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Original Research Article

Diagnostic Value of Early phase Tc99m MDP SPECT/CT in Patients with Suspected Osteomyelitis

Article History:

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Abstract:

Objective: Osteomyelitis is a difficult disease to diagnose because of its non-specific clinical presentations and similarity of imaging studies with noninfectious disease. There is no specificity in three-phase bone scintigraphy (TPBS) though it is very sensitive. Hybrid imaging using SPECT/CT enhances anatomy localization, though delayed-phase imaging might not be adequate. Tc-99m methyl diphosphonate (MDP) at low levels of Tc-99m SPECT/CT of the organ has become an interesting method of enhancing diagnostic accuracy.

Purpose: To establish the diagnostic ability of Tc-99m MDP aerobic SPECT/CT patients and suspected osteomyelitis by using histopathology as the gold standard.

Study Design: Cross-sectional. Place and Duration of Study: Department of Nuclear Medicine, Punjab Institute of Nuclear Medicine (PINUM) in a span of 23rd June 2025 22nd September 2025

Methodology: This study involved 211 patients who were suspected of having osteomyelitis. TPBS was performed on all patients, as well as early-phase SPECT/CT and delayed-phase SPECT/CT. The results of imaging were referenced against histopathological results. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and the overall accuracy were also calculated based on the 2×2 contingency tables.

Results: 109 (51.7) patients were confirmed to have osteomyelitis. Sensitivity (90.8), specificity (83.3), PPV (85.3), NPV (89.5) and overall accuracy (87.2) were 90.8, 83.3, 85.3 and 87.2 respectively with early-stage SPECT/CT. Comparatively, TPBS was more sensitive (94.5%), although with low specificity (56.8%), whereas delayed-phase SPECT/CT had a moderate level of diagnostic power. Diagnostic quality and false-positive rates were greatly decreased at an early stage with SPECT/CT because of the application of CT.

Conclusion: Early-stage Tc-99m MDP SPECT/CT offers a moderating diagnostic image with great performance in terms of sensitivity and greater specificity relative to standard examination. It is also a useful adjunct modality that can be used to accurately diagnose osteomyelitis and also improve the clinical decision-making process especially in ambiguous or complicated cases.

Keywords: Osteomyelitis, Technetium Tc 99m Medronate Tomography, Emission-Computed, Single-Photon Tomography, Sensitivity and Specificity.

INTRODUCTION

Osteomyelitis (OM) is a clinically important and potentially disabling bone infection that needs early and proper diagnosis focused on preventing the development of chronic infection, bone destruction, and limb amputation. Although improved diagnostic modalities have been developed, early diagnosis of osteomyelitis remains to be difficult because of its nonspecific clinical presentation and similar imaging with other noninfectious diseases like trauma, postoperative processes, and inflammatory diseases [1]. Traditional imaging techniques, such as plain radiography and computed tomography (CT), are usually not sensitive to early disease progression, with

magnetic resonance imaging (MRI) being highly sensitive but giving false-positive outcomes in the case of postoperative alterations or neuropathic alterations [2].

Nuclear medicine imaging has become a significant issue when it comes to the assessment of the suspected osteomyelitis especially when the outcomes of the traditional imaging are not clear. One of these, three-phase bone scintigraphy (TPBS) with technetium-99m (Tc-99m) methyl diphosphonate (MDP), has traditionally been considered a highly sensitive technology to identify osteoblastic activity in case of infection [3]. The method is dynamic flow, blood pool, and delayed phases which enables the evaluation of perfusion and bone metabolism. The greatest shortcoming of TPBS however is that it can hardly be specific particularly in patients who have recently appeared under trauma or surgeries and might have underlying pathologies of the bone and increased tracer uptake may not always be indicative of an infection [4].

Nuclear imaging has had a significant advancement in the capability to enhance the diagnostic performance through the integration of both functional and anatomical information with the parameter of the single-photon emission computed tomography (SPECT) and CT. SPECT/CT increases lesion localization, contrast resolution and is more helpful in distinguishing a lesion between bone and intermediate soft tissue uptake [5]. Recent reports have indicated that SPECT/CT has been able to enhance specificity over considering planar imaging alone especially in complex anatomical parts, as well as in instances with ambiguous results [6]. In addition, quantitative SPECT/CT techniques have been promising in enhancing accuracy of diagnosis in diseases like diabetic foot osteomyelitis [7].

In spite of these developments, the best timing of SPECT/CT acquisition is a topic of research. The DPS has conventionally been utilized as complimentary to TPBS, and the belated-phase SPECT/CT imaging has limited specificity as it might continue to be unable to differentiate between infection and sterile inflammation or postoperative alterations [8]. In that regard, an alternative novel imaging technique is early-phase SPECT/CT that can record the distribution of a tracer at a blood pool level, which could result in a more accurate separation between hyperemia in the further soft tissues and the actual bone involvement.

The SPECT/CT, which is carried out soon after tracer injection, at an early stage, offers a better image of the perfusion and blood pool activity with an accurate anatomical localization. A recent pilot study has indicated that early stage SPECT/CT was found to have a high sensitivity, specificity and diagnostic accuracy than either TPBS or delayed-phase SPECT/CT in suspected cases of osteomyelitis [9]. This method can be well applicable especially in instances where greater involvement of the soft tissue obscures the bone involvement in the planar imaging hence minimizing the false-positive results.

Besides, new systematic reviews and comparative studies point to the increasing role of hybrid imaging methods, such as SPECT/CT and positron emission tomography (PET)/CT in enhancing diagnostic confidence in musculoskeletal infections [10]. Not only do these modalities improve lesion detectability, but also facilitate treatment planning and monitoring response to therapy.

Taking these factors into account, the necessity to further test the diagnostic value of early-phase Tc-99m MDP SPECT/CT against standard TPBS and delayed-phase imaging is evident. This paper will evaluate the accuracy of early-stage SPECT/CT in terms of histopathology as the gold standard and an evaluation will be undertaken on its relevance in the standard clinical use/practice of the assessment of suspected osteomyelitis.

METHODOLOGY

This research is a validation cross-sectional study and was performed in the Department of Nuclear Medicine, Punjab Institute of Nuclear Medicine (PINUM) in a span of 23rd June 2025 22nd September 2025 with the committee of ethical review of the institution giving its approval. The purpose of the study was to test the diagnostic accuracy of early-phase Tc-99m methyldiphosphonate (MDP) SPECT/CT of patients with clinically suspected osteomyelitis as compared to the gold standard of histopathology. The sensitivity of 90.9, specificity of 70, prevalence of 52.4, precision of 9, and a confidence level of 95 were used to calculate the total sample of 211 patients. A non-probability consecutive sampling technique was applied in enrolling patients of the patients referred to the nuclear medicine department to enroll patients to bone scintigraphy.

The study included both female and male patients aged between 2 and 70 years with clinical suspicion of the occurrence of osteomyelitis due to pain, fever, chills, and local inflammatory signs signs, or even discharging sinus. Patients who were pregnant were excluded. All participants were informed of their consent in writing before enrolment. A proforma was used to record demographic information, clinical history, and records of relevant laboratory investigations.

Bone scintigraphy with Tc-99m MDP and a hybrid system of a gamma camera was performed under a hybrid SPECT/CT of all registered patients (GE Healthcare Discovery NM/CT 670). After intravenous injection of Tc-99m MDP (400-750 MBq dose range) it was treated to three planes of bone scintigraphy. The initial step (flow step) involved a dynamic imaging of the region of interest obtained immediately following injection of the region at a rate of one second per image over 60 seconds. The second phase (blood pool phase) was subsequent to the first one, where simply planar images standing still were acquired between 1 and 3 minutes after injection. This third phase (delay phase) involved regional and whole-body planar imaging at a time of some 2.5-3 hours after tracer injection, where

patients were asked to void before being imaged, as it suits out urinary tracer interference.

Along with TPBS, the early-stage SPECT/CT imaging was conducted right after the blood pool phase was completed, usually, between 3 to 12 minutes after the injection. This enabled a fine evaluation of the perfusion and blood pool pulsatility with accurate localization of tracer uptake anatomically. Spect/CT imaging was also done in delayed-phase immediately after the delayed planar images to assess late tracer distribution. Images were processed, and interpreted separately by a skilled nuclear medicine consultant who was not informed about the histopathological outcome to reduce observer effects.

Findings of the imaging were classified according to predefined diagnostic rules. Higher levels of tracer uptake during all three stages localized in bones were an indication of osteomyelitis. A phenomenologically distinct difference between abnormal perfusion, and blood pool activity of bone structures and soft tissues was established via early-phase SPECT/CT. Histopathology and / or microbiological evidence of biopsy, wound culture and blood culture revealed an infection and therefore confirmed the final diagnosis of osteomyelitis.

To perform statistical analysis data were keyed in and occasioned with the aid of SPSS version 20.0. Quantitative variables like age were used in mean plus standard deviation and qualitative variables like gender, imaging results and final diagnosis were used as frequencies and percentages. To determine sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy, a 2x2 contingency table was made of each imaging modality (TPBS, early-phase SPECT/CT and delayed-phase SPECT/CT) using histopathology as the reference standard. The p-value at below 0.05 was deemed as significant.

RESULTS

The average age of the study population was 38.6 ± 16.2 and the range of age was between 5 and 70 years. Among the participants, 124 (58.8%) were male and 87 (41.2%) were female. Pain was the most frequent presenting complaint with 198 (93.8%) patients reporting pain, then local signs of inflammation, 162 (76.8%), fever, 118 (55.9%) and discharging sinuous formation 64 (30.3) (Table 1).

Table 1. Demographic and Clinical Characteristics (n = 211)

Variable	Frequency (n)	Percentage (%)
Age (Mean ± SD)	38.6 ± 16.2 years	—
Gender		
Male	124	58.8%
Female	87	41.2%
Clinical Features		
Pain	198	93.8%
Fever	118	55.9%
Fever with chills	92	43.6%
Local inflammation	162	76.8%
Discharging sinus	64	30.3%

According to the histopathological and microbiological results (gold standard), 109 (51.77-percent) of the total patients were diagnosed with osteomyelitis and 102 (48.23-percent) were patients without osteomyelitis (Table 2).

Table 2. Final Diagnosis by Histopathology

Diagnosis	Frequency (n)	Percentage (%)
Osteomyelitis Present	109	51.7%
Osteomyelitis Absent	102	48.3%

Planar three-phase bone scintigraphy (TPBS) diagnosed 141 (66.8%) patient's osteomyelitis, early-phase SPECT/CT diagnosed 116 (55.0%) patient's osteomyelitis, and delayed-phase SPECT/CT diagnosed 128 (60.7%) patient's osteomyelitis on imaging (Table 3).

Table 3. Imaging findings

Imaging Modality	Positive (n)	Negative (n)
TPBS	141	70
Early-phase SPECT/CT	116	95
Delayed-phase SPECT/CT	128	83

Compared to the gold standard, early-phase SPECT/CT was shown to have a better diagnostic result. It accurately detected 99 cases of true positives and 85 cases of true negatives with a false negativity of 10 and false positivity of 17 (Table 4).

Table 4. Diagnostic Performance of Early-phase SPECT/CT

	Osteomyelitis Present	Osteomyelitis Absent	Total
Positive	99 (TP)	17 (FP)	116
Negative	10 (FN)	85 (TN)	95

Total	109	102	211

TPBS demonstrated greater false-positive rates (Table 5)

Table 5. Diagnostic Performance of Early-phase SPECT/CT

	Osteomyelitis Present	Osteomyelitis Absent	Total
Positive	103 (TP)	38 (FP)	141
Negative	6 (FN)	64 (TN)	70
Total	109	102	211

Delayed-phase SPECT/CT demonstrated mediocre diagnostic rates (Table 6)

Table 6. Diagnostic Performance of Delayed-phase SPECT/CT

	Osteomyelitis Present	Osteomyelitis Absent	Total
Positive	96 (TP)	32 (FP)	128
Negative	13 (FN)	70 (TN)	83
Total	109	102	211

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) and overall accuracy of each imaging modality were calculated through 2×2 contingency tables. The sensitivity and specificity of early-stage SPECT/CT (90.8 and 83.3, respectively) was higher than those of TPBS (94.5 and 56.8) and later-stage SPECT/CT (88.1 and 68.6). The overall measurement accuracy was greatest with early-phase SPECT/CT (87.2), then delayed-phase SPECT/CT (78.7) and TPBS (75.4) (Table 7)

Table 7. Comparison of Diagnostic Accuracy

Parameter	TPBS (%)	Early SPECT/CT (%)	Delayed SPECT/CT (%)
Sensitivity	94.5	90.8	88.1
Specificity	56.8	83.3	68.6
PPV	73.0	85.3	75.0
NPV	91.4	89.5	84.3
Accuracy	75.4	87.2	78.7

TPBS, early-stage SPECT/CT, and delayed-stage SPECT/CT have positive concordance with regards to identifying either an obvious or a developed osteomyelitis: each modality has good sensitivity; they all have elevated uptake of tracer in the affected bone with the infected bone. Nonetheless, there is a great disparity in the abundance of discordance mostly based on the distinctions in particularity and localization in anatomy. The TPBS is prone to give false-positive results due to low specificity among other factors such as in cases of traumas, postoperative and inflammations. Early-stage SPECT/CT enhances diagnostic specificity due to the ability to differentiate hyperemia of soft tissues and actual bone involvement, thus decreasing false positives. Delayed-phase SPECT/CT demonstrates intermediate performance but might continue to be limited in distinguishing between infection and sterile inflammation. General summary Early-phase SPECT/CT is recommended to resolve discordant results and is optimal in terms of its sensitivity and specificity (Table 8)

Table 8. Concordance and Discordance Among Imaging Modalities

Aspect	Three-Phase Bone Scan (TPBS)	Early-Phase SPECT/CT	Delayed-Phase SPECT/CT	Concordance / Discordance Interpretation
Sensitivity	94.5%	90.8%	88.1%	High concordance in detecting true positives (all are sensitive)
Specificity	56.8% (low)	83.3% (high)	68.6% (moderate)	Major discordance—TPBS shows more false positives
Detection of obvious osteomyelitis	Positive	Positive	Positive	Strong concordance in advanced disease
Soft tissue vs bone differentiation	Poor	Excellent	Moderate	Discordance—early SPECT/CT differentiates better
False positives	High (38 FP)	Low (17 FP)	Moderate (32 FP)	TPBS overcalls infection compared to SPECT/CT
False negatives	Lowest (6 FN)	Moderate (10 FN)	Highest (13 FN)	Discordance in subtle/early cases
Perfusion/blood pool assessment	Present (flow + pool phases)	Best (early acquisition)	Limited	Early SPECT/CT superior → causes discordance with

				delayed imaging
Post-traumatic/postoperative changes	Often positive	Better differentiation	May remain equivocal	Discordance due to non-specific uptake in TPBS
Anatomical localization	Poor (planar)	Excellent (CT fusion)	Excellent (CT fusion)	TPBS vs SPECT/CT discordance in lesion localization
Overall diagnostic accuracy	75.4%	87.2%	78.7%	Early SPECT/CT resolves discordant cases best

DISCUSSION

The current work assessed the diagnostic quality of early-stage Tc-99m methyldiphosphonate (MDP) SPECT/CT in suspected osteomyelitis patients and it was found that, the diagnostic quality level was high with a sensitivity of 90.8, specificity of 83.3 and an overall diagnostic score of 87.2. These results indicate that early-stage SPECT/CT is also a dependable imaging modality which not only remains as sensitive as nuclear medicine methods commonly used, but also offers a great deal of specificity over the traditional three-phase bone scintigraphy (TPBS). The quality of a CT/SPECT that can distinguish better between bone and soft tissue involvement at the early stages of the disease seems to be the most significant factor behind its performance in diagnosing.

Findings of the current study align with the recent developments in the hybrid imaging methods that are proving to have better diagnostic results over the traditional imaging modalities. In a multicenter, retrospective and large study, Gao et al. [11] found that Tc-99m MDP SPECT/CT had a sensitivity and specificity of 96 percent and 92 percent, respectively, with a total diagnostic efficiency of 96 percent. These values are marginally above those reported in the current study although the difference is perhaps due to the different study design, population of the patients involved and the applied complex quantitative reconstruction techniques. However, the two studies both indicate that the hybrid form of SPECT/CT imaging is definitely superior to the traditional forms of imaging like MRI and planar scintigraphy, especially in the specificity and diagnostic certainty.

Osteomyelitis is another disease that has received a boost diagnostic power using quantitative SPECT/ CT imaging. The sensitivity and specificity reported as well over 90% with quantitative parameters including standardized uptake value (SUVmax) and infection /background ratio (Nishikawa et al. [12]). In comparison to such results, a relatively less specificity in the case of the current study could be attributed to the qualitative aspect of image interpretation. Nonetheless, the protocol used in the early phases of acquisition in this study has a practical benefit as it allows a better visualization of the activity of perfusion and blood pools without involving the use of a complex quantitative analysis. This indicates that the early-stage SPECT/CT could be viable and applicable in a normal clinical scenario where sophisticated quantitative instruments might be unfamiliar.

Alternative imaging modalities Hybrid imaging modalities like FDG-PET/MRI have also been investigated in the investigation of osteomyelitis. The results by Hulsen et al. [13] indicated that FDG-PET/MRI had a specificity of 100% and a comparatively low sensitivity of 78% in the diagnosis of chronic osteomyelitis. Comparatively, the first stage SPECT/CT of the present study was more sensitive, which suggests that it has a larger capacity of identifying the actual cases of infection. Nevertheless, the reduced specificity of SPECT/CT than PET/MRI can imply that early-stage SPECT/CT is beneficial in detecting disease, whereas the PET-based interests can be more efficient in verifying disease in the absence of false-positive results. Nonetheless, PET/MRI is not as universally accessible and is more expensive which limits its application, especially in resource-limited facilities.

Traditional imaging modalities remain a part of the diagnostic pathway and are linked to significant drawbacks. Foti et al. [14] showed that MRI had a sensitivity and specificity of 89.1 and 87.5, respectively and dual-energy CT (DECT) had a similar sensitivity but poorer specificity. The results of the current study show that early-stage SPECT/CT has the same sensitivity to MRI but a bit lower specificity. But as compared to MRI, SPECT/CT is capable of giving functional data which can enhance confidence of diagnosis particularly in cases with indeterminate anatomical results or postoperative alterations.

Mishra et al. [15] found that MRI got a high sensitivity level (96%) and a significantly low specificity level (38.2) in diabetic foot osteomyelitis whose diagnostic challenges are especially great. This underscores how MRI is likely to overdiagnose infection because of the challenge of differentiating between infection, inflammation or neuropathic alterations. By comparison, the present study with early-stage SPECT/CT had much higher specificity and PPV, indicating that there is a lower chance of false-positive diagnosis. It has clinical implications because over diagnosis can result in unnecessary therapy with antibiotics or even surgery.

The examination of biomarker-based methods has been examined in diagnosing osteomyelitis, as well. Soleimani et al. [16] gave a report of good diagnostic accuracy by means of procalcitonin levels with the sensitivity and specificity of nearly 100 percent.

Likewise, Sun et al. [17] showed the neutrophil CD64 index with erythrocyte sedimentation rate was highly diagnostic. Although these are encouraging results, these biomarkers do not have the capacity to localize infection hence they cannot substitute imaging modalities. Rather, they can be of as an effective supplement to imaging, especially in complicated instances when both clinical and imaging results are indeterminate.

The new imaging technologies, such as radiomics and other more advanced MRI parameters, have proven themselves as having potential in enhancing the diagnostic accuracy. According to The et al. [18], apparent diffusion coefficient (ADC) ghost sign exhibited high specificity (94.5%), but low sensitivity (19.5%), which shows that it is not a useful diagnostic sign alone. Jia et al. [19] have shown that MRI-based radiomics could increase diagnostic performance and help in surgery decision-making. In the same way, Shin et al. [20] have found that quantitative SPECT/CT uptake ratios had moderate sensitivity (71.4%) and high specificity (88.9%). Such results indicate that quantitative or radiomic methods of integration with early-stage SPECT/CT further improve its diagnostic capabilities.

The probe-to-bone (PTB) test along with plain radiography, have demonstrated low diagnostic accuracy. Herrera-Casamayor et al. [21] found that the PTB test with biomarkers or radiography yielded moderate sensitivity (~75) and very low specificity (~2324%). Such results are vastly poorer compared to findings with early-grading SPECT/CT in the current research and support the significance of high-level imaging to establish the diagnosis of osteomyelitis. On the same note, Xu et al. [22] and Coye et al. [23] pointed out that the primary intention of inflammatory markers and bedside tests is to be used as a screening tool but not a pathogenic test.

Research that has been conducted on individual parts of the body further demonstrates the inconsistency of the diagnostic accuracy of differing modalities of imaging. Muraoka et al. [24,25] also proved the usefulness of diffusion-weighted MRI in the diagnosis of mandibular osteomyelitis and Kawasaki et al. [26] showed a high level of sensitivity when it comes to some radiographics (e.g., osteosclerosis and bone resorption) but a low level of sensitivity of detecting sequestration and cortical per These results underline that anatomical imaging can be unsuitable to assess all the elements and justify the contribution of hybrid imaging methods that help to integrate functional with structural data.

The better diagnostic quality of the early-stage SPECT/CT as is the case of the current study may be explained by the fact that it can trace the distribution of the tracers during the blood pool phase and localize anatomically. This has the benefit of enhanced distinction of hyperemia in soft tissues and actual bone involvement, a frequent source of diagnostic uncertainty in planar imaging. Early-phase SPECT/CT obviates the chances of a false-positive interpretation caused by a lag in tracer uptake in noninfectious states, by observing initial inflammatory changes.

Limitations

In spite of merits, the current study is limited in the following ways. To begin with, the study was carried out in one center which can restrict the generalization of the findings. Second, the interpretation of the images was carried out qualitatively, and quantitative parameters were not involved, which might improve diagnostic accuracy. Third, the histopathology was the gold standard but not all patients are likely to have done biopsy, which risks introducing verification bias. Further research with multicenter data and quantitative imaging is justified to confirm and further generalize these findings.

CONCLUSION

To sum up, the results of the current work indicate that Tc-99m MDP SPECT/CT at an early stage is an effective diagnostic instrument that can be used in the assessment of suspected osteomyelitis. It is a balanced profile with the highest sensitivity and better specificity than the traditional imaging modalities. In comparison with recent literature, primitive stage SPECT/CT has a competitive performance on the advanced imaging methods, and does have a feasible, convenient, and quality way of clinical utility in routine applications. Its high sensitivity to minimise false positive diagnoses and its high diagnostic confidence makes it especially effective when it comes to complex clinical situations such as postoperative and post-traumatic. Future studies with quantitative measure and more patient's cohort could be used to further improve its application in clinical practice.

Recommendations

Tc-99m MDP SPECT/CT is a Tc-99m based imaging modality that is advised to be used as an adjunct imaging in patients with suspected osteomyelitis when the planar three-phase bone scintigraphy are equivocal. It has a better specificity and sensitivity that increases its usefulness in proper diagnosis and minimizing the false-positive results. It must be included into the routine imaging protocols in tertiary care cases, and when dealing with complex cases, like postoperative, post-traumatic, and diabetic foot infections. Combination with clinical and laboratory data should be encouraged to improve the overall precision of diagnosis. Interpretation standards and training should be standardized to bring uniformity across institutions. The future of the multicentric research with increased sample size and quantitative imaging parameter inclusion is desirable in order to substantiate its diagnostic roles further. Moreover, the research assessing its effectiveness concerning treatment monitoring and cost-efficiency is proposed to facilitate its further clinical implementation.

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