

INPLASY2024100131

doi: 10.37766/inplasy2024.10.0131

Received: 30 October 2024

Published: 31 October 2024

Jin, CB; Cheng, LY; Zhang, H; Yang, TS; Tao, WJ.

**Corresponding author:**

Weijing Tao

weijingtao2021@vip.163.com

**Author Affiliation:**

Department of Nuclear Medicine,  
The Affiliated Huai'an No. 1 People's  
Hospital of Nanjing Medical  
University, Huai'an, Jiangsu, China.

**ADMINISTRATIVE INFORMATION****Support** - The study was conducted without any commercial or financial relationships that could be considered a potential conflict of interest.**Review Stage at time of this submission** - Data analysis.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2024100131**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 October 2024 and was last updated on 31 October 2024.**INTRODUCTION**

**Review question / Objective** The subjects were esophageal cancer patients (Population) who underwent PET scanning with the radiolabeled FAPI tracer (Intervention), and the results were compared with those of 18F-FDG PET imaging (Comparison). The results of the study aimed to evaluate the uptake of FAPI in primary or metastatic lesions of esophageal cancer and the detection rate of FAPI PET in patients with esophageal cancer (Outcome).

**Condition being studied** In 2022, the incidence of esophageal cancer ranked 11th and the mortality rate ranked 7th. Despite recent advances in medical technology, including endoscopic surgery after neoadjuvant chemotherapy and combined immunotherapy and chemoradiotherapy, the overall prognosis of esophageal cancer patients has improved, but the overall survival rate is still not high. According to the SEER database, the 5-year relative survival rate for esophageal cancer

from 2014 to 2020 was 21.6%. Long-term survival of esophageal cancer patients remains a challenge, and early diagnosis and appropriate clinical management are critical to improving the prognosis of esophageal cancer patients. However, false-positive uptake of 18F-FDG limits its use in differentiating between inflammatory esophageal tissue and residual or recurrent tumor. The development of new tracers to complement or even replace 18F-FDG has been a hot topic. FAPI is a novel PET tracer that targets fibroblast activation protein in the tumor microenvironment, thereby facilitating tumor detection. This technology not only improves the sensitivity of esophageal cancer detection, but also helps to more accurately assess treatment efficacy and disease progression. Esophageal cancer ranked 11th in terms of incidence and 7th in terms of mortality in 2022. The incidence and mortality rates are two to three times higher in the male population than in the female population. Although advances in medical technology in recent years, including endoscopic surgery after neoadjuvant

chemotherapy and combined immunotherapy and chemoradiotherapy, have improved the overall prognosis of patients with esophageal cancer, the overall survival rate is still not high. According to statistics from the SEER database, the 5-year relative survival rate for esophageal cancer between 2014 and 2020 was 21.6%. Long-term survival of patients with esophageal cancer remains a challenge and has a significant impact on global health. Early diagnosis and appropriate clinical management are critical to improving the prognosis of patients with esophageal cancer.

## METHODS

**Search strategy** We performed a systematic search of three databases (PubMed, Embase and Web of Science) from inception until August 10th, 2024, using the following search syntax: (“FAPI” OR “fibroblast activation protein”) AND ((carcin\* or cancer\* or neoplas\* or tumour\* or tumor\* or cyst\* or growth\* or adenocarcin\* or malig\*)AND(esophagus or oesophagus or esophageal or oesophageal)). The citations of the included studies were also thoroughly reviewed to identify additional studies that might strengthen the validity of the research. No language restrictions were applied.

**Participant or population** Studies using radionuclide-labeled FAPI and FDG as radiotracers for PET diagnosis of esophageal cancer were included.

**Intervention** Diagnostic Tools of radionuclide-labeled FAPI.

**Comparator** Diagnostic Tools of 18F-FDG PET imaging.

**Study designs to be included** Original article with a comparative analysis of the diagnostic efficacy and visualization of FAPI and 18F-FDG in the assessment of esophageal cancer.

**Eligibility criteria** The following article types were excluded: reviews, editorials, letters, case reports, out-of-scope studies, and preclinical studies.

**Information sources** We performed a systematic search of three databases (PubMed, Embase and Web of Science) from inception until August 10th, 2024.

**Main outcome(s)** Performance of 18F-FDG PET imaging and FAPI PET imaging in the assessment of esophageal cancer, including detection rates and semi-quantitative metabolic parameters.

**Quality assessment / Risk of bias analysis** We used the QUDAS-2 assessment scale for risk assessment. risk of bias assessment includes four areas (patient selection, indicator testing, reference criteria, flow, and timing). Applicability assessment consists of three areas (patient selection, indicator testing, and reference criteria).Assessment of publication bias using funnel plots and Egger's test.

**Strategy of data synthesis** Data analysis was performed using the R language and Stata version 16.0. Heterogeneity between studies was assessed using I<sup>2</sup> and Q test statistics. I<sup>2</sup>≥50% indicates statistical heterogeneity. When heterogeneity is high, the random effects model is used to pool results. Otherwise, the fixed effects model is used. A p-value of less than 0.05 is considered statistically significant. The results are presented as forest plots.

**Subgroup analysis** The subgroup analysis aims to analyze the SUV uptake of primary lesions, lymph nodes and distant metastases of esophageal cancer.

**Sensitivity analysis** According to the results of the forest plot, some studies with low quality, obvious methodological heterogeneity, or clinical heterogeneity were excluded, and then meta-analysis was performed. The effect of excluding some studies on the combined effect size was examined by comparing the combined effect sizes before and after exclusion. If the combined effect size did not change significantly after excluding some studies, it indicates that the results of the meta-analysis are relatively robust; otherwise, it indicates that the results of the meta-analysis are less stable and should be interpreted with caution when drawing conclusions.

**Language restriction** No language restrictions were applied.

**Country(ies) involved** China.

**Keywords** FAPI; fibroblast-activating protein inhibitor; PET; esophageal cancer; SUVmax; standardized uptake values; TBR; tumor-to-background uptake ratio; GTV;gross tumor volume.

### Contributions of each author

Author 1 - Chaobo Jin.  
Email: 18269777926@163.com  
Author 2 - Luyi Cheng.  
Author 3 - Huai Zhang  
Author 4 - Tianshuo Yang.  
Author 5 - Weijing Tao.