X-Ray Versus Magnetic Resonance Imaging in Diabetic Foot Osteomyelitis: A Clinical Comparison

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Abstract: OBJECTIVE Radiographic imaging is an important diagnostic tool in diabetic foot osteomyelitis (DFO). It is unknown whether DFO cases diagnosed with conventional X-ray versus positive Magnetic Resonance Imaging (MRI) differ regarding epidemiology and treatment outcome. Theoretically, signs of inflammation on MRI without bone lesions might be easier to treat and predominate among selected clinical variables. METHODS Our clinical pathway for diabetic foot infections discourages the use of MRI for the diagnosis of DFO. We compared the epidemiology and therapy of non-amputated DFO with positive features on conventional X-ray, MRI, or both. Radiology specialists interpreted the images. The intraoperative aspect of bone during amputation and the results of bone cultures were considered gold standard for DFO diagnosis. RESULTS We prospectively followed 390 DFO episodes in 186 adult patients for a median of 2.9 years and performed 318 conventional X-rays (median costs 100 Swiss Francs; 100 US)$and47(47/390; 12\%)MRIscans(median800SwissFrancs; 800US)$. Among them, 18 episodes were associated with positive MRI findings but lacked bone lesions on X-ray. After debridement, the median duration of systemic antibiotics was 28 days for MRI-only episodes and 30 days for X-ray-positive cases (Wilcoxon-ranksum-test; p=0.26). The corresponding median numbers of surgical debridements were 1 and 1; and remission was achieved in 25% and 27%, respectively. In multivariate logistic regression analysis, MRI-only episodes did not alter remission rate (odds ratio 0.5, 95%CI 0.1-5.2). CONCLUSIONS According to our clinical pathway, DFO episodes with positive MRI findings only did not differ epidemiologically and did not influence the choice of therapy nor remission rate.

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X-Ray Versus Magnetic Resonance Imaging in Diabetic Foot Osteomyelitis: A Clinical Comparison

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Abstract: ***Objective:*** Radiographic imaging is an important diagnostic tool in diabetic foot osteomyelitis (DFO). It is unknown whether DFO cases diagnosed with conventional X-ray versus positive Magnetic Resonance Imaging (MRI) differ regarding epidemiology and treatment outcome. Theoretically, signs of inflammation on MRI without bone lesions might be easier to treat and predominate among selected clinical variables.

Methods: Our clinical pathway for diabetic foot infections discourages the use of MRI for the diagnosis of DFO. We compared the epidemiology and therapy of non-amputated DFO with positive features on conventional X-ray, MRI, or both. Radiology specialists interpreted the images. The intraoperative aspect of bone during amputation and the results of bone cultures were considered gold standard for DFO diagnosis.

Results: We prospectively followed 390 DFO episodes in 186 adult patients for a median of 2.9 years and performed 318 conventional X-rays (median costs 100 Swiss Francs; 100 US$) and 47 (47/390; 12%) MRI scans (median 800 Swiss Francs; 800US$). Among them, 18 episodes were associated with positive MRI findings but lacked bone lesions on X-ray. After debridement, the median duration of systemic antibiotics was 28 days for MRI-only episodes and 30 days for X-ray-positive cases (Wilcoxon-ranksum-test; p=0.26). The corresponding median numbers of surgical debridements were 1 and 1; and remission was achieved in 25% and 27%, respectively. In multivariate logistic regression analysis, MRI-only episodes did not alter remission rate (odds ratio 0.5, 95%CI 0.1-5.2).

Conclusions: According to our clinical pathway, DFO episodes with positive MRI findings only did not differ epidemiologically and did not influence the choice of therapy nor remission rate.

Keywords: Diabetic foot osteitis; X-ray; MRI; clinical associations; outcomes.

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INTRODUCTION

Recent studies failed to identify a minimal optimal duration of systemic antibiotic therapy for chronic osteomyelitis, especially in diabetic foot osteomyelitis (DFO)[1-8]. Since DFO might be clinically silent, radiologic studies remain important for diagnosis of DFO[9, 10], with multiple available modalities. Conventional X-ray falls behind, with an 80% specificity and a 60% sensitivity due to significant delay in the occurrence of abnormal findings[9]. In contrast, Magnetic Resonance Imaging (MRI) detects inflammation in advance of established bone alterations, with a 90% sensitivity and 80% specificity[9, 11, 12]. DFO with mild signs of inflammation on MRI might be easier to treat than cases with more advance disease with alterations on conventional X-ray[13]. However, this assumption remains unverified. We compared the epidemiology and management of DFO with positive MRI findings only versus infections with both X-ray and MRI anomalies. This assessment may lead to a different approach for patients presenting DFO with only MRI anomalies such as a reduced antibiotherapy duration or reduced surgical approach.

METHODS

The Geneva University Hospitals ran a clinical pathway for adult DFO patients between 2013 and 2018. As part of a hospital-wide quality program, patients were not required to provide informed consent for storing key clinical data. Patients admitted to the orthopedic department of Geneva University hospital for an episode of DFO were included prospectively and analyzed retrospectively. Our clinical pathway discouraged using MRI for diagnosis of DFO, but it was performed in unclear cases. The diagnosis of DFO was based on radiological findings using X-ray and/or MRI. . Radiology specialists interpreted all MRIs and most X-rays. Both were performed within two weeks of admission. Patients with radiologically proven osteomyelitis were included in the analysis. Exclusion criteria were patients without both X-ray and MRI performed and patients requiring a immediate amputation for ischemia.

Radiologic signs used to define the presence of osteomyelitis on X-ray were lytic lesions, periosteal thickening, osteopenia, new bone apposition or loss of trabecular architecture. For MRI, the radiologic signs used to detect osteomyelitis were signal change from bone marrow edema (decreased on T1-weighted and increased on T2-weighted imaging sequences). We excluded episodes with less than three months of active follow-up, those with Charcot osteoarthropathy, and all DFOs with curative amputations. Those with partial amputations were included. We compared groups using the Pearson-χ^2 or Wilcoxon-ranksum tests and performed a multivariate logistic regression analysis with the term "remission" as the outcome[14]. Analysis were performed using the STATA software (14.0, USA).

RESULTS

General results and treatment

Among 1071 adult diabetic foot infections, 390 DFOs met our study criteria (186 patients; 98 [25%] females; median age, 69 years) (Figure **1**). The median number of distinct DFO episodes per patient was two (range, 1-13 episodes). DFO mostly involved the forefoot (321 [83%]). The mid- and hindfeet were involved in 44 (11%) and 25 (6%) cases, respectively. On admission, median transcutaneous oxygen tension on the forefoot was 30 mmHg (interquartile range (IQR), 28-32 mmHg), median ankle-brachial index was 0.9 (IQR, 0.9-1.1), median serum C-reactive protein level was 76 mg/L (IQR, 64-87 mg/L), and most DFOs showed similar clinical signs of infection and necrosis. Thirty-five episodes were bacteremic and 248 occurred in patients with peripheral arterial disease. Debridement was performed in all cases, along with partial amputations in 294 (75%). The median number of debridements was 1 (range, 0-7). The median duration of post-surgical antibiotic therapy was 28 days, with a median parenteral administration of 6 days. We used 26 different antibiotic regimens on 53 distinct intraoperative combinations of microbiological results. 148 DFO episodes involved *Staphylococcus aureus* and 26 *Pseudomonas aeruginosa* infections. All patients were instructed in pressure offloading. Surgeons used vacuum-assisted negative pressure therapy in 24 episodes, and patients underwent hyperbaric oxygen therapy in 39 cases (median, 30 times). The duration between X-ray and first surgical procedure did not differ between both groups (7.5 vs 8.1 days; p=0.51).

Radiological assessment

We performed 381 conventional X-rays (381/390 episodes [98%]; median costs, 100 Swiss Francs [100 US$]) and 47 MRIs (47/390 [12%]; median, 800 Francs [800 US$]). Among the latter, only 38 scans were concomitantly accompanied by an X-ray. In 18 episodes, radiological anomalies were found on MRI only, and they were positive on both modalities in 20 episodes. In contrast, we found no single DFO case with established bone lesions on conventional X-ray without any signs on concomitant MRI.

Outcomes and multivariate adjustment

Overall clinical recurrence occurred after a median of 1 year following the previous episode. From a microbiological standpoint, concordance between the initial and subsequent DFOs was found in only 24% of cases (21/86 recurrences). We compared clinical features of DFOs with positive findings on MRI scan only, versus DFOs with other combinations of radiographic findings (Table **1**). In this group comparison, MRI-only DFOs were not associated with particular variables, or with a lower rate of recurrence. In view of the considerable case-mix, we performed a multivariate logistic regression analysis (Table **2**). The results confirmed the lack of association between MRI-only DFOs and remission rate. The goodness-of-fit result

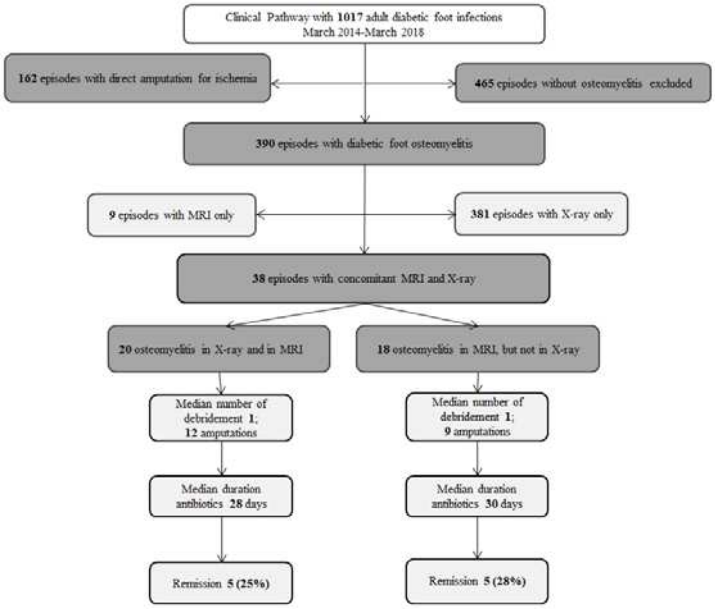

Fig. (1). Study flow chart.

of our final model was non-significant (p=0.45) and the Receiver-Operating-Curve (ROC) value was 0.85, highlighting a more than acceptable accuracy of our final model.

Table 1. Characteristics of diabetic foot osteomyelitis that was visible solely in MRI, but not in standard X-ray.

n = 38	Visible in MRI & X-ray, n = 20	*p* value*	Visible only in MRI, n = 18
Female sex	4 (20%)	0.57	5 (28%)
Median Diabetes duration	15.3 years	0.41	14.8 years
Median BMI	27.9 kg/m^2	0.84	28.1 kg/m^2
Glycosylated haemoglobulin	7.2%	0.74	7.4%
Insulin-dependant diabetes mellitus	12 (60%)	0.41	10 (55.5%)
Diabetic neuropathy	16 (80%)	0.57	14 (77.8%)
Diabetic nephropathy	9 (45%)	0.48	9 (50%)
Median serum C-reactive protein level	59 mg/L	0.81	71 mg/L
White blood cell count	11. 86 x10^3	0.64	12. 59 x10^3
Clinical peripheral arterial disease	9 (45%)	0.52	10 (56%)
Bacteraemic infection	2 (10%)	0.28	1 (6%)
Calcaneal osteomyelitis	1 (5%)	0.49	2 (11%)
Mean duration between X-ray and first surgical intervention	7.5 days	0.51	8.1 days
Number of surgical interventions (median)	1 (range, 0-6)	0.83	1 (range, 0-5)
Partial amputation of bone	12 (60%)	0.53	9 (50%)
Vacuum-assisted negative pressure therapy	1 (5%)	0.45	2 (12%)
Duration of antibiotic treatment (median)	28 days	0.26	30 days
Duration of intravenous antibiotics (median)	10 days	0.96	4 days
Recurrence	5 (25%)	0.85	5 (28%)

Significant p values ≤ .05 (two-tailed) are displayed ***in bold and italic***. Pearson-χ^2 and Wilcoxon-ranksum-tests, as appropriate

Table 2. Logistic regression analyses with the outcome "remission" ***(odds ratio with 95% confidence intervals)***

n = 390	*Univariate*	*Multivariate*
Female sex	1.1, 0.6-1.9	n.d.
Serum C-reactive protein level	1.0, 1.0-1.0	n.d.
Clinical peripheral arterial disease	0.6, 0.4-1.1	n.d.
Ankle-Brachial index	1.2, 0.3-5.5	n.d.
Transcutaneous oxygen tension forefoot	1.0, 1.0-1.0	n.d.
Bacteremia	0.9, 0.4-2.1	n.d.
Partial amputation	*0.4, 0.3-0.7*	n.d.
Number of surgeries	0.8, 0.6-1.1	n.d.
Use of vacuum-assistance	1.1, 0.9-1.2	n.d.
Use of hyperbaric oxygen therapy	1.2, 0.5-3.2	n.d.
Duration of total antibiotics	1.0, 1.0-1.0	1.1, 0.9-1.2
Duration of parenteral antibiotics	1.0, 1.0-1.0	n.d.
Hyperbaric oxygen therapy	1.7, 0.8-3.4	n.d.
Use of MRI despite the availability of X-ray	1.2. 0.6-2.5	n.d.
MRI pathologic only	0.9, 0.2-3.7	0.5, 0.1-5.2

n.d. = not done

DISCUSSION

In this single-center prospective clinical pathway of 390 adult DFO patients, episodes with abnormal findings on MRI only, but not on conventional X-ray, occurred very rarely (5%). This subset of DFO cases was not associated with specific clinical parameters or differences in therapeutic outcomes. MRI positive-only DFO episodes were treated the same way as other DFO cases with X-ray lesions, and had a similar remission rate of 25% during the long-term follow-up. Moreover, neither total duration of antibiotic therapy nor the number of surgical debridements impacted the rate of remission, in accordance with the results our previous study. Only partial amputation was protective against clinical recurrence.

This study, apart from being retrospective, has several limitations. Firstly, patients who received treatment outside of our hospital may have been lost to follow-up. However, this is unlikely a major bias since our hospital has been the largest and only public reference center in the Geneva area for decades. Secondly, we focused mainly on moderate and severe DFO requiring hospitalization with potential surgery. Thus, our data may not reflect outcomes for mild cases that are treated entirely in the ambulatory setting. Thirdly, local wound care, especially pressure off-loading of the affected limb, is crucial for treating and preventing DFO. While the rationale of such measures is easily understandable, effectively implementing them depends on patient education and adherence, which we could not monitor. Fourthly, our definition of DFO, by design, relied on the positivity of bone culture. This definition is common, but might also lead to selection bias by excluding culture-negative cases, which might occur with prior antibiotic exposure[15]. However, our previous database studies of DFO patients failed to detect different treatment outcomes between culture-negative and culture-positive osteomyelitis, which speaks against a substantial bias. Finally, our hospital is set in a resource-rich country. Many centers worldwide either lack access to MRI, or tend to overuse it [16, 17]. Our 12% prevalence regarding the use of MRI can be considered an intuitive balance between both.

CONCLUSION

In conclusion, according to our clinical pathway, DFOs with positive findings on MRI only did not differ in epidemiology or clinical outcomes after standardized treatment, when compared to those with findings on both MRI and conventional X-ray. Although MRI is a more sensitive modality, it does not seem to alter outcome by detecting early cases of DFO. This suggests that clinical management in terms of antibiotherapy or surgical procedure should not differ in patients with only positive MRI.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are the basis of this research.

CONSENT FOR PUBLICATION

Not applicable.

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DATA AVAILABILITY

The data used to support the findings of this study are available from the corresponding author upon request.

CONFLICT OF INTEREST

KG, DL, SB and BK declare no conflict of interest. IU has received research donations from Innocoll Ltd. for another project.

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