Original Article

Role of magnetic resonance imaging and 18-fluorodeoxyglucose positron emission tomography-computed tomography in identifying pain generators in patients with chronic low back pain

ABSTRACT

Objective: Low back pain (LBP) is a major cause of pain and disability. Identification of the pathology accurately or the pain generators is sometimes difficult with the conventional modalities such as magnetic resonance imaging (MRI), computed tomography (CT), or X-ray. Nuclear medicine investigations such as single-photon emission CT (SPECT/CT) or 18-fluorodeoxyglucose positron emission tomography-CT (18-FDG PET-CT) have emerged as an adjuvant tool in these cases. In this study, we evaluated and analyzed the role of 18-FDG PET-CT in identifying active pain generators and the outcomes of interventions based on that compared to MRI.

Methodology: This study included all patients who fell under inclusion criteria presented with chronic LBP with or without radiculopathy. History and clinical examination were done as well as Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) scores were calculated. All the patients underwent MRI lumbosacral spine with sacroiliac (SI) joint and 18-FDG PET-CT whole spine. Patients in whom PET-CT was positive and active pain generator was identified were managed for the specific level or pain generator responsible by appropriate modalities, i.e. surgery, interfacetal injections, transforaminal epidural injections, and SI joint injections. Patients in whom PET-CT was negative were managed according to the pain generator identified on the basis of MRI and clinical correlation. Patients were told to follow-up after 1 week and 1 month, and subsequent improvement was evaluated on the basis of VAS after 1 week and 1 month and ODI score after 1 month.

Results: A total of 20 patients were included in the study, with a mean age of 41.9 ± 13.53 years. Twelve patients had multiple level pathology without the indication of significant pain generator and eight patients' symptoms did not correlate with the MRI findings. 18-FDG PET-CT was done in all patients. 10% (2/20) patients were identified with active pain generators on PET-CT which were not identified on MRI. Eleven out of twenty patients underwent intervention in the form of surgery or pain injections. The mean VAS and ODI score in the patients intervened on the basis of 18-FDG PET-CT improved by 70.59% and 50%, respectively, whereas in patients who underwent intervention on the basis of MRI had improvement in mean VAS and ODI score by 58.57% and 30.81%, respectively after 1 month.

Conclusion: Inflammation and associated degenerative process in the spine is a continuous process and affects multiple levels and might not be easily picked up on MRI or other conventional modalities. Thus, 18-FDG PET-CT is useful in identifying these active inflammatory processes and thereby helping in the localization of active pain generators. Treating these active pain generators has a better outcome in patients after intervention in terms of better pain relief and quality of life and also reduces the levels being treated.

Keywords: 18-fluorodeoxyglucose positron emission tomography, low back pain, Oswestry Disability Index, spinal pain generators, Visual Analog Scale

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Submitted: 02-Aug-23 **Accepted:** 27-Aug-23
Published: 29-Nov-23

How to cite this article: Sharma DN, Yerramneni VK, Srivastava MK, Yerragunta T, Akurati S. Role of magnetic resonance imaging and 18-fluorodeoxyglucose positron emission tomography-computed tomography in identifying pain generators in patients with chronic low back pain. J Craniovert Jun Spine 2023;14:381-7.

Access this article online	
Website: www.jcvjs.com	Quick Response Code
DOI: 10.4103/jcvjs.jcvjs_88_23	

INTRODUCTION

Low back pain (LBP) is a major cause of pain and disability that is experienced across all ages. It still continues to be responsible for more years lived with disability than any other disorders.[1] The literature shows that 30% of adolescents worldwide experience at least one LBP episode in their lifetime.[2] Andersson estimated the annual worldwide LBP incidence in adults to be 15% and the point prevalence to be 30%.[3] Clinicians evaluating patients with LBP or radicular symptoms tend to focus on the anterior spinal column, specifically on disc pathology, often overlooking the role of the posterior elements in pain generation which can be potential source of pain and not easily diagnosed by conventional modalities. Facet joints, pedicles, spinal ligaments, spinous processes, transitional lumbosacral (LS) segments, and sacroiliac (SI) joints have all been implicated as sources of axial back and neck pain and may be causal of radicular symptoms.[4]

Oftentimes, the patient's history and physical examination point to a spinal pain generator, but the two typical imaging (dynamic radiography, magnetic resonance imaging [MRI], and computed tomography [CT]) fail to identify its exact location.[5] Identifying the cause and managing this segment of patients have brought the attention of the clinicians to nuclear medicine investigations such as single-photon emission CT (SPECT/CT) or 18-fluorodeoxyglucose (FDG) positron emission tomography-CT (PET-CT) to identify the pain generators where conventional imaging modalities failed. A study published in May 2021 in *the Journal of Nuclear Medicine* described the role of 18-FDG PET-CT in identifying inflammation and microcalcification in patients of LBP.[6] Another study published in May 2006 described the role of PET-CT in identifying facet joint arthropathy.[7] Thus, in this study, we have studied the role of 18-FDG PET-CT as an adjunct tool to MRI in identifying the pain generators in patients of LBP where conventional MRI was inconclusive or unable to do so. Furthermore, we have tried to establish the role of 18-FDG PET-CT in the management of these patients for a better outcome by detecting the exact cause of pathology that is, the active pain generator and its treatment, thus reducing the risk of failure of interventions.

METHODOLOGY

This is a prospective observational study. The study included twenty patients. All aspects of the study had been approved by the Research Committee And Institutional Ethical Committee. The study was conducted at Nizam's Institute of Medical Sciences, Hyderabad from October 2021 to March 2023 (18 months).

This study included all the patients who fell under inclusion criteria presented with chronic LBP with or without radiculopathy. History and clinical examination were done as well as Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) scores were calculated. All the patients underwent MRI LS spine with SI joint and 18-FDG PET-CT whole spine. On PET-CT, the pain generators appeared as hypermetabolic foci. Patients in whom PET-CT was positive and active pain generator was identified were managed for the specific level or pain generator responsible by appropriate modalities, i.e. surgery, interfacetal injections, transforaminal epidural injections, and SI joint injections. Patients in whom PET-CT was negative were managed according to the pain generator identified on the basis of MRI and clinical correlation. Patients were told to follow-up after 1 week and 1 month, and subsequent improvement was evaluated on the basis of VAS after 1 week and 1 month and ODI score after 1 month [Figure 1].

Inclusion criteria

1 Patients with multiple level pathology on MRI or without any clear identification of pain generator.
2 Patients with a history of surgery but had no relief in pain after surgery (failed back syndrome).
3 Symptoms not correlating with MRI.

Exclusion criteria

1 Patients with suspected metastatic lesion or infected lesion (such as tuberculosis).
2 Traumatic spine injuries such as fractures.
3 Patients with a history suggestive of inflammatory back pain.
4 Psychiatric illness or emotional instability.

Statistics analysis

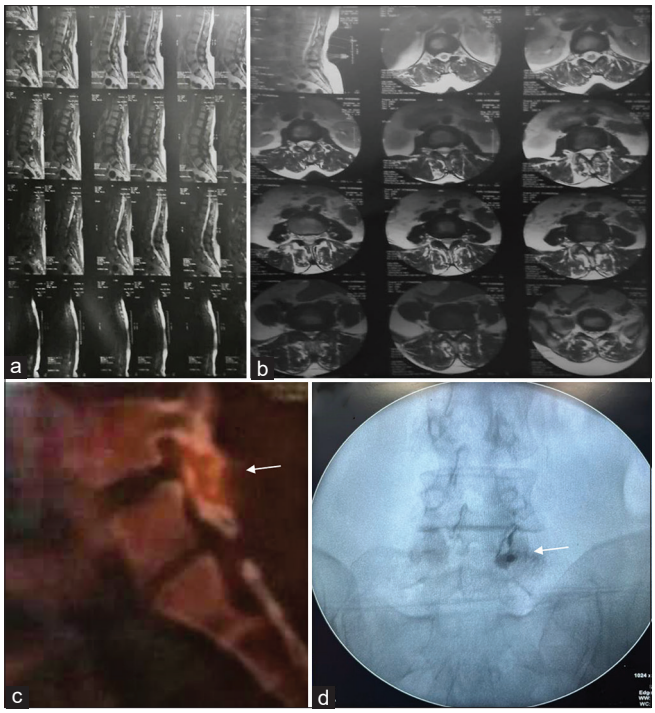
All the data were organized using a spreadsheet. Categorical variables were expressed in percentages. Continuous data were expressed as mean and standard deviation.

RESULTS

A total of 20 patients were included in the study. All patients underwent MRI LS spine with SI joint and 18-FDG PET-CT. Two out of twenty patients were identified with active pain generators on 18-FDG PET-CT and were treated based on it, whereas the remaining 18 patients with no active pain generator on 18-FDG PET-CT were treated based on probable pain generator on MRI and clinical correlation.

Demographics

The mean age of the study group was 41.9 ± 13.53 years. Among the 20 patients included in the study, a majority



Case Illustration 1 : A 48-year old female presented with LBP with left radiculopathy but no deficits. Figure 1a and 1b:- shows MRI L-S spine sagittal(a) and axial view(b) respectively, depicting disc bulges at multiple levels. Figure 1c:- 18-FDG PET-CT showing mild FDG uptake in bilateral L4 pars interarticularis which is depicted with white arrow. Patient was given bilateral L4-5 facetal injections. Figure 1d shows site of L4-5 interfacetal injection with contrast in the facet joint marked by white arrow. the VAS score of the patient changed from 8 to 2 and the ODI score from 40% to 22% at the end of 1 month.

with 55% belonged to 40–60-year age group, followed by 30% in 20–40-year age group. Furthermore, the majority of the patients were of female gender, i.e., 70% and 30% were of male gender.

Clinical presentation

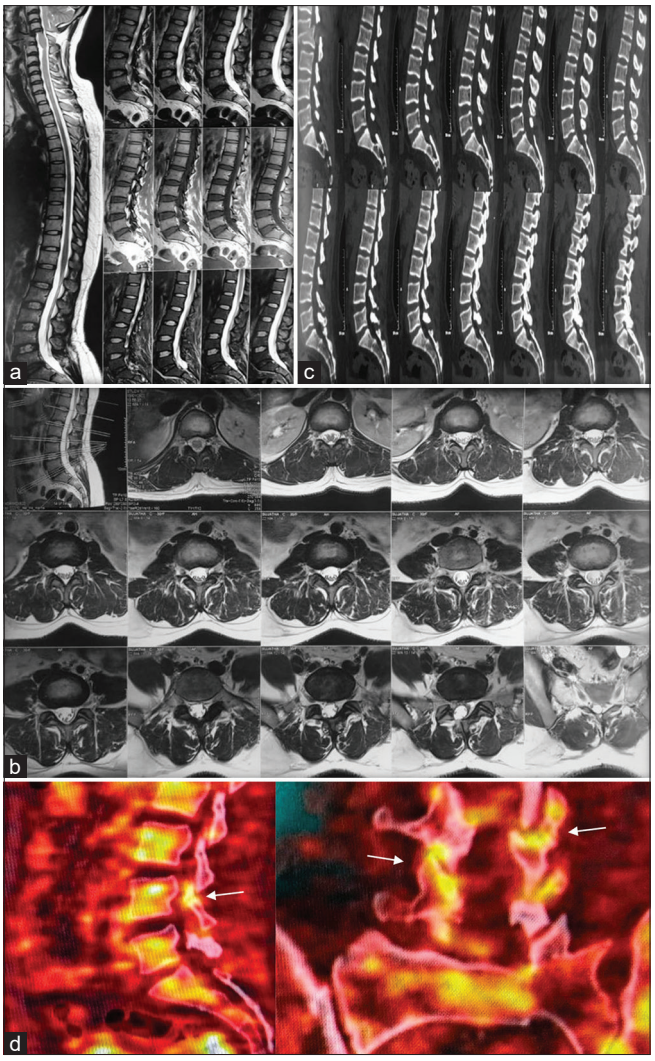
Among the study group, all the patients presented with chronic axial LBP. Out of 20, nine patients (45%) had left radiculopathy, five patients (25%) had right radiculopathy, and four patients (20%) with bilateral radiculopathy. Two patients (10%) among the study group had no radiculopathy.

Magnetic resonance imaging findings

Among the study group, 12 patients (60%) had multiple level pathology on MRI, and out of these 12 patients, one patient was of failed back syndrome, whereas in the rest eight patients (40%), the symptoms did not correlate with the MRI findings, i.e., either the MRI was normal or the pathology was not significant to cause the symptoms.

18-fluorodeoxyglucose positron emission tomography-computed tomography findings

It was observed that, 18-FDG PET-CT in two patients(10%) was positive that is, it showed active pain generators (Table 1, Case Illustration 1 and Case Illustration 2).



Case illustration 2: A 30-year old female post-L5 laminectomy and L5-S1 discectomy presented with LBP with bilateral radiculopathy (R>L). Figure 2a and 2b :-MRI L-S Spine sagittal(2a) and axial view(2b) respectively, depicting mild diffuse disc bulges at L3-4, L4-5, and L5-S1 level. Figure 2c shows CT LS spine showing degenerative changes in L5 pars . Figure 2d:- mild FDG uptake in bilateral L4 and right L5 pars interarticularis on 18-FDG PET-CT sagittal and Coronal view depicted with white arrow. The patient underwent L4-L5-S1 open transforaminal lumbar interbody fusion (TLIF). The VAS score improved from 9 to 3 and the ODI score from 56% to 26% at the end of 1 month.

Table 1: Comparison of pain generators on magnetic resonance imaging and 18-fluorodeoxyglucose positron emission tomography-computed tomography in patients with positive positron emission tomography-computed tomography

Pain generators on MRI	Active pain generators on PET-CT
Multiple level lumbar disc bulges	Mild FDG uptake in bilateral pars interarticularis of L4
L4/5, L5/S1 PIVD, S/P L5 laminectomy	Mild FDG uptake in bilateral L4 and right L5 pars interarticularis

MRI – Magnetic resonance imaging; PET-CT – Positron emission tomography-computed tomography; FDG – Fluorodeoxyglucose; PIVD – Prolapsed intervertebral disc

Treatment based on investigations (positron emission tomography-computed tomography and magnetic resonance imaging)

Two patients among the study group were treated based on the active pain generators identified on 18-FDG PET-CT. Out of these two patients, one patient underwent surgery (TLIF) and one patient was given interfacetal injection. While the rest 18 patients were treated based on the MRI findings, of which one patient underwent surgery (TLIF), eight patients were treated with pain injections (seven transforaminal epidural and one SI joint) and nine patients were treated conservatively [Table 2].

Visual Analog Scale and Oswestry Disability Index scores of patients treated on the basis of pain generators on 18 fluorodeoxyglucose positron emission tomography-computed tomography and magnetic resonance imaging

Preintervention versus postintervention scores in patients intervened on the basis of 18 fluorodeoxyglucose positron emission tomography-computed tomography

Visual Analog Scale score

The two patients who were treated based on the 18-FDG PET-CT presented with severe pain. On intervention, the condition improved, and the patients complained of moderated pain after 1 week of intervention. It further improved, and the patients had mild pain by 1 month of intervention [Table 3].

The mean VAS score of the two patients who were treated on the basis of the pain generators detected on 18 FDG-PET/CT was 8.5 ± 0.71 at presentation. A mean VAS score of 6.0 ± 00, 5.00 ± 00, and 2.5 ± 0.71 was observed immediately after the intervention, 1 week after intervention, and 1 month after intervention, respectively. It was observed that there was an improvement in VAS score by 29.41% immediately after the initiation of treatment, while an improvement by 41.18% and 70.59% was noted in patients after 1 week and 1 month of treatment, respectively.

Table 2: Treatment modality distribution on the basis of magnetic resonance imaging and positron emission tomography-computed tomography in the study group

Treatment modality	Conservative management	Intervention	
		Injections	Surgery
PET-CT	0	1	1
MRI	9	8	1

MRI – Magnetic resonance imaging; PET-CT – Positron emission tomography-computed tomography

Oswestry Disability Index score

Among the patients treated based on the pain generators reported on 18 FDG-PET/CT, one patient had severe disability and one had moderate disability at the time of presentation. After treatment, the patient with severe disability improved and exhibited moderate disability [Table 3].

The mean ODI scores of the patients treated based on the PET-CT findings were 48.0 ± 11.31 and 24.0 ± 2.83 pre- and post-intervention, i.e., at 1 month. It was observed that there was an improvement in ODI score by 50% after treatment, i.e., at 1 month [Table 4].

Table 3: Visual Analog Scale and Oswestry Disability Index scores of patients treated on the basis of pain generators on 18-fluorodeoxyglucose positron emission tomography-computed tomography and magnetic resonance imaging

VAS range	Pretreatment	Posttreatment			ODI range	Pretreatment	Posttreatment
		Immediate	1 week	1 month			
PET-CT: Intervention (n=2)							
No pain (0)	0	0	0	0	Minimal disability (0–20)	0	0
Mild pain (1–3)	0	0	0	2	Moderate disability (21–40)	1	2
Moderate pain (4–6)	0	2	2	0	Severe disability (41–60)	1	0
Severe pain (7–9)	2	0	0	0	Crippled (61–80)	0	0
Worst pain (10)	0	0	0	0	Bed bound (81–100)	0	0
MRI: Intervention (n=9)							
No pain (0)	0	0	0	0	Minimal disability (0–20)	1	3
Mild pain (1–3)	0	0	0	5	Moderate disability (21–40)	6	6
Moderate pain (4–6)	1	8	9	4	Severe disability (41–60)	2	0
Severe pain (7–9)	8	1	0	0	Crippled (61–80)	0	0
Worst pain (10)	0	0	0	0	Bed bound (81–100)	0	0
MRI: Conservative management (n=9)							
No pain (0)	0	0	0	0	Minimal disability (0–20)	1	2
Mild pain (1–3)	0	0	0	2	Moderate disability (21–40)	5	6
Moderate pain (4–6)	1	1	4	6	Severe disability (41–60)	2	1
Severe pain (7–9)	8	8	5	1	Crippled (61–80)	1	0
Worst pain (10)	0	0	0	0	Bed bound (81–100)	0	0

MRI – Magnetic resonance imaging; PET-CT – Positron emission tomography-computed tomography; VAS – Visual Analog Scale; ODI – Oswestry Disability Index

Table 4: Comparison of mean Visual Analog Scale and Oswestry Disability Index scores pre- and post-treatment on the basis of pain generators on 18-fluorodeoxyglucose positron emission tomography-computed tomography and magnetic resonance imaging

	VAS score				ODI score	
	Pretreatment	Posttreatment			Pretreatment	Posttreatment
		Immediate	1 week	1 month		
PET-CT: Intervention (n=2)						
Mean±SD	8.5±0.71	6.0±00	5.0±0.0	2.5±0.71	48.0±11.31	24.0±2.83
Improvement by (%)	-	29.41	41.18	70.59	-	50
MRI: Intervention (n=9)						
Mean±SD	7.78±0.97	5.67±1.12	5.0±0.87	3.22±0.83	38.22±11.07	26.44±7.55
Improvement by (%)	-	27.14	35.71	58.57	-	30.81
MRI: Conservative management (n=9)						
Mean±SD	7.67±0.87	7.67±0.87	6.44±0.73	4.67±1.5	36.56±13.52	29.89±9.62
Improvement by (%)	-	0	15.94	39.13	-	18.24

MRI – Magnetic resonance imaging; PET-CT – Positron emission tomography-computed tomography; VAS – Visual Analog Scale; ODI – Oswestry Disability Index; SD – Standard deviation

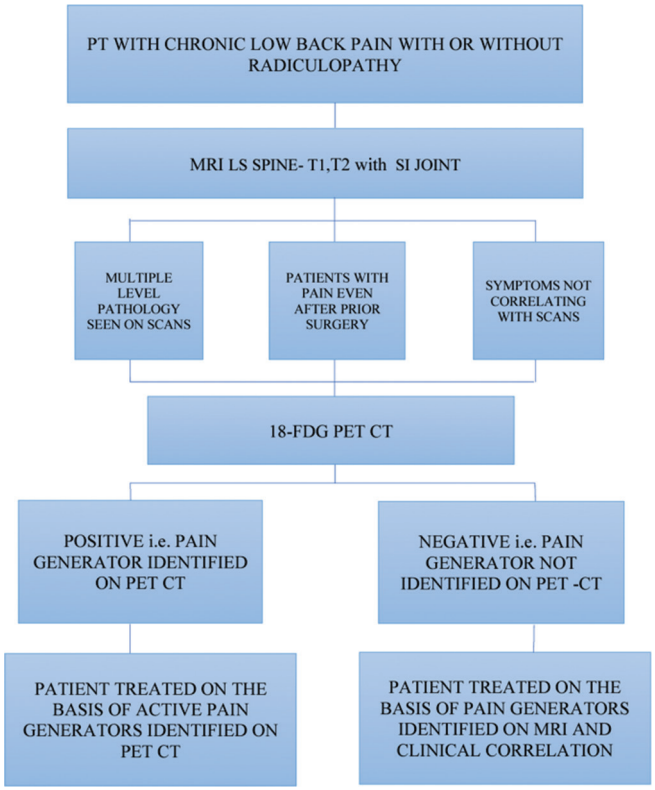


Figure 1: Flowchart depicting methodology. PT – Patient; MRI – Magnetic resonance imaging; LS – Lumbosacral; SI – Sacroiliac; PET-CT – Positron emission tomography-computed tomography; 18-FDG – 18-Fluorodeoxyglucose

Preintervention versus postintervention scores in patients intervened on the basis of magnetic resonance imaging

Visual Analog Scale score

Among the nine patients who underwent intervention based on the MRI findings, majority with eight patients presented with severe pain and one patient with moderate pain. Immediately after intervention, only one patient presented with severe pain and rest eight patients complained of moderate pain. After 1 week, none complained of severe pain and all nine patients were in moderate pain category. The symptoms further improved by 1 month of intervention and majority of five patients complained of mild pain, whereas the rest four had moderate pain [Table 3].

Nine patients who underwent intervention based on the pain generators identified on MRI, the mean VAS score before the intervention was 7.78 ± 0.89. A mean VAS score of 5.67 ± 1.12, 5.0 ± 0.87, and 3.22 ± 0.83 was observed immediately postintervention, 1 week after intervention, and 1 month after intervention, respectively. It was observed that there was an improvement in VAS score by 27.14% immediately postintervention, whereas improvement by 35.71% and 58.57% in VAS score was noted in patients after 1 week and 1 month of intervention, respectively [Table 4].

Oswestry Disability Index score

Majority, i.e. six patients who underwent intervention based on the pain generators identified on MRI, presented with moderate disability, whereas two had severe disability and one with minimal disability. One month postintervention, six patients were in moderate disability category, whereas three were in minimal disability category [Table 3].

The mean ODI score preintervention in the patients intervened on the basis of MRI findings was 38.22 ± 11.07, and after 1 month postintervention mean ODI was 26.44 ± 7.55. It was observed that there was an improvement in ODI score by 30.81% after 1 month of intervention [Table 4].

Preconservative management versus postconservative management scores

Visual Analog Scale score

Among the nine patients who were treated conservatively based on MRI findings, majority of eight patients presented with severe pain and one patient with moderate pain. Immediately after intervention, there was no improvement

in the pain. After 1-week postconservative management improvement was seen where four patients had moderate pain, whereas the rest five had severe pain. Further improvement was noted after 1 month, wherein only one patient was in severe pain, two patients in mild, and rest six in moderate pain category [Table 3].

The mean VAS score of the nine patients, who were treated conservatively based on the MRI findings, was 7.67 ± 0.87. A mean VAS score of 7.67 ± 0.87, 6.44 ± 0.73, and 4.67 ± 1.5 was observed immediately after the initiation of conservative treatment, 1 week and 1 month after the conservative management, respectively. It was observed that there was no immediate improvement in mean VAS score, whereas improvement by 15.94% and 39.13% in mean VAS score was noted in patients after 1 week and 1 month of conservative management, respectively [Table 4].

Oswestry Disability Index score

Among the patients who were treated conservatively, one patient was crippled, two had severe disability, five had moderate disability, and one had mild disability. After 1 month of conservative management, one patient had severe disability, six had moderate disability, and two had minimal disability and no patient was in the crippled category [Table 3].

The mean ODI score of nine patients treated conservatively was 36.56 ± 13.52 before treatment and 29.89 ± 9.62 posttreatment, i.e., at 1 month. It was observed that there was an improvement in ODI score by 18.24% after treatment, i.e., at 1 month [Table 4].

DISCUSSION

Identification of the primary pain generator in patients with chronic LBP due to degenerative spine disease can be very difficult. Oftentimes, the patient's history and physical examination point to a spinal pain generator, but the typical imaging (dynamic radiography, MRI, and CT) fail to identify the exact location of the pain generator.[5] There has been increased interest in recent years to use 18-FDG PET-CT in the diagnosis of axial spinal pain. Physiologic imaging such as radionuclide bone scanning or 18-FDG PET-CT and functional imaging with weight-bearing or axial loading may demonstrate findings more specific to the subset of degenerative age-related changes that are actually responsible for the patient's pain.[4] 18-FDG PET-CT can help for the precise anatomical localization of the areas with increased bone metabolism. The iliac bones and the vertebral bodies, particularly in young patients, have a naturally high concentration of osteoblasts and therefore often show a physiologically increased signal. The reliability of 18-FDG PET-CT in determining the primary spinal pain generator appears to be good. Targeted treatments based on the 18-FDG PET-CT findings might have more chances to show positive results.

A study published in May 2021 in the *Journal of Nuclear Medicine* described the role of 18-FDG PET-CT in identifying inflammation and microcalcification in patients of LBP.[6] Another study published in May 2006 described the role of PET-CT in identifying facet joint arthropathy.[7]

In the *Journal of Nuclear Medicine*, a study was published in September 2012 which suggested that 18-FDG PET-CT is better and more accurate in diagnosing spondylodiscitis patients than SPECT/CT.[8]

Diagnostic accuracy and anatomic localization further improves with 18-FDG PET-CT. Foci of increased radiotracer uptake may be observed in the posterior elements associated with facet arthritis/synovitis, acute or subacute pars interarticularis defects/fractures, and Baastrup phenomenon of the spinous processes. It can identify facet arthropathy with active findings related to inflammation and hypervascularity, which therefore is more likely to benefit from treatment.[9]

Case reports and small series have shown that 18-FDG PET-CT may also show foci of increased FDG uptake corresponding to facet osteoarthrosis, most commonly in the lumbar spine.[7,9,10] Case report of 56-year-old woman with a history of lung nodule and chronic LBP underwent whole-body PET-CT, in which there was no uptake in the lung, but it showed uptake in facet joints at the level of L4/L5.[7]

In a study conducted by Rosen *et al.*, 150 patients who underwent 18-FDG PET-CT, 22% of patients had incidental finding of degenerative spine disease either in disc space or facets excluding metastasis and it was most common in LS spine[9] [Table 5].

Table 5: Comparison of the present study with findings of a study by Rosen *et al*.[9]

	Rosen *et al*.[9]	Our study
Patient selection	All patients >18 years for unknown or suspected malignancy	All patients with chronic LBP
Positive findings in spine for degenerative spine disease, *n* (%)	33/150 (22)	2/20 (10)
Most common site	Lumbosacral (23/150)	Lumbosacral (2/20)
Active pain generators on PET-CT	Disc space and facet joints	Pars interarticularis

PET-CT – Positron emission tomography-computed tomography; LBP – Low back pain

In our study, we decided to assess the role of 18-FDG PET-CT in adjunct to MRI in patients with chronic LBP and it showed that 10% of the patients had active pain generators identified on 18-FDG PET-CT which was not identified on MRI. There was an improvement by 70.59% and 50% in VAS and ODI scores respectively in patients who were intervened on the basis of 18-FDG PET CT findings, whereas, an improvement by 58.57% and 30.81% in VAS and ODI scores respectively was noted in patients who underwent treatment on the basis of MRI findings. Although the sample size is small, our study shows that 18-FDG PET-CT is a helpful tool in identifying the active pain generators by detecting the underlying active inflammation which cannot be seen on MRI and thus targeting these active pain generators gives a better outcome.

The process of degenerative disease and the inflammatory process in the disc and facet joints should be viewed as a continuous process during which there is a variable degree of inflammation evident on 18-FDG PET-CT, which over the years results in the abnormalities seen on anatomic imaging. The time at which the PET scan is done or patients using anti-inflammatory medications before scan might be some factors responsible for a negative scan. Our study had 10% of patients with positive PET-CT and rest 18/20 (90%) had negative PET-CT which might be due to the use of previous medications, on which the significant data were not available. Hence, considering all the factors, 18-FDG PET-CT can be considered an adjunct modality to MRI in patients with chronic LBP, where MRI is inconclusive in identifying pain generator. This not only will help to identify the active pain generator but also will improve the yield of outcome after intervention, reducing the levels to be treated and thus improving the quality of life of the patients.

CONCLUSION

This study suggests that 18-FDG PET-CT can be a helpful noninvasive tool that can be used adjunct to MRI in identifying active pain generators in patients with axial low back pain with or without radiculopathy. Inflammation and associated degenerative process in the spine is a continuous process and affects multiple levels in the spine. This continuous process and its changes might not be easily picked up on MRI or other conventional modalities. Thus, 18-FDG PET-CT is useful in identifying these active inflammatory processes and thereby helping in localization of active pain generators. Treating these active pain generators has a better outcome in patients after intervention and also reduces the levels being treated. Although the primary investigation in patients with back pain patients is MRI and it cannot be replaced, in patients where MRI is unable to indicate a definite pain generator and give an accurate diagnosis, 18-FDG PET-CT can be used as an adjunct tool to identify the pain generator to have better pain relief in patients.

Limitations

There are several limitations to this study. The sample size is small, and it needs to be studied on a bigger sample size to design protocol or guidelines regarding the inclusion of 18-FDG PET-CT in patients presenting with chronic axial LBP. There was unavailability of data on the history of medications in patients, which affects the inflammatory process and can lead to negative PET scan. Degeneration in the spine is a multilevel and ongoing process, thus treating a particular level does not ensure a prolonged symptom-free period postintervention.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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