BMJ Open

Foot health and quality of life in patients with rheumatoid arthritis: a cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-036903
Article Type:	Original research
Date Submitted by the Author:	18-Jan-2020
Complete List of Authors:	Reinoso-Cobo, Andres; Hospital Universitario Virgen de las Nieves Gijon-Nogueron, Gabriel; University of Malaga, Nursing and Podiatry Ferrer-Gonzalez, Miguel Angel; Hospital Universitario Virgen de las Nieves Vallejo-Fernandez1, Maria Teresa; Hospital Universitario Virgen de las Nieves Caliz-Caliz1, Rafela; Hospital Universitario Virgen de las Nieves Miguel Morales-Asencio, Jose; University of Malaga, Nursing and Podiatry Ortega-Avila, Ana Belen; Universidad de Malaga Facultad de Ciencias de la Salud, Nursing and Podiatry
Keywords:	RHEUMATOLOGY, Foot & ankle < ORTHOPAEDIC & TRAUMA SURGERY, PRIMARY CARE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Foot health and quality of life in patients with rheumatoid arthritis: a cross-sectional study

Andres Reinoso-Cobo[1] MSc andres.reinoso.sspa@juntadeandalucia.es

Gabriel Gijon-Nogueron[2,3], PhD gagijon@uma.es

Rafela Caliz-Caliz[1] MD,PhD antonior.caliz.sspa@juntadeandalucia.es

Miguel Angel Ferrer-González[1] MD PhD maferrer@fundacionhvn.org

Maria Teresa Vallejo-Fernandez[1], MsC tvallejo@ibsgranada.es

Jose Miguel Morales-Asencio[2,3] PhD jmmasen@uma.es

Ana Belen Ortega-Avila[3] PhD anaortavi@uma.es

1. Departamento de Reumatologia, Hospital Universitario Virgen de las Nieves, Granada, Granada, Spain
2. Instituto de Investigación Biomédica de Málaga (IBIMA), Malaga, Spain
3. Department Nursing and Podiatry, Universidad de Málaga, Malaga. Spain

Corresponding author: Gabriel Gijon-Nogueron

Faculty of Health Sciences. Arquitecto Francisco Penalosa 3. Ampliación de Campus de Teatinos, 29071 Malaga. Spain. gagijon@uma.es

Word count: 2249 words without references

References: 26

Abstract: 363 words

Tables: 3

Funding: This study did not receive any funding.

Conflict of interest: All the authors declare that they have no conflict of interest derived from the outcomes of this study.

Abstract

Objective: The aim of this study is to identify foot health factors related to the quality of life in patients with RA.

Setting: The cross-sectional in total, 293 subjects were analysed, with 229 patients in the RA group and 64 in the control group. In the RA group, 173 patients were female, as were 50 of the control group

Participants: Patients with foot pain and RA (according to the 1987 American College of Rheumatology revised criteria) and with foot pain but no RA were recruited (Granada, Spain).

Intervention: Two researchers independently interviewed the patients to obtain the study data

Primary and secondary outcome measures: Clinical data were obtained using the SF-12 questionnaire (Quality of life) (Primary outcome), visual analogue scales for pain (VAS pain), the Manchester Foot Pain Disability Index questionnaire (MFPDI) and the Foot Function Index (FFI). Anthropometric measurements were obtained by means of a foot measurement platform, the Foot Posture Index (FPI) and the Manchester Hallux Valgus Scale.(secondary outcomes)

Results

Of the 293 subjects, 76.1% were female. Significant differences were observed between the RA and control groups ($p<0.001$) according to VAS pain (general, foot and hand), the MFPDI and the FFI. In terms of anthropometric measurements, significant differences were only recorded for midfoot and forefoot width ($p=0.03$). In the data for the physical component, the multivariable linear regression with the parameters age, gender, VAS pain (general) and the presence of RA presented an R2 value of 48.8%, while for the mental health component, the corresponding value was 5.6%.

Conclusion

Morphological and structural characteristics of the foot are not necessarily associated with pain, disability and loss of function. The presence of RA, a higher score in VAS pain (general), female gender and greater age are all associated with the physical component of the quality of life for patients with RA.

Key words

Rheumatoid arthritis; foot health; quality of life; functionality; pain.

Strengths and limitations of this study

- The foot-related parameters are strongly associated with the quality of life
- The presence of RA, a higher score for general VAS pain, female gender and greater age are all related to a reduced quality of life in the physical component for patients with RA
- The physical and the mental components were analysed at a moment that might have coincided with an aggravation of the RA experienced

Introduction

Rheumatoid arthritis (RA) is a chronic rheumatic disease that affects 0.5% to 1% of the population in Europe [1]. The most characteristic symptom is swelling, which provokes important changes in joint structures and limits function [2].

RA mainly affects the small joints of the hands and feet [3]. In the foot, it provokes deformities in the forefoot and hindfoot. The most common pathologies are hallux valgus, metatarsal subluxation, and hammer or claw toes [4]. As the disease progresses, first metatarsophalangeal joint and pes planus may also be observed. These pathologies occur as the deterioration affects the joints and ligaments [5], thus limiting movement in the ankle and the foot. It also produces an unequal distribution of pressures and therefore makes it painful to remain in a standing position [6].

RA is a systemic disease that not only presents extra-articular manifestations but also has psychological affects [7], in many cases provoking mental health and functional problems as a consequence of ageing [8], oxidative damage to DNA and systemic inflammatory stress [9], thus limiting leisure and family-related activities and restricting social relationships [10]. The simultaneous impact of RA and a reduced quality of life imposes a major burden on patients, caregivers, the health system and society in general [11].

The mental and physical components of RA can reduce adherence to treatment, leading to poorer health outcomes and a worsened quality of life [12].

In patients with RA, the foot has been analysed from various standpoints, such as hallux valgus, claw fingers or morphological alterations [13]. Psychological and social aspects of the disease have also been analysed [14,15]. However, to date no studies have been undertaken to determine whether RA in the foot has a negative impact on the quality of life, in physical and mental terms.

The aim of the present study, therefore, is to identify foot health factors related to the quality of life in patients with RA.

Method

Ethical approval: Institutional review board that approved the protocol for the study: Medical Research Ethics Committee of University of Malaga (CEUMA-91-2015-H) and PEIBA Andalucia (ARC0001), Spain.

Design: Cross-sectional study

Participants

A convenience sample was obtained of 246 patients with foot pain and RA (according to the 1987 American College of Rheumatology revised criteria) [16], of whom seventeen subsequently declined to participate, citing lack of time (the study questionnaire required 30 minutes to complete) and 64 patients with foot pain but no RA. The patients were enrolled at hospital outpatient clinics from January to December 2018. All those included in the study had a history of subtalar and/or ankle and/or talonavicular or hindfoot pain, did not make daily use of walking aids, and were able to achieve the normal range of motions in the ankle, subtalar and midtarsal joints [6]. The exclusion criteria applied were the presence of concomitant musculoskeletal disease, central or peripheral nervous system disease or endocrine disorders (especially diabetes mellitus).

Patients who met the criteria for inclusion were approached by members of the rheumatology service at the Virgen de la Nieves Hospital (Granada, Spain), given an information sheet and invited to participate. Those who agreed were then interviewed and given further details of the study. All participants provided written consent prior to starting the interviews.

Data collection

Demographic and clinical characteristics

The demographic characteristics recorded included the patient's age, gender, disease duration and current therapy. The clinical data recorded were those obtained from the SF-12 questionnaire [17], a visual analogue scale for pain (VAS pain), both general [18] and specific to the foot and hand, the Manchester Foot Pain Disability Index (MFPDI) [19] and the Foot Function Index (FFI) [20].

For the anthropometric measurements, a foot measurement platform [21] was used to measure the foot length (weight bearing and non weight bearing), the midfoot, forefoot and heel width and the midfoot height. Each participant was asked first to stand on the

platform and then to be seated, in both cases with the body weight distributed evenly between the two feet, arms beside the body and facing forwards. The measurements were obtained with the patient's heels placed in the heel cups, as far back as possible, and the first metatarsal heads located against the limit surface.

Other measurements were obtained using the Foot Posture Index, a reliable instrument for this purpose [22], and the Manchester Scale of hallux valgus [23].

The data availability statement No additional data available

Procedure

Two researchers (ARC and GGN) independently interviewed the patients to obtain the study data. The clinical interview was conducted in one room, where the patients were asked to complete the SF-12 (adapted version for a Spanish population) [24], MFPDI and VAS questionnaires. In a separate room, each patient was measured using a validated foot platform (intraclass correlation coefficient for the instrument, ICC, 0.96-0.98). Foot posture was determined according to the Foot Posture Index (FPI) (ICC for the clinician, 0.94-0.96). Each criterion was scored as −2, −1, 0, +1 or +2. The following FPI cut-off points, defining foot type category were used: a) highly supinated −12 to −4, b) supinated −3 to 0, c) neutral 1 to 7, d) pronated 8 to 10 and e) highly pronated 11 to 12 [25]. The presence/absence of hallux valgus was determined according to the Manchester Scale of Hallux Valgus (ICC for the instrument, 0.93-0.97), a clinical tool consisting of photographs of feet with four levels of hallux valgus: none, mild, moderate and severe [23].

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in the design or conduct of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants

Statistical analysis

The results obtained are reported as the median and interquartile range, due to the non-normal distribution of the variables. The normality of the distributions was examined by the Kolmogorov-Smirnov test and the intra-rater reliability of the measurement instruments was calculated by a two-way mixed-consistency ICC model. Bivariate

analysis was performed with a non-parametric test (the Mann-Whitney U test), in view of the non-normal distribution observed in most cases. Finally, a multivariable linear regression model was obtained to evaluate the predictors of quality of life, according to the physical and mental health components of the SF-12 questionnaire. In constructing the models, the regression assumptions of homoscedasticity, normality and independence of the residuals and collinearity were tested. Homoscedasticity was evaluated by analysing the distribution of predicted values and scatterplots of the residuals. Normality of the residuals was tested by analysing histograms and by graphs of standardised residuals. Independence of the residuals was evaluated by the Durbin-Watson statistic. Finally, the presence of collinearity was tested by calculating the variance inflation factor, the tolerance and partial correlations. The significance level was set at $p<0.05$, with two-tailed tests. All statistical analyses were conducted using SPSS v. 24.0 statistical software (SPSS Inc., Chicago, IL, USA) and GPower 3.1.92 for the post-hoc analyses.

Results

In total, 293 subjects were analysed, with 229 patients in the RA group (average duration of RA, 15.44, SD 10.54 years) and 64 in the control group. In the RA group, 173 patients were female, as were 50 of the control group. The values for median age and interquartile range (IR) were 59 and 16 years for the patients with RA and 53 and 21 years for those in the control group. The median values for height and weight were 162 cm (IR: 10) and 70 kg (IR: 19), respectively, for the RA group, and 162 cm (IR: 10) and 65 kg (IR: 15), respectively, for the control group. The patients with RA were treated with biological disease-modifying antirheumatic drugs (bDMARDs) (42%), methotrexate (35%) or nonsteroidal anti-inflammatory drugs (NSAIDs) / corticosteroids (20%).

The instruments used to measure pain, disability and functionality (VAS pain, MFPDI and FFI) revealed significant differences between the patients with RA and the control group, for both genders ($p<0.001$). However, among those used to obtain foot measurements and posture data, only the midfoot height values ($p=0.007$ and $p=0.004$) for male and female participants and midfoot width ($p=0.03$) for the females were statistically significant. The FPI and the other anthropometric measurements were not statistically significant (Table 1).

The results for the SF-12 quality of life questionnaire revealed significant differences in the physical component, with $p<0.001$ (females) and $p=0.02$ (males) and in the mental

component in the female participants (p=0.04) (Table 2). Among the male participants, no differences in the mental health component were observed between the RA and control groups.

Bivariate analyses were performed to determine the relations between the physical and mental health components, taking into account the sociodemographic, clinical and anthropometric characteristics of the participants. Among these results, especially noteworthy was the value of -0.630 with $p<0.001$ obtained for VAS pain (general) and that of -0.505 with $p<0.001$ for the presence of RA. Neither the anthropometric characteristics, foot posture nor disease duration presented any correlation with either of these variables.

Multivariate models were then constructed, using as predictors the variables that had presented a significant association in the bivariate models, adjusted for age and gender. Two models were calculated, with the physical and mental health components respectively as dependent variables.

According to the data for the physical component, the multivariable linear regression presented an R^2 value of 48.8%. (Table 3). Post-hoc analysis yielded a power of 0.95 for this four-predictor model. The multivariable linear regression of the mental health component presented an R^2 value of 5.6%. There was no collinearity in the model (maximum VIF 1.39 and minimum tolerance of 0.72) and the residuals were independent (Durbin-Watson, 1.19), using the same parameters (i.e. age, gender, general VAS pain and the presence of RA).

Discussion

The aim of this study is to determine and analyse foot health factors related to the quality of life of patients with RA. The multivariate regression results obtained suggest that patients with foot pain and RA perceive a significantly lower level of health than those with foot pain but no RA (control group) ($p<0.001$). However, these findings are not directly related to the clinical parameters that might have triggered the increased level of pain. The deformations which are typical of this disease and which are located in the forefoot (such as hallux valgus, hallux rigidus, floating of the lesser toes or synovial inflammation of the metatarsophalangeal joints) or in the hindfoot (such as hindfoot valgus or flat foot) are often believed to aggravate pain and disability among this

population. Nevertheless, this expectation was not borne out by our study results, possibly because the presence of RA in itself is painful, while other patients with similar foot deformities but no RA might not experience pain. If this were the case, then the deformity would not be the cause of pain, but merely the outcome of a degenerative process in the foot. However, analysis of plantar pressures shows that this localised pain is not correlated with peak plantar pressure, which is received in the hindfoot.

Structural alterations in the foot not only cause physical deterioration due to reduced mobility, but can also lead to emotional deterioration. Nevertheless, according to our study findings, these alterations are not in themselves the cause of increased pain. Instead, this outcome may be influenced by an external component such as the choice of footwear, a factor that is strongly influenced by the appearance of structural alterations in the foot. Many patients, both male and female, have considerable difficulty in obtaining appropriate footwear, i.e. that which is comfortable, adapted to the deformities of the foot, of assistance in performing the gait cycle and acceptable aesthetically [26,27].

The latter characteristic is the area in which most negative impressions are caused among the population with RA, since many patients do not choose their footwear in strict accordance with the deformities present in their feet [28]. This discordance can produce a negative impact, either in terms of the mental component (the perceived quality of life), when the personal image is compared with that of the non-affected population, or because of increased plantar pain, when the footwear chosen is uncomfortable and prevents the proper mobilisation of the musculoskeletal structures of the foot, thereby limiting the performance of the activities of daily life. These outcomes are often associated with dissatisfaction and even depression among the population affected.

With advancing age, musculoskeletal deformities and, in particular, structural alterations in the foot increase, as a greater number of structures are damaged. These alterations may also be caused by increased neuropathy in the foot, which in turn would heighten pain and reduce functionality [1], thus worsening the perceived quality of life [29].

This research presents certain limitations. Firstly, it is based on a cross-sectional study of a heterogeneous sample population, rather than on a longitudinal study. This characteristic of the study design may have influenced the results obtained in two respects. On the one hand, in our sample the number of participants with RA significantly exceeded that of those not presenting this alteration. Therefore, if the size of the control

group were increased, somewhat different results might be obtained. Moreover, as the analysis was transversal, both the physical and the mental components were analysed at a moment that might have coincided with an aggravation of the RA experienced, thus altering the study results obtained.

Another limitation of our study is that it is based on a convenience sample, which means that the homogeneity of the participants cannot be assured. In future research, therefore, the size and composition of the study groups should be controlled to optimise their homogeneity. Finally, attention should be paid to the question of whether foot pain is determined by the characteristics of the foot, or whether RA pain affects certain foot types in particular.

Our study shows that patients with RA are more likely to present structural alterations in the foot and hence to experience physical and/or psychosocial deterioration than when this condition is absent [30]. Furthermore, the long-term evolution of the disease may be directly related to psychosocial and emotional perceptions. It should be also be taken into account that in our study groups most of the patients were female, although this reflects their prevalence among the general population affected by RA and foot pain [31,32].

On the other hand, the study also has important strengths. Although the results obtained do not show that foot-related parameters are strongly associated with the quality of life of these patients, they do highlight the need for further, longitudinal studies addressing parameters such as the evolution of the disease, the treatment received and psychosocial aspects that could influence the patient's perception of the impact of RA with respect to daily activities and musculoskeletal pain.

In the clinical context, our study raises an important question, namely that the pain and the reduced quality of life experienced by patients with RA may be provoked by the disease itself, and not by the alterations in the foot. If this were so, the presence of the latter might not be related to the pain experienced.

Conclusions

Morphological and structural characteristics of the foot are not necessarily associated with pain, disability and loss of function. The presence of RA, a higher score for general VAS pain, female gender and greater age are all related to a reduced quality of life in the physical component for patients with RA.

Author Contributions

Conceptualization, Gabriel Gijon-Nogueron, Rafael Caliz-Caliz, Jose Miguel Morales-Asencio and Ana Belen Ortega-Avila; Data curation, Andres Reino-Cobo; Formal analysis, Gabriel Gijon-Nogueron, Jose Miguel Morales-Asencio and Ana Belen Ortega-Avila; Methodology, Gabriel Gijon-Nogueron, Rafael Caliz-Caliz, Miguel Angel Ferrer-Gonzalez and Ana Belen Ortega-Avila; Project administration, Maria Teresa Vallejo-Velazquez; Writing – original draft, Andres Reino-Cobo, Gabriel Gijon-Nogueron and Ana Belen Ortega-Avila; Writing – review & editing, Andres Reino-Cobo, Gabriel Gijon-Nogueron, Rafael Caliz-Caliz, Jose Miguel Morales-Asencio and Ana Belen Ortega-Avila.

References

1 de Andrade AP, Inoue EN, Nisihara R, *et al.* Foot function in rheumatoid arthritis patients: a cross-sectional study. *Clin Rheumatol* 2018;**37**:3427–30. doi:10.1007/s10067-018-4215-y

2 Gabriel SE, Michaud K. Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. Arthritis Res. Ther. 2009;**11**. doi:10.1186/ar2669

3 Stolt M, Suhonen R, Leino-Kilpi H. Foot health in patients with rheumatoid arthritis—a scoping review. Rheumatol. Int. 2017;**37**:1413–22. doi:10.1007/s00296-017-3699-0

4 Siddle HJ, Hodgson RJ, Hensor EMA, *et al.* Plantar plate pathology is associated with erosive disease in the painful forefoot of patients with rheumatoid arthritis. *BMC Musculoskelet Disord* 2017;**18**. doi:10.1186/s12891-017-1668-0

5 Jaakkola JI, Mann RA. A review of rheumatoid arthritis affecting the foot and ankle. Foot Ankle Int. 2004;**25**:866–74. doi:10.1177/107110070402501205

6 Otter SJ, Lucas K, Springett K, *et al.* Foot pain in rheumatoid arthritis prevalence, risk factors and management: an epidemiological study. *Clin Rheumatol* 2010;**29**:255–71. doi:10.1007/s10067-009-1312-y

7 Margaretten M, Julian L, Katz P, *et al.* Depression in patients with rheumatoid arthritis: Description, causes and mechanisms. *Int J Clin Rheumtol* 2011;**6**:617–23. doi:10.2217/ijr.11.62

8 Lu MC, Guo HR, Lin MC, *et al.* Bidirectional associations between rheumatoid arthritis and depression: A nationwide longitudinal study. *Sci Rep* 2016;**6**. doi:10.1038/srep20647

9 Malemud CJ, Miller AH. Pro-inflammatory cytokine-induced SAPK/MAPK and

JAK/STAT in rheumatoid arthritis and the new anti-depression drugs. Expert Opin. Ther. Targets. 2008. doi:10.1517/14728222.12.2.171

10 Matcham F, Rayner L, Steer S, *et al.* The prevalence of depression in rheumatoid arthritis: A systematic review and meta-analysis. *Rheumatol (United Kingdom)* Published Online First: 2013. doi:10.1093/rheumatology/ket169

11 Sambamoorthi U, Shah D, Zhao X. Healthcare burden of depression in adults with arthritis. Expert Rev. Pharmacoeconomics Outcomes Res. 2017;**17**:53–65. doi:10.1080/14737167.2017.1281744

12 DiMatteo MR, Lepper HS, Croghan TW. Depression Is a Risk Factor for Noncompliance With Medical Treatment. *Arch Intern Med* 2000;**160**:2101. doi:10.1001/archinte.160.14.2101

13 Hafström I, Engvall I-L, Rönnelid J, *et al.* Rheumatoid factor and anti-CCP do not predict progressive joint damage in patients with early rheumatoid arthritis treated with prednisolone: a randomised study. *BMJ Open* 2014;**4**:e005246. doi:10.1136/bmjopen-2014-005246

14 Vamos M. Body image in rheumatoid arthritis: The relevance of hand appearance to desire for surgery. *Br J Med Psychol* 1990;**63**:267–77. doi:10.1111/j.2044-8341.1990.tb01619.x

15 Williams AE, Graham AS. 'My feet: visible, but ignored . . .' A qualitative study of foot care for people with rheumatoid arthritis. *Clin Rehabil* 2012;**26**:952–9. doi:10.1177/0269215511434995

16 Van Der Linden MPM, Knevel R, Huizinga TWJ, *et al.* Classification of rheumatoid arthritis: Comparison of the 1987 American College of Rheumatology criteria and the 2010 American College of Rheumatology/European League Against Rheumatism criteria. *Arthritis Rheum* Published Online First: 2011. doi:10.1002/art.30100

17 Luo X, George ML, Kakouras I, *et al.* Reliability, validity, and responsiveness of the short form 12-item survey (SF-12) in patients with back pain. *Spine (Phila Pa 1976)* Published Online First: 2003. doi:10.1097/01.BRS.0000083169.58671.96

18 Sendlbeck M, Araujo EG, Schett G, *et al.* Psychometric properties of three single-item pain scales in patients with rheumatoid arthritis seen during routine clinical care: A comparative perspective on construct validity, reproducibility and internal responsiveness. *RMD Open* Published Online First: 2015. doi:10.1136/rmdopen-2015-000140

19 Gijon-Nogueron G, Ndosi M, Luque-Suarez A, *et al.* Cross-cultural adaptation and validation of the Manchester Foot Pain and Disability Index into Spanish. *Qual Life Res* 2013;:571–9. doi:10.1007/s11136-013-0507-5

20 Paez-Moguer J, Budiman-Mak E, Cuesta-Vargas AI. Cross-cultural adaptation and validation of the Foot Function Index to Spanish. *Foot Ankle Surg* 2014;**20**:34–9. doi:10.1016/j.fas.2013.09.005

21 McPoil TG, Vicenzino B, Cornwall MW, *et al.* Can foot anthropometric measurements predict dynamic plantar surface contact area? *J Foot Ankle Res* 2009;**2**:1–9. doi:10.1186/1757-1146-2-28

22 Redmond AC, Crosbie J, Ouvrier RA. Development and validation of a novel rating system for scoring standing foot posture: The Foot Posture Index. *Clin Biomech* 2006;**21**:89–98. doi:10.1016/j.clinbiomech.2005.08.002

23 Garrow AP, Papageorgiou A, Silman AJ, *et al.* The grading of hallux valgus. The Manchester Scale. *J Am Pod Med Assoc* 2001.

24 Schmidt S, Vilagut G, Garin O, *et al.* Normas de referencia para el Cuestionario de Salud SF-12 versión 2 basadas en población general de Cataluña. *Med Clin (Barc)* Published Online First: 2012. doi:10.1016/j.medcli.2011.10.024

25 Redmond AC, Crane YZ, Menz HB. Normative values for the Foot Posture Index. *J Foot Ankle Res* 2008;**1**:6. doi:10.1186/1757-1146-1-6

26 Naidoo S, Anderson S, Mills J, *et al.* 'I could cry, the amount of shoes I can't get into': A qualitative exploration of the factors that influence retail footwear selection in women with rheumatoid arthritis. *J Foot Ankle Res* 2011;**4**. doi:10.1186/1757-1146-4-21

27 Goodacre LJ, Candy FJ. 'If I didn't have RA I wouldn't give them house room': The relationship between RA, footwear and clothing choices. *Rheumatology* 2011;**50**:513–7. doi:10.1093/rheumatology/keq347

28 Reina-Bueno M, Vázquez-Bautista M del C, Pérez-García S, *et al.* Effectiveness of custom-made foot orthoses in patients with rheumatoid arthritis: a randomized controlled trial. *Clin Rehabil* 2019;**33**:661–9. doi:10.1177/0269215518819118

29 Perry MG, Richards L, Harbuz MS, *et al.* Sequential synovial fluid sampling suggests plasma and synovial fluid IL-6 vary independently in rheumatoid arthritis [2]. Rheumatology. 2006;**45**:229–30. doi:10.1093/rheumatology/kei196

30 Gates LS, Arden NK, Hannan MT, *et al.* Prevalence of Foot Pain Across an International Consortium of Population-Based Cohorts. *Arthritis Care Res*

2019;**71**:661–70. doi:10.1002/acr.23829

31 Sokka T, Toloza S, Cutolo M, *et al.* Women, men, and rheumatoid arthritis: Analyses of disease activity, disease characteristics, and treatments in the QUEST-RA Study. *Arthritis Res Ther* 2009;**11**. doi:10.1186/ar2591

32 Kvien TK, Uhlig T, Ødegård S, *et al.* Epidemiological aspects of rheumatoid arthritis: The sex ratio. In: *Annals of the New York Academy of Sciences*. 2006. 212–22. doi:10.1196/annals.1351.019

	Overall(n=293)					Female (n=173)					Male (n=120)				
	Patients with foot pain and RA (group)		Patients with foot pain but no RA (control group)			Patients with foot pain and RA (group)		Patients with foot pain but no RA (control group)			Patients with foot pain and RA (group)		Patients with foot pain but no RA (control group)		
	Median	Interquartile range	Median	Interquartile range	P value	Median	Interquartile range	Median	Interquartile range	P value	Median	Interquartile range	Median	Interquartile range	P value
Age (years)	59	16	53	21	0,003	59	16	53	21	0.001	58	16	53.5	24	0.845
Height (cm)	162	10	162	10	0,401	160	10	160.5	9	0.536	170	10	171	15	0.578
Weight (kg)	70	19	65	15	0,168	65	15	62.5	11	0.134	78	18	76.5	13	0.35
Gen. VAS (0-100)	6	3	1,5	4	<0.001	6	3	2	5	<0.001	5	4	0	1	<0.001
Hand VAS	6	3	0	3	<0.001	6	4	1	3	<0.001	5	4	0	1	<0.001
Feet VAS	6	5	2	5	<0.001	6	4	2	5	<0.001	4	5	0	1	<0.001
MFPDI	21	18	4	10	<0.001	22	17	4.5	11	<0.001	19	18	0.5	6	<0.001
FFI Total	43,91	45	6,52	18	<0.001	48.3	39	9.1	23	<0.001	30.4	51	0	5	<0.001
FFI Pain	48	38	8	29	<0.001	50	34	14	33	<0.001	41.5	47	0	4	<0.001
FFI Disability	49	58	0	14	<0.001	51	50	2	18	<0.001	24	56	0	0	<0.001
FFI Physical activity	6	19	0	2	<0.001	7	20	0	2	<0.001	3	15	0	0	<0.001
W/b r/foot	242	22	244	18	0,339	237	15	240.5	17	0.127	261	18	261	22	0.777
W/b 1st MTPJ r/foot	180	16	180,5	15	0,843	178	11	177	14	0.249	195.5	14	189.5	19	0.9
W/b r/MF height	53,8	9,7	56,265	10,31	<0.001	51.4	8.2	54.4	9.4	0.007	58.8	6.3	65.8	16	0.004
W/b r/MF width	77	8,63	74,965	8,93	0,035	75.5	6.7	73.9	6.9	0.03	83.5	7.2	81.5	8.7	0.559
W/b r/forefoot	91,38	9,34	91,69	7,08	0,508	89.7	7	88.5	6.8	0.289	97.3	7.8	96.4	7.4	0.941
W/b r/hindfoot	66,52	7,29	66,105	6,16	0,089	65.7	6.2	65.2	6.6	0.157	71.8	7.6	68.5	4.2	0.39
FPI TOTAL (r/ foot)	5	7	5	4	0,338	5	6	5	5	0.307	2	8	5	3	0.205

Table 1. Characteristics of the study groups W/b: Weight bearing; r/: Right; MTPJ: Metatarsophalangeal joints; MF: midfoot *Mann-Whitney U-test

	Female					Male				
	RA (n=173)		Control group (n=50)			RA (n=56)		Control group (n=14)		
	Mean	**SD**	**Mean**	**SD**	**P value***	**Mean**	**SD**	**Mean**	**SD**	**P value***
Physical health component (Ref. Spanish population)	36.50	7.91	48.88	7.55	p<0.001	39.07	2.91	49.09	8.22	0.02
Mental health component (Ref. Spanish population)	32.10	7.97	35.08	5.00	0.04	33.76	1.65	36.14	4.66	0.35

* Mann-Whitney U-test

Table 2. Characteristics of the sample group according to the SF 12 results

					95%CI	
	Adjusted coefficient	**B**	**β**	**p**	**Lower**	**Upper**
Age	-0.175	-0.082	-0.113	0.038	-0.159	-0.005
Gender	-1.361	-0.603	-0.028	0.607	-2.908	1.703
VAS pain – General	-2.177	-1.609	-0.474	<0.001	-2.024	-1.193
RA	-11.769	-6.461	-0.292	<0.001	-9.111	-3.811

Table 3: Model of multivariate regression for the perception of physical health

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7
Generalisability	21	Discuss the generalisability (external validity) of the study results	7-8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Foot health and quality of life in patients with rheumatoid arthritis: a cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-036903.R1
Article Type:	Original research
Date Submitted by the Author:	06-Apr-2020
Complete List of Authors:	Reinoso-Cobo, Andres; Hospital Universitario Virgen de las Nieves Gijon-Nogueron, Gabriel; University of Malaga, Nursing and Podiatry Caliz-Caliz, Rafael; Hospital Universitario Virgen de las Nieves Ferrer-Gonzalez, Miguel Angel; Hospital Universitario Virgen de las Nieves Vallejo-Velazquez, Maria Teresa; Hospital Universitario Virgen de las Nieves Miguel Morales-Asencio, Jose; University of Malaga, Nursing and Podiatry Ortega-Avila, Ana Belen; Universidad de Malaga Facultad de Ciencias de la Salud, Nursing and Podiatry
Primary Subject Heading:	Rheumatology
Secondary Subject Heading:	Rheumatology
Keywords:	RHEUMATOLOGY, Foot & ankle < ORTHOPAEDIC & TRAUMA SURGERY, PRIMARY CARE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Foot health and quality of life in patients with rheumatoid arthritis: a cross-sectional study

Andres Reinoso-Cobo[1] MSc andres.reinoso.sspa@juntadeandalucia.es
Gabriel Gijon-Nogueron[2,3], PhD gagijon@uma.es
Rafela Caliz-Caliz[1] MD,PhD antonior.caliz.sspa@juntadeandalucia.es
Miguel Angel Ferrer-González[1] MD PhD maferrer@fundacionhvn.org
Maria Teresa Vallejo-Fernandez[1], MsC tvallejo@ibsgranada.es
Jose Miguel Morales-Asencio[2,3] PhD jmmasen@uma.es
Ana Belen Ortega-Avila[3] PhD anaortavi@uma.es

1. Departamento de Reumatologia, Hospital Universitario Virgen de las Nieves, Granada, Granada, Spain
2. Instituto de Investigación Biomédica de Málaga (IBIMA), Malaga, Spain
3. Department Nursing and Podiatry, Universidad de Málaga, Malaga. Spain

Corresponding author: Gabriel Gijon-Nogueron

Faculty of Health Sciences. Arquitecto Francisco Penalosa 3. Ampliación de Campus de Teatinos, 29071 Malaga. Spain. gagijon@uma.es

Word count: 2645 words without references

References: 39

Abstract: 302 words

Tables: 3

Funding: This study did not receive any funding.

Conflict of interest: All the authors declare that they have no conflict of interest derived from the outcomes of this study.

Abstract

Objective: The aim of this study is to identify foot health factors related to the quality of life in patients with RA.

Setting: The cross-sectional study in total, 293 subjects were analysed, with 229 patients in the RA group and 64 in the control group. In the RA group, 173 patients were female, as were 50 of the control group

Participants: Patients with foot pain and RA (according to the 2010 ACR/ EULAR Rheumatoid Arthritis classification criteria) and with foot pain but no RA were recruited (Granada, Spain).

Intervention: Two researchers independently interviewed the patients to obtain the study data

Primary and secondary outcome measures: Clinical data were obtained using the SF-12 questionnaire (Quality of life) (Primary outcome), visual analogue scales for pain (VAS pain), the Manchester Foot Pain Disability Index questionnaire (MFPDI) and the Foot Function Index (FFI). Anthropometric measurements were obtained by means of a foot measurement platform, the Foot Posture Index (FPI) and the Manchester Hallux Valgus Scale.(secondary outcomes)

Results

Of the 293 subjects, 76.1% were female. Significant differences were observed between the RA and control groups ($p<0.001$) according to VAS pain (general, foot and hand), the MFPDI and the FFI. In terms of anthropometric measurements, significant differences were only recorded for midfoot and forefoot width ($p=0.03$). In the data for the physical component, the multivariable linear regression with the parameters age, gender, VAS pain (general) and the presence of RA presented an R2 value of 48.8%, while for the mental health component, the corresponding value was 5.6%.

Conclusion

Morphological and structural characteristics of the foot are not necessarily associated with pain, disability and loss of function. The presence of RA, a higher score in VAS pain (general), female gender and greater age are all associated with the physical component of the quality of life for patients with RA.

Key words

Rheumatoid arthritis; foot health; quality of life; functionality; pain.

Strengths and limitations of this study

- This research presents a new framework the foot-related parameters in Rheumatoid Arthritis(RA) associated with the quality of life(QoL)
- This method provides identification of foot parameters stratified by gender, related to QoL in RA
- This study has been the first to show how people with RA experience a negative impact on their QoL related to foot parameter.
- The QoL were analysed at a moment that might coincide with an aggravation of the RA
- The result could be different if they study should be a longitudinal study

Introduction

Rheumatoid arthritis (RA) is a chronic rheumatic disease that affects 0.5% to 1% of the population in Europe [1]. The most characteristic symptom is swelling, which provokes important changes in joint structures and limits function [2].

RA mainly affects the small joints of the hands and feet [3]. In the foot, it provokes deformities in the forefoot and hindfoot. The most common pathologies are hallux valgus, metatarsal subluxation, and hammer or claw toes [4]. As the disease progresses, the first metatarsophalangeal joint and pes planus may also be associated. These pathologies occur as the deterioration affects the joints and ligaments [5], thus limiting movement in the ankle and the foot. It also produces an unequal distribution of pressures and therefore makes it painful to remain in a standing position [6].

RA is a systemic disease that not only presents extra-articular manifestations but also has psychological affects [7], in many cases provoking mental health and functional problems as a consequence of ageing [8], oxidative damage to DNA and systemic inflammatory stress [9], thus limiting leisure and family-related activities and restricting social relationships [10]. The simultaneous impact of RA and a reduced quality of life imposes a major burden on patients, caregivers, the health system and society in general [11].

The mental and physical components of RA can reduce adherence to treatment, leading to poorer health outcomes and a worsened quality of life [12].

In patients with RA, the foot has been analysed from various standpoints, such as hallux valgus, clawed toes or morphological alterations [13]. Psychological and social aspects of the disease have also been analysed such as anxiety, depression or affectivity [14,15][16]. However, to date no studies have been undertaken to determine whether RA in the foot has a negative impact on the quality of life, in physical and mental health terms.

The aim of the present study, therefore, is to identify foot health factors related to the quality of life in patients with RA.

Method

Ethical approval: Institutional review board that approved the protocol for the study: Medical Research Ethics Committee of University of Malaga (CEUMA-91-2015-H) and PEIBA Andalucia (ARC0001), Spain.

Design: Cross-sectional study

Participants

A convenience sample was obtained of 246 patients with foot pain and RA (according to the 2010 ACR/ EULAR Rheumatoid Arthritis classification criteria)[17], of whom seventeen subsequently declined to participate, citing lack of time (the study questionnaire required 30 minutes to complete) and 64 patients with foot pain but no RA. The patients were enrolled at hospital outpatient clinics from January to December 2018.

All those included in the study had a history of subtalar and/or ankle and/or talonavicular or hindfoot pain, did not make daily use of walking aids, and were able to achieve the normal range of motions in the ankle, subtalar and midtarsal joints. Although the patient could not reach the maximum range of movement within those joints in terms of dorsiflexion, pronation or supination, if reducing their length of the step, patients could achieve the enough range of movement to walk [6][18].

The exclusion criteria applied were the presence of concomitant musculoskeletal disease, central or peripheral nervous system disease or endocrine disorders (especially diabetes mellitus).

Patients who met the criteria for inclusion were approached by members of the rheumatology service at the Virgen de la Nieves Hospital (Granada, Spain), given an information sheet and invited to participate. Those who agreed were then interviewed and given further details of the study. All participants provided written consent prior to starting the interviews.

Data collection

Demographic and clinical characteristics

The demographic characteristics recorded included the patient's age, gender, disease duration and current therapy. The clinical data recorded were those obtained from the SF-12 questionnaire [19], a visual analogue scale for pain (VAS pain), both general [20] and specific to the foot and hand, the Manchester Foot Pain Disability Index (MFPDI) [21] and the Foot Function Index (FFI) [22].

For the anthropometric measurements, a foot measurement platform [23] was used to measure the foot length (weight bearing and non weight bearing), the midfoot, forefoot and heel width and the midfoot height. Each participant was asked first to stand on the platform and then to be seated, in both cases with the body weight distributed evenly between the two feet, arms beside the body and facing forwards. The measurements were obtained with the patient's heels placed in the heel cups, as far back as possible, and the first metatarsal heads located against the limit surface.

Other measurements were obtained using the Foot Posture Index, a reliable instrument for this purpose [24], and the Manchester Scale of hallux valgus [25].

The data availability statement No additional data available

Procedure

Two researchers (ARC and GGN) independently interviewed the patients to obtain the study data. The clinical interview was conducted in one room, where the patients were asked to complete the SF-12 (adapted version for a Spanish population) [26], MFPDI and VAS questionnaires. In a separate room, each patient was measured using a validated foot platform (intraclass correlation coefficient for the instrument, ICC, 0.96-0.98). Foot posture was determined according to the Foot Posture Index (FPI) (ICC for the clinician, 0.94-0.96). Each criterion was scored as −2, −1, 0, +1 or +2. The following FPI cut-off points, defining foot type category were used: a) highly supinated −12 to −4, b) supinated −3 to 0, c) neutral 1 to 7, d) pronated 8 to 10 and e) highly pronated 11 to 12 [27]. The presence/absence of hallux valgus was determined according to the Manchester Scale of Hallux Valgus (ICC for the instrument, 0.93-0.97), a clinical tool consisting of photographs of feet with four levels of hallux valgus: none, mild, moderate and severe [25].

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in the design or conduct of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants

Statistical analysis

The results obtained are reported as the median and interquartile range, due to the non-normal distribution of the variables. The normality of the distributions was examined by the Kolmogorov-Smirnov test and the intra-rater reliability of the measurement instruments was calculated by a two-way mixed-consistency ICC model. Bivariate analysis was performed with a non-parametric test (the Mann-Whitney U test), in view of the non-normal distribution observed in most cases. Finally, a multivariable linear regression model was obtained to evaluate the predictors of quality of life, according to the physical and mental health components of the SF-12 questionnaire. In constructing the models, the regression assumptions of homoscedasticity, normality and independence of the residuals and collinearity were tested. Homoscedasticity was evaluated by analysing the distribution of predicted values and scatterplots of the residuals. Normality of the residuals was tested by analysing histograms and by graphs of standardised residuals. Independence of the residuals was evaluated by the Durbin-Watson statistic. Finally, the presence of collinearity was tested by calculating the variance inflation factor, the tolerance and partial correlations. The significance level was set at $p<0.05$, with two-tailed tests. All statistical analyses were conducted using SPSS v. 24.0 statistical software (SPSS Inc., Chicago, IL, USA) and GPower 3.1.92 for the post-hoc analyses.

Results

In total, 293 subjects were analysed, with 229 patients in the RA group (average duration of RA, 15.4, SD 10.5 years) and 64 in the control group. In the RA group, 173 patients were female, as were 50 of the control group. The values for median age and interquartile range (IQR) were 59 and 16 years for the patients with RA and 53 and 21 years for those in the control group. The median values for height and weight were 162 cm (IQR: 10) and 70 kg (IQR: 19), respectively, for the RA group, and 162 cm (IQR: 10) and 65 kg (IQR: 15), respectively, for the control group. The patients with RA were treated with biological disease-modifying antirheumatic drugs (bDMARDs) (42%),

methotrexate (35%) or nonsteroidal anti-inflammatory drugs (NSAIDs) / corticosteroids (20%).

The instruments used to measure pain, disability and functionality (VAS pain, MFPDI and FFI) revealed significant differences between the patients with RA and the control group, for both genders ($p<0.001$). However, among those used to obtain foot measurements and posture data, only the midfoot height values ($p=0.007$ and $p=0.004$) for male and female participants and midfoot width ($p=0.03$) for the females were statistically significant. The FPI and the other anthropometric measurements were not statistically significant (Table 1).

The results for the SF-12 quality of life questionnaire revealed significant differences in the physical component, with $p<0.001$ (females) and $p=0.02$ (males) and in the mental component in the female participants ($p=0.04$) (Table 2). Among the male participants, no differences in the mental health component were observed between the RA and control groups.

Bivariate analyses were performed to determine the relations between the physical and mental health components, taking into account the sociodemographic, clinical and anthropometric characteristics of the participants. Among these results, especially noteworthy was the value of -0.630 with $p<0.001$ obtained for VAS pain (general) and that of -0.505 with $p<0.001$ for the presence of RA. Neither the anthropometric characteristics, foot posture nor disease duration presented any correlation with either of these variables.

Multivariate models were then constructed, using as predictors the variables that had presented a significant association in the bivariate models, adjusted for age and gender. Two models were calculated, with the physical and mental health components respectively as dependent variables.

According to the data for the physical component, the multivariable linear regression presented an R^2 value of 48.8%. (Table 3). Post-hoc analysis yielded a power of 0.95 for this four-predictor model. The multivariable linear regression of the mental health component presented an R^2 value of 5.6%. There was no collinearity in the model (maximum VIF 1.39 and minimum tolerance of 0.72) and the residuals were

independent (Durbin-Watson, 1.19), using the same parameters (i.e. age, gender, general VAS pain and the presence of RA).

Discussion

The aim of this study is to determine and analyse foot health factors related to the quality of life of patients with RA. The multivariate regression results obtained suggest that patients with foot pain and RA perceive a significantly lower level of health than those with foot pain but no RA (control group) ($p<0.001$). However, these findings are not directly related to the clinical parameters that might have triggered the increased level of pain. The deformations which are typical of this disease and which are located in the forefoot (such as hallux valgus, hallux rigidus, floating of the lesser toes or synovial inflammation of the metatarsophalangeal joints) or in the hindfoot (such as hindfoot valgus or flat foot) are often believed to aggravate pain and disability among this population. Nevertheless, this expectation was not borne out by our study results, possibly because the presence of RA in itself is painful, while other patients with similar foot deformities but no RA might not experience pain. If this were the case, then the deformity would not be the cause of pain, but merely the outcome of a degenerative process in the foot. However, analysis of plantar pressures shows that this localised pain is not correlated with peak plantar pressure, which is received in the hindfoot.

Structural alterations in the foot not only cause physical deterioration due to reduced mobility, but can also lead to emotional deterioration. Nevertheless, according to our study findings, these alterations are not in themselves the cause of increased pain. Instead, this outcome may be influenced by an external component such as the choice of footwear, a factor that is strongly influenced by the appearance of structural alterations in the foot. Patients should prioritize factors such as fit and comfort when choosing footwear.[28]

Many patients, both male and female, have considerable difficulty in obtaining appropriate footwear, especially females, i.e. that which is comfortable, adapted to the deformities of the foot, of assistance in performing the gait cycle and acceptable aesthetically [29,30].

The latter characteristic is the area in which most negative impressions are caused among the population with RA, since many patients do not choose their footwear in

strict accordance with the deformities present in their feet [31]. This discordance can produce a negative impact, either in terms of the mental component (the perceived quality of life), when the personal image is compared with that of the non-affected population, or because of increased plantar pain, when the footwear chosen is uncomfortable and prevents the proper mobilisation of the musculoskeletal structures of the foot, thereby limiting the performance of the activities of daily life. These outcomes are often associated with dissatisfaction and even depression among the population affected.

With advancing age, musculoskeletal deformities and, in particular, structural alterations in the foot increase, as a greater number of structures are damaged. These alterations may also be caused by increased neuropathy in the foot, which in turn would heighten pain and reduce functionality [1], thus worsening the perceived quality of life (anxiety and depression status) [32][33].

This research presents certain limitations. Firstly, it is based on a cross-sectional study of a heterogeneous sample population, rather than on a longitudinal study. This characteristic of the study design may have influenced the results obtained in two respects. On the one hand, in our sample the number of participants with RA significantly exceeded that of those not presenting this alteration. Therefore, if the size of the control group were increased, somewhat different results might be obtained. Moreover, as the analysis was transversal, both the physical and the mental components were analysed at a moment that might have coincided with an aggravation of the RA experienced, thus altering the study results obtained.

Another limitation of our study is that it is based on a convenience sample, which means that the homogeneity of the participants cannot be assured. In future research, therefore, the size and composition of the study groups should be controlled to optimise their homogeneity. Finally, attention should be paid to the question of whether foot pain is determined by the characteristics of the foot, or whether RA pain affects certain foot types in particular.

Our study shows that patients with RA are more likely to present structural alterations in the foot and hence to experience physical and/or psychosocial deterioration than when this condition is absent [34]. Furthermore, the long-term evolution of the disease may be directly related to psychosocial and emotional perceptions. It should be also be

taken into account that in our study groups most of the patients were female, although this reflects their prevalence among the general population affected by RA and foot pain [35,36] Females has their psychosocial life altered due to some factors, such as being active in terms of work or their self-image perception.[37][38][39]

On the other hand, the study also has important strengths. Although the results obtained do not show that foot-related parameters are strongly associated with the quality of life of these patients, they do highlight the need for further, longitudinal studies addressing parameters such as the evolution of the disease, the treatment received and psychosocial aspects that could influence the patient's perception of the impact of RA with respect to daily activities and musculoskeletal pain.

In the clinical context, our study raises an important question, namely that the pain and the reduced quality of life experienced by patients with RA may be provoked by the disease itself, and not by the alterations in the foot. If this were so, the presence of the latter might not be related to the pain experienced.

Conclusions

Morphological and structural characteristics of the foot are not necessarily associated with pain, disability and loss of function. The presence of RA, a higher score for general VAS pain, female gender and greater age are all related to a reduced quality of life in the physical component for patients with RA.

Author Contributions

Conceptualization, Gabriel Gijon-Nogueron, Rafael Caliz-Caliz, Jose Miguel Morales-Asencio and Ana Belen Ortega-Avila; Data curation, Andres Reino-Cobo; Formal analysis, Gabriel Gijon-Nogueron, Jose Miguel Morales-Asencio and Ana Belen Ortega-Avila; Methodology, Gabriel Gijon-Nogueron, Rafael Caliz-Caliz, Miguel Angel Ferrer-Gonzalez and Ana Belen Ortega-Avila; Project administration, Maria Teresa Vallejo-Velazquez; Writing – original draft, Andres Reino-Cobo, Gabriel Gijon-Nogueron and Ana Belen Ortega-Avila; Writing – review & editing, Andres Reino-Cobo, Gabriel Gijon-Nogueron, Rafael Caliz-Caliz, Jose Miguel Morales-Asencio and Ana Belen Ortega-Avila.

References

1 de Andrade AP, Inoue EN, Nisihara R, *et al.* Foot function in rheumatoid arthritis patients: a cross-sectional study. *Clin Rheumatol* 2018;**37**:3427–30. doi:10.1007/s10067-018-4215-y

2 Gabriel SE, Michaud K. Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. Arthritis Res. Ther. 2009. doi:10.1186/ar2669

3 Stolt M, Suhonen R, Leino-Kilpi H. Foot health in patients with rheumatoid arthritis—a scoping review. Rheumatol. Int. 2017. doi:10.1007/s00296-017-3699-0

4 Siddle HJ, Hodgson RJ, Hensor EMA, *et al.* Plantar plate pathology is associated with erosive disease in the painful forefoot of patients with rheumatoid arthritis. *BMC Musculoskelet Disord* 2017;**18**:1–9. doi:10.1186/s12891-017-1668-0

5 Jaakkola JI, Mann RA. A review of rheumatoid arthritis affecting the foot and ankle. Foot Ankle Int. 2004. doi:10.1177/107110070402501205

6 Otter SJ, Lucas K, Springett K, *et al.* Foot pain in rheumatoid arthritis prevalence, risk factors and management: An epidemiological study. *Clin Rheumatol* Published Online First: 2010. doi:10.1007/s10067-009-1312-y

7 Margaretten M, Julian L, Katz P, *et al.* Depression in patients with rheumatoid arthritis: Description, causes and mechanisms. *Int J Clin Rheumtol* Published Online First: 2011. doi:10.2217/ijr.11.62

8 Lu MC, Guo HR, Lin MC, *et al.* Bidirectional associations between rheumatoid arthritis and depression: A nationwide longitudinal study. *Sci Rep* 2016;**6**. doi:10.1038/srep20647

9 Malemud CJ, Miller AH. Pro-inflammatory cytokine-induced SAPK/MAPK and JAK/STAT in rheumatoid arthritis and the new anti-depression drugs. Expert Opin. Ther. Targets. 2008. doi:10.1517/14728222.12.2.171

10 Matcham F, Rayner L, Steer S, *et al.* The prevalence of depression in rheumatoid arthritis: A systematic review and meta-analysis. *Rheumatol (United Kingdom)* Published Online First: 2013. doi:10.1093/rheumatology/ket169

11 Sambamoorthi U, Shah D, Zhao X. Healthcare burden of depression in adults with arthritis. Expert Rev. Pharmacoeconomics Outcomes Res. 2017. doi:10.1080/14737167.2017.1281744

12 DiMatteo MR, Lepper HS, Croghan TW. Depression Is a Risk Factor for Noncompliance With Medical Treatment. *Arch Intern Med* Published Online First: 2000. doi:10.1001/archinte.160.14.2101

13 Hafström I, Engvall I-L, Rönnelid J, *et al.* Rheumatoid factor and anti-CCP do not predict progressive joint damage in patients with early rheumatoid arthritis

treated with prednisolone: a randomised study. *BMJ Open* 2014;**4**:e005246. doi:10.1136/bmjopen-2014-005246

14 Vamos M. Body image in rheumatoid arthritis: The relevance of hand appearance to desire for surgery. *Br J Med Psychol* Published Online First: 1990. doi:10.1111/j.2044-8341.1990.tb01619.x

15 Williams AE, Graham AS. 'My feet: visible, but ignored . . .' A qualitative study of foot care for people with rheumatoid arthritis. *Clin Rehabil* 2012;**26**:952–9. doi:10.1177/0269215511434995

16 Rathbun AM, Reed GW, Harrold LR. The temporal relationship between depression and rheumatoid arthritis disease activity, treatment persistence and response: A systematic review. *Rheumatol (United Kingdom)* 2013;**52**:1785–94. doi:10.1093/rheumatology/kes356

17 Aletaha D, Neogi T, Silman AJ, *et al.* 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum. 2010;**62**:2569–81. doi:10.1002/art.27584

18 Dubbeldam R, Baan H, Nene A V., *et al.* Foot and ankle kinematics in rheumatoid arthritis: Influence of foot and ankle joint and leg tendon pathologies. *Arthritis Care Res* 2013;**65**:503–11. doi:10.1002/acr.21852

19 Luo X, George ML, Kakouras I, *et al.* Reliability, validity, and responsiveness of the short form 12-item survey (SF-12) in patients with back pain. *Spine (Phila Pa 1976)* Published Online First: 2003. doi:10.1097/01.BRS.0000083169.58671.96

20 Sendlbeck M, Araujo EG, Schett G, *et al.* Psychometric properties of three single-item pain scales in patients with rheumatoid arthritis seen during routine clinical care: A comparative perspective on construct validity, reproducibility and internal responsiveness. *RMD Open* Published Online First: 2015. doi:10.1136/rmdopen-2015-000140

21 Gijon-Nogueron G, Ndosi M, Luque-Suarez A, *et al.* Cross-cultural adaptation and validation of the Manchester Foot Pain and Disability Index into Spanish. *Qual Life Res* 2014;**23**:571–9. doi:10.1007/s11136-013-0507-5

22 Paez-Moguer J, Budiman-Mak E, Cuesta-Vargas AI. Cross-cultural adaptation and validation of the Foot Function Index to Spanish. *Foot Ankle Surg* 2014;**20**:34–9. doi:10.1016/j.fas.2013.09.005

23 McPoil TG, Vicenzino B, Cornwall MW, *et al.* Can foot anthropometric

measurements predict dynamic plantar surface contact area? *J Foot Ankle Res* 2009;**2**:1–9. doi:10.1186/1757-1146-2-28

24 Redmond AC, Crosbie J, Ouvrier RA. Development and validation of a novel rating system for scoring standing foot posture: The Foot Posture Index. *Clin Biomech* 2006;**21**:89–98. doi:10.1016/j.clinbiomech.2005.08.002

25 Garrow AP, Papageorgiou A, Silman AJ, *et al.* The grading of hallux valgus. The Manchester Scale. *J Am Pod Med Assoc* 2001.

26 Schmidt S, Vilagut G, Garin O, *et al.* Normas de referencia para el Cuestionario de Salud SF-12 versión 2 basadas en población general de Cataluña. *Med Clin (Barc)* Published Online First: 2012. doi:10.1016/j.medcli.2011.10.024

27 Redmond AC, Crane YZ, Menz HB. Normative values for the Foot Posture Index. *J Foot Ankle Res* 2008;**1**:6. doi:10.1186/1757-1146-1-6

28 Tovaruela-Carrión N, Becerro-de-Bengoa-Vallejo R, Losa-Iglesias ME, *et al.* Accurately Determining Proper Shoe Size in Patients With Rheumatoid Arthritis. *Rehabil Nurs* 2018;**43**:285–9. doi:10.1097/rnj.0000000000000040

29 Naidoo S, Anderson S, Mills J, *et al.* 'I could cry, the amount of shoes I can't get into': A qualitative exploration of the factors that influence retail footwear selection in women with rheumatoid arthritis. *J Foot Ankle Res* Published Online First: 2011. doi:10.1186/1757-1146-4-21

30 Goodacre LJ, Candy FJ. 'If I didn't have RA I wouldn't give them house room': The relationship between RA, footwear and clothing choices. *Rheumatology* 2011;**50**:513–7. doi:10.1093/rheumatology/keq347

31 Reina-Bueno M, Vázquez-Bautista M del C, Pérez-García S, *et al.* Effectiveness of custom-made foot orthoses in patients with rheumatoid arthritis: a randomized controlled trial. *Clin Rehabil* 2019;**33**:661–9. doi:10.1177/0269215518819118

32 Perry MG, Richards L, Harbuz MS, *et al.* Sequential synovial fluid sampling suggests plasma and synovial fluid IL-6 vary independently in rheumatoid arthritis [2]. Rheumatology. 2006. doi:10.1093/rheumatology/kei196

33 Li Y, Jiang L, Zhang Z, *et al.* Clinical characteristics of rheumatoid arthritis patients with peripheral neuropathy and potential related risk factors. *Clin Rheumatol* 2019;**38**:2099–107. doi:10.1007/s10067-019-04521-5

34 Gates LS, Arden NK, Hannan MT, *et al.* Prevalence of Foot Pain Across an International Consortium of Population-Based Cohorts. *Arthritis Care Res* 2019;**71**:661–70. doi:10.1002/acr.23829

35 Sokka T, Toloza S, Cutolo M, *et al.* Women, men, and rheumatoid arthritis: Analyses of disease activity, disease characteristics, and treatments in the QUEST-RA Study. *Arthritis Res Ther* Published Online First: 2009. doi:10.1186/ar2591

36 Kvien TK, Uhlig T, Ødegård S, *et al.* Epidemiological aspects of rheumatoid arthritis: The sex ratio. In: *Annals of the New York Academy of Sciences*. 2006. doi:10.1196/annals.1351.019

37 Kobelt G, Texier-Richard B, Mimoun S, *et al.* Rheumatoid arthritis and sexuality: A patient survey in France. BMC Musculoskelet. Disord. 2012;**13**:170. doi:10.1186/1471-2474-13-170

38 Lacaille D, White MA, Backman CL, *et al.* Problems faced at work due to inflammatory arthritis: New insights gained from understanding patients' perspective. *Arthritis Care Res* 2007;**57**:1269–79. doi:10.1002/art.23002

39 López-López D, Becerro-De-Bengoa-Vallejo R, Losa-Iglesias ME, *et al.* Evaluation of foot health related quality of life in individuals with foot problems by gender: A cross-sectional comparative analysis study. *BMJ Open* 2018;**8**:e023980. doi:10.1136/bmjopen-2018-023980

	Overall(n=293)					Female (n=173)					Male (n=120)				
	Patients with foot pain and RA (group)		Patients with foot pain but no RA (control group)			Patients with foot pain and RA (group)		Patients with foot pain but no RA (control group)			Patients with foot pain and RA (group)		Patients with foot pain but no RA (control group)		
	Median	Interquartile range	Median	Interquartile range	P value	Median	Interquartile range	Median	Interquartile range	P value	Median	Interquartile range	Median	Interquartile range	P value
Age (years)	59	16	53	21	0,003	59	16	53	21	0.0	58	16	53.5	24	0.845
Height (cm)	162	10	162	10	0,401	160	10	160.5	9	0.9	170	10	171	15	0.578
Weight (kg)	70	19	65	15	0,168	65	15	62.5	11	0.1	78	18	76.5	13	0.35
Gen. VAS (0-100)	6	3	1,5	4	<0.001	6	3	2	5	<0.0	5	4	0	1	<0.001
Hand VAS	6	3	0	3	<0.001	6	4	1	3	<0.0	5	4	0	1	<0.001
Feet VAS	6	5	2	5	<0.001	6	4	2	5	<0.0	4	5	0	1	<0.001
MFPDI	21	18	4	10	<0.001	22	17	4.5	11	<0.0	19	18	0.5	6	<0.001
FFI Total	43,91	45	6,52	18	<0.001	48.3	39	9.1	23	<0.0	30.4	51	0	5	<0.001
FFI Pain	48	38	8	29	<0.001	50	34	14	33	<0.0	41.5	47	0	4	<0.001
FFI Disability	49	58	0	14	<0.001	51	50	2	18	<0.0	24	56	0	0	<0.001
FFI Physical activity	6	19	0	2	<0.001	7	20	0	2	<0.0	3	15	0	0	<0.001
W/b r/foot	242	22	244	18	0,339	237	15	240.5	17	0.05	261	18	261	22	0.777
W/b 1st MTPJ r/foot	180	16	180,5	15	0,843	178	11	177	14	0.84	195.5	14	189.5	19	0.9
W/b r/MF height	53,8	9,7	56,265	10,31	<0.001	51.4	8.2	54.4	9.4	0.00	58.8	6.3	65.8	16	0.004
W/b r/MF width	77	8,63	74,965	8,93	0,035	75.5	6.7	73.9	6.9	0.0	83.5	7.2	81.5	8.7	0.559
W/b r/forefoot	91,38	9,34	91,69	7,08	0,508	89.7	7	88.5	6.8	0.55	97.3	7.8	96.4	7.4	0.941
W/b r/hindfoot	66,52	7,29	66,105	6,16	0,089	65.7	6.2	65.2	6.6	0.1	71.8	7.6	68.5	4.2	0.39
FPI TOTAL (r/ foot)	5	7	5	4	0,338	5	6	5	5	0.8	2	8	5	3	0.205

Table 1. Characteristics of the study groups W/b: Weight bearing; r/: Right; MTPJ: Metatarsophalangeal joints; MF: midfoot *Mann-Whitney U-test

	Female					Male				
	RA (n=173)		Control group (n=50)			RA (n=56)		Control group (n=14)		
	Mean	**SD**	**Mean**	**SD**	**P value***	**Mean**	**SD**	**Mean**	**SD**	**P value***
Physical health component (Ref. Spanish population)	36.50	7.91	48.88	7.55	p<0.001	39.07	2.91	49.09	8.22	0.02
Mental health component (Ref. Spanish population)	32.10	7.97	35.08	5.00	0.04	33.76	1.65	36.14	4.66	0.35

* Mann-Whitney U-test

Table 2. Characteristics of the sample group according to the SF 12 results

					95%CI	
	Adjusted coefficient	**B**	**β**	**p**	**Lower**	**Upper**
Age	-0.175	-0.082	-0.113	0.038	-0.159	-0.005
Gender	-1.361	-0.603	-0.028	0.607	-2.908	1.703
VAS pain – General	-2.177	-1.609	-0.474	<0.001	-2.024	-1.193
RA	-11.769	-6.461	-0.292	<0.001	-9.111	-3.811

Table 3: Model of multivariate regression for the perception of physical health

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7
Generalisability	21	Discuss the generalisability (external validity) of the study results	7-8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Foot health and quality of life in patients with rheumatoid arthritis: a cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-036903.R2
Article Type:	Original research
Date Submitted by the Author:	16-Apr-2020
Complete List of Authors:	Reinoso-Cobo, Andres; Hospital Universitario Virgen de las Nieves Gijon-Nogueron, Gabriel; University of Malaga, Nursing and Podiatry Caliz-Caliz, Rafael; Hospital Universitario Virgen de las Nieves Ferrer-Gonzalez, Miguel Angel; Hospital Universitario Virgen de las Nieves Vallejo-Velazquez, Maria Teresa; Hospital Universitario Virgen de las Nieves Miguel Morales-Asencio, Jose; University of Malaga, Nursing and Podiatry Ortega-Avila, Ana Belen; Universidad de Malaga Facultad de Ciencias de la Salud, Nursing and Podiatry
Primary Subject Heading:	Rheumatology
Secondary Subject Heading:	Rheumatology
Keywords:	RHEUMATOLOGY, Foot & ankle < ORTHOPAEDIC & TRAUMA SURGERY, PRIMARY CARE

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Foot health and quality of life in patients with rheumatoid arthritis: a cross-sectional study

Andres Reinoso-Cobo[1] MSc andres.reinoso.sspa@juntadeandalucia.es
Gabriel Gijon-Nogueron[2,3], PhD gagijon@uma.es
Rafael Caliz-Caliz[1] MD,PhD antonior.caliz.sspa@juntadeandalucia.es
Miguel Angel Ferrer-González[1] MD PhD maferrer@fundacionhvn.org
Maria Teresa Vallejo-Velazquez[1], MsC tvallejo@ibsgranada.es
Jose Miguel Morales-Asencio[2,3] PhD jmmasen@uma.es
Ana Belen Ortega-Avila[3] PhD anaortavi@uma.es

1. Departamento de Reumatologia, Hospital Universitario Virgen de las Nieves, Granada, Granada, Spain
2. Instituto de Investigación Biomédica de Málaga (IBIMA), Malaga, Spain
3. Department Nursing and Podiatry, Universidad de Málaga, Malaga. Spain

Corresponding author: Gabriel Gijon-Nogueron

Faculty of Health Sciences. Arquitecto Francisco Penalosa 3. Ampliación de Campus de Teatinos, 29071 Malaga. Spain. gagijon@uma.es

Word count: 2645 words without references

References: 39

Abstract: 302 words

Tables: 3

Funding: This study did not receive any funding.

Conflict of interest: All the authors declare that they have no conflict of interest derived from the outcomes of this study.

Abstract

Objective: The aim of this study is to identify foot health factors related to the quality of life in patients with RA.

Setting: The cross-sectional study in total, 293 subjects were analysed, with 229 patients in the RA group and 64 in the control group. In the RA group, 173 patients were female, as were 50 of the control group

Participants: Patients with foot pain and RA (according to the ACR/EULAR 2010 rheumatoid arthritis classification criteria) and with foot pain but no RA were recruited (Granada, Spain).

Intervention: Two researchers independently interviewed the patients to obtain the study data

Primary and secondary outcome measures: Clinical data were obtained using the SF-12 questionnaire (Quality of life) (Primary outcome), visual analogue scales for pain (VAS pain), the Manchester Foot Pain Disability Index questionnaire (MFPDI) and the Foot Function Index (FFI). Anthropometric measurements were obtained by means of a foot measurement platform, the Foot Posture Index (FPI) and the Manchester Hallux Valgus Scale.(secondary outcomes)

Results

Of the 293 subjects, 76.1% were female. Significant differences were observed between the RA and control groups ($p<0.001$) according to VAS pain (general, foot and hand), the MFPDI and the FFI. In terms of anthropometric measurements, significant differences were only recorded for midfoot and forefoot width ($p=0.03$). In the data for the physical component, the multivariable linear regression with the parameters age, gender, VAS pain (general) and the presence of RA presented an R2 value of 48.8%, while for the mental health component, the corresponding value was 5.6%.

Conclusion

Morphological and structural characteristics of the foot are not necessarily associated with pain, disability and loss of function. The presence of RA, a higher score in VAS pain (general), female gender and greater age are all associated with the physical component of the quality of life for patients with RA.

Key words

Rheumatoid arthritis; foot health; quality of life; functionality; pain.

Strengths and limitations of this study

- The foot-related parameters are strongly associated with QoL.
- RA, higher score for VAS pain, female sex and age are all related to the physical component of QoL.
- Neither FPI nor any other anthropometric measurements are related to QoL.
- QoL was analysed at a moment that might coincide with an aggravation of RA.
- A longitudinal study might obtain different results.

Introduction

Rheumatoid arthritis (RA) is a chronic rheumatic disease that affects 0.5% to 1% of the population in Europe [1]. The most characteristic symptom is swelling, which provokes important changes in joint structures and limits function [2].

RA mainly affects the small joints of the hands and feet [3]. In the foot, it provokes deformities in the forefoot and hindfoot. The most common pathologies are hallux valgus, metatarsal subluxation, and hammer or claw toes [4]. As the disease progresses, the first metatarsophalangeal joint and pes planus may also be associated. These pathologies occur as the deterioration affects the joints and ligaments [5], thus limiting movement in the ankle and the foot. It also produces an unequal distribution of pressures and therefore makes it painful to remain in a standing position [6].

RA is a systemic disease that not only presents extra-articular manifestations but also has psychological affects [7], in many cases provoking mental health and functional problems as a consequence of ageing [8], oxidative damage to DNA and systemic inflammatory stress [9], thus limiting leisure and family-related activities and restricting social relationships [10]. The simultaneous impact of RA and a reduced quality of life imposes a major burden on patients, caregivers, the health system and society in general [11].

The mental and physical components of RA can reduce adherence to treatment, leading to poorer health outcomes and a worsened quality of life [12].

In patients with RA, the foot has been analysed from various standpoints, such as hallux valgus, clawed toes or morphological alterations [13]. Psychological and social aspects of the disease have also been analysed such as anxiety, depression and affectivity, have

also been analysed [14,15][16]. However, to date no studies have been undertaken to determine whether RA in the foot has a negative impact on the quality of life, in physical and mental health terms.

The aim of the present study, therefore, is to identify foot health factors related to the quality of life in patients with RA.

Method

Ethical approval: Institutional review board that approved the protocol for the study: Medical Research Ethics Committee of University of Malaga (CEUMA-91-2015-H) and PEIBA Andalucia (ARC0001), Spain.

Design: Cross-sectional study

Participants

A convenience sample was obtained of 246 patients with foot pain and RA (according to the ACR/EULAR rheumatoid arthritis classification criteria)[17], of whom seventeen subsequently declined to participate, citing lack of time (the study questionnaire required 30 minutes to complete) and 64 patients with foot pain but no RA. The patients were enrolled at hospital outpatient clinics from January to December 2018.

All those included in the study had a history of subtalar and/or ankle and/or talonavicular or hindfoot pain, did not make daily use of walking aids, and were able to perform the normal range of motions in the ankle, subtalar and midtarsal joints. Even if maximum dorsiflexion, pronation or supination in these joints could not be produced, a sufficient range of motion was achieved by adjusting the dynamics, for example by reducing stride length[6][18].

The exclusion criteria applied were the presence of concomitant musculoskeletal disease, central or peripheral nervous system disease or endocrine disorders (especially diabetes mellitus).

Patients who met the criteria for inclusion were approached by members of the rheumatology service at the Virgen de la Nieves Hospital (Granada, Spain), given an information sheet and invited to participate. Those who agreed were then interviewed and given further details of the study. All participants provided written consent prior to starting the interviews.

Data collection

Demographic and clinical characteristics

The demographic characteristics recorded included the patient's age, gender, disease duration and current therapy. The clinical data recorded were those obtained from the SF-12 questionnaire [19], a visual analogue scale for pain (VAS pain), both general [20] and specific to the foot and hand, the Manchester Foot Pain Disability Index (MFPDI) [21] and the Foot Function Index (FFI) [22].

For the anthropometric measurements, a foot measurement platform [23] was used to measure the foot length (weight bearing and non weight bearing), the midfoot, forefoot and heel width and the midfoot height. Each participant was asked first to stand on the platform and then to be seated, in both cases with the body weight distributed evenly between the two feet, arms beside the body and facing forwards. The measurements were obtained with the patient's heels placed in the heel cups, as far back as possible, and the first metatarsal heads located against the limit surface.

Other measurements were obtained using the Foot Posture Index, a reliable instrument for this purpose [24], and the Manchester Scale of hallux valgus [25].

The data availability statement No additional data available

Procedure

Two researchers (ARC and GGN) independently interviewed the patients to obtain the study data. The clinical interview was conducted in one room, where the patients were asked to complete the SF-12 (adapted version for a Spanish population) [26], MFPDI and VAS questionnaires. In a separate room, each patient was measured using a validated foot platform (intraclass correlation coefficient for the instrument, ICC, 0.96-0.98). Foot posture was determined according to the Foot Posture Index (FPI) (ICC for the clinician, 0.94-0.96). Each criterion was scored as −2, −1, 0, +1 or +2. The following FPI cut-off points, defining foot type category were used: a) highly supinated

−12 to −4, b) supinated −3 to 0, c) neutral 1 to 7, d) pronated 8 to 10 and e) highly pronated 11 to 12 [27]. The presence/absence of hallux valgus was determined according to the Manchester Scale of Hallux Valgus (ICC for the instrument, 0.93-0.97), a clinical tool consisting of photographs of feet with four levels of hallux valgus: none, mild, moderate and severe [25].

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in the design or conduct of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to the study participants

Statistical analysis

The results obtained are reported as the median and interquartile range, due to the non-normal distribution of the variables. The normality of the distributions was examined by the Kolmogorov-Smirnov test and the intra-rater reliability of the measurement instruments was calculated by a two-way mixed-consistency ICC model. Bivariate analysis was performed with a non-parametric test (the Mann-Whitney U test), in view of the non-normal distribution observed in most cases. Finally, a multivariable linear regression model was obtained to evaluate the predictors of quality of life, according to the physical and mental health components of the SF-12 questionnaire. In constructing the models, the regression assumptions of homoscedasticity, normality and independence of the residuals and collinearity were tested. Homoscedasticity was evaluated by analysing the distribution of predicted values and scatterplots of the residuals. Normality of the residuals was tested by analysing histograms and by graphs of standardised residuals. Independence of the residuals was evaluated by the Durbin-Watson statistic. Finally, the presence of collinearity was tested by calculating the variance inflation factor, the tolerance and partial correlations. The significance level was set at $p<0.05$, with two-tailed tests. All statistical analyses were conducted using SPSS v. 24.0 statistical software (SPSS Inc., Chicago, IL, USA) and GPower 3.1.92 for the post-hoc analyses.

Results

In total, 293 subjects were analysed, with 229 patients in the RA group (average duration of RA, 15.4, SD 10.5 years) and 64 in the control group. In the RA group, 173 patients were female, as were 50 of the control group. The values for median age and interquartile range (IQR) were 59 and 16 years for the patients with RA and 53 and 21 years for those in the control group. The median values for height and weight were 162 cm (IQR: 10) and 70 kg (IQR: 19), respectively, for the RA group, and 162 cm (IQR: 10) and 65 kg (IQR: 15), respectively, for the control group. The patients with RA were treated with biological disease-modifying antirheumatic drugs (bDMARDs) (42%), methotrexate (35%) or nonsteroidal anti-inflammatory drugs (NSAIDs) / corticosteroids (20%).

The instruments used to measure pain, disability and functionality (VAS pain, MFPDI and FFI) revealed significant differences between the patients with RA and the control group, for both genders ($p<0.001$). However, among those used to obtain foot measurements and posture data, only the midfoot height values ($p=0.007$ and $p=0.004$) for male and female participants and midfoot width ($p=0.03$) for the females were statistically significant. The FPI and the other anthropometric measurements were not statistically significant (Table 1).

The results for the SF-12 quality of life questionnaire revealed significant differences in the physical component, with $p<0.001$ (females) and $p=0.02$ (males) and in the mental component in the female participants ($p=0.04$) (Table 2). Among the male participants, no differences in the mental health component were observed between the RA and control groups.

Bivariate analyses were performed to determine the relations between the physical and mental health components, taking into account the sociodemographic, clinical and anthropometric characteristics of the participants. Among these results, especially noteworthy was the value of -0.630 with $p<0.001$ obtained for VAS pain (general) and that of -0.505 with $p<0.001$ for the presence of RA. Neither the anthropometric characteristics, foot posture nor disease duration presented any correlation with either of these variables.

Multivariate models were then constructed, using as predictors the variables that had presented a significant association in the bivariate models, adjusted for age and gender.

Two models were calculated, with the physical and mental health components respectively as dependent variables.

According to the data for the physical component, the multivariable linear regression presented an R^2 value of 48.8%. (Table 3). Post-hoc analysis yielded a power of 0.95 for this four-predictor model. The multivariable linear regression of the mental health component presented an R^2 value of 5.6%. There was no collinearity in the model (maximum VIF 1.39 and minimum tolerance of 0.72) and the residuals were independent (Durbin-Watson, 1.19), using the same parameters (i.e. age, gender, general VAS pain and the presence of RA).

Discussion

The aim of this study is to determine and analyse foot health factors related to the quality of life of patients with RA. The multivariate regression results obtained suggest that patients with foot pain and RA perceive a significantly lower level of health than those with foot pain but no RA (control group) ($p<0.001$). However, these findings are not directly related to the clinical parameters that might have triggered the increased level of pain. The deformations which are typical of this disease and which are located in the forefoot (such as hallux valgus, hallux rigidus, floating of the lesser toes or synovial inflammation of the metatarsophalangeal joints) or in the hindfoot (such as hindfoot valgus or flat foot) are often believed to aggravate pain and disability among this population. Nevertheless, this expectation was not borne out by our study results, possibly because the presence of RA in itself is painful, while other patients with similar foot deformities but no RA might not experience pain. If this were the case, then the deformity would not be the cause of pain, but merely the outcome of a degenerative process in the foot. However, analysis of plantar pressures shows that this localised pain is not correlated with peak plantar pressure, which is received in the hindfoot.

Structural alterations in the foot not only cause physical deterioration due to reduced mobility, but can also lead to emotional deterioration. Nevertheless, according to our study findings, these alterations are not in themselves the cause of increased pain. Instead, this outcome may be influenced by an external component such as the choice of footwear, a factor that is strongly influenced by the appearance of structural alterations in the foot. We conclude, therefore, that patients should prioritise factors such as fit and comfort when choosing footwear.[28]

Many patients, especially women, have considerable difficulty in obtaining appropriate footwear, i.e. that which is comfortable, adapted to the deformities of the foot, of assistance in performing the gait cycle and acceptable aesthetically [29,30].

The latter characteristic is the area in which most negative impressions are caused among the population with RA, since many patients do not choose their footwear in strict accordance with the deformities present in their feet [31]. This discordance can produce a negative impact, either in terms of the mental component (the perceived quality of life), when the personal image is compared with that of the non-affected population, or because of increased plantar pain, when the footwear chosen is uncomfortable and prevents the proper mobilisation of the musculoskeletal structures of the foot, thereby limiting the performance of the activities of daily life. These outcomes are often associated with dissatisfaction and even depression among the population affected.

With advancing age, musculoskeletal deformities and, in particular, structural alterations in the foot increase, as a greater number of structures are damaged. These alterations may also be caused by increased neuropathy in the foot, which in turn would heighten pain and reduce functionality [1], thus worsening the perceived quality of life (impacting on anxiety and depression status in particular) [32][33].

This research presents certain limitations. Firstly, it is based on a cross-sectional study of a heterogeneous sample population, rather than on a longitudinal study. This characteristic of the study design may have influenced the results obtained in two respects. On the one hand, in our sample the number of participants with RA significantly exceeded that of those not presenting this alteration. Therefore, if the size of the control group were increased, somewhat different results might be obtained. Moreover, as the analysis was transversal, both the physical and the mental components were analysed at a moment that might have coincided with an aggravation of the RA experienced, thus altering the study results obtained.

Another limitation of our study is that it is based on a convenience sample, which means that the homogeneity of the participants cannot be assured. In future research, therefore, the size and composition of the study groups should be controlled to optimise their homogeneity. Finally, attention should be paid to the question of whether foot pain

is determined by the characteristics of the foot, or whether RA pain affects certain foot types in particular.

Our study shows that patients with RA are more likely to present structural alterations in the foot and hence to experience physical and/or psychosocial deterioration than when this condition is absent [34]. Furthermore, the long-term evolution of the disease may be directly related to psychosocial and emotional perceptions. It should be also be taken into account that in our study groups most of the patients were female, although this reflects their prevalence among the general population affected by RA and foot pain [35,36] Psychosocial status was also increased in this female population, due to factors such as their being in employment or the presence of positive body image perceptions [37][38][39]

On the other hand, the study also has important strengths. Although the results obtained do not show that foot-related parameters are strongly associated with the quality of life of these patients, they do highlight the need for further, longitudinal studies addressing parameters such as the evolution of the disease, the treatment received and psychosocial aspects that could influence the patient's perception of the impact of RA with respect to daily activities and musculoskeletal pain.

In the clinical context, our study raises an important question, namely that the pain and the reduced quality of life experienced by patients with RA may be provoked by the disease itself, and not by the alterations in the foot. If this were so, the presence of the latter might not be related to the pain experienced.

Conclusions

Morphological and structural characteristics of the foot are not necessarily associated with pain, disability and loss of function. The presence of RA, a higher score for general VAS pain, female gender and greater age are all related to a reduced quality of life in the physical component for patients with RA.

Author Contributions

Conceptualization, Gabriel Gijon-Nogueron, Rafael Caliz-Caliz, Jose Miguel Morales-Asencio and Ana Belen Ortega-Avila; Data curation, Andres Reinoso-Cobo; Formal analysis, Gabriel Gijon-Nogueron, Jose Miguel Morales-Asencio and Ana Belen Ortega-Avila; Methodology, Gabriel Gijon-Nogueron, Rafael Caliz-Caliz, Miguel Angel Ferrer-Gonzalez and Ana Belen Ortega-Avila; Project administration, Maria Teresa Vallejo-Velazquez; Writing – original draft, Andres Reinoso-Cobo, Gabriel

Gijon-Nogueron and Ana Belen Ortega-Avila; Writing – review & editing, Andres Reinoso-Cobo, Gabriel Gijon-Nogueron, Rafael Caliz-Caliz, Jose Miguel Morales-Asencio and Ana Belen Ortega-Avila.

References

1 de Andrade AP, Inoue EN, Nisihara R, *et al.* Foot function in rheumatoid arthritis patients: a cross-sectional study. *Clin Rheumatol* 2018;**37**:3427–30. doi:10.1007/s10067-018-4215-y

2 Gabriel SE, Michaud K. Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. Arthritis Res. Ther. 2009. doi:10.1186/ar2669

3 Stolt M, Suhonen R, Leino-Kilpi H. Foot health in patients with rheumatoid arthritis—a scoping review. Rheumatol. Int. 2017. doi:10.1007/s00296-017-3699-0

4 Siddle HJ, Hodgson RJ, Hensor EMA, *et al.* Plantar plate pathology is associated with erosive disease in the painful forefoot of patients with rheumatoid arthritis. *BMC Musculoskelet Disord* 2017;**18**:1–9. doi:10.1186/s12891-017-1668-0

5 Jaakkola JI, Mann RA. A review of rheumatoid arthritis affecting the foot and ankle. Foot Ankle Int. 2004. doi:10.1177/107110070402501205

6 Otter SJ, Lucas K, Springett K, *et al.* Foot pain in rheumatoid arthritis prevalence, risk factors and management: An epidemiological study. *Clin Rheumatol* Published Online First: 2010. doi:10.1007/s10067-009-1312-y

7 Margaretten M, Julian L, Katz P, *et al.* Depression in patients with rheumatoid arthritis: Description, causes and mechanisms. *Int J Clin Rheumtol* Published Online First: 2011. doi:10.2217/ijr.11.62

8 Lu MC, Guo HR, Lin MC, *et al.* Bidirectional associations between rheumatoid arthritis and depression: A nationwide longitudinal study. *Sci Rep* 2016;**6**. doi:10.1038/srep20647

9 Malemud CJ, Miller AH. Pro-inflammatory cytokine-induced SAPK/MAPK and JAK/STAT in rheumatoid arthritis and the new anti-depression drugs. Expert Opin. Ther. Targets. 2008. doi:10.1517/14728222.12.2.171

10 Matcham F, Rayner L, Steer S, *et al.* The prevalence of depression in rheumatoid arthritis: A systematic review and meta-analysis. *Rheumatol (United Kingdom)* Published Online First: 2013. doi:10.1093/rheumatology/ket169

11 Sambamoorthi U, Shah D, Zhao X. Healthcare burden of depression in adults with arthritis. Expert Rev. Pharmacoeconomics Outcomes Res. 2017. doi:10.1080/14737167.2017.1281744

12 DiMatteo MR, Lepper HS, Croghan TW. Depression Is a Risk Factor for Noncompliance With Medical Treatment. *Arch Intern Med* Published Online First: 2000. doi:10.1001/archinte.160.14.2101

13 Hafström I, Engvall I-L, Rönnelid J, *et al.* Rheumatoid factor and anti-CCP do not predict progressive joint damage in patients with early rheumatoid arthritis treated with prednisolone: a randomised study. *BMJ Open* 2014;**4**:e005246. doi:10.1136/bmjopen-2014-005246

14 Vamos M. Body image in rheumatoid arthritis: The relevance of hand appearance to desire for surgery. *Br J Med Psychol* Published Online First: 1990. doi:10.1111/j.2044-8341.1990.tb01619.x

15 Williams AE, Graham AS. 'My feet: visible, but ignored . . .' A qualitative study of foot care for people with rheumatoid arthritis. *Clin Rehabil* 2012;**26**:952–9. doi:10.1177/0269215511434995

16 Rathbun AM, Reed GW, Harrold LR. The temporal relationship between depression and rheumatoid arthritis disease activity, treatment persistence and response: A systematic review. *Rheumatol (United Kingdom)* 2013;**52**:1785–94. doi:10.1093/rheumatology/kes356

17 Aletaha D, Neogi T, Silman AJ, *et al.* 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum. 2010;**62**:2569–81. doi:10.1002/art.27584

18 Dubbeldam R, Baan H, Nene A V., *et al.* Foot and ankle kinematics in rheumatoid arthritis: Influence of foot and ankle joint and leg tendon pathologies. *Arthritis Care Res* 2013;**65**:503–11. doi:10.1002/acr.21852

19 Luo X, George ML, Kakouras I, *et al.* Reliability, validity, and responsiveness of the short form 12-item survey (SF-12) in patients with back pain. *Spine (Phila Pa 1976)* Published Online First: 2003. doi:10.1097/01.BRS.0000083169.58671.96

20 Sendlbeck M, Araujo EG, Schett G, *et al.* Psychometric properties of three single-item pain scales in patients with rheumatoid arthritis seen during routine clinical care: A comparative perspective on construct validity, reproducibility and internal responsiveness. *RMD Open* Published Online First: 2015.

doi:10.1136/rmdopen-2015-000140

21 Gijon-Nogueron G, Ndosi M, Luque-Suarez A, *et al.* Cross-cultural adaptation and validation of the Manchester Foot Pain and Disability Index into Spanish. *Qual Life Res* 2014;**23**:571–9. doi:10.1007/s11136-013-0507-5

22 Paez-Moguer J, Budiman-Mak E, Cuesta-Vargas AI. Cross-cultural adaptation and validation of the Foot Function Index to Spanish. *Foot Ankle Surg* 2014;**20**:34–9. doi:10.1016/j.fas.2013.09.005

23 McPoil TG, Vicenzino B, Cornwall MW, *et al.* Can foot anthropometric measurements predict dynamic plantar surface contact area? *J Foot Ankle Res* 2009;**2**:1–9. doi:10.1186/1757-1146-2-28

24 Redmond AC, Crosbie J, Ouvrier RA. Development and validation of a novel rating system for scoring standing foot posture: The Foot Posture Index. *Clin Biomech* 2006;**21**:89–98. doi:10.1016/j.clinbiomech.2005.08.002

25 Garrow AP, Papageorgiou A, Silman AJ, *et al.* The grading of hallux valgus. The Manchester Scale. *J Am Pod Med Assoc* 2001.

26 Schmidt S, Vilagut G, Garin O, *et al.* Normas de referencia para el Cuestionario de Salud SF-12 versión 2 basadas en población general de Cataluña. *Med Clin (Barc)* Published Online First: 2012. doi:10.1016/j.medcli.2011.10.024

27 Redmond AC, Crane YZ, Menz HB. Normative values for the Foot Posture Index. *J Foot Ankle Res* 2008;**1**:6. doi:10.1186/1757-1146-1-6

28 Tovaruela-Carrión N, Becerro-de-Bengoa-Vallejo R, Losa-Iglesias ME, *et al.* Accurately Determining Proper Shoe Size in Patients With Rheumatoid Arthritis. *Rehabil Nurs* 2018;**43**:285–9. doi:10.1097/rnj.0000000000000040

29 Naidoo S, Anderson S, Mills J, *et al.* 'I could cry, the amount of shoes I can't get into': A qualitative exploration of the factors that influence retail footwear selection in women with rheumatoid arthritis. *J Foot Ankle Res* Published Online First: 2011. doi:10.1186/1757-1146-4-21

30 Goodacre LJ, Candy FJ. 'If I didn't have RA I wouldn't give them house room': The relationship between RA, footwear and clothing choices. *Rheumatology* 2011;**50**:513–7. doi:10.1093/rheumatology/keq347

31 Reina-Bueno M, Vázquez-Bautista M del C, Pérez-García S, *et al.* Effectiveness of custom-made foot orthoses in patients with rheumatoid arthritis: a randomized controlled trial. *Clin Rehabil* 2019;**33**:661–9. doi:10.1177/0269215518819118

32 Perry MG, Richards L, Harbuz MS, *et al.* Sequential synovial fluid sampling

suggests plasma and synovial fluid IL-6 vary independently in rheumatoid arthritis [2]. Rheumatology. 2006. doi:10.1093/rheumatology/kei196

33 Li Y, Jiang L, Zhang Z, *et al.* Clinical characteristics of rheumatoid arthritis patients with peripheral neuropathy and potential related risk factors. *Clin Rheumatol* 2019;**38**:2099–107. doi:10.1007/s10067-019-04521-5

34 Gates LS, Arden NK, Hannan MT, *et al.* Prevalence of Foot Pain Across an International Consortium of Population-Based Cohorts. *Arthritis Care Res* 2019;**71**:661–70. doi:10.1002/acr.23829

35 Sokka T, Toloza S, Cutolo M, *et al.* Women, men, and rheumatoid arthritis: Analyses of disease activity, disease characteristics, and treatments in the QUEST-RA Study. *Arthritis Res Ther* Published Online First: 2009. doi:10.1186/ar2591

36 Kvien TK, Uhlig T, Ødegård S, *et al.* Epidemiological aspects of rheumatoid arthritis: The sex ratio. In: *Annals of the New York Academy of Sciences*. 2006. doi:10.1196/annals.1351.019

37 Kobelt G, Texier-Richard B, Mimoun S, *et al.* Rheumatoid arthritis and sexuality: A patient survey in France. BMC Musculoskelet. Disord. 2012;**13**:170. doi:10.1186/1471-2474-13-170

38 Lacaille D, White MA, Backman CL, *et al.* Problems faced at work due to inflammatory arthritis: New insights gained from understanding patients' perspective. *Arthritis Care Res* 2007;**57**:1269–79. doi:10.1002/art.23002

39 López-López D, Becerro-De-Bengoa-Vallejo R, Losa-Iglesias ME, *et al.* Evaluation of foot health related quality of life in individuals with foot problems by gender: A cross-sectional comparative analysis study. *BMJ Open* 2018;**8**:e023980. doi:10.1136/bmjopen-2018-023980

	Overall(n=293)					Female (n=173)					Male (n=120)				
	Patients with foot pain and RA (group)		Patients with foot pain but no RA (control group)			Patients with foot pain and RA (group)		Patients with foot pain but no RA (control group)			Patients with foot pain and RA (group)		Patients with foot pain but no RA (control group)		
	Median	Interquartile range	Median	Interquartile range	P value	Median	Interquartile range	Median	Interquartile range	P value	Median	Interquartile range	Median	Interquartile range	P value
Age (years)	59	16	53	21	0,003	59	16	53	21	0.0	58	16	53.5	24	0.845
Height (cm)	162	10	162	10	0,401	160	10	160.5	9	0.9	170	10	171	15	0.578
Weight (kg)	70	19	65	15	0,168	65	15	62.5	11	0.1	78	18	76.5	13	0.35
Gen. VAS (0-100)	6	3	1,5	4	<0.001	6	3	2	5	<0.0	5	4	0	1	<0.001
Hand VAS	6	3	0	3	<0.001	6	4	1	3	<0.0	5	4	0	1	<0.001
Feet VAS	6	5	2	5	<0.001	6	4	2	5	<0.0	4	5	0	1	<0.001
MFPDI	21	18	4	10	<0.001	22	17	4.5	11	<0.0	19	18	0.5	6	<0.001
FFI Total	43,91	45	6,52	18	<0.001	48.3	39	9.1	23	<0.0	30.4	51	0	5	<0.001
FFI Pain	48	38	8	29	<0.001	50	34	14	33	<0.0	41.5	47	0	4	<0.001
FFI Disability	49	58	0	14	<0.001	51	50	2	18	<0.0	24	56	0	0	<0.001
FFI Physical activity	6	19	0	2	<0.001	7	20	0	2	<0.0	3	15	0	0	<0.001
W/b r/foot	242	22	244	18	0,339	237	15	240.5	17	0.05	261	18	261	22	0.777
W/b 1st MTPJ r/foot	180	16	180,5	15	0,843	178	11	177	14	0.84	195.5	14	189.5	19	0.9
W/b r/MF height	53,8	9,7	56,265	10,31	<0.001	51.4	8.2	54.4	9.4	0.00	58.8	6.3	65.8	16	0.004
W/b r/MF width	77	8,63	74,965	8,93	0,035	75.5	6.7	73.9	6.9	0.0	83.5	7.2	81.5	8.7	0.559
W/b r/forefoot	91,38	9,34	91,69	7,08	0,508	89.7	7	88.5	6.8	0.55	97.3	7.8	96.4	7.4	0.941
W/b r/hindfoot	66,52	7,29	66,105	6,16	0,089	65.7	6.2	65.2	6.6	0.1	71.8	7.6	68.5	4.2	0.39
FPI TOTAL (r/ foot)	5	7	5	4	0,338	5	6	5	5	0.8	2	8	5	3	0.205

Table 1. Characteristics of the study groups W/b: Weight bearing; r/: Right; MTPJ: Metatarsophalangeal joints; MF: midfoot *Mann-Whitney U-test

	Female					Male				
	RA (n=173)		Control group (n=50)			RA (n=56)		Control group (n=14)		
	Mean	**SD**	**Mean**	**SD**	**P value***	**Mean**	**SD**	**Mean**	**SD**	**P value***
Physical health component (Ref. Spanish population)	36.50	7.91	48.88	7.55	p<0.001	39.07	2.91	49.09	8.22	0.02
Mental health component (Ref. Spanish population)	32.10	7.97	35.08	5.00	0.04	33.76	1.65	36.14	4.66	0.35

* Mann-Whitney U-test

Table 2. Characteristics of the sample group according to the SF 12 results

					95%CI	
	Adjusted coefficient	**B**	**β**	**p**	**Lower**	**Upper**
Age	-0.175	-0.082	-0.113	0.038	-0.159	-0.005
Gender	-1.361	-0.603	-0.028	0.607	-2.908	1.703
VAS pain – General	-2.177	-1.609	-0.474	<0.001	-2.024	-1.193
RA	-11.769	-6.461	-0.292	<0.001	-9.111	-3.811

Table 3: Model of multivariate regression for the perception of physical health

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7
Generalisability	21	Discuss the generalisability (external validity) of the study results	7-8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.