete the examination; pregnancy or possible pregnancy; breastfeeding; and noncompliance.

Treatment Schemes

The NAC treatment was based on the SOX regimen (tegafur gimeracil oteracil potassium capsule for 2 wk with oxaliplatin on day 1, every 3 wk for 3 courses). According to randomization, 16 received the SOX regimen alone, 4 received the SOX regimen combined with apatinib, and 8 received the SOX regimen combined with apatinib and camrelizumab. Surgery was performed at a median of 30.5 d (range, 3–6 wk) after NAC completion.

PET/CT Imaging

^{68}Ga-FAPI-04 was prepared according to a previous procedure (*18*). Briefly, radioactive gallium (^{68}Ga) was extracted from a ^{68}Ge/^{68}Ga generator and added to a reactor vial with 20 μg of DOTA-FAPI-04 (CSBio) and then mixed with NaOAc (1 mol/L, 1 mL) to achieve a pH of 4. An automated synthesis module (Trasis) was used to react the mixture further at 100°C for 10 min. ^{18}F-FDG was routinely synthesized. Patients underwent ^{18}F-FDG PET/CT and ^{68}Ga-FAPI-04 PET/CT imaging covering the whole body (from the top of the head to the upper thigh) at baseline and the upper abdomen after 1 NAC cycle. The interval between ^{18}F-FDG and ^{68}Ga-FAPI-04 PET/CT scans was within 7 d, and the interval between the first cycle of NAC treatment and the postcycle 1 PET/CT scan was 15–20 d. After being injected with ^{18}F-FDG (3.7–4.44 MBq/kg) or ^{68}Ga-FAPI-04 (1.85–2.96 MBq/kg), patients rested for 60–90 or 30–60 min, respectively. Patients with excluded contraindications were then administered 20 mg of hyoscine-*N*-butylbromide intravenously and then drank approximately 500 mL of water to distend the stomach before scanning. PET/CT scans

TABLE 1
Clinical and Pathologic Characteristics of Patients

Characteristic	*n*	%
Patients	28	
Sex		
Male	21	75.00
Female	7	25.00
Histologic type		
Containing PCC	14	50.00
Without PCC	14	50.00
Pathologic tumor staging		
ypT0	1	3.57
ypT1	2	7.14
ypT2	5	17.86
ypT3	12	42.86
ypT4	8	28.57
Pathologic lymph node staging		
ypN0	15	53.57
ypN1	8	28.57
ypN2	3	10.72
ypN3	2	7.14
Degree of differentiation		
Well	0	0.00
Moderately	9	32.14
Poorly	18	64.29
Not applicable	1	3.57
Lauren classification		
Intestinal subtype	12	42.86
Mixed subtype	3	10.71
Diffuse subtype	11	39.29
Not applicable	2	7.14
TRG		
0	1	3.57
1	5	17.86
2	16	57.14
3	6	21.43

Median age is 61 y (range, 38–75 y). Pathologic staging is according to eighth American Joint Committee on Cancer Post–Neoadjuvant Therapy Classification system.

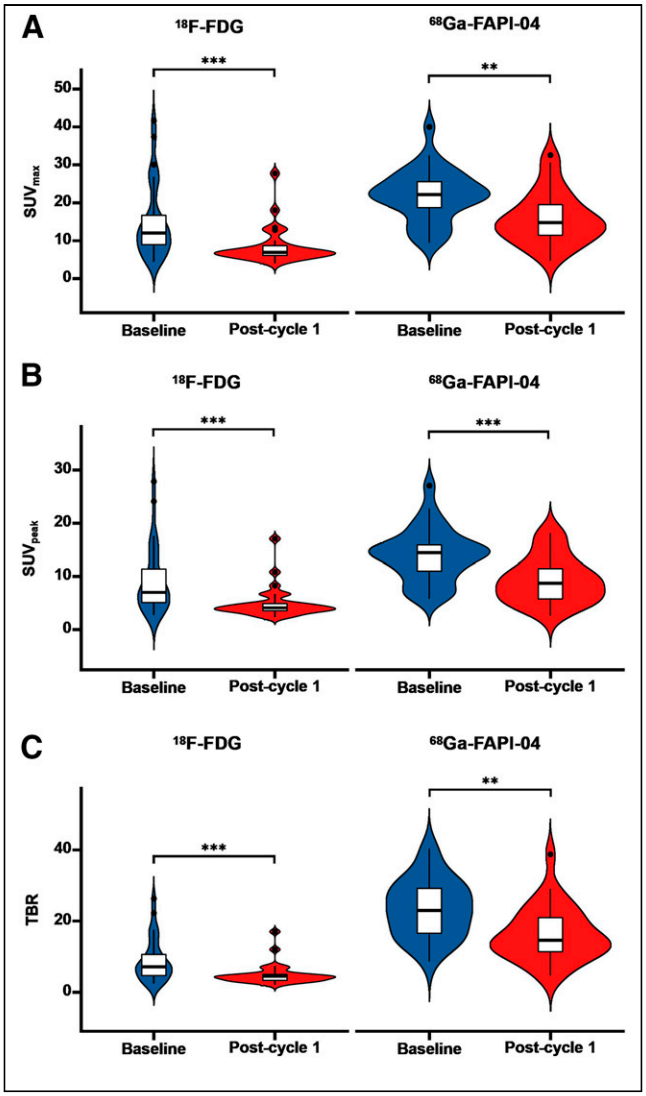

FIGURE 2. Changes in PET parameters at baseline and after 1 NAC cycle: SUV_{max} (A), SUV_{peak} (B), and TBR (C) from ^{18}F-FDG and ^{68}Ga-FAPI-04 PET. $^{**}P < 0.01$. $^{***}P < 0.001$.

were performed using a dedicated PET/CT scanner (Biograph Vision 450; Siemens Healthineers). CT images were captured using CARE Dose4D (Siemens) technique (120 kV, automatic mA-modulation), whereas PET images were captured in 3-dimensional mode and reconstructed in a 440 × 440 matrix (iterations, 4, subsets, 5) using the TrueX + TOF (ultraHD-PET; Siemens) method.

Image Analysis

All PET/CT images were independently evaluated by 2 experienced nuclear medicine physicians. Both baseline and postcycle 1 ^{18}F-FDG PET/CT and ^{68}Ga-FAPI-04 PET/CT images were analyzed using the syngo.via software (Siemens Molecular Imaging). A spheric region of interest was drawn around tumor lesions, and it was automatically adjusted to a 3-dimensional volume of interest at 60% isocontour (*19*). PET parameters including the SUV_{max} and the SUV_{peak} were recorded. To measure the SUV_{mean} of the mediastinal blood pool background, we set a 10-mm-diameter volume of interest on the descending aorta. Furthermore, we calculated the tumor-to-background ratio (TBR) as tumor lesion SUV_{max}/mediastinal blood pool background SUV_{mean}; the change rate of SUV (%SUV) as [postcycle 1 SUV − baseline SUV]/baseline SUV × 100%; and the change rate of TBR (%TBR) as [postcycle 1 TBR − baseline TBR]/baseline TBR × 100%.

Pathologic Assessment

The postoperative specimens were examined histopathologically, and the TRG was based on the following: grade 0, complete regression with no viable cancer cells; grade 1, moderate regression with single cancer cells or a small cluster of cancer cells; grade 2, minimal regression with residual cancer but less than fibrosis; grade 3, poor regression with extensive residual cancer, or minimal or no cancer cell death (*20*). Grades 0 and 1 indicate a major pathologic response, whereas grades 2 and 3 indicate a minor pathologic response.

Statistical Analysis

Statistical analysis was performed using the IBM SPSS Statistics 26.0 software. Continuous variables for SUV, TBR, %SUV, and %TBR are presented as medians and interquartile ranges, whereas categoric variables are expressed as numbers and percentages. The Wilcoxon signed-rank test was used to compare ^{18}F-FDG and ^{68}Ga-FAPI-04 PET parameters, as well as PET parameters at baseline and after 1 NAC cycle. The Mann–Whitney *U* test was used to compare PET parameters between the major and minor pathologic responders. The Kruskal–Wallis test was used to compare PET parameters between the different regimens. The correlation between variables was assessed using the Spearman rank correlation coefficient. The area under the curve (AUC) was obtained using the receiver operating characteristic curve, and the optimal predictive threshold was further calculated using the Jorden index (i.e., sensitivity + specificity − 1). The predictive performance for tumor pathologic response, including sensitivity, specificity, positive predictive value, negative predictive value, and accuracy, was also analyzed. All statistical data were analyzed using the 2-tailed test, and a *P* value of less than 0.05 was considered statistically significant.

RESULTS

Patients

Of the 33 potentially eligible patients, 28 were ultimately enrolled and succeeded in completing the study. Figure 1 presents the study's flowchart. Within the cohort, 6 patients were major pathologic responders, whereas 22 were minor pathologic responders. Table 1 summarizes the clinical and pathologic characteristics of the 28 patients.

Comparison of PET Parameters at Baseline and 1 Cycle After NAC in Patients with LAGC

At baseline, all 28 patients were ^{68}Ga-FAPI-04–avid, whereas 23 of 28 were ^{18}F-FDG–avid. Five patients with non–^{18}F-FDG–avid tumors were confirmed as having PCC (with partial SRCC). Moreover, baseline ^{68}Ga-FAPI-04 SUV_{max} was significantly higher than ^{18}F-FDG SUV_{max} (22.15 [18.44–26.59] vs. 12.05 [8.25–19.32], $P = 0.007$), as well as SUV_{peak} (14.43 [10.73–15.90] vs. 7 [5.05–13.00], $P = 0.003$) and TBR (23.01 [15.93–29.24] vs. 7.17 [4.51–11.54], $P < 0.001$). After 1 NAC cycle, ^{18}F-FDG PET parameters (SUV_{max}, SUV_{peak}, and TBR) significantly decreased ($P < 0.001$, $P < 0.001$, and $P < 0.001$, respectively), as did ^{68}Ga-FAPI-04 PET parameters ($P = 0.001$, $P < 0.001$, and $P = 0.001$, respectively). Figure 2 shows the changes in ^{18}F-FDG and ^{68}Ga-FAPI-04 PET parameters at baseline and after 1 NAC cycle in patients with LAGC.

Correlations Between PET Parameters and Pathologic Features

Figure 3 presents the correlations between ^{18}F-FDG and ^{68}Ga-FAPI-04 PET parameters and the pathologic features. First, the

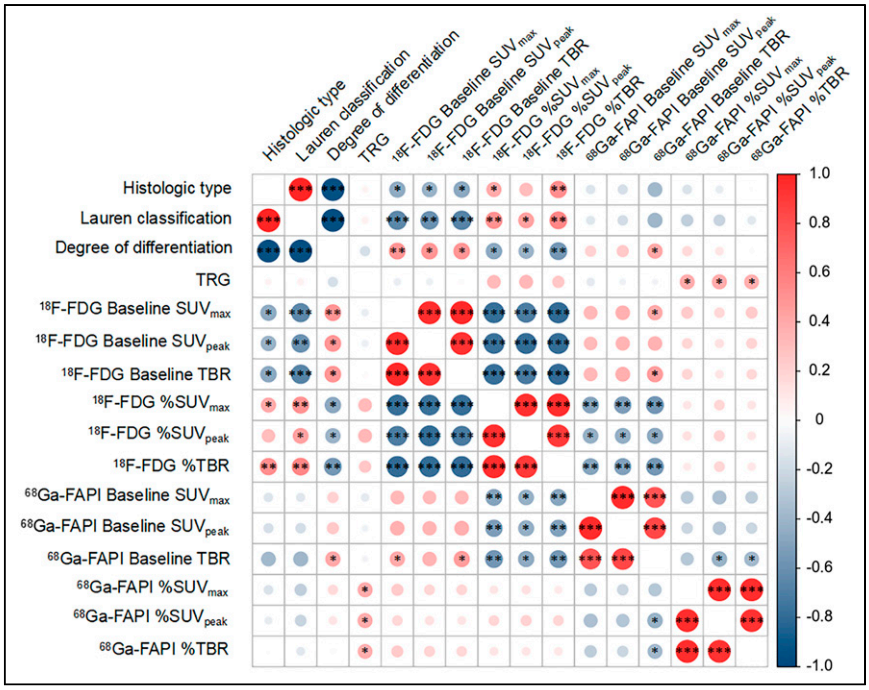

FIGURE 3. Correlations between PET parameters and pathologic features. Red circle denotes positive correlation between 2 factors, whereas blue circle denotes negative correlation. Darker color indicates stronger correlation. *P* values show statistical difference in correlation between 2 factors. $^{*}P < 0.05$. $^{**}P < 0.01$. $^{***}P < 0.001$.

^{18}F-FDG baseline and change rate parameters correlated with histologic type, Lauren classification, and differentiation degree, whereas most of the ^{68}Ga-FAPI-04 PET parameters did not correlate with the abovementioned pathologic characteristics. Second, TRG correlated with ^{68}Ga-FAPI-04 change rate parameters including %SUV$_{max}$, %SUV$_{peak}$, and %TBR but not with the baseline or change rate parameters of ^{18}F-FDG PET. Additionally, the ^{18}F-FDG PET parameters partially correlated with ^{68}Ga-FAPI-04 parameters, but there was no correlation between ^{18}F-FDG and ^{68}Ga-FAPI-04 PET change rate parameters.

Comparison of PET Parameters Between NAC Major and Minor Pathologic Responder Groups

Table 2 compares the ^{18}F-FDG and ^{68}Ga-FAPI PET parameters between the NAC major and minor pathologic responders in the whole cohort. The results showed that major pathologic responders had significantly lower ^{68}Ga-FAPI change rate parameters including %SUV$_{max}$, %SUV$_{peak}$, and %TBR ($P = 0.009$, $P = 0.022$, and $P = 0.007$, respectively) than minor pathologic responders, whereas both ^{18}F-FDG and ^{68}Ga-FAPI baseline PET parameters and ^{18}F-FDG change rate parameters showed no significant difference between the 2 groups. Supplemental Table 1 further compares the ^{18}F-FDG PET parameters between the 2 responder groups in 23 patients with ^{18}F-FDG–avid tumors (supplemental materials are available at http://jnm.snmjournals.org). The results were consistent with those of the overall cohort. Figure 4 displays representative cases of a major and a minor pathologic responder.

TABLE 2
Comparison of PET Parameters Between NAC Major and Minor Pathologic Responder Groups

	Major pathologic responder ($n = 6$)		Minor pathologic responder ($n = 22$)			
Parameter	Median	IQR	Median	IQR	Z	*P*
^{18}F-FDG						
Baseline SUV$_{max}$	12.98	5.43 to 16.71	11.19	8.96 to 26.37	−0.336	0.737
Baseline SUV$_{peak}$	7.89	3.41 to 11.19	6.59	5.09 to 14.03	−0.168	0.867
Baseline TBR	7.37	2.64 to 10.60	7.17	4.69 to 14.80	−0.672	0.502
%SUV$_{max}$	−49.54	−62.30 to −14.03	−35.96	−51.64 to −12.88	−0.840	0.401
%SUV$_{peak}$	−42.86	−74.92 to −22.87	−37.38	−59.84 to −22.73	−0.784	0.433
%TBR	−47.82	−64.05 to −12.65	−35.66	−52.60 to −17.36	−0.728	0.467
^{68}Ga-FAPI-04						
Baseline SUV$_{max}$	21.97	13.33 to 34.38	22.47	18.73 to 25.58	−0.224	0.823
Baseline SUV$_{peak}$	12.76	7.39 to 23.84	14.43	11.19 to 15.89	−0.056	0.955
Baseline TBR	24.22	13.98 to 39.25	23.01	18.43 to 28.92	−0.280	0.780
%SUV$_{max}$	−62.74	−65.63 to −42.29	−16.92	−37.26 to 1.03	−2.631	0.009*
%SUV$_{peak}$	−64.00	−66.35 to −46.52	−21.19	−52.71 to −10.30	−2.296	0.022†
%TBR	−65.06	−67.61 to −42.25	−25.46	−41.46 to 7.25	−2.687	0.007*

*$P < 0.01$.
†$P < 0.05$.
IQR = interquartile range.

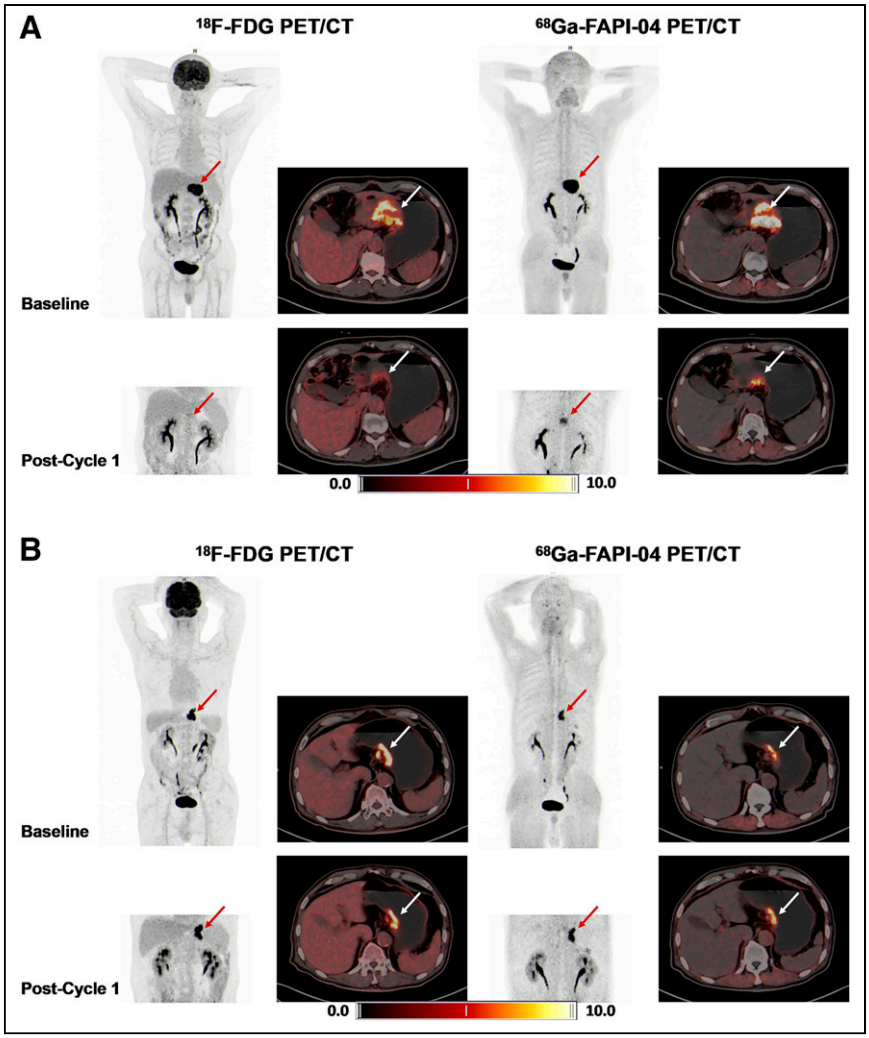

FIGURE 4. ^{18}F-FDG and ^{68}Ga-FAPI-04 PET/CT images at baseline and after 1 NAC cycle: major pathologic responder with TRG grade 0 (arrows, A) and minor pathologic responder with TRG grade 3 (arrows, B).

Performance of PET Parameters in Early Prediction of Pathologic Response to NAC

Supplemental Table 2 and Figure 5 present the receiver operating characteristic curves assessing the predictive accuracy of PET parameters in identifying major and minor pathologic responders to NAC. The AUCs for ^{68}Ga-FAPI %SUV$_{max}$, %SUV$_{peak}$, and %TBR were significant (0.856, 0.811, and 0.864, respectively) among the various PET parameters. Table 3 displays the predictive performance of significant PET parameters in early prediction of pathologic response to NAC. ^{68}Ga-FAPI %SUV$_{max}$, %SUV$_{peak}$, and %TBR had the same accuracy of 89.29%, with the thresholds of decrease to at least 52.43%, 60.46%, and 52.96%, respectively; the sensitivity, specificity, positive predictive value, and negative predictive value were 83.33%, 90.91%, 71.43%, and 95.24%, respectively.

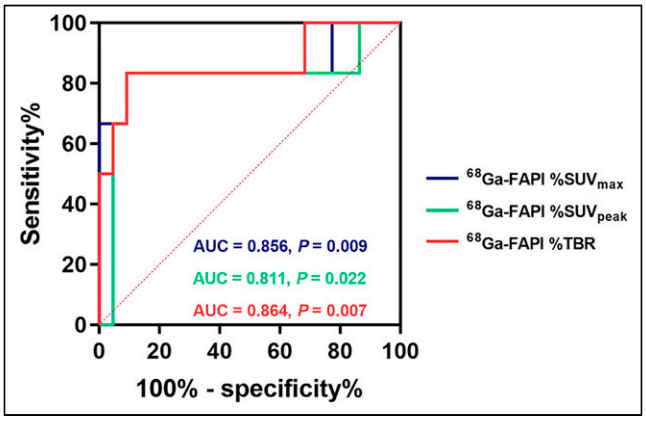

FIGURE 5. Receiver operating characteristic curves for ability of PET parameters to predict pathologic response to NAC early.

Comparison of PET Parameters Between Different NAC Regimens

Figure 6 further compares the ^{18}F-FDG and ^{68}Ga-FAPI change rate parameters among the 3 different regimens. The results showed that ^{68}Ga-FAPI %SUV$_{max}$ and %TBR were significantly lower in the SOX-plus-apatinib-plus-camrelizumab group than in the SOX group (P = 0.028 and 0.028, respectively). However, there were no significant differences between the other groups and for other PET parameters. According to the postoperative pathology, in the SOX, SOX-plus-apatinib, and SOX-plus-apatinib-plus-camrelizumab groups, there were 1 of 16, 0 of 4, and 5 of 8 patients, respectively, who achieved a major pathologic response.

DISCUSSION

In this study, TRG correlated with ^{68}Ga-FAPI change rate parameters including %SUV$_{max}$, %SUV$_{peak}$, and %TBR. Major pathologic responders had significantly lower ^{68}Ga-FAPI change rate parameters than minor pathologic responders. ^{68}Ga-FAPI %SUV$_{max}$, %SUV$_{peak}$, and %TBR could provide an early indication of pathologic response to NAC in LAGC and outperformed ^{18}F-FDG PET parameters. ^{68}Ga-FAPI %SUV$_{max}$ and %TBR may be better predictors of therapeutic response between different treatment regimens.

Considering the heterogeneity of gastric cancer, the therapeutic response to NAC is highly variable and is strongly associated with patient prognosis. A 2-center study found that the 3- and 5-y survival rates of patients with gastric cancer with TRG 0–1 after NAC plus surgery were 85.2% and 74.5%, respectively, compared with 28.2%–56.1% and 23%–44.1%, respectively, in patients with TRG 2–3 (*7*). An earlier metaanalysis of 17 studies on gastroesophageal cancer demonstrated that compared with no or minimal pathologic response after NAC, a major pathologic response is significantly associated with higher overall survival and disease-free survival (*8*). Therefore, we sought to obtain indirect prognostic information using PET/CT imaging techniques to predict pathologic response to NAC early.

Several studies have explored the value of ^{18}F-FDG PET for therapeutic monitoring in gastric cancer but obtained controversial findings (*21*). In our study, ^{18}F-FDG PET parameters did not

TABLE 3
Performance of PET Parameters in Early Prediction of Pathologic Response to NAC

Parameter	AUC	*P*	Threshold	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
^{68}Ga-FAPI %SUV$_{max}$	0.856	0.009*	−52.43	83.33	90.91	71.43	95.24	89.29
^{68}Ga-FAPI %SUV$_{peak}$	0.811	0.022†	−60.46	83.33	90.91	71.43	95.24	89.29
^{68}Ga-FAPI %TBR	0.864	0.007*	−52.96	83.33	90.91	71.43	95.24	89.29

*$P < 0.01$.
†$P < 0.05$.
PPV = positive predictive value; NPV = negative predictive value.

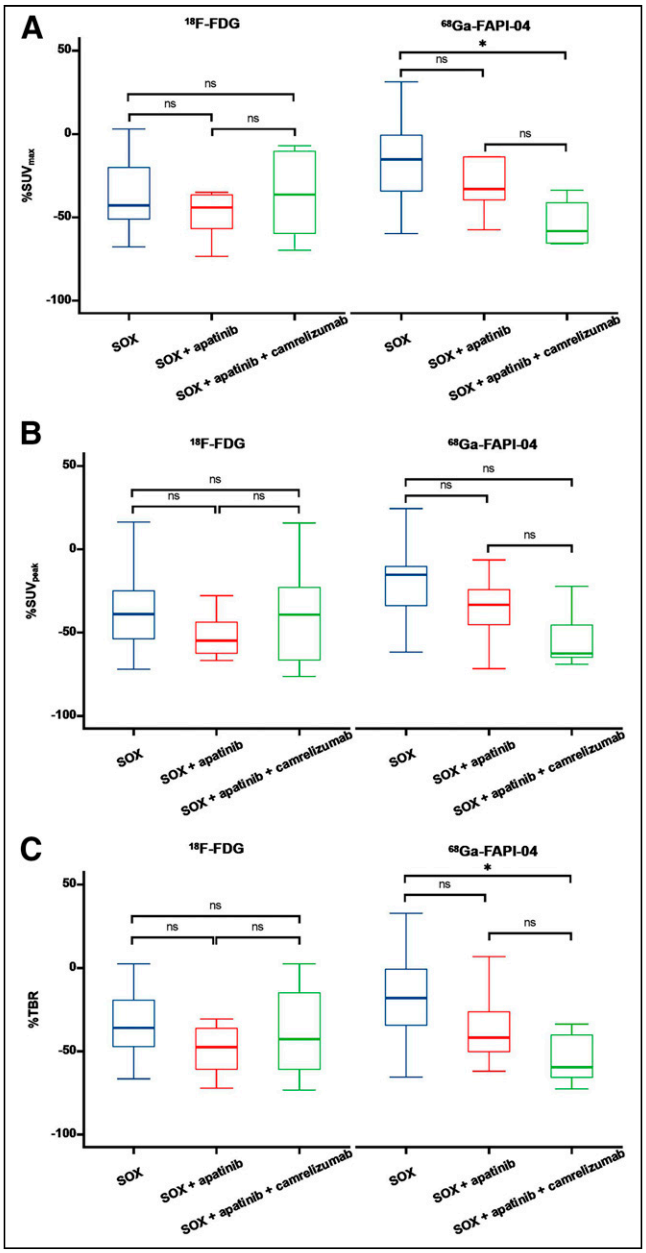

FIGURE 6. Comparison of change rate parameters between different NAC regimens: %SUV$_{max}$ (A), %SUV$_{peak}$ (B), and %TBR (C) from ^{18}F-FDG and ^{68}Ga-FAPI-04 PET. *$P < 0.05$. ns = not statistically significant.

correlate with TRG and were not significantly different between major and minor pathologic responders. This was further verified in ^{18}F-FDG–avid LAGC, as the assessment of metabolic response in non–^{18}F-FDG–avid gastric tumors was considered limited. For PCC (including SRCC), the incidence is on the rise, with a higher proportion of younger women and advanced-stage patients than for non-PCC subtypes, which tend to present as non–^{18}F-FDG–avid tumors, in part due to high mucus content, low tumor cell density, and low glucose transporter 1 expression (*22–24*). Given their poorer prognosis, effective assessment tools are needed.

Numerous studies revealed that ^{68}Ga-FAPI PET is preferable to ^{18}F-FDG in gastric cancer staging and restaging (*22,25–29*). Our previous study also confirmed the superiority of ^{68}Ga-FAPI PET over ^{18}F-FDG in detecting gastric cancer primary lesions and peritoneal metastases, especially in PCC including SRCC (*18*). As observed in our present study, most of the ^{68}Ga-FAPI-04 PET parameters had no significant correlation with the histologic type, Lauren classification, and degree of differentiation of the tumors, consistent with our previous finding (*18*). This may be because FAPI reflects the characteristics of the tumor stroma rather than the tumor cells. In addition, the value of ^{68}Ga-FAPI PET/CT in the early prediction of NAC treatment response in LAGC remains unclear.

Although previous case reports and series showed the initial value of FAPI PET in monitoring treatment response of breast myeloid sarcoma, peritoneal carcinomatosis, and gastric cancer, our prospective study further indicated that ^{68}Ga-FAPI PET change rate parameters (%SUV$_{max}$, %SUV$_{peak}$, and %TBR) could predict the pathologic response to NAC in LAGC early (*27,29–31*). Of these, ^{68}Ga-FAPI %SUV$_{max}$ and %TBR further discriminated the treatment response between different treatment regimens, suggesting that ^{68}Ga-FAPI PET may have potential applicability for monitoring the efficacy of different treatment regimens. However, baseline ^{68}Ga-FAPI PET parameters did not correlate with therapeutic response in our study—a finding that is inconsistent with the findings of Hu et al. (*32*). This may be attributed to different criteria used to evaluate the therapeutic response. Additionally, 5 patients with non–^{18}F-FDG–avid tumors (confirmed as PCC with partial SRCC) were all avid on ^{68}Ga-FAPI-04 PET, suggesting the potential of ^{68}Ga-FAPI PET parameters to predict NAC pathologic response early, especially in non–^{18}F-FDG–avid gastric cancer such as PCC (including SRCC). A typical case is shown in Figure 7. However, the fact that no significant changes in ^{68}Ga-FAPI PET parameters were observed in one of our major pathologic responders—possibly because of superimposition of inflammation or fibrosis after chemotherapy—may be a potential pitfall in predicting NAC efficacy that requires further investigation (*33*).

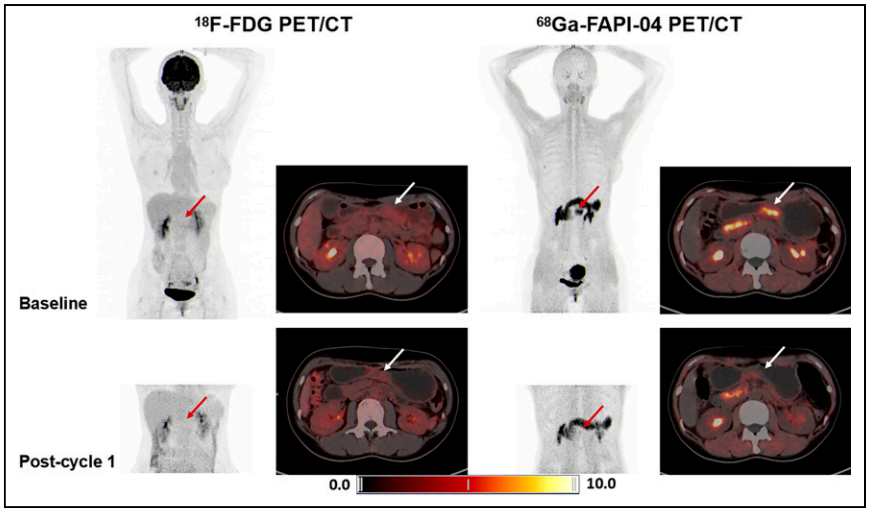

FIGURE 7. ^{18}F-FDG and ^{68}Ga-FAPI-04 PET/CT images at baseline and after 1 NAC cycle in major pathologic responder with TRG grade 1. Patient had non–^{18}F-FDG–avid LAGC (arrows), confirmed as PCC.

This study had several limitations. First, the sample size was relatively small. Especially, the number of patients showing a major response to NAC was limited, preventing further stratification analysis according to clinicopathologic characteristics. Second, an upper abdominal local PET/CT scan was used as an early evaluation scheme in our study; its use may contribute to underestimation because of the heterogeneity of tumor sensitivity to chemotherapy. For example, one of our patients had a new metastatic lesion in the pelvic peritoneum detected by laparoscopy after NAC completion, despite a significant reduction of ^{68}Ga-FAPI uptake in the primary lesion after 1 NAC cycle. In addition, our study was conducted at a single center; further large, multicenter clinical trials are needed to confirm our conclusion.

CONCLUSION

This preliminary study suggests that ^{68}Ga-FAPI-04 PET change rate parameters appear to be more predictive of the pathologic response at an early stage than ^{18}F-FDG PET parameters. ^{68}Ga-FAPI %SUV$_{max}$ and %TBR may be better predictors of therapeutic response between different treatment regimens, but this possibility needs to be verified in a larger cohort. This insight may help us understand the sensitivity of chemotherapy and thus optimize treatment regimens.

KEY POINTS

QUESTION: Can PET parameters from ^{18}F-FDG and ^{68}Ga-FAPI-04 PET/CT predict a pathologic response to NAC early in patients with LAGC?

PERTINENT FINDINGS: ^{68}Ga-FAPI PET parameters (including %SUV$_{max}$, %SUV$_{peak}$, and %TBR) could provide an early indication of pathologic response to NAC in LAGC and outperformed ^{18}F-FDG PET parameters. ^{68}Ga-FAPI %SUV$_{max}$ and %TBR may be better predictors of therapeutic response between different treatment regimens.

IMPLICATIONS FOR PATIENT CARE: Our preliminary findings may help optimize treatment for patients with LAGC.

DISCLOSURE

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