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## Reliability of knee joint sonography in the evaluation of gouty arthritis

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### Keywords

ultrasound,  
sensitivity,  
specificity,  
gouty arthritis,  
meta-analysis

### Abstract

**Objective:** To determine the reliability of knee joint sonography in the evaluation of gouty arthritis. **Methodology:** A search of Google Scholar, PubMed, NCBI, MEDLINE, and Medscape databases, from 1988 up to 2020. The key search terms used were knee joint; knee joint ultrasound; gout; gouty arthritis, knee joint pain; sensitivity; specificity. The reviewer independently screened the titles and abstracts of the relevant articles and full-text downloads to determine whether the inclusion or exclusion criteria were met. **Results:** In total, 103 articles were identified through the database search. In addition, 11 articles were identified through other sources. Then, screening was performed, and 9 articles were removed due to duplication. Further screening was done for 105 articles, and 27 articles were excluded due to insufficient information. Seventy-eight full-text articles were assessed for eligibility. A total of 13 full-text articles were excluded due to research performed on animals, as the study had been designed as a review of only human studies. Sixty-three studies were included that had a qualitative synthesis. **Conclusion:** The knee is a weight-bearing joint and may be affected by a myriad of different pathological conditions, therefore a proper diagnosis is of prime importance for a proper management plan. Ultrasound is a non-invasive, radiation-free, and readily available modality that has high sensitivity and specificity in the evaluation of gouty arthritis.

## Introduction

The knee is a weight-bearing joint and can be affected by several pathological conditions ranging from a simple muscular sprain and strain to tendon and ligament tears, and bone fractures. Knee joint pain and disability is one of the most common musculoskeletal disorders that accounts for the greatest proportion of visits to orthopedic clinics<sup>(1)</sup>. Knee joint sonography is the second common examination technique after shoulder sonography. It consumes a substantial amount of budget every year. Gouty arthritis is one of the widespread causes of knee pain and disability<sup>(2)</sup>.

Monosodium urate (MSU) crystal deposition in articular or peri-articular tissues and the renal tract is linked to the clinical manifestations of gout. Usually, the natural history of articular gout consists of three stages: asymptomatic hyperuricemia, outbreaks of asymptomatic acute gout attacks, and chronic gout arthritis<sup>(3)</sup>. In comparison, it is potentially easier to treat and cure gout in cases with a relatively low urate crystal load, though there is

insufficient knowledge on the occurrence of urate deposits in the joints of patients with uncomplicated gout<sup>(4)</sup>.

Ultrasonography (US) is a beneficial method for detecting deposits of intra-articular urate<sup>(5)</sup>. The double contour (DC) sign formed by the deposition of urate crystals on the surface of the articular cartilage and hyperechoic cloudy areas representing urate deposits inside the joint and tendons or soft tissues are considered to be two characteristic sonographic features of gout<sup>(5–9)</sup>. Ultrasound scanning is routinely performed to diagnose gouty arthritis but a high degree of discordance is found in the literature as to its reliability. A review and pooling of the results of studies in the literature were needed to gain insights into the reliability of the examination.

## Material and methods

A search of Google Scholar, PubMed, NCBI, MEDLINE, and Medscape databases, from 1988 up to 2020 was performed.

**Tab. 1.** Variables of the study (N/A represents that no data related to particular variables were available in the studies)

No.	Author (year)	Sensitivity	Specificity	Country	Sample size	Disease	Journal
1	Cajas <i>et al.</i> (1988) <sup>(22)</sup>	N/A	N/A	Italy	20	Gout	Acta Radiol
2	Nalbant <i>et al.</i> (2003) <sup>(23)</sup>	N/A	N/A	USA	26	Gout	The Journal of Rheumatology
3	Grassi <i>et al.</i> (2006) <sup>(24)</sup>	N/A	N/A	Italy	60	Gout	Semin Arthritis Rheum
4	Rettenbacher <i>et al.</i> (2007) <sup>(25)</sup>	96	73	Austria	105	Gout	European Radiology
5	Thiele & Schlesinger (2007) <sup>(7)</sup>	N/A	N/A	USA	23	Gout	Rheumatology
6	Wright <i>et al.</i> (2007) <sup>(6)</sup>	67%	71%	UK	39	Gout	Annals of the Rheumatic Diseases
7	Filippucci <i>et al.</i> (2008) <sup>(8)</sup>	43.70%	99%	France	132	Gout	Osteoarthritis and Cartilage
8	Iagnocco <i>et al.</i> (2011) <sup>(26)</sup>	N/A	N/A	Italy	N/A	Gout	Semin Ultrasound CT MR
9	Perez-Ruiz <i>et al.</i> (2009) <sup>(5)</sup>	96%	73%	Spain	N/A	Gout	Arthritis Research & Therapy
10	Carter <i>et al.</i> (2009) <sup>(27)</sup>	N/A	N/A	USA	27	Gout	Rheumatology
11	Filippucci <i>et al.</i> (2010) <sup>(28)</sup>	N/A	N/A	Italy	100	Gout	Clin Exp Rheumatol
12	Thiele (2011) <sup>(14)</sup>	96%	83.70%	New York	N/A	Gout	Current Rheumatology Reports
13	Pineda <i>et al.</i> (2011) <sup>(29)</sup>	N/A	N/A	Mexico	102	Gouty Arthritis	Arthritis Research & Therapy
14	Howard <i>et al.</i> (2011) <sup>(30)</sup>	N/A	N/A	New York	50	Gout	Arthritis Care & Research
15	de Ávila Fernandes <i>et al.</i> (2011) <sup>(31)</sup>	83.30%	61.60%	Brazil	31	Gout	Skeletal Radiology
16	Filippucci <i>et al.</i> (2011) <sup>(33)</sup>	85%	79%	Italy	50	Gout	European Radiology
17	Ottaviani <i>et al.</i> (2011) <sup>(34)</sup>	75%	62.50%	France	15	Gout	Experimental Rheumatology
18	Choi <i>et al.</i> (2011) <sup>(35)</sup>	78%	93%	USA	40	Gout	Annals of Rheumatic Diseases
19	Dalbeth <i>et al.</i> (2011) <sup>(36)</sup>	81%	76%	USA	33	Gout	Annals of Rheumatic Diseases
20	Glazebrook <i>et al.</i> (2011) <sup>(37)</sup>	100%	89%	New York	12	Gout	Radiology
21	De Miguel <i>et al.</i> (2011) <sup>(32)</sup>	43%	99%	Spain	26	Gout	Annals of Rheumatic Diseases
22	Roddy <i>et al.</i> (2013) <sup>(38)</sup>	90%	93%	UK	40	Gout	Joint Bone Spine
23	McQueen <i>et al.</i> (2012) <sup>(39)</sup>	N/A	N/A	New Zealand		Gout	Postgraduate Medical Journal
24	Ottaviani <i>et al.</i> (2012) <sup>(40)</sup>	67%	100%	France	500	Gout	Clin Exp Rheumatol
25	Girish <i>et al.</i> (2013) <sup>(41)</sup>	N/A	N/A	USA	N/A	Gout	Hindawi
26	Bergner <i>et al.</i> (2013) <sup>(42)</sup>	92%	72%	Germany	103	Gout	Annals of the Rheumatic Diseases
27	Huppertz <i>et al.</i> (2014) <sup>(43)</sup>	84.60%	85.70%	Berlin	60	Gout	Rheumatology International
28	Zhang <i>et al.</i> (2014) <sup>(44)</sup>	95.59%	68%	China	32	Gout	Journal of Sichuan University
29	Lamers-Karnebeek <i>et al.</i> (2014) <sup>(45)</sup>	77%	96%	Netherlands	54	Gout	Clinical Rheumatology
30	Naredo <i>et al.</i> (2014) <sup>(46)</sup>	84.60%	83.30%	Spain	91	Gout	Annals of the Rheumatic Diseases
31	Löffler <i>et al.</i> (2015) <sup>(20)</sup>	85%	80%	Germany	225	Gout	Journal of Rheumatology
32	Atik <i>et al.</i> (2015) <sup>(47)</sup>	46.30%	99%	Italy	N/A	Gout	Medical Ultrasonography
33	Zufferey <i>et al.</i> (2015) <sup>(48)</sup>	60%	90%	Switzerland	109	Gout	Arthritis Research & Therapy
34	Bongartz <i>et al.</i> (2015) <sup>(49)</sup>	90%	83%	USA	40	Gout	Annals of Rheumatic Diseases
35	Diekhoff <i>et al.</i> (2015) <sup>(50)</sup>	100%	100%	Germany	3	Gout	Skeletal radiology
36	Ogdie <i>et al.</i> (2017) <sup>(18)</sup>	76.90%	84.30%	New Zealand	824	Gout	Arthritis and Rheumatology
37	Das <i>et al.</i> (2016) <sup>(51)</sup>	86.25%	100%	India	38	Gout	Modern Rheumatology
38	Elsama <i>et al.</i> (2016) <sup>(19)</sup>	85.90%	86.70%	Germany	100	Gout	Ultrasound Med Biol
39	Zhu <i>et al.</i> (2017) <sup>(52)</sup>	97.14%	74.29%	China	195	Gout	Journal of Ultrasound in Medicine
40	Elsaman <i>et al.</i> (2016) <sup>(19)</sup>	86%	87%	Egypt	100	Gout	Ultrasound Med Biol
41	Ahmad <i>et al.</i> (2016) <sup>(53)</sup>	100%	48%	India	30	Gout	Int J Rheum Dis
42	Ventura-Rios <i>et al.</i> (2016) <sup>(54)</sup>	69.60%	92%	Mexico	35	Gout	Clinical Rheumatology
43	Stewart <i>et al.</i> (2017) <sup>(55)</sup>	N/A	N/A	New Zealand	86	Gout	Journal of Foot and Ankle Research
44	Stewart <i>et al.</i> (2017) <sup>(56)</sup>	N/A	N/A	New Zealand	34	Gout	Arthritis Care & Research
45	Das <i>et al.</i> (2017) <sup>(12)</sup>	69.40%	100%	India	62	Gout	Int J Rheum Dis
46	Lee & Song (2017) <sup>(57)</sup>	65.10%	89.00%	Korea	938	Gout	Semin Arthritis Rheum
47	Pattampaspong <i>et al.</i> (2017) <sup>(58)</sup>	58%	92%	Thailand	89	Gout	Skeletal Radiology
48	Zhang <i>et al.</i> (2018) <sup>(44)</sup>	66%	92%	China	13	Gout	PLOS ONE
49	Tekaya <i>et al.</i> (2018) <sup>(59)</sup>	N/A	N/A	Tunisia	1	Gout	Egyptian Rheumatologist
50	Bhadu <i>et al.</i> (2018) <sup>(60)</sup>	87.20%	84%	India	47	Gout	Int J Rheum Dis
51	Gamala <i>et al.</i> (2018) <sup>(61)</sup>	N/A	N/A	Netherlands	147	Gout	Clinical Rheumatology
52	Dalbeth & Doyle (2018) <sup>(62)</sup>	N/A	N/A	New Zealand	60	Gout	Rheumatology
53	Jia <i>et al.</i> (2018) <sup>(63)</sup>	80.88%	88.24%	China	221	Gout	Clinical Rheumatology
54	Ramon <i>et al.</i> (2018) <sup>(64)</sup>	90%	80%	France	1502	Gout	Clinical Rheumatology

55	Di Matteo <i>et al.</i> (2019) <sup>(65)</sup>	N/A	N/A	Portugal	40	Gout	Joint Bone Spine
56	Cazenave <i>et al.</i> (2019) <sup>(66)</sup>	N/A	N/A	Germany	13	Gout	Rheumatology International
57	Murayama <i>et al.</i> (2019) <sup>(67)</sup>	N/A	N/A	N/A	1	Gout	Mod Rheumatol Case Rep
58	Micu & Dogaru (2019) <sup>(68)</sup>	N/A	N/A	N/A	1	Gout	Clinical Rheumatology
59	Persons & Kissin (2020) <sup>(69)</sup>	N/A	N/A	USA	1	Gout	J Med Ultrasound
60	Sakellariou <i>et al.</i> (2020) <sup>(70)</sup>	79%	69%	Italy	943	Gout	Frontiers in Medicine

The key search terms used were knee joint; knee joint ultrasound; gout; gouty arthritis, knee joint pain; sensitivity; specificity. The reviewer independently screened the titles and abstracts of the relevant articles and full-text downloads to determine whether the inclusion or exclusion criteria were met. Any disagreement was resolved through a consensus. The studies were eligible if they included information about gout and the role of ultrasound in the diagnosis of gouty arthritis. Studies involving research on animals were excluded from the review process. The eligible studies were categorized, and then data analysis was performed according to specific pathological conditions. This literature review retrieved study sample size, gouty arthritis, sensitivity, specificity of the ultrasound in the diagnosis of gout. From all the data retrieved, descriptive statistics were compiled for further analysis. A table was created, with predefined sub-groups, for all the variables included in the study (Tab. 1). The variables included the year of the study, first author of the research article, country, sensitivity, specificity, sample

size, disease, and journal name. The studies were included if complete information was available for all the variables in a human study. The studies were excluded if incomplete information was given about the variables of the study. In total, 103 articles were identified through the database search. In addition, 11 articles were identified through other sources. Then, screening was performed, and 9 articles were removed due to duplication. Further screening was performed for 105 articles, and 27 articles were excluded due to insufficient information. Seventy-eight full-text articles were assessed for eligibility. A total of 13 full-text articles were excluded due to research performed on animals, as the study had been designed as a review of only human studies. Sixty-three studies were included that had a qualitative synthesis. In addition, 63 quantitative syntheses were included (meta-analysis). The flow diagram depicts the flow of information through the different phases of the systematic review. It maps out the number of records identified, included, and excluded, and the reasons for their exclusion (Fig. 1).

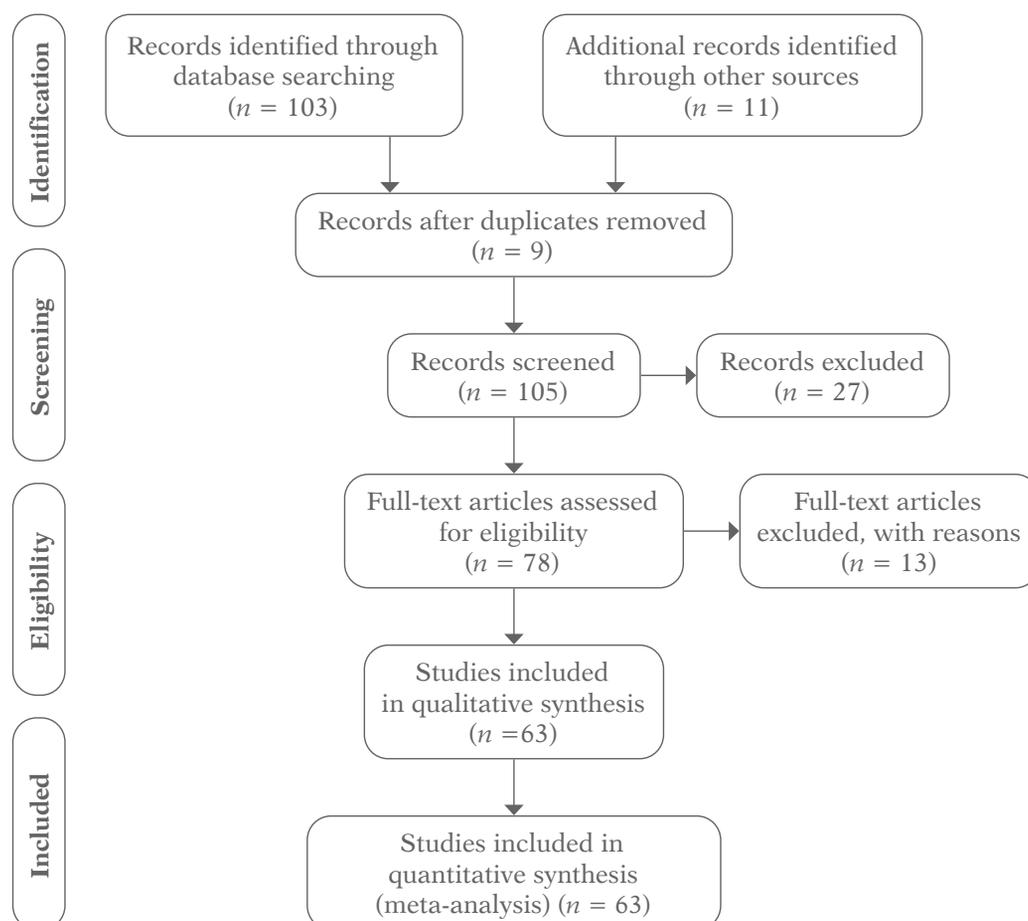
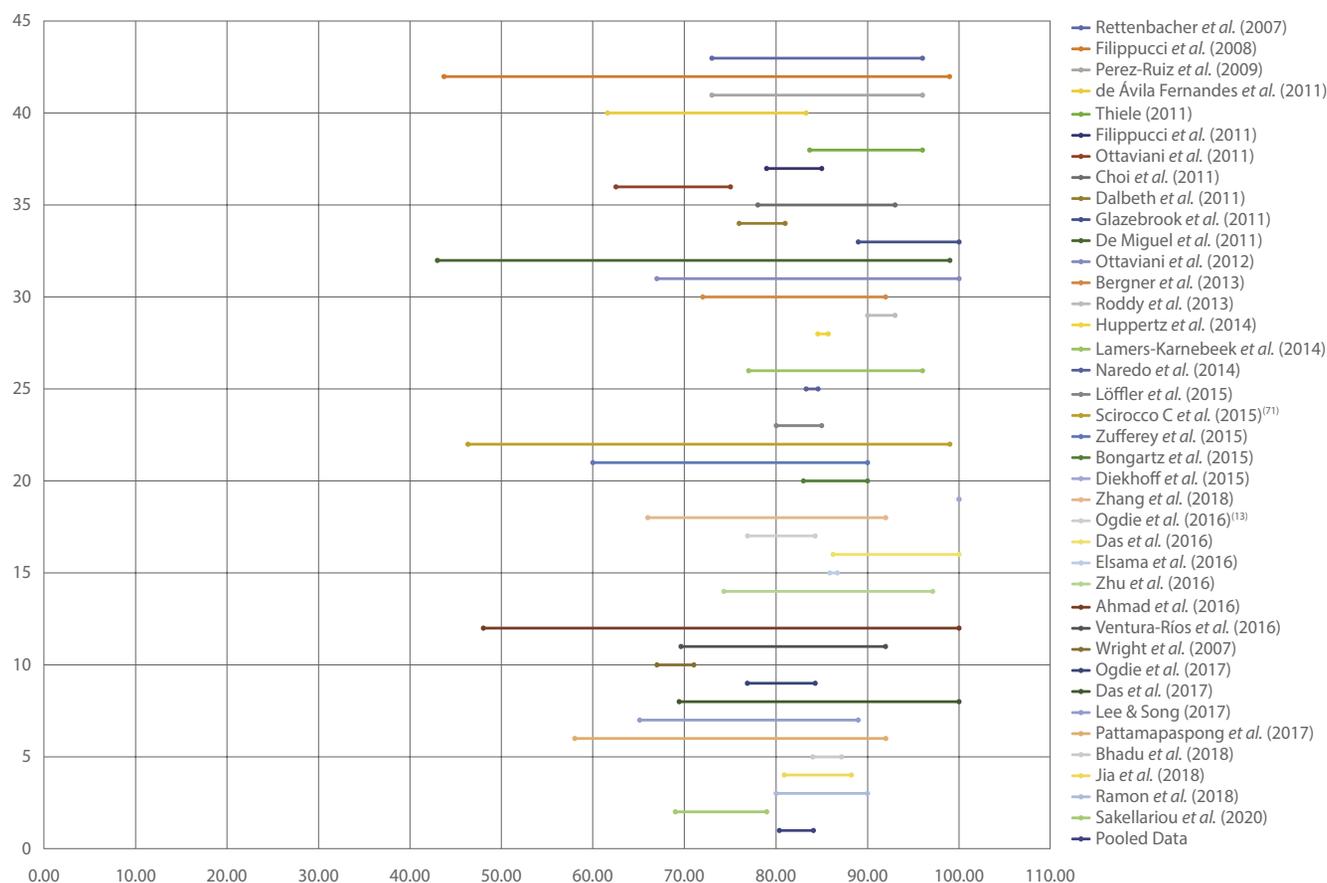


Fig. 1. PRISMA 2009 Flow Diagram



**Fig. 2.** Forest plot showing the sensitivities and specificities of the studies, and pooled results (represented with a thick horizontal line at the bottom of the plot)

## Results

The articles included in the literature review were published in 1988–2020. The disease under study was gouty arthritis which causes pain in the knee joint and was confirmed with the help of ultrasonography (Tab. 1). A forest plot was made for each study having the sensitivity and specificity of gouty arthritis. The pooled sensitivity of the ultrasound in the diagnosis of gouty arthritis in the patients having knee joint pain was 80.35%, while the specificity was 84.09% (Fig. 2).

## Discussion

Gout is a prevalent arthritic disorder that affects around 1% of the population. In men, the prevalence is higher, and rising with age. The pathogenesis of gout involves disturbed purine metabolism, reduced uric acid renal excretion, elevated levels of uric acid in the blood, and deposition of crystals of monosodium urate (MSU) in the joints and soft tissues<sup>(10)</sup>. Episodic acute monoarthritis of the first metatarsophalangeal joint (MTP) with overlying erythema is the usual gout presentation. However, the clinical appearance can become atypical as the disease progresses; for example, polyarticular attacks involving the hand joints and prolonged arthritis duration may occur<sup>(11)</sup>. Needle aspiration of joint effusion

and detection of MSU crystals by polarizing microscopy is the gold standard procedure for diagnosing gout<sup>(12)</sup>. However, in a subset of arthritic patients, arthrocentesis is not done, and these patients frequently undergo empirical treatment with an indefinite diagnosis<sup>(10)</sup>. In several joint diseases, ultrasonography (US) is a helpful evaluation tool, offering assistance in disease detection, assessment of results, and aspiration and local injection procedures<sup>(13)</sup>. Ultrasound has also been found to be a useful modality for the diagnosis of gout, as early deposition of MSU crystals can be identified in certain joint structures, such as hyaline cartilage surface and synovium<sup>(14)</sup>. It is also possible to use the US to measure synovial thickness, synovial effusion, and bone degradation. Power Doppler US may evaluate synovial inflammation<sup>(15)</sup>. The diagnostic utility of US for gout, however, varies across studies; thus, additional research is needed to confirm the usefulness of US in diagnosing gout<sup>(16)</sup>. Such research would have to evaluate the characteristic sonographic features of gouty arthritis and to assess the diagnostic importance of gouty arthritis in the US. While gout is widespread, an actual diagnosis of crystals is rarely pursued<sup>(16)</sup>. Polarizing microscopy, the diagnostic gold standard, joint aspiration and crystal analysis require technical expertise and equipment. Consequently, patient-friendly, effective modalities for the diagnostic work-up would be highly desirable. Ideally, such a test would be non-invasive, affordable, effective, highly sensitive and precise, and would involve repeated testing to determine patient response to the

procedures. Imaging, such as classical (CR) radiography, CT, MRI and ultrasound (US) are currently used for diagnosis. Guidance on the protocol and evaluation of the treatment response in gout. Ultrasonography is a readily accessible technique worldwide<sup>(17)</sup>. US was used for assessing the crystalline deposits present in and around joints<sup>(18)</sup>. The urate of monosodium (MSU) tophi can best be sonographically visualized<sup>(19)</sup>. While it is possible to see calcified concretions on CR, MSU tophi are not commonly seen on CR<sup>(20)</sup>. Ultrasound was found to be more sensitive in detecting bony erosions in rheumatoid arthritis when compared with radiography<sup>(21)</sup>. According to the results of our study ultrasound has high sensitivity and specificity in the diagnosis of gouty arthritis.

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## Conclusion

The knee is a weight-bearing joint and may be affected by a myriad of different pathological conditions. Therefore, a proper diagnosis is of prime importance for a proper management plan. Ultrasound is a non-invasive, radiation-free, and readily available modality characterized by high sensitivity and specificity in the evaluation of gouty arthritis.

## Conflict of interest

*The authors have no conflict of interest.*

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