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REVIEW

FDG PET/CT FOR INFECTION AND INFLAMMATION: A PRACTICAL APPROACH

Spondylodiscitis

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ABSTRACT

Diagnosis of spondylodiscitis remains a challenge for clinicians. It results from various causative agents and conditions that can be challenging to identify. Prompt and appropriate treatment are necessary to prevent long-term irreversible complications and sequelae. The diagnosis of spondylodiscitis often constitutes a major challenge for the clinicians, and relies on the combination of clinical, laboratory and imaging findings. Various imaging techniques can be used for the workup of spondylodiscitis, with magnetic resonance imaging and 18-fluoro-deoxy-glucose positron emission tomography, combined with a CT being the most commonly used in daily practice. The aim of this review is to provide general information about indications and protocols for [^{18}F]FDG PET/CT imaging in spinal infections, focusing on spondylodiscitis, in adults.

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KEY WORDS: Discitis; Positron emission tomography computed tomography; Spine; infection; Osteomyelitis.

Spinal infections constitute a heterogeneous group of diseases that can arise through hematogenous spread from infection at another site (primary) or caused by direct inoculation during spinal instrumentation or contiguous spread in patients with pressure sores (secondary). Spondylodiscitis involves the vertebral body or disc, and may also extend to the epidural space, posterior elements and paravertebral soft tissues.[1]

Spondylitis involves the vertebral bodies, particularly when the infection is limited to the vertebral bodies without involving the intervertebral disc. Spondylitis can appear in the early stages of classic spondylodiscitis, especially in elderly or immunocompromised patients, and is often associated with granulomatous infections, such as those caused by *Mycobacterium tuberculosis*.[2]

Discitis involves the intervertebral disc. It frequently coexists with spondylodiscitis, particularly in cases of hematogenous spread or post-surgical complications. Diagnosis relies on imaging techniques like MRI due to the non-specific nature of clinical and laboratory findings.[2]

Spondylodiscitis involves the vertebral body and intervertebral disc, often referred to as vertebral osteomyelitis or septic discitis. It commonly affects the lumbar spine, followed by the thoracic and cervical regions. The condition is typically pyogenic, with *Staphylococcus aureus* being the most frequent causative agent, although other bacteria like *Enterobacter* and non-pyogenic pathogens such as *Mycobacterium tuberculosis* and fungi can also be involved (Figure 1).[2]

Spondylodiscitis accounts for 2-7% of all vertebral infections and is most common in older adults, especially men, and peaks between ages 50 and 70. The incidence of spondylodiscitis is rising, reaching 6.5/100,000 cases each year[3, 4] due to an ageing population, increased spinal surgeries, intravenous drug use, immunosuppressive treatments, and better diagnostic methods.[5]

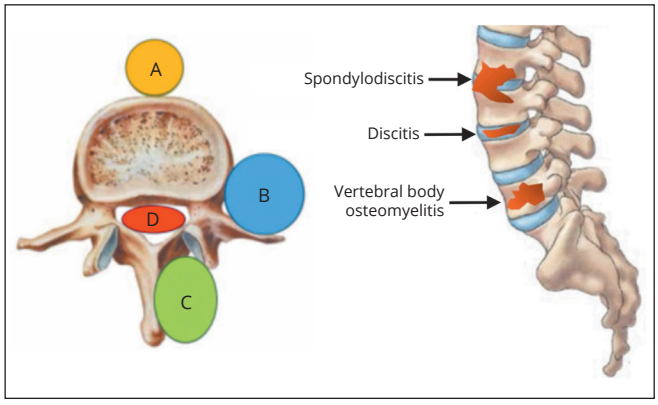

Figure 1.—On the left: location of perivertebral abscesses. A) Anterior or prevertebral space; B) lateral space, including the psoas; C) posterior space or vertebral drip; D) abscess in epidural space. On the right: Types of spinal infection: spondylodiscitis, discitis and vertebral osteomyelitis.

Most cases are bacterial, but tuberculosis and fungal infections occur more often in immunocompromised patients. The infection commonly affects the lumbar spine (60%), followed by the thoracic (30%) and cervical (10%) regions.[2] Symptoms include spinal pain, present in 80-90% of cases, and fever, observed in one-third of patients.[6] Neurological deficits such as radiculopathy or paralysis occur in about 34% of cases. Patients usually present with inflammatory syndrome with increased biomarkers such as c-reactive protein or erythrocyte sedimentation rate.

In adults, spondylodiscitis typically starts from hematogenous spread into the vertebral body, then extending to the avascularized intervertebral disc. The infection can extend to posterior bone elements, paraspinal tissues, and the epidural space, resulting in vertebral plate erosion, disc collapse, and bone destruction.[7] In contrast, the intervertebral disc is vascularized in children and they, may develop isolated discitis without adjacent bone involvement.[8]

Etiology and risk factors

Primary spondylodiscitis

Direct contamination occurs during interventional spinal procedures, such as spinal surgery or lumbar puncture. The incidence varies between 1-7%, depending on the type of procedure. The most common pathogens in postoperative infections include *Staphylococcus aureus* (accounting for 50% of cases), *E. coli, Staphylococcus coagulase negative coagulase negative* and other gram-negative bacteria such as *E. coli, Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. *M. tuberculosis* typically begins in the anteroinferior region of the vertebral body and may spread to contiguous or distant bodies through the anterior longitudinal ligament, with relative preservation of intervertebral disc in early stages. Table I highlights the main differences between pyogenic and mycobacterial spondylodiscitis.

Secondary spondylodiscitis

The main causative agent is *Staphylococcus aureus,* other pathogens include Gram-negative bacteria such as *Escherichia coli* and *Pseudomonas* species, especially in individuals with underlying conditions like endocarditis. Cases caused by *Mycobacterium tuberculosis* remains an important cause, especially in endemic regions or among immunocompromised patients.[1]

In children, hematogenous dissemination typically originates from an oropharyngeal primary source of infection, the main etiology being *Staphylococcus aureus* and, in young children typically under 6 years, *Kingella kingae*, a gram-negative facultative anaerobe commonly found in the oropharynx.[9]

The main risk factors include diabetes mellitus, rheumatoid arthritis, concurrent infections, multi-system trauma, prior surgery, alcoholism, chronic hepatitis, chronic kidney failure, organ transplants, congenital and acquired immunosuppression (*e.g.*, HIV), prolonged steroid therapy, chemotherapy, use of urinary or central venous catheters, and substance abuse.

Indications for the use of [^{18}F]FDG PET/CT

Nuclear medicine techniques detect infection earlier by highlighting increased cellular activity and glucose metabolism, an advantage over CT, which identifies structural changes that may remain normal for up to three weeks in

TABLE I.—*Differentiating features between M. Tuberculosis and pyogenic spondylodiscitis.*

Parameter	*M. tuberculosis*	Pyogenic (*e.g. S. aureus*)
Symptoms	Chronic	Acute
Disc damage	Late	Early
Abscesses	Large	Small
Affected spine	More in lower dorsal spine / dorsolumbar union	More in lumbar
Affection of posterior spinal elements	Possible	Unusual

case of spondylodiscitis. However, CT is superior in detecting collections, vertebral destruction, complications, and spinal stability. MRI is superior to CT and is the imaging modality of choice with a sensitivity and specificity nearing 100%, offering accurate diagnosis, localization and assessment of complications, such as epidural abscess.[10]

According to the EANM/SNMMI Guidelines,[11] the main indications for the use of [^{18}F]FDG PET/CT in patients with suspected spondylodiscitis are:

- suspected spondylodiscitis in patients without spinal hardware, particularly if MRI is contra-indicated;
- suspected spondylodiscitis in patients with spinal hardware, preferably performed 3-4 months after surgery;
- suspected spondylodiscitis with inconclusive/indeterminate MRI and elevated inflammatory markers (ESR and/or CRP);
- evaluation of multi-level spondylodiscitis;
- identification of the source and/or extent of dissemination of infection in established spondylodiscitis;
- evaluation of antibiotic therapy response in primary and secondary spondylodiscitis.

[^{18}F]FDG PET/CT is recommended for spondylodiscitis diagnoses in cases with inconclusive MRI findings, multilevel involvement, or post-surgical scenarios to evaluate infection spread.

Diagnostic performance of [^{18}F]FDG PET/CT

[^{18}F]FDG PET/CT is increasingly recognized as a valuable modality for diagnosing spondylodiscitis. Treglia *et al.*[12] reviewed 12 studies (396 patients), confirming [^{18}F]FDG PET/CT's excellent diagnostic performance with sensitivity and specificity of 94.8% and 91.4%, respectively. Another large study by Maamari *et al.*,[13] which included 20 studies (1.123 scans), found [^{18}F]FDG PET/CT had higher specificity (80%) than MRI (72%) for diagnosing pyogenic spondylodiscitis. Additionally, a meta-analysis focusing on pyogenic spondylitis without previous spine surgery reported a pooled sensitivity and specificity of 93% and 91%, respectively, for PET/CT, showing superior accuracy compared to postoperative cases.[14] Overall, these findings suggest that [^{18}F]FDG PET/CT is a highly effective tool, particularly in challenging cases or when MRI is inconclusive. However, MRI remains an appropriate first-line modality depending on local availability.

Table II summarizes the results of the systematic reviews in more detail.[12-16]

[^{18}F]FDG PET/CT is the first-choice imaging modality in nuclear medicine in patients with high suspicion of spine infection.

Patient preparation and acquisition pearls specific to imaging spondylodiscitis

The patient preparation adheres to the general recommendations specified in the EANM guidelines for [^{18}F]FDG PET/CT.[11, 17] Similarly, the CT acquisition parameters are aligned with the detailed guidance provided in the EANM guidelines.[17]

Metallic artifact reduction techniques should be used whenever available and indicated.

A multi-society joint consensus document containing detailed evidence-based recommendations and a flow chart for the diagnosis of spondylodiscitis was published in 2019 (Figure 2).[18, 19]

Guidelines for an appropriate use of criteria for imaging in musculoskeletal infections were also published in 2021. According to Palestro *et al.*,[20] [^{18}F]FDG PET is the nuclear medicine imaging modality of choice for diagnosing spondylodiscitis, regardless of the presence of spinal hardware.

[^{18}F]FDG PET/CT has been included in the diagnostic algorithms for spondylodiscitis, being useful in patients with a history of surgery with metallic implants, in cases of contraindicated MRI (pacemakers or valve prostheses) or inconclusive MRI. Another possible future indication would be the evaluation of response to treatment.

TABLE II.—*Performance values in five meta-analyses on [^{18}F]FDG PET/CT in patients with suspected spondylodiscitis.*[12-16]

Authors, ref.	N. studies (patients)	Se% (95% CI)	Sp% (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR (95% CI)
Yin *et al.*[15]	6 (191)	96% (84–99)	90% (79–96)	9.83 (4.39-22.03)	0.05 (0.01-0.19)	124.08 (39.04-394.34)
Kim *et al.*[16]	7 (212)	95% (87-98)	88% (73-95)	7.6 (3.4-17.2)	0.05 (0.02-0.14)	141 (44-444)
Treglia *et al.*[12]	26 (833)	95% (89-98)	91% (78-97)	4.7 (2.9-7.7)	0.11 (0.07-0.16)	63.4 (28.9-139)
Maamari *et al.*[13]	20	93%	80%	NA	NA	NA
Zhang *et al.*[14]	18 (660)	91% (84–95)	90% (79–95)	NA	NA	86 (31–240)

Se: sensitivity; Sp: specificity; LR+: positive likelihood ratio; LR-: negative likelihood ratio; DOR: diagnostic odds ratio; NA: not available.

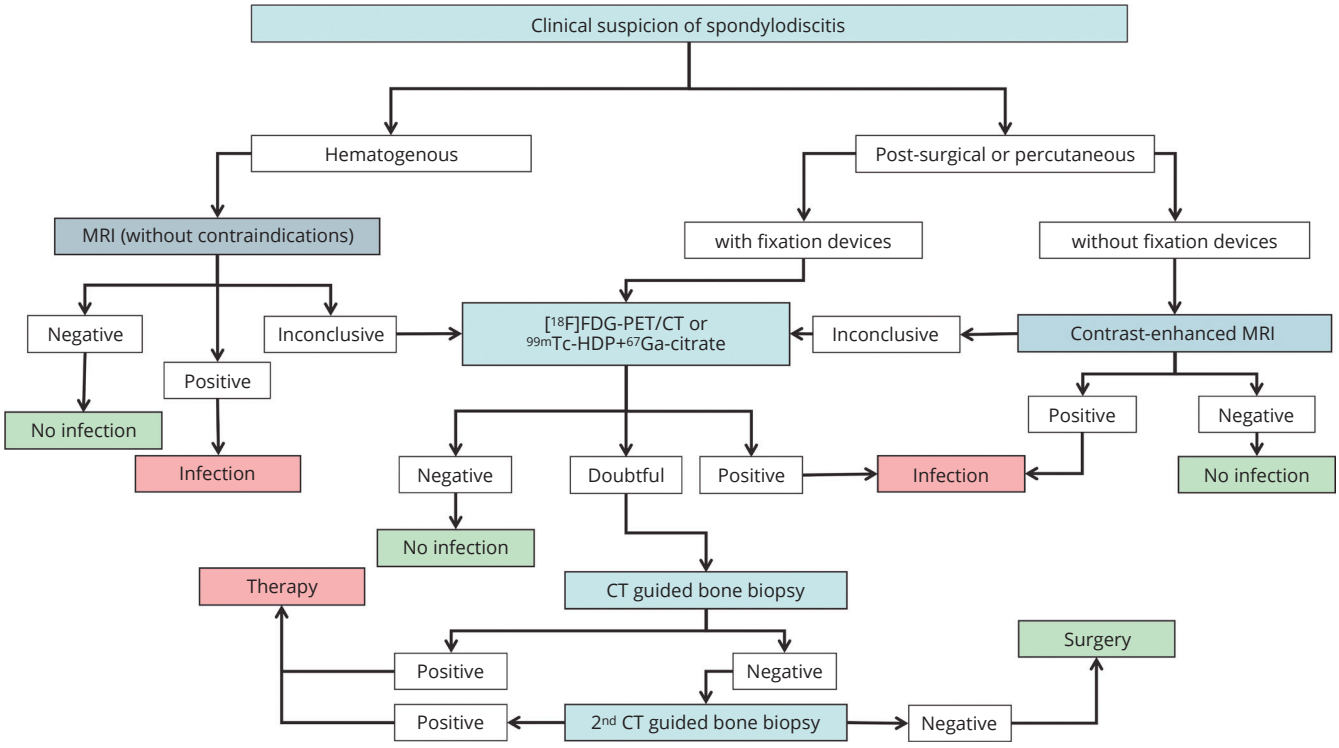

Figure 2.—Diagnosis flow chart (modified from Lazzeri *et al.*).[18]

Interpretation criteria

Establishing reliable interpretation criteria for [18F]FDG PET/CT in spondylodiscitis is essential to improve diagnostic specificity and sensitivity.

- First of all, sagittal slices should be routinely evaluated to analyze the spine;
- [18F]FDG PET/CT is regarded as negative for spondylodiscitis when there is either no uptake or if the [18F]FDG uptake at the suspected site appears homogenous, with an intensity matching that of the neighboring vertebrae and surrounding soft tissue;
- conversely, [18F]FDG PET/CT is considered positive for spondylodiscitis if the [18F]FDG uptake at the suspected location is higher than in the adjacent vertebrae and surrounding soft tissue[18, 19] and/or if [18F]FDG uptake extends to the adjacent soft tissues in the pre- or paravertebral space or in the epidural space;
- important aspects include differentiating between infection and sterile inflammation, understanding uptake patterns in infected *versus* noninfected bone structures, and quantifying metabolic activity using SUV;
- dual time-point imaging, lesion-to-background ratios, and correlation with CT findings are additional considerations that enhance the accuracy of interpretation.
- it is important to distinguish between infectious uptake and degenerative or mechanical inflammation patterns. Hungenbach *et al.* proposed the use of uptake patterns as interpretation criteria to predict or exclude spondylodiscitis.[21]
- Score 0: normal findings and physiological distribution of [18F]FDG (consistent with absence of infection);
- Score 1: slightly elevated uptake in the intervertebral or paravertebral region (consistent with absence of infection);
- Score 2: clearly elevated uptake of a linear or disciform pattern in the intervertebral space (consistent with discitis; Figure 3);
- Score 3: clearly elevated uptake of a linear or disciform pattern in the intervertebral space and involvement of the endplate or superior plate or both plates of adjacent vertebrae (consistent with spondylodiscitis).
- Score 4: clearly elevated uptake of a linear or disciform pattern in the intervertebral space and involvement of the endplate or superior plate or both plates of adjacent vertebrae and surrounding soft tissue abscess (consistent with spondylodiscitis; Figure 4).

Semi-quantitative analysis has limited value in diagnos-

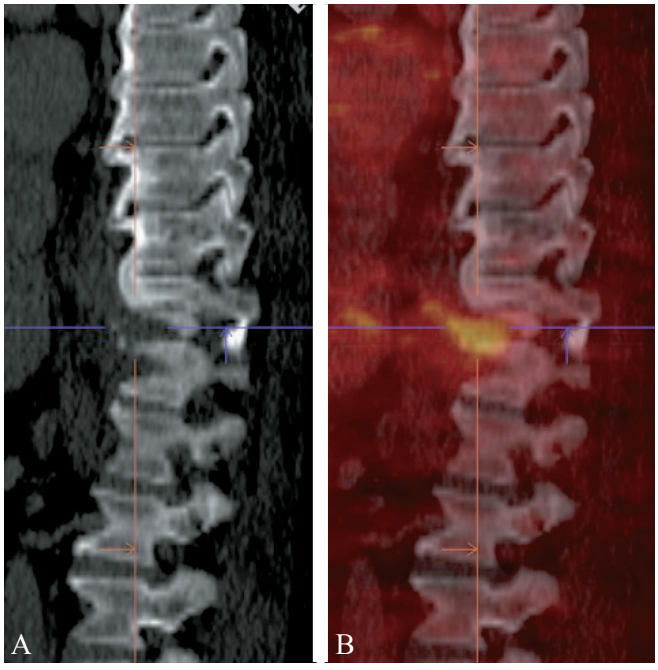

Figure 3.—[18F]FDG PET/CT assembly showing linear uptake in the T10-T11 space indicative of discitis. CT (A) and fused sagittal PET/CT (B) images.

ing spondylodiscitis, with SUV_{max} being the most widely validated parameter. Although no definitive cut-off values exist to differentiate positive from negative findings[22] it could also be valuable for evaluating treatment response; a decrease in SUV_{max} during follow-up compared to baseline suggests a positive therapeutic response. The literature proposes a ΔSUV_{max} cut-off of 25-43% [calculated as (SUV_{max} before treatment − SUV_{max} after treatment)/SUV_{max} before treatment] as indicative of a metabolic response to treatment.[23, 24] However, this is not evidence-based and depends on the camera systems used.

According to the EANM/SNMMI guidelines, the following findings are suggestive of spondylodiscitis.

In patients *without* a spinal device:[11]

• focal or linear increased uptake in one or more adjacent vertebral plates above the intensity of normal bone marrow activity;

• there may also be increased uptake in the adjacent disc space and/or paravertebral soft tissues; the extent of abnormal uptake into the epidural space should be assessed (Figure 5);

• in some patients, it may be difficult to distinguish infection from mildly elevated [18F]FDG uptake associated with degenerative changes, but the distinction can usually be made based on the exact localization of increased [18F]FDG uptake (*i.e.*, intervertebral disc in case of spondylodiscitis) and clinical presentation;

• CT may reveal endplate irregularities, erosions and/or destruction (Figure 6), extension into adjacent soft tissues or the presence of abscesses. However, these findings may be absent in early stages of the disease.

In patients with spinal device:[11]

• intense and confluent uptake in soft tissue and bone adjacent to the device at multiple contiguous levels, extending to the bone-device interface of one or more interpedicular screws;

• Increased uptake in one or two hooks, screws or anchors, usually in the upper or lower portions of the device, are suggestive of aseptic inflammation due to loosening or bone remodeling; extension of abnormal uptake, particularly to the epidural space, should be assessed;

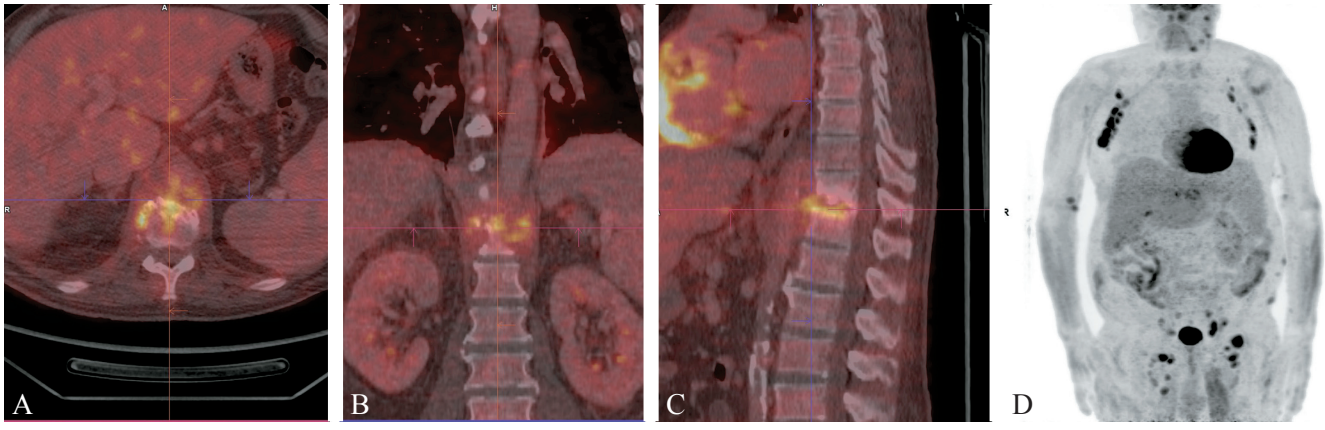

Figure 4.—Axial (A), coronal (B) and sagittal (C) fused PET/CT images and MIP image (D) showing spondylodiscitis and abscess between the T11 and T12 vertebrae.

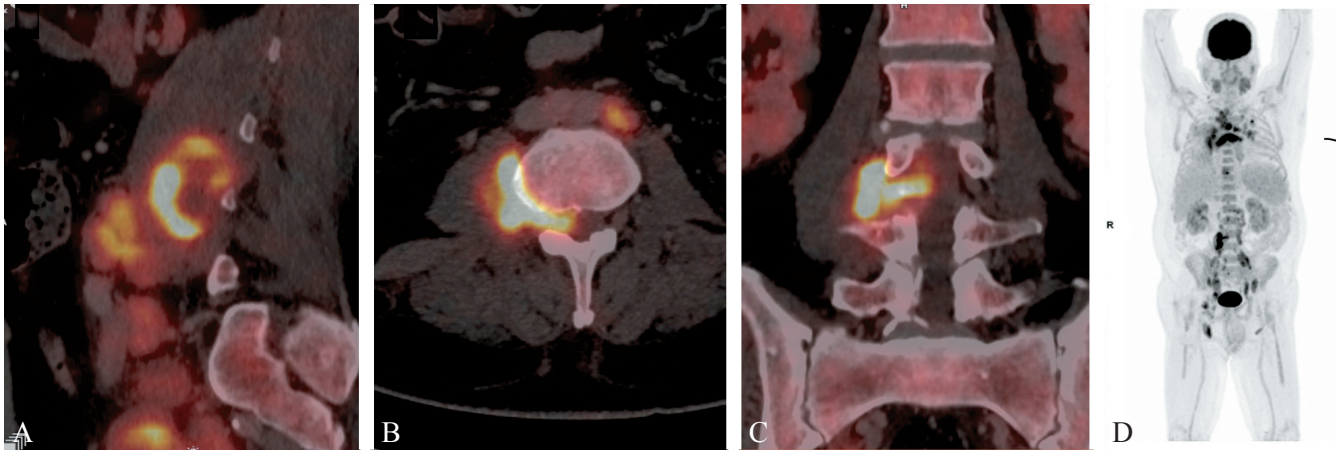

Figure 5.—Sixty-five-years-old patient immunosuppressed man with HIV. ^{18}F-FDG shows a markedly increased uptake at the right side of the L3-L4 vertebral endplates, extending laterally into the right psoas muscle and posteriorly into the vertebral canal, corresponding to spondylodiscitis with psoas abscess and epiduritis. Mycobacterium tuberculosis infection was confirmed by bone biopsy. Sagittal (A), axial (B) and coronal (C) fused PET/CT images and MIP image (D).

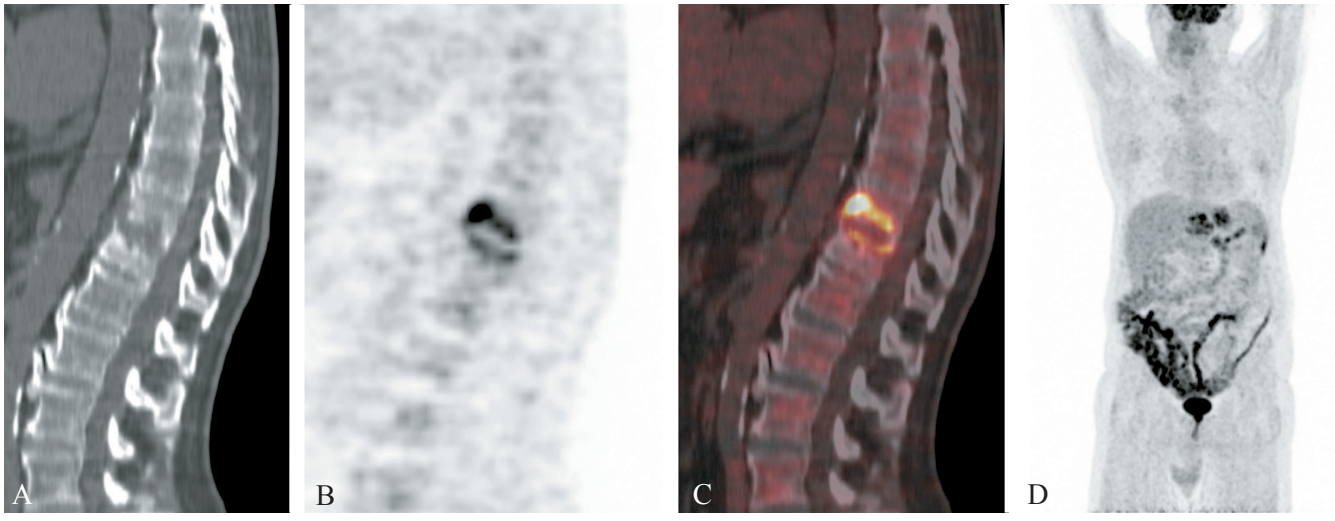

Figure 6.—[^{18}F]FDG PET/CT imaging in a 48 years old patient with back pain, fever and *S. epidermidis* infection of the lumbar spine confirmed by positive microbiology culture of the vertebral biopsy. Sagittal CT (A); PET (B); fused images (C) and MIP (D) showed spondylodiscitis with bone destruction between T11 and T12.

• correlative CT findings supportive for infection: endplate irregularities, erosions and/or destruction, extension to adjacent soft tissues or presence of collections (Figure 7). However, these findings may be absent early in the disease.

Studies suggest that the [^{18}F]FDG uptake pattern is more reliable than the uptake intensity for distinguishing patients with active infection from those without or those who have responded successfully to therapy.[10] Kloiber *et al.*[25] analyzed pattern-based interpretation criteria, achieving with a sensitivity and specificity of 98% and 100% for the initial diagnosis of spondylodiscitis. The same data were analyzed using intensity-based criteria. The optimal cut-off value for SUV_{max} was determined by receiver operating characteristic (ROC) analysis. The sensitivity and specificity of intensity-based criteria using the optimal cut-off value of 4.2 were significantly lower, 93% and 68% ($P<0.01$). The negative predictive value of [^{18}F]FDG PET/CT using pattern-based criteria to exclude the presence of residual active spondylodiscitis after treatment was 97%. The true negative rate for intensity-based criteria dropped to 55% due to a false positive rate of 45% ($P<0.001$).

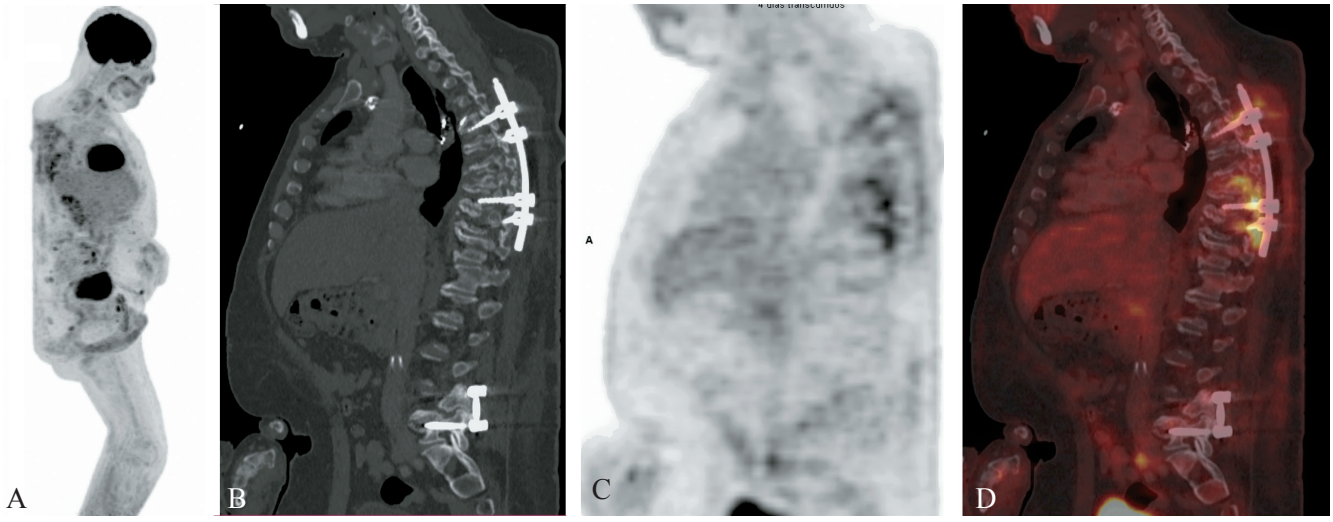

Figure 7.—MIP image (A) and sagittal CT (B) PET (C) and PET/CT fusion (D) images showing postoperative spondylodiscitis with increased ^{18}F-FDG uptake around the spinal implants and the surrounding soft tissues at multiple contiguous levels.

Differential diagnosis

Several diseases can mimic spinal infections, and radiological features may be used to differentiate spondylodiscitis from other diseases *e.g.* degenerative endplate changes, SAPHO, microcrystalline spondylodiscitis, Charcot, or chronic neuropathic disorder.

Mechanically induced non-septic inflammation (MNI) shows normal discs and degenerated discs with narrowing but no bone-on bone contact typically shows low or absent activity on [^{18}F]FDG PET/CT. Destroyed joints with bone-on-bone contact may be [^{18}F]DG-positive in the absence of spondylodiscitis.

When activity is confined to the edges of a destroyed disc with bone-on-bone contact, it aligns with MNI. This typically appears as a single line of activity if the bones remain in close contact (Figure 8A).[25] In patients with collapsed vertebrae and kyphotic deformity, the disc space may open in the supine position, causing activity to show as thin "tramlines" on the exposed bone surface (Figure 8B). This pattern often occurs alongside a vacuum disc phenomenon, with MNI activity spreading throughout the joint. If the annulus is pushed out from the disc, its location can be identified on localization CT due to attached bone fragments. Activity extending to the annulus is considered part of MNI (Figure 8C, 9A).[25] Similarly, if CT reveals well-defined fissures from the damaged joint into fragmented endplates, with activity confined within these fissures, this also signifies MNI (Figure 8D) and should not be mistaken for soft tissue or bone activity indicative of active spondylodiscitis. Since the damaged joint and its connected structures form a single virtual space, MNI generally displays uniform intensity throughout any joint. Differing intensities across compartments may suggest ongoing infection.

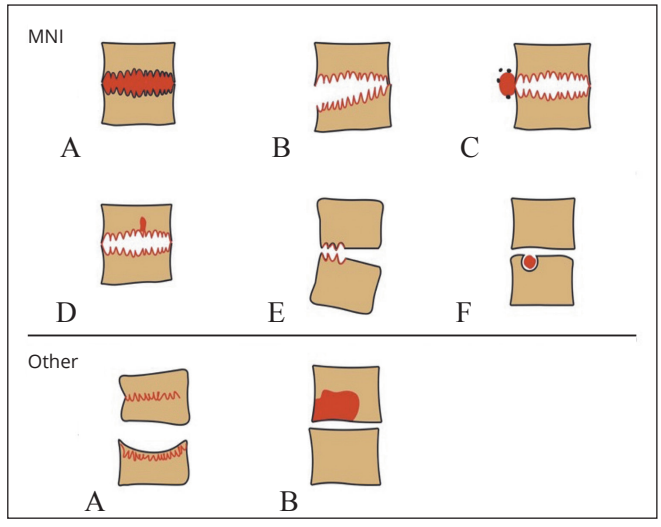

Figure 8.—Jagged vertebral endplates indicate denuded exposed bone. Abnormal metabolic activity is shown in red. Top row with different pattern of mechanical non-septic inflammation (MNI). Botton row with others spine patterns: post-traumatic and insufficiency fractures (A). Rounded, well-demarcated focal lesions are usually neoplastic (B) (modified from Kloiber *et al.*).[25]

Complete disc destruction can also be seen in non-septic degenerative arthritis, whereas partial disc damage or

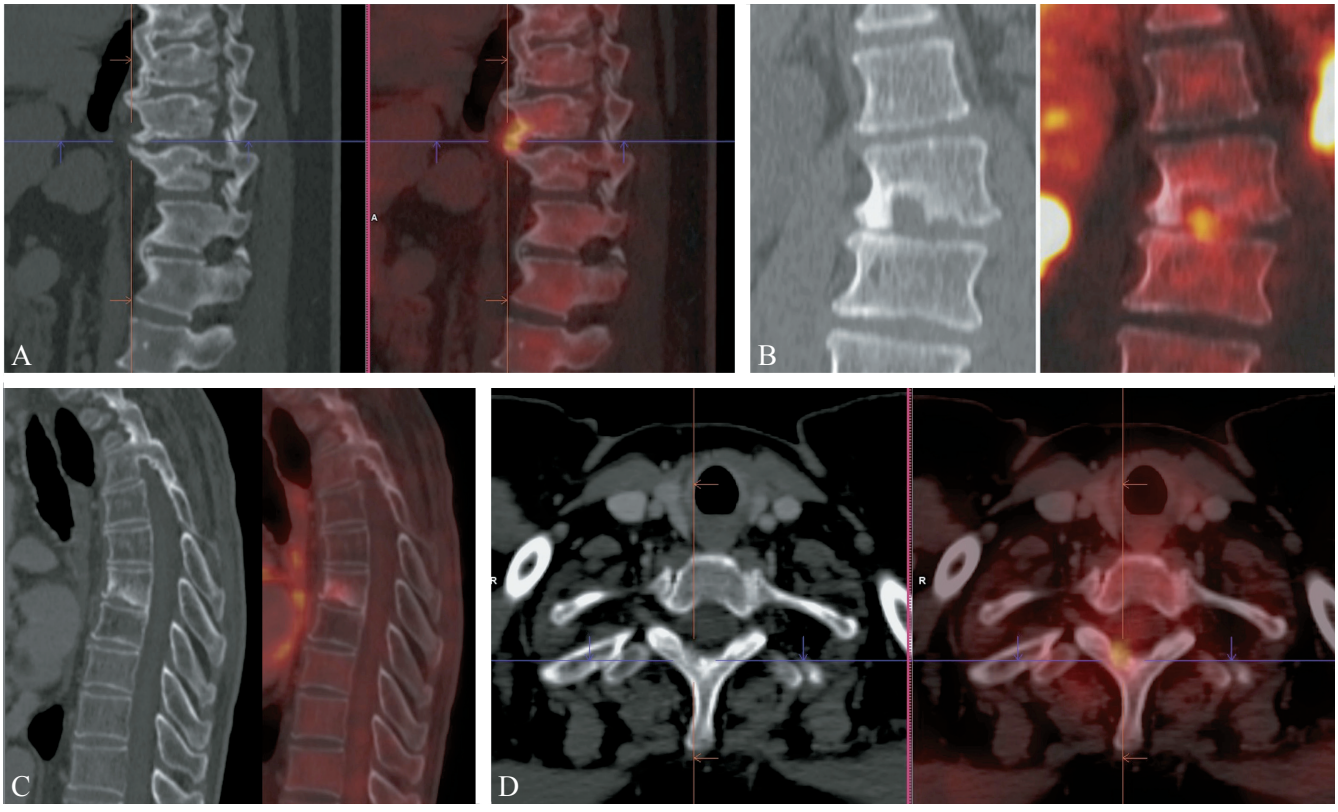

Figure 9.—A) Sagittal CT (left) and sagittal fused images (right) demonstrate an intense focus of increased ^{18}F-FDG uptake in the dorsolumbar spine corresponding to a T12-L1 osteophytic conflict. B) Coronal CT (left) and sagittal fused images (right) demonstrate focal metabolism corresponding Schmorl's nodes (modified from Kloiber *et al.*).[25] C) Sagittal CT (left) and sagittal fused images (right) demonstrate degenerative changes, Modic I changes. D) Axial CT (left) and fused sagittal images (right) show a lytic tumor lesion in the right posterior T2 arc with well-demarcated focal hypermetabolism.

localized endplate changes (such as Schmorl's nodes) are not related to spondylodiscitis (Figure 8E, F, Figure 9B). If joint destruction results in spontaneous fusion, there will be no mechanical motion to generate MNI.

Post-traumatic and insufficiency fractures are common non-infectious diagnoses. Vertebral deformity is typical on localisation CT. [^{18}F]FDG PET shows a linear increase in metabolic activity. The discs remain intact, and the activity cannot be attributed to MNI (Figure 8A).

Infection usually extends through tissue planes. Rounded, well-demarcated focal lesions are usually neoplastic (Figure 8B, Figure 9D). Spondylodiscitis superimposed on another diagnosis can be problematic.

Pitfalls

Given the low specificity of [^{18}F]FDG in distinguishing infection from acute or chronic sterile inflammation, along with the absence of standardized interpretation criteria, several potential pitfalls must be taken into account.[18, 26] The build-up of leukocytes, macrophages, monocytes, lymphocytes, and giant cells is part of the body's response to injury and infection. Following such events, regulation of glucose transporters has been observed, which contributes to [^{18}F]FDG uptake in areas of infection and inflammation, as well as in regenerative and traumatic processes. Readers should be aware of [^{18}F]FDG's limitations; for instance, recent fractures may result in increased [^{18}F]FDG uptake, but careful evaluation of CT is mandatory for differential diagnosis.

Increased [^{18}F]FDG uptake may be challenging, and differential diagnoses include, infection, inflammation, bone tumors, metastases, surgical reinterventions, fractures, osteophytes, enthesopathies, or degenerative changes, among others (Figure 10). In a healthy musculoskeletal system, no physiological [^{18}F]FDG uptake should be visible.[26] In early stages of the degenerative process, the intervertebral discs are dehydrated and consequently the

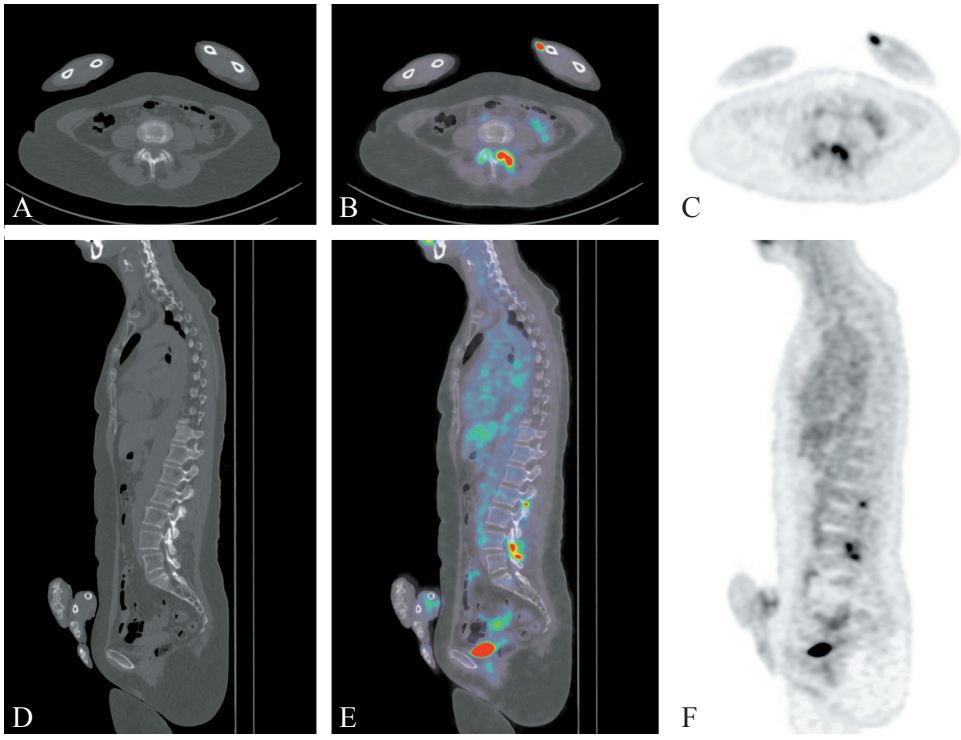

Figure 10.—A 66-year-old female presenting with fever and lumbosacral pain. [18F]FDG PET/CT reveals intense uptake at the left L4-L5 facet joint extending into the periarticular tissues, with lesser uptake observed at the right L4-L5 and left L2-L3 facet joints. CT images demonstrate erosions at the facet joints. Findings are consistent with multilevel septic facet joint arthritis. Axial CT (A) PET/CT fusion (B) and PET (C) images. Sagittal CT (D) PET/CT fusion (E) and PET (F) images.

vertebral discs are subjected to repeated micro-impacts. This evokes an inflammatory reaction resulting in fibrous tissue formation and oedema that is mainly present at the adjacent vertebral endplates (known as Modic I changes; Figure 9C), and which is responsible for the increased [18F]FDG uptake and gadolinium enhancement, also present in infectious spondylodiscitis.

Patients with suspected or proven infection are usually treated with antibiotics. A longer duration of antibiotic treatment may be associated with a lower likelihood of finding an infectious focus on [18F]FDG PET/CT, but the literature on this issue is contradictory.[27] According to the EANM guidelines, studies should ideally be conducted before starting antibiotic treatment or as soon as possible afterwards, ensuring no delay in the commencement of treatment. [18F]FDG PET/CT scans performed during antibiotic therapy in patients with suspected infection require careful interpretation. A reduction in intensity and alterations in the distribution pattern of [18F]FDG uptake in known infections are parameters used to evaluate the effectiveness of antibiotic therapy. In all cases involving microbiologically confirmed infections where patients were receiving appropriate antibiotic treatment, [18F]FDG PET/CT has accurately identified areas of increased uptake consistent with infection, without yielding false-negative results. Positive findings were observed in a small subset of patients with severe infection who failed to respond even after a month of adequate antibiotic treatment.[11, 19] The optimal duration of antibiotic-free time prior to image-guided biopsy has not been established.

After surgery, non-specific [18F]FDG uptake may be detected in healing tissues and may continue for months after surgery.

False-negative results are possible in case of infection with low-virulence bacteria, previous antimicrobial therapy, epidural abscesses or extensive vertebral arthrodesis.

The presence of spinal hardware may provoke an inflammatory response, resulting in increased [18F]FDG uptake around noninfected implants, confounding the interpretation of the study. It's essential to review PET images both with and without attenuation correction, especially if the patient has vertebral osteosynthesis material. The presence of metallic implants or devices causes CT artefacts and degrades image quality that may lead to false-positive uptake interpretations.[2] Other false positive cases are often related to post-surgical changes or spinal metastases.

Dual time-point imaging may help differentiate malignant disease from infection and inflammation. Given the variations in glucose metabolism, [18F]FDG uptake typically remains elevated for a longer duration in malignant

TABLE III.—*Summary of [18F]FDG PET/CT pitfalls imaging in inflammation and infections.*

Parameter	False positive	False negative
Spine infections	Inflammatory or degenerative disc diseases Bone tumors or metastases Recent vertebral fractures Post-surgical inflammation	Low-virulence bacterial infections Previous antimicrobial treatment Epidural abscesses Extensive arthrodesis

lesions compared to infections or inflammatory processes. This difference can be observed by performing [18F]FDG PET/CT scans at two separate time intervals. Although dual time-point imaging can enhance the specificity of elevated [18F]FDG uptake in certain cases – such as distinguishing between chronic inflammatory lesions in sarcoidosis and malignancy – the differentiation may still prove challenging.[27, 28]

Considering these factors may enhance the diagnostic accuracy of [18F]FDG PET/CT in spondylodiscitis cases, by reducing the risk of misinterpretation (Table III).

[18F]FDG PET/CT false positives images: post-surgical inflammation, degenerative changes, and low-grade infections can mimic spondylodiscitis.

[18F]FDG PET/CT false negatives images: result from prior antibiotic use or infections with low virulence organisms.

Imaging to guide biopsy

Image-guided biopsy is a crucial diagnostic tool for spondylodiscitis, allowing definitive diagnosis through histopathological and microbiological analysis of infected tissue. Blood cultures, the first non-invasive diagnostic step, identify the causative pathogen in up to 60% of cases but have a lower yield in postoperative infections.

CT or fluoroscopy-guided biopsy is the primary invasive diagnostic method, achieving pathogen identification in up to 91% of cases. It is particularly important in postoperative spondylodiscitis, where blood cultures often yield negative results. The diagnostic success of biopsies depends on factors such as prior antibiotic use, clinical features, radiologist expertise, and sample quality. Biopsy specimens should undergo Gram staining, aerobic and anaerobic cultures, and histopathological analysis, which can distinguish between pyogenic and granulomatous diseases and identify tumor etiology if suspected. For patients with specific risk factors, cultures for mycobacteria, fungi, or Brucella, and molecular methods, can improve pathogen detection.[19]

[18F]FDG PET/CT could also assist spine/neuro surgeons for planning surgical interventions by delineating the extent of infection and identifying areas of abscess formation or spinal cord compression, thereby improving surgical debridement, and overall patient outcomes (Figure 11).[29]

Role in response to therapy

Assessing treatment response is essential in managing infectious diseases, but reliable non-invasive biomarkers remain a subject of debate. Therapeutic response is typically evaluated based on symptomatic improvement and normalization of inflammatory markers. Imaging studies are generally not recommended for patients showing a favorable clinical response, as follow-up primarily relies on clinical and biological assessments. There is insufficient evidence to support the routine use of [18F]FDG PET/CT for monitoring in clinical practice. Repeated imaging

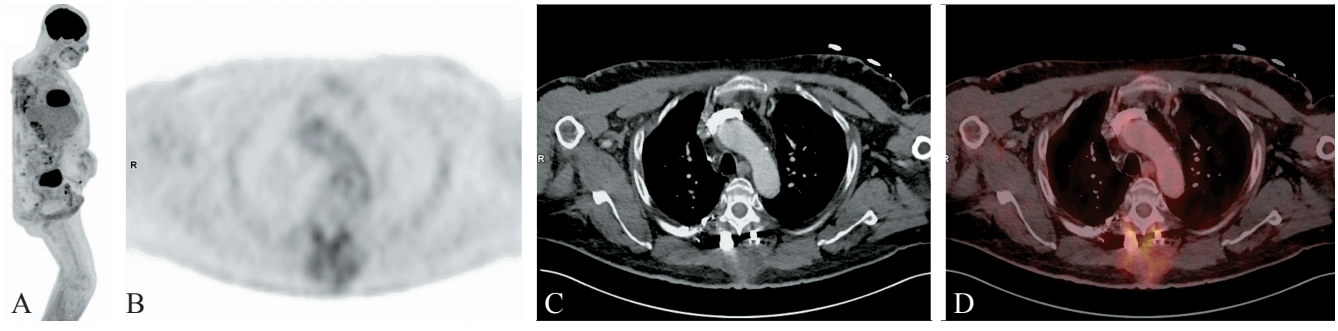

Figure 11.—MIP image (A) and axial PET (B), CT (C) and PET/CT fusion (D) images showing dorsal paravertebral abscess formation where [18F]FDG PET/CT helps guide biopsy in a Staphylococcus aureus infection.

should be reserved for cases of non-response to treatment or worsening symptoms. [^{18}F]FDG PET/CT should be performed just prior to the end of the prescribed course of antibiotics in patients who are not responding clinically. Scanning too early in the courses of treatment may lead to equivocal results because of a partial treatment response. A reduction in activity has been reported as early as 2 weeks after initiation of antibiotic treatment; however, a baseline [^{18}F]FDG PET/CT is needed which may not be available in clinical practice.[25]

Some studies that have evaluated the [^{18}F]FDG PET/CT to assess response to treatment have used different parameters, such as changes in SUV between baseline and follow-up imaging and treatment response after a decrease in SUV_{max} between the baseline and the follow-up studies (Figure 12, Figure 13).[23, 24, 30, 31] Elevated SUVs indicate increased metabolic activity, aiding in the identification of active infections. Serial [^{18}F]FDG PET/CT scans can track metabolic changes over time, enabling early detection of treatment failure or recurrence and distinguishing between treatment response and post-treatment changes. This information supports adjustments in antimicrobial therapy or surgical intervention.[29]

Some problems associated with quantifying response in infection include:

- in clinical practice, a baseline study is unlikely to have been done;
- limited data and poor correlation between serum biomarkers and imaging biomarkers;
- SUV cutoff value (threshold) not established;
- Delta SUV_{max} between two studies (baseline and follow-up) not established;

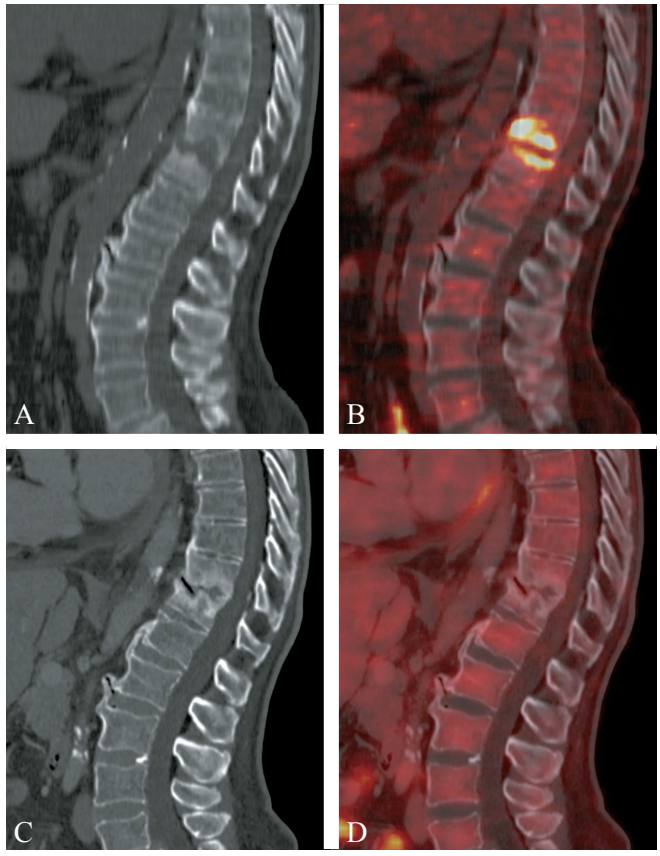

Figure 12.—Pre- and post-treatment [^{18}F]FDG PET/CT images of a 45-year-old man with fever and back pain. Initial [^{18}F]FDG PET/CT revealed increased ^{18}F-FDG uptake at the T11-T12 level (A: CT; B: Fused PET/CT), with spondylodiscitis confirmed by spinal biopsy identifying S. Aureus. After three months of antibiotic therapy, follow-up PET/CT showed no ^{18}F-FDG uptake (C: CT; D: Fused PET/CT), consistent with reactive post-treatment changes following successful management of spondylodiscitis.

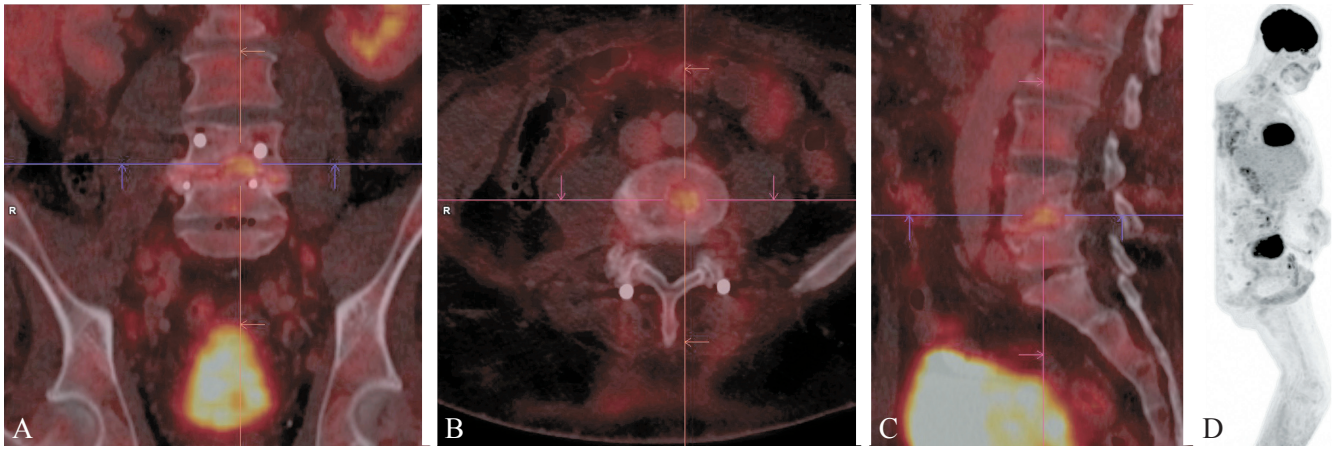

Figure 13.—Coronal (A), axial (B) and sagittal (C) fused PET/CT images and MIP image (D) showing re-infection after osteosynthesis L4-L5 due to spondylodiscitis.

• time point during the course of treatment when the follow-up scan must be done;

• definition of the region of interest is more difficult than with solid tumors;

• no clear guidelines on interpretation of mixed response (especially in tuberculosis).

[^{18}F]FDG-PET/CT may be considered for follow-up in patients with treatment non-response or worsening symptoms.

Reduction in [^{18}F]FDG uptake on PET/CT after treatment indicates a positive response, but residual activity in severely damaged joints may not signify ongoing infection.

Conclusions

The use of [^{18}F]FDG is rapidly expanding within the field of inflammation and infection imaging. Current literature demonstrates the excellent diagnostic performances of [^{18}F]FDG PET/CT in patients with suspected spondylodiscitis, especially in cases when MRI is unavailable, contraindicated or inconclusive. Numerous studies demonstrated the utility of [^{18}F]FDG PET/CT in the assessment of postoperative spine infections and some studies show a potential role for monitoring treatment response. Integrating [^{18}F]FDG PET/CT into the multidisciplinary management of spondylodiscitis offers significant potential to improve diagnostic accuracy, treatment planning, and patient outcomes. Effective collaboration between radiologists, nuclear medicine specialists, infectious disease experts, and neurosurgeons is critical to maxime the role of [^{18}F]FDG PET/CT in clinical decision-making, ultimately improving care for patients with spondylodiscitis.

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions
Edel Noriega-Álvarez has given substantial contributions to the conception or the design of the manuscript; Andor W. Glaudemans and Olivier Gheysens to analysis and interpretation of the data. All authors have participated to drafting the manuscript, Andor W. Glaudemans and Olivier Gheysens revised it critically. All authors read and approved the final version of the manuscript.

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