

## Comparison of foot pain and foot care among rheumatoid arthritis patients taking and not taking anti-TNF $\alpha$ therapy: an epidemiological study

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**Abstract** Epidemiological studies report foot pain affects more than 90% of people with rheumatoid arthritis (RA). Most data about foot involvement in RA were collected prior to the availability of novel treatments such as biologics. The objective of this study is to compare the prevalence of foot symptoms, frequency of foot examination, and access to foot care services among RA patients currently treated with anti-TNF $\alpha$  to those not receiving biologics. This study is a cross-sectional epidemiological study: a 28-item self-administered questionnaire was posted to 1,040 people with RA throughout the UK. Overall, 585 (55%) useable replies were received, and 120 (20.5%) respondents were currently

taking anti-TNF $\alpha$  medication. Prevalence of current foot pain was 99% among the biologics group compared with 76% not treated with biologics. Stiffness, swelling, and numbness in the feet were all significantly more common in the anti-TNF $\alpha$  group ( $P < 0.05$ ). Most respondents (90%) taking biologics discussed their foot pain with their rheumatologist, but only 70% were receiving podiatry (compared to 78% not taking anti-TNF $\alpha$ ). Subjects reported that their feet were examined significantly less frequently ( $P < 0.001$ ) than their hands. Foot complaints are common in this group, and allied health professions could enhance rheumatological care by undertaking foot assessment.

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### Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory poly-arthritis typically affecting up to 1% of the population leading to joint damage causing disability and deformity [1, 2]. Foot complaints are frequently seen in people with RA [3, 4], and the extent of these pathologies contributes to the overall disability experienced [5]. Involvement of the foot in RA has been shown to be an important marker for impaired mobility and reduced functional capacity; this subsequent loss of mobility due to foot pathology can have a profoundly negative impact on social interaction [6–8]. Novel therapies for RA have brought about substantial changes in quality of life and symptoms in people with RA. In particular, anti-TNF $\alpha$  therapies are now widely used throughout the UK, and managing foot complaints in these patients can impact on their overall rheumatological care [9]. Therefore, we aimed at investigating the effect of anti-TNF $\alpha$  on foot symptoms among a cohort of people with RA.

## Methods

### Subjects

In this cross-sectional study, two groups of people with RA were identified. The first cohort was recruited according to their membership of a British charity, the National Rheumatoid Arthritis Society (NRAS,  $n = 650$ ). The second cohort ( $n = 390$ ) comprised all people with RA attending outpatient appointments at three major hospitals over the course of 1 month in a Teaching Hospital NHS Trust in the UK. A questionnaire was developed from items generated by focus groups with people with RA as well as podiatrists and rheumatologists. Items were then triangulated with validated tools previously used among those with RA [10, 11], in systemic disorders where foot complaints are common [12] (e.g., diabetes) and measures for other chronic foot complaints [13]. We tested the questionnaire in two stages on people with RA attending a podiatry clinic and utilised their feedback in producing the final tool. The questionnaire enquired about demographics, duration and severity of disease, medication, foot symptoms, foot examination, and access to foot care services.

### Data collection

Every subject ( $n = 1,040$ ) was mailed a questionnaire [4], accompanied by a prepaid reply envelope and covering letter. Ethical approval was granted from University of Brighton (REC05-59) and Brighton and Hove Local

Research Ethics Committees (06/Q1907/12). A system of reminders for non-responders was not initiated at the specific behest of the research ethics committee.

### Statistical analysis

Data were cleaned and entered into SPSS v17. Categorical data were summarised using frequency counts and percentages. Continuous data were summarised by means ( $\pm$ standard deviations). The Student's *t*-test, analysis of variance (with post hoc Tukey multiple comparison where appropriate), chi-square, and correlation coefficients were used to test for significant associations between foot symptoms, with significance set at the  $P < 0.05\%$  confidence level.

## Results

### Demographic data

In total, 585 usable replies were received (56% response rate), and of these, 120 (20.5%) respondents were currently being prescribed anti-TNF $\alpha$  medication. No respondents reported taking other categories of biological agents (e.g., B-cell inhibitors). The demographic characteristics of all respondents, those taking and not taking anti-TNF $\alpha$  medication, which are outlined in Table 1, were broadly similar except for age and BMI. Of the 120 respondents prescribed anti-TNF $\alpha$  medication, 78% ( $n = 94$ ) were taking at least

**Table 1** Demographic and symptom characteristics of respondents

Characteristic	Anti-TNF $\alpha$ group ( $n = 120$ )	Non-anti-TNF $\alpha$ group ( $n = 465$ )	Significance
Mean age ( $\pm$ SD)	54 years ( $\pm 11.5$ )	58 years ( $\pm 12.8$ )	$P = 0.01$
Gender M:F	16 M : 104 F	93 M : 366 F	$P = 0.09$
Mean duration RA ( $\pm$ SD)	12.8 years (9.6)	11.9 years (11.2)	$P = 0.15$
Mean BMI ( $\pm$ SD)	25.4 (5.77)	25 (4.6)	$P = 0.018$
Symptoms			
Currently experiencing morning stiffness	Yes = 91% ( $n = 107$ )	Yes = 86% ( $n = 385$ )	$P = 0.015$
Mean duration of morning stiffness (range, ( $\pm$ SD))	3 h (10 min—24 h, (5.5))	2.9 h (10 min—24 h, (5.7))	$P = 0.84$
Current foot pain due to RA	Yes = 99%	Yes = 76%	$P = 0.012$
Severity of current foot pain (0–10 cm VAS) mean ( $\pm$ SD)	4.5 (2.4)	5.3 (2.9)	$P = 0.08$
Proportion of respondents who always or sometimes experience stiffness in their feet	95%	89%	$P = 0.050$
Proportion of respondents who always or sometimes experience swelling in their feet	97%	88%	$P = 0.014$
Proportion of respondents who always or sometimes experience numbness in their feet	96%	55%	$P = 0.044$

another disease-modifying anti-rheumatic drug (DMARD) in combination with their biological therapy.

Prevalence of foot symptoms

A significantly greater proportion of subjects in the anti-TNF $\alpha$  group reported current foot ( $P = 0.012$ ), compared with those not taking anti-TNF $\alpha$  medication (Table 1). Other symptoms characteristics of foot complaints in RA (i.e., stiffness, swelling, and numbness) were also found to be significantly more prevalent in the anti-TNF $\alpha$  group (all  $P \leq 0.05$ ). A comparison of severity of current foot pain (using a 10 cm visual analogue scale), a trend towards reduced pain scores in the anti-TNF $\alpha$  group (mean 4.5,  $\pm$  SD 2.4) compared with the non-anti-TNF $\alpha$  group (mean 5.3,  $\pm$  SD 4.6), was noted, although this did not reach statistical significance ( $P = 0.08$ ). The location of

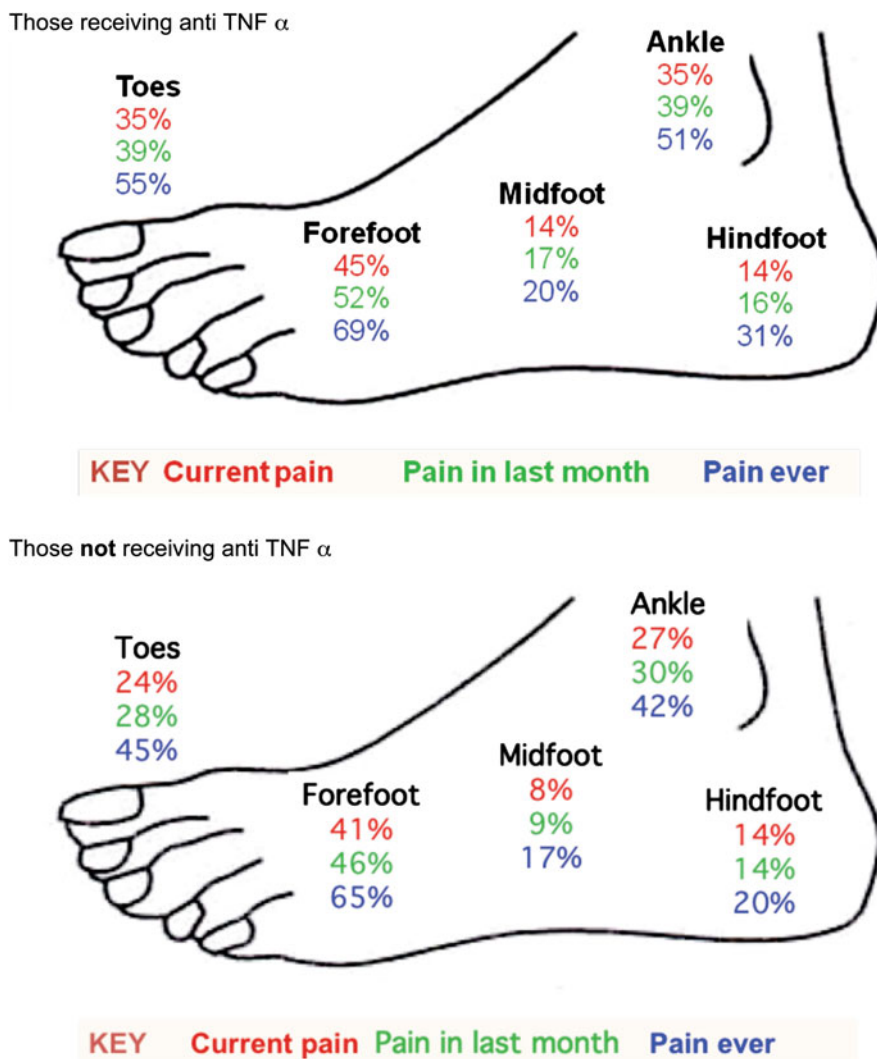
foot pain is reported in Fig. 1, where pain in the ankle and forefoot predominated.

Assessment and management of foot complaints

Those taking anti-TNF $\alpha$  medication reported hand examination was undertaken on average every 4.1 months (SD 5.28) compared with every 6.6 months (SD 11.3) in those **not** prescribed anti-TNF $\alpha$  medication. People taking anti-TNF $\alpha$  recalled foot examination on average every 15.7 months (SD 26), compared with foot examination every 15.4 months (SD 28.6) for those **not** taking anti-TNF $\alpha$  medication ( $P < 0.001$ ).

Overall, 78 (94%) of the anti-TNF $\alpha$  group reported experiencing difficulty with basic foot care (defined as ability to cut own toenails), compared with 299 (64%) of the non-anti-TNF $\alpha$  group. Overall, 90% of anti-TNF $\alpha$

**Fig. 1** Location of current pain in the foot



N.B. Figures expressed as percentages for ease of comparison, sections may total more than 100 as respondents could select more than one anatomical area

respondents reported discussing their foot problems with their rheumatologist: 70% were currently receiving podiatry care compared to 78% not taking anti-TNF $\alpha$ .

## Discussion

This is the first study to report on the prevalence of foot symptoms among RA patients taking, compared with those not taking, anti-TNF $\alpha$  medication. The results suggest that those receiving biologics are significantly more likely to be affected by foot pain, stiffness, swelling, and numbness compared with those prescribed traditional DMARD therapy. Counter-intuitively, however, it appeared that a greater proportion of the conventional treatment group were currently receiving specialist foot care by a podiatrist compared with those currently prescribed anti-TNF $\alpha$  therapy. According to respondent's recollection, all subjects (receiving and not receiving biologics) had significantly more frequent hand than foot assessment.

According to NICE guidance in the UK, anti-TNF $\alpha$  drugs are reserved for those with RA with the most severe uncontrolled inflammation despite at least two DMARDs, one of which must be methotrexate [14]. Given that anti-TNF $\alpha$  drugs are therefore used as a 'step-up' therapy under current UK guidelines, it may be that the increased prevalence of foot symptoms simply underlines that those receiving biological drugs are those most severely affected by RA. However, the results of clinical trials with anti-TNF $\alpha$  drugs show remarkable and dramatic reductions in VAS pain scores, and indeed, pain improvement is a part of assessment of disease activity captured by a DAS-28 score [15]. It is possible however that the greater number of foot symptoms in the TNF $\alpha$  group might be because patients have a greater degree of mobility as a result of the effectiveness of biological agents.

Our results suggested that those prescribed anti-TNF $\alpha$  medication recalled foot examination having been performed less frequently than those taking conventional therapy and considerably less often than hand examination. While it must be borne in mind that this may be a consequence of recall bias, there was no obvious reason to expect a selective recall bias for foot examination compared with hand examination. Clinicians limited by time constraints in clinic might perform a quick hand examination for signs of synovitis in all or most RA patients but perhaps perform foot examination only when foot symptoms are specifically mentioned. It may be a consequence of the well-validated DAS 28 scoring system [15], which specifically does not incorporate foot/ankle examination that respondents perceive that their feet/ankles are less frequently assessed, and it may be that our results reflect increasing use of formalised joint scoring in clinical settings [16].

The results of our study suggest that foot symptoms are ubiquitous in RA even among those treated with the most aggressive forms of therapy. This highlights a specific need for specialist foot care in this group, especially in the face of a varied pattern of provision of foot care services around the UK [17]. In particular, RA patients are at high risk of foot ulceration (reported prevalence between 4 and 8%) [10, 18]; consequently, it is clearly vital that early signs of decreased tissue viability are detected and managed aggressively, especially in immunocompromised patients [19].

## Conclusions

In conclusion, we have found that foot symptoms remain a major problem for those with RA even when treated with biological therapies. Respondents perceived that examination of their feet was carried out less regularly than that of their hands. It may be that clinicians target their examination to joints in which the worst symptoms are reported. If this is the case, specific enquiry about foot symptoms in every patient with RA should be 'best practice'. This may lead to more people needing their feet examining in clinic and highlights the role of the multidisciplinary team where a podiatrist or extended scope specialist nurse could undertake routine foot assessment as part of a defined care pathway.

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**Conflict of interest** None.

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