Seminars in Arthritis and Rheumatism 57 (2022) 152107

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Defining the clinical utility of PET or PET-CT in idiopathic inflammatory myopathies: A systematic literature review

Georgia Bentick [a,1], Jessica Fairley [a,b,1], Suba Nadesapillai [a,c], Ian Wicks [a,b,d], Jessica Day [a,b,d,*]

[a] The Royal Melbourne Hospital, Rheumatology, Parkville, Australia
[b] The University of Melbourne, Parkville, Australia
[c] The Royal Melbourne Hospital, Nuclear Medicine, Parkville, Australia
[d] The Walter and Eliza Hall Institute of Medical Research, Inflammation Division, Parkville, Australia

ARTICLE INFO

Keywords:
Myositis
PET
PET-CT
Malignancy screening
Interstitial lung disease
Inflammatory myopathies

ABSTRACT

Objectives: Positron emission tomography (PET), often combined with computed tomography (CT), is a well-established tool for diagnosing malignancy and inflammatory disease. The idiopathic inflammatory myopathies (IIM) are chronic, multi-system diseases characterised by skeletal muscle inflammation, the potential for extramuscular manifestations such as interstitial lung disease (ILD) and an increased risk of malignancy. We performed a systematic literature review to evaluate the utility of PET or PET-CT in evaluation of IIM.
Methods: A search of Medline and EMBASE from 1990 to 2022 using keywords related to IIM and PET was performed. English language studies of adults with IIM who had PET or PET-CT were included.
Results: Our search identified 1173 potentially relevant abstracts, 19 of which were included. The majority of studies used [18F] fluorodeoxyglucose (FDG) PET or PET-CT scans, while the remainder used [18F] florbetapir and [^{11}C] Pittsburgh compound B ([^{11}C] PIB). The sensitivity and specificity of 18F-FDG-PET or 18F-FDG-PET-CT for diagnosing malignancy compared with standard detection methods was 66.7–94% and 80–97.8%, respectively. The sensitivity of 18F-FDG PET-CT for ILD was 93–100% when high-resolution CT was used as the reference standard. 18F-PET and 18F-FDG-PET-CT appear to accurately detect muscle inflammation, although correlations with clinical measures of IIM disease activity were variable. [18F] florbetapir PET-CT and [^{11}C] PIB PET were able to differentiate sporadic inclusion body myositis (IBM) from non-IBM IIM.
Conclusion: PET-CT holds promise as a single tool that can simultaneously evaluate multiple aspects of IIM. These include screening for associated malignancy, achieving an early diagnosis of ILD and evaluating muscle inflammation.

Key messages

- PET-CT is a promising tool to evaluate multiple aspects of IIM
- Further data are required to validate the use of PET-CT in IIM evaluation

Introduction

The idiopathic inflammatory myopathies (IIM) are a group of systemic autoimmune diseases characterised by chronic skeletal muscle inflammation, which may also be accompanied by a range of extramuscular manifestations. IIM can be classified into several subtypes including dermatomyositis (DM), polymyositis (PM), anti-synthetase syndrome (ASyS), sporadic inclusion body myositis (IBM), immune mediated necrotising myopathy (IMNM) and overlap myositis (OM). While skeletal muscle weakness is a major cause of morbidity for people with IIM, cardiorespiratory involvement including interstitial lung disease (ILD) and malignancy are major contributors to mortality [1–3]. An increased risk of malignancy in IIM is well-described, particularly in DM and PM [4,5]. This association is particularly strong in the presence of certain myositis-specific antibodies (MSA) such as anti-transcription intermediary factor 1γ (anti-TIF1γ) and anti-nuclear matrix protein 2

* Corresponding author at: Department of Rheumatology, Royal, Melbourne Hospital, 300 Grattan Street, Parkville, Victoria 3050, Australia.
E-mail address: jessica.day2@mh.org.au (J. Day).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.semarthrit.2022.152107

Available online 18 October 2022

(anti-NXP2) [6,7]. Although there is no uniformly agreed-upon cancer screening strategy for IIM, evidence-based algorithms have been proposed [8].

Positron emission tomography (PET) is a non-invasive imaging technique that detects both morphologic and functional changes according to tissue avidity for tracer uptake. In recent years, PET has been combined with computed tomography (CT) to provide more accurate anatomical information [9]. While [18F] fluorodeoxyglucose (FDG) is used to evaluate the presence of inflammatory disease or malignancy, alternative tracers (18F-florbetapir and [^{11}C] Pittsburgh compound B ([^{11}C] PIB)) are available for detection of amyloid. Given its ability to detect increased metabolic activity in inflamed muscle and other potentially involved tissues such as lung, joints and skin, there are multiple potential benefits of PET-CT scanning in IIM. Moreover, PET-CT is a sensitive tool to detect malignancy in other populations [10, 11], although its role in detecting malignancy in IIM cohorts has not yet been defined.

Accordingly, we systematically reviewed the literature to determine the utility of PET or PET-CT in IIM, including detection of malignancy, muscle inflammation and extramuscular manifestations, such as ILD.

Methods

A detailed study protocol has been submitted to the PROSPERO Register of systematic reviews. An electronic search of EMBASE and MEDLINE from 1990 to June 2022 was conducted using keywords and MeSH terms related to PET scanning and IIM (Fig. ES1). We cross-checked the reference lists of these articles to identify additional studies of potential significance. Two authors (GB, JF) screened the abstracts to determine their relevance, using the blinded Covidence systematic review data software system. Discrepancies were resolved by discussion and consultation with an additional author (JD) where necessary (Fig. 1). Full texts were reviewed by three authors (GB, JF, JD). Data extraction was performed by one author (GB or JF) and cross-checked by two authors (JF, JD).

Inclusion/exclusion criteria

We included studies if they met the following eligibility criteria: English language; clinical trial or observational study design, or case series including five or more participants; adult population; PET scan performed to investigate IIM (to assess skeletal muscle inflammatory activity, extramuscular manifestations or malignancy). Case reports, reviews, comments, letters to the editor and conference abstracts were excluded. Manuscripts where data from the same cohort was represented were reviewed by two authors and one record excluded to avoid duplication of data.

Population

We included papers which studied people with IIM, excluding non-inflammatory forms of myopathy.

Intervention

We included studies with any form of PET scanning techniques and radiotracers, including 18F-FDG-PET, 18F-FDG-PET-CT, 18F-florbetapir amyloid PET-CT and [^{11}C]PIB-PET.

Comparator/control

Studies were not required to have a comparison or control group for inclusion. However, when a control or comparator was available, we used this to compare efficacy of PET scanning in assessing the desired

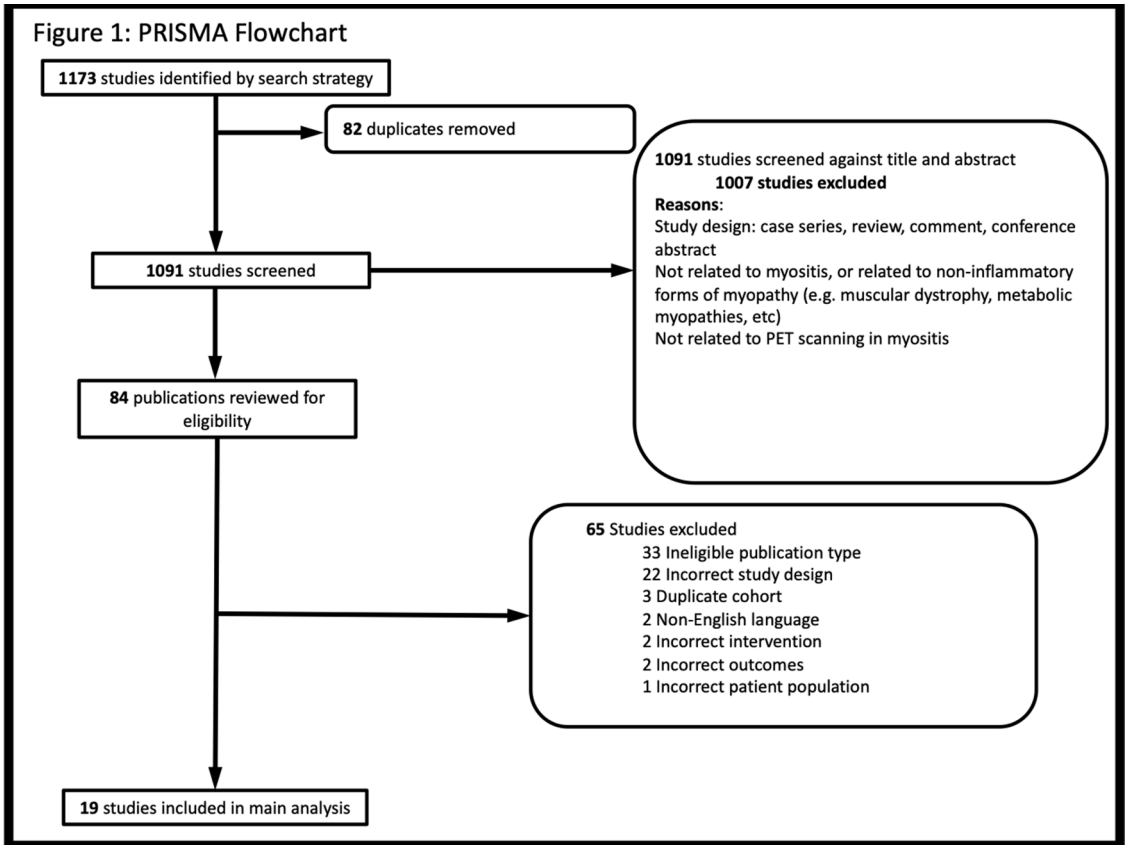

Fig. 1. PRISMA Flowchart.

outcome (e.g. conventional malignancy screening compared to PET, or magnetic resonance imaging (MRI) or muscle biopsy for detection of muscle inflammation).

Outcomes

Primary outcomes

Our primary outcome was use of PET or PET-CT to assess any pre-specified measure of muscle involvement, extramuscular manifestations of IIM or for the presence of malignancy. To compare the accuracy of PET with standard diagnostic techniques, we extracted method of diagnosis or classification of IIM and, where relevant, screening methods used for detection of malignancy and other extramuscular manifestations such as ILD.

Secondary outcomes

We extracted demographic data including disease subtype, disease severity and MSA profile where available.

Statistical analysis

We performed a qualitative synthesis of data summarised in descriptive tables. Meta-analysis was not possible due to significant heterogeneity in study design, interventions, comparison groups and PET scanning protocols.

Risk of bias estimation

Risk of bias assessments were performed using the National Heart, Lung and Blood Institute quality assessment tool for Observational Cohort and Cross-Sectional Studies. Each domain was identified as present, absent or unclear. Studies were deemed "Low" risk of bias if all criteria were present, "Moderate" risk of bias if up to two criteria were absent and up to two criteria were unclear, or "High" risk of bias if more than two criteria were absent and/or more than two criteria unclear. Risk of bias assessments were performed in duplicate (JF, GB).

Results

Description of included studies

Our search strategy identified 1173 potentially relevant studies. Of these, 82 were removed as duplicates, and 1007 were excluded for other reasons (Fig. 1: PRISMA Flowchart). Eighty-four full texts were assessed for eligibility, and 19 studies included in the main analysis. The primary diagnosis was most commonly PM or DM [12–30], including clinically amyopathic dermatomyositis (CADM) [15,17,19,27] and DM sine dermatitis [19]. The other primary diagnoses included IBM [18,20,28–30], OM [18,20,27], myositis not otherwise specified (MNOS) [18,30], orbital myositis [18] and IMNM [20,27]. Six studies were scored as being at moderate risk of bias [13,19,23,26,29,30], and 13 studies at high risk of bias [12,14–18,20–22,24,25,27,28] (Fig. ES2).

The included studies were all observational with a prospective [13,16,22,23,28–30] or retrospective [12,14,15,17–21,24–27] design. Study populations ranged from 9 to 131 people with IIM. Four studies performed PET or PET-CT prior to commencement of treatment [14,21,24,25]; eight studies performed PET or PET-CT after commencing treatment (including corticosteroids) in some participants [13,15,17,19,20,22,26,28], and the remainder did not record treatment information [12,16,18,23,27,29,30].

All studies used PET or PET-CT to identify one or more of the following outcomes: detection of muscle inflammation, amyloid deposition, malignancy and ILD. The majority of studies used either 18F-FDG PET-CT [14–27] or 18F-FDG PET alone [12,13,26] to examine people with IIM. The remainder used [18F] florbetapir PET-CT [28] or [11C] PIB-PET for amyloid deposition characteristic of IBM [29,30]. Heterogeneous visual and quantitative methods were used to determine PET positivity. Visual methods typically involved analysis of PET or PET-CT by nuclear medicine physicians and/or radiologists. Quantitative analysis typically involved measurement of standardised uptake values (SUVs) to determine the tracer activity in regions of interest. The application of SUVs to the quantitative analysis of each study is detailed in Table 1.

Detection of muscle pathology in IIM

18F-FDG PET and PET-CT

Ten studies evaluated either 18F-FDG PET-CT or 18F-FDG PET alone for its ability to detect muscle inflammation in IIM [13–15,19–22,24–26] (Table 2A). PET or PET-CT demonstrated a statistically significant difference in muscle uptake when compared with non-myopathic controls in the nine studies utilising such controls [13–15,19,20,22,24–26]. Most studies used IIM classification criteria as the reference standard, including American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) [20], Bohan and Peter (B&P) [13–15,22,24–26] and European Neuromuscular Centre (ENMC) [19] criteria. However, one study used magnetic resonance imaging (MRI) of muscle [21] as the reference standard.

Detection of muscle inflammation on PET or PET-CT was made by the visual analysis of a radiologist or nuclear medicine physician, or by a quantitative method (calculation cut-off SUV values) (Table 1). The sensitivity of PET and PET-CT for detection of muscle inflammation ranged from 33.3% to 100%, with specificity of 50% to 100% [13,14,19–22,24–26]. Analysing only studies that used PET-CT (a more modern approach), sensitivity ranged from 50 to 100% [14,19–22,24–26]. Quantitative assessment of PET or PET-CT was found to be more sensitive than visual analysis for differentiating IIM from controls in another study (50% sensitivity for visual analysis vs. 100% sensitivity for quantitative assessment) [20]. The sensitivity and specificity of PET-CT for detecting muscle inflammation when MRI was used as the reference standard was 87.5% and 50%, respectively [21].

Skeletal muscle FDG uptake was described as symmetrical in four studies [13,14,19,26] and involving proximal limbs in eight studies [13,14,19,20,22,24–26]. Limb muscle FDG uptake was predominant in three studies [14,15,22], though the pattern of FDG uptake was inconsistently reported (Table 2A).

In two studies, PET-CT detected subclinical inflammatory muscle signal in people with CADM [15,19]. Indeed, one study revealed no significant difference in skeletal muscle FDG uptake between DM and CADM [19]. However, the sensitivity of PET-CT for differentiating DM from controls in this study was only 50% [19], perhaps owing to corticosteroid or immunosuppressive treatment prior to PET-CT (9/24) [19]. Another study demonstrated higher skeletal muscle FDG uptake in PM/DM than in people with CADM [15]. No other studies evaluated the ability of 18F-FDG PET or PET-CT to differentiate between IIM subtypes [13–15,19–22,24–26].

Other PET tracers

Two studies evaluated [11C]PIB-PET [29,30] and one study evaluated [18F] florbetapir PET-CT [28] for its ability to detect muscle amyloid deposition and hence identify IBM (Table 2A). PET/PET-CT was able to differentiate IBM from non-IBM IIM in all three studies [28–30]. In the two studies that reported sensitivity and specificity of PET or PET-CT for detection of muscle amyloid in IBM, sensitivity ranged from 80% to 88.9%, while specificity was 100% in both [28,30]. Forearm and leg muscle uptake for both [18F]florbetapir and [11C]PIB-PET was greater in IBM compared with other IIM in the two studies reporting the distribution of muscle involvement [28,30].

Table 1
Details of included studies.

Author (Year) Country	N	Characteristics of IIM patients examined	Study design	IIM Criteria	Exclusions	PET Outcome
18F-FDG PET						
Berner (2003) Germany	13 IIM	DM (13) with suspected paraneoplastic syndrome Age (mean): 56.1 years (range 31–74); Female: 53.8% Clinical follow-up 1–6 years Treatment data not available	Retrospective	C	NR	Malignancy Diagnosis: - VA - Cut-off SUV-LBM >2.5
Owada (2012) Japan	24 IIM 69 NMC	DM (13) PM (11) Age (mean): 56.8 years (range 17–75); Female: 67% All patients with active myositis and elevated serum CK 6/24 IIM patients were on immunotherapy	Prospective	B&P	NR	Malignancy Diagnosis, Muscle Inflammatory Activity, ILD Diagnosis: - VA (FDG uptake ≥ liver FDG uptake)
18F-FDG PET/CT						
Arai-Okuda (2020) Japan	28 IIM 28 NMC	DM (18) PM (10) Age (mean): 66 years (range 42–77 years) Female: 79% 18F-FDG PET/CT before receiving initial corticosteroid treatment	Retrospective	B&P	NR	Myositis Inflammatory Activity: - VA (FDG uptake ≥ (liver FDG uptake OR mediastinal blood vessel uptake) - Cut-off SUV-mean > 1.12 - SUV-max
Li (2017) China	38 IIM 22 NMC	DM (18) CADM (17) PM (3) Age (mean ± SD): 56.0 ± 12.5 years (ranged 24– 83 years); Female: 60.5% 30/38 IIM treated with 1.0–2.0 mg/kg daily Glucocorticoid before PET/CT imaging	Retrospective	B&P; S	NR	Malignancy Diagnosis, Muscle Inflammatory Activity, ILD Diagnosis: - VA - SUV-max
Li (2020) China	75 IIM	DM (75); Age (mean ± SD) 52.9 ± 10.1 years; Female: 52% Follow-up rate of 100%; Median follow-up of 36.5 months (range 12–52 months) Treatment data not available	Prospective	B&P	Previous history of malignancy.	Malignancy Diagnosis: - VA
Liang (2021) China	61 IIM	DM (31) PM (9) CADM (12) ILD (100%) Age (mean ± SD): 56.7 ± 11.3 years (ranged 24– 83 years); Female: 59.0% Median follow-up of 11.9 months (range 4.0–23.8 months) Immunosuppressive and/or corticosteroid treatment prior to all FDG-PET/CT examinations	Retrospective	ACR/ EULAR	Clarified overlap syndromes with other CTDs. Myopathy related to thyroid dysfunction, strenuous exercise, inherited metabolic disorders, drug-induced myositis. Hospitalization for reasons unrelated to myositis and its complications. Newly identified or unresolved malignancies. Loss to follow-up without death from any cause within 3 months after hospitalization.	ILD Diagnosis: - VA - SUV-mean
Maliha (2019) Canada	63 IIM	DM (32); Age (mean ± SD) 54 ± 17; Female: 77% OM (25); Age (mean ± SD) 53 ± 11; Female: 88% PM (1); Age (mean) 40; Female: 100% IBM (1); Age (mean) 67; Female: 0% Orbital myositis (1); Age 55; Female: 100% MNOS (4); Age (mean ± SD) 53 ± 28; Female: 67% Treatment data not available	Retrospective	C, Serological	Insufficient follow up. Indeterminant diagnosis of IIM. Malignancy diagnosed before 18F-FDG PET/CT.	Malignancy Diagnosis: -VA
Martis (2019) France	24 IIM 24 NMC	DM (17) CADM (4), DM sine dermatitis (3) Age (median): 63 years (range 27–85 years); Female: 63% Life-threatening clinical signs at time of diagnosis in 11/24 Median time from diagnosis to FDG-PET 13 days (IQR 7–21) 9/24 IIM patients had received immunosuppressive treatment and/or corticosteroids at the time of FDG-PET	Retrospective	ENMC, H	Patients with ASyS or IMNM were excluded.	Muscle Inflammatory Activity: - Cut-off SUVPROX/ SUVMLT- >1.73
Matuszak (2019) France	34 IIM 20 NMC	34 IIM patients with 44 PET examinations (10/34 repeat scans) DM (16) OM (9) IMNM (4) IBM (3) PM (1) OM and DM (1)	Retrospective	ACR/ EULAR	NR	Muscle Inflammatory Activity: - VA

(*continued on next page*)

Table 1 (*continued*)

Author (Year) Country	N	Characteristics of IIM patients examined	Study design	IIM Criteria	Exclusions	PET Outcome
		Active muscle disease (26); Age (mean ± SD) 59.3 ± 13.9; Female: 73% Low/no muscle disease (18); Age (mean ± SD) 56.4 ± 19.4; Female: 67 Immunosuppressive and/or corticosteroid treatment prior to 31/44 FDG-PET/CT examinations				- Muscle SUV-max/ liver SUV-mean > 0.66
Motegi (2019) Japan	22 IIM	DM (22) Age (mean ± SD) 50.9 ± 2.6; Female: 59% PET/CT performed prior to treatment	Retrospective	B&P; S	NR	Muscle Inflammatory Activity, ILD Diagnosis: - VA - SUV-max
Pipitone (2012) Italy	12 IIM 14 NMC	DM (10) PM (2) Age (Median): 59.8 years Disease duration (median): 10 months Female: 92% 10/12 IIM patients had received immunosuppressive treatment and/or corticosteroids at the time of FDG-PET/CT	Prospective	B&P	NR	Muscle Inflammatory Activity: - Cut-off SUV muscle/liver > 0.45
Selva-O'Callaghan (2010) Spain	55 IIM	DM (33) PM (6) Age (Median (IQR)): 57.5 years (46.1–68.9) Female: 67% Treatment data not available	Prospective	B&P	Previous cancer, an active infection that could produce misleading FDG-PET uptake (e.g., tuberculosis), critical clinical situation.	Malignancy Diagnosis: - VA
Sun (2018) China	22 IIM 22 NMC	DM/PM (22) Age (mean ± SD) 52.1 ± 13.1 years Female: 73% PET/CT performed prior to treatment	Retrospective	B&P	NR	Muscle Inflammatory Activity: - VA - Cut-off SUV-max > 1.86
Tanaka (2013) Japan	20 IIM 20 NMC	DM (15) PM (5) Age (Median (IQR)): 62 (34-67) years Female: 80% Follow up (Median): 19 months All patients underwent PET/CT before receiving corticosteroid therapy	Retrospective	B&P	CADM	Muscle Inflammatory Activity: - Cut-off mean proximal muscle SUV> 0.83
Tateyama (2015) Japan	33 IIM 22 NMC	DM (11) PM (11) PM/DM with other collagen disease (8) Age (mean): 56 ± 17.9 years Female: 70% FDG PET performed after commencement of corticosteroid treatment in 8/11: mean 6.1 days (range 2–9 days)	Retrospective	B&P	IBM	Muscle Inflammatory Activity: - VA (FDG uptake ≥ mediastinal blood vessels FDG uptake) - SUV-max Eight patients underwent **18F-FDG PET** and 25 patients underwent **18F-FDG PET/CT**
Trallero-Araguas (2022) Spain	131 IIM; PET in 77/131	DM (61; CADM 23/61) PM (6) IMNM (21) OM (43; ASyS 32, SSc with myositis 11) Age (median): 55 (IQR 42–66) years Female: 62.5% Treatment data not available	Retrospective	ENMC	NR	Malignancy diagnosis: VA
Other PET tracer						
Lilleker (2019) UK	16 IIM	IBM (10): Age (mean at diagnosis): 64.3; Female: 10%; Disease duration at scan (mean): 4.0 years PM (6): Age (mean at diagnosis): 58.2; Female: 33.3%; Disease duration at scan (mean): 1.5 years 3/10 IBM and 6/6 PM patients had received immunosuppressive treatment and/or corticosteroids at the time of FDG-PET/CT	Prospective	IBM: ENMC PM: B&P	Age < 45 years for PM cohort	**[18F] florbetapir amyloid PET/CT**IBM Diagnosis, Muscle Inflammatory Activity: - Cut-off total SUVR ≥ 1.28
Maetzler (2011) Germany	9 IIM 4 NMC	IBM (7) PM (2) Demographic data NR Treatment data not available	Prospective	C, H	NR	**[^{11}C] PIB-PET**IBM Diagnosis, Muscle Inflammatory Activity: - VA - SUV
Noto (2020) Japan	13 IIM	IBM (9); Age (mean ± SD) 73.8 ± 3.9 years; Female: 44%; Disease duration (mean): 57.3 months Other IIM: DM (3) MNOS (1); Age (mean ± SD) 68.0 ± 10.4 years; Female: 75%; Disease duration (mean): 98.0 months Treatment data not available	Prospective	ENMC	NR	**[^{11}C] PIB-PET**IBM Diagnosis, Muscle Inflammatory Activity: - VA - SUV-mean ≥ 0.301

Abbreviations: [^{11}C]PIB = Pittsburgh compound B; ACR/EULAR = American College of Rheumatology/European League Against Rheumatism; ASyS = anti-synthetase syndrome; B&*P* = Bohan and Peter; C = clinical; CADM = clinically amyopathic dermatomyositis; CK = creatinine kinase; CT = computed tomography; CTD = connective tissue disease; DM = dermatomyositis; ENMC = European Neuromuscular Centre; FDG = fluorodeoxyglucose; *H* = histological; IBM = sporadic inclusion body myositis; IIM = idiopathic inflammatory myopathy; ILD = interstitial lung disease; IMNM = immune mediated necrotising myopathy; IQR = interquartile range; MNOS = myositis not otherwise specified; MRI = magnetic resonance imaging; NMC = non myositis controls; NR = not reported; OM = overlap myositis; PET = positron emission tomography; PM = polymyositis; *S* = Sontheimer's; SUV = standardised uptake value; SUV-LBM = standardised uptake value-lean body mass; SUV-max = standardised uptake value- maximum; SUVMLT = standardised uptake value musculus longissimus thoracis; SUVPROX = standardised uptake value proximal muscles; SUVR = standardised uptake value ratio; VA = visual analysis; vFDG = visual FDG.

Correlation with clinical markers of muscle disease activity and severity

Biomarkers

Five studies reported positive correlation of muscle FDG uptake on PET or PET-CT with serum creatine kinase (CK) level [14,15,20,21,25]. However, no correlation was found in four studies [13,19,22,26] (Table 2B). One study demonstrated that serum CK did not correlate with mean FDG uptake in proximal limb muscles, but did correlate with FDG uptake in cervical, thoracic and lumbar muscle groups [24]. Two studies reported a significant correlation between muscle FDG uptake and aldolase levels [14,25], but one other study demonstrated none [21].

Muscle strength

Muscle FDG uptake on PET-CT correlated with decreased muscle strength in three of six studies assessing strength [15,24,25]. Regional FDG uptake correlated with the degree of weakness in the corresponding muscle group in one study [25].

Severity and treatment response

One study demonstrated that a maximal SUV > 0.66 successfully differentiated high muscle disease activity (defined using the Myositis Intention to Treat Activity Index, MITAX) from low or no muscle disease activity with 92.3% sensitivity and 88.9% specificity [20]. A reduction in muscle FDG uptake with treatment was also reported [20].

Non-FDG tracers

Amyloid detection using PET or PET-CT did not correlate with clinical measures of disease severity including decreased strength [28–30] (Table 2B). The presence of degenerative biopsy features and fatty infiltration on MRI did not correlate with amyloid detection [28].

Malignancy

Seven studies investigated the ability of 18F-FDG PET-CT or 18F-FDG PET alone or to detect malignancy in people with IIM [12,13,15,16,18,23,27] (Table 3). To assess the diagnostic performance of PET or PET-CT, results were compared with highly heterogenous conventional malignancy screening algorithms in three of the seven studies [12,18,23]. Screening algorithms included variable combinations of bone scan, blood tests, CT, chest x-ray, endoscopy, endovaginal ultrasound and mammography [12,18,23]. Four studies did not report their comparative malignancy screening protocol [13,15,16,27].

When reported, the sensitivity and specificity of PET or PET-CT for diagnosing malignancy compared with standard detection methods was 66.7–94% and 80–97.8%, respectively [12,16,23,27]. Only one study prospectively compared the diagnostic performance of a standardised set of conventional malignancy screening tests with FDG-PET-CT and reported that these approaches had equivalent overall predictive value (both 92.7%) [23].

False positive cases for malignancy were observed in benign neoplasm and inflammatory lesions, including reactive lymph nodes [12,16,18,27]. One study demonstrated that both false positive PET-CT scans and conventional screening methods led to additional investigations, including imaging and biopsies [18]. Another study observed no side effects or damage due to further investigation of false positive PET-CT scans [27]. False negative PET/PET-CT scans for malignancy included lung cancer [12], breast cancer [16,18,23], vaginal carcinoma [23], multiple myeloma [18] and skin cancer [18]. However, it is known that some primary tumours are not readily visualised on PET or PET/CT, including small non-invasive breast cancers [32] or vaginal carcinoma [35]. PET cannot detect cancers occurring outside its field of view; in one study skin cancer was detected distal to where the PET-CT scan was performed [18].

Extramuscular manifestations of IIM

ILD was the only extramuscular manifestation evaluated by the included studies (Table 4).

ILD

Four studies investigated the role of PET in ILD associated with IIM [13,15,17,21]. The prevalence of ILD in these studies ranged from 75%–100% [13,15,17,21]. Three studies reported autoantibody data; the most commonly reported positive autoantibodies in IIM-ILD were anti-Jo1 [13,17,21], anti-MDA5 [17,21] and anti-Ro52 [17]. In one cohort, all anti-MDA5 positive participants ($n = 11$) had ILD, with four of these developing rapidly progressive ILD (RP-ILD) [21]. In another cohort, 3/4 anti-Jo1 positive participants had ILD [13].

Three studies reported the ability of PET or PET-CT to detect ILD, compared with HRCT as the reference standard [13,15,21]. The sensitivity of 18F-FDG PET-CT to detect ILD compared with HRCT was 93–100% [15,21], while 18F-FDG PET alone was only 39% [13], highlighting the value of combined PET-CT imaging.

Importantly, FDG uptake appeared to have a role in determining progression and severity of ILD, RP-ILD and unfavourable outcomes. Bilateral lung FDG uptake and abnormal mediastinal lymph nodes on PET-CT were significantly correlated with the development of RP-ILD [17]. FDG uptake in each lung was significantly positively correlated with the lung HRCT severity score [21], and FDG lung uptake was significantly increased in people with RP-ILD as compared to those with non-RP-ILD [15,17]. Furthermore, people with ILD who died within 3 months were found to have a higher bilateral lung mean SUV ($p = 0.019$) [17].

Discussion

People with suspected IIM typically undergo a series of tests to confirm the diagnosis, evaluate disease activity and extent of muscle involvement, and to screen for malignancy and extramuscular manifestations, including ILD. These tests are time consuming and burdensome; for hospital inpatients additional tests (e.g. mammography, cervical or bowel cancer screening) can prolong the length of stay or require follow up with a primary care provider post-discharge. 18F-FDG PET-CT has appeal as a hybrid technique that permits simultaneous assessment of multiple aspects of IIM including the presence of many malignancies, the burden and distribution of muscle inflammation and the presence of ILD, which is a critical extramuscular manifestation (Fig. 2).

Despite its potential, the role of PET or PET-CT in IIM evaluation and management is poorly defined. This review demonstrates that PET/PET-CT performs relatively well as a malignancy screening tool in IIM and that PET-CT can detect ILD, and may help to predict its severity and clinical progression. While PET-CT may help identify the burden and

Table 2
Studies using PET/PET-CT to describe muscle pathology (including diagnosis, distribution and disease activity).

Table 2A: Detection and Distribution of Muscle Pathology

Author (Year)	Population	PET Parameters	Diagnostic performance Statistically significant difference when compared with Controls	Sensitivity	Specificity	Notes
FDG-PET or FDG-PET/CT studies						
Arai-Okuda (2020)	28 IIM 28 NMC Gold Standard-B&P	18F-FDG PET/CT	Yes ($p < 0.001$)	85.7%	96.4%	FDG muscle uptake showed an almost symmetrical distribution. Proximal limb muscle uptake was most frequent (shoulders, buttocks and upper part of thighs).
Li (2017)	38 IIM 22 NMC Gold Standard-B&P; S	18F-FDG PET/CT	Yes (p value NR)	NR	NR	FDG limb uptake in PM/DM > CADM > controls.
Martis (2019)	24 IIM 24 NMC Gold Standard - ENMC	18F-FDG PET/CT	Yes ($p = 0.0012$)	50%	83.3%	No significant difference between DM and CADM ($p = 0.079$). All but those with CADM had FDG uptake that was symmetrical and proximal (limb).
Matuszak (2019)	34 IIM 20 NMC Gold Standard - ACR/EULAR	18F-FDG PET/CT	Yes ($p < 0.05$)	100%	92%	SUV-max in IBM was increased compared with controls but to a lesser extent than in other IIMs. Quantitative assessment was more sensitive than VA for diagnosis of IIM. Proximal (limb and trunk) muscle uptake was observed in IIIM.
Motegi (2019)	22 IIM Gold Standard-MRI	18F-FDG PET/CT	NR	87.5%	50%	Used MRI as gold standard for diagnosis of muscle inflammation. FDG uptake observed in muscles exhibiting myositis on MRI. In three cases, FDG uptake observed in muscles which did not have myositis on MRI. Did not report pattern of muscle FDG uptake.
Owada (2012)	24 IIM 69 NMC Gold Standard-B&P	18F-FDG PET	Yes ($p = 0.0004$)	33.3%	97.1%	FDG-PET sensitivity for detecting muscle involvement was 33.3%, which was significantly lower than the sensitivity of EMG (72.6%), MRI (57.1%) and muscle biopsy (100%) Patients with FDG muscle uptake had increased endomysial cell infiltration. Muscle FDG uptake in IIIM was mainly symmetrical and proximal (limb and trunk).
Pipitone (2012)	12 IIM 14 NMC Gold Standard-B&P	18F-FDG PET/CT	Yes ($p < 0.001$)	75%	100%	Proximal limb muscle uptake was observed in IIIM, with similar uptake in upper and lower limbs.
Sun (2018)	22 IIM 22 NMC Gold Standard-B&P	18F-FDG PET/CT	Yes ($p < 0.001$)	95.5%	95.5%	Proximal limb and paraspinal muscle uptake was observed in IIIM.
Tanaka (2013)	20 IIM 20 NMC Gold Standard-B&P	18F-FDG PET/CT	Yes ($p < 0.001$)	90%	100%	Proximal (limb and trunk) muscle uptake was observed in IIIM. Mean proximal muscle SUVs were similar in PM and DM.
Tateyama (2015)	33 IIM 22 NMC Gold Standard-B&P	18F-FDG PET (8) and 18F-FDG PET/CT (25)	Yes ($p < 0.0001$)	60.6%	NR	SUV-max reflected proximal symmetrical muscle involvement for PM/DM. Pattern of proximal muscle FDG uptake was variable.
Studies investigating amyloid deposition						
Lilleker (2019)	16 IIM (10 IBM, 6 PM) Gold Standard-IBM: ENMC; PM: B&P	[18F]florbetapir amyloid PET/CT	Yes ($p = 0.005$) (for differentiating IBM from PM)	80%	100%	[18F]florbetapir amyloid limb muscle uptake was greater in IBM compared with PM.
Maetzler (2011)	9 IIM (7 IBM, 2 PM) 4 NMC Gold Standard-muscle biopsy	[^{11}C]PIB-PET	Yes ($p = 0.004$) (for differentiating IBM from non-IBM)	NR	NR	All IBM patients had [11C] PIB-SUV levels above 0.5 in at least 1 muscle. All non-IBM subjects presented with [11C] PIB-SUV levels below 0.5. Did not report pattern of muscle uptake.
Noto (2020)	13 IIM 9 IBM, 3 DM, 1	[^{11}C]PIB-PET		88.9%	100%	

(*continued on next page*)

Table 2 (*continued*)

Table 2A: Detection and Distribution of Muscle Pathology						
Author (Year)	Population	PET Parameters	Diagnostic performance Statistically significant difference when compared with Controls	Sensitivity	Specificity	Notes
	MNOS Gold Standard - ENMC		Yes ($p = 0.031$) (for differentiating IBM from other IIM)			[^{11}C]PIB-PET uptake was greater in the forearm and lower-leg muscles of IBM compared to other IIM.
Table 2B: Muscle Disease Activity						
Author (Year)	Population	PET parameter	Correlation of PET parameters with muscle disease activity	Notes		
			CK	Decreased Muscle Strength#	Other	
FDG-PET or FDG-PET/CT studies						
Arai-Okuda (2020)	28 IIM 28 NMC	18F-FDG PET/CT	Yes (Mean SUV-mean, $p = 0.002$) (Mean SUV-max, $p = 0.010$)	NR	Mean SUV-mean, and mean SUV-max showed significant correlations with aldolase ($P = 0.005$, 0.038, respectively).	
Li (2017)	38 IIM 22 NMC	18F-FDG PET/CT	Yes ($p = 0.042$)	Yes ($p < 0.001$) #MMT grade		
Martis (2019)	24 IIM 24 NMC	18F-FDG PET/CT	No	No #MRC scale		
Matuszak (2019)	34 IIM 20 NMC	18F-FDG PET/CT	Yes ($p < 0.0001$)	NR	Reduced muscle FDG uptake with treatment. #MITAX score	SUV-max > 0.66 differentiated: - High muscle disease activity vs. low or no muscle disease activity: 92.3% sensitivity, 88.9% specificity.
Motegi (2019)	22 IIM	18F-FDG PET/CT	Yes ($p < 0.05$)	NR	No correlation between SUV-max of muscles and serum CRP or aldolase.	
Owada (2012)	24 IIM 69 NMC	18F-FDG PET	No ($p = 0.31$)	No ($p = 1.00$) #MMT		
Pipitone (2012)	12 IIM 14 NMC	18F-FDG PET/CT	No	No #MMT	No correlation with MRI muscle oedema scores.	
Sun (2018)	22 IIM 22 NMC	18F-FDG PET/CT	No (proximal muscle) Yes (cervical, thoracic and lumbar regions ($p < 0.05$))	Yes ($p = 0.004$) #MMT		
Tanaka (2013)	20 IIM 20 NMC	18F-FDG PET/CT	Yes ($p = 0.015$)	Yes ($p = 0.028$) #MMT	Mean proximal muscle SUVs significantly correlated aldolase levels ($p = 0.002$).	Regional FDG uptake reflects the corresponding weakness of the same muscle group. SUVs in proximal muscles from which biopsy specimens were obtained significantly correlated with the histological grade for the infiltration of inflammatory cells.
Tateyama (2015)	33 IIM 22 NMC	18F-FDG PET (8) and 18F-FDG PET/CT (25)	No ($p = 0.20$)	NR		Histological grades of biopsied muscles correlated with both the mean SUV-max and number of VA FDG-positive regions.
Amyloid studies						
Lilleker (2019)	16 IIM	18F]florbetapir amyloid PET/CT	NR	No #MMT	[18F]florbetapir SUVRs correlated poorly with fatty infiltration on MRI and the presence of degenerative biopsy features.	
Maetzler (2011)	9 IIM 4 NMC	[^{11}C]PIB-PET	NR	NR	Clinically severely affected muscles did not show increased [11C]PIB binding on PET/CT and no PIB staining within muscle fibres.	
Noto (2020)	13 IIM	[^{11}C]PIB-PET	NR	No #MRC scale	There was no correlation between SUVs and clinical parameters in IBM patients (i.e., disease duration and disease severity scores).	

#Measure of muscle strength used for comparison.

Abbreviations: [^{11}C]PIB = Pittsburgh compound B; ACR/EULAR = American College of Rheumatology/European League Against Rheumatism; ASyS = anti-synthetase syndrome; B&P = Bohan and Peter; C = clinical; CT = computed tomography; CXR = chest x-ray; DM = dermatomyositis; ENMC = European Neuromuscular Centre; FDG = fluorodeoxyglucose; H = histological; IBM = sporadic inclusion body myositis; IIM = idiopathic inflammatory myopathy; ILD = interstitial lung disease; IMNM = immune mediated necrotising myopathy; MNOS = myositis not otherwise specified; MMT = manual muscle testing; MRC scale = medical research council scale;

MRI = magnetic resonance imaging; NR = not reported; OM = overlap myositis; PET = positron emission tomography; PM = polymyositis; *S* = Sontheimer's; SUV = standardised uptake value; SUV-max = standardised uptake value- maximum; SUVR = standardised uptake value ratio; US = ultrasound; VA = visual analysis.

distribution of skeletal muscle inflammation in IIM, whether this offers utility above standard diagnostic tests and measures of muscle disease activity remains unclear. Preliminary data suggest PET-amyloid has promise as a non-invasive diagnostic test to subtype IBM from non-IBM myopathic disease.

Cancer is a well-known association of IIM, particularly DM and PM [4,5]. Our review highlights the lack of a standard approach in current malignancy screening practices [12,18,23], and emphasises the need for consensus guidelines for malignancy screening in IIM. The risk of malignancy in people with IIM varies according to disease subtype, clinical features and the presence of certain MSAs. Clinical risk factors include older age at disease onset, male gender, dysphagia, cutaneous necrosis or vasculitis, rapid onset, refractory disease and elevated inflammatory markers [6,36]. The presence of specific MSAs, namely anti-TIF1γ and anti-NXP2, confer a higher risk for cancer [6,7]. A recent systematic review of cancer screening in IIM indicates that while CT may be a useful cancer screening modality, there is preliminary evidence to suggest that PET-CT may also be an effective strategy to identify malignancy, among other IIM manifestations [37]. Our review indicates that when compared to standard detection methods, PET or PET-CT performs relatively well for detecting malignancy (sensitivity 66.7–94%, specificity 80–97.8%) [12,16,23,27]. In the single prospective study, the diagnostic performance of FDG-PET-CT was equivalent to conventional malignancy screening [23]. However, PET or PET-CT is not without limitation as a single malignancy screening test: lesions that are small or have low glycolytic activity such as carcinoid tumours and low-grade lymphomas [38,39], and malignancy outside the standard field of view (e.g. melanoma in the distal extremities) may be missed [18]. Furthermore, non-specific inflammatory uptake can be difficult to differentiate from malignancy [12,16,40]. False positives may lead to burdensome, invasive and costly investigations, although this risk also applies to conventional screening modalities [14]. While PET or PET-CT performs well for malignancy screening, it cannot replace thorough clinical assessment and standard, age-appropriate malignancy screening. Cancer screening with PET-CT may be most suitable for high-risk IIM cohorts such as those with clinical risk factors or anti-TIF1γ or anti-NXP2 positivity.

Interstitial lung disease is the leading cause of morbidity and mortality in IIM [1,2]. Recent evidence suggests that pulmonary FDG uptake can be successfully used to monitor inflammatory pulmonary disease in studies of people with connective tissue disease [41] and systemic sclerosis-related ILD [42]. Our review indicates that 18F-FDG PET-CT is also a valuable imaging tool for the detection of IIM-ILD, demonstrating a sensitivity of 93–100% when compared with HRCT [15,21]. It also highlights the ability of PET-CT to determine the progression and severity of IIM-ILD, with multiple studies demonstrating that lung FDG uptake was significantly increased in people with RP-ILD as compared to those with non-RP-ILD [15,17]. Further studies examining well-characterised cohorts are required to evaluate the prognostic significance of PET-CT for IIM-ILD.

Evaluating muscle activity in IIM typically involves clinical assessment and measurement of muscle enzymes. MRI is a non-invasive imaging technique to identify the presence and pattern of muscle inflammation, although muscle biopsy remains the gold standard for diagnosis. Our review indicates that 18F-FDG-PET or PET-CT may provide information about muscle inflammation, although its utility beyond standard techniques is unclear. The sensitivity of PET-CT for detecting muscle inflammation in IIM ranged from 50 to 100% [13,14,19–22,24–26]: prior administration of corticosteroids may have suppressed muscle inflammation and hence FDG uptake in several cohorts [13,15,19,20,22,26]. Importantly, muscle FDG uptake on PET is non-specific, and can occur with exercise [31], poor participant positioning in the scanner [34] and denervation [43]. This was reflected in the variable specificity of PET or PET-CT for muscle activity in IIM compared with controls, which ranged from 50 to 100% [13,14,19–22,24–26]. A benefit of PET-CT is its ability to rapidly assess muscle groups that are difficult to assess clinically and are not routinely evaluated using standard muscle MRI or EMG. This was demonstrated by the FDG uptake in paraspinal muscles that was observed in one study [24]. Serum CK and manual muscle strength testing (MMT) are included in the International Myositis Assessment and Clinical Studies Group (IMACS) disease activity core set measures, however it is well recognised that the relationship between these measures and disease activity is variable [44,45]. Our review indicates that the relationship between FDG uptake and these disease activity measures such as serum CK and muscle strength is unclear [13–15,19–22,24–26]. While other biomarkers of myositis activity have been proposed, such as serum ferritin, these were not assessed in any of the studies included in our review [46]. Whether FDG-PET-CT could aid the diagnosis of IIM by identifying a representative muscle sample for histological examination was not addressed by the included studies. PET scans using 18F-florbetapir and [^{11}C] PIB are a well described tool for the detection of amyloid-beta in the brains of people with Alzheimer's Disease [47,48]. Although the composition of amyloid deposits in IBM are not identical to those in Alzheimer's Disease, PET using 18F-florbetapir or [^{11}C] PIB can potentially detect the amyloid deposits in IBM [49]. An important finding of our review was that PET-amyloid may be able to subtype IBM from non-IBM myopathic disease [28–30]. This has promise as a non-invasive diagnostic test, though will require careful validation in larger cohorts, as well as analysis of the effects of age on amyloid muscle deposition.

A range of other extramuscular manifestations, including cardiac involvement, skin lesions, arthritis, hemophagocytic lymphohistiocytosis (HLH) and pulmonary hypertension can occur in IIM. While we did identify one study, which evaluated the clinical utility of PET-CT in secondary HLH in IIM [33], this was not included in our final review, as it was a duplicate cohort [17]. Furthermore, the studies included our review did not evaluate the utility of PET for detecting other non-ILD extramuscular manifestations of IIM. In addition to its potential for increasing the cancer detection yield, extending the PET scan field of view would permit a more accurate assessment of extramuscular manifestations, as it may capture the distal small joints and inflammatory skin lesions, such as Gottron's papules. Cardiac involvement is another potentially serious complication of IIM [50] and the role of cardiac protocol PET to detect cardiac involvement merits further investigation.

Strengths and limitations

This review provides a current and comprehensive synopsis of the utility of PET or PET-CT for multiple applications in IIM and hence provides a framework to guide clinicians in the use of PET-CT scans for people with this disease. Despite this, our review has limitations. The included studies were small and observational in nature. All studies were at moderate to high risk of bias. Additionally, the methods of PET or PET-CT interpretation were highly heterogenous between each study, precluding calculation of pooled effect estimates. Certain techniques reported within the studies (e.g. using PET alone) are outdated and have largely been replaced by PET-CT, which may underestimate the diagnostic yield of PET-CT presented in these data.

Conclusion

FDG-PET-CT is a promising hybrid imaging tool that may be useful to evaluate the burden of muscle inflammation and achieve an early diagnosis of RP-ILD in people with IIM. PET-CT should be strongly considered as an upfront test in high-risk patients for malignancy at IIM diagnosis. PET-amyloid may be able to differentiate IBM from non-IBM

Table 3
Studies describing malignancy diagnosis.

Author (Year)	Population	Possible malignancy on PET (Positive tests)	Confirmed malignancy (True +)	False +	Negativetests	False negative	Sensitivity	Specificity	Conventional malignancy screen	Malignancy diagnosis	Notes
Berner (2003)	13 IIM	4/13	3/4	1/4	9/13	1/9	75%	88.9%	Bone scan, CT, CXR, Endoscopy, MRI, US*	Histology	Benign neoplasm (adrenal adenoma) also demonstrated increased tracer uptake. False negative- lung cancer.
Li (2017)	38 IIM 22 NMC	8/38	7/8	1/8	30/38	NR	NR	NR	NR	Histology	Increased FDG uptake foci (SUV-max ranged 3.5–12.8) accompanied with soft tissue density masses were seen in all 7 cases with malignant tumours on PET/CT.
Li (2020)	75 IIM	19/75	16/19	3/19	56/75	1/56	94%	95%	NR	Histology	False positive cases observed in benign tumours and inflammatory reaction sites. False negative- breast cancer.
Maliha (2019)	63 IIM 100 scans in 63 patients	9/63	0/9	9/9	54/63	3/64	NR	NR	CT, CXR, Endoscopy, Endovaginal US, Mammography, SPEP, Tumour Markers*	Histology	PET was false positive for malignancy in 13/100 scans. This led to 11 additional imaging investigations and 8 biopsies. Conventional screening was false positive 21 times in 21 individuals, which led to 10 additional imaging investigations and 12 biopsies. The false negatives malignancies comprised: multiple myeloma (anti-MDA5), 7 mm breast cancer (anti-Mi2) and skin squamous cell carcinoma (anti-TIF1γ).
Owada (2012)	24 IIM 69 NMC	1/24	1/1	NR	NR	NR	NR	NR	NR	NR	
Selva-O'Callaghan (2010)	55 IIM	7/55	6/7	1/7	44/55	3/44	66.7%	97.8%	Physical exam, CBC, serum chemistry, Thoracoabdominal CT, gynecologic Examination, Mammography, tumor Markers, Pelvic US	Histology	PET inconclusive for malignancy in 4 patients. The overall predictive value of broad conventional screening was the same as that of FDG-PET/CT (92.7 vs 92.7). The false negative malignancies comprised: breast cancer detected during follow up and vaginal carcinoma.
Trallero-Araguas (2022)	131 IIM; PET in 77/131	24/77	11/24	13/24	53/77	1/53	91.2%	80%	Only performed in 11/88 participants. Protocol not recorded	Histology where available.	One patient died of cancer complications prior to definitive malignancy investigation. 36 procedures (21 invasive in 17 participants) performed in 23 participants. 7 participants ultimately free from cancer underwent invasive procedures. No side effects or damage due to complementary tests observed.

* Screening was not standardised across patients

Abbreviations: CBC = complete blood count; CT = computed tomography; CXR = chest x-ray; FDG = fluorodeoxyglucose; IIM = idiopathic inflammatory myopathy; MRI = magnetic resonance imaging; NR = not reported; PET = positron emission tomography; SPEP = serum protein electrophoresis; SUV = standardised uptake value; SUV-max = standardised uptake value- maximum; US = ultrasound;.

Table 4
Studies investigating interstitial lung disease (ILD).

Author (Year)	Population	Autoantibody Status	HRCT detection of ILD	PET ILD detection (HRCT gold standard)	Notes
Li (2017)	DM [18] CADM [17] PM [3]	NR	30/38	28/30 (PET/CT)	On PET/CT imaging, the degree and extent of FDG uptake were significantly increased in the patients with RP-ILD, compared to those with chronic ILD. When SUV-max $\geq$ 2.4 was used as the threshold to predict RP-ILD, the diagnostic sensitivity, specificity, and accuracy was 100.0% (7/7), 87.0% (20/23), and 90.0% (27/ 30), respectively.
Liang (2021)	DM [31] CADM [12] PM [9]	Anti-Ro-52 31/61, Anti-MDA5 25/61, Anti-NXP2 7/61, Anti-SAE1 5/61, Anti-TIF1γ 4/61, Anti-Mi-2α 2/61, Anti-Mi-2β 4/61, Anti-SRP 3/61, Anti-PM-Scl75 3/61, Anti-Ku 2/61 Antisynthetase Ab: Anti-Jo-1 5/61, Anti-PL-7 6/61, Anti-EJ 1/61, Anti-OJ 1/61, Anti-PL-12 2/61	61/61 (only IIM patients with ILD selected for this study)	NR	Bilateral lung FDG uptake and abnormal mediastinal lymph nodes on PET/CT were significantly correlated with the development of RP-ILD in IIM-ILD patients. When bilateral lung SUV-mean > 0.454 was used as the threshold to predict RP-ILD, the diagnostic sensitivity was 95.2%, and the specificity was 62.5%. IIM-ILD patients who died within 3 months were found to have a higher bilateral lung SUV-mean (p = 0.019).
Motegi (2019)	DM [22]	Anti-MDA5 11/22 (all anti-MDA5 patients had ILD, 4 developed RP-ILD) Anti-ARS 3/22	21/22	21/21 (PET/CT)	The location of FDG uptake localised to the ILD region detected by HRCT. There was a significant positive correlation between lung HRCT score and SUV-max in each lung.
Owada (2012)	24 IIM	Anti-Jo-1 4/24 Anti-Jo-1 with ILD 3/4	18/24	7/18 (PET)	All patients with FDG uptake in the lung had active ILD as defined by respiratory symptoms, progressive ground-glass opacities, or a decrease in PaO2.

Abbreviations: CADM = clinically amyopathic dermatomyositis; CT = computed tomography; DM = dermatomyositis; FDG = fluorodeoxyglucose; HRCT = high resolution computed tomography; IIM = idiopathic inflammatory myopathy; ILD = interstitial lung disease; NR = not reported; PET = positron emission tomography; PM = polymyositis; RP-ILD = rapidly-progressive ILD; SUV = standardised uptake value; SUV-max = standardised uptake value- maximum;.

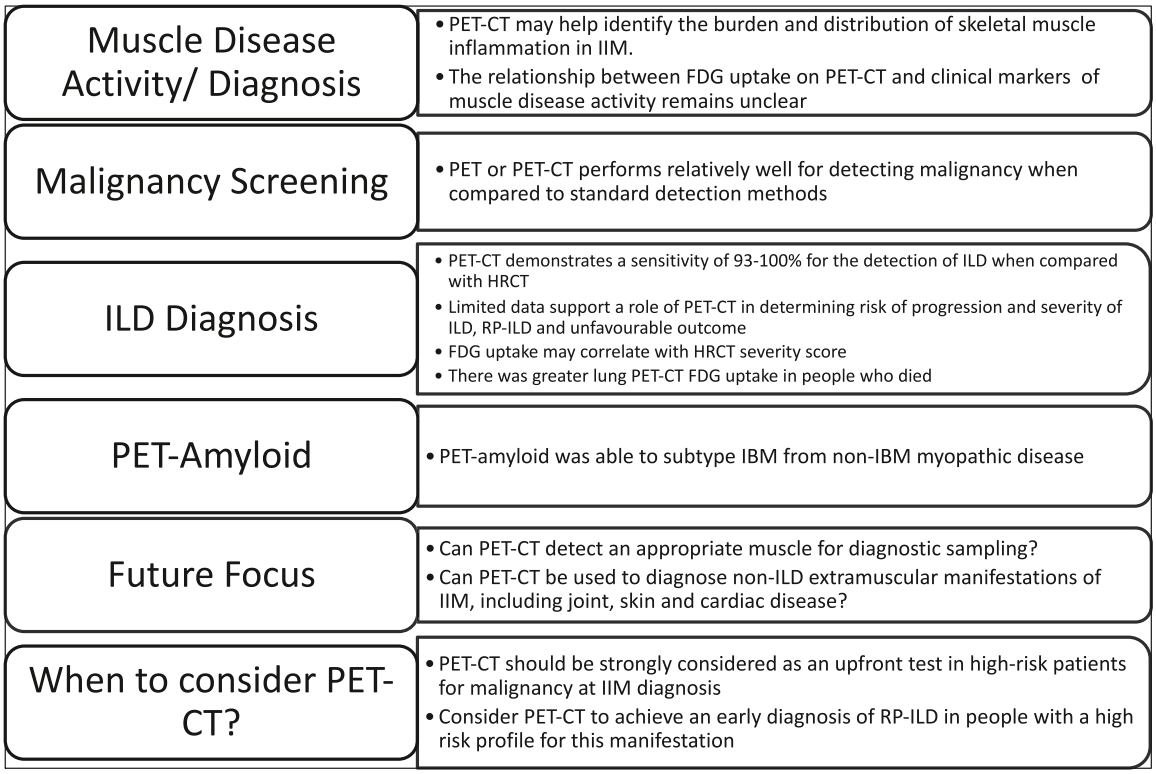

Fig. 2. PET and PET-CT in Idiopathic Inflammatory Myopathies: Key Points and Knowledge Gaps.

myopathic disease. Further well-designed research in larger cohorts is required to validate the use of PET for these purposes, and to determine its practical and economic feasibility beyond the current standard available techniques.

Funding

No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Data availability statement

The data supporting this article are available in the article and in its online supplementary material.

Declaration of Competing Interest

The authors have declared no conflicts of interest.

Acknowledgments

Acknowledgements: JD is the recipient of the Sylvia and Charles Viertel Charitable Foundation Clinical Investigator Award, the John T Reid Charitable Trust Centenary Fellowship and the RACP Australian Rheumatology Association & D.E.V Starr Research Establishment Fellowship. JF is the recipient of a National Health and Medical Research Council (NHMRC) Postgraduate Scholarship and is supported by an Australian Government Research Training Program Scholarship. IW is the recipient of a National Health and Medical Research Council Medical Research Future Fund Practitioner Fellowship (1154325) and receives research support from the John T Reid Charitable Trust.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.semarthrit.2022.152107.

References

[1] Shappley C, Paik JJ, Saketkoo LA. Myositis-related interstitial lung diseases: diagnostic features, treatment, and complications. Curr Treatm Opt Rheumatol 2019;5(1):56–83.
[2] Barba T, Mainbourg S, Nasser M, Lega JC, Cottin V. Lung diseases in inflammatory myopathies. Semin Respir Crit Care Med 2019;40(2):255–70.
[3] Dobloug GC, Svensson J, Lundberg IE, Holmqvist M. Mortality in idiopathic inflammatory myopathy: results from a Swedish nationwide population-based cohort study. Ann Rheum Dis 2018;77(1):40–7.
[4] Buchbinder R, Forbes A, Hall S, Dennett X, Giles G. Incidence of malignant disease in biopsy-proven inflammatory myopathy. A population-based cohort study. Ann Intern Med 2001;134(12):1087–95.
[5] Yang Z, Lin F, Qin B, Liang Y, Zhong R. Polymyositis/dermatomyositis and malignancy risk: a metaanalysis study. J Rheumatol 2015;42(2):282–91.
[6] Moghadam-Kia S, Oddis CV, Ascherman DP, Aggarwal R. Risk factors and cancer screening in myositis. Rheum Dis Clin N Am 2020;46(3):565–76.
[7] Fiorentino DF, Chung LS, Christopher-Stine L, Zaba L, Li S, Mammen AL, et al. Most patients with cancer-associated dermatomyositis have antibodies to nuclear matrix protein NXP-2 or transcription intermediary factor 1γ. Arthritis Rheum 2013;65(11):2954–62.
[8] Selva-O'Callaghan A, Martinez-Gómez X, Trallero-Araguás E, Pinal-Fernández I. The diagnostic work-up of cancer-associated myositis. Curr Opin Rheumatol 2018;30(6):630–6.
[9] Tong S, Alessio AM, Kinahan PE. Image reconstruction for PET/CT scanners: past achievements and future challenges. Imaging Med 2010;2(5):529–45.
[10] Chen YK, Ding HJ, Su CT, Shen YY, Chen LK, Liao AC, et al. Application of PET and PET/CT imaging for cancer screening. Anticancer Res 2004;24(6):4103.
[11] Xu G, Zhao L, He Z. Performance of whole-body PET/CT for the detection of distant malignancies in various cancers: a systematic review and meta-analysis. J Nucl Med 2012;53(12):1847.
[12] Berner U, Menzel C, Rinne D, Kriener S, Hamscho N, Dobert N, et al. Paraneoplastic syndromes: detection of malignant tumors using [18F]FDG-PET. Q J Nucl Med 2003;47(2):85–9.
[13] Owada T, Maezawa R, Kurasawa K, Okada H, Arai S, Fukuda T. Detection of inflammatory lesions by F-18 fluorodeoxyglucose positron emission tomography in patients with polymyositis and dermatomyositis. J Rheumatol 2012;39(8):1659–65.
[14] Arai-Okuda H, Norikane T, Yamamoto Y, Mitamura K, Fujimoto K, Takami Y, et al. 18F-FDG PET/CT in patients with polymyositis/dermatomyositis: correlation with serum muscle enzymes. Eur J Hybrid Imaging 2020;4(1):14.
[15] Li Y, Zhou Y, Wang Q. Multiple values of 18F-FDG PET/CT in idiopathic inflammatory myopathy. Clin Rheumatol 2017;36(10):2297–305.
[16] Li X, Tan H. Value of (18)F-FDG PET/CT in the detection of occult malignancy in patients with dermatomyositis. Heliyon 2020;6(4):e03707. -e.
[17] Liang J, Cao H, Liu Y, Ye B, Sun Y, Ke Y, et al. The lungs were on fire: a pilot study of 18F-FDG PET/CT in idiopathic-inflammatory-myopathy-related interstitial lung disease. Arthritis Res Ther 2021;23(1):198.
[18] Maliha PG, Hudson M, Abikhzer G, Singerman J, Probst S. 18F-FDG PET/CT versus conventional investigations for cancer screening in autoimmune inflammatory myopathy in the era of novel myopathy classifications. Nucl Med Commun 2019;40(4):377–82.
[19] Martis N, Viau P, Zenone T, Andry F, Grados A, Ebbo M, et al. Clinical value of a [18F]-FDG PET-CT muscle-to-muscle SUV ratio for the diagnosis of active dermatomyositis. Eur Radiol 2019;29(12):6708–16.
[20] Matuszak J, Blondet C, Hubele F, Gottenberg JE, Sibilia J, Bund C, et al. Muscle fluorodeoxyglucose uptake assessed by positron emission tomography-computed tomography as a biomarker of inflammatory myopathies disease activity. Rheumatology 2019;58(8):1459–64 (Oxford).
[21] Motegi SI, Fujiwara C, Sekiguchi A, Hara K, Yamaguchi K, Maeno T, et al. Clinical value of 18F-fluorodeoxyglucose positron emission tomography/computed tomography for interstitial lung disease and myositis in patients with dermatomyositis. J Dermatol 2019;46(3):213–8.
[22] Pipitone N, Versari A, Zuccoli G, Levrini G, MacChioni P, Bajocchi G, et al. 18F-fluorodeoxyglucose positron emission tomography for the assessment of myositis: a case series. Clin Exp Rheumatol 2012;30(4):570–3.
[23] Selva-O'Callaghan A, Grau JM, Gamez-Cenzano C, Vidaller-Palacin A, Martinez-Gomez X, Trallero-Araguas E, et al. Conventional cancer screening versus PET/CT in dermatomyositis/polymyositis. Am J Med 2010;123(6):558–62.
[24] Sun L, Dong Y, Zhang N, Lv X, Chen Q, Wei W. [18F]Fluorodeoxyglucose positron emission tomography/computed tomography for diagnosing polymyositis/dermatomyositis. Exp Ther Med 2018;15(6):5023–8.
[25] Tanaka S, Ikeda K, Uchiyama K, Iwamoto T, Sanayama Y, Okubo A, et al. [18F]FDG uptake in proximal muscles assessed by PET/CT reflects both global and local muscular inflammation and provides useful information in the management of patients with polymyositis/dermatomyositis. Rheumatology 2013;52(7):1271–8 (Oxford).
[26] Tateyama M, Fujihara K, Misu T, Arai A, Kaneta T, Aoki M. Clinical values of FDG PET in polymyositis and dermatomyositis syndromes: imaging of skeletal muscle inflammation. BMJ Open 2015;5(1):e006763.
[27] Trallero-Araguás E, Gil-Vila A, Martínez-Gómez X, Pinal-Fernández I, Alvarado-Cardenas M, Simó-Perdigó M, et al. Cancer screening in idiopathic inflammatory myopathies: ten years experience from a single center. Semin Arthritis Rheum 2022;53:151940.
[28] Lilleker JB, Hodgson R, Roberts M, Herholz K, Howard J, Hinz R, et al. Florbetapir positron emission tomography: identification of muscle amyloid in inclusion body myositis and differentiation from polymyositis. Ann Rheum Dis 2019;78(5):657–62.
[29] Maetzler W, Reimold M, Schittenhelm J, Vorgerd M, Bornemann A, Kotter I, et al. Increased [11C]PIB-PET levels in inclusion body myositis are indicative of amyloid beta deposition. J Neurol Neurosurg Psychiatry 2011;82(9):1060–2.
[30] Noto YI, Kondo M, Tsuji Y, Matsushima S, Mizuno T, Tokuda T, et al. Diagnostic value of muscle [11C] PIB-PET in inclusion body myositis. Front Neurol 2020;10:1386.
[31] Shiozawa H, Ohsawa T, Tsushima Y, Higuchi T, Takagishi K, Chikuda H. Evaluation of muscle activity just after straight leg raising exercise by using (18) FDG-PET. J Orthop Sci 2018;23(2):328–33.
[32] Ben-Haim S, Ell P. 18F-FDG PET and PET/CT in the evaluation of cancer treatment response. J Nucl Med 2009;50(1):88.
[33] Liang J, Cao H, Wu B, Liu Y, He Y, Xu B, et al. Clinical value of (18)F-FDG PET/CT scan and cytokine profiles in secondary hemophagocytic lymphohistiocytosis in idiopathic inflammatory myopathy patients: a pilot study. Front Immunol 2021;12:745211.
[34] Parida GK, Roy SG, Kumar R. FDG-PET/CT in skeletal muscle: pitfalls and pathologies. Semin Nucl Med 2017;47(4):362–72.
[35] Lamoreaux WT, Grigsby PW, Dehdashti F, Zoberi I, Powell MA, Gibb RK, et al. FDG-PET evaluation of vaginal carcinoma. Int J Radiat Oncol Biol Phys 2005;62(3):733–7.
[36] Lu X, Yang H, Shu X, Chen F, Zhang Y, Zhang S, et al. Factors predicting malignancy in patients with polymyositis and dermatomyostis: a systematic review and meta-analysis. PLoS ONE 2014;9(4):e94128.
[37] Oldroyd AGS, Allard AB, Callen JP, Chinoy H, Chung L, Fiorentino D, et al. A systematic review and meta-analysis to inform cancer screening guidelines in idiopathic inflammatory myopathies. Rheumatology 2021;60(6):2615–28 (Oxford).
[38] Iwano S, Ito S, Tsuchiya K, Kato K, Naganawa S. What causes false-negative PET findings for solid-type lung cancer? Lung Cancer 2013;79(2):132–6.
[39] Chang JM, Lee HJ, Goo JM, Lee HY, Lee JJ, Chung JK, et al. False positive and false negative FDG-PET scans in various thoracic diseases. Korean J Radiol 2006;7(1):57–69.
[40] Long NM, Smith CS. Causes and imaging features of false positives and false negatives on F-PET/CT in oncologic imaging. Insights Imaging 2011;2(6):679–98.

[41] Uehara T, Takeno M, Hama M, Yoshimi R, Suda A, Ihata A, et al. Deep-inspiration breath-hold 18F-FDG-PET/CT is useful for assessment of connective tissue disease associated interstitial pneumonia. Mod Rheumatol 2016;26(1):121–7.
[42] Peelen DM, Zwezerijnen BGJC, Nossent EJ, Meijboom LJ, Hoekstra OS, Van der Laken CJ, et al. The quantitative assessment of interstitial lung disease with positron emission tomography scanning in systemic sclerosis patients. Rheumatology 2020;59(6):1407–15 (Oxford).
[43] Choi JS, Seo HG, Oh BM, Choi H, Cheon GJ, Lee SU, et al. 18F-FDG uptake in denervated muscles of patients with peripheral nerve injury. Ann Clin Transl Neurol 2019;6(11):2175–85.
[44] Oldroyd A, Dixon W, Chinoy H, Howells K. Patient insights on living with idiopathic inflammatory myopathy and the limitations of disease activity measurement methods - a qualitative study. BMC Rheumatol 2020;4:47.
[45] Rider LG, Aggarwal R, Machado PM, Hogrel JY, Reed AM, Christopher-Stine L, et al. Update on outcome assessment in myositis. Nat Rev Rheumatol 2018;14(5):303–18.
[46] Benveniste O, Goebel HH, Stenzel W. Biomarkers in inflammatory myopathies-an expanded definition. Front Neurol 2019;10:554.
[47] Clark CM, Schneider JA, Bedell BJ, Beach TG, Bilker WB, Mintun MA, et al. Use of florbetapir-PET for imaging beta-amyloid pathology. JAMA 2011;305(3):275–83.
[48] Klunk WE, Engler H, Nordberg A, Wang Y, Blomqvist G, Holt DP, et al. Imaging brain amyloid in Alzheimer's disease with Pittsburgh compound-B. Ann Neurol 2004;55(3):306–19.
[49] Pinal-Fernandez I, Mammen AL. Amyloid-PET: a new tool for diagnosing IBM? Nat Rev Rheumatol 2019;15(6):321–2.
[50] Fairley JL, Wicks I, Peters S, Day J. Defining cardiac involvement in idiopathic inflammatory myopathies: a systematic review. Rheumatology 2022;61(1):103–20 (Oxford).