

DIAGNOSTIC CAPABILITIES OF $^{68}\text{GA-FAPI}$ PET/CT IN GASTRIC CANCER

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ABSTRACT

Relevance: Gastric cancer remains a significant medical issue due to its high incidence and mortality rates. Hybrid imaging techniques, including positron emission tomography/computed tomography (PET/CT), play an important role in the diagnosis of malignant tumors, including gastric cancer. The development and clinical evaluation of radiopharmaceuticals used in oncology continues to advance.

The study aimed to evaluate the diagnostic capabilities of PET/CT using fibroblast activation protein inhibitor labeled with gallium-68 ($^{68}\text{Ga}\text{F}\text{API-PET/CT}$) in gastric cancer.

Methods: This review includes data from 8 clinical studies (both prospective and retrospective) comparing the diagnostic performance of $^{68}\text{Ga}\text{F}\text{API-PET/CT}$ and fluorodeoxyglucose labeled with fluorine-18 ($^{18}\text{F}\text{FDG}$) in patients with histologically confirmed gastric cancer. The number of patients in the studies ranged from 13 to 112, totaling 379 patients. The parameters analyzed included maximum standardized uptake value (SUV_{max}), tumor-to-background ratio (TBR), and the sensitivity in detecting primary gastric tumors, as well as lymph node and peritoneal metastases.

Results: According to multiple clinical studies, $^{68}\text{Ga}\text{F}\text{API}$ demonstrated higher SUV_{max} and TBR values compared to $^{18}\text{F}\text{FDG}$, especially in the visualization of diffuse, mucinous, and signetring cell histological subtypes of gastric cancer. This is associated with strong expression of FAP in the tumor stroma, enabling effective tracer accumulation in affected areas. Furthermore, $^{68}\text{Ga}\text{F}\text{API-PET/CT}$ showed higher sensitivity in detecting primary gastric lesions (100% vs. 53%), lymph node metastases (79% vs. 54%), and peritoneal metastases (96% vs. 55%) compared to $^{18}\text{F}\text{FDG-PET/CT}$. In 11-67% of patients, the use of $^{68}\text{Ga}\text{F}\text{API-PET/CT}$ led to a change in tumor staging and influenced the formulation of an individualized treatment plan.

Conclusion: $^{68}\text{Ga}\text{F}\text{API-PET/CT}$ demonstrated greater diagnostic performance compared to $^{18}\text{F}\text{FDG-PET/CT}$ in staging gastric malignancies, particularly in histological subtypes with low glycolytic activity. The method offers superior sensitivity and visualization of peritoneal, visceral, and lymphatic metastases, playing a crucial role in determining treatment strategies.

Keywords: gallium-68 labeled fibroblast activation protein inhibitor ($^{68}\text{Ga}\text{F}\text{API}$), gastric cancer (GC), positron emission tomography/computed tomography (PET/CT), cancer staging, fibroblast activation protein (FAP).

Introduction: According to GLOBOCAN 2022, gastric cancer (GC) remains one of the leading causes of cancer-related mortality worldwide, ranking fifth in terms of the number of new cases and deaths among all malignant neoplasms (MNs). It is estimated that in 2022, 968,784 new cases and 660,175 deaths related to this pathology were recorded, indicating that gastric cancer is one of the most prevalent types of oncological diseases [1]. Gastric MNs have risk factors, most of which are immutable characteristics [2].

The diagnostics of gastrointestinal MNs is conducted using standard imaging methods, such as radiographic examination, ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) [3]. Each method has its advantages and limitations, including in assessing the extent of the malignant process [4].

Modern approaches to the diagnostics and staging of GC require high sensitivity, specificity, and reproducibility [5]. An important aspect of the diagnostic process remains hybrid imaging methods, particularly positron

emission tomography/computed tomography (PET/CT) with the radiopharmaceutical (RPh) 18-fluorodeoxyglucose ($^{18}\text{F}\text{FDG}$). However, the informativeness of this method is significantly reduced in cases of mucinous, poorly differentiated, and undifferentiated tumors [6]. One of the reasons for this is the low glucose metabolism in some histological subtypes of gastric tumors, which results in insufficient accumulation of $^{18}\text{F}\text{FDG}$ for their detection [7]. Fibroblast activation protein (FAP), expressed in cancer-associated fibroblasts (CAF), plays a key role in remodeling the tumor microenvironment, invasion, and metastasis [8, 9]. FAP belongs to the family of dipeptidyl peptidases and has enzymatic activity involved in the remodeling of the extracellular matrix, contributing to the progression and invasion of epithelial tumors [10]. In 90% of all epithelial-origin tumors, increased FAP expression is observed [11]. Given that the tumor stroma can predominate in the structure of the neoplasm, targeted imaging of its components, such as activated fibroblasts, represents a more sensitive alternative compared to the visualization of tumor cells alone [12]. The RPh fibroblast ac-

tivation protein inhibitor labeled with gallium-68 ($[^{68}\text{Ga}]$ F⁰API), developed as a high-affinity ligand to FAP, demonstrates a high degree of accumulation in most MNs, including gastric MNs. It has high affinity to FAP, rapid clearance from the blood, and low nonspecific accumulation in normal tissues [13]. $[^{68}\text{Ga}]$ F⁰API has become widely used in oncological imaging following the demonstration of its high affinity to FAP and its potential for radiolabeling for PET diagnostics [14]. Experience with the use of $[^{68}\text{Ga}]$ F⁰API in patients with other solid tumors, including thyroid tumors, confirms its universality and high diagnostic effectiveness [15]. Studies have also shown widespread accumulation of F⁰API in patients with various solid tumors, including gastrointestinal tumors [16]. $[^{68}\text{Ga}]$ F⁰API-PET/CT has demonstrated clinical significance in planning radiation therapy and delineating the radiation volume [17]. Aggregated data confirm the high safety of $[^{68}\text{Ga}]$ F⁰API and its high accuracy in visualizing gastrointestinal tumors [18]. It should also be noted that the accumulation of $[^{68}\text{Ga}]$ F⁰API is independent of the glycolytic activity of the tumor, making it particularly useful for signet-ring cell tumors of the stomach and other forms with low glucose metabolism [19]. Several studies have shown that $[^{68}\text{Ga}]$ F⁰API has advantages in detecting peritoneal metastases and metastatic lymph nodes, as well as in identifying early disease recurrence after treatment [20]. Peritoneal metastases are the most common form of spread in GC and are responsible for nearly half of the mortality cases, highlighting the need for accurate methods to detect them at early stages. Additionally, $[^{68}\text{Ga}]$ F⁰API has proven effective in diagnosing tumors with low glucose metabolism and in cases with negative $[^{18}\text{F}]$ FDG-PET/CT results [21]. Thus, $[^{68}\text{Ga}]$ F⁰API is a versatile tool for imaging the tumor microenvironment and staging the tumor [22].

The study aimed to evaluate the diagnostic capabilities of PET/CT using fibroblast activation protein inhibitor labeled with gallium-68 ($[^{68}\text{Ga}]$ F⁰API-PET/CT) in gastric cancer.

Materials and Methods: This study includes the results of 8 prospective and retrospective clinical studies published between 2018 and 2024, focusing on the comparison of diagnostic efficacy between $[^{68}\text{Ga}]$ F⁰API-PET/CT and $[^{18}\text{F}]$ FDG-PET/CT in patients with confirmed gastric cancer (GC). The search was conducted in PubMed, Scopus, Web of Science, and Google Scholar databases using the following keywords: "68Ga-F⁰API", "PET/CT", "gastric cancer", "fibroblast activation protein". Inclusion criteria for the publications were: histological confirmation of the diagnosis, performance of both $[^{68}\text{Ga}]$ F⁰API-PET/CT and $[^{18}\text{F}]$ FDG-PET/CT, reporting of maximum standardized uptake value (SU-Vmax) and tumor-to-background ratio (TBR), indication of TNM stage, and data on the impact of the method on treatment strategies.

Standardized PET/CT protocols were used in all included studies: intravenous injection of RPh, a field of view

from the head to the upper third of the thighs, and hybrid PET/CT imaging.

Effectiveness of imaging was assessed by comparing SUVmax and TBR between $[^{68}\text{Ga}]$ F⁰API and $[^{18}\text{F}]$ FDG in primary lesions, lymph nodes, and metastatic sites.

Results: An analysis of the results from 8 prospective and retrospective clinical studies allowed for a comprehensive overview of the existing evidence. Table 1 presents the clinical and methodological parameters of studies on the use of $[^{68}\text{Ga}]$ F⁰API-PET/CT in gastric cancer.

Study Design. 5/8 sources included in the review describe prospective studies, which enhances the evidence strength of the presented results. 3/8 studies followed a retrospective design, which potentially increases the risk of systematic errors and biases related to data selection and the lack of control over variables. Sample size varied from 13 patients [19] to 112 patients [3].

Indications for $[^{68}\text{Ga}]$ F⁰API. The indications to perform $[^{68}\text{Ga}]$ F⁰API-PET/CT were staging, restaging, diagnostics of $[^{18}\text{F}]$ FDG-PET/CT negative cases, visualization of specific histological subtypes, and peritoneal metastatic lesions. These indications highlight the expanding clinical use of $[^{68}\text{Ga}]$ F⁰API beyond standard diagnostics.

Patients (n). A total of 8 clinical studies with 379 patients were included. Larger samples (e.g., S. Zhang [3], Y. Sun [7]) allow for statistically significant conclusions, while smaller series focus on more specialized subtypes.

Activity. The RPh activity used in the studies ranged from 1.11 to 2.96 MBq/kg. In 2 out of 8 studies, the activity was between 1.11-1.85 MBq/kg, in 2 studies it was 1.85 MBq/kg, in 2 studies it ranged from 1.8 to 2.2 MBq/kg, and one study used $[^{68}\text{Ga}]$ F⁰API activity in the range of 2.0-2.5 MBq/kg and 1.85-2.96 MBq/kg. The standard activity dosage range is 1.8-3.7 MBq/kg.

Interval. This parameter indicates the period from the intravenous injection of the RPh to the PET/CT scan. In 7 out of 8 studies, this interval was 60 minutes, and in 1 out of 8 studies, the PET/CT scan was performed between 60 and 90 minutes after the RPh injection.

Stage Correction. The highest frequency of stage modification was noted in the study by A. Selçuk [18], 2025, which was 67%, potentially related to the selection of patients with $[^{18}\text{F}]$ FDG-negative tumors. Similarly, a high percentage of stage progression was observed in the studies by J. Kuten [19], 2022 (38.5%), and Z. Shumao [20], 2022 (27.9%). The lowest frequency of stage correction, 5.8%, was observed in the study by Y. Sun [7], 2024, which can be attributed to the prevalence of signet-ring cell and mucinous subtypes of gastric MNs with high F⁰API accumulation, but without significant revision of the TNM stage.

Treatment Adjustment. The performance of $[^{68}\text{Ga}]$ F⁰API-PET/CT also impacted treatment strategies. In 4 out of 8 studies where this parameter was specifically tracked, changes in therapy ranged from 12.9% [4] to 67% [18]. In the study by S. Zhang, the proportion of therapy adjust-

ments was 17.9%, confirmed by the decision of a multidisciplinary team [3].

Table 2 presents a comparative analysis of $[^{68}\text{Ga}]$ F⁺API and $[^{18}\text{F}]$ FDG in the visualization of gastric cancer (GC) based on the data from 8 studies.

Table 2 provides a comparative analysis of the diagnostic characteristics of $[^{68}\text{Ga}]$ F⁺API and $[^{18}\text{F}]$ FDG based on data from 8 clinical studies. All studies included patients with confirmed GC, including difficult-to-visualize histological types such as signet-ring cell carcinoma (SRCC), mucinous carcinoma (MAC), and diffuse adenocarcinoma types. In some studies, the TBR value was not provided. In such cases, the contrast between the tumor and background tissues was calculated using the formula

$$\text{TBR} = \frac{\text{SUVmax опухоли.}}{\text{SUVmean фона}} \quad (1)$$

The average SUVmean value of the ascending aorta (SUVmean \approx 2.5) was used as the standard for background accumulation in evaluating the effectiveness of $[^{68}\text{Ga}]$ F⁺API-PET/CT. Given the repeatability of these values in several publications (e.g., [4, 6, 7]), the adopted value can be considered a reasonably acceptable benchmark for comparative analysis.

The comparative analysis of the studies presented in the table confirms a consistent advantage of $[^{68}\text{Ga}]$ F⁺API-PET/CT over $[^{18}\text{F}]$ FDG in terms of SUVmax and TBR in patients with GC, including aggressive histological subtypes and cases with low glucose metabolism.

J. Kuten et al. demonstrated that the SUVmax for $[^{68}\text{Ga}]$ F⁺API was 16.6, while for $[^{18}\text{F}]$ FDG it was 11.6. The median TBR value for $[^{68}\text{Ga}]$ F⁺API was 11.9, compared to 3.2 for $[^{18}\text{F}]$ FDG. These data were accompanied by 100% detection of primary tumors using $[^{68}\text{Ga}]$ F⁺API, while $[^{18}\text{F}]$ FDG showed only 50% sensitivity [17].

In the study by Y. Pang et al., the SUVmax for $[^{68}\text{Ga}]$ F⁺API was 12.7, while for $[^{18}\text{F}]$ FDG it was 3.7. The TBR was also significantly higher for $[^{68}\text{Ga}]$ F⁺API, with $[^{18}\text{F}]$ FDG showing values of 7.6 versus 2.2. All tumors (n=20) were visualized with $[^{68}\text{Ga}]$ F⁺API, while $[^{18}\text{F}]$ FDG detected only 53%, emphasizing the limitations of $[^{18}\text{F}]$ FDG in non-intestinal tumor types [8].

A. Selçuk et al. reported a primary tumor SUVmax of 14.8 for $[^{68}\text{Ga}]$ F⁺API and 6.8 for $[^{18}\text{F}]$ FDG. For peritoneal metastases, the values were 6.9 and 3.3, respectively. The calculated TBR for $[^{68}\text{Ga}]$ F⁺API was 5.92, while for $[^{18}\text{F}]$ FDG it was 2.72. $[^{68}\text{Ga}]$ F⁺API enabled stage modification in 30% of patients [18].

In the study by S. Zhang et al., the average SUVmax for primary tumors with $[^{68}\text{Ga}]$ F⁺API was 10.28 versus 3.20 for $[^{18}\text{F}]$ FDG. For metastatic lesions, the values were also higher for $[^{68}\text{Ga}]$ F⁺API: in lymph nodes, 9.20 versus 3.15, and in distant metastases, 8.00 versus 4.20, respectively. Based on our calculations, the TBR for $[^{68}\text{Ga}]$ F⁺API was 4.11, while for $[^{18}\text{F}]$ FDG it was 1.28. This allowed for stage modification in 7 out of 25 patients [20].

D. Jiang et al. presented the most detailed comparison of SUVmax based on tumor size and T-stage: Overall SUVmax: 7.4 ($[^{68}\text{Ga}]$ F⁺API) vs. 6.5 ($[^{18}\text{F}]$ FDG); Tumors >4 cm: 11.0 ± 4.5 ($[^{68}\text{Ga}]$ F⁺API) vs. 6.3 ± 1.8 ($[^{18}\text{F}]$ FDG); T2-T4: 9.7 ± 4.4 ($[^{68}\text{Ga}]$ F⁺API) vs. 5.6 ± 1.9 ($[^{18}\text{F}]$ FDG); T1: 3.1 ± 1.5 ($[^{68}\text{Ga}]$ F⁺API) vs. 2.7 ± 0.9 ($[^{18}\text{F}]$ FDG); TBR: 9.2 ± 5.9 ($[^{68}\text{Ga}]$ F⁺API) vs. 5.9 ± 4.2 ($[^{18}\text{F}]$ FDG) [6].

Y. Miao et al. demonstrated the highest absolute SUVmax among all studies: 18.81 for $[^{68}\text{Ga}]$ F⁺API compared to 10.44 for $[^{18}\text{F}]$ FDG, also confirming the superiority of $[^{68}\text{Ga}]$ F⁺API across all stages and histological subtypes. The TBR for $[^{68}\text{Ga}]$ F⁺API was 12.9 and 4.5 for $[^{18}\text{F}]$ FDG, respectively [4].

Y. Sun et al. studied $[^{68}\text{Ga}]$ F⁺API in patients with mucinous and signet-ring cell carcinoma (MAC/SRCC), showing a primary tumor SUVmax of 9.3 for $[^{68}\text{Ga}]$ F⁺API compared to 3.1 for $[^{18}\text{F}]$ FDG. For peritoneal metastases, the values were 6.9 and 3.3, respectively. The TBR calculation indicated that $[^{68}\text{Ga}]$ F⁺API (3.7) outperformed $[^{18}\text{F}]$ FDG (1.2). In the study by Y. Sun et al., F⁺API outperformed $[^{18}\text{F}]$ FDG in sensitivity for peritoneal and intestinal metastases. For peritoneal metastases, SUVmax was: 5.66 ± 1.97 for $[^{68}\text{Ga}]$ F⁺API versus 4.28 ± 2.70 for $[^{18}\text{F}]$ FDG, and TBR was: 4.22 ± 1.47 for $[^{68}\text{Ga}]$ F⁺API versus 1.41 ± 0.89 for $[^{18}\text{F}]$ FDG. For tumor implantation into the intestinal wall, SUVmax for F⁺API was 6.70 ± 0.25 , and for $[^{18}\text{F}]$ FDG it was 7.58 ± 1.66 , but the TBR was still higher for $[^{68}\text{Ga}]$ F⁺API (5.63 vs. 2.20) [7].

S. Zhang et al. provided the following values for $[^{68}\text{Ga}]$ F⁺API: SUVmax=13.6, TBR=5.44. For $[^{18}\text{F}]$ FDG in this study, SUVmax and TBR values were not provided [3].

Advantages. Table 2 reflects the qualitative parameters highlighted by the authors of the original studies, and the comparative analysis of these allows the assessment not only of numerical parameters such as SUVmax and TBR but also the practical significance of each method. In 5 out of 8 of the analyzed sources, a clear advantage of detecting metastatic lesions was identified. The remaining studies emphasize that $[^{68}\text{Ga}]$ F⁺API-PET/CT provides a clear visualization of primary gastric MNs, histological subtypes like MAC and SRCC, and lymph nodes.

Discussion: FAP is expressed in the tumor microenvironment, particularly in activated fibroblasts, making it a valuable target for stromal imaging [22, 23]. FAP expression in the microenvironment of gastrointestinal tumors opens new opportunities for targeted visualization of stromal components, particularly in clinical scenarios where the effectiveness of conventional imaging modalities, such as CT, MRI, and $[^{18}\text{F}]$ FDG PET/CT, is limited due to cirrhotic changes or high background activity in normal tissues [24]. Despite its high specificity, it is known that F⁺API can accumulate in areas of inflammation, trauma, and IgG4-related diseases, which must be taken into account when interpreting imaging results [25]. $[^{68}\text{Ga}]$ F⁺API PET/CT demonstrates superior contrast and faster clearance kinetics, making it more suitable for use in frail patients [26]. The

increased sensitivity of $[^{68}\text{Ga}]$ F⁺PI in detecting peritoneal metastatic lesions is a critically important factor in surgical decision-making, particularly concerning the need for laparoscopy and the extent of surgical intervention [27]. F⁺PI, expressed by activated fibroblasts in the tumor microenvironment, has been identified as a key factor in tumor progression and has emerged as a promising target for the development of next-generation RPhs [28].

In contrast to $[^{18}\text{F}]$ FDG, which reflects glucose metabolism, $[^{68}\text{Ga}]$ F⁺PI accumulates more uniformly within the tumor background and is effective in tumors with low glycolytic activity, such as mucinous adenocarcinoma and signet ring cell carcinoma. Consequently, it can detect lesions that are poorly visualized by $[^{18}\text{F}]$ FDG PET/CT [29]. Due to the low metabolic activity of $[^{18}\text{F}]$ FDG and potential physiological confounders, the method has certain limitations in imaging specific subtypes of gastrointestinal tumors, including MAC and SRCC [30].

In recent years, $[^{68}\text{Ga}]$ F⁺PI PET/CT has demonstrated expanding clinical utility in the diagnosis and staging of GC [31]. Several studies emphasize its superiority over traditional imaging methods, including $[^{18}\text{F}]$ FDG PET/CT and CT, particularly in identifying peritoneal metastases, regional lymphatic spread, and tumors with low glucose metabolism [32, 33]. The high reproducibility across different histological tumor types, consistent uptake parameters, and high selectivity of $[^{68}\text{Ga}]$ F⁺PI for tumor stroma underscore its diagnostic value [34]. Systematic reviews and meta-analyses confirm the superiority of $[^{68}\text{Ga}]$ F⁺PI not only in terms of imaging performance but also in clinical relevance, from more accurate staging to direct influence on treatment strategies [35]. Furthermore, the use of $[^{68}\text{Ga}]$ F⁺PI is actively discussed in contemporary clinical guidelines, including national protocols in China, where it is considered a potential alternative to $[^{18}\text{F}]$ FDG PET/CT [36]. Its integration into preoperative diagnostics remains a promising direction, including the detection of $[^{18}\text{F}]$ FDG-negative metastatic lesions, helping to avoid unnecessary surgical procedures and improve therapy personalization. The two tables presented in this study summarize both methodological and clinical parameters as well as the comparative diagnostic advantages of $[^{68}\text{Ga}]$ F⁺PI relative to conventional $[^{18}\text{F}]$ FDG.

Aggregated data from eight studies demonstrated that $[^{68}\text{Ga}]$ F⁺PI PET/CT was used for initial staging and evaluation of disease extent, including signet ring cell carcinoma, mucinous adenocarcinoma, and other diffuse forms of GC. These histological tumor types are traditionally characterized by low glucose metabolism, limiting the sensitivity of $[^{18}\text{F}]$ FDG PET/CT. In this context, F⁺PI shows an advantage by accumulating in the tumor stroma regardless of the glycolytic activity of tumor cells. Notably, all studies employed standardized protocols (60-minute interval post-injection, scan coverage from head to upper/mid-thigh, PET/CT acquisition), ensuring data comparability. Particular attention is given to "Treatment Correction." In

7 out of 8 studies, the impact was quantified numerically (ranging from 12.9% to 67.0%), where F⁺PI PET/CT findings led to changes in treatment strategy, including the choice between surgical and pharmacological approaches. In the remaining cases, the impact was reflected in improved staging, detection of peritoneal metastases, or clarification of tumor resectability. These data indicate that $[^{68}\text{Ga}]$ F⁺PI PET/CT functions not only as a diagnostic tool but also as a patient management aid.

The second analytical section focuses on the comparison between $[^{68}\text{Ga}]$ F⁺PI and $[^{18}\text{F}]$ FDG. In all included studies, $[^{68}\text{Ga}]$ F⁺PI outperformed $[^{18}\text{F}]$ FDG in terms of SUV_{max} and tumor-to-background ratio (TBR), primarily due to lower physiological background in abdominal organs when using $[^{68}\text{Ga}]$ F⁺PI. This is especially significant for visualizing: SRCC and MAC, which often yield false-negative results on $[^{18}\text{F}]$ FDG PET/CT; Peritoneal metastases, where F⁺PI imaging enabled detection of lesions not visible with conventional PET or CT; Metastatic and small-volume lesions, including lymph nodes and subserosal spread. To date, $[^{18}\text{F}]$ FDG PET/CT remains the imaging standard in oncology. However, in GC – particularly undifferentiated and mucinous forms – its effectiveness is limited. In the review by X. Liu et al., $[^{68}\text{Ga}]$ F⁺PI PET/CT demonstrated 100% sensitivity in detecting primary gastric tumors and 96% sensitivity for peritoneal metastases, significantly surpassing $[^{18}\text{F}]$ FDG, which showed 53% and 55%, respectively [37].

$[^{68}\text{Ga}]$ F⁺PI also outperformed $[^{18}\text{F}]$ FDG in detecting lymphatic metastases, with sensitivities of 79% and 54%, respectively [6, 38, 39]. $[^{68}\text{Ga}]$ F⁺PI exhibited rapid and selective accumulation in the tumor microenvironment with minimal background uptake, enabling high-contrast visualization of peritoneal metastatic lesions [40]. These findings underscore the advantages of F⁺PI for imaging tumors with low glucose metabolism, particularly metastatic lesions. Several studies consistently confirm that $[^{68}\text{Ga}]$ F⁺PI PET/CT improves the detection of malignant peritoneal involvement, which is often difficult to diagnose using conventional imaging methods [41, 42]. Additionally, the low background activity associated with $[^{68}\text{Ga}]$ F⁺PI-04 provides a clearer contrast between tumor and surrounding tissues compared to $[^{18}\text{F}]$ FDG, enhancing lesion visualization [43].

In all studies, $[^{68}\text{Ga}]$ F⁺PI demonstrated superiority in SUV_{max} and TBR compared to $[^{18}\text{F}]$ FDG. This was especially evident in difficult-to-visualize forms of gastric MNs and in cases where $[^{18}\text{F}]$ FDG yielded negative results [44].

Thus, $[^{68}\text{Ga}]$ F⁺PI is a more sensitive imaging tool for diffuse, mucinous, and metastatic disease forms. $[^{68}\text{Ga}]$ F⁺PI PET/CT for GC staging demonstrates high effectiveness in detecting peritoneal metastases and histologically challenging tumor types [45, 46]. $[^{68}\text{Ga}]$ F⁺PI has proven to be an effective component of a comprehensive therapeutic approach, facilitating optimized preoperative planning and objective assessment of tumor resectability [47, 48].

Table 1 – Clinical and methodological parameters of studies on the use of $[^{68}\text{Ga}]$ FAPI-PET/CT in gastric cancer patients

Study	Year	Study Design	Indications	Patients (n)	Potency (MBq/kg)	Interval (min.)	Staging Correction (%)	Treatment Correction (%)
Kuten J. [19]	2022	P	Staging/restaging	13	1.8-2.2	60	38.5	30.8
Pang Y. [8]	2021	R	Staging	20	1.8-2.2	60	21.0	21.0
Sevincuk A. [18]	2025	P	$[^{18}\text{F}]$ FDG-negative/ peritoneal metastases	23	2.0-2.5	60	67	67
Shumao Z. [20]	2022	R	Staging/restaging	25	1.85	60	27.9	27.9
Jiang D. [6]	2021	P	Staging/peritoneal metastases	38	1.11-1.85	60	10.5	n/a
Miao Y. [4]	2023	P	Staging	62	1.85-2.96	60-90	12.9	12.9
Sun Y. [7]	2024	P	Histological subtype	86	1.85	60	5.8	30.0
Shunyu Z. [3]	2025	R	Restaging	112	1.11-1.85	60	18.8	17.9

Table 2 – Comparative analysis of the effectiveness of $[^{68}\text{Ga}]$ FAPI and $[^{18}\text{F}]$ FDG in gastric cancer imaging

Study	Radio pharmaceutical	SUVmax ($[^{68}\text{Ga}]$ FAPI)/ $[^{18}\text{F}]$ FDG)	TBR ($[^{68}\text{Ga}]$ FAPI)/ $[^{18}\text{F}]$ FDG)	Advantages $[^{68}\text{Ga}]$ FAPI
Kuten J. [19]	$[^{68}\text{Ga}]$ FAPI $[^{18}\text{F}]$ FDG	16.6 / 11.6	11.9 / 3.2	Detection of peritoneal metastatic foci, $[^{18}\text{F}]$ FDG-negative cases
Pang Y. [8]	$[^{68}\text{Ga}]$ FAPI $[^{18}\text{F}]$ FDG	12.7 / 3.7	7.6 / 2.2	Better visualization of tumors and lymph nodes in $[^{18}\text{F}]$ FDG-negative cases
Sevincuk A. [18]	$[^{68}\text{Ga}]$ FAPI $[^{18}\text{F}]$ FDG	14.8 / 6.8	5.92 / 2.72	Detection of peritoneal metastases in $[^{18}\text{F}]$ FDG-negative cases
ShumaoZ. [20]	$[^{68}\text{Ga}]$ FAPI $[^{18}\text{F}]$ FDG	10.28 / 3.20	4.11 / 1.28	Effective in $[^{18}\text{F}]$ FDG-negative cases, early detection of peritoneal metastatic foci
Jiang D. [6]	$[^{68}\text{Ga}]$ FAPI $[^{18}\text{F}]$ FDG	7.4 / 6.5	9.2 / 5.9	Clear visualization of primary tumors, early detection of metastases
Miao Y. [4]	$[^{68}\text{Ga}]$ FAPI $[^{18}\text{F}]$ FDG	18.81 / 10.44	12.9 / 4.5	High contrast of lymph nodes, submucosal lesions
Sun Y. [7]	$[^{68}\text{Ga}]$ FAPI $[^{18}\text{F}]$ FDG	9.3 / 3.1	3.7 / 1.2	Clear visualization of SRCC and MAC histological sub-types
Shunyu Z. [3]	$[^{68}\text{Ga}]$ FAPI $[^{18}\text{F}]$ FDG	13.60 / n. a.	5.44 / n/a	Early detection of peritoneal metastatic foci

Note: MAC – Mucinous adenocarcinoma, SRCC – Signet ring cell carcinoma, SUVmax – Maximum standardized uptake value, TBR – Tumor-to-background ratio

Its inclusion in clinical guidelines and research protocols confirms its practical value and clinical promise [49, 50]. Further research should aim to explore the prognostic significance of FAPI, its role in therapy monitoring, and the potential therapeutic use of FAPI-based RPhs.

Conclusion: $[^{68}\text{Ga}]$ FAPI-PET/CT is a promising imaging method for GC staging, demonstrating high accuracy in detecting peritoneal metastases and difficult-to-diagnose tumor forms. This makes $[^{68}\text{Ga}]$ FAPI a valuable tool in a multimodal approach to treatment. The potential of this method is confirmed by its integration into clinical guidelines and research protocols.

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АНДАТПА

^{68}GA -FAP1 ПЭТ/КТ-НЫҢ АСҚАЗАННЫҢ ҚАТЕРЛІ ІСІГІНІҢ ДИАГНОСТИКАСЫНДАҒЫ МҮМКІНДІКТЕРІ

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Озектілігі: Асқазанның қатерлі (АҚ) ісігі аурушаңдық пен олім-жітімділік деңгейінің жоғары болуына байланысты медицинаның озекті мәселесі болып табылады. Гибридті визуализация, соның ішінде ПЭТ/КТ қатерлі ісіктердің, сонымен қатар АҚ ісігінің диагностикасында маңызды орын алады. Онкологияда қолданылатын радиофармацевтикалық препараттардың өзірлеу және зерттеу жұмыстары жалғасуда.

Зерттеудің мақсаты – асқазанның қатерлі ісігінде ^{68}Ga -FAP1-ПЭТ/КТ диагностикалық мүмкіндіктерін зерттеу.

Әдістері: Зерттеуге гистологиялық түрде расталған АҚ ісігі бар науқастарға жүргізілген ^{68}Ga -FAP1-ПЭТ/КТ және ^{18}F -FDG-ПЭТ/КТ диагностикалық көрсеткіштерін салыстырмалы аспекттіде зерттелген 8 клиникалық зерттеудің (проспективті және ретроспективті) нәтижелері енгізілді. Зерттеулердегі науқастар саны 13-тен 112-ге дейін, жалпы саны – 379 пациентті құрады. SUV_{max} , TBR мәндері, асқазанның алгаңқы ісігін, лимфа түйіндеріндегі және ішпәрделегі метастатикалық зақымдануды анықтаудағы сезімтандық талданды.

Нәтижелері: Бірқатар клиникалық зерттеулердің мәліметтері бойынша, ^{68}Ga -FAP1 визуализация кезінде ^{18}F -FDG-мен салыстырғанда жоғары SUV_{max} және TBR көрсеткіштерін көрсетті, өсіреле диффузды, мүцинозды және шырышты жасаушалы АҚ жағдайларында. Бұл FAP ақуызының ісік стромасында жоғары экспрессиясымен түсіндіріледі, нәтижесінде препарат зақымданған ошақтарда тиімді жинақталады. Сонымен қатар, ^{68}Ga -FAP1-ПЭТ/КТ ^{18}F -FDG-ПЭТ/КТ-мен салыстырғанда асқазандагы алгаңқы ісік ошақтарын (100% қарсы 53%), лимфа түйіндеріндегі метастаздарды (79% қарсы 54%) және ішпәрделік метастаздарды (96% қарсы 55%) визуализациялауда жоғары сезімтандық көрсетті. ^{68}Ga -FAP1-ПЭТ/КТ зерттеуінен кейін науқастардың 11-67%-ында ісік процесінің сатысы нақтыланып, ем жоспарын даралау мүмкін болды.

Корытынды: ^{68}Ga -FAP1-ПЭТ/КТ әдісі ^{18}F -FDG-ПЭТ/КТ-мен салыстырғанда АҚ сатылдыруда анықтамалы ақпараттылығы жоғары болды, өсіреле гликогенитикалық метаболизмі төмен ісік гистотиптері жағдайында. Бұл әдіс ішпәрделік, висцералдық және лимфогендік метастаздарды жоғары сезімтандықпен анықтауга мүмкіндік береді және емдеу тактикасын анықтауда маңызды рол атқарады.

Түйінді сөздер: фибробласттардың белсендену ақуызының тежегіші, галлий-68-мен таңбаланған (^{68}Ga -FAP1), асқазан обыры (АҚ), позитрон-эмиссиялық томография/компьютерлік томография (ПЭТ/КТ), қатерлі ісік сатысы, фибробласттардың белсендену ақуызы (FAP).

АННОТАЦИЯ

ДИАГНОСТИЧЕСКИЕ ВОЗМОЖНОСТИ ^{68}GA -FAP1 ПЭТ/КТ ПРИ РАКЕ ЖЕЛУДКА

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Актуальность: Рак желудка (РЖ) является актуальной проблемой медицины, в связи с высокими показателями заболеваемости и смертности. Гибридная визуализация, в том числе позитронно-эмиссионная томография/компьютерная томография (ПЭТ/КТ), имеет важное значение в диагностике злокачественных опухолей, включая РЖ. Разработка и изучение возможностей радиофармпрепараторов, применяемых в онкологии, продолжаются.

Цель исследования – изучить диагностические возможности ПЭТ-КТ с применением ингибитора белка активации фибробластов, меченного галлием-68 (^{68}Ga -FAP1-ПЭТ/КТ) при раке желудка.

Методы: Проведено сравнение результатов 8 клинических проспективных и ретроспективных исследований, в которых приведены диагностические показатели ПЭТ/КТ с применением ингибитора белка активации фибробластов, меченного галлием-68 (^{68}Ga -FAP1-ПЭТ/КТ) и фтордезоксиглюкозы, меченной фтором-18 (^{18}F -FDG-ПЭТ/КТ) при гистологически верифицированном РЖ. Количество пациентов в исследованиях было от 13 до 112 пациентов, общее количество составило – 379. Проанализированы значения максимального стандартизованного накопления (SUV_{max}), отношения опухоли к фону (TBR),

чувствительность обнаружении первичного очага в желудке, а также метастатических изменений в лимфатических узлах и брюшине.

Результаты: Согласно данным проанализированных клинических исследований, $[68\text{Ga}]F\text{API}$ продемонстрировал более высокие значения SUV_{max} и TBR по сравнению с $[18\text{F}]FDG$, особенно при визуализации диффузных, муцинозных и перстневидноклеточных форм РЖ. Это связано с выраженной экспрессией FAP в опухолевом строме, что обеспечивает эффективное накопление препарата в пораженных участках. Кроме того, $[68\text{Ga}]F\text{API}$ -ПЭТ/КТ характеризуется более высокой чувствительностью при визуализации первичных очагов РЖ (100% против 53% для $[18\text{F}]FDG$ -ПЭТ/КТ), метастатического поражения лимфатических узлов (79% против 54%), перитонеальных метастатических очагов (96% против 55%). У 11-67% пациентов проведение $[68\text{Ga}]F\text{API}$ -ПЭТ/КТ позволило уточнить стадию опухолевого процесса и повлияло на формирование индивидуального плана лечения.

Заключение: Применение $[68\text{Ga}]F\text{API}$ -ПЭТ/КТ показало более высокую информативность по сравнению с $[18\text{F}]FDG$ -ПЭТ/КТ при стадировании злокачественных опухолей желудка, особенно при гистологических подтипах с низким гликогенитическим метаболизмом. $[68\text{Ga}]F\text{API}$ -ПЭТ/КТ обеспечивает более высокую чувствительность и более качественную визуализацию перитонеальных, висцеральных и лимфогенных метастатических очагов, что играет важную роль в определении тактики лечения.

Ключевые слова: ингибитор белка активации фибробластов, меченный галлием-68 ($[68\text{Ga}]F\text{API}$), рак желудка (РЖ), позитронно-эмиссионная томография/компьютерная томография (ПЭТ/КТ), стадирование рака, белок активации фибробластов (FAP).

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