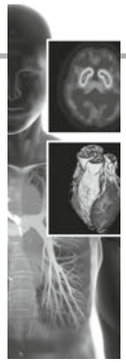
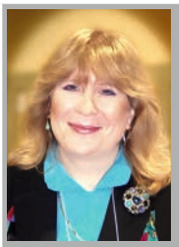


The role of ultrasonography in imaging of gouty arthritis

"*Crystalline material in joints reflects US waves stronger than the surrounding tissues, such as unmineralized hyaline cartilage or synovial fluid, is very echogenic on US and thus can be readily distinguished.*"

KEYWORDS: gouty arthritis ■ ultrasonography



Naomi Schlesinger

Department of Medicine, UMDNJ-Robert Wood Johnson Medical School, One Robert Wood Johnson Pl., P.O. Box 19, New Brunswick, NJ 08903-0019, USA
Tel.: +1 732 235 7702
Fax: +1 732 235 7702
schlesna@umdnj.edu

Gouty arthritis: overview

Gouty arthritis is the most common form of inflammatory arthritis in the USA affecting 8.3 million US citizens [1]. Gouty arthritis is caused by monosodium urate (MSU) crystal deposition within joints and soft tissues resulting from hyperuricemia [2]. Above serum urate (SU) levels of 6.8 mg/dl, MSU crystals fall out of solution and deposit in joints and soft tissues. MSU crystal deposition can lead to inflammation and result in an acute gouty arthritis attack manifesting as extreme pain, tenderness, warmth, swelling, erythema, and loss of function of the affected joint or joints [3,4]. It has recently become clear that during the intercritical period, when the patient is asymptomatic, chronic inflammation is often present [5]. If MSU crystal deposition and chronic inflammation persist, recurrent acute attacks may increase in frequency and severity [4], and a chronic destructive gouty arthritis characterized by disfiguring tophi, joint destruction and persistent pain may ensue.

"*Doppler US helped show that gouty arthritis is frequently a chronic inflammatory arthropathy.*"

The increasing prevalence of gouty arthritis worldwide contributes to the need to identify gouty arthritis patients early into their disease. The current gold standard for establishing a definite diagnosis of gouty arthritis has been demonstrating the presence of MSU crystals via needle aspiration of joint fluid or tophaceous material (MSU crystal deposits) and evaluation with polarizing microscopy for MSU crystals. Conventional radiography (CR) is not useful in detecting early MSU crystal deposition in joints, and soft tissue radiographs of joints affected by gouty arthritis are frequently normal; this is due to MSU crystals being radiolucent. Only 45% of patients with gouty arthritis have radiographic bone changes suggestive of gouty arthritis [4]. Well-defined, 'punched out', periarticular erosions with overhanging edges are seen radiographically only 6–12 years after the initial acute gouty arthritis attack [6,7]. Thus, changes seen on CR indicate the chronicity of the disease process. These include normal mineralization, joint space preservation, sharply marginated erosions with sclerotic borders and overhanging edges, and asymmetric polyarticular distribution.

Ultrasonography in gouty arthritis

Ultrasonography (US) is as a promising new imaging modality for gouty arthritis. Over the past decade there has been a growing interest in musculoskeletal ultrasonography (MSKUS) imaging by rheumatologists [8,9]. US is a user- and patient-friendly noninvasive imaging modality to evaluate joints, periarticular tissue, tendons, muscles, bursae and nerves. US lacks radiation; is less costly than CT and MRI; has high resolution; and has multiplanar imaging capability. It is useful for US-guided procedures, such as synovial fluid and tophi aspiration, as well as synovial biopsies.

US has long been used to detect calcified urolithiasis and gallstones. US visualizes tissues as acoustic reflections. Reflection of ultrasound waves through the body tissues depends on their composition and generates grayscale US images in B-mode. The physics of US makes it an imaging modality able to detect crystalline material in soft tissues. Crystalline material in joints reflects US waves stronger than the surrounding tissues, such as unmineralized hyaline cartilage or synovial fluid, is very echogenic on US and thus can be readily distinguished.

part of future medicine fsg

Diagnosis of gouty arthritis

US may aid in the diagnosis of acute and chronic gouty arthritis. US was found to be a reliable, noninvasive method for diagnosing gouty arthritis [10]. Histopathological studies found crystallization of MSU crystals on hyaline cartilage to be the hallmark of gouty arthritis [11]. Such deposition on the surface of hyaline cartilage, together with microtophi, represent the earliest changes of gouty arthritis [12]. We found several specific US diagnostic features suggestive of gouty arthritis [10]. These included: a hyperechoic, irregular band over the superficial margin of the articular cartilage, described as a double contour sign (icing), in 92% of gouty joints and in none of the controls ($p < 0.001$). The icing was found exclusively in gouty arthritis, and hypoechoic to hyperechoic, inhomogeneous material surrounded by a small anechoic rim, representing tophaceous material, was seen only in gouty joints and in none of the controls ($p < 0.001$). Erosions were seen in 65% of metatarsophalangeal joints and in 25% of MCP joints. Wright *et al.* found US changes suggestive of gouty arthritis were found in metatarsophalangeal joints [13] not previously affected by an acute gouty arthritis attack. In this study, US aided in the diagnosis of gouty arthritis by identifying US features suggestive of gouty arthritis in clinically silent joints. In yet another study comparing US to CR [14], US was found to be more sensitive than CR but less specific. CR was found to have a sensitivity of 31% (32/102) and a specificity of 93% (55/59) in showing features of gouty arthritis versus US that had a sensitivity of 96% (98/102) and a specificity of 73% (43/59) in showing features of gouty arthritis. Thus, US was more sensitive in detecting bony erosions in gouty arthritis when compared with CR. Another study [15] comparing the use of MRI, high-resolution CT, CR and 3D rendering in patients with crystal proven gouty arthritis found US to be superior in detecting changes of gouty arthritis compared with MRI, CR, CT and 3DR imaging. CR, MRI and CT scanning were less helpful in diagnosing radiological changes secondary to gouty arthritis, and therefore led to inappropriate referrals and procedures. Thus, US holds great promise in diagnosing gouty arthritis since joint aspiration can be challenging.

Doppler US in gouty arthritis

The Doppler technique detects the movement of red blood cells in vessels. Color Doppler US detects the direction of the blood flow with contrasting colors and power Doppler US encodes the 'power' of the blood flow in the vessel. During acute gouty arthritis attacks the fibrovascular matrix vessels will be engorged leading to a positive color and power Doppler signal. In addition to the inflammation during the acute attack. It has recently become apparent that there is ongoing inflammation in chronic tophaceous gouty arthritis inbetween attacks, when the patient is usually asymptomatic. We found [15] persistent inflammatory changes in more than half of asymptomatic tophaceous gouty arthritis patients. Tophi and their surrounding anechoic corona were associated with erosion formation in gouty arthritis. Doppler US helped show that gouty arthritis is frequently a chronic inflammatory arthropathy.

Response to treatment

Serial US images can help assess a treatment response to anti-inflammatory therapy or urate-lowering therapy. Tophus size can be measured using US and can be repeated at repeat patient visits [16]. Changes in tophus size can be observed. Most of the tophi that showed change in maximal diameter or volume were in patients with proper control of SU level, although changes were also rarely observed in patients with higher SU levels.

MSU deposition on the hyaline cartilage too can be sensitive to change early into the treatment with urate-lowering therapy [17]. The double contour sign was seen in all gouty arthritis patients. Disappearance of the double contour sign was influenced by urate-lowering drugs once SU levels remain ≤6 mg/dl for 7 months or more. In patients who achieved SU levels of <6 ml/dl, this sign had disappeared at follow-up. By contrast, disappearance of the double contour sign was not seen in patients who maintained an SU level of 7 mg/dl.

A glance into the future

The advances in US imaging of gouty arthritis joints suggest future exciting possibilities. These include diagnosing gouty arthritis, understanding the role of inflammation, as well as possibly serving as a tool to screen a population at risk for preclinical gouty arthritis. In addition, US can be used to assess early damage from gouty arthritis and as an outcome measure of success of anti-inflammatory treatment given for acute gouty arthritis as well as an outcome measure of the success of urate-lowering drugs in reducing joint damage and monitoring response to therapy. Future studies are needed to further assess the role of US in gouty arthritis.

Financial & competing interests disclosure

N Schlesinger has received grants from Novartis; is on the advisory boards for Novartis, Takeda, Savient, Enzyme Rx and URL Pharma; has acted as a consultant for Novartis; and is on the Speakers Bureau for Takeda, Savient and Novartis. The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

References

1 Zhu Y, Pandya B, Choi H. Prevalence of gout and hyperuricemia in the US general population. *Arthritis Rheum.* 3136–3141 (2011).

2 Choi HK, Mount DB, Reginato AM. Pathogenesis of gout. *Ann. Intern. Med.* 143(7), 499–516 (2005).

3 Schlesinger N. Diagnosis of gout. *Am. J. Manag. Care* 11, S443–S450 (2005).

4 Schlesinger N. Diagnosis of gout. *Minerva Med.* 98, 759–767 (2007).

5 Schlesinger N, Thiele RG. The pathogenesis of bone erosions in gouty arthritis. *Ann. Rheum. Dis.* 69(11), 1907–1912 (2010).

6 Peh WCG. Tophaceous gout. Imaging consultation. *Am. J. Orthop.* 30, 665 (2001).

7 Buckley TJ. Radiographic features of gout. *Am. Fam. Physician* 54, 1232–1238 (1996).

8 Balint P, Sturrock RD. Musculoskeletal ultrasound imaging: a new diagnostic tool for the rheumatologist? *Br. J. Rheumatol.* 36(11), 1141–1142 (1997).

9 Wakefield RJ, Gibbon WW, Emery P. The current status of ultrasonography in rheumatology. *Rheumatology* 38(3), 195–198 (1999).

10 Thiele R, Schlesinger N. Diagnosis of gout by ultrasound. *Rheumatology* 1116–1121 (2007).

11 Sokoloff L. Pathology of gout. *Arthritis Rheum.* 8(5), 707–713 (1965).

12 Yu JS, Chung C, Recht M, Dailiana T, Jurdi R. MR imaging of tophaceous gout. *AJR Am. J. Roentgenol.* 168(2), 523–527 (1997).

13 Wright SA, Filippucci E, McVeigh C *et al.* High-resolution ultrasonography of the first metatarsal phalangeal joint in gout: a controlled study. *Ann. Rheum. Dis.* 66(7), 859–864 (2007).

14 Rettenbacher T, Ennemoser S, Weirich H *et al.* Diagnostic imaging of gout: comparison of high-resolution US versus conventional X-ray. *Eur. J. Radiol.* 18(3), 621–630 (2008).

15 Thiele RG, Schlesinger N. Ultrasound detects more erosions in gout than conventional radiography. *Arthritis Rheum.* 62(Suppl. 10), S889 (2010).

16 Perez-Ruiz F, Martin I, Canteli B. Ultrasonographic measurement of tophi as an outcome measure for chronic gout. *J. Rheumatol.* 34, 1888–1893 (2007).

17 Thiele RG, Schlesinger N. Ultrasonography shows disappearance of monosodium urate crystal deposition on hyaline cartilage after sustained normouricemia is achieved. *Rheumatol. Int.* 30(4), 495–503 (2011).