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18F-FDG PET/CT in the Diagnostic Workup of Fever and Inflammatory Syndromes of Unknown Origin in the Elderly: A Valuable Tool with a Need for Clinical Finesse

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Keywords

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Commentary

Fever and inflammatory syndromes of unknown origin (FUO and IUO) represent some of the most challenging diagnostic entities in clinical medicine [1]. These conditions often trigger extensive investigations, prolonged hospitalizations, and sometimes empirical treatments with limited benefit. The diagnostic complexity is even greater in the elderly, where clinical presentations are frequently atypical, underlying conditions are numerous, and physiological responses to illness are blunted or masked [1]. In this context, advanced imaging modalities such as 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) have emerged as promising tools, offering a whole-body metabolic assessment capable of identifying hidden foci of inflammation, infection, or malignancy.

Despite the increasing use of PET/CT in internal medicine and rheumatology, its role in the geriatric population remains underexplored. A retrospective study conducted between 2013 and 2018 on patients aged 75 and older provides important insights into the real-world clinical utility of PET/CT in this demographic [2]. With a mean patient age exceeding 82 years, the study highlights both the diagnostic and therapeutic contributions of PET/CT in a population where non-invasive, yet effective, diagnostic tools are urgently needed.

The findings are compelling: PET/CT led to a definitive diagnosis in nearly one-third of cases. Notably, the spectrum of diseases uncovered was broad and clinically significant—infections (19.8%), inflammatory or autoimmune conditions (19.8%), and malignancies (14.3%)—all entities requiring targeted treatment. Perhaps more importantly, nearly 40% of patients underwent targeted diagnostic procedures, including directed biopsies, as a direct consequence of PET/CT findings. In over one-third of cases, this imaging modality resulted in a change in clinical management, including both the initiation and discontinuation of treatments.

These results are consistent with broader literature (**Table 1**). For instance, a study by Georga *et al*. reported that 18F-FDG PET/CT contributed to the diagnosis in 70% of patients with FUO, with a sensitivity of 94.7% and a specificity of 50% [3]. Similarly, a meta-analysis by Bharucha *et al.* found that the diagnostic efficacy of 18F-FDG PET/CT in FUO was 56%, with 69% of scans being abnormal. These findings underscore the potential of PET/CT to uncover underlying causes of FUO, including infections, inflammatory diseases, and malignancies [4].

Table 1. Diagnostic performance of 18F-FDG PET/CT in FUO and IUO: Summary of published studies.

Study (Year)	Population (n)	Condition	Diagnostic Yield (%)	Sensitivity (%)	Specificity (%)	Notable Findings
Bleeker-Rovers et al. (2007) [1]	70	FUO	60	67	78	PET/CT contributed to diagnosis in 60% of cases.
Donga et al. (2014) [7]	388	FUO	58	98.2	85.9	High sensitivity and specificity reported.
Bharucha et al. (2017) [4]	905	FUO	56	Not specified	Not specified	Meta-analysis showing moderate diagnostic yield.
Takeuchi et al. (2022) [8]	2058	FUO	58	86	52	Comprehensive review indicating high sensitivity.
Meller et al. (2000) [6]	48	FUO	67	Not specified	Not specified	PET/CT helped establish diagnosis in 67% of patients.
Balink et al. (2014) [5]	317	IUO	75.1	Not specified	Not specified	PET/CT was contributory in 75.1% of cases.
Georga et al. (2020) [3]	Not specified	FUO/IUO	70	94.7	50	High sensitivity reported in a Greek referral center.
Zhu et al. (2020) [9]	89	FUO	Not specified	84.5	25.8	PET/CT had high sensitivity but low specificity.
Buchrits et al. (2021) [10]	303	FUO	Not specified	88.7	80.9	PET/CT showed superior sensitivity compared to CT.

However, enthusiasm must be tempered by caution. The study reports a false-positive rate of approximately 15%, which is not trivial. Inflammation from atherosclerosis, age-related degenerative changes, or recent infections can all produce misleading uptake [5]. In frail patients, such inaccuracies can lead to unnecessary biopsies, overtreatment, or emotional distress. Therefore, the interpretation of PET/CT in the elderly must be highly contextualized, ideally involving multidisciplinary discussion, geriatric expertise, and a careful risk–benefit analysis [6].

Another critical consideration is the ethical dimension of diagnostic escalation in the elderly. While the identification of a disease is important, it must be paired with an actionable plan that aligns with the patient's health status, frailty, and personal goals of care. The mere detection of pathology is not always synonymous with therapeutic benefit. The decision to pursue a PET/CT should be guided by the likelihood that the findings will meaningfully alter management — for instance, prompting a curative or palliative intervention that is tolerable and appropriate in the context of the patient's global condition.

From a health systems perspective, the increasing availability of PET/CT and its proven utility should prompt updated guidelines for its use in elderly patients with FUO/IUO, emphasizing careful patient selection [1,6]. Geriatric patients should not be excluded from advanced diagnostics on the basis of age alone. On the contrary, they are often the patients who benefit most from a strategic, non-invasive approach—but this must be grounded in clinical reasoning, not algorithmic automation.

In conclusion, 18F-FDG PET/CT represents a powerful tool in the diagnostic workup of unexplained fever and inflammatory syndromes, particularly when conventional tests fail to provide clarity. In the elderly, it holds the potential to uncover treatable conditions and guide clinical decisions in a timely and effective manner. Nevertheless, its use must be deliberate, integrated into a broader clinical strategy, and tailored to the unique vulnerabilities and priorities of the aging patient. As medicine continues to evolve alongside demographic shifts, such tools must be deployed with precision and compassion—not merely to diagnose disease, but to optimize care.

Links of Interest

None directly relevant to the content of this manuscript.

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