

USE OF 18F-FDG PET IN ASSESSING RESPONSE TO TREATMENT IN ADULTS WITH PULMONARY SARCOIDOSIS: A SYSTEMATIC LITERATURE REVIEW

Oliver Vij¹, Mathangi Krishnakumar², Helen Elwell³, Mrinalini Dey⁴, Koushan Kouranloo^{5,6}

¹Addenbrookes Hospital, Cambridge University Hospitals, Cambridge, United Kingdom; ²Department of Radiology, Wrexham Maelor Hospital, Croesnewydd, Wrexham, Wales, United Kingdom; ³British Medical Association Library, BMA House, Tavistock Square, London, United Kingdom; ⁴Centre for Rheumatic Diseases, Denmark Hill Campus, King's College London, London, United Kingdom; ⁵School of Medicine, Cedar House, University of Liverpool, Ashton Street, Liverpool, United Kingdom ; ⁶Department of Rheumatology, University Hospital Lewisham, Lewisham High Street, London, United Kingdom

ABSTRACT. *Background and aim:* Symptoms, severity and response to treatment of sarcoidosis can follow a heterogenous pattern, presenting a clinical challenge. Use of Fludeoxyglucose F18 Positron Emission Tomography (18F-FDG PET) in disease monitoring remains uncertain. We undertook a systematic literature review on the use of 18F-FDG PET in assessing response to treatment in adults with pulmonary sarcoidosis. *Methods:* Articles discussing 18F-FDG PET use in response to treatment in pulmonary sarcoidosis published until January 2024 were included. All article types were eligible except opinion pieces, case reports, case series of ≤10 patients and reviews. *Results:* Time between baseline 18F-FDG PET and follow-up scan ranged from 2 to 6 months. Compared to clinical response, sensitivity of 18F-FDG PET in determining response to treatment ranged from 56% to 100%, with mean sensitivity of 74.3% (standard error; SE 7.3). *Conclusions:* 18F-FDG PET could be considered in monitoring response to immunosuppression in patients with pulmonary sarcoidosis.

KEY WORDS: FDG PET, 18F-FDG PET, PET-CT, sarcoidosis, autoimmune disease

INTRODUCTION

Sarcoidosis is a chronic, multisystem, granulomatous disease affecting many organs but predominantly the lungs (1). Immunosuppressants, particularly corticosteroids, are the mainstay of treatment (2). Symptoms, severity and response to treatment can follow a heterogenous pattern and assessment of inflammatory activity in chronic sarcoidosis patients with persistent symptoms is still lacking a gold standard (2,3). This presents a clinical challenge when assessing response to treatment in patients

with sarcoidosis. Many markers indicative of disease activity have been investigated in sarcoidosis. These are broadly categorised as: macrophage and granuloma associated, such as angiotensin-converting-enzyme (ACE) and calcitriol; lymphocyte associated, such as soluble interleukin-2 receptors (sIL-2R) and interferon gamma; and extracellular matrix associated, such as procollagen III peptide and fibronectin (3). Of these ACE levels are the most widely used, but there is poor correlation between ACE level and disease severity (4). Fludeoxyglucose F18 (18F-FDG) PET can be used to distinguish between benign and malignant tumours, based mainly on the fact that cancer cells have abnormally high rates of glycolysis (5,6). Likewise, active granulomatous sarcoid lesions have high glycolytic activity resulting in the accumulation of FDG in activated macrophages and CD4+ T lymphocytes (7,8). This allows for *in vivo* visualisation of active granulomas in sarcoidosis

Received: 28 November 2024

Accepted: 27 January 2025

Correspondence: Oliver Vij, MB BChir

Oral and Maxillofacial Department, Addenbrookes Hospital, Cambridge, United Kingdom, CB2 0QQ

E-mail: ov221@cantab.ac.uk

ORCID: 0009-0005-5787-6649

through 18F-FDG PET (9). Histological confirmation of non-caseous granulomas is required for a diagnosis of sarcoidosis (10). 18F-FDG PET can therefore be used to identify both highly inflammatory lesions and those which are more accessible, thus increasing biopsy yield (9). Indeed, imaging with the use of 18F-FDG PET has been recommended by the American Thoracic Society (ATS) guidelines in choosing an appropriate biopsy site (11). However, the use of 18F-FDG PET in disease monitoring remains uncertain. A large proportion of patients with sarcoidosis are treated with corticosteroids, however, between 16% and 75% of patients relapse with cessation or tapering of corticosteroids (2,12). Disease monitoring in sarcoidosis is therefore important, and 18F-FDG PET is being increasingly used for this purpose (9). We undertook a systematic literature review (SLR) on the utility of 18F-FDG PET in assessing response to treatment in adults with pulmonary sarcoidosis.

METHODS

This SLR was undertaken in accordance with the Cochrane Handbook and reported as per the Preferred Reporting Items for Systematic Review and Meta-Analysis (13,14). The protocol was registered in the PROSPERO database of systematic reviews (CRD42023416412) (15). The review question was framed and structured using the ‘Patients, Intervention, Comparator or Control and Outcome’ (PICO) format (16): What is the utility of PET imaging in prognosis, response to treatment and outcomes of pulmonary sarcoidosis? The “population” comprised adults with a biopsy-confirmed diagnosis of pulmonary sarcoidosis with the “intervention” as PET-CT use. The outcomes included: changes on PET-CT imaging before and after treatment; physiological parameters; patient reported outcome in symptoms. PET was compared to clinician assessment of clinical improvement in symptoms defined as “clinical response”. Intervention and comparator terms were not relevant to this search.

Search strategy, databases and study selection

To ensure comprehensive coverage, indexing terms (MeSH, applicable to Medline and Cochrane, and Emtree headings on Embase) as well as keyword searching were used. The full search strategy

is available in the supplementary material. Medline, Embase and Cochrane databases were searched for articles discussing the use of PET-CT in sarcoidosis until 2nd January 2024. Medline from 1946, Embase from 1974, Cochrane CDSR from 1995, and Cochrane CENTRAL from inception in 1996. Cochrane CENTRAL first began publication in 1996, but its composite nature means that it does not have an inception (start) date, in the way that other traditional biomedical databases do (17). The search was restricted to English-language articles. All article types were eligible except opinion pieces, case reports, case series of ≤ 10 patients and reviews. Full length articles were uploaded into Rayyan (www.Rayyan.ai) with duplicates removed. Articles meeting inclusion criteria were examined by one author (MD), with 20% validity screening (KK). In addition to basic demographics, information was extracted on: Siltzbach classification of subjects; treatment; additional tests performed; time between baseline and follow-up PET-CT. Meta-analysis using a random effects model was conducted for sensitivity of PET-CT in determining response to treatment. This approach accounts for both within-study sampling error and between-study variability, providing a more generalised estimate of the overall effect size. A minimum of five values was deemed acceptable to be able to conduct meta-analysis. The analysis was performed using the metafor package in R Studio (v4.3.1), which offers robust tools for implementing random-effects models. The sensitivity of PET-CT was extracted from each of the included studies. Sensitivities and their corresponding variances were extracted from each study and pooled using the random-effects model. Risk of bias of included studies, all of which were cohort studies, was assessed using the Newcastle-Ottawa scale (18) (Table 1). An overall risk of bias score for each paper, and statement was subsequently formulated, based on the results of the assessment.

RESULTS

Qualitative results

Initially, 2502 articles were retrieved, reducing to 1950 after deduplication. Ultimately, six articles were included (Figure 1). Three prospective studies and three retrospective cohort studies were included. Cohort and case-control studies were assessed for

Table 1. Newcastle-Ottawa Quality Assessment for risk of bias for cohort studies

Cohort studies	Selection				Comparability	Outcome			Total (9*)
	Representativeness of exposed cohort (*)	Selection of non-exposed cohort (*)	Ascertainment of exposure (*)	Outcome of interest does not present at start of study (*)	(**)	Assessment of outcome (*)	Length of follow-up (*)	Adequacy of follow up (*)	
Braun et al. 2008 (19)	*	-	*	*	-	*	*	*	6*
Chen et al. 2018 (20)	*	-	*	*	-	*	*	*	6*
Keijsers et al. 2008 (21)	*	-	*	*	-	*	*	*	6*

risk of bias using the Newcastle-Ottawa quality assessment (Table 1). This gave a pooled total of 130 patients with pulmonary sarcoidosis with 43.0% male and a mean age 46.3 years (standard deviation; SD 3.7). Study populations were from France (n=1), China (n=1), The Netherlands (n=1), India (n=2) and Serbia (n=1). Treatment for pulmonary sarcoidosis varied markedly amongst the included studies, including systemic corticosteroids (n=3) and infliximab (n=1), with the treatment being unknown in two studies. All studies used 18F-FDG PET, with one study comparing the use of 18F-FDG PET and Gallium-67 in localising active disease (19).

Additional tests performed across all studies included spirometry, chest radiograph, serum ACE levels and sIL-2R levels. These results are summarised in Table 2. Only two studies commented on chest radiography post-treatment. Chest radiographic state did not change in any of 11 clinically responding patients in one study (21). In the second study, complete radiological response, defined as total resolution of mediastinal and peripheral lymphadenopathy to less than 1cm and >90% resolution of parenchymal changes, was seen in eight patients. Partial response, defined as decrease in size of lymph nodes but with still with significant residual nodes was seen in eight patients (22). All studies concluded that 18F-FDG PET correlates with clinical response to treatment and is useful for prognostication, aside from one study which concluded that metabolic response on 18F-FDG PET can predict future risk of relapses but does not correlate with clinical response (23). More specifically, it is decreased 18F-FDG

PET activity after initiation or modification of treatment that has been shown to correlate with clinical signs of improvement, thus showing 18F-FDG PET is a good marker for monitoring disease activity (21).

Quantitative results

Time between baseline PET-CT and follow-up scan ranged from two months to six months. Compared to clinical response, sensitivity of 18F-FDG PET in determining response to treatment ranged from 56% to 100%, with a pooled sensitivity of 74.3% (standard error; SE 7.3), as calculated in our meta-analysis. One study reported post-treatment pulmonary function tests. There was a statistically significant improvement in diffusion capacity of the lung for carbon monoxide (DLCO) following treatment, but no significant correlation between SUVmax and DLCO. The average decrease in SUVmax was correlated with an improvement of vital capacity ($P<0.01$) (21). Serum angiotensin converting enzyme (ACE) was measured in three studies. Two studies reported a decrease in serum ACE with treatment, whereas another study found no significant difference in serum ACE levels before and after treatment (21,22,24). Of the five studies that referenced SUVmax, all studies found a significant decrease in SUVmax when compared with baseline 18F-FDG PET (20–24).

DISCUSSION

To our knowledge, this is the first SLR summarising the use of 18F-FDG PET in assessing

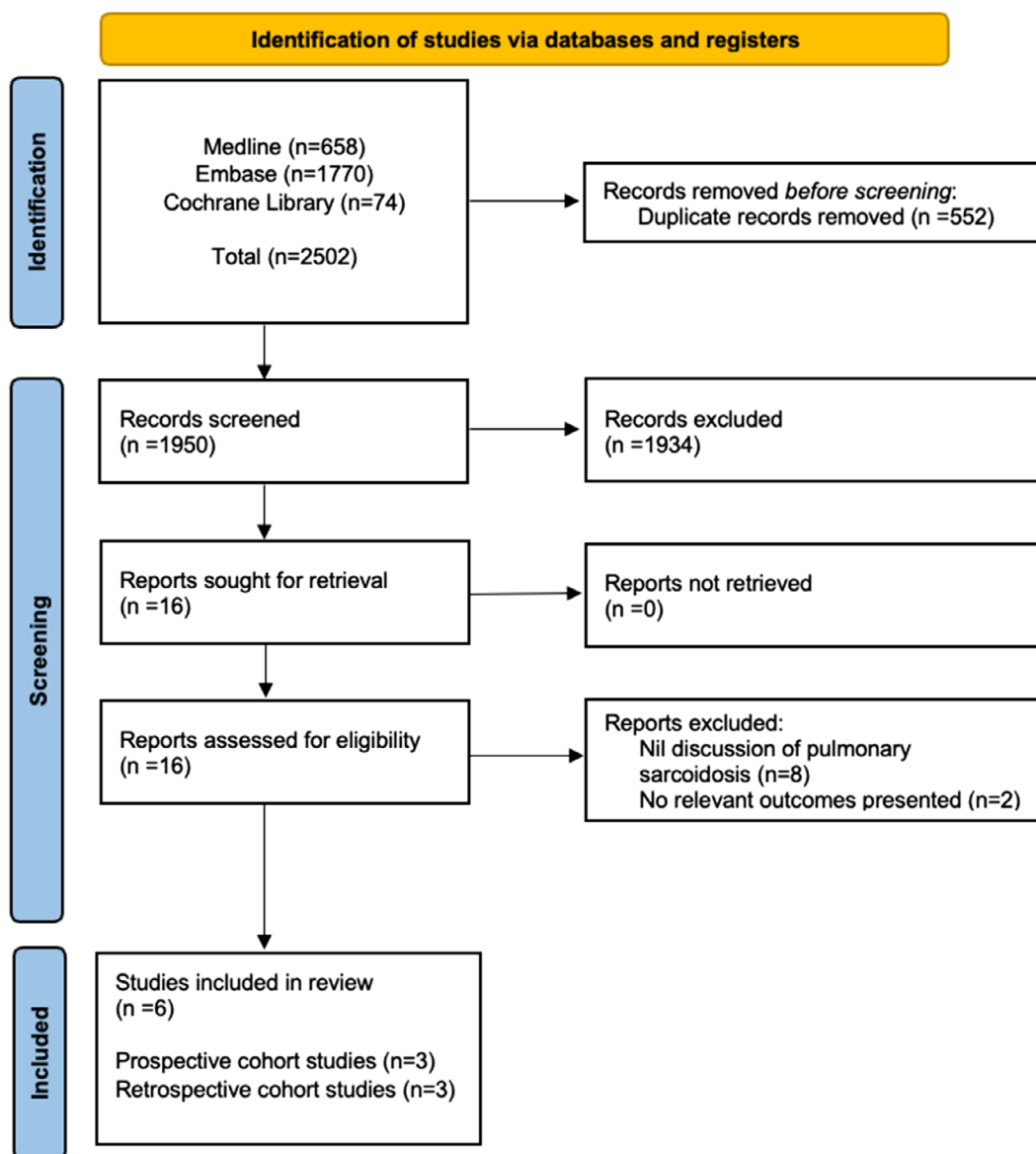


Figure 1. Flow diagram of stages of systematic literature review. Cochrane Library encompasses library of: systematic reviews; systematic review protocols; controlled clinical trials.

response to treatment in adults with pulmonary sarcoidosis. Our findings suggest that 18F-FDG PET is useful in determining response to treatment with a mean sensitivity of 74.3% across a pool of 130 patients. The papers were overall deemed to be of uncertain risk of bias, as per assessment using the Newcastle-Ottawa scale. At present, assessment of inflammatory activity in chronic sarcoidosis patients with persistent symptoms is challenging due to the lack of a gold standard (3). Despite this, 18F-FDG

PET has been shown to be a useful parameter for measuring disease activity in sarcoidosis (25–28). However, a positive 18F-FDG PET is not always specific for sarcoidosis as increased FDG uptake can also be seen in infectious and neoplastic aetiologies. Hence, tissue biopsy plays a crucial role in obtaining a histopathological diagnosis (10,29–31). 18F-FDG PET is, however, recommended by the ATS guidelines for selecting an appropriate site for biopsy (11). 18F-FDG PET helps in depicting the most

Table 2. Summary of included studies with PET technique and tracers, sensitivity, comparators and summary of treatments and follow up

Title	Sample size	Chest radiographic stage	PET technique	PET tracers	Sensitivity of PET to determine response	PET comparator	Time to repeat PET	Other tests performed	Drug treatment
Braun et al. 2008 (19)	13 (5 followed up after treatment)	I (2); II (3); III (1); IV (7)	PET CT	18F-FDG, 67Ga	100%	Clinical response	2 months	67Ga scintigraphy, biopsy, endoscopy, chest radiograph, pulmonary function tests, BAL, HRCT	50mg/day prednisolone, tapering regime
Chen et al. 2018 (20)	23	I (13); II (7); III (0); IV (3)	PET CT	18F-FDG	56.6%	Clinical response	3 months	Biopsy, HRCT	3 months systemic corticosteroid (dose and type unknown)
Guleria et al. 2014 (22)	25 (21 with follow up scan)	0 (4); I (15); II (4); III (2); IV (0)	PET CT	18F-FDG	66%	Clinical response	6 months	Chest radiograph, serum ACE	0.5-1mg/kg/day of prednisone, tapering regime
Keijzers et al. 2008 (21)	12	I (3); II (6); III (2); IV (1)	PET	18F-FDG	91.7%	Clinical response	6 months	Chest radiograph, serum ACE, DLCO, vital capacity, soluble IL-2 receptor	6 cycles infliximab
Maturu et al. 2016 (23)	27 (16 pulmonary)	I (22); II (5)	PET CT	18F-FDG	56%	Clinical response	3 months	Pulmonary function tests, serum ACE, chest CT	Unknown
Sobic-Saranovic et al. 2013 (24)	30	I (2); II (15); III (11); IV (2)	PET CT	18F-FDG	80%	Clinical response	6 months	Serum ACE	Unknown

metabolically active lesion which is likely to produce the highest biopsy yield. 18F-FDG PET applications for sarcoidosis are therefore more applicable for assessing response to treatment and deciding the most suitable biopsy site, rather than for definitive diagnosis. Our results found that 18F-FDG PET had a pooled sensitivity of 74.3% when compared with clinical response, suggesting it could be a useful adjunct in detecting treatment response to sarcoidosis. A potential challenge for the use of PET CT is that it is not always positive in patients with sarcoidosis, with negative pulmonary 18F-FDG PET findings more common in patients with radiographic stage 0, I and IV sarcoidosis (32,33). Despite this, the majority of patients with persistent disabling symptoms do have positive PET findings (25,34). The results for serum ACE measurements in response to treatment amongst the studies included in this review were discordant, with two studies reporting a reduction in serum ACE and another reporting no significant change before and after treatment (21,22,24). The sensitivity of serum ACE levels for sarcoidosis ranges from 22 to 86%, with the specificity ranging from 54 to 95% (35). The use of serum ACE as a diagnostic or prognostic tool is a matter of ongoing debate (36). In contrast, 18F-FDG PET has been found to be very sensitive (94%) for assessing active sarcoidosis when compared to ACE levels (34). The single study reporting lung function showed a correlation between the average decrease in maximum standardised uptake value (SUV_{max}) and improvement of vital capacity ($P < 0.01$) (21). This could suggest that 18F-FDG PET could be used as a predictive tool in sarcoidosis (28). It has been shown that 18F-FDG PET activity correlates with future deterioration in lung function tests (37,38). More specifically, SUV_{max} , which is the most commonly used semi-quantitative value of 18F-FDG PET, and total lung glycolysis (TLuG) can predict changes in lung function in sarcoidosis patients after treatment with infliximab (39). In addition, it has been suggested that baseline SUV_{max} and metabolic response could predict the prognosis of sarcoidosis patients treated with corticosteroids (20). Both these results indicate that 18F-FDG PET could be used to reliably stratify patients treated with both corticosteroids and infliximab. 18F-FDG PET has also been shown to influence clinical management of sarcoidosis. Positive 18F-FDG PET findings were associated with changes in therapy as it is able to detect sites of active inflammation in patients

with normal ACE and in older patients with more pronounced symptoms, providing a justification for changes to therapy (40,41). This is particularly important as appropriate dosage modification of corticosteroids is conducive to mitigating side effects and this ability to adjust doses depends on accurate treatment response evaluation (42). It has been suggested that 18F-FDG PET is a more sensitive parameter of therapeutic effect than clinical manifestations which could ultimately benefit patients in making suitable treatment decisions (20). There are several co-morbidities and complications associated with sarcoidosis that can co-exist at the time of diagnosis or develop throughout the course of the disease which contribute to the unpredictable heterogeneous nature of sarcoidosis. (43). The presence of pulmonary hypertension and/or fibrosis can complicate assessment of the response to treatment of pulmonary sarcoidosis both clinically and with 18F-FDG PET (43). In contrast to idiopathic pulmonary fibrosis (IPF), pulmonary fibrosis in sarcoidosis can still be accompanied by inflammation (27). There is, however, evidence to suggest 18F-FDG PET could be beneficial to identify any occult inflammation or active granulomas in sarcoidosis with pulmonary fibrosis (44). Likewise, there may be a role for 18F-FDG PET to assess for active inflammation in sarcoidosis associated pulmonary hypertension (43). Further research is required to determine the efficacy and usefulness of 18F-FDG PET in distinguishing between pulmonary sarcoidosis and related complications which also result in active inflammation. 18F-FDG PET has also been used in cardiac sarcoidosis, both in terms of diagnosis and in assessing treatment response (45,46). Indeed, a recent meta-analysis has shown that 18F-FDG PET has a sensitivity of 84% and specificity of 83% for diagnosing cardiac sarcoidosis (47). Similarly to pulmonary sarcoidosis, 18F-FDG PET has been shown to be a good technique to follow patients undergoing immunosuppressive therapy and evaluate their response to treatment through SUV_{max} (48). The utility of 18F-FDG PET in cardiac sarcoidosis has similar challenges to pulmonary sarcoidosis, with co-morbidities presenting with cardiac inflammation potentially resulting in misdiagnosis (45,49). Despite this, 18F-FDG PET has been demonstrated to give the best cost-benefit ratio in terms of diagnosing cardiac sarcoidosis and can potentially avoid unnecessary invasive procedures (45). Unfortunately, there are limits to the application of 18F-FDG PET in

clinical practice due to its availability and cost. Black subjects, and in particular black females, are most affected by sarcoidosis (50). The average number of PET-CT scanners per 1 million population in low-income countries, including those in Africa with a potentially higher black population, is only 0.006. In contrast, high income countries have 1.664 PET-CT scanners per 1 million population (51). This suggests that the use of PET-CT may be limited amongst the patient group with the highest burden of sarcoidosis.

Future directions

Further work, with larger patient cohorts, is required to confirm the utility of 18F-FDG PET in the management of pulmonary sarcoidosis. These studies could also attempt to evaluate the use of PET-CT in discriminating between pulmonary sarcoidosis and its complications such as pulmonary hypertension and fibrosis as well as determining the ideal timing for serial follow up with 18F-FDG PET. Future studies should also consider appropriate representation of populations disproportionately affected by sarcoidosis. In addition, cost-effectiveness evaluation into the use of 18F-FDG PET compared with other diagnostic tools in assessing treatment response to sarcoidosis is required.

Limitations

This systematic review demonstrates that 18F-FDG PET could be considered as a tool for monitoring treatment in patients with pulmonary sarcoidosis. However, our study included only six studies due to the specific condition and imaging modality that was assessed. The sample sizes for each study ranged from 12 to 30 participants, which are relatively small in number and therefore reduce the accuracy of statistical analyses. In addition, this systematic review did not include any randomised control trials (RCTs) as they were not available for analysis. It is therefore important not to infer that 18F-FDG PET can currently be used as a predictive tool in pulmonary sarcoidosis as more detailed studies with larger cohorts are required to establish this accurately. The endpoints of the included studies were different, with follow 18F-FDG PET ranging from two to six months. These differences between included studies make it more difficult to accurately compare the sensitivity of 18F-FDG PET to response to sarcoidosis treatment

as they are compared at different time points following initiation of treatment. The included studies were conducted in China, France, India, Serbia and the Netherlands, which are all areas with relatively low proportion of black subjects (52). This could mean the included studies do not accurately represent populations which would be most affected by sarcoidosis.

CONCLUSION

To our knowledge, this is the first SLR summarising the use of 18F-FDG PET in assessing response to treatment in adults with pulmonary sarcoidosis. 18F-FDG PET is a useful parameter for monitoring sarcoidosis disease activity and in determining response to treatment and prognosis in pulmonary sarcoidosis (20,41). It has also been shown to have potential as both a predictive tool through the assessment of SUV_{max} and to influence clinical management (20,28,37,39).

Clinical implications

18F-FDG PET could be considered in monitoring response to immunosuppression in patients with pulmonary sarcoidosis. However, further studies are necessary to further evaluate its utility for this indication.

Acknowledgements: All data available on request. The authors declare no competing interests.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors' Contributions: The study's design was influenced by all the writers. Initial searches were conducted by HE. The articles were then selected for inclusion by MD and KK. The first draft of work was written by OV. The initial draft was edited by OV, MK, MD and KK and the final manuscript was approved by all writers.

REFERENCES

- Rossi G, Cavazza A, Colby TV. Pathology of sarcoidosis. Clin Rev Allergy Immunol 2015;49:36-44. doi: 10.1007/s12016-015-8479-6
- Ungprasert P, Ryu JH, Matteson EL. Clinical manifestations, diagnosis, and treatment of sarcoidosis. Mayo Clin Proc Innov Qual Outcomes 2019;3:358. doi: 10.1016/j.mayocpiqo.2019.04.006
- Society ER. Consensus conference: activity of sarcoidosis. Third WASOG meeting, Los Angeles, USA, September 8-11, 1993. Eur Respir J 1994;7:624-7. doi: 10.1183/09031936.94.07030624

4. Keijsers RGM, Grutters JC. In which patients with sarcoidosis is FDG PET/CT indicated? *J Clin Med* 2020;9:890. doi: 10.3390/jcm9030890
5. Farwell MD, Pryma DA, Mankoff DA. PET/CT imaging in cancer: current applications and future directions. *Cancer* 2014;120:3433-45. doi: 10.1002/cncr.28860
6. Warburg O. The metabolism of tumours. Constable and Company 1930
7. Koiwa H, Tsujino I, Ohira H, et al. Images in cardiovascular medicine: imaging of cardiac sarcoid lesions using fasting cardiac 18F-fluorodeoxyglucose positron emission tomography: an autopsy case. *Circulation* 2010;122:535-6. doi: 10.1161/CIRCULATIONAHA.110.952184
8. EACVI Reviewers, et al. A joint procedural position statement on imaging in cardiac sarcoidosis: from the Cardiovascular and Inflammation & Infection Committees of the European Association of Nuclear Medicine, the European Association of Cardiovascular Imaging, and the American Society of Nuclear Cardiology. *Eur Heart J Cardiovasc Imaging* 2017;18:1073-89. doi: 10.1093/ehjci/jex146
9. Régis C, Benali K, Rouzet F. FDG PET/CT imaging of sarcoidosis. *Semin Nucl Med* 2023;53:258-72. doi: 10.1053/j.semnucmed.2022.08.004
10. Statement on sarcoidosis. *Am J Respir Crit Care Med* 1999;160:736-55. doi: 10.1164/ajrccm.160.2.ats4-99
11. Diagnosis and detection of sarcoidosis. *Am J Respir Crit Care Med* (ATS guideline) [year n.d.];[volume n.d.];[pages n.d.] – ATS guideline title only, DOI given in URL; DOI removed per rules.
12. Nagai S, Handa T, Ito Y, et al. Outcome of sarcoidosis. *Clin Chest Med* 2008;29:565-74. doi: 10.1016/j.ccm.2008.03.006
13. Cochrane Handbook for Systematic Reviews of Interventions. [anno n.d.];[vol n.d.];[pp n.d.]
14. Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ* 2021;372:n160. doi: 10.1136/bmj.n160
15. PROSPERO: International prospective register of systematic reviews: what are the PET imaging use in prognosis, response to treatment and outcomes of pulmonary sarcoidosis? [anno n.d.];[vol n.d.];[pp n.d.] – titolo riportato, ma senza formato standard.
16. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017;358:j4008. doi: 10.1136/bmj.j4008
17. Cochrane Controlled Register of Trials (CENTRAL). [anno n.d.]; [vol n.d.];[pp n.d.]
18. Wells G, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Non-Randomized Studies in Meta-Analysis. 2000
19. Braun JJ, Kessler R, Constantinesco A, et al. 18F-FDG PET/CT in sarcoidosis management: review and report of 20 cases. *Eur J Nucl Med Mol Imaging* 2008;35:1537-43. doi: 10.1007/s00259-008-0770-9
20. Chen H, Jin R, Wang Y, et al. The utility of 18F-FDG PET/CT for monitoring response and predicting prognosis after glucocorticoids therapy for sarcoidosis. *Biomed Res Int* 2018;2018:1823710. doi: 10.1155/2018/1823710
21. Keijsers RGM, Verzijlbergen JF, van Diepen DM, et al. 18F-FDG PET in sarcoidosis: an observational study in 12 patients treated with infliximab. *Sarcoidosis Vasc Diffuse Lung Dis* 2008;25:143-9
22. Guleria R, Jyothidasan A, Madan K, et al. Utility of FDG-PET-CT scanning in assessing the extent of disease activity and response to treatment in sarcoidosis. *Lung India* 2014;31:323-30. doi: 10.4103/0970-2113.142092
23. Maturu VN, Rayamajhi SJ, Agarwal R, et al. Role of serial F-18 FDG PET/CT scans in assessing treatment response and predicting relapses in patients with symptomatic sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis* 2016;33:372-80
24. Sobic-Saranovic DP, Grozdic IT, Videnovic-Ivanov J, et al. Responsiveness of FDG PET/CT to treatment of patients with active chronic sarcoidosis. *Clin Nucl Med* 2013;38:516-21. doi: 10.1097/RLU.0b013e31828731f5
25. Mostard RLM, Vöö S, van Kroonenburgh MJPG, et al. Inflammatory activity assessment by F18 FDG-PET/CT in persistent symptomatic sarcoidosis. *Respir Med* 2011;105:1917-24. doi: 10.1016/j.rmed.2011.08.012
26. Mostard RL, Kuijk SMV, Verschakelen JA, et al. A predictive tool for an effective use of 18F-FDG PET in assessing activity of sarcoidosis. *BMC Pulm Med* 2012;12:57. doi: 10.1186/1471-2466-12-57
27. Mostard RLM, Verschakelen JA, van Kroonenburgh MJPG, et al. Severity of pulmonary involvement and (18)F-FDG PET activity in sarcoidosis. *Respir Med* 2013;107:439-47. doi: 10.1016/j.rmed.2012.11.011
28. Treglia G, Annunziata S, Sobic-Saranovic D, et al. The role of 18F-FDG-PET and PET/CT in patients with sarcoidosis: an updated evidence-based review. *Acad Radiol* 2014;21:675-84. doi: 10.1016/j.acra.2014.01.008
29. Treglia G, Cason E, Fagioli G. Recent applications of nuclear medicine in diagnostics (I part). *Ital J Med* 2010;4:84-91. doi: 10.4081/itjm.2010.84
30. Treglia G, Cason E, Fagioli G. Recent applications of nuclear medicine in diagnostics: II part. *Ital J Med* 2010;4:159-66. doi: 10.4081/itjm.2010.159
31. Sobic-Saranovic D, Artiko V, Obradovic V. FDG PET imaging in sarcoidosis. *Semin Nucl Med* 2013;43:404-11. doi: 10.1053/j.semnucmed.2013.06.007
32. Adams H, van Rooij R, van Moorsel CHM, et al. Volumetric FDG PET analysis of global lung inflammation: new tool for precision medicine in pulmonary sarcoidosis? *Sarcoidosis Vasc Diffuse Lung Dis* 2018;35:44-54. doi: 10.36141/svdlld.v35i1.5807
33. Teirstein AS, Machac J, Almeida O, et al. Results of 188 whole-body fluorodeoxyglucose positron emission tomography scans in 137 patients with sarcoidosis. *Chest* 2007;132:1949-53. doi: 10.1378/chest.07-1178
34. Keijsers RG, Verzijlbergen FJ, Oyen WJ, et al. 18F-FDG PET, genotype-corrected ACE and sIL-2R in newly diagnosed sarcoidosis. *Eur J Nucl Med Mol Imaging* 2009;36:1131-7. doi: 10.1007/s00259-009-1097-x
35. Ramos-Casals M, Retamozo S, Sisó-Almirall A, et al. Clinically-useful serum biomarkers for diagnosis and prognosis of sarcoidosis. *Expert Rev Clin Immunol* 2019;15:391-405. doi: 10.1080/1744-666X.2019.1568240
36. Kraaijvanger R, Janssen Bonás M, Vorselaars ADM, et al. Biomarkers in the diagnosis and prognosis of sarcoidosis: current use and future prospects. *Front Immunol* 2020;11:1443. doi: 10.3389/fimmu.2020.01443
37. Adams H, Keijsers RG, Korenromp IHE, et al. FDG PET for gauging of sarcoid disease activity. *Semin Respir Crit Care Med* 2014;35:352-61. doi: 10.1055/s-0034-1376866
38. Keijsers RG, Verzijlbergen EJ, van den Bosch JM, et al. 18F-FDG PET as a predictor of pulmonary function in sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis* 2011;28:123-9
39. Schimmelpennink MC, Vorselaars ADM, Veltkamp M, et al. Quantification of pulmonary disease activity in sarcoidosis measured with 18F-FDG PET/CT: SUVmax versus total lung glycolysis. *EJNMMI Res* 2019;9:54. doi: 10.1186/s13550-019-0505-x
40. Ambrosini V, Zompatori M, Fasano L, et al. 18F-FDG PET/CT for the assessment of disease extension and activity in patients with sarcoidosis: results of a preliminary prospective study. *Clin Nucl Med* 2013;38:e171-7. doi: 10.1097/RLU.0b013e31827a27df
41. Sobic-Saranovic D, Grozdic I, Videnovic-Ivanov J, et al. The utility of 18F-FDG PET/CT for diagnosis and adjustment of therapy in patients with active chronic sarcoidosis. *J Nucl Med* 2012;53:1543-9. doi: 10.2967/jnumed.112.104380

42. Judson MA. Advances in the diagnosis and treatment of sarcoidosis. *F1000Prime Rep* 2014;6:89. doi: 10.12703/P6-89
43. Tana C, Drent M, Nunes H, et al. Comorbidities of sarcoidosis. *Ann Med* 2022;54:1014-35. doi: 10.1080/07853890.2022.2063375
44. Asif H, Ribeiro Neto ML, Culver DA. Pulmonary fibrosis in sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis* 2023;40:e2023027. doi: 10.36141/svdlld.v40i3.14830
45. Tana C, Mantini C, Donatiello I, et al. Clinical features and diagnosis of cardiac sarcoidosis. *J Clin Med* 2021;10:1941. doi: 10.3390/jcm10091941
46. Al Hayja MA, Vinjamuri S. Cardiac sarcoidosis: the role of cardiac MRI and 18F-FDG-PET/CT in the diagnosis and treatment follow-up. *Br J Cardiol* 2023;30:7. doi: 10.5837/bjc.2023.007
47. Kim SJ, Pak K, Kim K. Diagnostic performance of F-18 FDG PET for detection of cardiac sarcoidosis; a systematic review and meta-analysis. *J Nucl Cardiol* 2020;27:2103-15. doi: 10.1007/s12350-018-01582-y
48. Furuya S, Manabe O, Ohira H, et al. Which is the proper reference tissue for measuring the change in FDG PET metabolic volume of cardiac sarcoidosis before and after steroid therapy? *EJNMMI Res* 2018;8:94. doi: 10.1186/s13550-018-0447-8
49. Ramirez R, Trivieri M, Fayad ZA, et al. Advanced imaging in cardiac sarcoidosis. *J Nucl Med* 2019;60:892-8. doi: 10.2967/jnumed.119.228130
50. Hena KM. Sarcoidosis epidemiology: race matters. *Front Immunol* 2020;11:537382. doi: 10.3389/fimmu.2020.537382
51. Gallach M, Lette MM, Abdel-Wahab M, et al. Addressing global inequities in positron emission tomography-computed tomography (PET-CT) for cancer management: a statistical model to guide strategic planning. *Med Sci Monit* 2020;26:e926544-1-e926544-8. doi: 10.12659/MSM.926544
52. African diaspora. *Encyclopedia.com*. Available from: <https://www.encyclopedia.com/social-sciences-and-law/anthropology-and-archaeology/human-evolution/african-diaspora> [accessed 2024 Aug 19].