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Foot and Ankle Characteristics in Gout: A Systematic Review

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ABSTRACT

Objectives: Gout has a predilection for the foot and ankle, but the impact of gout has limited presence in the literature. The aim of this systematic review was to synthesise existing literature which has investigated the characteristics of foot and ankle involvement in gout; identifying consensus and highlighting areas for further study.

Methods: Studies were included if they were published in English and involved participants over 18 years of age with gout, and presented original findings relating to outcome measures associated with the foot and ankle. Methodological quality was assessed using a modified version of the Quality Index Tool.

Results. Of 707 studies identified, 16 met the inclusion criteria and were included in this review. The mean (range) quality score was 68.1% (38.9%-88.9%). Compared to controls, participants with gout reported higher levels of activity limitation, foot-related pain and disability and walked more slowly. Plain radiography, dual-energy Computer Tomography and diagnostic ultrasound consistently demonstrated pathological features of gout in the first metatarsophalangeal joint and Achilles tendon. However, studies offered limited quality, particularly around recruitment strategies, validity and potential impact of confounding factors, making definitive statements difficult.

Conclusions: This systematic review highlights the negative impact of gout on the structure and function of the foot and ankle causing significant impairment and disability. To effectively guide management, improvements in methodological quality are recommended.

Keywords: Gout, Foot, Ankle

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Significance & Innovations

- Gout involves frequent deposition of monosodium urate crystals within joints and soft tissues, more commonly the first metatarsophalangeal joint and the Achilles Tendon, negatively impacting on function.
- People with gout exhibit altered gait strategies that may be reflective of increased pain or walking apprehensively in anticipation of foot pain
- Greater loss of lower limb muscle strength is associated with gout compared to age/sex match controls
- Future research should include primary and secondary care-based participants using clear recruitment criteria

Introduction

Gout is a common cause of inflammatory arthritis occurring as a result of a metabolic inefficiency of purine metabolism, typically affecting middle-aged men [1]. Monosodium urate (MSU) crystal deposition is the key pathological origin and the subsequent rapid, inflammatory response causes an acute arthritis characterised by intense, debilitating pain and swelling of the affected joint [2]. However, the impact of gout goes beyond the episodic acute attack. Sustained hyperuricaemia results in the formation of subcutaneous tophi, chronic synovitis, bone erosions and eventual joint destruction in a proportion of individuals [3-5]. Consequently, people with gout can experience ongoing pain, impairment and disability in the absence of acute arthritis [6]. Gout most commonly affects peripheral structures with a propensity for the first metatarsophalangeal joint (MTPJ) [7]. In a systematic review [8] Stewart et al., identified substantial patient-reported pain and disability. However, this review only focussed on the first MTPJ, whereas more recent evidence highlights the impact of gout on the wider foot and ankle [9,10]. Predilection for the foot and ankle in gout is well recognised in the literature, yet the effect of MSU crystal deposition on structure and function are not well documented [9]. To this end, an in-depth understanding of how gout affects the foot and ankle is key to informing evidence-based interventions to effectively improve patient-centred outcomes. No formal synthesis of current literature has been conducted to describe the impact of gout on the foot and ankle [11]. To address this gap, this systematic review aimed to evaluate and summarise existing literature that reports on the characteristics of the foot and ankle in people with gout.

Materials and methods

Data sources & searches

A comprehensive systematic electronic search was performed to include literature published from January 1999 to December 2020 using AMED, CINAHL, COCHRANE, Health Research Premium Collection, PubMed, SCOPUS, SPORTDiscuss and ZETOC databases. Our search strategy used subject headings combined with keywords, ultilising a similar approach described previously [8]. To combine keywords, the Boolean phrases 'OR' and 'AND' in addition to truncations (*) were used (supplemental file 1). The same search terms were applied to the title and abstracts in all databases. All articles were screened by their title, followed by their abstract before full texts were collated and screened. The database search was supplemented with hand-searching of reference lists of all potentially eligible full text articles and selected review articles to ensure adequate capture of all relevant literature. To reduce the risk of publication bias, a search was conducted of the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) meetings for relevant conference abstracts. All abstracts with ‘gout’ in the title were screened. Where studies were identified as an abstract and a published paper, the published paper was included. Studies were eligible provided they reported on clinical outcome measures relating to the foot and ankle in gout. Such items included descriptions of clinical features, imaging features, and structural and functional characteristics.

Study selection

One author (KB) undertook the searches and assessed potential studies against the inclusion criteria at all stages. After the initial searches, the author reviewed all resulting titles and abstracts for eligibility. Only articles published in English that had adult study participants (>18 years) with gout were considered, and searches were limited to randomised controlled trials, qualitative, cohort, case-controlled and cross-sectional studies. Articles were excluded if they were retrospective, case reports, case series of less than five participants, or review articles. Studies assessing the efficacy of pharmacological or surgical interventions and research evaluating diagnostic tests or tools were also excluded as were articles reporting acute gout attacks.

Data extraction and synthesis

We extracted the following information from included studies: study author, publication date, demographic characteristics of participants, method of gout diagnosis, study location. Potential sources of methodological heterogeneity were also extracted, including study design and assessed outcomes. The quality of the included studies was evaluated independently by two authors (KH, BA). Any discrepancies were resolved by consensus. Quality was assessed using a modified version of the Quality Index Tool (QIT) [12]. The QIT was developed to assess the methodological quality of both interventional and observational studies and can be modified if required. This comprehensive tool has been shown to have high internal consistency, good inter-rater reliability and good test-retest reliability [12]. The original QIT consists of 27 items allowing the reviewer to assess the study's internal and external validity, quality of reporting of bias and study power. However, questions regarding the allocation mechanism used only relate to randomised trials. For this systematic review the QIT was modified to exclude questions that were not relevant, as interventional studies were not included in our original search criteria. We followed a similar approach applied in a systematic review on foot and ankle characteristics in systemic lupus erythematosus [13]. In total ten questions were omitted, all relating to interventional study designs (questions 4, 8, 13-15, 17, 19, 23-24, 27). This resulted in the retention of seventeen questions assessing the quality of reporting (questions 1-3, 5-7, 9-10), external validity (questions 11-12), and internal validity (questions 16, 18, 20-22, 25 and 26). The items were scored using grades for each question of either * = not relevant to review, 1 = yes, 0 = no, or U0 = unable to determine, apart from question 5 which scored 2 = yes, 1 = partially, 0 = no. Some questions were not relevant to all studies, the number of quality index items included for each paper varied, items that were not applicable to the study were not scored. To produce a homogeneous value which is consistent and easily comparable, the scores for the included items were summated for each study and divided by the total number of index items, generating an overall percentage score. While the original instrument did not describe an overall cut-off score to categorise study quality, a previous systematic review using the QIT cri-teria [14] applied the following values to describe overall quality: ≥85% high quality, 61% to 84% moderate quality and <61% poor quality.

Data analysis

To present a qualitative synthesis of the results from this systematic review, data analysis involved synthesis of the descriptions of the outcomes relating to the characteristics of the foot and ankle in gout, together with the QIT for each article. This systematic review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [15] and we utilised definitions proposed by a consensus statement [16]. Meta-analysis assessment was not deemed appropriate based on heterogeneity of the included studies, which contained a variation in disease duration, differing definition of gout, primary outcomes and outcome measures and differences in disease severity.

Results

Literature search results

Our search strategy retrieved 1298 articles in addition to 3 articles obtained through hand-searching. Of these papers, 594 were removed as duplicates, leaving 707 articles to be screened based on the title and abstract. A further 462 items were excluded for methodological reasons. The remaining 245 full text articles were evaluated and screened for eligibility, whereby 229 were excluded as they failed to meet the inclusion criteria, leaving 16 articles included in this review (supplementary file 2).

Study characteristics

The studies involved nine different cohorts of participants (some studies analysed data from the same cohort), details of the included studies are presented in table 1. Studies were located primarily in New Zealand (n=15), a combined NZ/USA dataset and one UK dataset. The pooled sample size totalled 593 participants, of which 425 had gout, the majority (91%) were male. The mean age of the gout participants across studies ranged between 58 to 70.6 years, the mean disease duration of gout varied from 9 to 25 years.

Methodological quality

Table 2 details the quality assessment. Overall QIT scores varied widely (range between 38.9% to 88.9% (mean 68.1%). Two studies were deemed of high quality (QIT score ≥85%) and two were deemed of poor quality (QIT score <61%). Many of those deemed of moderate quality comprised limited information on the methods of study recruitment, creating difficulty in assessing the generalisability of the results, consequently reducing their external validity. The articles retrieved for review reported on one or more of the following outcomes relating to the foot and ankle: clinical characteristics, gait characteristics, muscle strength and kinematics in addition to imaging features.

Clinical characteristics

The core clinical characteristics reported included foot pain, disability, clinical evidence of tophi and foot ulceration. Using a 100mm Visual Analog Scale to measure foot pain, five studies documented mean participant-reported pain ranged from 5.7mm to 28.5mm - significantly greater than control subjects [10, 17-21]. Four studies used three different outcome measures to determine pain, function and disability [6, 21-23]. All used the Health Assessment Questionnaire [24], together with the Foot Function index [25] and/or the Leeds Foot Impact scale [26]. Compared to controls, participants with gout reported higher levels of foot pain and activity limitation. Foot-related pain and disability was specifically measured in four studies [19,20,27,28], with mean Manchester Foot Pain and Disability Index [29]: scores ranging from 12.4-13.4, significantly higher than control subjects (mean scores 1.8-2.1). One study [9] reported the presence of clinically evident tophi, the Achilles tendon being the most common location (36% prevalence) followed by the second toe (30%), the least common sites being the second and fourth MTPJ (both 2%). Participants with palpable tophi had significantly greater foot pain and disability scores compared to those without clinically evident tophi. One study reported on the clinical characteristics of foot ulceration in gout [22], but with low numbers of participants. Altered foot structure was described via clinical assessment of hallux valgus severity using the validated Manchester Scale [30], where compared to controls, participants with gout had an increased odds ratio of having more severe hallux valgus in addition to greater disability and poorer lower limb function [19].

Gait characteristics

Overall, the temporal-spatial gait parameters demonstrated significant differences, suggesting that people with gout walk slower, with reduced step, stride length and cadence. Utilising a self-selected and fast walking speed, compared to controls, people with gout walked with increased step and stance time, reduced velocity and reduced cadence [28]. Similar results were seen with barefoot walking, whereby people with gout demonstrated significantly increased step and stance time and decreased velocity. [31] In terms of plantar pressure analysis, participants with gout had significantly reduced pressure at the heel and hallux and increased pressure at the midfoot [31]. Comparable results were previously reported with significantly reduced peak plantar pressures and pressure-time integrals beneath the hallux and increased pressure-time integrals under the midfoot [6].

Muscle strength and kinematics

Peak isokinetic concentric muscle strength was tested using dynamometry in four studies [9,20,21,27]. Compared to controls, participants with gout had significantly reduced first MTPJ plantarflexion force in addition to reduced range of motion [19]. People with gout demonstrated significantly reduced plantarflexion, eversion and inversion muscle strength compared to controls [27]. Similarly, after adjusting for age, disease duration and pain score, participants with foot or ankle tophi had significantly reduced muscle force compared to those without tophi during plantarflexion, dorsiflexion, inversion, and eversion [9]. Significantly decreased peak ankle joint angular velocity was recorded in participants with gout but no differences were found for ankle motion in the sagittal or frontal planes (P=0.08) [21]. Despite differences in muscle strength being reported, no differences were observed for peak ankle joint power, force or moment [21].

Imaging features

Various imaging modalities including plain radiography, dual energy computed tomography (DECT) and ultrasonography have assessed urate crystal deposition [3,7,17], the presence of tophi [17,23,32,33], synovial pathology [20,32], tendon pathology [17, 33] and osseous changes [3,18,32]. However, considerable differences were reported between imaging modalities. Utilising DECT, tophi were observed in 48.6% of MTPJs [23], compared with 13% tophi presence at the first MTPJ using ultrasonography [32]. Using DECT MSU crystals were most commonly reported in the first MTPJ [3,18], second most frequently at the fifth MTPJ and least commonly at the fourth MTPJ [18]. The Achilles tendon was the most involved tendon/ligament site to demonstrate MSU crystals with DECT [3,17,18] followed by the peroneal tendons [7]. The presence of intra-tendinous tophus/aggregates varied between 38% to 73% [17,33]. The enthesis and tendon body being the most prevalent sites [17]. Using shear wave elastography significantly reduced tendon stiffness was reported in those with gout compared to controls, with no relationship between the presence of tophi and shear wave values being detected [33]. Synovial pathology included synovial hypertrophy, synovitis and joint effusion [20,32]. Synovitis was reported in 44 % of those with gout and gout was associated with an increased odds ratio of having synovitis [32]. Joint effusion was only reported in 9% of those with gout and synovial hypertrophy was equally uncommon, reported in <11% of joints, with no significant difference for the presence of effusion or synovial hypertrophy between those with gout and controls [22]. In terms of bony pathology, plain film radiography and ultrasonography demonstrated erosions most frequently in the first MTPJ [3,18, 32]. However, in these studies rates varied between 33%-79%. Bone erosions were eight-fold more likely to occur at sites with MSU crystal deposition compared to those without [18]. The least frequent site for erosions was at the third and fourth MTPJs [3,18]. Other osseous radiographic features included spur formation, joint space narrowing, osteophytes, sclerosis and periosteal new bone formation [18].

Discussion

Our aim was to summarise and evaluate the characteristics of the foot and ankle in people with gout from published quantitative studies. Based on 16 studies combining 425 gout patients across three continents, we found that people with gout experience a multitude of foot and ankle pathologies characterised by increased pain and functional disability. Consequently, it is clear from this review that the impact of gout in the foot and ankle extends beyond the episodic acute attack [6,10,11]. With the recognised association with metabolic syndrome and comorbidities such as diabetes [34], one may speculate that the foot in gout is also at greater risk of further complications including pain, impaired function and ulceration.

Increased foot pain was a consistent finding, with most studies utilising a visual analogue scale (VAS). Commonly used in practice and research, there is an implicit assumption such a scale is interval in nature. However, some have reported low test-retest reliability [35] and RASCH analysis indicates a VAS operates as an ordinal scale [36]. Consequently, care should be exercised in using VAS scores to compare data with parametric statistical techniques. Outcome measures to assess foot function such as the Foot Function Index (FFI) [25] and the Leeds Foot Impact Scale (LIFS) [26] were originally developed/validated for use in other inflammatory arthropathies, specifically rheumatoid arthritis. A review has identified limited use of the FFI in gout; but highlighted good psychometric properties of the FFI across a range of other diagnosis [37]. Recent work reported the LFIS did not have adequate content validity for use in Psoriatic arthritis [38]. Similar validation has not been carried out in gout, but indicates the heterogeneity associated with foot complaints in different types of inflammatory arthritis.

Compared with age/sex-matched controls, people with gout walked more slowly with reduced cadence and reduced step and stride length, reduced velocity and cadence and exhibited increased stance times. Differences in results between studies may reflect methodological variation e.g. shod and barefoot conditions. Nevertheless, by walking slowly, people with gout demonstrate gait patterns consistent with first MTPJ pain-avoidance strategies [6]. The development of methods for pain/fear-avoidance could persist following acute arthritis or become a learned motor pattern as an attempt to prevent triggering an episode of acute gout [28]. Qualitative research has reported people with gout attempt to walk more cautiously with an adjusted foot position to relieve hallux pain during an acute gout attack [39]. Changes in plantar pressure patterns further reflect the pain-avoidance strategies to offload pressure at the first MTPJ [6,31]. Abnormal first MTPJ loading at propulsion may also be exacerbated by biomechanical strain resulting from MSU crystal deposition within tendons [7]. The extent of tophi deposition varied considerably between studies, which may reflect different sampling techniques, variations in inclusion criteria, relatively low participant numbers across trials and/or different imaging techniques. The impact of tophi presence on muscular activation is worthy of further examination, particularly considering the reported negative interaction on cell viability and function between tenocytes and MSU crystals [40]. While gouty tophi presence assessed by clinical examination may not reflect the true burden in people with gout, the varying prevalence of subclinical deposition of tophi highlights the value of imaging recommendations and reporting guidelines [41, 42]. Equally, concomitant foot osteoarthritis may affect joint range of motion and muscle strength [43,44]: with Roddy et al., [45] suggesting that one in six older adults are affected by foot osteoarthritis. This indicates the need for more research to confirm the role of osteoarthritis and reduced range of motion at the first MPTJ in those with gout.

Reduced lower limb muscle strength/function has been widely reported in people with gout using dynamometry [9,19,27], 3D motion analysis [21] and shearwave elastography [33]. It is plausible that apropulsive and/or antalgic gait strategies adopted by people with gout can result in reduced muscle strength due to disuse muscle atrophy or possibly secondary to pain-avoidance strategies. The underpinning pathogenesis remains unclear with some studies pointing to the association with tophi [9] and others finding no relationship [33]. In terms of methodological quality however, the construct validity of dynamometry relative to dynamic muscle forces during gait has not been clearly determined. Static dynamometry in particular has good clinical utility, but has limited validity in testing stronger muscle groups (e.g. plantarflexors) where test participants can overpower examiners.

The studies we included all had limitations which may restrict the generalisability of their data. There were considerable variations in participant numbers (n= 6 to n=153), which may reduce external validity. Clinical heterogeneity also results from variability in recruitment strategies including the definition of gout, which further limits the interpretation of the findings. Gout was typically classified based on the 1977 ACR clinical criteria [46] rather than a recommended gold standard [47]. The primary intention of classification criteria is to provide researchers with a validated and standardised means of identifying participants for enrolment, enabling creation of uniform cohorts which become comparable across different studies and geographical locations [48]. Furthermore, there is a potential for classification bias as not all comparator participants underwent arthrocentesis to confirm their 'control' status. Most participants were of European descent or described as Caucasian. Thus, their described foot and ankle characteristics cannot be extended to other ethnic groups, as different ethnicities have functional differences in foot loading and morphology during gait [49]. Most studies were conducted in New Zealand, which has one of the highest reported prevalence of gout worldwide [50]. Therefore, data may not fully represent people with gout from other countries. Methodological heterogeneity existed, with variability in trial design and quality, which jeopardises the generalisability of the findings. For example, most of the studies analysed were cross-sectional, which limits the investigation of the cause-effect relationship between gout and the characteristics of the foot and ankle. The absence of a recommended outcome measure to assess patient-reported outcomes pertaining to the foot and ankle in gout creates challenges in the comparison of the studies. Finally, none of the studies reviewed included the significant influence of psychosocial factors on foot related pain and/or disability [45].

The strengths and limitations of this review should be acknowledged. We systematically searched eight electronic databases using a comprehensive search strategy designed in collaboration with an experienced librarian. However, our inclusion of studies may have been limited by a single reviewer conducting the search inadvertently leading to bias. Secondly, the methodology adopted may have introduced selection bias as only English language studies being included, and as in any review, publication bias may reduce available studies for inclusion.

Future research should consider the methodological limitations of current published literature, aiming to assess the impact of gout on the foot and ankle whilst focusing on a more homogeneous set of outcomes. It is recommended that such research should include assessment of multiple areas of the foot and ankle. In addition, to increase study quality and recruit a more representative population it can be recommended that future studies include:

- More robust and defined methods of study recruitment
- Larger study populations
- Alternative geographic study locations
- Incorporating a combination of participants recruited from secondary and primary care
- Using a standardized definition of gout for participant inclusion

By establishing the true impact of gout on the foot and ankle, further research may investigate the effectiveness of management strategies that specifically target foot and ankle problems in people with gout whilst seeking to improve foot function and patient-reported outcomes.

The results from this systematic review suggest that gout involves frequent deposition of MSU crystals within joints and soft tissues, more commonly the first MTPJ and Achilles tendon. People with gout walk more slowly and exhibit apropulsive gait strategies implying they walk apprehensively in anticipation of foot pain, which may subsequently result in disuse muscle atrophy. Further research is required to strengthen the body of evidence and guide appropriate decision making in the context of ongoing foot and ankle management in gout.

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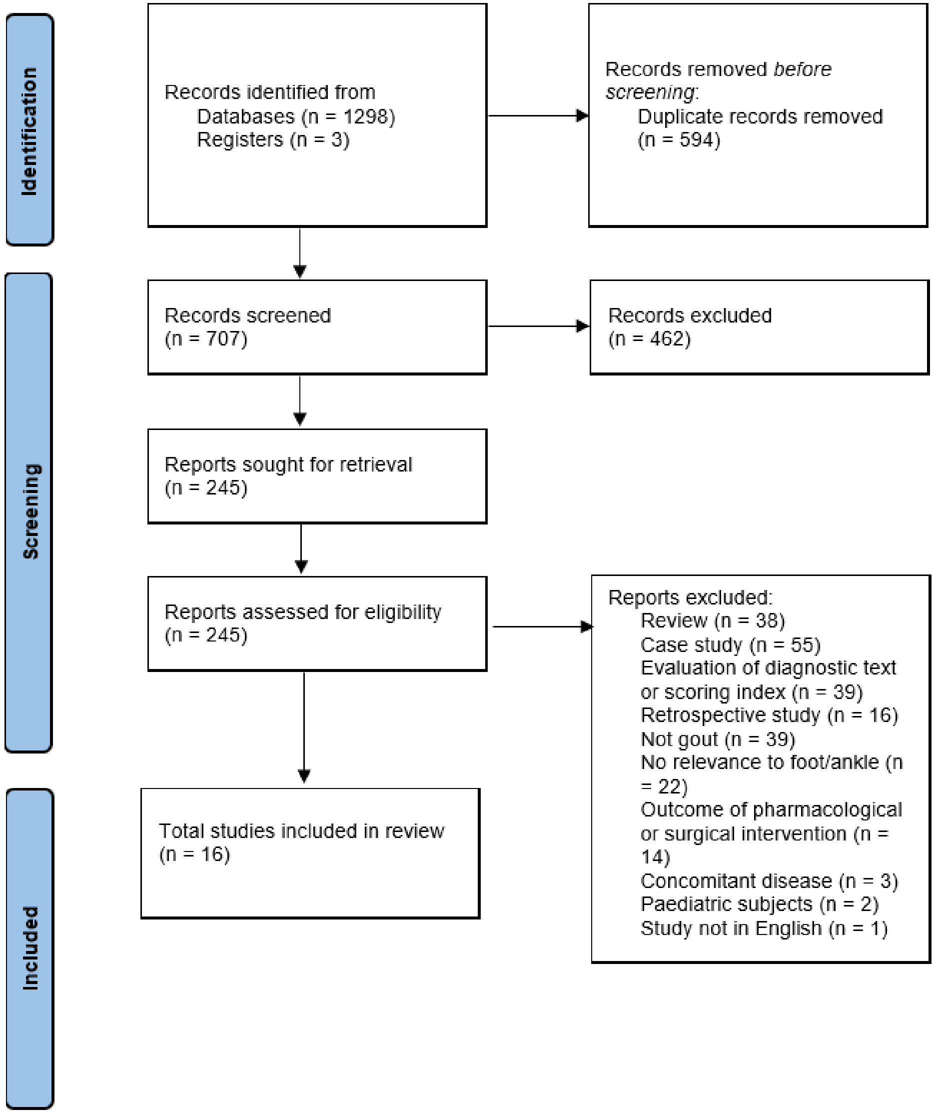
Table 1. *Search terms*

#1	Gout* OR "crystal arthropathy" OR "uric acid" OR urate OR hyperuric* OR toph* OR "monosodium urate" OR MSU
#2	*foot OR foot OR feet OR toe* OR digit OR ankle OR podiatry OR “metatarsophalangeal” OR “metatarsal phalangeal” OR MTPJ OR MTP OR hallux OR “big toe” OR “first toe” OR podagra OR 1mtp* OR subtalar OR STJ
#3	Imaging OR sonograph* OR ultraso* OR “doppler” OR radiograph* OR xray OR x-ray OR “magnetic resonance” OR MRI OR “computed tomograph*” OR CT OR "dect" OR “dual energy” OR anatomy OR structure OR epidemiology OR characteristic*
#4	Histol* OR microscop* OR cutaneous OR skin OR nail* OR ulcer*
#5	Biomechanic* OR musculoskeletal OR musc* OR function* OR gait OR walk* OR “plantar pressure” OR *flexion OR flex* OR dorsi* OR plantar* OR pressure* OR postur* OR alignment OR "range of motion" OR motion OR movement OR deformit* OR tendon* OR joint* OR strength OR erosive OR *erosive OR inflammat* OR pain OR force OR kinematic* OR kinetic*
#6	#1 AND #2
#7	#3 OR #4 OR #5
#8	#6 AND #7

Final search: ((Gout* OR "crystal arthropathy" OR "uric acid" OR urate OR hyperuric* OR toph* OR "monosodium urate" OR MSU) AND (*foot OR foot OR feet OR toe* OR digit OR ankle OR podiatry OR “metatarsophalangeal” OR “metatarsal phalangeal” OR MTPJ OR MTP OR hallux OR “big toe” OR “first toe” OR podagra OR 1mtp* OR subtalar OR STJ)) AND ((Imaging OR sonograph* OR ultraso* OR “doppler” OR radiograph* OR xray OR x-ray OR “magnetic resonance” OR MRI OR “computed tomograph*” OR CT OR "dect" OR “dual energy” OR anatomy OR structure OR epidemiology OR characteristic*) OR (Histol* OR microscop* OR cutaneous OR skin OR nail* OR ulcer*) OR (Biomechanic* OR musculoskeletal OR musc* OR function* OR gait OR walk* OR “plantar pressure” OR *flexion OR flex* OR dorsi* OR plantar* OR pressure* OR postur* OR alignment OR "range of motion" OR motion OR movement OR deformit* OR tendon* OR joint* OR strength OR erosive OR *erosive OR inflammat* OR pain OR force OR kinematic* OR kinetic*))

PRISMA flow diagram of literature search for foot and ankle characteristics in gout



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Table 1. *Summary of included articles*

Author year	*Location*	*Study design*	*Participants (% male)*	*Age, years mean (SD),*	*Gout disease duration, years mean (SD),*	*Gout Diagnosis*	*Findings*	*Outcome measures*
Carroll, et al., 2017 [17]	NZ	Cross-sectional	Gout: 24 (92) Non-gout: 24 (92)	Gout: 61.9 (12) Non-gout: 61.7 (12.3) [1]	17.4 (11.9)	ACR *	Tophus deposition was observed in 73% of Achilles tendons in people with tophaceous gout. Entheseal calcifications, calcaneal bone cortex irregularities and calcaneal ethesophytes were observed in both gout and control participants without differences between groups	Imaging features of the Achilles tendon using ultrasound
Carroll, et al., 2018 [21]	NZ	Cross-sectional	Gout: 24 (92) Control: 24 (92)	Gout: 61.9 (12) Control: 61.7 (12.3) [1]	17.4 (11.9)	ACR criteria	The severity of foot pain, generic pain, global function and activity limitation was assessed using the Health Assessment Questionnaire (HAQ)-II. The spatial and temporal parameters of gait were assessed using a 9-camera motion analysis system. Peak ankle joint angular velocity was significantly decreased in participants with gout ($p<0.01$), but no differences were found in ankle ROM or peak ankle joint power or force	Ankle biomechanics during gait using three-dimensional gait analysis
Dalbeth, et al., 2013 [7]	NZ	Cross-sectional	Gout: 92 (93)	Gout: 58 (40) [4]	22 (14)	ACR criteria	DECT used to assess the foot and ankle in tophaceous gout. The Achilles tendon was the most commonly involved tendon/ligament site (39.1%) followed by the peroneal tendons (18.1%). Tibialis anterior and the extensor tendons were involved less commonly (7.6-10.3%), and the other flexor tendons, plantar fascia and deltoid ligaments were rarely involved (<5%). Enthesis involvement alone was more common in the Achilles tendon. The authors observed MSU deposits most frequently at the first metatarsal head (49% of participants), second most commonly at the distal fibula (39%) and the proximal calcaneus (38%), then the fifth metatarsal head	Imaging features of the foot and ankle in gout using DECT and plain radiography (SvdH)

							(29%) and base (24%), and least commonly observed at the first (4%) and second (3%) metatarsal base, and finally the cuneiform (2%)	
Dalbeth, et al., 2015 [18]	NZ	Cross-sectional	Gout: 92 (93)	Gout: 58 (40) [4]	22 (14)	ACR criteria	DECT used in tophaceous gout, found crystal deposition was more frequently observed in joints with erosions. Both were most frequent at the first MTPJ (38% MSU deposition, 79.3% prevalence of first MTPJ erosions) and least common at the fourth MTPJ (4.9% and 6%)	Imaging features of the 1st MTPJ in gout using DECT and plain radiography (SvdH)
Otter et al. 2020 [33]	UK	Case-control	Gout 24 (79% male) Control 26 (81% male)	Gout 70.6 (11) Control 72.3 (10)	9.39 (8.49)	ACR criteria	Ultrasonography found small proportion with tophi in Achilles tendon, with neovascularity in a third of those with gout. Elastography demonstrated significantly reduced tendon stiffness in those with gout compared to controls: right Achilles mdiff =1.04 m/s (95% CI (0.38 to 1.7) p = 0.003 and left Achilles mdiff = 0.7 m/s (95% CI 0.09 to 1.32) p = 0.025.	Ultrasonography & Shear wave elastography
Rome, et al., 2011 [6]	NZ	Case-control	Gout: 25 (75) Controls: 25 (75)	Gout: 61.2 (11.7) Controls: 57.3 (12.2)	22.4 (13.2)	ACR criteria (including 44% crystal proven gout)	The severity of foot pain, generic pain, global function and activity limitation was assessed using the HAQ and Leeds Foot Impact Scale (LFIS). People with chronic gout had higher levels of general and foot-specific disability, pain and impairment. The Foot Function Index assessed pain and showed a mean score of 28.2, which was significantly greater than controls (P<0.001). People with gout had a LFIS mean score of 24 compared to a score of 1 for controls (p<0.001), significantly lower peak plantar pressures in the hallux (p<0.05), significantly higher pressure-time integrals at the midfoot (p<0.05), but lower values were observed at the hallux (p<0.05). The spatial and temporal parameters of gait	Functional characteristics of 1st MTPJ in gout

							was assessed using GAITMAT-11. People with gout walked slower, with longer step and stride length compared to controls	
Rome, et al., 2014 [22]	NZ	Cross-sectional	Gout: 6 (83)	Gout: 66.7 (17.3)	22.3 (6.3)	ACR criteria	The severity of foot pain, generic pain, global function and activity limitation was assessed using the HAQ-II. The dorsal aspect of the third distal interphalangeal joint was the most commonly ulcerated. Moderate scores of foot pain, disability, impairment and health-related quality of life were observed. Most foot ulcers were small (<0.5cm²) and were of partial thickness. Tophus was present in four out of six participants	Skin characteristics
Sapsford, et al., 2017 [23]	NZ	Cross-sectional	Gout: 92 (93)	Gout: 58 (40) [4]	22 (14)	ACR criteria	SvdH scoring method to grade joints for radiographic damage. Erosions were most common at the first MTPJ (79.3%), followed by the fifth MTPJ (34.4%) and least common at the fourth MTPJ (6%)	Imaging features of 10 MTPJs using DECT and conventional radiography
Stewart, et al. 2015 [19]	NZ	Cross-sectional	Gout: 24 (100) Asymptomatic hyperuricemia: 29 (100) Control: 34 (100)	Gout: 58 (13) Asymptomatic hyperuricemia: 58 (19) Control: 58 (14) [2]	17 (11)	ACR criteria used in 18 participants (75%), Crystal proven in 6 participants (25%)	The severity of foot pain, generic pain, global function and activity limitation was assessed using the HAQ-DI. Compared to controls, participants with gout had greater first MTPJ pain (p=0.014), greater foot pain and disability (p<0.001), increased odds of having disabling foot pain (OR 13.4, p<0.001), decreased lower limb function for daily living (p=0.002) and recreational activities (p<0.001), increased activity limitation (p=0.002), reduced overall wellbeing (p=0.034), reduced ROM (p<0.001), reduced plantarflexion force (p=0.012) and increased odds of having more severe hallux valgus (OR 0.3, p=0.041)	Foot pain, disability and functional characteristics of the 1st MTPJ in gout

Stewart, e t al. 2016 [31]	NZ	Cross-sectional	Gout: 24 (100) Asymptomatic hyperuricaemia: 29 (100) Controls: 34 (100)	Gout: 58 (13) Asymptomatic hyperuricaemia: 58 (19) Controls: 58 (14) [2]	17 (11)	ACR criteria	The spatial and temporal parameters of gait was assessed using GAITRite During barefoot walking, compared to normouricemic controls, participants with gout demonstrated increased step time (p=0.022) and stance time (p=0.022), and reduced velocity (p=0.050). Participants with gout walked with decreased peak pressure at the heel (p=0.012) and hallux (p=0.036) and increased peak pressure (p<0.001) and pressure time integrals (p=0.005) at the midfoot	Gait characteristics including plantar pressures and spatiotemporal gait parameters
Stewart, et al., 2016 [27]	NZ	Cross-sectional	Gout: 20 (95) Control: 20 (95)	Gout: 60 (7) Control: 53 (12) [3]	16 (11)	ACR criteria	Gout participants demonstrated reduced muscle strength at both the 30°/s and 120°/s testing velocities for plantarflexion, inversion and eversion (p<0.05). They also displayed a reduced plantarflexion-to-dorsiflexion strength ratio (p<0.05). Foot pain and disability was significantly higher in people with gout (p<0.0001)	Foot pain and disability and functional characteristics of the foot and ankle in gout
Stewart, et al., 2016 [28]	NZ	Cross-sectional	Gout: 20 (95) Control: 20 (95)	Gout: 60 (7) Control: 53 (12) [3]	16 (11)	ACR criteria (including 20% crystal proven gout)	The spatial and temporal parameters of gait was assessed using GAITRite at a self-selected walking speed, gout participants demonstrated increased step time (p=0.017), stance time (p=0.012) and reduced velocity (p=0.036) and cadence (p=0.009)	Gait characteristics including foot pain and disability
Stewart, et al., 2017 [10]	NZ	Cross-sectional	Gout without clinically evident tophi: 35 (89) Gout with clinically evident tophi: 22 (86)	Gout without clinically evident tophi: 60 (14) Gout with clinically evident tophi: 60 (12)	Gout without clinically evident tophi: 11 (10) Gout with clinically evident tophi: 25 (13)	ACR criteria	Tophus was more prevalent at the Achilles tendon (73%). Participants with tophi had significantly reduced muscle force during plantarflexion (p<0.001), dorsiflexion (p=0.003), inversion (p=0.003) and eversion (p=0.001) compared to those without tophi. Those with Achilles tophi had significantly reduced force during plantarflexion (p<0.001), inversion (p=0.008) and eversion (p=0.001)	Functional characteristics of foot and ankle in gout

Stewart, et al., 2017 [20]	NZ	Cross-sectional	Gout: 23 (100) Control: 34 (100) Asymptomatic hyperuricemia: 29 (100)	Gout: 58 (14) Control: 58 (14) Asymptomatic hyperuricemia: 58 (19) [2]	18 (11)	ACR criteria (including 26% crystal proven)	Using ultrasonography reported a prevalence of the double contour sign in 37% of first MTPJs. Double contour sign was associated with higher foot pain and disability scores (p<0.001). Ultrasound tophus was associated with higher foot pain and disability scores (p<0.001), increased temperature (p=0.005), and reduced walking velocity (p=0.001). No associations were observed between ultrasound synovitis or erosion and clinical characteristics. The spatial and temporal parameters of gait was assessed using GAITRite	Imaging features and clinical characteristics of the 1st MTPJ in people with gout
Stewart, et al., 2017 [31]	NZ	Cross-sectional	Gout: 23 (100) Control: 34 (100) Asymptomatic hyperuricemia: 29 (100)	Gout: 58 (14) Control: 58 (14) Asymptomatic hyperuricemia: 58 (19) [2]	18 (11)	ACR criteria (including 26% crystal proven)	Participants with gout had more frequent double contour sign (OR 3.91, p=0.011), more erosions (OR 10.13, p=0.001) and synovitis (OR 9.00, p<0.001). Reported a prevalence of the double contour sign in 37% of first MTPJs	Imaging features of the 1st MTPJ in gout using ultrasound
Yokose, et al., 2019 [3]	USA and NZ	Cross-sectional	Gout: 153 (92)	Gout: 58.5 (11.4)	14.9 (10.3)	ACR criteria	In the feet/ankles, bone erosions were observed in a clustered manner and was symmetrical in presence. Erosions were eight-fold more likely to be present in sites with MSU crystal deposition compared to those without	Imaging features of the foot and ankle in gout using DECT

[1], [2], [3], [4] denote studies which analyse the same cohort of participants

*ACR diagnostic criteria [47]

Table 2 *Modified Quality Index Tool* scores

	Reporting								*External Validity*		*Internal Validity (Bias)*			*Internal Validity (Con-founding)*				*Score*
Study	1	2	3	5	6	7	9	10	11	12	16	18	20	21	22	25	26	*(%)*
Ankle joint function during walking in tophaceous gout: A biomechanical gait analysis study [21] *Carroll 2018*	1	1	1	2	1	1	U0	1	U0	0	1	1	1	0	U0	0	U0	12 (66.7)
Are ultrasound features at the first metatarsophalangeal joint associated with clinically-assessed pain and function? A study of people with gout, asymptomatic hyperuricaemia and normouricaemia [20] *Stewart 2017*	1	1	1	2	1	1	U0	1	U0	0	1	1	1	0	U0	0	U0	11 (61.1)
Characteristics of the first metatarsophalangeal joint in gout and asymptomatic hyperuricaemia: a cross-sectional observational study [19] *Stewart 2015*	1	1	1	2	1	1	*	1	U0	0	1	1	1	0	U0	1	*	12 (66.7)
Clinical characteristics of foot ulceration in people with chronic gout [22] *Rome 2014*	1	1	1	*	1	0	1	*	0	0	1	0	1	*	*	0	0	7 (38.9)
Clinically-evident tophi are associated with reduced muscle force in the foot and ankle in people with gout: a cross-sectional study [10] *Stewart 2017*	1	1	1	2	1	1	*	1	0	0	1	1	1	0	U0	1	*	12 (66.7)

Foot and ankle muscle strength in people with gout: A two-arm cross-sectional study [27] Stewart 2016	1	1	1	2	1	1	*	1	1	0	1	1	1	1	U0	1	*	14 (77.8)
Foot-related pain and disability and spatio-temporal parameters of gait during self-selected and fast walking speeds in people with gout: A two-arm cross sectional study [28] Stewart et al 2016	1	1	1	2	1	1	*	1	0	0	1	1	1	0	U0	1	*	14 (77.8)
Functional and biomechanical characteristics of foot disease in chronic gout: a case-control study [6] Rome et al 2011	1	1	1	1	1	1	*	1	0	0	1	1	1	0	U0	0	*	10 (56)
Radiologic evidence of symmetric and polyarticular monosodium urate crystal deposition in gout - A cluster pattern analysis of dual-energy CT [3] Yokose et al 2019	1	1	0	*	1	1	*	*	U0	0	1	1	1	*	*	U0	*	7 (38.9)
Relationship between structural joint damage and urate deposition in gout: a plain radiography and dual-energy CT study [18] Dalbeth et al 2015	1	1	1	2	1	1	1	1	U0	UO	1	1	1	1	1	1	1	16 (88.9)
Relationship of bone erosion with the urate and soft tissue components of the tophus in gout: a dual energy computed tomography study [23] Sapsford et al 2017	1	1	1	2	1	1	1	1	U0	UO	1	1	1	1	1	1	1	16 (88.9)

Spatiotemporal gait parameters and plantar pressure distribution during barefoot walking in people with gout and asymptomatic hyperuricemia: Comparison with healthy individuals with normal serum urate concentrations [31] *Stewart et al 2017*	1	1	1	1	1	1	*	1	U0	U0	1	1	1	0	U0	1	*	14 (77.8)
Tendon involvement in the feet of patients with gout: a dual-energy CT study [7] *Dalbeth et al 2013*	1	1	1	*	1	1	*	1	U0	U0	1	1	1	*	*	U0	*	14 (77.8)
Ultrasound features of the first metatarsophalangeal joint in gout and asymptomatic hyperuricaemia: comparison with normouricaemic individuals [32] *Stewart et al 2017*	1	1	1	1	1	1	*	1	U0	UO	1	1	1	0	U0	1	1	13 (72.3)
Ultrasound Characteristics of the Achilles Tendon in Tophaceous Gout: A Comparison with Age- and Sex-matched Controls [17] *Carroll et al 2017*	1	1	1	1	1	1	*	1	U0	0	1	1	1	0	U0	1	*	11 (61.1)
Differences in Achilles tendon stiffness in people with gout: a pilot study [33] Otter et al 2020	1	1	1	1	1	1	*	1	U0	1	1	1	1	1	1	0	*	13 (72.3)

All items scored using the following scale: 1 = yes, 0 = no, U0 = unable to determine, * = not applicable to study

Question 5 scored as 2 = yes, 1 = partially, 0 = no