Original Article

Utility of FDG-PET-CT scanning in assessing the extent of disease activity and response to treatment in sarcoidosis

Randeep Guleria, Amudhan Jyothidasan, Karan Madan, Anant Mohan, Rakesh Kumar[1], Ashu Seith Bhalla[2], Arun Malhotra[1]

Departments of Pulmonary Medicine and Sleep Disorders, [1]Nuclear Medicine and [2]Radio-Diagnosis, All India Institute of Medical Sciences, New Delhi, India

ABSTRACT

Background: Radionuclide imaging modalities have increasingly been evaluated in the assessment of organ involvement in sarcoidosis. Fluoro-deoxyglucose positron emission tomography–computed tomography (FDG–PET–CT) scanning has received increasing attention in the recent years. The aim of our study was to evaluate the utility of FDG–PET–CT in determining the extent of organ involvement and disease activity in patients of sarcoidosis and to assess its utility in the evaluation of response to therapy. The secondary objective was to compare the agreement between clinical, radiological (HRCT) and metabolic indices (FDG–PET–CT) of disease activity. **Materials and Methods:** This was a prospective observational study conducted between March 2007 and December 2008 at a tertiary care referral center in north India. Twenty-five symptomatic and histopathologically proven cases of sarcoidosis underwent FDG–PET–CT scanning at baseline and a follow-up scan in 21 patients at 6-9 months post-treatment with glucocorticoids. **Results:** FDG–PET–CT scan detected metabolic disease activity in 24 of the 25 patients with clinically active sarcoidosis. It also demonstrated many clinically inapparent sites of disease activity. Complete or partial metabolic response was seen in 17 of the 21 patients in whom a follow-up scan was available. Substantial degree of agreement was found between the metabolic response and the radiological response, whereas moderate agreement was found between clinical and metabolic responses. **Conclusions:** FDG–PET–CT scanning is a useful imaging modality to assess disease activity, extent of disease involvement and response to treatment in clinically active sarcoidosis. There is substantial agreement between the HRCT and metabolic parameters of disease activity. Further, large sample size studies are proposed in order to identify the subset of patients who are likely to benefit the most from this sensitive modality of imaging, especially in developing countries where the cost of the procedure is an important concern.

KEY WORDS: Bronchoscopy, computed tomography, granuloma, positron-emission tomography, respiratory tract, sarcoidosis

Address for correspondence: Dr. Randeep Guleria, Department of Pulmonary Medicine and Sleep Disorders, All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110 029, India. E-mail: randeepg@hotmail.com

INTRODUCTION

Sarcoidosis is a chronic inflammatory multisystem disease that usually affects middle-aged adults and frequently presents with bilateral hilar lymphadenopathy, pulmonary parenchymal involvement and ocular and skin lesions. Diagnosis is established by a clinico-radiological picture consistent with sarcoidosis along with tissue confirmation of non-caseating granulomas and exclusion of other granulomatous conditions.

Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/0970-2113.142092

The term "activity" in sarcoidosis refers to ongoing inflammation that necessitates appropriate therapy. Several biochemical and radiological markers have been used as indices of disease activity, but there is often a lack of concordance in these markers and no gold standard is available to validate these markers. Treatment of sarcoidosis remains controversial and there is little consensus on the optimum duration of therapy and assessment of disease activity.

The role of fluoro-deoxy glucose–positron emission tomography (FDG–PET) scanning in assessing the extent

of disease spread or metastasis and its utility in assessing response to treatment in the form of chemotherapy or radiotherapy is well defined in many neoplastic conditions, and its utility has also been recognized in certain inflammatory conditions. FDG–PET and a combination of this procedure with computed tomography scanning (FDG–PET–CT) has gained prominent attention in patients with sarcoidosis over the last two decades as a means to assess disease activity and response to therapy. Its role has also been evaluated in patients with cardiac sarcoidosis. Herein, we present our preliminary experience on the utility of 18F-FDG–PET–CT scanning in assessing the extent of disease activity and response to treatment in sarcoidosis patients from a tertiary care referral hospital in north India.

MATERIALS AND METHODS

The aim of our study was to evaluate the utility of FDG–PET–CT scan in determining the extent of organ involvement and disease activity in patients of sarcoidosis and to assess its utility in the evaluation of response to therapy. The secondary objective was to compare the agreement between clinical, radiological (HRCT) and metabolic indices (FDG–PET–CT) of disease activity.

Newly diagnosed symptomatic and treatment-naïve patients of sarcoidosis were included in the study. The study design was prospective with one baseline FDG–PET–CT scan and a follow-up scan at 6-9 months duration following treatment. Patients willing to participate in the study and satisfying the American Thoracic Society (ATS) diagnostic criteria,[1] i.e. compatible clinico-radiological features and tissue biopsy showing non-caseating granulomas, were included in the study. Exclusion criteria were asymptomatic disease, any obvious associated comorbid illness that may cause false-positive FDG uptake (like active malignancy/other inflammatory conditions, uncontrolled diabetes mellitus) and pregnancy. The study protocol was approved by the ethics committee of the institute and written informed consent was obtained from each of the participants.

Baseline investigations included routine biochemical investigations and complete hemogram. Levels of serum calcium, serum angiotensin-converting enzyme (ACE) and erythrocyte sedimentation rate were measured. Chest radiograph, tuberculin skin test, spirometry with pulmonary diffusing capacity for carbon monoxide (DLCO) using single breath technique, ophthalmological evaluation for uveitis and a contrast-enhanced CT examination of the thorax (including high-resolution scan images of the lung) were also performed. As part of diagnostic evaluation, all patients underwent a flexible bronchoscopy examination wherein samples of transbronchial lung biopsy and bronchial biopsy were obtained. Diffusion capacity for carbon monoxide was performed using the single breath technique. High-resolution images of the lungs were obtained in all the patients at the time of the CT examination. Enrolled participants subsequently underwent a whole body FDG–PET–CT scan.

Whole body FDG–PET–CT scan procedure

Patients were kept fasting for 4 h before the injection of 18F-FDG. FDG–PET–CT scans were performed on the dedicated scanners (SiemensWashington, USA, [Biograph 64]). The blood glucose level was checked to ensure that it was less than 150 mg/dL before the injection of 18F-FDG. 18F-FDG was administered in a dose of 5.2 MBq (0.14 mCi)/kg through a peripheral vein 1 h before imaging. Initial CT acquisition was performed without oral or intravenous contrast injection, followed by PET scan. During the uptake phase, patients sat quietly in a dimly lit room and were asked to refrain from talking, walking and any other muscular activity to prevent non-specific FDG uptake in the skeletal muscles. Sequential overlapping emission scans of the neck, chest, abdomen and pelvis were acquired 60 min after the injection of the radiotracer.

Data interpretation was performed by an experienced nuclear medicine physician who was blinded to the clinical findings. PET images were looked for area of increased radiotracer uptake. Corresponding area in the CT images and fused PET–CT images were corroborated. Lesions with increased tracer uptake in the PET scan were considered to be metabolically active disease sites. The extent of disease was determined by the presence of tracer uptake in the involved organs, such as the thoracic and extrathoracic lymph nodes, lungs, spleen, liver, bone, muscle, skin, parotid glands, etc. Tracer uptake was quantified in terms of standardized uptake value (SUV). SUV was taken as an index of disease activity. The maximum SUV (SUVmax) in the pathological sites of uptake in whole-body PET was taken as the pre-treatment SUVmax.

Treatment and follow-up

Patients were started on treatment based on the treatment protocol of ATS (1999). For pulmonary sarcoidosis, the initial dosage was 0.5-1 mg/kg/d of prednisone. The dose was then slowly tapered to 5-10 mg daily or an every other day regimen over 6 months. Treatment was continued for a minimum of 12 months in most patients. Patients were on a regular follow-up. After 6-9 months of therapy, the patients were reassessed with all the parameters studied earlier, including a repeat FDG–PET–CT scan for disease activity.

Response assessment

Clinical response was assessed as complete, partial and no response based on the complete resolution of symptoms, persistence of one or more symptoms and clinical worsening, respectively. Radiological response was assessed based on the degree of resolution of lymphadenopathy and parenchymal changes.

Complete radiological response

Total resolution of mediastinal and peripheral lymphadenopathy to less than 1 cm and >90% resolution of parenchymal changes excluding chronic changes such as bullae, emphysema, traction bronchiectasis, bronchial distortion, parenchymal bands and fibrosis.

Incomplete radiological response
Decrease in the size of lymph nodes but the residual nodes were still significant, i.e. more than 1 cm in size, as well as a 10-90% decrease in lung parenchymal abnormalities.

No response or worsening radiologically
Increase in the size of existing lymph nodes and/or presence of new groups of lymph nodes or worsening of parenchymal lesions with or without the appearance of new lesions.

Metabolically active disease was said to be present on the basis of abnormal tracer uptake in the involved tissue on FDG–PET–CT. Metabolic response was assessed by the change in the uptake quantified in terms of SUV. Non-physiological tracer uptake in the various organs was documented.

Complete metabolic response
If there was more than 70% fall in post-treatment SUV over pre-treatment SUV.

Partial metabolic response
Twenty percent to 70% fall in post-treatment SUV over pre-treatment SUV.

No response or disease progression
If there was less than 20% fall or an increase in post-treatment SUV over pre-treatment SUV.

Statistical analysis
Results of the FDG–PET–CT scan were compared with the clinical, biochemical and radiological response. Non-parametric tests were used in most comparisons in view of the small sample size. The Wilcoxon signed rank test was used for comparison of continuous variables before and after treatment. The Kappa test was used as a measure of agreement among clinical, radiological, metabolic and biochemical responses. The Chi-square test was used to determine the association between various CT findings and metabolic activity in PET scan. Correlation between the initial SUVmax and clinical response to therapy was performed using the Spearman correlation.

RESULTS

Thirty-three patients of sarcoidosis who were satisfying the inclusion criteria were screened between the period March 2007 and December 2008. Four patients were excluded as they did not consent to participate. Five patients were excluded as they were clinically asymptomatic. Twenty-five patients were finally recruited for the study. All the patients were histopathologically proven cases of sarcoidosis. Histologic evidence was established by flexible bronchoscopy and transbronchial lung biopsy in 24 patients and by endomyocardial biopsy in one patient. Twenty-one patients were successfully followed-up after 6-9 months of steroid treatment.

Baseline clinical characteristics of the patients are summarized in Table 1. Constitutional symptoms like fatigue, weight loss, loss of appetite with or without fever along with respiratory complaints like cough and shortness of breath were the most common presenting complaints (60%). One patient presented with nephrolithiasis secondary to hypercalcemia. Another patient presented with ventricular arrhythmias with bradycardia in whom endomyocardial biopsy showed evidence of non-caseating granulomas and a diagnosis of cardiac sarcoidosis was made. One patient presented with hip pain secondary to bone sarcoidosis. Nine of the 25 patients had received anti-tuberculous medications prior to the diagnosis of sarcoidosis and were referred to our center for non-response to therapy.

Baseline FDG–PET–CT scan findings
Of the 25 study patients, PET–CT scan showed tracer uptake in 24 patients. Uptake was quantified in terms of SUVmax for each patient. SUVmax of a given patient is the maximum non-physiological uptake in the whole body PET–CT scan irrespective of the tissue or organ involved. However, the site of maximum uptake was also noted in order to compare the same organ or tissue in the post-treatment scan. Extent of involvement as detected by pathological tracer uptake in various organs was also noted. The most common site of increased metabolic activity was the mediastinal lymph nodes, followed by lung parenchyma. Intraabdominal and peripheral lymph nodes, spleen, liver, muscle, bone and skin were the other organs that showed an increased metabolic activity as detected by the PET–CT scan. One patient had uptake in thyroid gland while another in the stomach. The findings are summarized in Figure 1. Median SUVmax

Table 1: Baseline clinical characteristics of the study subjects

Age	41.4±9.3 years
Sex	Male-12 patients (48%)
	Female-13 patients (52%)
Cigarette smokers	2 patients (8%)
Constitutional symptoms	15 patients (60%)
Large joint arthralgias	12 patients (48%)
Uveitis	4 patients (16%)
Erythema nodosum	3 patients (12%)
History of receiving antitubercular treatment prior to diagnosis	9 patients (36%)
Serum calcium (mg/dl)	9.7±0.88
Serum ACE levels (U/L)	77.88±41.4
Tuberculin skin testing	No induration (negative) 21 patients (84%)
	Indeterminate 2 patients
	Induration>10 mm 2 patients
Spirometry	Normal 14 patients (56%)
	Obstructive pattern 3 patients
	Restrictive 8 patients
Scadding stage (chest radiographic)	Stage 0: 4 patients
	Stage I: 15 patients (60%)
	Stage II: 4 patients
	Stage III: 2 patients
	Stage IV: None

ACE: Angiotensin-converting enzyme

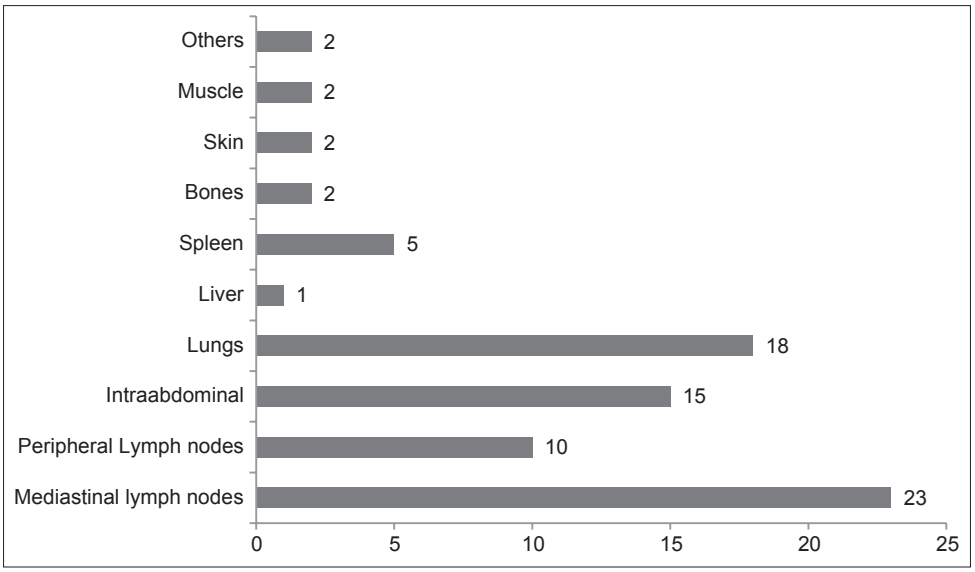

Figure 1: Positron emission tomography–computed tomography tracer uptake of involved organs at the baseline in 25 study subjects

is found to be 6.4 (range 1.1-37). The mean SUVmax was 9.36 ± 7.40.

Follow-up data

Four patients were lost to follow-up and follow-up data were available for 21 patients. All patients received treatment with oral prednisolone and clinical response was assessed after 2 months, after which the steroid doses were tapered accordingly. After 6-9 months of therapy, the patients were reassessed for clinical symptoms and relevant hematological and biochemical investigations along with spirometry, CT thorax and whole body PET–CT scan were repeated.

Response to therapy

Clinical response

Complete clinical response was noted in nine patients and partial response was seen in 11 patients [Figure 2]. One patient with cardiac sarcoidosis had recurrence of arrhythmias and congestive cardiac failure on tapering of steroid doses and was considered as having clinical worsening. Joint pain was the most common symptom that persisted at the end of the follow-up period. ESR (baseline levels 39.4 ± 16.5, follow-up levels 20.66 ± 12.48; $P < 0.001$) and serum ACE levels (baseline levels 80.2 ± 38.7, follow-up levels 33.7 ± 16.8; $P < 0.001$) reduced significantly post-treatment in the 21 patients who could be followed-up. There was no significant change in serum calcium levels, FEV_1 and DLCO post-treatment.

Radiological response

Complete radiological response was seen in eight patients while partial response was noted in nine patients [Figure 3]. Four patients did not show any radiological signs of improvement.

Metabolic response

Complete metabolic response as seen by total resolution of pathological tracer uptake is seen in eight patients [Figure 4]. Partial response was seen in nine patients. Therefore, cumulatively, 17 of 21 patients showed evidence of improvement following steroid therapy, with a decrease or total absence of metabolic activity. Four patients had an apparent absence of response or disease progression in terms of persistence of metabolic activity to pre-treatment levels or an increase in SUVmax in comparison with the pre-treatment values. The patterns of complete, partial and no metabolic response are shown in Figures 5-7.

Comparison of clinical response, radiological response and metabolic response

In patients who had a complete clinical response, 66% showed a complete metabolic response as well while 22% still had evidence of residual disease activity (partial metabolic response) in PET–CT. One patient apparently had a persistence of metabolic activity (pre-treatment SUVmax 5.6 and post-treatment 7.1) in the involved sites. In patients who had a partial or incomplete clinical response, majority of them showed an incomplete metabolic response as well and a few showed an increase in metabolic activity. One patient with cardiac sarcoidosis had a relapse of disease and developed recurrence of ventricular arrhythmias. The PET–CT scan showed an increase in metabolic activity.

Among the 14 patients who had elevated serum ACE levels at the time of diagnosis, 11 showed normalization of levels during follow-up. Of the patients who had normalization of serum ACE levels on follow-up, complete metabolic response was seen in four patients and partial metabolic response was seen in four patients, while the other three had no response or worsening in the PET–CT scan. Serum ACE levels increased in two patients on follow-up while the PET–CT scan in them showed a decrease in metabolic activity on follow-up. The agreement of PET–CT response with other indices of disease activity is shown in Figure 8.

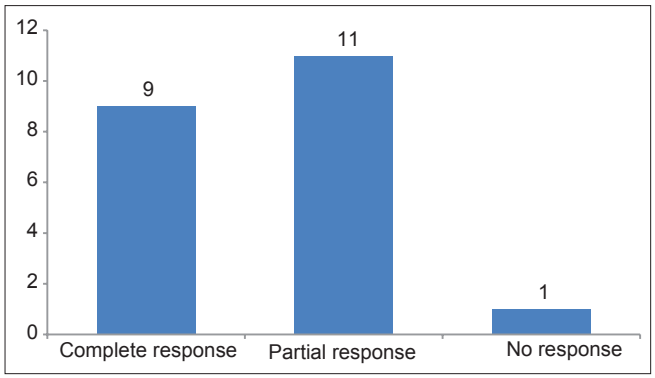

Figure 2: Clinical response on follow-up in 21 study subjects

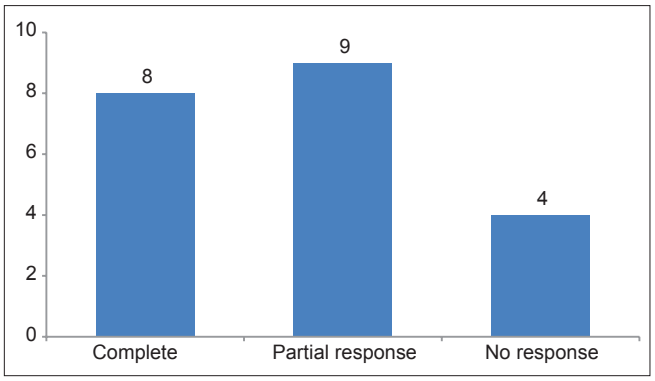

Figure 3: Radiological response on follow-up in 21 study subjects

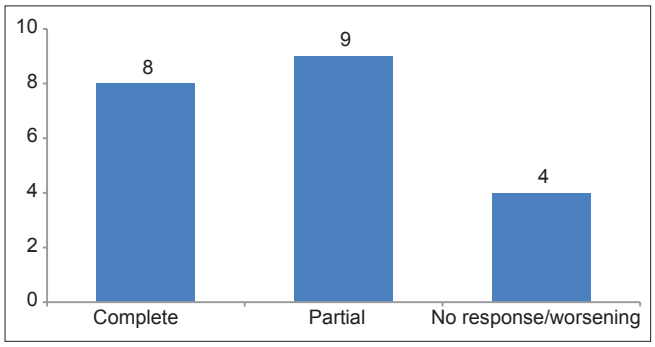

Figure 4: Metabolic response on follow-up in 21 study subjects

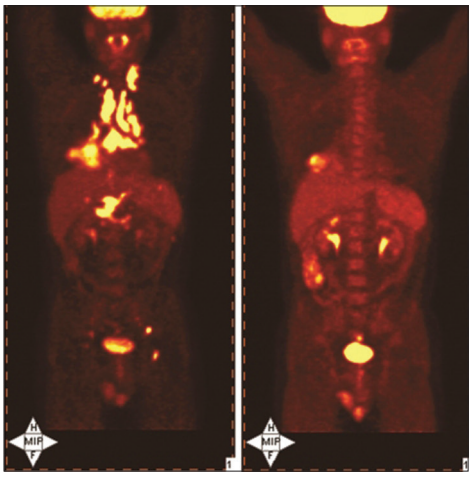

Figure 5: Baseline (left panel) and follow-up (right panel) positron emission tomography images of patient with complete metabolic response

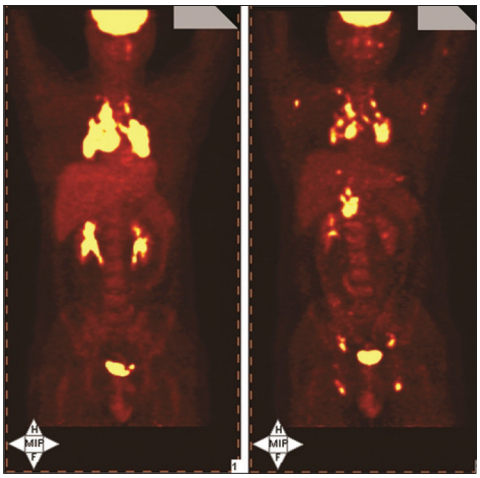

Figure 6: Baseline (left panel) and follow-up (right panel) positron emission tomography images of patient with partial metabolic response

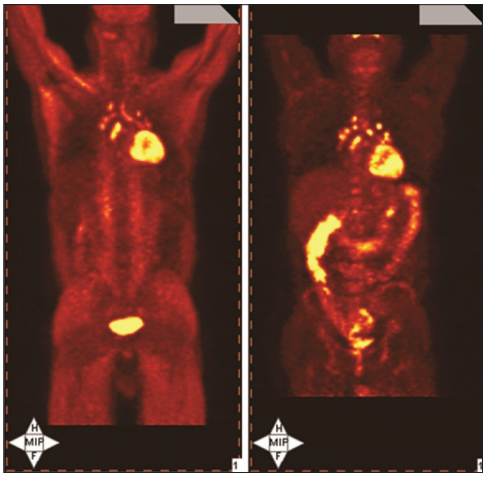

Figure 7: Baseline (left panel) and follow-up (right panel) positron emission tomography images of patient with no metabolic response

DISCUSSION

There is no consensus on the optimal duration of immunosuppressive treatment in patients with sarcoidosis, and the accurate assessment of disease activity still remains an area of active interest. Disease activity in sarcoidosis is not precisely defined and there is no general consensus on its meaning. Chest radiographs are insensitive in differentiation between active disease and inactive fibrotic disease.[2] HRCT is a very useful modality for the assessment of lung parenchymal involvement in sarcoidosis patients; however, correlates of HRCT findings with the extent of active/inactive disease are also not well defined. Also, large sample patient data on the utility of serial HRCT scanning for follow-up assessment of pulmonary sarcoidosis patients and their correlation with

Comparison	Kappa value	Degree of agreement	Level of significance
Metabolic vs clinical	0.44	Moderate	0.003
Metabolic vs radiological	0.70	Substantial	<0.001
Metabolic vs ESR	0.32	Fair	0.006
Metabolic vs ACE levels	−0.06	No	0.755
Radiological vs clinical	0.52	Moderate	<0.001

Figure 8: Agreement of positron emission tomography -computed tomography response with other indices of disease activity

change in lung function parameters is also not available.[3] In patients with a predominance of fibrotic opacities on the chest radiographs/CT scans, assessment of disease activity is very difficult but nonetheless extremely important. Identification of active disease in this subset of patients can allow institution of appropriate treatment, which can possibly halt the decline in pulmonary function.

Nuclear medicine imaging modalities that have been studied in patients with sarcoidosis include Gallium-67 scinitgraphy, somatostatin receptor scintigraphy and PET imaging. Gallium scintigraphy is now used sparingly at many centers. Compared with FDG–PET scanning, the sensitivity of Gallium scintigraphy is poorer (97% vs. 88%) and the radiation dose is nearly three times higher.[4] Another disadvantage of the technique is prolonged procedure time as image acquisition is delayed after 24 h of agent administration. However, a negative gallium scan combined with normal levels of serum ACE has a high negative predictive value for ruling out the disease.[5] Somatostatin receptor scintigraphy is performed most commonly using the radiopharmaceutical, Indium-111 pentetreotide and has been found to be a useful modality for diagnosis of thoracic involvement with sarcoidosis. However, a disadvantage of this technique is that it can miss many sites of extrathoracic disease involvement.[6]

Over the last decade, FDG–PET scanning has emerged as a potentially useful modality of imaging in patients with sarcoidosis. FDG–PET is a metabolic imaging technique. It relies on the principle of increased accumulation and metabolism of glucose by the malignant or inflammatory areas. FDG is a radioactive analogue of glucose that enters cells via the same receptors that are involved in glucose uptake and gets converted into FDG 6 phosphate by the enzyme hexokinase, similar to glucose metabolism by the glycolytic pathway. FDG 6 phosphate is not metabolized further and gets entrapped in the cell. Therefore, the level of FDG uptake is proportional to the level of glycolysis is the tissue. This explains the mechanism of increased uptake of FDG in malignancy, inflammatory and infectious processes.[3] A combined modality using FDG–PET and CT scanning (FDG–PET–CT), which was used in our study, has been found to be more sensitive than PET in isolation.

In a study by Teirstein *et al.*, 137 patients with sarcoidosis underwent 188 whole body FDG–PET examinations.[7] The SUVmax ranged between 2 and 15.8, and most patients had an SUV of more than 3. The median SUVmax in our study was 6.4 (range 1.1-37). The most common FDG avid sites were mediastinal lymph nodes (54 scans), extrathoracic lymph nodes (30 scans) and lung (24 scans). There were 31 positive scan findings in six other organs. Forty-eight of the repeat scans were performed to follow the results of therapy, primarily in patients with cardiac sarcoidosis. Of the repeat scans, 11 exhibited therapy-related decreased SUVs. In most patients, symptoms, conventional imaging findings and physiologic data paralleled the improvement seen on the PET scans, as was also seen in our study. It was found that PET adequately demonstrates sites of active disease that can be used to obtain biopsies in apparently occult disease.

Braun *et al*. described 20 patients of sarcoidosis (13 thoracic and seven cases of extrathoracic) in whom FDG–PET was performed.[8] To evaluate the response to treatment, five enrolled patients underwent a second 18F-FDG–PET–CT. Complete regression of all foci of pathological tracer uptake was shown in two cases, permitting corticosteroid withdrawal after 2 and 6 months. Improvement but incomplete regression of mediastinal and pulmonary disease occurred in two patients treated with corticosteroids for 19 and 21 months. Disease progression was detected in one patient.

PET scanning has also been reported to have a prognostic role in patients of sarcoidosis as uptake on PET correlates with BAL fluid neutrophil count. A high number of neutrophils in the BAL has been demonstrated to be a poor prognostic marker in patients with sarcoidosis.[9] Recent studies have also highlighted the possible clinical utility of PET–CT in influencing clinical management decisions in patients with sarcoidosis.[10]

A number of questions have emerged after the utilization of PET scanning in patients with sarcoidosis. In the study by Teirstein *et al.*, of the 11 patients who had a partial clinical response, no decrease in SUV was observed in two patients. Similar observations were seen in our study, wherein nearly one-fifth of the patients who had complete clinical response had evidence of active tracer uptake on their follow-up PET scans. On the contrary, treatment response as evidenced by total resolution of pathological tracer uptake in the published literature has been noted to occur as early as 2 months of steroid therapy in some cases.[11] These observations raise an important issue as to whether PET–CT scanning could be used to guide the optimum duration of therapy in these patients. The first scenario suggests that clinical response occurs earlier than metabolic response and taking clinical response alone as the criterion to stop therapy might not be appropriate and disease activity may flare. The second suggests that in some patients the resolution of metabolic activity can be pretty dramatic; hence, a shorter duration of treatment might be equally effective rather that

prolonged treatment. Large sample follow-up data in this regard may be able to answer these questions more appropriately in the future.

Another issue is as to when to perform a repeat PET scanning for the assessment of disease activity in sarcoidosis. Repeating the PET scan at 2-3 months is unlikely to help in therapeutic decision in patients with partial clinical response as most of these patients may not show a complete metabolic response. For clinically unresponsive patients, it may be useful to perform the scan early as an increase in the uptake would point toward a need for possible relooking at the diagnosis and/or optimization or change of treatment regimen. However, the optimum duration of follow-up scanning in this regard still needs to be determined.

In our study, there was a good agreement between radiological and metabolic response. Of the three patients in whom there were discordant findings, two showed a partial resolution of radiological abnormalities while the PET–CT showed a modest increase in the uptake. In one patient, there was persistent mediastinal lymph nodal enlargement on follow-up CT suggesting no response; however, PET showed reduction in tracer uptake. These findings suggest that CT still remains an extremely useful and cost-effective modality for follow-up response assessment. It would be important to identify the subgroup of patients who would be likely to benefit from the addition of PET-CT imaging for response assessment, which may be useful for predicting the outcome. In our opinion, this group of patients is likely to comprise of patients in whom the radiological picture predominantly consists of irreversible changes like fibrosis and bronchiectasis and the physician is considering the possibility of disease activity within those lesions. Future studies targeted at this group of patients will likely answer this issue more appropriately.

There are inherent limitations of our study owing to a smaller sample size as it was a preliminary study at our center. However, our study lays the ground for further larger sample-sized studies on the utility of FDG–PET–CT in Indian patients with sarcoidosis. Use of SUVmax for surrogate of disease activity as has been used in previous studies needs to be considered in the light of the pattern of disease involvement. As disease involvement in sarcoidosis is diffuse in contrast to solid organ tumors, which usually have a primary large focal lesion, quantified uptake of FDG might be more relevant than SUVmax estimation at a focal area. However, studies are not yet available that have tried to correlate quantified FDG uptake with clinical parameters.[3] It is difficult to precisely quantify clinical response; therefore, a comparison with objective measures like SUV and metabolic response cannot be accurate. Most patients in our study had stage 1 or stage 2 disease patterns. It has been proposed in previous studies that PET scan may be useful in patients with stage 3 and 4 disease to differentiate reversible component needing steroid treatment from irreversible fibrotic changes. Hence, our results may not reflect the results that will be obtained in such a population. The extent of involvement as a prognostic factor becomes important with the presence of cardiac or neurologic sarcoidosis. The protocol used for the whole body PET–CT scan in this study could have missed asymptomatic cardiac or neurosarcoidosis. Histological proof of the involvement in all the organs showing uptake is not possible to obtain, and the same has been the case with previous studies. Another issue is differentiatingf non-specific uptake or uptake due to intercurrent infection from sarcoidosis disease activity.

The results of our study show that FDG–PET–CT scanning is a sensitive nuclear imaging modality that adequately demonstrates sites of disease activity in patients with sarcoidosis. There is a good correlation of PET–CT findings with conventional markers of disease activity, like the clinical response and CT findings. In difficult clinical scenarios, it can also guide in planning the site of biopsy in order to establish a histopathological diagnosis. However, important issues exist regarding the evaluation of this investigation modality in resource-constrained settings. As the procedure is costly (nearly five times the cost of a contrast-enhanced CT examination of the thorax in an Indian setting), it is extremely important to use this modality judiciously and to identify those patients who are most likely to benefit from its performance, and it makes a difference to their overall outcome. The answer to these questions will require the conductance of large, well-conducted studies with follow-up assessment corroborated with histopathological measures to better delineate the utility of FDG–PET–CT imaging in patients of sarcoidosis.

REFERENCES

1. Statement on sarcoidosis. Joint Statement of the American Thoracic Society (ATS), the European Respiratory Society (ERS) and the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) adopted by the ATS Board of Directors and by the ERS Executive Committee, February 1999. Am J Respir Crit Care Med1999;160:736-55.
2. Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med 2007;357:2153-65.
3. Keijsers RG, van den Heuvel DA, Grutters JC. Imaging the inflammatory activity of sarcoidosis. Eur Respir J 2013;41:743-51.
4. Keijsers RG, Grutters JC, Thomeer M, Du Bois RM, Van Buul MM, Lavalaye J, *et al*. Imaging the inflammatory activity of sarcoidosis: Sensitivity and inter observer agreement of (67)Ga imaging and (18) F-FDG PET. QJNucl MedMol Imaging 2011;55:66-71.
5. Baughman RP, Shipley R, Eisentrout CE. Predictive value of gallium scan, angiotensin-converting enzyme level, and bronchoalveolar lavage in two-year follow-up of pulmonary sarcoidosis. Lung 1987;165:371-7.
6. Lebtahi R, Crestani B, Belmatoug N, Daou D, Genin R, Dombret MC, *et al*. Somatostatin receptor scintigraphy and gallium scintigraphy in patients with sarcoidosis. J Nucl Med 2001;42:21-6.
7. Teirstein AS, Machac J, Almeida O, Lu P, Padilla ML, Iannuzzi MC. Results of 188 whole-body fluorodeoxyglucose positron emission tomography scans in 137 patients with sarcoidosis. Chest 2007;132:1949-53.
8. Braun JJ, Kessler R, Constantinesco A, Imperiale A. 18F-FDG PET/CT in

sarcoidosis management: Review and report of 20 cases. Eur J Nucl Med Mol Imaging 2008;35:1537-43.
9. Drent M, Jacobs JA, de Vries J, Lamers RJ, Liem IH, Wouters EF. Does the cellular bronchoalveolar lavage fluid profile reflect the severity of sarcoidosis? Eur Respir J 1999;13:1338-44.
10. Ambrosini V, Zompatori M, Fasano L, Nanni C, Nava S, Rubello D, *et al*. (18)F-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.
11. Basu S, Asopa RV, Baghel NS. Early documentation of therapeutic response at 6 weeks following corticosteroid therapy in extensive sarcoidosis: Promise of FDG-PET. Clin Nucl Med 2009;34:689-90.

How to cite this article: Guleria R, Jyothidasan A, Madan K, Mohan A, Kumar R, Bhalla AS, *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.

Source of Support: Nil, **Conflict of Interest:** None declared.