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ORIGINAL ARTICLE

Hybrid imaging with 99mTc-WBC SPECT/CT to monitor the effect of therapy in diabetic foot osteomyelitis

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Abstract

This study sought to assess the utility of monitoring response to treatment of diabetic foot osteomyelitis (DFO) with Tc-99m WBC-labelled single photon emission computed tomography (SPECT/CT) imaging. This is a retrospective cohort study of 20 patients with DFO with sequential Tc-99m WBC-labelled SPECT/CT imaging. Radiologic findings of osteomyelitis were evaluated and imaging results were correlated with clinical outcomes subtracted from chart review. Successful treatment of osteomyelitis was defined by wound healing and/or lack of re-admission for bone infection of the same site within 1 year. The sensitivity, specificity, positive predictive value and negative predictive value of SPECT/CT to determine osteomyelitis treatment remission were 90%, 56%, 69% and 83%, respectively. Tc-99m WBC-labelled SPECT/CT imaging may be useful to help determine treatment outcomes for DFO.

Introduction

Diagnosis of osteomyelitis in diabetic foot infections (DFIs) is challenging; more challenging, however, is monitoring the response to treatment and resolution of bone infection. Currently, the duration of antibiotic therapy is largely based on convention rather than reliable and repeatable clinical criteria. The lack of a more definitive measurement of response is one of the main barriers in determining when therapy should be stopped or prolonged. Magnetic resonance imaging (MRI) is one of the most common imaging techniques used for the initial diagnosis of osteomyelitis. Unfortunately, if there has been a bone surgery, trauma or fracture in combination with the bone infection, local bone marrow oedema may persist for many months, rendering MRI unreliable for monitoring resolution (1,2).

Radiolabelled white blood cell (WBC) imaging seems to be more specific than MRI in detecting an active infection in the diabetic foot (3); however, separating soft tissue from bone involvement is difficult because of low spatial resolution and sensitivity (4). With the combination of single photon emission computed tomography (SPECT/CT) localisation of labelled WBC and high-resolution diagnostic-quality CT (Tc-99m-WBC SPECT/CT), improvements in both the assessment of local WBC scintigraphic intensity and depiction of cortical bone destruction can be gained (5). Using this process, images differentiate infection from inflammation in the diabetic foot, bone involvement is better visualised and absence of WBC accumulation may possibly demonstrate the resolution of infection after therapy. This hybrid imaging technique has previously been used to diagnose and stage diabetic foot osteomyelitis (DFO). Erdman *et al.* (6) incorporated key anatomic and physiologic parameters available from Tc-99 WBC SPECT/CT images in a computed Composite Severity

Key Messages

- SPECT/CT imaging might have a role in monitoring the success of therapy in diabetic foot osteomyelitis
- medical charts of 20 patients with diabetes who received sequential SPECT/CT imaging were reviewed for this study
- the sensitivity, specificity, positive predictive value and negative predictive value of SPECT/CT to determine osteomyelitis treatment remission were 90%, 56%, 69% and 83%, respectively

Index to assess the prognostic value in DFIs. Masked retrospective image interpretation was performed in 77 patients with suspected DFI-associated osteomyelitis and SPECT/CT was accurate at predicting therapeutic outcome. Therefore, SPECT/CT seems to offer many advantages without the limitations that MRI has in monitoring DFO.

Materials and methods

We retrospectively reviewed a 20-patient cohort with pre- and post-intervention Tc-99 WBC SPECT/CT in an attempt to determine if SPECT/CT imaging could be used to monitor response to treatment in patients with DFO. Electronic medical records of diabetic patients with clinically suspected DFO were retrospectively reviewed from November 2010 through November 2013 at the University of Texas Southwestern Medical Center, Dallas, Texas. Those patients who underwent both baseline and subsequent Tc-99m WBC SPECT/CT scans within 7 months after initial therapy (follow-up median 9·35 weeks, SD ±3·7) were included in our study ($n = 20$). Clinical failure of treatment of DFO was defined as failure of wound healing and/or re-admission for the same ulcer within 1 year from the initial intervention. Clinical and radiographic outcomes were then compared using the Fisher's exact test (two-sided).

Imaging methods

SPECT/CT images of the feet and ankles were acquired on a Siemens Truepoint scanner, low-energy high-resolution collimation, matrix size 256 × 256. SPECT parameters were of a matrix size of 128 × 128, no magnification, 360° rotation, step and shoot mode, 120 or 128 steps, 20 seconds per stop. CT-based reconstruction was performed of the images using 1·25 mm CT slices, OSEM reconstruction was performed with measured attenuation correction, OSEM iterations 2, maximum number OSEM subsets 10, smoothing filter Butterworth: cut-off frequency 0·5, order 10. The CT images were generated for the purpose of optimising the SPECT images and for anatomical correlation of SPECT findings.

Image interpretation

Sequential Tc-99m-labelled WBC SPECT/CT scans and reports were retrospectively reviewed by attending physicians experienced in clinical nuclear medicine and radiology. Interpreters used the conventional, osteomyelitis versus no osteomyelitis, criteria (WBC activity that abutted the bone cortex or extended into the marrow space was reported as osteomyelitis). Scintigraphic activity of each WBC focus was quantified via WBC activity in the region of the posterior tibial and/or peroneal vessels on the Maximum Intensity Projection image (6).

Results

Table 1 provides a summary of the characteristics of the included patients. The mean antibiotic duration, including intravenous and oral medications (for the total group), was 16·5 weeks and the duration ranged from 1 to 9 months.

All 20 patients had osteomyelitis of the foot at baseline, based on clinical evaluation and conventional interpretation of osteomyelitis on SPECT/CT. Table 2 shows the results of the sequential SPECT/CT scan compared with successful therapy based on clinical criteria (wound healing and no re-admission results in 1 year). One patient did not complete the 12 months follow-up period. The mean interval between the two sequential SPECT/CT images was 9·35 weeks, ranging from 1 to 6 months. The sensitivity and specificity of SPECT/CT to determine success of osteomyelitis treatment were 90% and 56%, respectively. The positive predictive value (PPV) and negative predictive value (NPV) were 69% and 83%, respectively. The correlation coefficient between the two outcomes (Fisher's exact test, two-sided) was 0·057.

Discussion

Monitoring resolution of infection in patients with DFO remains a challenge for the clinician, especially when other processes such as fractures, recent bone surgery and neuropathic joints are present. Currently, there are no proven laboratory tests or imaging studies to determine when antibiotic therapy for DFO can be discontinued (7). As a result, the duration of parenteral and oral antibiotic therapy reported in the medical literature varies widely from a few weeks to more than a year (8). An objective way to determine treatment success could reduce bacterial resistance and reduce antibiotic-related complications.

Recent studies have reported high sensitivity and specificity and positive and NPVs of SPECT/CT in diagnosing and monitoring musculoskeletal infection (9,10). The validity and reliability of ^{99m}Tc-WBC SPECT/CT to diagnose osteomyelitis were determined in a small pilot study by Przybylski *et al.* (11). Fourteen patients underwent SPECT/CT for suspected DFO; the sensitivity, specificity, PPV and NPV of Tc99mWBC-labelled SPECT/CT were 87·5%, 71·4%, 77·8% and 83·3%, respectively. Vouillarmet *et al.* (12) evaluated 29 patients to determine remission of DFO. Based on clinical outcomes, they reported that the sensitivity, specificity, PPV and NPV were 100%, 91·5%, 71·5% and 100%, respectively. In contrast, our results showed lower sensitivity, specificity, PPV and NPV of 90%, 56%, 69% and 83%, respectively. In our series, the PPV of Tc-WBC-labelled SPECT/CT imaging was about the same as that obtained when flipping a coin. If Vouillarmet *et al.* are correct, this approach could dramatically reduce the risk of prolonged antibiotic treatment, especially in patients with chronic kidney disease and multiple comorbidities.

There are several important limitations to the present study. Firstly, diagnosis of bone infection was not confirmed by either histopathology or culture of bone in all patients and may have yielded false-positive results (this was also the case with the study by Erdman *et al.*). Secondly, the retrospective design and the small number of patients in this study make the interpretation of results difficult. Thirdly, our selection of patients may have been biased for patients who were more likely to have had a complicated treatment course. The study was probably repeated in patients who failed to respond as expected to standard therapy and it was probably unlikely that the study was

Table 1 Patient characteristics

	SPECT/CT positive ($n=13$)	SPECT/CT negative ($n=7$)	Total ($n=20$)
Age, years, mean ± SD	53·3 ± 8·4	48·6 ± 9·6	51·7 ± 8·9
Sex, male (%)	11 (85)	7 (100)	18 (90)
Diabetes, type II (%)	11 (85)	7 (100)	18 (90)
Tobacco use			
Current (%)	5 (39)	1 (14)	6 (30)
Past (%)	2 (15)	1 (14)	3 (15)
Never (%)	6 (46)	5 (72)	11 (55)
Comorbidities			
PAD (%)	6 (46)	2 (29)	8 (40)
CKD (%)	7 (54)	2 (29)	9 (45)
CAD (%)	3 (23)	0 (0)	3 (15)
Hep (%)	1 (8)	0 (0)	1 (5)
Type of therapy			
IV (%)	1 (8)	1 (14)	2 (10)
Oral (%)	1 (8)	0 (0)	1 (5)
IV and oral (%)	4 (30)	3 (43)	7 (37)
IV, oral and PFA (%)	7 (54)	2 (29)	9 (48)
Duration of antibiotic therapy (weeks)	19·2 ± 12·5	11·5 ± 4·7	16·5 ± 10·9 (range 4–36)

CAD, coronary artery disease; CKD, chronic kidney disease; Hep, hepatitis; IV, intravenous antibiotics; Oral, oral antibiotics; PAD, peripheral artery disease; PFA, partial foot amputation; SD, standard deviation.

Table 2 SPECT/CT results compared with clinical success

		Clinical success*		
		Yes	No	
Sequential SPECT/CT	Positive	9	4	13
	Negative†	1	5	6
		10	9	19

SPECT, single photon emission computed tomography.
*Defined as wound healing and lack of re-admission within 1 year follow-up.
†One patient lost to follow-up.

ordered for patients who seemed to respond quickly to treatment.

Further prospective studies with larger numbers of patients are needed to determine the role of nuclear imaging in monitoring success of therapy in DFO. Factors that may contribute to inaccurate study results need to be identified in order to only use reliable studies to determine treatment success and failure.

References

1. Morrison WB, Schweitzer ME, Batte WG, Radack DP, Russel SM. Osteomyelitis of the foot: relative importance of primary and secondary MR imaging signs. *Radiology* 1998;**207**:625–32.
2. Ahmadi ME, Morrison WB, Carrino JA, Schweitzer ME, Raikin SM, Ledermann HP. Neuropathic arthropathy of the foot with and without superimposed osteomyelitis: MR imaging characteristics. *Radiology* 2006;**238**:622–31.
3. Devillers A, Moisan A, Hennion F, Garin E, Poirier JY, Bourguet P. Contribution of technetium-99m hexamethylpropylene amine oxime labeled leucocyte scintigraphy to the diagnosis of diabetic foot infection. *Eur J Nucl Med* 1998;**25**:132–8.
4. Capriotti G, Chianelli M, Signore A. Nuclear medicine imaging of diabetic foot infection: results of meta-analysis. *Nucl Med Commun* 2006;**27**:757–64.
5. Heiba SI, Kolker D, Mocherla B, Kapoor K, Jiang M, Son H, Rangaswamy B, Kostakoglu L, Savitch I, DaCosta M, Machac J. The optimized evaluation of diabetic foot infection by dual isotope SPECT/CT imaging protocol. *J Foot Ankle Surg* 2010;**49**:529–36.
6. Erdman W, Buethe J, Bhore R, Ghayee HK, Thompson C, Maewal P, Anderson J, Klemow S, Oz OK. Indexing severity of diabetic foot infection with 99m Tc-WBC SPECT/CT hybrid imaging. *Diabetes Care* 2012;**35**:1826–31.
7. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, Deery HG, Embil JM, Joseph WS, Karchmer AW, PInzur MS, Senneville E. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 2012;**54**:e132–73.
8. Embil JM, Rose G, Trepman E, Math MC, Duerksen F, Simonsen JN, Nicolle LE. Oral antimicrobial therapy for diabetic foot osteomyelitis. *Foot Ankle Int* 2006;**27**:771–9.
9. Horger M, Eschmann SM, Pfannenberg C, Storek D, Dammann F, Vonthein R, Claussen CD, Bares R. The value of SPECT/CT in chronic osteomyelitis. *Eur J Nucl Med Mol Imaging* 2003;**30**:1665–73.
10. Filippi L, Schillaci O. Tc-99m HMPAO-labeled leukocyte scintigraphy for bone and joint infections. *J Nucl Med* 2006;**47**:1908–13.
11. Przybylski MM, Holloway S, Vyce SD, Obando A. Diagnosing osteomyelitis in the diabetic foot: a pilot study to examine the sensitivity and specificity of Tc99m white blood cell-labelled single photon emission computed tomography/computed tomography. *Int Wound J* 2014; ISSN: 1742-4801.
12. Vouillarmet J, Morelec I, Thivolet C. Assessing diabetic foot osteomyelitis remission with white blood cell SPECT/CT imaging. *Diabet Med* 2014;**31**:1093–9.