Performance and value of ^{18}F-FDG PET/CT in patients with fever of unknown origin

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Abstract. Fever of unknown origin (FUO) is a common clinical and diagnostic challenge. The main aim of the present study was to evaluate the diagnostic accuracy of ^{18}F-fluorodeoxyglucose (^{18}FDG) positron emission tomography (PET)/CT in patients who present with FUO. Overall, 105 consecutive patients (61 men and 44 women) with a mean age of 51±35 years with FUO underwent ^{18}FDG PET/CT scans. The performance of ^{18}FDG PET/CT in determining the etiology of FUO was assessed. According to the PET/CT results, patients were classified into four groups: Group 1, patients with true-positive results (n=51; 49%), in whom abnormal ^{18}FDG uptake identified the final diagnosis; group 2, patients with false-positive results (n=24; 23%), in whom ^{18}FDG uptake was not consistent with the final diagnosis; group 3, patients with true-negative results (n=10; 9.5%), in whom the ^{18}FDG uptake was normal and no final disease was established; and group 4, patients with false-negative results (n=20; 19%), in whom ^{18}FDG uptake was normal and disease was finally established. Of the 51 patients with true-positive PET/CT results, 51% had infections, 35% had malignancies and 14% had inflammatory processes. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 72, 29, 68, 33 and 58%, respectively. In conclusion, the present results demonstrated that ^{18}FDG PET/CT established the final diagnosis of FUO in the majority of patients (72%). These results support the use of ^{18}FDG PET/CT in the initial evaluation and management of patients with FUO.

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Introduction

Fever of unknown origin (FUO) is a diagnostic challenge, despite recent advances in diagnostic modalities (1,2). FUO is defined as a prolonged febrile illness without a recognized cause, even after comprehensive laboratory tests and imagining workup. The current definition of FUO is as follows: i) Body temperature of ≥38.3˚C on at least two occasions; ii) duration of illness of ≥3 weeks; iii) not an immunocompromised setting; and iv) uncertain diagnosis despite thorough history taking, physical examination and laboratory assessments. These laboratory measures include the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), hemoglobin, platelet count, leukocyte count and differentiation, electrolyte levels, creatinine level, total serum protein, protein electrophoresis, alkaline phosphatase, aspartate aminotransferase, lactate dehydrogenase (LDH), ferritin, microscopic urinalysis, blood cultures and urine cultures. The most common radiological investigation includes chest X-ray and abdominal ultrasonography. Additional tests may include the tuberculin test or an interferon-γ release assay (3,4). The cause of FUO may be multifactorial and can be subdivided into four categories: Infections, malignancies, noninfectious inflammatory processes and miscellaneous causes (5). FUO is closely related to inflammation of unknown origin (IUO), and the causes and workups are the same for both FUO and IUO (6). Early identification of the cause of FUO is important for guiding the diagnostic workup and for initiating early and appropriate treatment without notable impacts on patient care (7).

Conventional anatomic imaging modalities, such as ultrasonography, and cross-sectional imaging with CT and MRI, are used as primary diagnostic modalities to manage FUO; however, they have limited sensitivity and specificity (8). Therefore, a significant number of patients with FUO (30-50%) leave the hospital without specific diagnoses (9). Positron emission tomography (PET)/CT using ^{18}F-fluorodeoxyglucose (^{18}FDG) is a well-accepted clinical tool for routine use in a wide range of malignancies. ^{18}FDG is a glucose analogue that accumulates in cells with high metabolic requirements, such as tumor and inflammatory cells. ^{18}FDG PET/CT is currently considered a useful noninvasive imaging modality for the evaluation of patients with FUO (10-13). However, only a few studies have assessed ^{18}FDG PET/CT in patients with FUO. Furthermore, most of these studies were performed

in developed countries and the geographic area of the study strongly influenced the determination of the final diagnosis. Studies have shown that the cause of FUO in developing countries was most often infectious (14,15), whereas noninfectious inflammatory processes were the most common drivers of FUO in developed countries.

Several meta-analyses have reported the positive impact of FDG PET/CT in establishing the final diagnosis of patients with FUO/IUO. The diagnostic yield of PET CT/CT in this population is 56-60%, which is ≥30% higher than that of conventional CT (16,17). However, most studies are retrospective studies, with significant heterogeneity of baseline study characteristics, definition of FUO/IUO and imaging parameters (18,19). In certain studies, FDG PET/CT was the only imaging modality that was able to establish a final diagnosis (18,19). The vast majority of the studies investigated the diagnostic value of PET/CT, with only a few studies investigating the cost-effectiveness of FDG PET/CT in the diagnostic work-up of patients with FUO (20). Based on the previous studies, patients with FUO/IUO are a challenging, heterogeneous population with a wide variety of differential diagnoses. Furthermore, there is a lack of an established work-up strategy. According to published data, it is important to further investigate the diagnostic impact of PET/CT, the cost-effectiveness, and when and how to perform PET/CT in the setting of FUO/FUI (21).

The purpose of the present study was to evaluate the performance and benefit of ^{18}FDG PET/CT in patients who presented with FUO at a tertiary academic general hospital in Riyadh, Saudi Arabia.

Patients and methods

Study population. The study was approved by the King Faisal Hospital and Research Center (Riyadh, Saudi Arabia) Institutional review board on 11/01/2021 (approval no. 2211019), and the requirement for informed consent was waived for the present retrospective study. A total of 105 patients {61 men and 44 women; median [interquartile range (IQR)] of age, 51 (31-65) years} who underwent ^{18}FDG PET/CT because of FUO between January 2016 and December 2019 were included in the present retrospective study. These patients met the definition criteria of FUO (febrile illness of >38.3˚C and no diagnosis after at least 3 days of inpatient or 3 weeks of outpatient investigation after thorough history taking, physical examination and standard diagnostic workup). Eligible patients were identified in the radiology information system by searching various categories, including FUO, IUO, unexplained fever and fever of unknown cause. Patients with nosocomial infection, known HIV infection, immunocompromised status and established etiology of FUO/IUO on conventional imaging were excluded from the present study.

Whole-body ^{18}FDG PET/CT was requested to determine the cause of fever. ^{18}FDG PET/CT was performed according to the standard protocol. The patients underwent imaging from the vertex of the skull to the mid-thigh area. Non-contrast CT images were used for attenuation correction and for anatomic localization. Any ^{18}FDG accumulation that could not be explained by physiologic distribution was designated abnormal. Both normal and abnormal ^{18}FDG results were evaluated for their diagnostic contribution to patient assessment. The ^{18}FDG PET/CT results were classified into four categories: i) True-positive if ^{18}FDG PET/CT identified the specific etiology of FUO that was confirmed with additional investigation or response to treatment; ii) false-negative if ^{18}FDG uptake was normal but a specific disease was identified by another diagnostic test or response to treatment; iii) false-positive if ^{18}FDG uptake could not identify the cause of FUO; and iv) true-negative if neither ^{18}FDG PET/CT nor standard diagnostic procedures found the cause of FUO. The nuclear medicine physicians reading the ^{18}FDG PET/CT scans had knowledge of the clinical history and results of prior imaging studies of each patient.

Statistical analysis. Descriptive statistics are presented as the mean ± SD for normally distributed numerical variables and as the median [interquartile range (IQR)] for non-normally distributed numerical variables. The Shapiro-Wilk test was used to test for normality. Frequencies and percentages were used for categorical variables. Comparison of the groups was performed using one-way analysis of variance for normally distributed numerical variables and the Kruskal-Wallis test for non-normally distributed numerical variables. Bonferroni correction was used as the post-hoc test. The χ^2 test was used to compare categorical variables. IBM SPSS statistics software (version 26; IBM Corp.) was used for the analysis. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. A total of 105 patients were included (61 men and 44 women), and the median (IQR) age was 51 (31-65) years. The mean ± SD ESR level was 71.5±40.6 mm/h. Additional acute-phase parameters were as follows: CRP, 139 (51-234) mg/l; white blood cell count (WBC), $8.9x10^3/\mu l$ ($4.5\text{-}1,210^3/\mu l$); LDH, 249 U/l; and ferritin, 672 (363-1,266) μg/l A total of 21 patients received corticosteroids before their ^{18}FDG PET/CT scans, 17 patients (16%) had positive blood cultures and 13 patients (12.4%) had positive urine cultures. Tissue biopsy was performed for 46 patients (34.3%). Blood cultures, urine cultures and tissue biopsy were performed according to standard procedures. Table I shows the patient characteristics.

Positive and negative ^{18}FDG PET/CT and classification of ^{18}FDG PET/CT results by final diagnosis. Of the 105 patients, 75 patients (72%) had positive PET/CT results and 30 patients (29%) had negative results. The CRP and ferritin values differed significantly between the two groups. The median CRP and ferritin levels were higher in the positive group than in the negative PET/CT group (P=0.019 and P=0.024 respectively; Table II). According to the final diagnoses, ^{18}FDG PET/CT results were classified into four categories: Group 1, patients with true-positive results (n=51; 49%), in whom abnormal ^{18}FDG uptake identified the process that directly led to the final diagnosis; group 2, patients with false-positive results (n=24; 23%), in whom ^{18}FDG uptake was not consistent with the final diagnosis reflecting the etiology of FUO; group 3, patients with true-negative results (n=10; 9.5%), in whom ^{18}FDG uptake was unremarkable and

Table I. Patient demographics, laboratory data and PET/CT results for the total study population (n=105).

Characteristic (normal ranges)	Value
Age, years	51 (31-65)
Sex	
Male	61 (58.1)
Female	44 (41.9)
Laboratory data	
WBC, x$10^3/\mu$l (4.5-11.0)	8.9 (4.5-12)
CRP, mg/l (8-10)	139 (51-234)
ESR, mm/h (<15)	71.5±40.6
LDH, U/l (140-280)	249 (184-444)
Ferritin, μg/l (24-336)	672 (363-1,266)
Positive blood culture	17 (16.2)
Positive urine culture	13 (12.4)
Biopsy performed	36 (34.3)
Patients treated with corticosteroids	21 (20)
PET/CT results	
True-positive	51 (48.6)
False-positive	24 (22.9)
True-negative	10 (9.5)
False-negative	20 (19)

Values are expressed as n (%) or median (interquartile range) or the mean ± standard deviation. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; PET, positron emission tomography; WBC, white blood cell count.

no final disease was established through follow-up or other diagnostic tests; and group 4, patients with false-negative results (n=20; 19%), in whom ^{18}FDG PET/CT uptake was normal and final disease was established with other tests or response to treatment. Patients in group 1 (true-positive) were heterogeneous and no single gold standard test was used to establish a final diagnosis. The final diagnosis was made by the referring physician and supported by other diagnostic studies, tissue biopsy, other laboratory tests and continued follow-up. There were no statistically significant differences among the four groups in terms of age, sex, WBC, ESR, LDH or ferritin values.

True-positive results. As shown in Table III, of the 51 patients with true-positive PET/CT results, 26 had infections (51%), 18 (35%) had malignancies and 7 (14%) had inflammatory noninfectious processes. For these patients, the different disease categories, infections, neoplasms and noninfectious inflammatory processes were compared. Examples of cases with true-positive PET/CT scans are shown in Figs. 1-3. The WBC and ferritin levels differed significantly among groups (group with infection, malignancies and inflammatory non-infectious). The WBC count was highest in patients with infections, i.e. 11.2 (6-13.9) $10^3/\mu$l compared to patients with neoplasms [3.5 (2-8.12)x$10^3/\mu$l] and patients with inflammatory/autoimmune disease [8.4 (8-11.52) $10^3/\mu$l] (P=0.018). Also, the ferritin levels were significantly different among the three true-positive groups, including infection, neoplasm and inflammatory/autoimmune disease (P=0.04).

False-positive results. In addition to the normal physiological distribution of ^{18}FDG, abnormal ^{18}FDG uptake was reported in 24 patients (23%), in whom no cause of FUO could be identified. These results were considered false-positives. The most common sites of abnormal ^{18}FDG uptake were the multiple lymph nodes above and below the diaphragm, the bone marrow, the pelvic and bowl (including focal or diffuse uptake), the head and neck, and the lung (areas of mediastinal and hilar adenopathy) (data not shown).

True-negative and false-negative ^{18}FDG PET/CT results. The ^{18}FDG PET/CT showed a normal tracer distribution and was reported as normal in 10 patients (9.5%), and no final diagnosis was established. These results were considered true negatives. False-negative PET/CT results were reported in 20 patients (19%), in whom ^{18}FDG PET/CT was reportedly normal, but a final diagnosis of infection (such as tuberculosis, brucellosis or enteric fever), malignancy (such as lymphoma) or inflammatory noninfectious disease (such as rheumatoid arthritis or adult-onset Still's disease) was established by other diagnostic or laboratory tests, or after a specific therapy (data not shown).

Sensitivity, specificity and positive- and negative-predictive values of PET/CT. The overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy was 72, 29, 68, 33 and 58%, respectively (Table IV). However, due to the small number of patients in each group, no additional analysis of the diagnostic performance of ^{18}FDG PET/CT was undertaken.

Discussion

To the best of our knowledge, the present study was the first study in Saudi Arabia and the Middle East to investigate the diagnostic value of ^{18}FDG PET/CT in identifying the underlying etiology of patients with disease with FUO. The present study investigated 105 patients with FUO and IUO, and revealed that ^{18}FDG PET/CT helped identify the etiology of the underlying disease and establish a final diagnosis in 49% of patients. This group was classified as the true-positive group, yielding a sensitivity of 72% and a positive predictive value of 68%. PET/CT was negative in 10% of patients, in whom there was no final diagnosis and PET/CT was considered a true negative, yielding a low specificity and negative predictive value of 29 and 33%, respectively. The final diagnoses of FUO etiology in this cohort included focal or systemic infections (51%), malignancies (35%) and inflammatory noninfectious processes (14%). These results are comparable to those of published studies of FUO, in which the sensitivity varied between 26 and 75% (22-31). Determining the diagnostic value and accuracy of ^{18}FDG PET/CT in the setting of FUO is complex and at times controversial. The sensitivity and specificity of ^{18}FDG PET/CT are difficult to establish in FUO because of the numerous potential differential diagnoses. The most common malignancy identified in the present cohort was lymphoma and leukemia, and other few miscellaneous malignancy as outlined in Table SI. Gafter-Gvili *et al* (13) reported

Table II. Patient characteristics based on positron emission tomography/CT results in the total study population (n=105).

Characteristic	Group 1, true-positive (n=51)	Group 2, false-positive (n=24)	Group 3, true-negative (n=10)	Group 4, false-negative (n=20)	P-value
Age, years	52 (38-66)	36 (23.5-65)	56 (29-72)	54.5 (30-64.5)	0.564
Sex					0.980
Male	30 (58.8)	13 (54.2)	6 (60)	12 (60)	
Female	21 (41.2)	11 (45.8)	4 (40)	8 (40)	
WBC, $10^3/\mu$l	8 (3.25-12)	10.1 (5.92-15.145)	8.9 (5.5-10.3)	9.5 (4.43-11.5)	0.595
CRP, mg/l	146.5 (70-230)	171 (75-280)	105 (7.4-154)	53 (11-234)	0.120
ESR, mm/h	154.2±100.6	190.4±170.3	107.9±106.5	115.8±124.9	0.179
LDH, U/l	244 (180-631)	267.5 (189.5-442)	263.5 (183-301)	223.5 (176-305.5)	0.705
Ferritin, μg/l	765 (452-1384)	606.5 (352-1785.5)	509 (342-782)	371 (149.5-1061)	0.135

Values are expressed as n (%), median (interquartile range) or the mean ± standard deviation. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; WBC, white blood cell count.

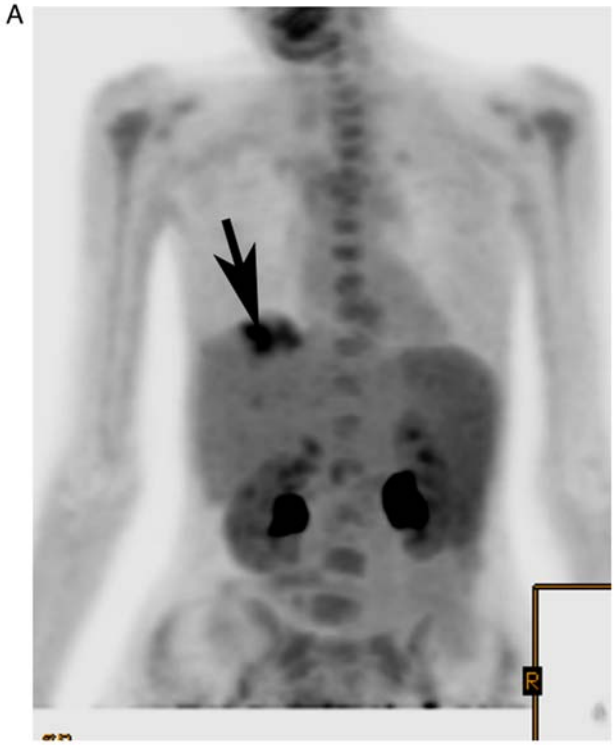
Table III. Patient characteristics and laboratory test results in true-positive patients (n=51).

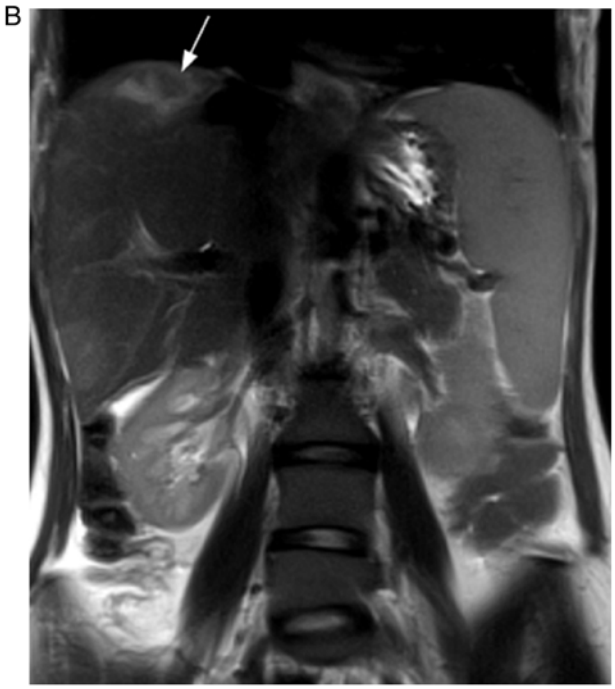
Characteristic	Infection (n=26)	Neoplasm (n=18)	Inflammation/ autoimmune (n=7)	P-value
Age, years	53±21.2	47.9±20.3	51.4±11	0.707
Sex				0.737
Male	14 (53.8)	11 (61.1)	5 (71.4)	
Female	12 (46.2)	7 (38.9)	2 (28.6)	
WBC, $10^3/\mu$l	11.2 (613.9)	3.5 (28.12)	8.4 (811.52)	0.018
CRP, mg/l	11.5 (55167)	19.0 (103 270)	14.4 (54181)	0.166
ESR, mm/h	78.3±33.6	84.3±32.9	96.3±44.9	0.477
LDH, U/l	236.5 (194438)	346 (216826)	162 (1211631)	0.128
Ferritin, μg/l	714.5 (45 886)	1115.5 (6713068)	562 (3771451)	0.043

Values are expressed as n (%), mean ± standard deviation or median (interquartile range). CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; WBC, white blood cell count.

14 cases of malignancy out of a total of 84 positive on FDG PET/CT (14%); of them, nine were non-Hodgkin's, two were Hodgkin's lymphoma, two were lung cancer and one was a sarcoma. In the present population, the prevalence of infectious disease was 51%, which is relatively higher than that in previous studies (32-34). According to several studies on FUO, the disease-associated FUO differs between developed countries and other countries. The percentages of classification of FUO were 19, 24, 12, 8 and 38% for infection, non-infection inflammatory, cancer, various etiologies and unknown, respectively in the developed countries, in contrast to 43, 20, 14, 7 and 16%, respectively, in developing countries (35). The main difference in cases of FUO between developed countries and developing countries is the high incidence of infectious disease; for instance, infectious disease was the most common cause of FUO in Iran (14) and Pakistan, in particular tuberculosis (15). The usefulness of PET/CT in the diagnostic process of FUO is also debatable. It is unknown whether only the true-positive findings can guide the final diagnosis or whether true-negative PET/CT results may rule out infection, inflammation or malignancies (36).

In contrast to a previous study, in which age >50 years, CRP level >30 mg/l and absence of fever were predictive of true-positive ^{18}FDG PET/CT results (37), the present study revealed no statistically significant association between PET/CT results and age, sex, WBC, CRP, ESR, LDH or ferritin levels among different diagnostic groups. This lack of association may be due to the wide variety of disease distribution and prevalence in FUO. In a previous study of more specific inflammatory diseases, such as rheumatoid arthritis, an association existed between CRP levels and ^{18}FDG uptake (38). When searching for clinical and laboratory tests associated with true-positive PET/CT results, elevated WBC counts and elevated serum levels of ferritin were associated with infection (P=0.018 and P=0.034, respectively) in the present study. Conversely, a previous study revealed no significant association between WBC values and ^{18}FDG PET/CT scan results, the clinical impact of ^{18}FDG PET/CT or the provision





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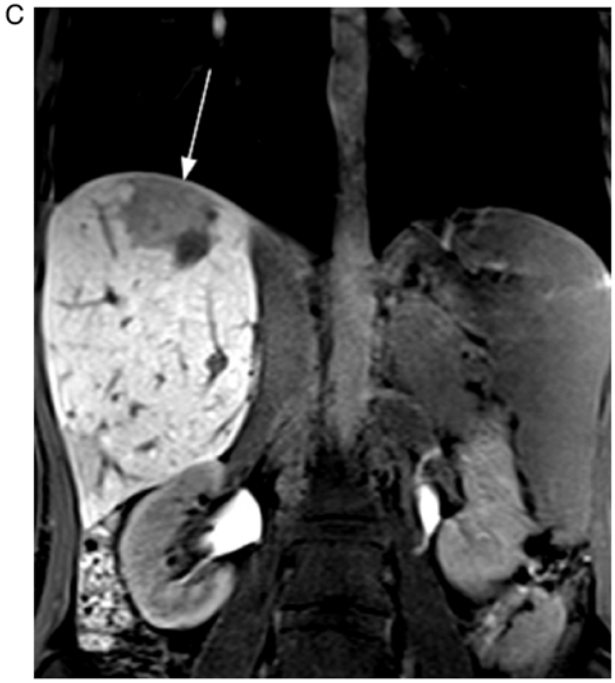
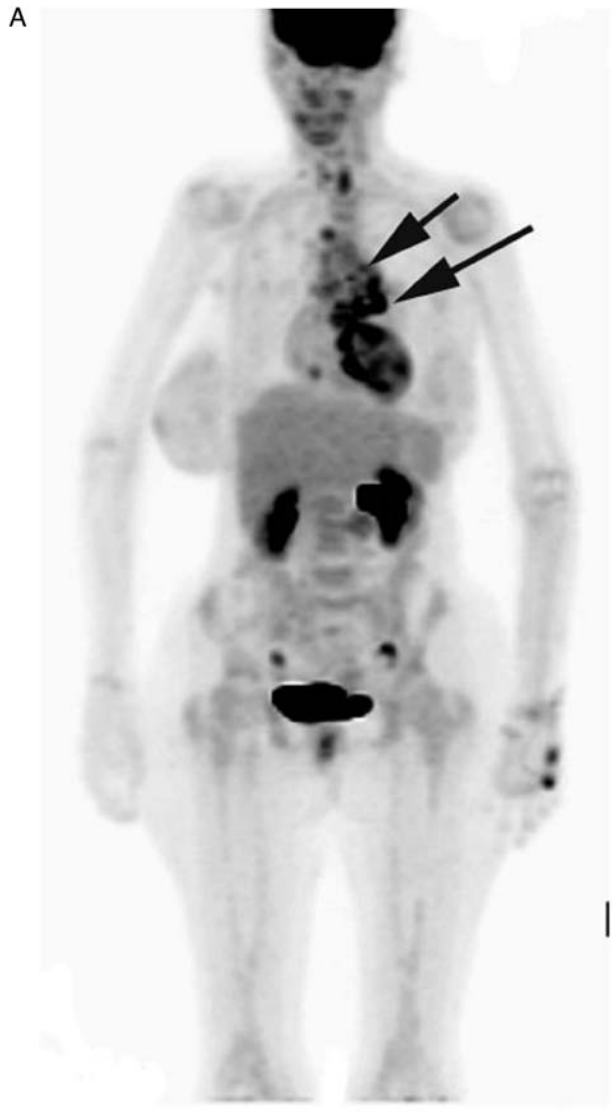


Figure 1. FDG positron emission tomography/computed tomography scan of a patient with fever of unknown origin diagnosed with liver phlegmon/abscess. (A) Coronal maximum intensity projection demonstrated abnormal focal uptake in the dome of the liver (arrow). (B) Coronal half-Fourier acquisition single-shot turbo spin-echo demonstrated a high signal area in the liver dome, corresponding to abnormal FDG uptake (arrow). (C) Coronal post-contrast T1-weighted image revealing a heterogonous area of low signal intensity in the same area in the liver dome (arrow). The patchy geographic areas of hepatic parenchyma signal alteration, and rim enhancing branching tubular structures were highly suggestive of an inflammatory/infectious process with phlegmonus changes but with no drainable hepatic abscesses. FDG, fluorodeoxyglucose.

of additional information. Other studies showed that anemia, lymphadenopathy and male sex correlated with diagnostic ^{18}FGD PET/CT results (13,23).

A significant number of false-positive results were reported in the present patients (23%), which reduced the positive predictive value to 68% and the overall diagnostic value in the study to 58%. This observation was most likely related to the normal physiological distribution of ^{18}FDG (in the kidney, urinary bladder, and small and large intestines). The discrimination between pathological and normal physiological uptake in such organs is difficult, which may explain the relatively high number of false-positives in the present study. In addition, ^{18}FDG uptake in the bone marrow and lymph nodes may be remarkable. Some investigators have suggested reclassifying ^{18}FDG uptake in the setting of FUO as a nonspecific sign of inflammation and considering the scan in such cases a true negative. This reclassification could greatly improve the positive predictive value and accuracy (39). Several issues may cause false-negative findings as well. For instance, small structures are not readily identified with PET/CT, as these small structures (such as temporal arteries) are beyond the resolution of PET/CT. The detection limit is ~10 mm. Furthermore, certain cancer types, such as prostate carcinoma and hepatocellular carcinoma, are not very FDG-avid (40).

Multiple previous studies have reported the value of ^{18}FDG PET/CT. However, comparing these studies is difficult, since the majority of these studies (including the present study) were retrospective with different inclusion and exclusion criteria with a possibility of selection bias. In addition, patients who undergo normal conventional imaging are more likely to have PET/CT scans than patients with positive conventional imaging results. In addition, certain studies included immunocompromised patients and comparing these patients with non-immunocompromised patients is difficult (41). Furthermore, in most studies, the definition of FUO was unspecified (42,43). One meta-analysis determined that only



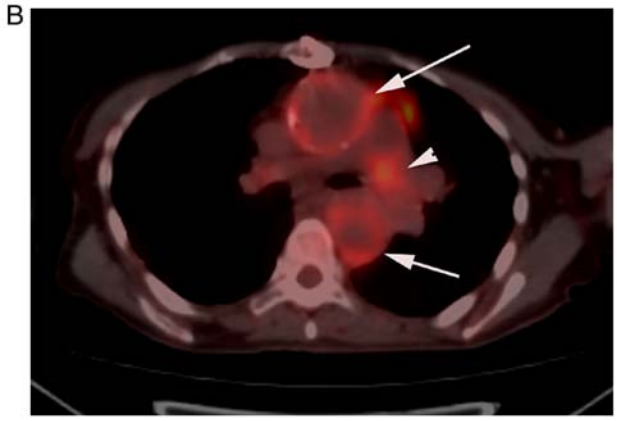


Figure 2. Continued.

a true-positive scan is helpful in diagnoses (44). In the present study, 51 patients (49%) had true-positive scans. However, this diagnostic approach has been questioned in a more recent meta-analysis, which suggested that true-negative scans must also be considered helpful, since patients with true-negative scans tend to have favorable prognoses and high spontaneous remission rates (45). Large, prospective, multicenter studies

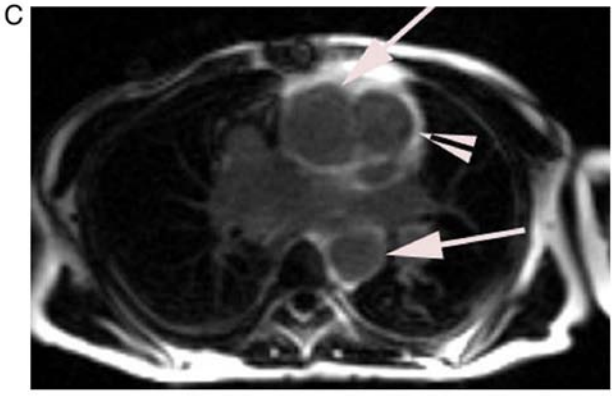
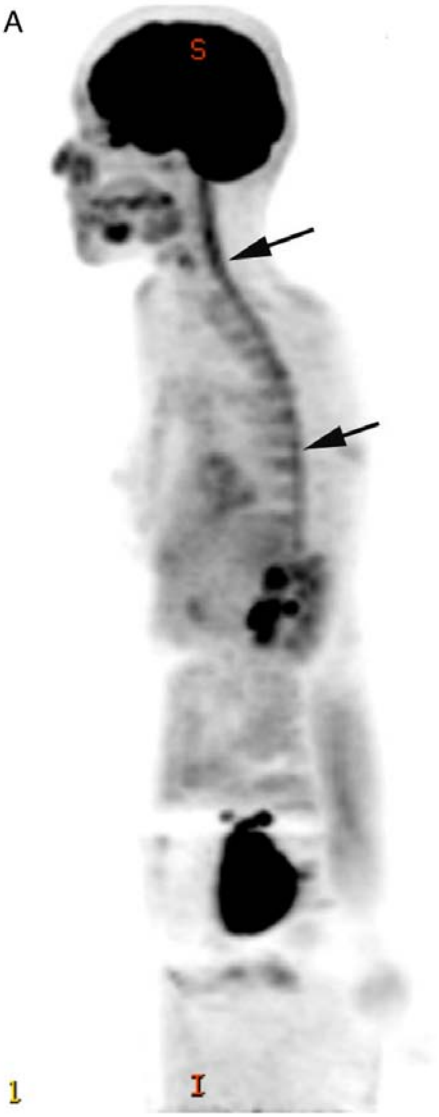


Figure 2. (A and B) FDG PET/CT scan and (C) MRI images of a patient diagnosed with Takayasu arteritis. (A) Coronal PET maximum intensity projection image demonstrating abnormal FDG uptake in the wall of the ascending aorta and pulmonary artery (arrows). (B) Axial fused image of FDG PET/CT confirming the abnormal FDG uptake in the ascending and descending aorta (arrow) and pulmonary artery (arrowhead). (C) Post gadolinium enhancement axial MRI at the level of the ascending aorta demonstrating abnormal wall thickening and gadolinium enhancement in the ascending aorta (arrow), and pulmonary artery wall (arrowhead). FDG, fluorodeoxyglucose; PET, positron emission tomography.



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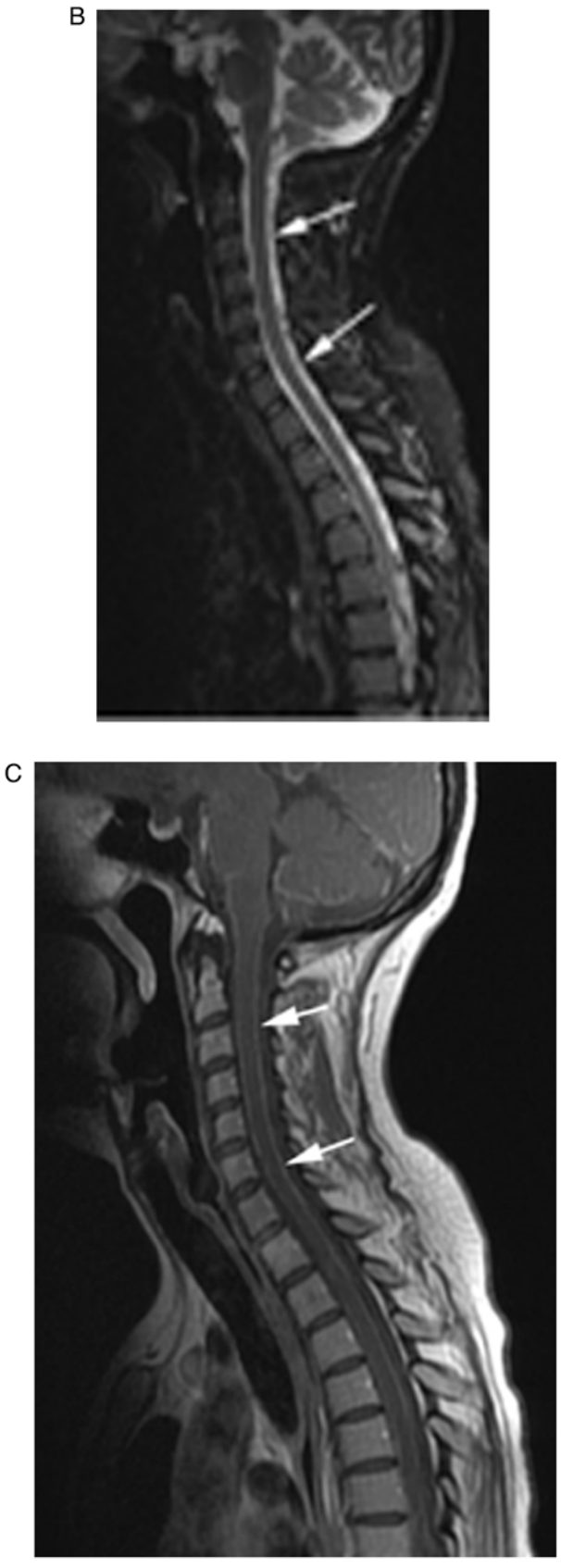

Figure 3. FDG PET/CT scan of a patient diagnosed with neurobrucellosis. (A) Sagittal FDG PET/CT PET maximum intensity projection image of the cervical spine showing diffuse and heterogeneous FDG uptake in the spinal cord (arrows). (B) Sagittal short-TI inversion recovery MRI of the cervical cord showing leptomeningeal hypointensity and thickening (arrows). (C) Sagittal post-gadolinium T1-weighted image showing diffuse leptomeningeal enhancement and thickening (arrows). FDG, fluorodeoxyglucose; PET, positron emission tomography.

Table IV. Sensitivity, specificity, and positive and negative predictive value of fluorodeoxyglucose positron emission tomography/CT.

Diagnostic performance	Value, %	95% CI, %
Sensitivity	71.83	59.90-81.87
Specificity	29.41	15.10-47.48
Positive predictive value	68.00	62.07-73.40
Negative predictive value	33.33	20.87-48.66
Accuracy	58.10	48.07-67.66

are needed to better investigate the role and value of ^{18}FDG PET/CT in patients with FUO.

The present study has certain important strengths and limitations. The study was a retrospective, small, single-tertiary care center study, and thus, the possibility of referral bias cannot be excluded. There was no structured protocol for a work-up of FUO. Both the diagnostic workup before ^{18}FDG PET/CT and the timing of the scan itself were performed according to the preference of the referring physicians. The significant variations among patients may have affected the disease prevalence and diagnostic accuracy of the test, which is one limitation of the study; the specificity was relatively low, only 29%, most likely due to heterogeneity of the population of the present study. The gold standard approach for patients with FUO/IUO is not well defined because of different patient populations among studies and the wide variety of etiologies. Finally, another limitation is that the cost of FDG PET/CT is relatively high and there is limited availability.

In conclusion, the present findings demonstrated that ^{18}FDG PET/CT substantially contributed to the establishment of a final diagnosis of FUO in a high percentage of patients (72%). ^{18}FDG PET/CT can detect metabolically active foci that may indicate infection, malignancies and inflammatory noninfectious processes, all of which may be the underlying etiology of the fever. PET/CT may be helpful by eliminating additional examinations that rule out focal processes; however, identifying focal ^{18}FDG activity may indicate false-positive findings and initiate additional examinations. Based on the present results and previous studies, it appears that ^{18}FDG PET/CT scans have a potential role in the initial diagnostic workup for investigation of the etiology of FUO. However, larger, prospective, multicenter studies with more specific referral criteria are warranted to better investigate the role and cost-effectiveness of ^{18}FDG PET/CT scans in the management of FUO.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

AF conceived the study, wrote the draft, prepared the figures and tables, and reviewed and edited the final manuscript. RB collected and analyzed data and prepared the draft of the manuscript. AF and RB confirm the authenticity of all the raw data. AA analyzed data and wrote, reviewed and edited the final manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

All procedures were performed in line with the ethical standards of the institutional research committee and conform to the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was conducted at the King Faisal Specialist Hospital and Research Centre (Riyadh, Saudi Arabia) after obtaining ethical approval from the Institutional Review Board on 11/01/2021 (approval reference no. 2211019). The consent to participate was waived by the ethics committee.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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