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Diagnostic Value of Dynamic Contrast-Enhanced MRI in Identifying Diabetic Foot Osteomyelitis Requiring Aggressive Treatment

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Abstract

Objective: Early identification of diabetic foot osteomyelitis (DFO) patients who will fail antibiotic therapy is critical for timely escalation to surgical or revascularization treatment. Dynamic contrast-enhanced MRI (DCE-MRI) quantifies tissue perfusion through time–signal intensity curves (TICs) and may provide a prognostic marker of treatment outcome beyond conventional morphological MRI.

Materials and Methods: In this prospective study, 21 patients with type 2 diabetes and clinically suspected foot osteomyelitis referred to the Yazd Diabetes Research Center underwent conventional MRI and DCE-MRI at Shahid Sadoughi Hospital. A 13-series dynamic acquisition was obtained over 270 seconds after intravenous gadolinium, and TICs were classified as F (rapid early enhancement), S (slow early enhancement), or O (weak or absent enhancement). Patients then received approximately six weeks of standard antibiotic therapy and were classified as treated (n= 8, 38%) or untreated/failed (n= 13, 62%) by clinical criteria.

Results: All 8 treated patients (100%) showed an F-type curve, whereas 10 of 13 untreated patients (77%) showed S- or O-type curves; the association between curve type and outcome was significant (P= 0.003). Treated patients had significantly higher maximum signal intensity (306.00 (± 28.55) vs. 157.38 (± 90.25), P= 0.001), higher average signal intensity (224.88 (± 28.78) vs. 109.31 (± 70.27), P< 0.001), and shorter time to bolus peak (38.13 (± 2.85) vs. 63.10 (± 13.90) seconds, P< 0.001).

Conclusion: F-type TIC and higher perfusion parameters on DCE-MRI were strongly associated with successful antibiotic therapy, whereas S- and O-type curves predicted treatment failure.

Keywords: Diabetic foot ulcer, Osteomyelitis, DCE-MRI, Time–signal intensity curve

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Introduction

Diabetes mellitus is among the most prevalent metabolic diseases worldwide, and its musculoskeletal complications, most notably diabetic foot ulcers, are a leading cause of morbidity and lower-extremity amputation. The combination of hemodynamic abnormalities, vasculopathy and neuropathy, and impaired tissue repair means that a substantial proportion of patients ultimately require amputation despite best medical care (1,2). Early and effective diagnosis and treatment can prevent the severe consequences of soft-tissue and bone infection in diabetic foot ulcers (3).

Systemic antibiotic therapy is the first-line treatment for mild-to-moderate (grade 1–3) diabetic foot ulcers, but its success depends on adequate hemodynamic status of the affected limb: impaired tissue perfusion prevents accumulation of antibiotics in infected tissue and leads to treatment failure (4,5). Knowledge of limb perfusion therefore helps clinicians decide between revascularization procedures, intensified medical therapy, or more invasive surgical management aimed at limb preservation (6).

Conventional MRI is the modality of choice for identifying the location and extent of osteomyelitis, with focal marrow signal change on T1- and fat-suppressed T2-weighted sequences as the hallmark findings (7–9). A recent systematic review and meta-analysis reported pooled sensitivity of 93% and specificity of 75% for MRI in diagnosing diabetic foot osteomyelitis, indicating that specificity in neuropathic or Charcot feet remains a clinical challenge (10-11). With advances in scanner hardware and post-processing software, dynamic contrast-enhanced MRI (DCE-MRI) has been increasingly applied to characterize tissue perfusion and microvascular permeability. Serial images acquired at fixed intervals after contrast injection allow construction of a time–signal intensity curve (TIC), from which pharmacokinetic parameters such as Ktrans and Ve, as well as descriptive indices (maximum signal intensity, average signal intensity, time to peak), can be derived (9).

The main purpose of this study was to evaluate the diagnostic and prognostic value of DCE-MRI-derived TIC patterns and perfusion parameters in identifying diabetic foot osteomyelitis patients who respond to antibiotic therapy versus those who require aggressive treatment.

Material and methods

Study design and patients:

This prospective study was conducted at the radiology department of Shahid Sadoughi Hospital, Yazd, in collaboration with the Yazd Diabetes Research Center. Patients with diabetic foot ulcers referred by treating clinicians were assessed clinically and paraclinically. Twenty-one patients with type 2 diabetes and clinically suspected foot osteomyelitis were enrolled.

Inclusion criteria were clinical suspicion of diabetic foot osteomyelitis, defined by local pain and fever or elevated CRP and/or ESR

Exclusion criteria were known pre-existing bone disease (e.g., fracture, tumor, Charcot arthropathy), incomplete MR examination, and contraindications to DCE-MRI such as significant renal or cardiac disease.

Of the 21 enrolled patients, 13 were male and 8 were female, with a mean age of 58.19 (± 6.96) years (range 47–73). The study was approved by the local ethics committee, and written informed consent was obtained from all patients.

MRI diagnostic criteria, Osteomyelitis was diagnosed on conventional MRI by focal decreased bone marrow signal intensity on T1-weighted images combined with increased marrow signal on fat-suppressed T2-weighted images relative to normal marrow, or focal marrow enhancement after contrast administration. Adjacent secondary findings-cellulitis, skin ulcers, soft-tissue abscesses, and sinus tracts strongly supported the diagnosis of osteomyelitis in the underlying bone.

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DCE-MRI acquisition and TIC classification, Patients first underwent conventional MRI according to the routine protocol. After intravenous injection of gadodiamide (Omniscan) at 0.1 mmol/kg (2.5 mmol vial per standard protocol), 13 dynamic series were acquired over 270 seconds at 20-second intervals. A region of interest of approximately 2.5 cm² was placed in the central area of the affected bone, and the time–signal intensity curve was generated using the scanner's basic software; other perfusion parameters were derived from these curves.

Curves were classified as: F (fast), rapid enhancement in the early phase; S (slow), slow early enhancement and O (absent/weak), very weak or no enhancement.

Treatment and outcome classification**:** After imaging, patients were referred back to their treating clinician for standard antibiotic treatment of osteomyelitis lasting approximately six weeks. Patients were then re-examined and classified as treated (successful outcome) or untreated (treatment failure) according to clinical criteria (resolution of local signs of infection, wound status, and inflammatory markers).

Variables and statistical analysis**:** Recorded variables were age, sex, duration of diabetes, duration of the current foot ulcer, osteomyelitis location, treatment outcome, TIC classification, maximum signal intensity (MSI), average signal intensity (SIA) and time to bolus peak (TBP).

Analyses were performed in SPSS version 18. Inter-observer variability of the permeability parameters was assessed with the intraclass correlation coefficient (ICC), and the distribution of continuous variables was tested with the one-sample Kolmogorov–Smirnov test. Descriptive statistics (means ± SD) were calculated, and treated versus untreated patients were compared using Student's *t*-test, with Levene's test for equality of variances reported. Sensitivity, specificity, and the area under the curve of TIC classification for predicting treatment failure were derived from the cross-tabulation. $P<0.05$ (two-sided) was considered statistically significant.

Ethical considerations

This study was approved by ethics committee of Shahid Sadoughi University of Medical Sciences, Yazd. (IR.SSU.MEDICINE.REC.1400.254).

Results

Patient characteristics and treatment outcome: The final analysis included 21 patients (13 male, 8 female; mean age 58.19 (± 6.96) years, range 47–73; mean diabetes duration 18 years). The most commonly involved bones were the metatarsals (11 cases), followed by the calcaneus (3), phalanges of the toes (2) and more than one bone (3). After approximately six weeks of standard antibiotic therapy, 8 patients (38%) were classified as treated and 13 (62%) as untreated (treatment failure) (Table 1).

The association between TIC type and treatment outcome was statistically significant ($P= 0.003$). All 8 treated patients (100%) had an F-type curve, whereas 10 of 13 untreated patients (77%) had S- or O-type curves. Conversely, an F-type curve identified successful antibiotic outcome with 100% sensitivity (8/8 treated) and 23% specificity (3/13 failures also showed F-type curves); an S- or O-type curve was 100% specific for treatment failure in this cohort (Tables 2-3).

In summary, treated patients showed significantly higher maximum and average signal intensities and a shorter time to bolus peak, consistent with preserved tissue perfusion, while untreated patients showed weaker and slower enhancement.

Discussion

The principal finding of this study is that the pattern of early enhancement on DCE-MRI the time–signal intensity curve was strongly associated with the outcome of antibiotic therapy in diabetic foot osteomyelitis.

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Table 1. Treatment outcome and TIC classification (n= 21)

TIC type	Treated (n= 8)	Untreated (n= 13)	Total
F (fast)	8 (100%)	3 (23%)	11 (52.4%)
S (slow)	0 (0%)	7 (54%)	7 (33.3%)
O (absent/weak)	0 (0%)	3 (23%)	3 (14.3%)
Total	8 (38.1%)	13 (61.9%)	21 (100%)

Table 2. Overall descriptive statistics of DCE-MRI parameters (n= 21)

Parameter	N	Min	Max	Mean	SD
Age (years)	21	47	73	58.19	6.96
Maximum Signal Intensity (MSI)	21	26	354	214.00	103.16
Average Signal Intensity (SIA)	21	13	263	153.33	80.99
Time to Bolus Peak (TBP, seconds)	18	35	81	52.00	16.39

Table 3. DCE-MRI parameters and age by treatment outcome

Parameter	Treated (n= 8)	Untreated (n= 13)	*P*-value
Age (years)	52.38 (± 4.37)	61.77 (± 5.76)	0.001
Maximum Signal Intensity (MSI)	306.00 (± 28.55)	157.38 (± 90.25)	< 0.001
Average Signal Intensity (SIA)	224.88 (± 28.78)	109.31 (± 70.27)	< 0.001
Time to Bolus Peak (TBP, seconds)*	38.13 (± 2.85) (n= 8)	63.10 (± 13.90) (n= 10)	< 0.001

Note:* Levene's test indicated unequal variances for MSI (F= 9.286, *P*= 0.007), SIA (F= 4.446, *P*= 0.048) and TBP (F= 11.628, *P*= 0.004); the Welch-corrected comparisons remained significant (MSI: t= 5.506, df= 15.516; SIA: t= 5.256, df= 17.238; TBP: t= −5.538, df = 9.936; all *P*< 0.001). TBP was available for 18 of 21 patients.

All patients whose curves were F-type (rapid early enhancement, indicating preserved perfusion) were successfully treated with antibiotics alone, whereas 77% of patients with S- or O-type curves failed medical therapy and presumably required more aggressive management such as revascularization or surgery.

This is biologically plausible. In osteomyelitis complicating a diabetic foot ulcer, antibiotic efficacy depends on delivery of the drug to the infected bone; impaired limb hemodynamics from peripheral arterial disease and microangiopathy reduces antibiotic accumulation and predicts failure (4-6). According to the literature on TIC patterns in osteomyelitis, limbs with normal hemodynamic function generally show F-type curves (rapid early enhancement), whereas delayed or absent enhancement indicates compromised perfusion (10-12). Our findings align with this framework and extend it by linking curve type to a hard clinical endpoint treatment outcome rather than diagnosis alone.

The quantitative perfusion indices reinforced the same signal: treated patients had roughly doubled the maximum and average signal intensities (MSI≈ 306 vs. 157; SIA≈ 225 vs. 109) and reached peak enhancement about 25 seconds earlier (≈ 38 vs. 63 seconds) than untreated patients (13-18). These differences were large and remained significant under Welch-corrected tests that account for the unequal variances observed between groups.

Our results should be interpreted alongside the broader diagnostic evidence. In a recent systematic review and meta-analysis of 29 studies, MRI achieved pooled sensitivity of 93% and specificity of 75% for diabetic foot osteomyelitis,with 18F-FDG-PET and 99mTc-HMPAO-labeled leukocyte scintigraphy offering higher specificity (11) (source S2). Because conventional MRI is sensitive but relatively non-specific particularly in neuropathic or Charcot feet (10,17) perfusion information from DCE-MRI may add functional characterization at low incremental cost, using the same examination without additional radiation.

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In our cohort, the S/O pattern was 100% specific for treatment failure, suggesting a potential triage role: patients with slow or absent enhancement might be considered earlier for revascularization or surgical pathways rather than prolonged, ultimately futile courses of antibiotics. Several cautions temper these conclusions. First, treated patients were significantly younger than untreated patients (52.4 vs. 61.8 years, *P*= 0.001) and older age is independently associated with peripheral arterial disease and poorer wound-healing outcomes. The present sample size did not permit multivariable adjustment, so part of the observed association between curve type and outcome could reflect confounding by age and vascular status. Second, TBP was missing in three patients and, with only three patients in the O category, subgroup inference for this pattern is unstable. Third, the outcome classification was clinical rather than biopsy-based; while this reflects real-world practice, it may have introduced outcome misclassification. Larger prospective studies with multivariable adjustment, and ideally direct comparison of DCE-MRI parameters against reference-standard bone biopsy, are required before TIC classification can be recommended for routine clinical decision-making.

Conclusion

Early performance of DCE-MRI and analysis of limb perfusion parameters in patients with diabetic foot ulcers and suspected osteomyelitis can predict the outcome of antibiotic treatment and identify patients at high likelihood of treatment failure. An F-type (rapid early enhancement) time–signal intensity curve, high maximum and average signal intensities, and short time to bolus peak characterize patients likely to respond to antibiotic therapy alone, whereas S- or O-type curves should prompt early consideration of revascularization or surgical management. DCE-MRI thus offers an accessible, radiation-free tool for risk stratification in diabetic foot osteomyelitis, pending validation in larger, confounder-adjusted cohorts.

Study limitations and declarations

The software available at the Shahid Sadoughi Hospital MRI facility could not compute diffusion-related pharmacokinetic parameters (Ktrans, Kep, Ve); only the time–signal intensity curve and its derived descriptive indices were available, and curve data required offline processing at another center because of software limitations (source S1). The small sample size (n= 21), with only three patients in the O category and missing TBP values in three patients, limited the statistical power and precluded multivariable adjustment for age and vascular status, which differed between outcome groups. Advanced age and reduced patient cooperation also complicated image acquisition and follow-up, and prolonged follow-up with incomplete cooperation may have led to attrition. Finally, the treatment outcome was classified clinically rather than by bone biopsy, the preferred reference standard.

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Conflict of Interest

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Authors' contributions

A.A. conceived and designed the study and drafted the manuscript; S.K.R.-R., R.N.M. and E.A. contributed to image acquisition and interpretation; N.N. contributed to study design and statistical analysis; M.S.A. contributed to data collection and manuscript revision. All authors read and approved the final manuscript.

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