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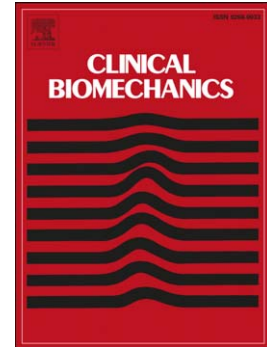
Foot and ankle muscle strength in people with gout: a two-arm cross-sectional study

Sarah Stewart, Grant Mawston, Lisa Davidtz, Nicola Dalbeth, Alain C. Vandal, Matthew Carroll, Trish Morpeth, Simon Otter, Keith Rome

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**TITLE**

Foot and ankle muscle strength in people with gout: a two-arm cross-sectional study

**AUTHORS**

\*Sarah Stewart<sup>a</sup>

Grant Mawston<sup>b</sup>

Lisa Davidtz<sup>a</sup>

Nicola Dalbeth<sup>c,d</sup>

Alain C. Vandal<sup>e,f</sup>

Matthew Carroll<sup>a</sup>

Trish Morpeth<sup>a</sup>

Simon Otter<sup>a,g</sup>

Keith Rome<sup>a</sup>

<sup>a</sup> School of Podiatry, Health & Rehabilitation Research Institute, Auckland University of Technology, Private Bag 92006, Auckland 1142, New Zealand.

<sup>b</sup> Department of Physiotherapy, School of Rehabilitation & Occupation Studies, Faculty of Health & Environmental Sciences, Auckland University of Technology, Private Bag 92006, Auckland 1142, New Zealand.

<sup>c</sup> Faculty of Medical and Health Sciences, The University of Auckland, Private Bag 92019, Auckland 1142, New Zealand.

<sup>d</sup> Department of Rheumatology, Auckland District Health Board, P.O. Box 92189, Auckland, New Zealand

<sup>e</sup> Department of Biostatistics & Epidemiology, School of Public Health & Psychosocial Studies, Faculty of Health and Environmental Sciences, Auckland University of Technology, Private Bag 92006, Auckland 1142, New Zealand.

<sup>f</sup> Health Intelligence and Informatics, Ko Awatea, Counties Manukau Health, Private Bag 93311, Auckland 1640, New Zealand

<sup>g</sup> School of Health Professions, University of Brighton, Darley Road, Eastbourne BN20 7UR, Brighton, United Kingdom.

\*Corresponding author: sarah.stewart@aut.ac.nz

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**ABSTRACT**

**Background** Foot and ankle structures are the most commonly affected in people with gout. However, the effect of gout on foot and ankle muscle strength is not well understood. The primary aim of this study was to determine whether differences exist in foot and ankle muscle strength for ankle plantarflexion, dorsiflexion, inversion and eversion between people with gout and age- and sex-matched controls. The secondary aim was to determine whether foot and ankle muscle strength was correlated with foot pain and disability.

**Methods** Peak isokinetic concentric muscle torque was measured for ankle plantarflexion, dorsiflexion, eversion and inversion in 20 participants with gout and 20 matched controls at two testing velocities (30°/s and 120°/s) using a Biodex dynamometer. Foot pain and disability was measured using the Manchester Foot Pain and Disability Index (MFPDI).

**Findings** Participants with gout demonstrated reduced muscle strength at both the 30°/s and 120°/s testing velocities for plantarflexion, inversion and eversion ( $p < 0.05$ ). People with gout also displayed a reduced plantarflexion-to-dorsiflexion strength ratio at both 30°/s and 120°/s ( $p < 0.05$ ). Foot pain and disability was higher in people with gout ( $p < 0.0001$ ) and MFPDI scores were inversely correlated with plantarflexion and inversion muscle strength at the 30°/s testing velocity, and plantarflexion, inversion and eversion muscle strength at the 120°/s testing velocity (all  $p < 0.05$ ).

**Interpretation** People with gout have reduced foot and ankle muscle strength and experience greater foot pain and disability compared to controls. Foot and ankle strength reductions are strongly associated with increased foot pain and disability in people with gout.

**KEYWORDS:** gout, ankle, torque, Biodex dynamometry

## 1 INTRODUCTION

Gout is a common form of inflammatory arthritis in adults and is caused by the deposition of monosodium urate (MSU) crystals in articular and peri-articular structures [1]. Gout typically presents as episodes of acute inflammatory arthritis interspersed with intercritical asymptomatic periods [2]. In the presence of prolonged hyperuricaemia, chronic gouty arthritis may develop with degenerative joint damage, soft tissue inflammation, tophus formation and altered structural integrity of tendons and ligaments [2, 3]. The structures of the foot and ankle are frequently affected in people with gout [4, 5]. Furthermore, imaging studies have demonstrated particular patterns of foot involvement in gout in which the most common sites for MSU deposition are the first metatarsophalangeal joint, ankle joint and tendons surrounding the ankle including the peroneal and Achilles tendons [6-8].

People with gout report difficulty walking and experience high levels of foot pain, disability and impairment [9-12]. Previous studies have also shown people with gout demonstrate a propulsive gait patterns with reduced walking speed and cadence [10, 12]. Despite the importance of lower limb and foot muscle strength requirements in major daily life activities, including walking, the strength of foot and ankle muscles in gout is poorly understood. Quantifying muscle strength may be useful in establishing the biomechanical impact of gout, providing further insight into the associated impairments and disabilities, characterising the natural progression of the disease, and consequently aid in monitoring the efficacy of therapies in a clinical setting.

The primary aim of this study was to determine whether there were significant differences in foot and ankle muscle strength for ankle plantarflexion, dorsiflexion, inversion and eversion between people with gout and age- and sex-matched controls. The secondary aim was to determine whether foot and ankle muscle strength was associated with foot pain and disability in people with gout and age- and sex-matched controls. It was hypothesized that those with gout would exhibit decreased muscle strength, and that decreased muscle strength would be associated with higher levels of foot pain and disability.

## 2 METHODS

A two-arm cross-sectional study was undertaken at the Auckland University of Technology (AUT), New Zealand. Twenty participants with gout were conveniently sampled from patients registered with the Rheumatology Department at Auckland District Health Board, New Zealand. All patients met the 1977 preliminary American Rheumatism Association classification criteria for gout [13]. Twenty age- and sex-matched controls were recruited from AUT University through poster advertisements and staff newsletters. Ethical approval was obtained from AUT Ethics Committee (AUTEK 13/100). Participants were excluded if they had a history of lower limb amputation, recent surgery or injury to the foot or ankle, or other rheumatic condition. Gout participants were also excluded if they were experiencing an acute flare at the time of assessment as determined by a registered podiatric clinician. Demographic information including age, sex, ethnicity, body mass index (BMI), current medications and co-morbidities was recorded for all participants. Disease duration and gout clinical characteristics, including flares in preceding 3 months, and the presence and number of subcutaneous tophi, were recorded for the gout participants.

Patient-reported foot pain and disability was assessed using the Manchester Foot Pain and Disability Index (MFPDI) [14]. This 19-item index measures foot-related items associated with functional limitation, pain, and physical appearance. Statements relating to each item were answered 'none of the time' (scored as 0), 'on some days' (scored as 1) and 'on most/every day(s)' (scored as 2) in the past month. A total score out of 38 was calculated for each participant.

Peak isokinetic concentric muscle strength was tested by a single researcher for four conditions: ankle plantarflexion, dorsiflexion, inversion and eversion using the Biodex System 3 Dynamometer (Biodex Medical Systems, Shirley, New York). Isokinetic dynamometry has been shown to be a reliable tool for measuring peak torque at the ankle joint [15, 16]. For all testing conditions, participants were seated in the adjustable chair of the dynamometer with the hip angle set at 70° to 85° flexion. The leg to be tested was elevated by a support arm under the knee which was flexed at 30° to 45°. To stabilize this position, straps were fit around the participant's torso, waist, and thigh. The participant's ankle was placed on a footplate, with the heel supported in a rubber heel cup at 90° flexion and the forefoot secured with two Velcro straps.

Prior to isokinetic testing each participant undertook a five minute warm up that involved walking at a self-selected pace. Participants were then seated in the Biodex device and the maximal range of motion was established for each test condition. In addition, to negate the effect of gravity on torque, each limb was weighed and the data corrected by the Biodex software [17]. Prior to testing, each participant received a verbal explanation of each test and was asked to perform four test-specific submaximal contractions to allow them to become familiar with each test procedure. Following the warm up each participant was asked to perform five maximal concentric isokinetic efforts. Verbal encouragement was given throughout testing. Both right and left limbs were tested for each condition at two velocities: 30°/s and 120°/s. Participants were given a two-minute rest period between each velocity condition. Participants were also given a five-minute rest period between plantarflexion-dorsiflexion testing and inversion-eversion testing. The maximum peak torque was calculated from the five contractions for each test condition and was normalised to the participant's body weight prior to analysis. In addition, the strength ratios of the antagonistic muscle groups (plantarflexion-to-dorsiflexion and eversion-to-inversion) were also calculated.

Descriptive statistics relating to participant demographics and muscle torque were presented as mean (SD) for continuous data and frequency (%) for categorical data. All muscle torque data was reviewed for normality using residuals from a linear model through both visual and formal tests including Kolmogorov-Smirnov and Shapiro-Wilk tests, with the participant group (gout or control) as the independent variable. Adjustments for gender, age group, and ethnicity were considered for each testing condition if they achieved at least 10% on an F test. A single adjusted model was sought for all testing conditions to facilitate interpretation. To determine whether the differences between gout and control groups were significant for each muscle test condition, mixed linear models were used. Models accounted for repeated measures taken from right and left feet of each participant through adopting a mixed models approach in which a participant-specific random effect and participant-nested random effect for foot-side were included. This analysis produces results identical to an analysis of measures averaged for each foot-side that would allow for a between-foot-side correlation, and also allows for any reweighting required due to missing values. For muscle groups which demonstrated significant between-group differences, Pearson correlation coefficients, denoted  $r$ , were used to assess for associations between the total MFPDI scores and muscle force. An  $r$  value of 0.1 was considered a small effect size, 0.3 a medium effect size, and 0.5 a large effect size [18]. No adjustments for multiplicity were used, but all test-statistics, their null distributions and their observed significance levels were reported. All data was analysed using SPSS v.20 (IBM Corporation) at a 5% level of significance unless otherwise noted.

### 3 RESULTS

Participants were predominantly middle-aged European men (Table 1). The mean MFPDI score was significantly higher in people with gout compared to control participants.

Descriptive statistics for peak torque were presented normalised to body weight (N·m/kg) (Table 2). All data conformed to a normal distribution. The participant-nested random effect for foot-side did not demonstrate significance for any muscle group tested. Age reached significance for all testing conditions (all  $p < 0.10$ ) and was therefore included as a covariate in the final models. Although ethnicity was explored as a covariate, the numbers in each group were too small to be able to account for it statistically. Furthermore, boxplots of random effects by ethnicity did not conclusively show a marked remaining difference between ethnic categories. Age-adjusted inferential statistics comparing each test condition between gout and controls demonstrated differences at both the 30°/s and 120°/s testing velocities for ankle plantarflexion ( $p = 0.010$  and  $0.008$ , respectively), inversion ( $p = 0.012$ ,  $0.005$ ), and eversion ( $p = 0.005$ ,  $0.028$ ), in which gout participants demonstrated reduced peak torque/kg values compared to controls (Table 3). No differences between gout and controls were observed for dorsiflexion torque/kg at either 30°/s ( $p = 0.280$ ) or 120°/s ( $p = 0.111$ ) testing velocities. The plantarflexion-to-dorsiflexion torque/kg ratio was higher in the gout participants when compared to control participants for both 30°/s ( $p = 0.035$ ) and 120°/s ( $p = 0.028$ ) testing velocities, while no significant differences were observed between gout and control groups for eversion-to-inversion torque/kg ratios at either 30°/s ( $p = 0.285$ ) or 120°/s ( $p = 0.285$ ).

The correlations between the MFPDI scores and muscle torque parameters showed that for people with gout, MFPDI scores were inversely correlated with plantarflexion at both 30°/s ( $r = -0.66$ ,  $p < 0.001$ ) and 120°/s ( $r = -0.44$ ,  $p = 0.008$ ) testing velocities, eversion at the 120°/s testing velocity ( $r = -0.36$ ,  $p = 0.45$ ) and inversion at both 30°/s ( $r = -0.49$ ,  $p = 0.005$ ) and 120°/s ( $r = -0.56$ ,  $p = 0.001$ ) testing velocities (Table 4). No significant correlation was observed between MFPDI scores and muscle torque in the control group.

#### 4 DISCUSSION

The aims of this study were to compare foot and ankle muscle strength in people with gout and age- and sex-matched controls and to determine whether strength was related to foot pain and disability. This study has shown that people with gout have significantly reduced plantarflexion, eversion and inversion muscle strength compared to controls. Consistent with our hypothesis this study has also demonstrated a negative correlation between these aspects of ankle strength and foot pain and disability in people with gout.

Previous research has observed tophaceous deposition in the Achilles, peroneal and the tibialis posterior muscle tendons in people with gout [6, 8]. Tendons have important functional roles, both in generating and absorbing mechanical work during ambulation [19]. The Achilles tendon in particular must withstand large muscle contractions during ankle plantarflexion at propulsion, as well as during deceleration of body movement in the stance phase of gait [20]. Eversion and inversion motions of the foot, which involve the peroneal and tibialis posterior muscles, are also important throughout the gait cycle, particularly for their contribution to shock absorption and stability [21]. Although the impact that MSU deposition in these ankle structures has on muscle strength remains unclear, several case studies investigating tendon ruptures of the ankle and foot in the gout populations have suggested that the presence of tophi reduces the tensile capacity of tendons [22-24]. Furthermore, the infiltration of tophi into muscle tissues may potentially reduce the functional cross-sectional muscle area (i.e. area of active working muscle) and thereby the potential to generate force [25].

The reduction in plantarflexion torque and the absence of a decrease in dorsiflexion torque was also illustrated in the lower plantarflexion-to-dorsiflexion ratio observed in our gout participants. Although large strength imbalances between ankle plantarflexion and dorsiflexion are not considered beneficial in terms of ankle stability and function, a specific range of plantarflexion-to-dorsiflexion ratio is important for normal walking [26]. Contrary to our hypothesis, our results indicate that the dorsiflexors of the ankle are not affected by strength deficits to the same extent as the plantarflexors of the ankle in people with gout. This finding may be related to the pattern of crystal deposition and patient symptoms reported in the foot and ankle, in which anterior ankle structures, including the tibialis anterior tendon are less frequently involved compared with the posterior ankle and Achilles tendon [6, 8]. Our results are consistent with previous studies investigating the ankle in other chronic inflammatory arthritic conditions [27] in which neural



(arthrogenic inhibition) and muscle volume (atrophy) changes have been found to be the main contributors to muscle weakness [28].

The findings from the current study are consistent with previous studies which have shown that foot-related pain, disability and impairment are not only features of acute gouty arthritis [9], but also present during intercritical periods [10, 11]. None of our gout participants were experiencing symptoms of acute arthritis at the time of the study which highlights the chronicity of foot pain in this population. Furthermore, we observed significant correlations between reduced muscle strength and increased MFPDI scores for plantarflexion, eversion and inversion. Although the causal link between muscle strength reduction and increased foot pain cannot be determined from this study, it is possible that foot pain may lead to muscle atrophy through disuse. Previous studies have observed a propulsive gait patterns consistent with pain-avoidance strategies in people with gout [10]. It has been proposed that such strategies would reduce plantarflexor muscle activity and the consequent disuse may contribute to muscle wasting [10].

This study has a number of limitations. The cross-sectional nature of the research design limits the ability to determine causality between patient-reported outcomes and muscle function. Furthermore, participants with gout were recruited from secondary care and may not be representative of less severe gout that is more commonly treated in primary care.

Further studies may employ advanced imaging methods to explore the relationships between muscle strength and the presence of tophi in associated lower limb and foot musculoskeletal structures. Additional gout disease characteristics, including the location of recent acute gouty arthritis in foot and ankle structures, could also be explored in terms of their impact on local muscle function. The findings from this study may be useful in directing future research which evaluates strengthening exercises and non-pharmacological interventions which specifically target ankle plantarflexion, inversion and eversion musculature. Our previous research has demonstrated that footwear featuring rocker sole characteristics facilitates a propulsive gait in patients with gout and improves patient-reported outcomes [29, 30]. Further studies may also determine whether sagittal plane muscle weakness and altered strength ratios are also present in the knee and hip musculature.

## **5 CONCLUSION**

In conclusion, the present study has demonstrated that muscle strength of the ankle plantarflexors as well as inversion and eversion of the foot is significantly reduced in people with gout.

Furthermore, reduced muscle strength in people with gout was strongly associated with increased levels of patient-reported foot pain and disability. We speculate that the muscle strength reductions may be a consequence of muscle atrophy secondary to pain-avoidance strategies.

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ACCEPTED MANUSCRIPT

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## TABLES

**Table 1:** Demographics & clinical characteristics

Variable	Control	Gout	<i>p</i>
N	20	20	
Gender, male, n (%)	19 (95%)	19 (95%)	0.998
Age, years, mean (SD)	53 (12)	60 (7)	0.056
Ethnicity, n (%)	European 20 (100%) Maori 0 (0%) Pacific 0 (0%) Asian 0 (0%)	European 12 (60%) Maori 1 (5%) Pacific 3 (15%) Asian 4 (20%)	<b>0.004</b>
BMI, kg/m <sup>2</sup> , mean (SD)	26.7 (4.3)	31.5 (5.9)	<b>0.006</b>
Diuretic use, n (%)	1 (5%)	3 (15%)	0.635
NSAID use, n (%)	0 (0%)	12 (60%)	0.998
Prednisone use, n (%)	0 (0%)	2 (10%)	0.998
Hypertension, n (%)	6 (30%)	12 (60%)	0.061
Cardiovascular disease, n (%)	1 (5%)	5 (25%)	0.108
Diabetes, n (%)	1 (5%)	4 (20%)	0.182
Microscopically proven gout	-	4 (20%)	-
Disease duration, years, mean (SD)	-	16 (11)	-
Serum urate, mmol/l, mean (SD)	-	0.37 (0.15)	-
Flares in preceding 3 months, mean (SD)	-	1.1 (1.6)	-
Any subcutaneous tophi, n (%)	-	12 (60%)	-
Subcutaneous tophus count, mean (SD)	-	3.9 (6.1)	-
Urate lowering therapy, n (%)	-	18 (95%)	-
MFPDI, total score, mean (SD)	2.1 (4.3)	12.4 (8.6)	<b>0.00001</b>

**Table 2:** Descriptive statistics: normalised peak torque, mean (SD), N·m/kg

Variable	Foot	Control	Gout
Plantarflexion 30°/s	right	0.94 (0.39)	0.52 (0.26)
	left	1.02 (0.41)	0.53 (0.25)
Dorsiflexion 30°/s	right	0.42 (0.09)	0.24 (0.05)
	left	0.41 (0.11)	0.26 (0.07)
Plantarflexion 120°/s	right	0.67 (0.39)	0.32 (0.28)
	left	0.56 (0.25)	0.28 (0.16)
Dorsiflexion 120°/s	right	0.38 (0.15)	0.21 (0.04)
	left	0.35 (0.10)	0.21 (0.06)
Eversion 30°/s	right	0.34 (0.12)	0.23 (0.07)
	left	0.33 (0.12)	0.24 (0.08)
Inversion 30°/s	right	0.36 (0.15)	0.26 (0.11)
	left	0.38 (0.17)	0.23 (0.11)
Eversion 120°/s	right	0.22 (0.07)	0.16 (0.05)
	left	0.22 (0.08)	0.16 (0.06)
Inversion 120°/s	right	0.24 (0.08)	0.17 (0.07)
	left	0.25 (0.08)	0.16 (0.07)
Plantarflexion/Dorsiflexion ratio 30°/s	right	2.27 (0.79)	1.84 (1.11)
	left	2.51 (0.88)	1.63 (0.63)
Plantarflexion/Dorsiflexion ratio 120°/s	right	2.13 (0.89)	1.51 (0.96)
	left	2.05 (0.75)	1.24 (0.71)
Eversion/Inversion ratio 30°/s	right	1.01 (0.27)	1.01 (0.29)
	left	0.98 (0.32)	1.24 (0.75)
Eversion/Inversion ratio 120°/s	right	0.91 (0.15)	0.90 (0.23)
	left	1.00 (0.23)	1.08 (0.34)

**Table 3:** Inferential statistics: normalised peak torque (N·m/kg)

Parameter		Mean Estimate	Difference	95% CI		<i>p</i>
				Lower	Upper	
Plantarflexion 30°/s	Control	0.94				
	Gout	0.65	-0.29	-0.51	-0.07	<b>0.010</b>
Dorsiflexion 30°/s	Control	0.41				
	Gout	0.37	-0.04	-0.10	0.03	0.280
Plantarflexion 120°/s	Control	0.51				
	Gout	0.32	-0.19	-0.32	-0.05	<b>0.008</b>
Dorsiflexion 120°/s	Control	0.25				
	Gout	0.22	-0.03	-0.06	0.01	0.111
Eversion 30°/s	Control	0.34				
	Gout	0.24	-0.09	-0.16	-0.03	<b>0.005</b>
Inversion 30°/s	Control	0.37				
	Gout	0.25	-0.12	-0.21	-0.03	<b>0.012</b>
Eversion 120°/s	Control	0.21				
	Gout	0.17	-0.04	-0.08	-0.01	<b>0.028</b>
Inversion 120°/s	Control	0.24				
	Gout	0.17	-0.07	-0.12	-0.02	<b>0.005</b>
Plantarflexion/Dorsiflexion ratio 30°/s	Control	2.33				
	Gout	1.79	-0.54	-1.05	-0.04	<b>0.035</b>
Plantarflexion/Dorsiflexion ratio 120°/s	Control	2.03				
	Gout	1.43	-0.60	-1.13	-0.07	<b>0.028</b>
Eversion/Inversion ratio 30°/s	Control	0.99				
	Gout	1.12	0.13	-0.12	0.38	0.285
Eversion/Inversion ratio 120°/s	Control	0.90				
	Gout	1.05	0.13	-0.12	0.38	0.285

**Table 4:** Correlations between MFPDI scores and normalised peak muscle torque (N·m/kg)

Strength Parameter	Control		Gout	
	Pearson's <i>r</i>	<i>p</i>	Pearson's <i>r</i>	<i>p</i>
Plantarflexion 30°/s	0.09	0.567	-0.66	<b>0.00002</b>
Plantarflexion 120°/s	0.00	0.979	-0.44	<b>0.008</b>
Eversion 30°/s	0.05	0.768	-0.28	0.117
Eversion 120°/s	0.05	0.758	-0.36	<b>0.045</b>
Inversion 30°/s	-0.04	0.794	-0.49	<b>0.005</b>
Inversion 120°/s	-0.03	0.864	-0.56	<b>0.001</b>



**Highlights**

- Peak isokinetic muscle torque of the foot and ankle was measured in people with gout
- Plantarflexion, inversion and eversion muscle strength is reduced in people with gout
- Reduced muscle strength is associated with increased foot pain and disability