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Imaging as a potential outcome measure in gout studies: A systematic literature review

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ABSTRACT

Objective: Despite major progress in the imaging of gout, it is unclear which domains these techniques can evaluate and whether imaging modalities have the potential to provide valid outcome measures. The aim of this study was to assess the use of imaging instruments in gout according to the Outcomes in Rheumatology Clinical Trials (OMERACT) filter to inform the development of imaging as an outcome measure.

Methods: A systematic literature search of imaging modalities for gout was undertaken. Articles were assessed by two reviewers to identify imaging domains and summarize information according to the OMERACT filter.

Results: The search identified 78 articles (one abstract). Modalities included were conventional radiography (CR) (16 articles), ultrasound (US) (29), conventional computed tomography (CT) (11), dual energy computed tomography (DECT) (20), and magnetic resonance imaging (MRI) (16). Three domains were identified as follows: urate deposition, joint damage, and inflammation. Although sufficient data were available to assess feasibility, validity, and reliability, comprehensive assessment of discrimination was not possible due to the paucity of prospective imaging studies. CR is widely accessible, inexpensive with a validated damage scoring system. US and MRI offer radiation-free methods of evaluating urate deposition, damage and inflammation, but may be limited by accessibility. DECT provides excellent definition of urate deposition and bone damage, but has restricted availability and requires radiation.

Conclusions: Imaging methods can detect urate deposition, damage, and inflammation in gout. More than one modality may be required depending on the domains and therapeutic agent of interest. No single imaging method currently fulfils all aspects of the OMERACT filter for any domain.

Introduction

In the last decade, there have been major advances in the imaging of gout. These include the development of a conventional radiography (CR) scoring system for joint damage in gout based on the Sharpe van der Heijde (SvdH) scoring system for rheumatoid arthritis [1], identification of ultrasound (US) lesions typical of gout [2], and development of dual energy computed tomography (DECT) that uses the chemical properties of urate to detect and quantify urate deposits [3]. Despite this progress in gout imaging, it is currently unknown which, if any, imaging techniques can provide valid outcome measures for clinical studies in gout.

The Outcomes in Rheumatology Clinical Trials (OMERACT) group define an outcome as “the effect of a treatment on a patient.” Imaging is considered an objective outcome measure and has been widely used in rheumatoid arthritis. To date imaging outcomes have not been used in clinical trials of gout therapy.

Although previous systematic reviews have addressed imaging for gout diagnosis [4], or specific modalities [5], no systematic review has assessed all major imaging methods for outcome measurement in gout studies. The aim of this systematic literature review was to evaluate imaging instruments used for gout using the pathophysiological components of the OMERACT filter 2.0 [6]

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to gauge their potential as outcome measures. We aimed to identify domains that could be assessed by different imaging modalities, and to determine the extent to which each imaging modality currently meets the filter requirements.

Materials and methods

A systematic search strategy was formulated to evaluate gout imaging with CR, US, magnetic resonance imaging (MRI), computed tomography (CT), and DECT. Electronic searches were performed in PubMed, Medline, and OVID using the search terms of gout (MeSH major heading) with variations of: "X-ray," "radiography," "imaging," "ultrasound," "computed tomography" (CT), "dual energy computed tomography," and "magnetic resonance imaging" (MRI). The search was limited to English language from 1960 to 1 May 2014 and the results were presented at the OMERACT 12 meeting in 2014. The search was updated in February 2015. Bibliographies were also reviewed for relevant papers. Abstract archives since 2002, from The American College of Rheumatology Annual Scientific Meeting and The European League Against Rheumatism Scientific Congress were also reviewed. A single abstract that had not appeared in full print with data pertinent to the OMERACT filter was included.

Articles were included if participants had gout and reported data regarding at least one imaging modality. Case reports, reviews, prevalence studies, and studies of conditions other than gout were excluded. A single case report [7] was included as it provided data about the construct validity of DECT. Manuscripts that compared two modalities were included in the analyses of both techniques.

Articles were assessed by two independent reviewers (L.D. and R.G.) and data addressing the components of OMERACT filter were entered into a standardized data extraction form formulated by all authors. Aspects of feasibility considered were patient acceptability, radiation use, equipment and training required, time of scanning and scoring, and cost. For the truth aspect of the filter, criterion and construct validity were assessed. Face validity was given general consideration but not formally evaluated. Criterion validity was considered in the context of "gold-standard verification." For urate deposition, the gold standard was microscopic MSU crystal confirmation. For bone pathology, CT or microscopic confirmation was considered acceptable. For other pathologies, microscopic confirmation was required as gold standard. Construct validity was considered to be present if the imaging finding had been confirmed with an alternative imaging modality in at least one study. Aspects of discrimination considered were reliability (intra- and inter-reader), within-group change sensitivity, and between-group difference sensitivity.

Results

Search results

The search strategy identified 1190 papers, with 841 articles remaining after removal of duplicates. Case reports ($n = 437$) and reviews ($n = 106$) were excluded. After review of the abstracts of the remaining 298 papers and removal of 234 papers not including people with gout and imaging, 64 papers remained for data extraction. These were presented at OMERACT 12 (2014). Review of bibliographies and updating the search in February 2015 identified 14 additional papers giving a total of 78 papers (Figure 1, supplementary text). The included papers examined gout and imaging by CR ($n = 16$), US ($n = 29 + 1$ abstracts [8]), CT ($n = 11$), DECT ($n = 20$) and MRI ($n = 16$) (articles which addressed more than one modality are included in the analyses of both).

Imaging domains

Three major imaging domains were identified as follows: urate deposition, joint damage, and inflammation. All imaging features analyzed within the articles are shown in the Supplementary tables. For the purposes of this review, we have focused on those imaging features that were most frequently reported. For urate deposition, these were urate crystals overlying articular cartilage (US-double contour sign), tophus (on US, CT, and MRI), and urate deposition visualized by DECT. For joint damage, bone erosion and cartilage damage/joint space narrowing (JSN) were the key findings. The inflammation features most frequently reported were synovitis and bone marrow oedema (osteitis) (Fig. 1).

Conventional radiography

In gout, CR can give information in the domains of damage (bone erosion and JSN) but not urate deposition or inflammation.

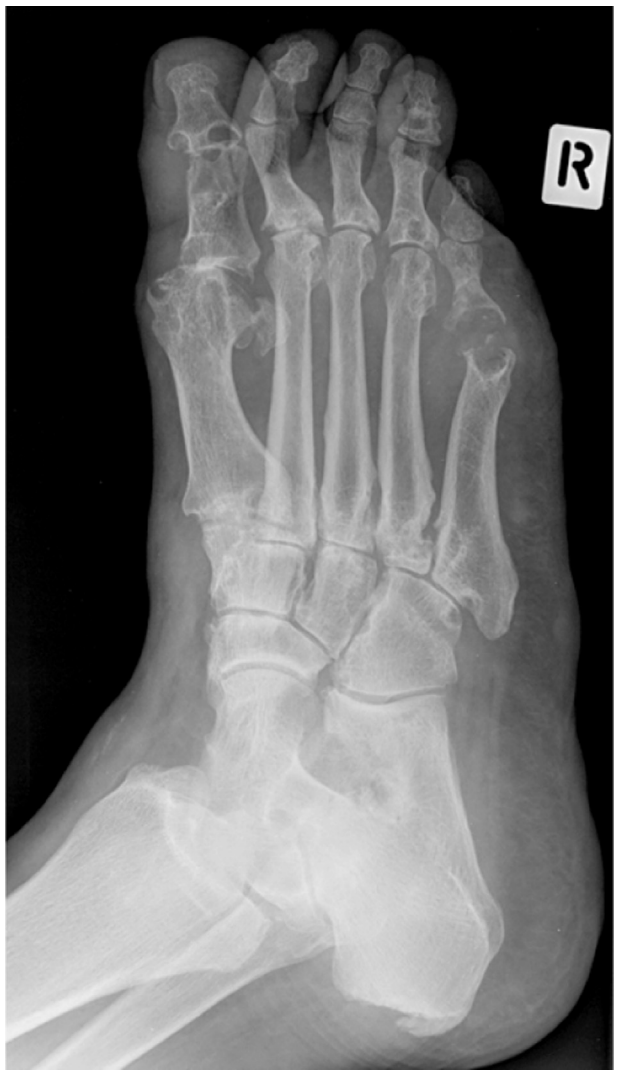

Fig. 1. Plain radiograph of the right foot (oblique view) in a patient with tophaceous gout showing the typical gouty erosions with well-defined sclerotic edges and overhanging margins. Both joint space narrowing (1st metatarsophalangeal joint) and joint space widening (5th metatarsophalangeal joint) is present in association with bone erosion. Note the distribution of disease including the 1st and 5th metatarsophalangeal joints, big toe interphalangeal joint and also the midfoot.