Analysis of the diagnostic effect of ^{18}F-FDG PET/CT in IIM patients and its relationship with disease severity

Binbin Wang[#] MD,
Lu Liu[#] MD,
Na Wang MD,
Yuqian Chen MD,
Yanpeng Sun MD

Department of Neurology, Taihe Hospital of Hubei University of Medicine, Shiyan, China

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Corresponding author:
Yanpeng Sun MD,
Department of Neurology, Taihe Hospital of Hubei University of Medicine, Shiyan, China
305213714@qq.com

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Abstract

Objective: To analyze the diagnostic effect of fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) in patients with idiopathic inflammatory myopathies (IIM) and its relationship with disease severity. **Subjects and Methods:** A retrospective analysis was conducted on the clinical and imaging data of 31 IIM patients treated in our hospital from April 2020 to April 2024, who were included in the lesion group. Additionally, 30 patients without muscle disease during the same period were selected as the control group. The maximum standardized uptake value (SUVmax) of the proximal limb girdle muscles was measured in both groups and compared. A receiver operating characteristic (ROC) curve was plotted to analyze the diagnostic value of SUVmax for IIM using ^{18}F-FDG PET/CT. Spearman rank correlation was used to analyze the relationship between muscle SUVmax in IIM patients and relevant laboratory indicators, including creatine kinase (CK), creatine kinase-MB (CK-MB), C-reactive protein (CRP), serum ferritin (SF), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and alanine aminotransferase (ALT). **Results:** The SUVmax level of the lesion group (2.94±0.58) was significantly higher than that of the control group (1.17±0.23) (t=15.568, P<0.05). A receiver operating characteristic curve analysis indicated that the optimal cut-off value of SUVmax for distinguishing the lesion group from the control group was 2.16g/mL, with a diagnostic sensitivity of 100%, specificity of 91.8%, and an area under the curve (AUC) of 0.952. Correlation analysis showed a positive correlation between SUVmax and CK (r=0.659), CK-MB (r=0.523), AST (r=0.458), and LDH (r=0.437) (P<0.05), but no significant correlation with CRP (r=0.219), SF (r=0.348), or ALT (r=0.237). **Conclusion:** Fluorine-18-FDG PET/CT demonstrates an ideal diagnostic effect for IIM patients, and its semi-quantitative parameter, SUVmax, holds good auxiliary diagnostic value for IIM. It can reflect the activity and severity of the disease to a certain extent.

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Introduction

Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune-mediated muscle diseases characterized primarily by skeletal muscle inflammation, weakness, and atrophy [1]. The pathogenesis is complex, involving environmental factors, genetic susceptibility, and immune abnormalities, but it is not yet fully understood [2]. Early diagnosis of IIM is crucial for timely intervention and improving prognosis. However, due to the diversity of clinical presentations and overlapping symptoms with other muscle diseases, accurate diagnosis can be challenging [3]. Imaging techniques play an important role in the diagnosis and assessment of IIM. Traditional imaging methods such as magnetic resonance imaging (MRI) and ultrasound can show pathological changes in the muscles, but their evaluation of disease activity and severity remains limited [4].

In recent years, flurorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) has emerged as an advanced molecular imaging technique that, due to its ability to detect metabolic features of active inflammation, has shown promising applications in the diagnosis and disease activity evaluation of IIM [5]. Flurorine-18-FDG PET/CT assesses inflammatory activity by measuring increased glucose metabolism in tissues, with maximum standardized uptake value (SUVmax) being a key parameter of semi-quantitative analysis, reflecting the level of metabolic activity in muscles [6]. However, current clinical studies on the application of ^{18}F-FDG PET/CT in IIM are still limited, and its diagnostic effect and relationship with disease severity have not been widely explored. Therefore, this study aims to retrospectively analyze the ^{18}F-FDG PET/CT imaging data of 31 IIM patients, explore the diagnostic value of SUVmax in IIM,

and analyze its relationship with disease severity, providing new imaging evidence for the early diagnosis and treatment of IIM.

Subjects and Methods

Basic information

A retrospective analysis was conducted on the clinical and imaging data of 37 IIM patients treated in our hospital from April 2020 to April 2024. Six patients were excluded due to incomplete data or recent corticosteroid treatment, leaving 31 patients to be included in the lesion group. In the lesion group, there were 14 males and 17 females; age range 51-77 years, with an average age of (55.86±7.98) years. Among these patients, 27 had dermatomyositis (DM) and 4 had polymyositis (PM). All patients met the diagnostic criteria by Bohan et al. (2021) [7]: 1) Symmetric proximal muscle weakness; 2) Elevated serum muscle enzymes; 3) Electromyography suggesting myogenic damage; 4) Muscle biopsy confirming inflammatory changes; 5) Characteristic rash of DM. Clinical information and laboratory test results of the 31 patients were collected, including treatment status, characteristic rash, muscle pain, muscle weakness, and levels of creatine kinase (CK), creatine kinase-MB (CK-MB), C-reactive protein (CRP), serum ferritin (SF), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and alanine aminotransferase (ALT). A control group of 30 patients without muscle disease, matched by gender and age, was selected for comparison, including 15 males and 15 females; age range 50-73 years, with an average age of (54.72±8.13) years. This study was approved by the medical ethics committee.

Examination methods

All patients underwent PET/CT examinations, following strict preparation protocols. Patients were required to fast for at least 6 hours to ensure blood glucose levels did not exceed 11.1mmol/L. Based on patient body weight, physicians calculated and injected the appropriate amount of the radiotracer ^{18}F-FDG, with doses ranging from 3.7 to 5.2MBq/kg. After injection, patients were instructed to lie quietly at rest for 60 minutes in a calm environment. Positron emission tomography/CT images were acquired with the patient in the supine position, breathing calmly. The imaging equipment used was the Philips GXL-16 PET/CT scanner, with a scanning range extending from the top of the head to the mid-thigh, and extending to the feet if necessary. Computed tomography scans were performed with a tube voltage of 120kV and a tube current of 100mA, with soft tissue algorithm reconstruction and a slice thickness of 2mm. Positron emission tomography scans typically covered 7 to 10 bed positions, with an acquisition time of 1.5 minutes per bed position. After the examination, the images were processed, including the reconstruction of transverse, sagittal, and coronal views for both PET and CT images. Positron emission tomography images were attenuation-corrected using CT data to improve accuracy. Finally, PET and CT images were fused using Syntegra software to generate clear PET/CT fusion images for diagnostic analysis.

Image analysis

Ensuring diagnostic accuracy during the analysis of PET/CT images is critical. All PET/CT images in this study were jointly evaluated by two experienced nuclear medicine specialists. In cases of disagreement between the two, a third equally qualified nuclear medicine expert was consulted for a final decision. During the evaluation, the specialists paid special attention to the patient's muscle tissues, closely examining the muscles of the upper arms, shoulders, paraspinal muscles of the cervical, thoracic, and lumbar spine, sternocleidomastoid muscle, buttocks, and upper thighs. For quantitative analysis, the specialists measured the SUVmax of these muscle regions and recorded the highest value. Standardized uptake value was calculated using the following formula: SUV (g/mL) = [Radioactive concentration in the region (Bq/mL)] / [Injected dose (Bq)/Body weight (g)].

Statistical analysis

GraphPad Prism 8 software was used for graphing, and SPSS 22.0 software was used for data processing. Measurement data following normal distribution were expressed as $\bar{x} \pm s$, and comparisons between groups were made using the Mann-Whitney U test. A receiver operating characteristic (ROC) curve was plotted to analyze the diagnostic value of SUVmax in ^{18}F-FDG PET/CT for IIM. Spearman rank correlation analysis was used to assess the relationship between muscle SUVmax in IIM patients and relevant laboratory indicators. A P-value of <0.05 was considered statistically significant.

Results

General data

All 31 IIM patients experienced varying degrees of proximal girdle muscle pain and weakness, 29 patients exhibited characteristic rash, 24 patients experienced shortness of breath, 13 patients had mild palpitations, and 19 patients showed muscle damage on electromyography. The average CK level was (427.69±1021.82) U/L, CK-MB (32.07±6.15) U/L, CRP (8.11±4.26) mg/L, LDH (522.83±407.95) U/L, SF (586.34±787.91) ng/mL, AST (113.92±108.84) U/L, and ALT (84.21±45.15) U/L.

Comparison of muscle SUVmax levels between the lesion group and control group

The SUVmax level in the lesion group (2.94±0.58) was significantly higher than that in the control group (1.17±0.23) ($t=15.568$, $P<0.05$), as shown in Figure 1. Additionally, 6 patients in the lesion group were found to have coexisting malignancies after PET/CT examinations, including 3 cases of prostate cancer, 2 cases of gastric cancer, and 1 case of Kaposi's sarcoma. Interstitial lung disease changes were observed in 21 patients, with an average SUVmax of (1.76±0.38) g/mL.

Diagnostic value of SUVmax in ^{18}F-FDG PET/CT for IIM

A receiver operating characteristic curve analysis results showed that the optimal cut-off value for SUVmax to differentiate between the lesion group and control group was 2.16g/mL, with a diagnostic sensitivity of 100%, specificity of 91.8%, and an AUC of 0.952, as shown in Figure 2.

Correlation analysis between muscle SUVmax and laboratory indicators in IIM patients

Correlation analysis results showed that SUVmax was positively correlated with CK (r=0.659), CK-MB (r=0.523), AST (r=0.458), and LDH (r=0.437) (P<0.05); however, no significant correlation was found with CRP (r=0.219), SF (r=0.348), or ALT (r=0.237), as shown in Figure 3.

Discussion

Idiopathic inflammatory myopathy is a rare group of chronic autoimmune diseases with a high risk of disability, characterized by skeletal muscle weakness, atrophy, and long-term inflammatory infiltration [8]. The main subtypes of IIM include dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM). Although these subtypes vary in clinical symptoms and pathological manifestations, they all share common features of varying degrees of proximal girdle muscle weakness and atrophy [9]. Moreover, inflammation plays a crucial role in these diseases, being the key pathological basis for muscle dysfunction [10]. In this study, the lesion group included 31 IIM patients, all of whom exhibited varying degrees of proximal girdle muscle pain and weakness. The ^{18}F-FDG PET/CT imaging showed that the SUVmax in the lesion group was significantly higher than in the control group (P<0.05), indicating that IIM patients had significantly higher glucose metabolism levels on PET/CT imaging compared to individuals without muscle disease. This increased uptake can be attributed to the active metabolic processes within inflammatory muscle tissues, especially the highly active macrophages and fibroblasts [11]. These cells absorb ^{18}F-FDG in a manner similar to tumor cells, due to the high expression of glucose transporter-1 (GLUT-1) and glucose transporter-3 (GLUT-3) on the surface of inflamma-

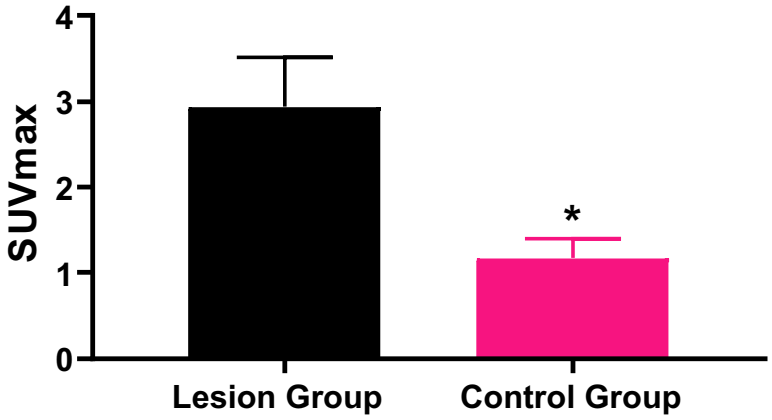

Figure 1. Comparison of muscle SUVmax levels between the lesion group and control group $\bar{x} \pm s$. Note: Comparison between groups, *P<0.05.

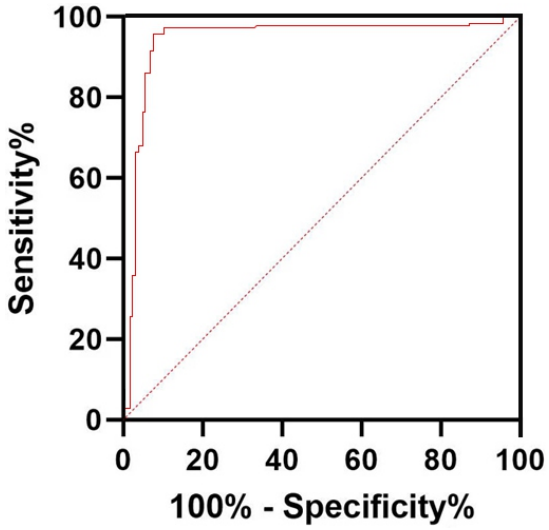

Figure 2. ROC curve analysis of SUVmax in the diagnosis of IIM by ^{18}F-FDG PET/CT.

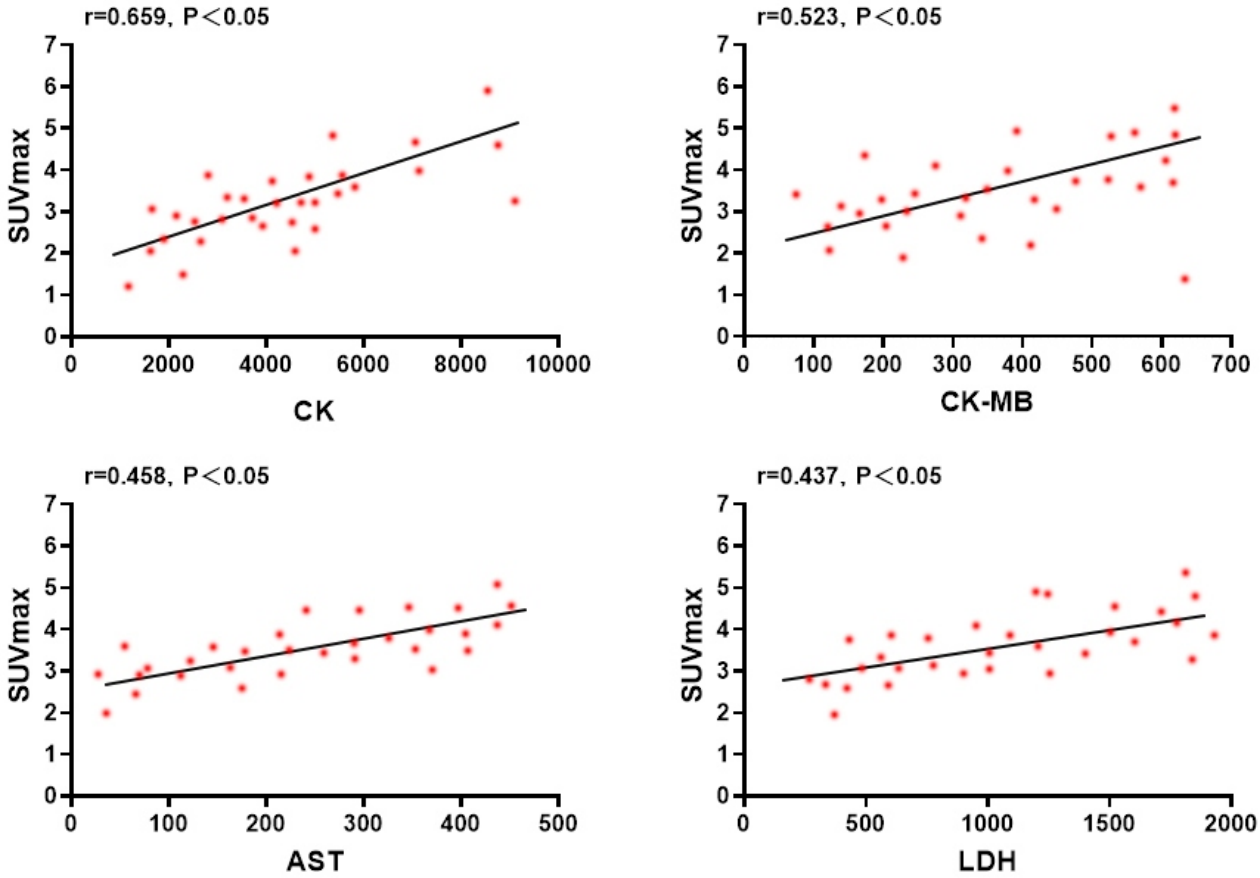

Figure 3. Correlation analysis between muscle SUVmax and laboratory indicators in IIM patients.

tory cells, thereby accelerating the glucose metabolism process. In inflammatory myopathies, this phenomenon reflects the level of muscle tissue inflammation. In recent years, an increasing number of studies [12, 13] have explored the application of ^{18}F-FDG PET/CT in various rheumatic immune diseases, such as rheumatoid arthritis, relapsing polychondritis, and adult-onset Still's disease. The value of ^{18}F-FDG PET/CT in these diseases lies mainly in its ability to detect active inflammation areas, helping doctors to assess disease activity more accurately. For IIM patients, this imaging tool has shown great potential in assessing the degree of muscle inflammation and diagnosing disease activity. In this study, the diagnostic value of SUVmax in IIM patients was analyzed using ROC. The results showed that when the SUVmax cut-off value was set at 2.16g/mL, PET/CT had a diagnostic sensitivity of 100% and a specificity of 91.8% in distinguishing between inflammatory muscles and normal muscles, with an AUC of 0.952. This further demonstrates the significant diagnostic value of ^{18}F-FDG PET/CT in IIM patients, especially in differentiating between subtypes such as DM and PM, making it highly promising for clinical application. Research by Tateyama et al. (2015) [14] also supports this conclusion, showing that the SUVmax in DM patients was closely related to the accumulation of macrophages in tissues, suggesting that SUVmax can not only reflect the degree of muscle inflammation but also serve as a biomarker for assessing disease activity. Therefore, ^{18}F-FDG PET/CT not only provides important imaging evidence for the diagnosis of IIM but also helps to assess the pathological activity of muscles through SUVmax, offering a reference for disease classification, treatment decisions, and prognosis evaluation.

In the clinical management of IIM patients, it is crucial to accurately grasp the activity of the lesions to formulate individualized treatment plans and evaluate efficacy [15]. Creatine kinase levels, as a commonly used laboratory marker, are often considered an important indicator reflecting the degree of muscle damage in patients [16]. However, CK levels can fluctuate and vary between individuals, which may limit their ability to assess disease activity. In this study, the average serum CK level in IIM patients was (427.69±1021.82) U/L, reflecting the extensive skeletal muscle damage in these patients. However, to assess the specific disease activity in different patients, a more comprehensive evaluation combining other methods is needed. In recent years, as a non-invasive imaging tool, ^{18}F-FDG PET/CT has provided a new means to assess the activity of lesions in patients with myositis due to its visual characteristics. In this study, muscle SUVmax was significantly positively correlated with serum CK levels (r=0.659, P< 0.05), indicating that as the glucose metabolism level of muscles increased, the levels of muscle damage markers CK also rose. This finding further confirms the potential of PET/CT in monitoring disease activity. Compared to traditional muscle biopsy or serological markers, SUVmax not only visually reflects the activity level of inflammation but also does so with-

out invasive procedures, greatly enhancing the feasibility of clinical applications. In addition to CK, this study also analyzed other important laboratory markers. The data showed that serum CK-MB, AST, and LDH levels in IIM patients were above the normal range, and muscle SUVmax was positively correlated with CK-MB (r=0.523), AST (r=0.458), and LDH (r=0.437) (P<0.05). These elevated markers are often associated with skeletal muscle and myocardial damage. In particular, CK-MB, as a sensitive marker of myocardial damage, usually indicates myocardial cell injury when elevated [17]. This study found a significant correlation between SUVmax and CK-MB, suggesting that the level of metabolic activity in muscles may be linked to the extent of myocardial involvement, which could provide an important reference for clinical assessment of whether IIM patients have myocardial lesions. Myocardial involvement in IIM patients is considered one of the major causes of death in patients with dermatomyositis and polymyositis, particularly in the context of complications such as myocarditis and heart failure [18]. Therefore, the application of PET/CT may not be limited to evaluating skeletal muscle damage, but could also provide diagnostic insights into lesions in other organs throughout the body. Aspartate aminotransferase is widely present in myocardial cells, and its elevated serum concentration usually indicates myocardial damage [19]. This study speculated that the elevated AST levels in IIM patients might be related to myocardial lesions, which also explains the positive correlation between SUVmax and AST. Lactate dehydrogenase is another important marker of tissue damage, mainly distributed in the heart, skeletal muscles, and kidneys [20]. The involvement of skeletal muscle and myocardium in patients with DM and PM leads to elevated LDH levels, and the positive correlation between SUVmax and LDH further confirms the accuracy of PET/CT in evaluating disease activity. Moreover, this study also explored the correlation between other acute phase reactants, such as CRP, SF, and ALT, with SUVmax. The results showed no significant correlations between SUVmax and CRP (r=0.219), SF (r=0.348), or ALT (r=0.237). A possible explanation is that IIM is a chronic inflammatory disease, while these markers are more commonly used to assess acute inflammation or organ damage, thus their sensitivity in chronic inflammation might be lower. Additionally, the limited sample size in this study may have affected the statistical results, leading to some bias.

Among the 31 IIM patients included in this study, 6 were diagnosed with concomitant malignancies after undergoing PET/CT examinations, including 3 cases of prostate cancer, 2 cases of gastric cancer, and 1 case of Kaposi's sarcoma. It is well known that DM patients have a higher risk of developing malignancies, and globally, the association between DM and malignancies shows significant regional and racial differences [21]. Many patients are diagnosed with cancer at an advanced stage, making early identification and intervention crucial for improving prognosis. As ^{18}F-FDG is a radiotracer with high tumor affinity, it can be rapidly taken up by tumor cells, and PET/CT, as a whole-body imaging tool, can accurately localize tumor lesions. This gives PET/CT an unparalleled advantage over conventional imaging methods in early tumor screening for IIM patients [22]. Therefore, PET/CT not only plays an important role in assessing muscle lesion activity in IIM patients, but also provides valuable diagnostic information for the early detection of potential malignancies. In addition, PET/CT has demonstrated its significant clinical application value in screening for pulmonary complications in IIM patients. This study found that 21 IIM patients showed interstitial pneumonia changes on PET/CT imaging, indicating that interstitial pneumonia is one of the common pulmonary complications in IIM patients and often affects patient prognosis. Among these pneumonia patients, the average SUVmax was (1.76±0.38) g/mL, indicating a moderate level of pulmonary inflammation activity. The association between interstitial lung disease and idiopathic inflammatory myopathies has been confirmed in several studies [23, 24], and certain types of pneumonia, such as rapidly progressive interstitial pneumonia, often carry a high mortality rate. Therefore, early identification and intervention are crucial. Li (2017) [25] and others have demonstrated that PET/CT can effectively predict whether IIM patients will develop rapidly progressive interstitial pneumonia, proposing an SUVmax of 2.4g/mL as the optimal diagnostic cut-off. At this threshold, PET/CT had a diagnostic sensitivity of 100%, specificity of 87%, and an overall accuracy of 90%. However, among the 21 pneumonia patients in this study, although 5 patients had lung SUVmax values exceeding 2.4g/mL, none of them developed rapidly progressive pneumonia after receiving glucocorticoid treatment. This result suggests that while PET/CT demonstrates high accuracy in predicting pulmonary complications, timely intervention in treatment can effectively prevent further disease progression. Therefore, in the pulmonary monitoring of IIM patients, PET/CT not only provides imaging evidence of disease activity but also helps clinicians assess potential risks in the patient's condition, thus guiding the formulation of individualized treatment strategies.

Conclusion and Limitations

Fluorine-18-FDG PET/CT has demonstrated significant clinical value in the diagnosis, disease assessment, and complication screening of IIM patients. As a non-invasive, visual molecular imaging technique, PET/CT not only aids in the early diagnosis of IIM but also assesses disease activity, monitors complications, and screens for potential malignancies. This suggests that PET/CT could become an important tool in the future management of IIM patients, providing clinicians with more comprehensive diagnostic information and helping to formulate individualized treatment plans, thereby improving patient outcomes. It should be noted that while this study provided important data on the diagnosis and disease assessment of IIM through ^{18}F-FDG PET/CT, there are still some limitations: 1) Small sample size: This study only included 31 IIM patients, which limits the generalizability of the findings to some extent; 2) Retrospective study design: This study is a retrospective analysis, which, although providing preliminary evidence for the application of PET/CT in IIM, has limitations in terms of establishing causal relationships; 3) Lack of longitudinal follow-up data: This study did not include follow-up data from patients, thus failing to evaluate the long-term application value of PET/CT in monitoring disease progression and treatment effica-

cy; 4) Insufficient exploration of other inflammatory markers: Although this study analyzed the correlation between SUVmax and several laboratory markers, it did not delve into other potential inflammatory markers, such as antinuclear antibodies (ANA) and anti-Jo-1 antibodies, which might provide more comprehensive diagnostic and prognostic information in relation to PET/CT results; 5) Treatment effects not considered: Since IIM patients may have undergone different treatment regimens (such as steroids and immunosuppressants), these treatments may affect PET/CT results, but this study did not fully control or analyze these factors, which may introduce some bias in the interpretation of results. In summary, future research should incorporate larger sample sizes, prospective designs, more comprehensive inflammatory marker detection, and include follow-up and treatment factors in the analysis to further clarify the full application value of PET/CT in IIM patients; 5) Treatment effects not considered: We acknowledge the importance of considering each patient's treatment type and duration when interpreting ^{18}F-FDG PET/CT results. In patients with idiopathic inflammatory myopathies (IIM), different therapies, such as immunosuppressants or corticosteroids, can influence ^{18}F-FDG uptake, potentially leading to variations in SUVmax. In this study, we did not specifically stratify patients based on treatment type or duration, which may introduce bias in the interpretation of results. Future research should aim to evaluate how these variables affect PET/CT findings in IIM patients, particularly in the context of malignancy risk, as outlined in international guidelines (ref. 23).

In conclusion, future research should incorporate larger sample sizes, prospective designs, more comprehensive inflammatory marker detection, and include follow-up and treatment factors in the analysis to further clarify the full application value of PET/CT in IIM patients.

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