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# Value of 18F-FDG PET/CT in guiding management of facet joint arthropathy

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## Abstract

**Background** Facet joint arthropathy is one of the causes of back and neck pain. Diagnosing facet arthropathy as the source of pain is a medical challenge. The purpose of this study was to investigate the potential role of 18F-FDG PET/CT imaging to precisely target the active inflammatory facet joints.

**Methods** A prospective study included 129 patients with chronic neck or back pain and no neurologic or radiologic findings to diagnose intervertebral-disk-related pain. 18F-FDG PET/CT imaging was performed to evaluate the cause of pain. None of the patients had any malignant or traumatic lesions in the spine. The PET findings were compared to the CT findings. In addition, the PET/CT findings were correlated with the clinical findings.

**Results** The images of PET/CT of 54 patients demonstrate abnormally increased FDG uptake in facet joints. Thirty patients had bilateral abnormally increased FDG uptake in facet joints (24 lumbar, 6 cervical facet joints). Of these 30 patients, 12 had a normal appearance of facet joints on CT, 12 had mild degenerative changes limited to the affected facet joints, and 6 had moderate multilevel degenerative changes affecting the facet joints on CT. Twenty-four patients had unilateral increased FDG uptake at facet joints (6 lumbar, 18 cervical facet joints). Among these 24 patients with unilateral increased FDG uptake at facet joints, 12 had a normal facet joints appearance on CT, while the other 12 had marked multilevel degenerative changes affecting the facet joints. The positive findings of PET or CT have been correlated with the neurological examination and injection therapy outcome.

**Conclusions** 18F-PET/CT has incremental value in the management of pain resulting from facet arthropathy by targeting the affected joints, especially when conventional imaging findings are non-specific or show no abnormality. The most effective management for facet arthropathy is nerve root block; therefore, PET/CT may outline and guide the management to target the active inflammatory facet joints.

**Keywords** FDG, PET/CT, Back pain, Facet joint arthropathy, Nerve block

## Background

Facet joint arthropathy of the spine is a common cause of back and neck pain with its first designation as the "facet syndrome." Although it overlaps clinically with other pathologies of the spine, the point prevalence for facet joint pain was found to be around 45–55%, 40–50% and 10–15% for the patients with neck, upper back and lower back pain, respectively [1, 2].

A typical presentation for patients with facet joint disease is similar to a discogenic pain pattern with additional features such as exacerbation with certain types of movement, such as sitting and coughing [3]. Pain can

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be caused by any component of the facet joint complex including the synovial membrane, fibrous capsule, hyaline cartilage, or the osseous component. Still, it is important to note that the likelihood of the etiology (discogenic vs. facetogenic pain) varies in different age groups [4, 5].

The pathophysiology behind facet joint arthropathy is associated with repetitive stress and minor trauma in relation to degenerative disk disease [6]. Facet joint pain can be caused by structural changes accompanied by degenerative intervertebral disks, spondylolisthesis, spondylolysis, as well as inflammatory joint diseases [5, 7]. Due to the possible overlap between other spine disorders and facet joint disease, it is crucial to have an accurate diagnostic strategy, to determine the appropriate approach to management [8].

Different investigation approaches have been used for the evaluation of back pain. Some limitations have been noted with single-modality imaging studies. Hence, hybrid imaging techniques, such as positron emission tomography/computed tomography (PET/CT), have been evolving as promising tools for superior assessment to guide management aiming to yield better outcomes [2, 9].

Combined PET/CT with the use of 18F-fluoro-2-deoxy-D-glucose (FDG), is well recognized in oncology imaging including staging, restaging and assessment of response to therapy of most malignancies. Furthermore, FDG PET/CT has been used in the characterization of infection and aseptic inflammation [10–15]. In addition, FDG concentrates on autoimmune disorders and granulomatous disease [16]. Considering joint diseases, the inflammatory changes of the synovium and hypertrophy of the lining layer are associated with FDG uptake in joints and have been associated with degenerative or inflammatory changes in joints [17, 18].

Some studies demonstrated the positive potential role of PET/CT in the diagnosis and evaluation of bone abnormalities in adolescent and young patients with back pain [19, 20]. Hence, the purpose of this study was to investigate the potential role of 18F-PET/CT imaging to precisely pinpoint the sites of active disease in the facet joints.

## Methods

### Patients and clinical data

This cross-sectional study was performed over a period from November 2016 to May 2021; 364 patients referred to our department presented with neck or back pain. Among them, 190 patients with neurological or radiological findings to diagnose intervertebral-disk-related pain were excluded. Additional 39 patients with malignant or traumatic lesions in the spine, 3 patients were unable to tolerate PET/CT imaging and 3 pregnant women were further excluded. Ultimately, this study included 129 patients (60 males and 69 females with a mean age of $52 \pm 16$ years). All the available clinical data as well as MRI reports of the spine when available were considered. Neurological examination and management data were reviewed. This study was conducted after being approved by the institutional ethical committee and obtaining Institutional review board (IRB) approval. Informed written consent was obtained from all patients who participated in the study.

### PET/CT imaging

The patients underwent PET/CT and diagnostic contrast CT imaging using a hybrid system with a 128-slice CT scanner (Biograph mCT 128, Siemens Healthineers, Erlangen, Germany). Patients are advised to avoid strenuous exercise for 24 h before PET/CT study. Patients have been asked to fast for 6 hours, during which they were encouraged to drink plain water. Both height and weight were recorded upon the patient arrival at our department. Blood sugar less than 11 mmol/L was required before injection of FDG at a dose of 4.3 MBq/Kg through a 20-gauge cannula in the antecubital vein followed by 20 mL of saline. After the FDG injection, the patient is instructed to relax in a quiet dim light room for about 60 min before PET/CT scan. During the wait time, the patient was instructed to drink about 1 L of water and should void before image acquisition to decrease the activity from the urinary bladder. At first low dose, CT scan from skull base to mid-thigh was performed for attenuation correction using 80 kVp. PET scan was performed after low-dose CT in 3D mode at 2 min sequential overlapping bed positions. Contrast CT study was acquired after intravenous injection of contrast (Ultravist® 370; Schering, Berlin, Germany) about 1.3 mL/Kg at the rate of 4 mL/s utilizing a contrast media injection system (Medrad Co., Inc., Pittsburgh, PA). PET images were reconstructed in ultra-high definition utilizing point-spread function (PSF) together with time of flight (TOF) (Siemens "ultraHD·PET"; iterations, 3; subsets, 21) with Gaussian filter applied. CT reconstruction with a slice thickness of 1 mm was acquired.

### Image interpretation

Studies were reviewed and interpreted using a commercial workstation (SyngoVia, Siemens Healthineers, Erlangen, Germany). CT scans were evaluated by an experienced radiologist with 18 years of experience, whereas the FDG PET and PET/CT fused images were assessed by an experienced nuclear medicine physician with 21 years of experience. The facet joints were defined based on the standard anatomical imaging [7]. Abnormally increased FDG uptake within facet joints was

considered positive on PET images. Positive CT characteristics for facet joint arthropathy include joint space narrowing, sclerosis, hypertrophy or osteophytes of the facet joints.

### Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Shapiro–Wilk test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation (SD). Quantitative nonparametric data were presented as the median and interquartile range (IQR). Qualitative variables were presented as frequency and percentage (%). The 18F-FDG PET and conventional imaging findings were evaluated by Spearman correlation coefficients. The receiver operating characteristic (ROC) curve was performed to assess the diagnostic efficacy of 18F-FDG PET/CT. Two-tailed *P* value < 0.05 was considered statistically significant.

**Table 1** Demographic data of 129 patients with back pain and no neurologic or radiologic findings of intervertebral disk abnormality

| | **(*n* = 129)** |
|---|---|
| Age (year) | 52 ± 16 (36–72) |
| *Gender* | |
| Male | 60 (46.5%) |
| Female | 69 (53.5%) |
| Duration of pain (months) | 112 ± 11.3 |
| *Onset of pain* | |
| Gradual | 56 (43.4%) |
| Acute | 73 (56.6%) |
| *Pain distribution* | |
| Bilateral | 89 (69%) |
| Unilateral | 40 (31%) |
| *Facet appearance on PET/CT* | |
| Normal | 75 (58%) |
| Active joints | 54 (42%) |
| *Facet appearance on CT* | |
| Normal | 57 (44.2%) |
| Degenerative | 72 (55.8%) |

Data are represented as mean ± SD, number (%), *CT* computed tomography

## Results

This study included 129 patients. Sixty (46.5%) patients were males and 69 (53.5%) were females. Their age ranged from 36 to 72 with a mean ± SD of 52 ± 16 years. All patients had chronic neck and back pain, 89 cases (69%) of them with bilateral symptoms and 40 cases (31%) with unilateral symptoms. Patients' demographics are given in Table 1. Specific facet joints were identified as the source of pain in 59 patients. In the remaining 70 patients, facet joints were not identified as the source of back pain. The final diagnosis was concluded based on nerve block in 96 patients, neurological examination in 26 patients and clinical follow-up in 7 patients.

As regards facet appearance on CT, 57 cases (44.2%) were normal and 72 (55.8%) cases demonstrated degenerative changes. According to FDG activity, there was abnormally increased uptake in 54 patients (Table 2), whereas 75 cases showed normal FDG uptake pattern in facet joints (Table 3). There was a strong agreement between the active facet joints as detected by FDG uptake and the identified facet joints as the source of pain with an agreement percent of 93%, kappa: 0.859 (95% confidence interval = 0.770–0.947). There was a slight agreement between CT findings and the actual involved facet as the source of pain. The agreement percent was 51.2%, kappa: 0.033 (95% confidence interval = − 0.136 to 0.202). The concordance rate for positive cases between FDG and CT findings was 23.3% (30 cases) (Fig. 1). On the other hand, 18F-FDG PET was positive, while CT was negative for degenerative changes in 18.6% (24 cases).

There have been 2 false positive and 7 false negative cases in the 18F-FDG PET results compared to 38 false positive and 25 false negative cases according to

**Table 2** Findings in the 54 patients with abnormally increased FDG uptake within the facet joints

| | **Cervical facets with abnormal FDG activity (*n* = 24)** | **Lumbar facets with abnormal FDG activity (*n* = 30)** | ***p* value** |
|---|---|---|---|
| *Distribution of activity* | | | |
| Unilateral | 18 (75%) | 6 (20%) | < 0.001* |
| Bilateral | 6 (25%) | 24 (80%) | |
| *Facet appearance on CT* | | | |
| Normal | 15 (62.5%) | 9 (30%) | 0.02* |
| Degenerative | 9 (37.5%) | 21 (70%) | |

*FDG* fluoro-2-deoxy-D-glucose, *CT* computed tomography, *MRI* magnetic resonance imaging

**p* value is significant

**Table 3** Findings in the 75 patients with normal FDG uptake pattern within the facet joints

| Facet appearance on CT | Cervical level ($n=23$) | Lumbar level ($n=52$) | *p* value |
|---|---|---|---|
| Normal | 12 (52.2%) | 18 (34.6%) | 0.15 |
| Mild single-level degenerative changes | 5 (21.7%) | 6 (11.5%) | 0.25 |
| Moderate multilevel degenerative changes | 2 (0.09%) | 17 (32.7%) | 0.02* |
| Marked multilevel degenerative changes | 4 (17.4%) | 11 (21.1%) | 0.71 |

*CT* computed tomography

**p* value is significant

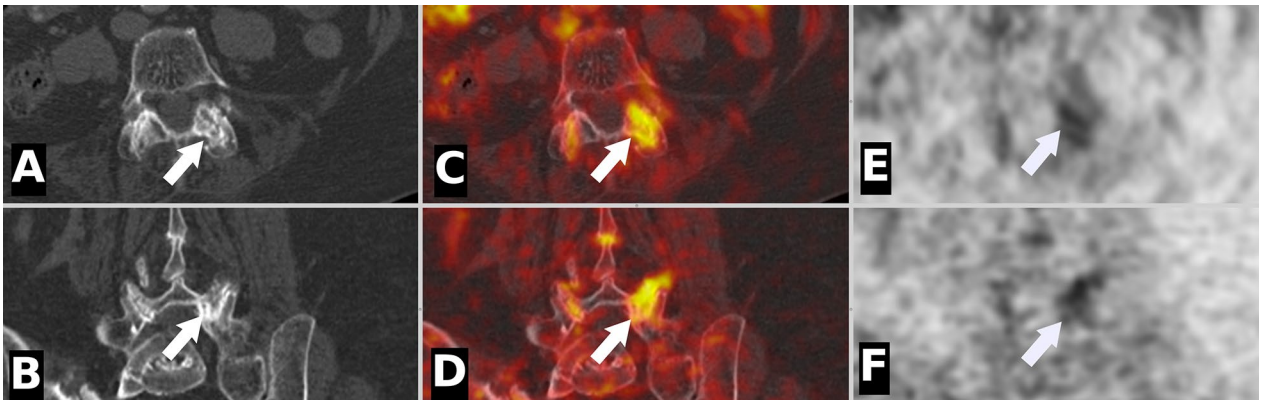


**Fig. 1** A case presented with low back pain. Multiplanar PET/CT images including CT bone window axial (**A**), coronal (**B**). Fused PET/CT axial (**C**), coronal (**D**), PET axial (**E**), coronal (**F**). Increased 18F-FDG uptake (arrows) related to bilateral L4/L5 facet joints, more on the left, with underlying degenerative changes on the corresponding CT images

**Table 4** Comparison of diagnostic performance between 18F-FDG PET and CT

| | 18F-FDG PET/CT | | Diagnostic CT | | *p* value |
|---|---|---|---|---|---|
| | % | 95% CI | % | 95% CI | |
| Sensitivity | 88.1 | 77.1–95.1 | 57.6 | 44.1–70.4 | < 0.01* |
| Specificity | 97.1 | 90.1–99.7 | 45.7 | 33.7–58.1 | < 0.01* |
| Accuracy | 93.0 | 87.2–6.8 | 51.2 | 42.2–60.1 | < 0.01* |
| Positive predictive value | 96.3 | 86.9–99.0 | 47.2 | 39.7–54.9 | < 0.01* |
| Negative predictive value | 90.7 | 82.9–95.1 | 56.1 | 46.4–65.5 | 0.01* |

*CT* computed tomography

**p* value is significant

the CT findings. Considering the localization of inflammatory facet joints, 18F-FDG PET/CT demonstrated significantly higher sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) compared to CT (Table 4).

## Discussion

The facet joint has been increasingly implicated as a significant source of pain which can arise from any structure within the facet joint complex including the fibrous capsule, synovial membrane, hyaline cartilage and bone. Facet arthropathy is prevalent in patients with low back pain and has been studied for an association with pain and for a potential impact on treatment indications and outcome. Facet osteoarthritis is the most frequent form of facet pathology [21, 22].

The aim of our study was to investigate the potential role of 18F-PET/CT imaging to precisely pinpoint the sites of active disease in the facet joints.

Our study demonstrates a strong correlation between FDG activity and the location of the painful facet joints even in the absence of underlying CT degenerative changes (Fig. 2). Increased FDG uptake in inflammatory cells, such as macrophages, has been documented in the literature. The pathophysiological of FDG activity in infection and inflammation can be explained by hyperemia which facilitates FDG delivery to the site of inflammation. In addition, enhanced glycolytic pathway and upregulation of glucose transporters increase the utilization of FDG [23, 24]. Irmler and co-workers showed a significant correlation between inflammatory cell bulk and the degree of FDG activity [25]. Arthropathy is a common disorder and is associated with physical and disability encumbrance of involved patients [26, 27]. 18F-FDG PET/CT can efficiently assess the

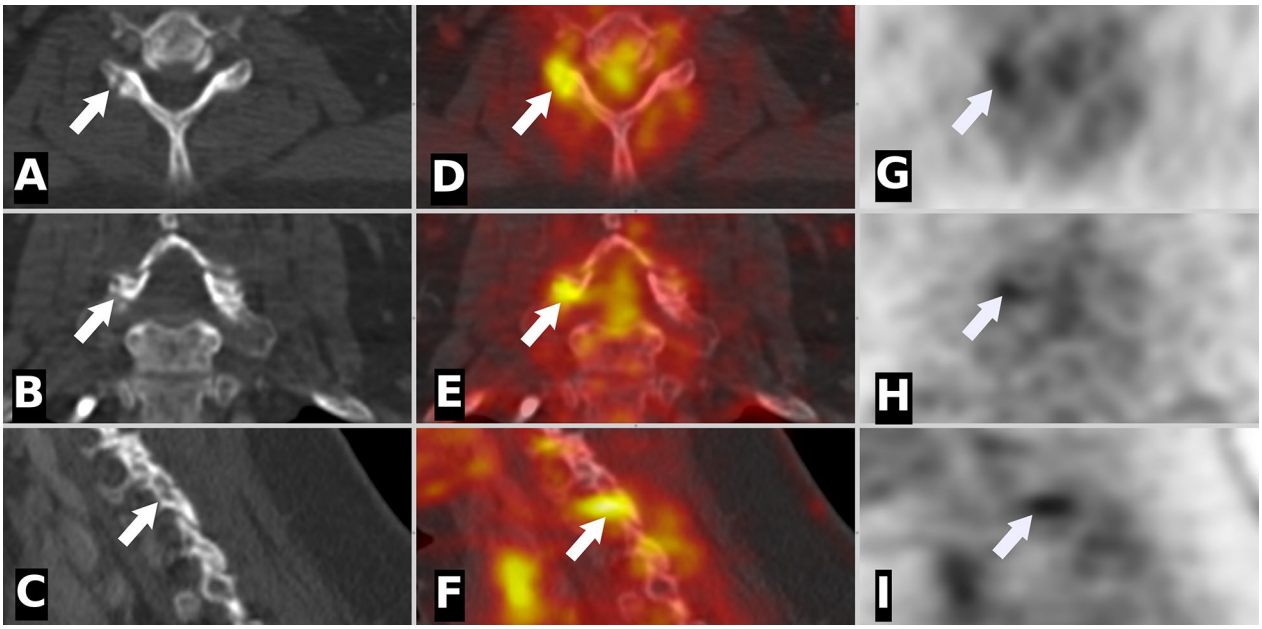


**Fig. 2** A case presented with neck pain. Multiplanar PET/CT images including CT bone window axial (**A**), coronal (**B**), and sagittal (**C**). Fused PET/CT axial (**D**), coronal (**E**), and sagittal (**F**). PET axial (**G**), coronal (**H**), and sagittal (**I**). Increased 18F-FDG uptake (arrows) related to right C6/C7 facet joint with no underlying CT changes. The pain has been improved after facet injection therapy at this level

disease extent and response to therapy in many musculoskeletal inflammatory disorders. Based on the glucose metabolism, 18F-FDG PET/CT can point to diseased joints by demonstrating inflammatory peripheral cells and fibroblasts [28]. Rosen et al. [29] evaluated the level of FDG uptake in the spine and correlated it with the findings from CT. The authors found a good correlation between the severity of FDG uptake and the severity of degeneration on CT.

This study shows the potential efficacy of 18F-FDG PET/CT in diagnosing abnormalities of cervical and lumbar facets in 129 adult patients who presented with neck or back pain. According to our results, CT diagnosed 72 patients with facet degenerative changes. From 59 patients with confirmed specific facet joints as the source of pain, 38 cases were false positive on CT images (Fig. 3). In addition, the FDG abnormality was not associated with clear degenerative changes on CT images in 18.6% of our cases. Several studies have

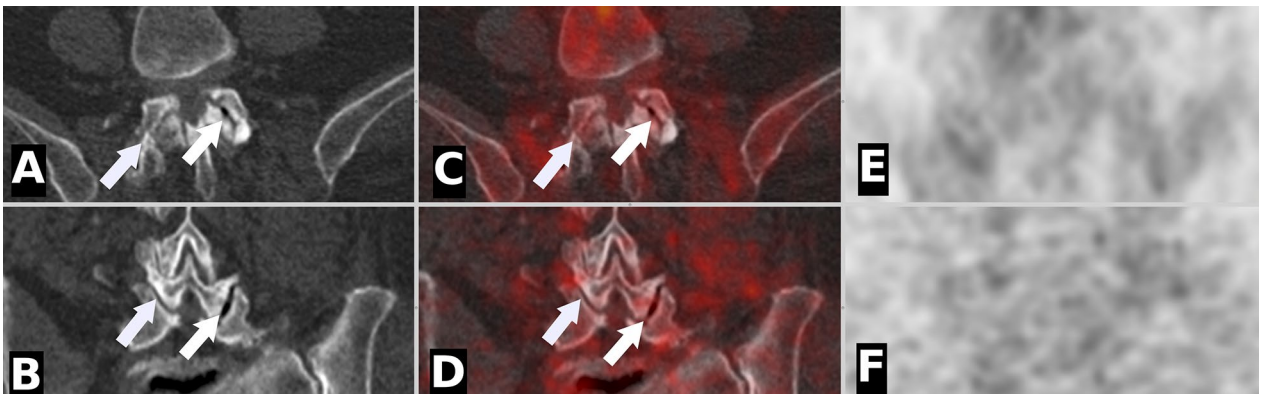


**Fig. 3** A case presented with low back pain. Multiplanar PET/CT images including CT bone window axial (**A**) and coronal (**B**). Fused PET/CT axial (**C**) and coronal (**D**). PET axial (**E**) and coronal (**F**). Advanced degenerative CT changes related to bilateral L4/L5 facet joints (arrows) with no abnormal 18F-FDG uptake on the corresponding PET images

reported that the CT facet joint degenerative changes are non-specific and not correlated with the actual site of pain generation [30–32].

Further, in the present study 18F-FDG PET/CT not only showed an additional asset in precisely identifying pain location, where 89 (69%) had bilateral distribution compared to 40 (31%) unilateral pain distribution, but also demonstrated significantly higher sensitivity and specificity compared to CT (88.1% vs. 57.6% and 97.1% vs. 45.7%, $p < 0.01$). Similarly, the drawbacks of CT were previously mentioned by Gorbach et al. [33] who reported that the degree of facet joint arthropathy as outlined by CT was not a significant predictor for the outcome in 42 patients who performed facet joint blocks ($p = 0.57–0.95$). Carrino et al. [34] measured inter-observer agreement, among 4 radiologists, in MR lumbar spine for facet arthropathy in 111 studies and found a variability of 0.54 (CI 95%: 0.50–0.57). The inconsistent variability indicated that MRI does not provide a clear assessment of facet arthropathy inflammatory status, and the report can be inconclusive. In the same study, the authors reported that conventional MRI and CT imaging convey facet arthropathy at multiple levels with no clear findings for those joints causing pain and no definite guide to the level of injection therapy.

There is scarce literature examining the role of 18F-FDG PET/CT imaging in facet joint arthropathy. Yet, our data corroborate that of Gamie et al. [35] where 67 patients with suspected facetogenic or discogenic pain were studied. Imaging studies were performed with 18F-FDG PET/CT without contrast. Abnormal uptake of the tracer was found in 56 patients (83.6%) with 45 of these patients having abnormal activity at the facet joint. Moreover, the authors reported a sensitivity of 84% overall, and a sensitivity of 88% for patients without a prior history of lumbar surgery. However, the study was not solely focused on facet joints, which suggests a different set of sensitivity values in reality.

This study has some limitations. Selection of patients based on back pain referral may cause selection bias. Nevertheless, all patients have been examined neurologically and with the aim of this study to explore the potential role of 18F-FDG PET/CT in patients with facet joint disorder, we think that the present data are informative. In the same context, an assessment of the effect of management was assigned to neurology physicians and may potentially result in some variability among them. However, as the assessment happened in a single center with a close experience level, we assume that the variability was insignificant.

## Conclusions

18F-FDG PET/CT has incremental value in the management of pain resulting from facet arthropathy by targeting the affected joints, especially when conventional imaging findings are non-specific or show no abnormality. The most effective management for facet arthropathy is facet nerve root block; therefore, PET/CT may outline and guide the management to target the active joint inflammatory process.

### Abbreviations

| | |
|---|---|
| 18F-FDG | 18F-fluoro-2-deoxy-D-glucose |
| 3D | Three-dimensional |
| IQR | Interquartile range |
| IRB | Institutional Review Board |
| kVp | Kilovoltage peak |
| L | Liter |
| MBq/Kg | Megabecquerel per kilogram |
| mL | Milliliter |
| mm | Millimeter |
| mL/s | Milliliter per second |
| mmol/L | Millimoles per liter |
| MRI | Magnetic resonance imaging |
| NPV | Negative predictive value |
| PET/CT | Positron emission tomography/computed tomography |
| PPV | Positive predictive value |
| PSF | Point-spread function |
| ROC | Receiver operating characteristic |
| SD | Standard deviation |
| TOF | Time of flight |
| ultraHD | Ultra-high definition |

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Not applicable.

### Author contributions

MH was responsible for study design, coordinating patients flow and follow-up, writing patients and methods and discussion, and manuscript proofing. GB was responsible for statistical analysis and writing the results. ME was responsible for clinical examination, clinical data and patients follow-up. HO was responsible for data collection, collaborating with a multidisciplinary team, and writing the introduction. All authors read and approved the final manuscript.

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### Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

## Declarations

### Ethics approval and consent to participate

This study was approved by the institution review board of the National Liver Institute and was given IRB Name: NLI IRB 00003413 FWA0000227 and IRB protocol number: 00338/2022.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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