

**Head-to-head comparison of [18F]FDG PET and [68Ga]Ga-FAPI-04 PET in the diagnosis of gastric or pancreatic cancer: A Systemic Review and Meta-analysis**

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Xie, WR<sup>1</sup>; Li, B<sup>2</sup>; Hong, ZZ<sup>3</sup>; Zhang, Y<sup>4</sup>.**ADMINISTRATIVE INFORMATION****Support** - None.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202380058**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 August 2023 and was last updated on 14 August 2023.**INTRODUCTION**

**Review question / Objective** P: patients with gastric cancer and pancreatic cancer; I: [68Ga]Ga-FAPI-04 PET; C: [18F]FDG PET; O: positivity rate (detection rate) of primary cancer, lymph node metastasis, bone metastasis, peritoneal metastases, liver metastasis; S: retrospective or prospective.

**Condition being studied** The World Health Organization (WHO) reclassifies digestive system tumors such as esophageal, stomach,rectal, large, small,pancreatic, and liver cancers as digestive system tumors. According to a recent study,there were about 5 million new cases of digestive cancer worldwide in 2020 and about 3.6 million deaths,and the incidence of various digestive cancers is gradually increasing, according to one study. Therefore,accurate image-based initial detection of the digestive tract is the key to

effective treatment that will provide maximum benefit to patients. [18F]-FDG PET/CT is currently the most commonly used imaging method for initial tumor staging,therapeutic response assessment, and detection of recurrence of most tumors. However, [18F]FDG may not be an ideal imaging agent for digestive tract tumors, as some limitations have been noted.

Fibroblast activating protein (FAP) has recently been found to be highly expressed in cancer-associated fibroblasts and is closely associated with cancer cell proliferation, tumor immunity, angiogenesis,extracellular matrix remodeling, and metastasis. FAP is low expressed in normal tissues and organs and is a good molecular target for tumor diagnosis and treatment. This imaging agent has good pharmacokinetic and biochemical distribution, high sensitivity, very clear tumor profile, and a high tumor background ratio in common solid tumors. Many studies have reported

the use of [68Ga] Ga-FAPI 04 PET/CT to detect gastrointestinal tumors.

## METHODS

**Participant or population** patients with gastric cancer or pancreatic cancer.

**Intervention** [68Ga]Ga-FAPI-04 PET.

**Comparator** [18F]FDG PET.

**Study designs to be included** Positivity rate of primary cancer, lymph node metastasis, bone metastasis, peritoneal metastases, liver metastasis.

**Eligibility criteria** Following criteria were included: (1) articles assessing the positivity rate of [68Ga]Ga-FAPI-04 PET and [18F]FDG PET for gastric cancer or pancreatic cancer; (2) a direct comparison between [68Ga]Ga-FAPI-04 PET and [18F]FDG PET for simultaneous diagnosis; (3) gold standard evaluation through histological pathology or follow-up imaging. The exclusion criteria were as follows: (1) irrelevant topics; (2) duplicated articles; (3) case reports, abstracts, letters, reviews, or meta-analyses; (4) unavailability of extracted positivity rates, which represent the proportion of patients or lesions with true-positive (TP) and false-positive (FP) results divided by the total number of patients or lesions.

**Information sources** A thorough search was performed on the PubMed, Embase, and Web of Science databases for all existing literature up until May 2023.

**Main outcome(s)** Positivity rate.

**Quality assessment / Risk of bias analysis** QUADAS-2 tool.

**Strategy of data synthesis** The positivity rates were evaluated using the DerSimonian and Laird method and transformed with the Freeman-Tukey double inverse sine transformation. The confidence intervals were calculated using the Jackson method. The Cochrane Q and  $I^2$  statistics were used to assess the heterogeneity within and between groups. If the heterogeneity between the studies differed significantly, meta regression analysis and sensitivity analysis were performed by reassessing the sensitivities or specificities following the omission of articles one by one. This was done to evaluate the robustness of the overall sensitivities or specificities and to identify single studies that may contribute to heterogeneity.

Publication bias was evaluated using a funnel plot and Egger's test. For all statistical tests except heterogeneity, a two-tailed p-value below 0.05 was deemed statistically significant. Statistical analyses were performed using the R software for statistical computing and graphics version 4.1.2.

**Subgroup analysis** Meta regression:(1)Study design:Retro,Pro;(2)Analysis:PB,LB;(3)Reference standard:Pathology,Pathologyand/or follow-up imaging;(4)Types of imaging tests:PET/CT,PET/MR;(5)No. of patients;(6)Country:China,Other country.

**Sensitivity analysis** positivity rate of [68Ga]Ga-FAPI-04 PET and [18F]FDG PET for gastric or pancreatic cancer.

**Country(ies) involved** China.

**Keywords** [68Ga]Ga-FAPI-04 PET; [18F]FDG PET; Gastric Cancer; Pancreatic Cancer; Meta-Analysis.

### Contributions of each author

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