ELSEVIER

Seminars in
NUCLEAR
MEDICINE

The value of [^{18}F]FDG PET/CT in fever of unknown origin (FUO): an update and future aspects

Domenico Albano,[a,b] Luca Urso,[c] Giorgio Treglia,[d,e,f] and Francesco Bertagna[a,b]

Fever of unknown origin (FUO) is a clinical diagnostic challenge because its symptoms are often vague and its causes varied. Although the use of 2-deoxy-2-[18F]-fluoro-D-glucose positron emission tomography/computed tomography ([^{18}F]FDG PET/CT) is on the rise to help solve these cases, the optimal timing and strategy for its application remains under debate. As a comprehensive whole-body imaging modality, [^{18}F]FDG PET/CT reveals areas of increased uptake and it is highly effective for detecting active oncological diseases, infectious or inflammatory foci that might be missed by radiological imaging. In FUO, [^{18}F]FDG PET/CT presents good diagnostic performances with a clinical impact in more than half of cases, also in special populations like pediatrics and critically ill patients. It may help to identify underlying causes of fever and to modify treatment and management procedures. Also a negative [^{18}F]FDG PET scan may help to exclude potential diseases and is associated with a good prognosis. And the future looks even more bright with huge developments in both camera systems (LAFOV PET/CT) and in specific infection and inflammation radiotracers.

Semin Nucl Med 00:1-7 © 2026 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)

Introduction

2-deoxy-2-[18F]-fluoro-D-glucose positron emission tomography/computed tomography ([^{18}F]FDG PET/CT) imaging is an increasingly valuable tool for diagnosing Fever of Unknown Origin (FUO).[1,2] Because FUO can stem from a broad spectrum of etiologies—including infections, non-infectious inflammatory diseases (NIID), malignancies, and other rare conditions—[^{18}F]FDG PET/CT helps narrow down the search in these complex cases.[3] The definition of FUO has evolved since Petersdorf and Beeson first established it in 1961.[4,5] but the main features remain similar: a persistent fever exceeding 38.3°C for over 3 weeks that remains undiagnosed after at least three days of inpatient testing or three outpatient consultations. Thus, FUO remains a diagnostic challenge with potential implications in the management of these patients. The primary objective in managing FUO should be the early and precise detection of the underlying cause, or, at minimum, the targeted guidance of secondary tests such as biopsies. Traditional diagnostic protocols, encompassing blood cultures, radiography, and ultrasonography, frequently yield inconclusive results in the presence of fever. Given the vast differential diagnosis associated with fever, relying solely on these methods often leads to a protracted and inefficient diagnostic process. This not only delays definitive care but can also subject the patient to redundant and unnecessarily invasive procedures. [^{18}F]FDG PET/CT seems to be a potential tool with high impact in this task. Unlike conventional CT or magnetic resonance imaging (MRI), which rely on structural changes that may not appear in the early stages of infection or inflammation.[6], [^{18}F]FDG PET/CT may recognize functional/metabolic alterations. This

[a]Nuclear Medicine, University of Brescia, Italy.
[b]Nuclear Medicine, ASST Spedali Civili di Brescia, Italy.
[c]Nuclear Medicine Unit, Onco-Hematology Department, University Hospital of Ferrara, Ferrara, Italy.
[d]Faculty of Biomedical Sciences, Università della Svizzera Italiana, Lugano, Switzerland.
[e]Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland.
[f]Division of Nuclear Medicine, Imaging Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Bellinzona, Switzerland.
Corresponding author at: Nuclear Medicine, Spedali Civili di Brescia, P.le Spedali Civili 1; 25123 Brescia Italy, Italy E-mail: domenico.albano@unibs.it

https://doi.org/10.1053/j.semnuclmed.2026.03.010
0001-2998/© 2026 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)

allows for earlier intervention and more informed therapeutic decision-making with a likely cost-effective approach.[1]

The evidence about the role of [18F]FDG PET/CT IN FUO

Diagnostic yield

Over the past two decades, several meta-analyses have reinforced the role of [18F]FDG PET/CT in evaluating FUO.[7-11] The main outcome measures derived by the literature were the overall diagnostic yield or helpfulness of [18F]FDG PET/CT in about 50-60% of patients (Table 1). The first meta-analysis.[7] was published in 2011 including 9 studies for a total of 174 patients but the populations were mixed because they were studied with PET only and PET/CT scanners. Despite these limitations, the diagnostic performances reported were very good with a sensitivity of 98% and a specificity of 86% and a positive clinical impact of 60%. Globally, there was a significant number of false positive reports and a very low rate of false negative findings. Moreover, there was no statistically significant difference between PET and PET/CT studies in terms of diagnostic performances. False positive reports are usually related to physiological area of uptake (muscular activity, brown fat activation, gastrointestinal activity) or iatrogenic conditions (post surgery, recent vaccinations). Instead, the main common causes of false negative scans are due to the resolution power of lesions (for example small vessel vasculitis), the not correct patient preparation (hyperglicemia, prolonged corticosteroid or antibiotic treatment) or the difficulties to investigate several organs with physiological [18F]FDG uptake (brain, urinary tracts).

Also Hao et al. [8] derived a good sensitivity (85%) considering only patients that performed [18F]FDG PET/CT, but also in this research the authors underlined the possibility of false positive reports on scan. In 2016, Besson et al.[9] focused on the potential contribution of [18F]FDG PET or PET/CT to the diagnostic assessment of FUO. They demonstrated that an abnormal PET was associated with a substantially increased final diagnostic rate in FUO (36%) and consequently they suggested to include [18F]FDG PET/CT in the first-line diagnostic work-up of FUO. One of the benefits of [18F]FDG PET/CT include the ability to conduct a comprehensive whole-body scan in a single imaging session, offering excellent resolution and high sensitivity for detecting low-grade and early-stage infections or inflammation, all while minimizing radiation exposure.

The significant diagnostic yield of [18F]FDG PET/CT in this setting was confirmed also by subsequent meta-analyses on larger populations.[10-12] In the last meta-analysis.[12] 23 studies for a total of 1927 patients were analyzed deriving a sensitivity of 84%, specificity of 63%, positive likelihood ratio of 2.3 (95% CI = 1.5-3.4), negative likelihood ratio of 0.25 (95% CI = 0.16-0.38) and diagnostic odds ratio of 9 (95% CI = 4.0-20). The clinical benefit of [18F]FDG PET/CT in the diagnostic process is certain, also in the exclusion of several diseases, in the guiding of further diagnostic and therapeutic decisions and in the avoiding of unnecessary invasive/not invasive procedures.

Cost-effectiveness

Beyond clinical utility, [18F]FDG PET/CT imaging may offer significant cost-effectiveness advantage. For instance, Becerra-Nakayo et al.[13] in a small group of patients with FUO ($n = 20$) observed that PET/CT was executed after an average 28-day hospitalization. Their analysis suggests that integrating [18F]FDG PET/CT in an early phase during the diagnostic process could reduce total costs by 49% (€5,471) per patient. Similarly, Balink et al.[14] compared outcomes for 92 patients and found that the PET/CT group incurred 42% (€5,298) lower costs while achieving a definitive diagnosis more than twice as often as those who did not receive the scan.

Patient management and prognostic role

Both a positive or negative [18F]FDG PET/CT scan may have a significant role in the diagnostic and therapeutic management of patients with FUO. A positive [18F]FDG PET/CT can be contributory by directly guiding treatment or subsequent diagnostic procedure. But also a negative [18F]FDG PET/CT may be equally important by excluding focal disease and it is associated with a favorable prognosis. Takeuchi et al. [15] investigated in a meta-analysis the association of [18F]FDGPET or PET/CT with spontaneous remission inf FUO. A meta-analysis was conducted on 13 studies involving 546 patients (418 via PET/CT and 128 via standalone PET). Specifically, patients with negative PET/CT results were significantly more likely to experience spontaneous regression than those with positive scans (RR = 5.6; $p < 0.001$. This

Table 1 Summary of meta-analysis concerning the role of PET/CT in FUO.

First author	Year	N° articles	N° patients	Device	Sensitivity	Specificity	Clinical impact
Dong[7]	2011	9	388	PET & PET/CT	98% (94-100%)	86% (75-93%)	60%
Hao[8]	2013	15	595	PET/CT	85% (81-88%)	nr	nr
Besson[9]	2016	14	712	PET & PET/CT	nr	nr	58%
Bharucha[10]	2017	18	905	PET/CT	nr	nr	56%
Takeuchi[11]	2016	22	1137	PET/CT	86% (81-90%)	52% (36-67%)	58%
Kan[12]	2019	23	1927	PET/CT	84% (79-89%)	63% (49-75%)	59%

Nr: not reported.

association was not observed in standalone PET scans. Furthermore, meta-regression confirmed that both the use of PET/CT (rRR = 7.4) and more recent publication years (rRR = 1.2 per year) were significantly linked to reported spontaneous remission. The bias of this work was that no study primarily focused on spontaneous remission as primary aim, and that in all studies the subsequent management after PET/CT was influenced by PET results. A recent multicentric Italian study.[16] including 929 patients from 12 centers demonstrated an overall sensitivity of 72%, specificity of 85%, positive predictive value of 94%, negative predictive value of 47%, and accuracy of 75%. Predictive markers for a positive [18F]FDG PET/CT were high C-reactive protein (CRP), high erythrocyte sedimentation rate (ESR), high neutrophil to lymphocyte ratio, the presence of fever at the time of PET and short duration of prior antibiotic therapy. Moreover, [18F]FDG PET/CT had a clinical impact on 73% of cases. Particularly, in 33% of patients, PET/CT findings modified patient treatment (starting a new therapy, or modulating ongoing therapy); in 21% guiding further invasive procedures (biopsies, endoscopic procedures, surgery); in 26% avoiding unnecessary invasive procedures and/or allowing antibiotic therapies to be interrupted; in 22% guiding further non-invasive procedures (imaging examinations).

Pre-scan tests

While the positive impact of [18F]FDG PET/CT in FUO is well demonstrated, the standard diagnostic pathway for FUO is yet under debate and strongly affected by regional/department rules and protocols.

C-reactive protein (CRP) remains the most established nonspecific marker in FUO and IUO, being elevated in the vast majority of cases. However, the optimal CRP threshold for predicting a contributory PET/CT scan remains debated. Several studies have demonstrated a significant association between elevated CRP levels and PET positivity; CRP > 30 mg/L was associated with higher diagnostic yield, with some evidence suggesting that patients with CRP > 50-100 mg/L derive the greatest benefit.[17-20] Other laboratory parameters have also shown predictive value. Elevated erythrocyte sedimentation rate (ESR), neutrophilia, and a high neutrophil-to-lymphocyte ratio have been associated with positive PET findings. Conversely, prolonged antibiotic therapy prior to PET/CT may reduce sensitivity by partially suppressing infectious foci. The presence of fever at the time of tracer injection also increases the likelihood of a contributory scan.

Wile about imaging examinations, chest X-rays and abdominal ultrasounds are the first-line tools also due to the fast execution, low-radiation dose and cheapness. More advanced 3D imaging (CT, MRI, PET/CT) or invasive procedures are generally reserved as second-line options. These are typically triggered by specific clinical findings or when initial tests fail to yield a diagnosis.[21] Until now, CRP seems to be the most established nonspecific marker of FUO.

Current evidence suggests that while no single threshold can definitively predict PET utility, patients with persistently elevated inflammatory markers despite negative first-line investigations are optimal candidates for early [18F]FDG PET/CT.

Patients preparation and protocols in FUO

[18F]FDG administration should be preceded by fasting for at least 6 hours. In patients with suspected cardiac disease (e.g. endocarditis, cardiac sarcoidosis) a prolonged fasting is recommended for at least 12−24 h, in combination with a high-fat and low-carbohydrate diet to ensure optimal suppression of physiological myocardial uptake. Supplemental intravenous low-dose unfractionated heparin (50 IU/kg 15 min prior to radiotracer injection) may also be considered especially in patients unable to complete long-term fasting and diet protocol, e.g. diabetics. Plasma glucose levels are recommended to be as lower as possible, despite a value less than 200 mg/dL in considered acceptable.

Concerning corticosteroids, it is recommended to perform the study prior to starting treatment (unless there is a risk of complications) since glucocorticoid administration can rapidly reduce [18F]FDG uptake. False negative results following steroid treatment are possible, but this risk seems to be not so evident if the oral corticosteroid therapy is started only few days before PET/CT.

Also for antibiotics is reported a potential effect on PET/CT scans, but the data are not shared.

Prolonged corticosteroid or antibiotic therapy may suppress FDG uptake in inflammatory or infectious foci, potentially causing false-negative scans. Whenever clinically safe, temporary discontinuation of these medications should be considered before PET/CT

A significant advantage of [18F]FDG PET/CT over ultrasound, CT and MRI is the ability to study the whole body in patients with suspected systemic disease and few diagnostic clues. The scan field should minimally include the vertex to mid-thighs, but a total-body acquisition could be considered especially when lower extremities involvement is suspected. When a process involving the heart is known or suspected, a dedicated myocardial suppression regimen is recommended to suppress physiological myocardial uptake and adherence to cardiac regimen prior to FDG administration should be verified and a delayed dedicated static (>90 minutes post injection) and cardiac gated acquisition can improve the diagnostic accuracy for selected indications.

Concerning CT of PET, a non-enhanced “low-dose” CT seems to be sufficient to detect the location of metabolic abnormalities that could lead to the final diagnosis. There is usually limited use of contrast-enhanced CT because of the often relatively minor morphological changes from infectious and inflammatory processes, especially at early stages.

Future aspects

Special populations

The effective role of [18F]FDG PET/CT in specific populations with FUO, such as in children and critically ill patients was only marginally investigated with promising results but

Table 2 Summary of meta-analysis concerning the role of PET/CT in FUO in pediatrics and critically ill patients.

First author	Year	Population	N° articles	N° patients	Sensitivity	Specificity	Clinical impact
Li[24]	2022	Pediatrics	6	191	nr	nr	A positive PET is strongly associate with achievement of a final diagnosis
Treglia[25]	2026	Critically ill patients	6	228	91% (80-96%)	78% (65-88%)	nr
Huang[26]	2020	Critically ill patients	4	87	94% (79-99%)	66% (45-83%)	65%

Nr: not reported.

not definitive consensus.[22,23] (Table 2). A 2025 review by Albano et al. specifically examined FUO/IUO in special populations, including end-stage renal disease and HIV patients, demonstrating that PET/CT maintains high diagnostic accuracy even in these complex clinical scenarios[23] Concerning pediatrics, the only meta-analysis available[24] founded that pediatric patients with abnormal PET findings were about 17 times more likely to achieve a definite diagnosis than those with normal PET findings, and that this contribution of abnormal PET findings remained stable across studies with different sample size, imaging modality, subclass of FUO origin, geographical area and length of follow-up. Overall, clinical impact of [^{18}F]FDG PET/CT ranged from 32% to 77% related to patients' features. The recent introduction in the clinical practice of total body/long axial field of view PET/CT devices might significantly reduce radiation exposure by injecting lower activities and to reduce the total acquisition time. In the pediatric population, these points could be crucial obviating potentially the need for anesthesia and encouraging the clinicians to ask PET/CT. Also for pediatrics, CRP is the best predictor for PET positivity.

About critically ill patients, a recent systematic review and meta-analysis.[25] demonstrated a very good sensitivity (91%) and a moderate specificity (78%). The underutilization of [^{18}F]FDG PET/CT in critical care stems largely from the logistical and clinical hurdles associated with the procedure. Unlike conventional CT scans, [^{18}F]FDG PET/CT requires prolonged imaging times, strict fasting protocols, and a post-injection uptake period of about one hour. For critically ill patients, these requirements are further complicated by the inherent risks of transport and out-of-unit monitoring, such as hemodynamic instability or respiratory distress. Consequently, the perceived complexity of managing these high-risk patients often outweighs the perceived benefits of the scan. Most contributions of [^{18}F]FDG PET/CT to patient management involved guiding interventional procedures and adjustments to medical therapy such as antimicrobial and corticosteroid treatment. Adverse events related to patient transport or [^{18}F]FDG PET/CT scan were not reported in most studies, with exception of one. Another meta-analysis showed a clinical yield of [^{18}F]FDG PET/CT in 65% of cases of critically ill patients analyzed.[26] Findings presented in the literature demonstrated a good diagnostic yield of [^{18}F]FDG PET/CT in the study of these patients affected by FUO with performances similar to adult general populations.

Innovative radiotracers and technology

While [^{18}F]FDG PET/CT remains a cornerstone in the localization of infection and inflammation, its lack of specificity remains a significant clinical hurdle. This limitation fuels the ongoing search for more precise radiopharmaceuticals and advanced imaging protocols. The research community is dedicated to refining diagnostic tools to move beyond simple detection: the ability to differentiate between infection, sterile inflammation, and malignancy with absolute precision. To reach this goal, current research is strategically concentrated on two primary pillars.[27] The paradigm shift toward personalized medicine, largely pioneered in oncology, is now fundamentally reshaping the management of infectious and inflammatory diseases. Nuclear medicine is uniquely positioned to drive this translation by targeting specific cell subpopulations and molecular markers within lesions. Beyond simple localization, modern tracers allow for the characterization of the immune microenvironment—highlighting specific lymphocytes, macrophages, or cytokine activity.[28] For example, FAPI-tracers was born originally an oncological imaging, but their usefulness in other conditions is increasingly emerging due to the ability to detect active fibroblasts in inflammatory states.[29] Furthermore, the development of pathogen-specific tracers suggests a future where imaging does not merely identify an infection but provides a "molecular biopsy" capable of distinguishing between Gram-positive and Gram-negative bacteria, thereby streamlining early, targeted antibiotic therapy.[30,31]

Furthermore, the development of pathogen-specific tracers promises to transform infection imaging. Tracers such as 2-deoxy-2-[^{18}F]fluoro-sorbitol ([^{18}F]FDS) exploit the sorbitol metabolism pathway present in Enterobacteriaceae, enabling specific detection of Gram-negative bacterial infections.[32] Similarly, [^{18}F]maltohexaose-based tracers target the bacterial maltodextrin transport system, showing promise for distinguishing live bacteria from sterile inflammation. Other emerging agents include ubiquicidin (^{19}F-FBEM-UBI), which binds to bacterial membranes, and ^{18}F-fluoropropyl-trimethoprim, which targets bacterial dihydrofolate reductase.

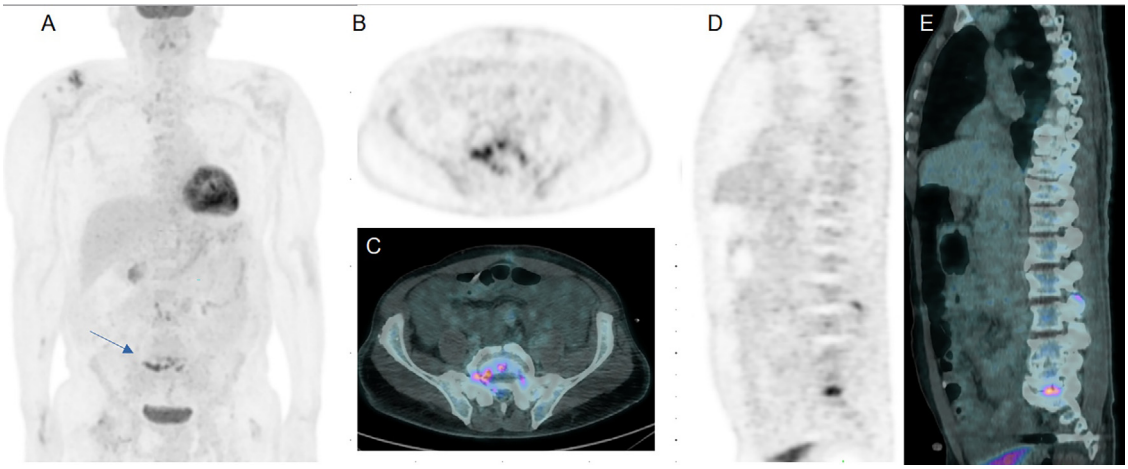


Fig. 1 A 69-year-old man with fever from more than 3 weeks not responsive to antibiotics executed an [18F]FDG PET/CT. MIP PET (A) showed the presence of a focal increased uptake in the column corresponding to the fourth and fifth lumbar vertebra. Subsequent axial PET (B), axial fused PET/CT (C), sagittal (B), sagittal PET (D) and sagittal PET/CT fused images (E) confirmed an increased [18F]FDG uptake in the intervertebral disk and adjacent vertebra consistent with spondylodiscitis.

CXCR4-targeted agents (e.g., [^{68}Ga]Ga-pentixafor) represent another promising class, as CXCR4 is overexpressed on inflammatory cells including macrophages and lymphocytes. Early studies in FUO/IUO suggest potential for characterizing the immune microenvironment and differentiating infectious from non-infectious inflammation. These emerging radiotracers, combined with advanced radiomics and artificial intelligence-based image analysis, may enable a future where PET/CT provides not only lesion detection but also etiological characterization—a true 'molecular biopsy.

Also from a technological point of view, there was a dramatic evolution. The emergence of Large Axial Field of View (LAFOV) PET/CT represents a paradigm shift in imaging performance. By drastically increasing sensitivity, LAFOV systems allow for significantly reduced scan times and lower tracer activities, effectively minimizing the radiation burden.[33] In the context of infection and inflammation, LAFOV technology offers several big clinical advantages: 1) ultrafast imaging: whole-body acquisitions are reduced to 2−3 minutes, facilitating the imaging of specific populations, such as pediatrics, critically ill, or high-pain patients who cannot tolerate the standard 15−20 minute protocols; 2) improvement in the detection rate: the superior sensitivity enables the visualization of low-metabolic processes (e.g., chronic low-grade infections) and subtle targets like biofilms or cranial vessel inflammation that often escape conventional PET/CT; 3) extended imaging windows: high sensitivity allows scanning at delayed time points (up to 4−5 half-lives), improving the signal-to-background ratio by allowing blood-pool activity to clear, which is vital for assessing large-vessel vasculitis or cardiac sarcoidosis; 4) ease in performing dynamic studies: all major organs can be captured simultaneously in a single field of view. This allows for dynamic imaging to map the distinct glucose kinetics of infection versus inflammation, potentially providing the specificity that static imaging lacks.[34,35] Beyond the current advancements in radiopharmaceutical chemistry and system instrumentation, a critical objective for the coming years remains the precise mapping of the immune landscape. The deep biological overlap between infectious, inflammatory, and oncological pathways presents a significant challenge for achieving the cellular specificity required for accurate imaging. Personalized medicine requires more than just better tracers; it requires a structural evolution. To move from a 'one-tracer-fits-all' model to a multi-probe diagnostic suite, we must bridge the gap between bench and bedside through targeted investment in decentralized radiopharmacy and distribution networks.

Conclusions

In conclusion, [^{18}F]FDG PET/CT has emerged as a cornerstone in the diagnostic algorithm for FUO, offering a high diagnostic yield by identifying infectious, inflammatory, and neoplastic etiologies that traditional imaging often misses. Its ability to provide whole-body metabolic information allows for the early detection of multi-focal diseases, significantly reducing the "time to diagnosis" and preventing unnecessary invasive procedures. However, to maximize its clinical utility, the scan should be integrated early into the workup, particularly in patients with elevated inflammatory markers, and interpreted with caution in the context of recent steroid or antibiotic therapy. Looking ahead, the implementation of LAFOV scanners and the introduction of new specific tracers promise to further enhance sensitivity and diagnostic accuracy. As technology evolves, [18F]FDG PET/CT is set to transition from a secondary tool to a primary, indispensable resource in the personalized management of patients with FUO. Fig. 1, Fig. 2, Fig. 3

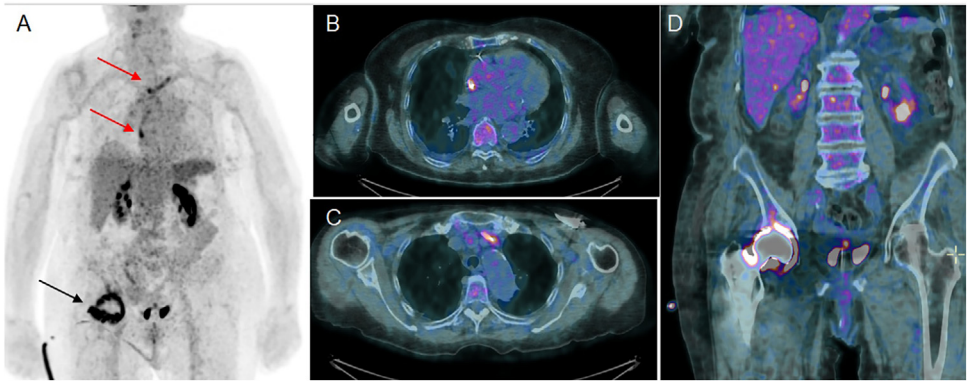


Fig. 2 A 48-year-old female with FUO underwent an [18F]FDG PET/CT scan. (A) The Maximum Intensity Projection (MIP) image shows several areas of increased uptake in the mediastinum (red arrows) and right hip (black arrow). Axial PET/CT images (B, C) show increased FDG uptake along the lead path, and the coronal PET/CT image (D) shows increased uptake around the hip prosthesis. The final diagnosis was prosthetic infection and cardiac device infection.

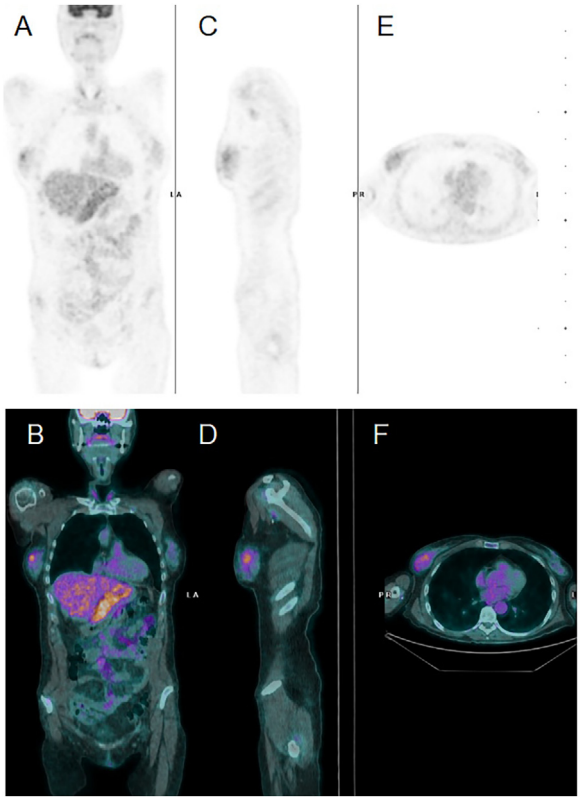


Fig. 3 A 54 year old woman admitted to the ICU for cerebrovascular event and fever performed [18F]FDG PET/CT for the search of any pathological uptake. Coronal PET (A), coronal PET/CT (B), sagittal PET (C), sagittal PET/CT (D), axial PET (E), axial PET/CT (F) revealed the presence of an increased uptake in the right breast corresponded to a hypodense area. The final diagnosis was abscess.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

The authors did not use any AI technology to support the writing of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Domenico Albano: Investigation, Methodology, Writing – original draft, Writing – review & editing. **Luca Urso:** Data curation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Giorgio Treglia:** Investigation, Methodology, Writing – original draft. **Francesco Bertagna:** Data curation, Investigation, Writing – original draft, Writing – review & editing.

References

1. Hess S, Noriega-Álvarez E, Leccisotti L, et al: EANM consensus document on the use of [18F]FDG PET/CT in fever and inflammation of unknown origin. Eur J Nucl Med Mol Imaging 51(9):2597-2613, 2024. https://doi.org/10.1007/s00259-024-06732-8
2. Abikhzer G, Treglia G, Pelletier-Galarneau M, et al: EANM/SNMMI guideline/procedure standard for [18F]FDG hybrid PET use in infection and inflammation in adults v2.0. Eur J Nucl Med Mol Imaging 52 (2):510-538, 2025. https://doi.org/10.1007/s00259-024-06915-3

ARTICLE IN PRESS

3. Mulders-Manders C, Simon A: Bleeker-Rovers C. Fever of unknown origin. Clin Med 15(3):280-284, 2015. https://doi.org/10.7861/clinmedicine.15-3-280
4. Petersdorf RG, Beeson PB: Fever of unexplained origin: report on 100 cases. Medicine 40:1-30, 1961. https://doi.org/10.1097/00005792-196102000-00001
5. Durack DT, Street AC: Fever of unknown origin—reexamined and redefined. Curr Clin Top Infect Dis 11:35-51, 1991
6. Ly KH, Costedoat-Chalumeau N, Liozon E, et al: Diagnostic value of 18F-FDG PET/CT vs. chest-abdomen-pelvis CT scan in management of patients with fever of unknown origin, inflammation of unknown origin or episodic fever of unknown origin: a comparative multicentre prospective study. J Clin Med 11(2):386, 2022.. d. 2022 Jan 13;11(2)
7. Dong MJ, Zhao K, Liu ZF, et al: A meta-analysis of the value of fluorodeoxyglucose-PET/PET-CT in the evaluation of fever of unknown origin. Eur J Radiol 80(3):834-844, 2011. https://doi.org/10.1016/j.ejrad.2010.11.018
8. Hao R, Yuan L, Kan Y, et al: Diagnostic performance of 18F-FDG PET/CT in patients with fever of unknown origin: a meta-analysis. Nucl Med Commun 34(7):682-688, 2013. https://doi.org/10.1097/MNM.0b013e328361cd0e
9. Besson FL, Chaumet-Riffaud P, Playe M, et al: Contribution of (18)F-FDG PET in the diagnostic assessment of fever of unknown origin (FUO): a stratification-based meta-analysis. Eur J Nucl Med Mol Imaging 43(10):1887-1895, 2016. https://doi.org/10.1007/s00259-016-3377-6
10. Bharucha T, Rutherford A, Skeoch S, et al: Diagnostic yield of FDG-PET/CT in fever of unknown origin: a systematic review, meta-analysis, and Delphi exercise. Clin Radiol 72(9):764-771, 2017. https://doi.org/10.1016/j.crad.2017.04.014
11. Takeuchi M, Dahabreh IJ, Nihashi T, et al: Nuclear imaging for classic fever of unknown origin: meta-analysis. J Nucl Med 57(12):1913-1919, 2016. https://doi.org/10.2967/jnumed.116.174391
12. Kan Y, Wang W, Liu J, et al: Contribution of 18F-FDG PET/CT in a case-mix of fever of unknown origin and inflammation of unknown origin: a meta-analysis. Acta Radiol 60(6):716-725, 2019. https://doi.org/10.1177/0284185118799512
13. Becerra Nakayo EM, Garcia Vicente AM, Soriano Castrejon AM, et al: Analysis of cost-effectiveness in the diagnosis of fever of unknown origin and the role of (18)F-FDG PET-CT: a proposal of diagnostic algorithm. Revista Esp De Med Nuclear e Imagen Mol. 31(4):178-186, 2012. https://doi.org/10.1016/j.remn.2011.08.007
14. Balink H, Tan SS, Veeger NJ, et al: (1)(8)F-FDG PET/CT in inflammation of unknown origin: a cost-effectiveness pilot-study. Eur J Nucl Med Mol Imaging 42(9):1408-1413, 2015. https://doi.org/10.1007/s00259-015-3010-0
15. Takeuchi M, Nihashi T, Gafter-Gvili A, et al: Association of 18F-FDG PET or PET/CT results with spontaneous remission in classic fever of unknown origin: a systematic review and meta-analysis. Medicine 97(43):e12909, 2018. https://doi.org/10.1097/MD.0000000000012909
16. Albano D, Lanfranchi M, Bauckneht M, et al: The diagnostic yield of [18F]FDG PET/CT in FUO: an Italian multicenter study on 929 patients. J Nucl Med 125:271525, 2026. https://doi.org/10.2967/jnumed.125.271525. jnumed
17. Garcia-Vicente AM, Tello-Galan MJ, Amo-Salas M, et al: Do clinical and laboratory variables have any impact on the diagnostic performance of 18F-FDG PET/CT in patients with fever of unknown origin? Ann Nucl Med 32(2):123-131, 2018. https://doi.org/10.1007/s12149-017-1226-8
18. P Akyüz Dağlı, Güven SC, Coşkun N, et al: Rheumatology experience with FDG PET /CT in inflammation of unknown origin: a single - centre report for determining factors associated with diagnostic precision. Clin Rheumatol 42(10):2861-2872, 2023. https://doi.org/10.1007/s10067-023-06673-x
19. Pereira AM, Husmann L, Sah BR, et al: Determinants of diagnostic performance of 18F-FDG PET/CT in patients with fever of unknown origin. Nucl Med Commun 37(1):57-65, 2016. https://doi.org/10.1097/MNM.0000000000000395
20. Tsuzuki S, Watanabe A, Iwata M, et al: Predictors of diagnostic contributions and spontaneous remission of symptoms associated with positron emission tomography with Fluorine-18-fluorodeoxy glucose combined with computed tomography in classic fever or inflammation of unknown origin: a retrospective study. J Korean Med Sci 36(22):e150, 2021. https://doi.org/10.3346/jkms.2021.36.e150
21. Crouzet J, Boudousq V, Lechiche C, et al: Place of (18)F-FDG-PET with computed tomography in the diagnostic algorithm of patients with fever of unknown origin. Eur J Clin Microbiol Infect Dis 31(8):1727-1733, 2012. https://doi.org/10.1007/s10096-011-1440-6
22. Olianti C, Trapani S, Secinaro A, et al: Fever of unknown origin in pediatrics: role of nuclear medicine. Q J Nucl Med Mol Imaging 68(1):48-57, 2024. https://doi.org/10.23736/S1824-4785.24.03546-5
23. Albano D, Rodella C, Guarneri A, et al: [18F]FDG PET/CT of FUO/IUO in special populations. Q J Nucl Med Mol Imaging 69(3):219-223, 2025. https://doi.org/10.23736/S1824-4785.25.03649-0
24. Li Q, Tian R, Wang H, et al: Quantifying the contribution of 18F-FDG PET to the diagnostic assessment of pediatric patients with fever of unknown origin: a systematic review and meta-analysis. Pediatr Radiol 52(8):1500-1511, 2022. https://doi.org/10.1007/s00247-022-05333-7
25. Treglia G, Albano D, Wittebole X, et al: Diagnostic value of [18F]FDG PET/CT for detection of infectious and inflammatory foci in critically ill patients: a systematic review and meta-analysis. Eur J Nucl Med Mol Imaging 2026. https://doi.org/10.1007/s00259-025-07759-1
26. Huang CK, Huang JY, Ruan SY, et al: Diagnostic performance of FDG PET/CT in critically ill patients with suspectedinfection: a systematic review and meta-analysis. J Formos Med Assoc 119(5):941-949, 2020. https://doi.org/10.1016/j.jfma.2019.09.010
27. Glaudemans AWJM, Gheysens O: Expert opinions in nuclear medicine: finding the "holy grail" in infection imaging. Front Med (Lausanne) 10:1149925, 2023. https://doi.org/10.3389/fmed.2023.1149925
28. Albano D, Rizzo A, Guarneri A, et al: Emerging PET-radiotracers in cardiovascular, neuro-inflammation, lung and rheumatological diseases: a narrative review. EJNMMI Rep 9(1):28, 2025. https://doi.org/10.1186/s41824-025-00263-7
29. Albano D, Rizzo A, Slart RHJA, et al: The role of fibroblast activation protein inhibitor positron emission tomography in inflammatory and infectious diseases: an updated systematic review. Pharmaceuticals 17(6):716, 2024. https://doi.org/10.3390/ph17060716
30. Albano D, Lauri C, Alberto S, et al: Nuclear medicine imaging to guide antibiotic therapy: an expert review. Br J Radiol 2026:tqag068. https://doi.org/10.1093/bjr/tqag068
31. Lauri C, Pontico M, Farina R, Signore A. Nuclear Imaging for therapy monitoring and response assessment in infectious diseases. Semin Nucl Med. Published online March 23, 2026. https://doi.org/10.1053/j.semnuclmed.2026.03.005
32. Rua M, Simón JA, Collantes M, et al: Infection-specific PET imaging with 18F-fluorodeoxysorbitol and 2-[18F]F-ρ-aminobenzoic acid: an extended diagnostic tool for bacterial and fungal diseases. Front Microbiol 14:1094929, 2023. https://doi.org/10.3389/fmicb.2023.1094929. Published 2023 Jan 25
33. Slart RHJA, Tsoumpas C, Glaudemans AWJM, et al: Long axial field of view PET scanners: a road map to implementation and new possibilities. Eur J Nucl Med Mol Imaging 48, 2021. 4326—245
34. Van Sluis J, Borra R, Tsoumpas C, et al: Extending the clinical capabilities of short- and long-lived positron-emitting radionuclides through high sensitivity PET/CT. Cancer Imaging 22:69, 2022. https://doi.org/10.1186/s40644-022-00507-w
35. Van Rijsewijk ND, van Leer B, Ivashchenko OV, et al: Ultra-low dose infection imaging of a newborn without sedation using long axial field-of-view PET/CT. Eur J Nucl Med Mol Imaging 50:622-623, 2022. https://doi.org/10.1007/s00259-022-05979-3