Toenail abnormalities in rheumatoid arthritis patients are associated with radiographic damage and impact disability: a cross sectional study nested within a cohort

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Abstract

Objective

Cutaneous involvement is an extra-articular manifestation of rheumatoid arthritis (RA). This includes nail abnormalities, which are often overlooked. We described nail findings in RA patients currently attending an early arthritis cohort (n=145), and associated them with disease activity and/or damage, as well as patient-reported outcomes.

Methods

A standardised nail examination was performed in 122 patients (84.1% of the cohort), concomitant to the rheumatic assessment. Disability, quality of life and perceived nail-related health were also assessed. Nail findings and their location were recorded and classified according to standardised definitions. Logistic and linear regression models were used to investigate predictors of nail findings and to identify the impact of toenail findings on disability, which was evaluated with the HAQ. Patients consented to participate.

Results

Patients were primarily middle-aged females, with median follow-up of 9 years, and had disease under control. Most patients (62.3%) had at least one nail finding and these patients scored lower their nail-related health. The median (IQR) of findings/abnormalities per patient was 3 (2–5) and the number of nails affected per patient was 10 (2–12). Age (OR: 1.04, 95%CI: 1.007–1.074) and erosive disease (OR: 2.26, 95%CI: 1.1–5.1) were associated with nail findings. Toenail involvement was consistently associated with HAQ score out of normal range (OR=3.4, 95%CI=1.24–9.35, p=0.02). There was a linear association between the number of toenails affected and the HAQ score.

Conclusion

Nail abnormalities are common and heterogeneous findings in RA patients; they are associated with erosive damage and impact disability.

Key words

nail abnormalities, fingernails, toenails, rheumatoid arthritis

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Significance and innovations
- *Nail abnormalities are frequent and heterogeneous findings in patients with RA.*
- *Nail abnormalities are associated with age and radiographic damage.*
- *Nail abnormalities have a linear impact on disability.*

Competing interests: none declared.

Introduction

Skin diseases can have a major impact on patients, affecting their psychological well-being, social functioning, and activities of daily living (1, 2). Dermatologists and clinicians at large recognise that in addition to the identification and treatment of skin diseases, it is crucial to gather information about their implication on different aspects of patients' lives. In that regard, *impairment* refers to the impact of the disease process on the affected organ, while *disability* describes the functional effect of this impairment; in turn, *handicap* describes the consequences the disability has in the patient's normal functioning in society (3). It is worth mentioning that techniques for creating specialty-specific measurements of handicap were first described for rheumatic diseases, such as rheumatoid arthritis (RA), almost four decades ago (4).

RA is a systemic inflammatory disorder with articular and extra-articular involvement that, if not properly controlled, can lead to significant joint structural damage and destruction, functional challenge, disability, reduced quality of life, and even increased mortality (5). Cutaneous manifestations are considered part of the extra-articular involvement in RA and are frequently overlooked. They have been characterised as either specific or non-specific, in addition to the dermatologic adverse effects related to anti-rheumatic therapies (6-8). Nails are skin appendages, and their evaluation is part of a standardised dermatologic examination (8). Nail abnormalities have been reported in RA (9-14), although information regarding their association with disease variables is quite scant. There are different potential explanations for nail changes in RA patients, which range from vascular involvement of the nail fold to the collateral effects of different systemic treatments. However, whether nail changes are associated with disease activity and/or secondary damage, has not been properly assessed.

Therefore, by using a synergist approach between rheumatologists and dermatologists, the aim of this study was to describe nail abnormalities in RA patients and to associate them with disease-specific variables (related to activity and/or damage), as well as patient-reported outcomes (PROs), particularly disability. We hypothesise an association between nails abnormalities and a more severe spectrum disease.

Patients and methods

Ethical considerations

The study was performed in compliance with the Helsinki Declaration (15). The Research Ethics Committee of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMyN-SZ) approved the study (ref. no.: IRE-2572-18-19/1). All participants provided written informed consent.

Study design, setting and study population

The study was cross sectional and performed between June 2018 and April 2019 in an early RA cohort, which was initiated in 2004 at the INCMyN-SZ, a national referral centre for rheumatic diseases in Mexico City (16).

Up to June 2018, the cohort included 199 RA patients, 54 of which had been lost to follow up. All the remaining patients (145) were invited to the study; 23 declined to participate because of time constraints to attend the dermatological exam. Patients entering the cohort had disease duration of less than one year and no specific rheumatic disease but RA; 94.3% of the patients met ACR 1987 RA classification criteria (17), and 98% of the 50 patients included from 2011 onwards met ACR/EULAR 2010 RA classification criteria (18).

Clinical evaluations at cohort entry and at follow-ups had been previously described (16) and included disease activity evaluation according to the disease activity score evaluated in 28 joints (DAS28) (19), comorbidity according to the Charlson score (20), laboratory tests and treatment assessments. During follow-up, patients received treat-to-target oriented treatment, primarily with traditional disease-modifying anti-rheumatic drugs (DMARDs) with or without corticosteroids. No standard therapeutic protocol was followed (16). Radiographic assessments were scheduled on annual basis; presence of erosions was identified on radiographs

(hands and feet) that were read in chronological order by the same rheumatologist and a radiologist. RA was classified as erosive (at least one unequivocal cortical bone defect or break) or as non-erosive disease by both physicians after a careful review of the radiographs; disagreement in classification was immediately resolved by consensus as previously published (16).

Dermatological evaluations, findings, classification and definitions

At study entry, patients had a complete standardised dermatological exam, which included nail examination, as well as their usual rheumatologic assessment. The dermatologist and the rheumatologist who examined the patients were blinded to each other's findings. All the dermatological exams were standardised and performed by a dermatology resident and a senior dermatologist, who confirmed the findings reported by the trainee according to photographs (Intra-observer correlation, κ=0.928; inter-observer correlation, κ=0.908).

Nail examination consisted of unmagnified vision of each nail, followed by the inspection of the proximal periungual fold capillary loops, nail bed, nail matrix, lateral periungual folds and hyponichium using a dermatoscope (10x magnification, Derm lite). Nail findings were recorded and classified into three categories as summarised in Table I: RA-related nail abnormalities, RA-unrelated nail abnormalities and nail diseases/syndromes. Standardised definitions (21-25) were used and are summarised in Supplementary Table S1**.** A record was also made of any nail that had been subjected to patient-reported-trauma, and the findings in these nails were excluded from the analysis. Only the current nail changes were recorded and the number and location of nails affected, although recorded, were not considered during the classification of the nail abnormalities. Nails from patients with clinical findings suggestive of fungal infection were sampled with nail scraping and KOH examination. Onychomycosis was defined by positive clinical findings and a positive nail scraping.

Patient-reported outcomes

Before the dermatologic exam, patients were asked if they were concerned about their nail health status (Yes/No) and to rate their perception of their nail-related health on a Visual Analogue Scale (VAS; 0–100 mm, where 100 mm reflects the best health) (8). Patients also completed the HAQ (26).

Statistical analysis

We performed a descriptive statistical analysis, presenting frequencies for categorical variables and median (interquartile range) for numerical variables. The Mann-Whitney U-test was used to compare continuous variables when they did not show a normal distribution (Kolmogorov-Smirnov). Fisher's exact test or χ^2 test were used to compare proportions.

Cumulative disease activity was obtained with DAS28 serial measurements, which were summarised as area under the curve (AUC) and presented standardised by the length of each patient follow-up (27).

Multiple logistic regression models (stepwise) were used to investigate factors associated to nail abnormalities, which was considered the dependent variable; secondary analyses were performed separately for fingernail and toenail alterations. Baseline variables (at cohort entry), DAS28 AUC and variables obtained at study entry, were included and tested as potentially associated factors in different models. Previously, correlations between specific variables were analysed and, when appropriate (Pearson correlation ≥0.70), one of them was selected, according to clinical relevance. In addition, the variables included in each model were selected according to their statistical significance in the univariate analysis, their clinical relevance and the number of outcomes (number of patients with nails abnormalities) identified; female sex was forced into the analysis as a confounding factor due to its association with a more severe spectrum disease. A similar (exploratory) sub-analysis was performed to identify factors associated to onychomycosis (dependent variable).

Multiple logistic regression analysis was additionally used to identify the impact of toenail findings/abnormalities on the HAQ score out of normal range and the steps performed were similar to those above described. Finally, linear regression analysis was applied, in order to define the impact of the number of toenail abnormalities and the number of toenails affected per patient on the HAQ score, defined as a continuous variable.

Receiving Operating Curve (ROC) were used to define the best age-cut-off to predict nail abnormalities/diseases.

Missing data were below 1.6% and applied to laboratory exams; no imputation was done. For regression analysis there were no patients with complete missing data.

All statistical tests were two-sided and evaluated at the 0.05 significance level. The statistical analysis was performed using the SPSS/PC programme (v. 17.0 Chicago IL).

Results

Population characteristics at study entry

The 122 patients finally included in the study were primarily middle-aged females and had median of 12 (IQR: 9–15) years of formal education. The median follow-up was 9 (5–13) years. Most patients (81.1% and 89.3%, respectively) had positive rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) (at cohort entry), and 46.7% had erosive disease. Also, most patients had disease activity under control according to (punctual) DAS28 score, and acute reactant phase determinations were within normal range; in accordance, median HAQ was within normal values. Forty percent of the patients had at least one additional (to RA) comorbid condition and median Charlson score was 1. Finally, almost 55% of the patients were on low-dose oral prednisone and up to 92% on DMARDs. Table II summarises clinical and demographic data.

Description of the nail examination and nail-related health patient's perception

Most patients (n=76, [62.3%]) had at least one nail abnormality (RA related,

Table I. Classification of nail findings and number (%) of RA patients affected with fingernail/toenail abnormalities.

RA-related nail abnormalities			RA-unrelated nail abnormalities			Nail diseases/syndromes		
	Hands	Feet		Hands	Feet		Hands	Feet
Bywaters	1	1	Erythema of the proximal nail fold	1	0	Onychomycosis	0	16
Muehrcke	0	0	Hapalonychia	3	0	Yellow nail syndrome	0	0
			Traumatic melanonychia	1	19			
			Fungal melanonychia	0	1			
			Short linear vessels	16	0			
			Splinter haemorrhages	0	4			
			True Leukonychia	0	1			
			Mycotic Leukonychia	0	7			
			Longitudinal striations (ridging)	14	11			
			Pachyonychia	0	4			
			Xanthonychia	0	25			
			Hyperkeratosis subungual	0	15			
			Onycholysis distal	0	3			
			Beau lines	5	8			
			Subungual haematoma	0	8			
			Onychocryptosis	0	5			
			Onicoatrophy	0	6			
			Transverse overcurvature nail	1	5			
			Longitudinal overcurvature nail	0	6			
			Frayed cuticles	8	0			

RA-unrelated and/or specific disease/syndrome). Among those, 35 patients (46.1%) had exclusively toenail findings, 27 (35.5%) had both toenail and fingernail findings, and there were 14 patients (18.4%) who had findings exclusively located on the fingernails. The median (IQR) of abnormalities/diseases per patient was 3 (2–5) and the number of nails affected per patient was 10 (2–12). Among patients with fingernail findings (n=41), there were 10 (range: 8–10) fingernails affected per patient; meanwhile, among the patients with toenail abnormalities (n=62), there were 4 (range: 2–10) toenails affected per patient (Fig. 1-2).

Most abnormalities were RA-unrelated, and they were more frequent in the feet, as summarised in Table I. This table also describes the distribution of patients with at least one abnormality.

Finally, 32 patients (26.2%) were concerned about their nail health status and the median nail-related health VAS of the entire RA population was 8 (7-9).

Factors associated with an abnormal nail examination

Patients with finger and toenail findings/diseases were compared to patients with a normal dermatological exam (Table II). Patients from the former group were older and had a higher frequency of erosive disease ($p<0.01$ for both); also, there was a trend for them to have a lower education level, longer disease duration, higher HAQ, and they were more likely to be on DMARDs. Also, as expected, more patients from the former group were concerned about their nail health status (28 patients [36.8%] *vs*. 4 [8.7%]) and rated lower in their nail-related health VAS (5 mm [2.3–6.8] *vs*. 7.5 mm [2.5–8.8], $p\leq0.001$ for both), compared to their counterparts. In the regression analy-

Table II. Population characteristics at study entry, and their comparison in the subpopulations defined according to presence/absence of finger and toenails abnormalities.

	Study population n=122	Patients with nail abnormalities n=76	Patients without nail abnormalities n=46	*p*
Characteristics				
Age, years	45.5 (36-58)	51 (39.3-59)	43 (32.8-52)	0.003
Females[1]	111 (91)	68 (89.5)	43 (93.5)	0.532
Formal education, years*	12 (9-15)	12 (9-14.8)	12 (9-16)	0.230
Disease duration, years	9 (5-13)	10 (5-13)	6 (4.8-12.3)	0.197
RF+[1]*	99 (81.1)	61 (80.3)	38 (82.6)	0.815
ACPA+[1]*	109 (89.3)	67 (88.2)	42 (91.3)	0.765
Hand and/or feet erosive disease[1]	57 (46.7)	43 (56.6)	14 (30.4)	0.005
Isolated hand erosions[1]	34 (27.9)	28 (36.8)	6 (13)	0.006
Isolated feet erosions[1]	48 (39.3)	35 (46.1)	13 (28.3)	0.058
Hand and feet erosions[1]	25 (20.2)	20 (26.3)	5 (10.9)	0.014
Incidental erosive disease[1],[2]	43 (35.2)	31 (40.8)	12 (26.1)	0.120
(Punctual) DAS28	1.6 (0.9-2.5)	1.7 (0.8-2.5)	1.5 (0.9-2.4)	0.794
(Cumulative) DAS28 AUC	3.8 (2.9-4.7)	3.8 (2.9-4.8)	3.6 (2.9-4.3)	0.34
ESR, mm/H	4 (2-11.3)	4 (2-12)	3 (2-11)	0.358
CRP, mg/dL	0.39 (0.14-0.12)	0.4 (0.13-1)	0.4 (0.14-0.84)	0.893
HAQ	0 (0-0.125)	0 (0-0.12)	0 (0-0)	0.356
Charlson score	1 (1-1)	1 (1-1)	1 (1-1)	0.203
Corticosteroids[1]	67 (54.9)	43 (56.6)	24 (52.2)	0.709
DMARDs[1]	112 (91.8)	72 (94.7)	40 (87)	0.175
no. of DMARDs/patient	1 (1-2)	1 (1-2)	1 (1-2)	0.853

Data presented as median (IQR) unless otherwise indicated. [1]Number (%) of patients. *Data obtained at cohort entry. [2]Patients without erosions at cohort entry but who developed erosions at study entry. RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; DAS28: disease activity score on 28 joints; AUC: area under the curve; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; HAQ: Health Assessment Questionnaire; DMARDs: disease-modifying anti-rheumatic drugs.

sis to identify factors associated to nail abnormalities (dependent variable), the following variables were included: age, years of formal education, disease duration, erosive disease, HAQ and number of DMARDs per patient; in addition, female sex and cumulative DAS28 were forced into the analysis. Age (OR: 1.04, 95%CI: 1.007–1.074, p=0.018) and erosive disease (OR: 2.26, 95%CI: 1.1–5.1, p=0.049) were the only variables associated with nail abnormalities/diseases. The age cut-off to predict nail abnormalities/diseases was 42.5 years (area under the curve=0.665; sensitivity=0.66; specificity=0.47; positive predictive value=0.77 and negative predictive value=0.52).

We further explored factors associated with onychomycosis, considering there may be differences with those associated with non-infectious nail abnormalities. There were 16 patients with onychomycosis. All of them had additional nail findings/abnormalities, with a median (IQR) of 5 (4–7) nail abnormalities per patient and 10 (3–15) finger/toenails affected per patient. We then identified differences between patients with isolated finger and toenail abnormalities (n=61) and those who additionally had onychomycosis (n=16). Results are summarised in Suppl. Table S2 and show that patients with concomitant fungal infection tend to be more frequently male, RF positive (at cohort entry), to present higher cumulative DAS28 and to have received more intensive RA treatment. In the models tested, we included combinations of 2 of the following variables: sex, cumulative disease activity, DMARDs per patient and RF as independent variables and results were consistent; male sex was the only variable retained in the model to explain concomitant onychomycosis and nail abnormalities (OR=4.7, 95% CI=1.2–21.3, p=0.047). Finally, more patients with concomitant onychomycosis and other nail abnormalities tend to be concerned about their nail health status (9 patients [56.3%]) and rated lower their nail-related health VAS (5 mm [2–7]) compared to their counterparts (*vs*. 20 patients [32.8%] and *vs*. 8 mm [6.5–9], p=0.15 and p=0.004, respectively).

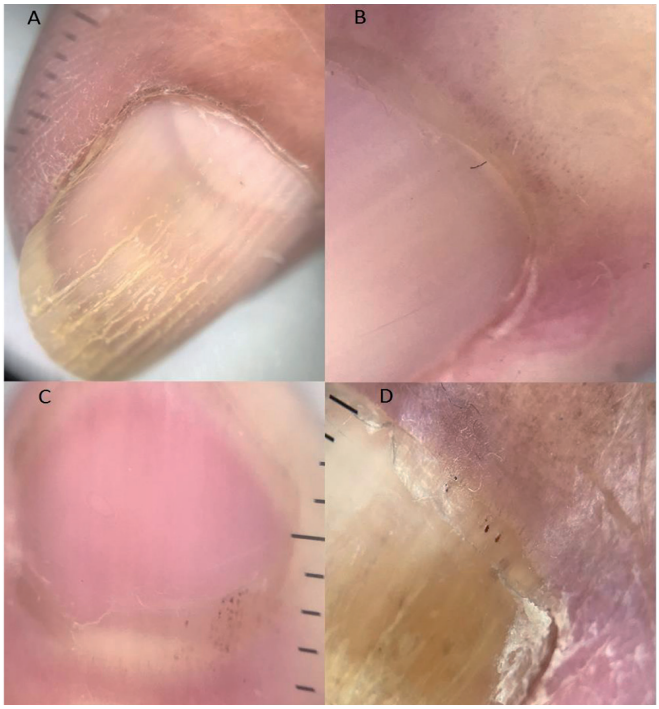

Fig. 1. Dermoscopic features of nail abnormalities.
A: Longitudinal striations.
B: Short linear vessels
C: Bywaters lesions in fingernails.
D: Bywaters lesions in toenails.

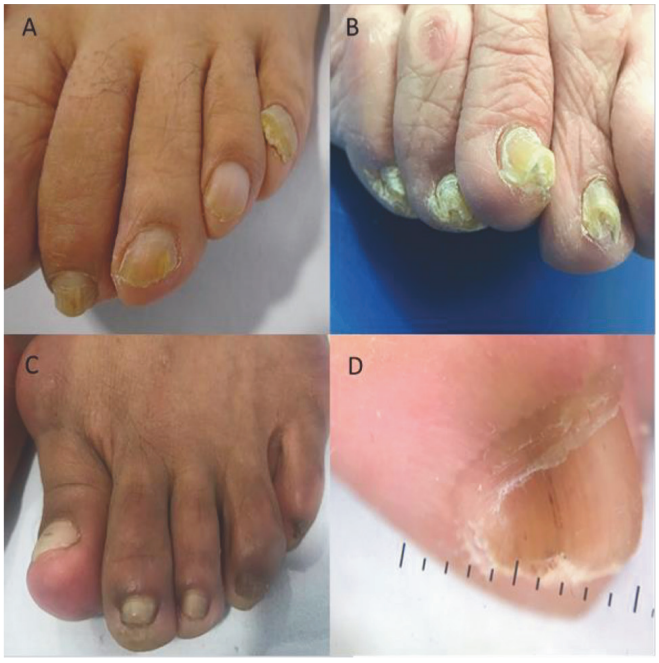

Fig. 2. Toenail abnormalities.
A: Xanthonychia in all toenails and pachyonychia in 5th toenail.
B: Severe foot deformation and nail abnormalities (xanthonychia, pachyonychia and onycogryphosis).
C: Traumatic melanonychia 4th and 5th toenail.
D: Dermoscopic features traumatic melanonychia and splinter haemorrhages.

Toenail abnormalities/diseases and disability

We first explored the association of nail findings/abnormalities with the HAQ score within/out of normal range. Most patients (n=99 [81%]) had a HAQ score within normal range which was defined as <0.25 (26). Table III summarises comparison of patients with HAQ score within normal range and their counterparts, and highlights that patients from the former group had lesser frequently incidental erosive disease and isolated hand erosions, had lower cumulative disease activity and lesser frequently toenails findings/abnormalities.

Multiple logistic regression analysis showed that in the different models tested, the presence of toenail abnormalities/diseases was consistently associated to HAQ score out of normal range (n=23 with HAQ≥0.25); in addition, incidental erosive disease was found to be associated to HAQ score

Table III. Comparison of demographic, disease characteristics and presence of nail abnormalities/findings in the subpopulations defined according to HAQ score within/out of normal range.

	Patients with HAQ score within normal range, n=99	Patients with HAQ score out of normal range, n=23	*p*
Characteristics			
Age, years	44 (35-56)	54 (38-63)	0.091
Females[1]	91 (91.9)	20 (87)	0.433
Formal education, years*	12 (9-15)	9 (6-12)	0.075
Disease duration, years	8 (5-12)	11 (6-14)	0.081
RF+[1]*	85 (85.9)	20 (87)	1
ACPA+[1]*	90 (90.9)	21 (91.3)	1
Hand and/or feet erosive disease[1]	41 (41.4)	16 (69.6)	0.2
Isolated hand erosions[1]	22 (22.2)	12 (52.2)	0.008
Isolated feet erosions[1]	37 (37.4)	11 (47.8)	0.478
Hand and feet erosions[1]	18 (18.2)	7 (30.4)	0.250
Incidental erosive disease[1],[2]	29 (29.3)	14 (60.9)	0.007
(Cumulative) DAS28 AUC	3.6 (2.8-4.4)	4.5 (3.5-5.1)	0.033
ESR, mm/H	3 (2-11)	7 (2-15)	0.525
CRP, mg/dL	0.35 (0.14-0.72)	0.53 (0.2-3.14)	0.103
Charlson score	1 (1-1)	1 (1-1)	0.387
Corticosteroids[1]	53 (53.5)	14 (60.9)	0.643
DMARDs[1]	90 (90.9)	22 (95.7)	0.686
N° of DMARDs/patient	1 (1-2)	1 (1-2)	0.830
Nail abnormalities/diseases[1]	34 (34.3)	7 (30.4)	0.810
Toenail abnormalities/diseases[1]	45 (45.5)	17 (73.9)	0.020
Fingernail abnormalities/diseases[1]	59 (59.6)	17 (73.9)	0.239

Data presented as median (IQR) unless otherwise indicated. [1]Number (%) of patients. *Data obtained at cohort entry. [2]Patients without erosions at cohort entry but who developed erosions at study entry. RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; DAS28: disease activity score on 28 joints; AUC: area under the curve; ESR: erythrocyte sedimentation rate; CRP: C reactive protein; HAQ: Health Assessment Questionnaire; DMARDs: disease-modifying anti-rheumatic drugs.

Table IV. (Stepwise) multiple logistic regression analysis to predict HAQ score out of normal range.

	Model 1 OR (95%CI)	Model 2 OR (95%CI)	Model 3 OR (95%CI)
Age			
Years of disease duration			
Incidental erosive disease		3.3 (1.25-8.56)[1]	
Hand and/or feet erosive disease			
Cumulative DAS28			
Toenail abnormalities/diseases	3.4 (1.24-9.35)[1]	2.9 (1.03-8.2)[2]	3.4 (1.24-9.34)[1]

OR: odds ratio; CI: confidence interval; DAS28: disease activity score on 28 joints. [1]$p \leq 0.018$; [2]$p \leq 0.044$. Model 1 also included hand and/or feet erosive disease, and cumulative DAS28; model 2 also included cumulative DAS28; model 3 also included age and years of disease duration.

out of normal range in model 2. In the different models tested which are summarised in Table IV, age, and disease duration were included as relevant confounding factors.

We then assessed through multiple linear regression analysis whether the number of toenails affected and of different toenail abnormalities/diseases per patient (from Table I) impacted the HAQ score; the model also included cumulative disease activity; the number of toenails affected per patient (B exponential: 0.39, 95%CI: 0.019–0.058, $p \leq 0.0001$) increased the HAQ score.

Discussion

Here, we assessed nail health in a large single-institution cohort of patients with RA, and observed that nail abnormalities were both, common and heterogeneous in presentation; in addition, the study showed an association between toenail abnormalities and disability. Nail health is an important indicator of personal health and nail examination is inexpensive and straightforward (8). Nail abnormalities are not only a sign of local disorders, but may also reflect the presence of systemic diseases (28). Our study highlights that in the clinical context of RA patients, (toe) nails abnormalities are associated to a more severe spectrum disease.

Physical function is a central aspect of life for patients with RA and, thus, its preservation remains a major goal in the treatment strategies. Disability has been associated with many adverse outcomes, such as loss of employment and decreases in income, and it also represents an important economic burden for health services (29). In clinical practice, physical function and disability are commonly evaluated with questionnaires, among which the HAQ-DI (Disability Index) is one of the most robust and widely used self-assessment instrument in patients with a variety of rheumatic diseases, including RA (30).

We found that toenail involvement was consistently associated with an abnormal HAQ score, and this association was independent of other factors that have been linked to functional disability, such as age and disease duration (26, 31). In one of the model tested, incidental erosive disease was additionally associated to a HAQ score out of normal range as previously published, particularly in patients with long-standing disease (32). In addition, a linear association was found between the number of toenails affected per patient and the HAQ score; such as, for every 6 toenails affected per patient, there was a 0.22 increase in the HAQ-DI, which is considered the minimal clinically important difference and translates into greater disability (33). To the best of our knowledge, this is the first study to link extensive toenail abnormalities with disability in RA patients.

The nail unit consists of different anatomical elements, all of which may be involved in nail diseases. In non RA-patients, nail disorders present a variety of symptoms that may be caused by different factors, such as chemicals (including medicinal drugs), infections, trauma and systemic and local diseases that can affect all, or some, of the components of the nail unit (34). Most of

these factors are frequently present in RA patients, in whom radiographic damage is more often identified in the feet joints (16). Moreover, even patients with early disease may present with clinically important changes in foot function (35). Ultimately, the interplay between disease activity and bone erosions determine specific biomechanical faults (36, 37), which are known to cause repetitive trauma and subsequent nail abnormalities (38, 39). Gait analysis has been incorporated to routine rheumatic assessments to gain a better understanding of the walking pattern of RA patients (35, 40), which we propose may contribute to toenail changes.

Our study revealed that nail abnormalities are highly prevalent in our RA population, being present in two thirds of evaluated patients. Calderón *et al*. (41) assessed frequency of nails alterations in 86 middle-aged Mexican females with cancer; previous chemotherapy, nails alterations were observed in 23% of the patients. Domínguez-Cherit *et al*. (42) observed that traumatic melanonychia was detected in 8.5% of 68 Mestizo Hispanic patients with melanonychia of any cause, meanwhile this type of melanonychia was observed in almost the totality of our patients. We additionally found that nail involvement was extensive when considering both, the number of nails affected per patient, and the wide spectrum of different nail findings in each individual patient. Factors associated with abnormal nail findings were age and erosive disease. Our results provide relevant information about different nail abnormalities in a specific RA population, consisting mostly of patients with adequately controlled disease. Since information reported in previous studies is quite scant (9-12, 21), we consider our results to be a valuable contribution that indicates a need for integral examination of RA patients, particularly of the skin and nails. Age has been consistently associated with nail alteration in the general population (36), as well as in RA patients (11), which is in line with our results. It needs to be emphasised that the age cut-off to predict nail findings in our study was 42.5 years, which is almost 10 years younger than the mean age described in a classical study that confirmed the association of nail disease in RA almost six decades ago (11). In older people (over 65–70 years old), one of the underlying mechanisms proposed to explain nail abnormalities has been dysfunctional circulation, which may happen earlier in RA patients, particularly in those with active disease (43). The literature also reports an association between disease activity and nail findings (44, 45). Although we did not find a direct association with disease activity, we observed an association with bone erosions. Erosions are indicative of damage, which could reflect persistent disease activity (46). However, there could be additional factors involved, such as the specific RA microenvironment, including the previously mentioned endothelial dysfunction, because other markers of activity, such as the cumulative DAS28, were not associated with nail abnormalities.

We observed onychomycosis in 13% of our sample; its presence was concomitant to additional abnormal nail findings. Interestingly, male sex was the only factor associated with the presence of both nail abnormalities and onychomycosis. Our results are similar to those described in the general population, where it has been demonstrated that men have a higher prevalence of toenail fungal infection than women. Vascular disease and sports have been found to be the most common predisposing factors (47). In our population, primarily integrated by middle-aged women, the inflammatory milieu characteristic of RA, which leads to endothelial dysfunction and subsequent vascular disease (43), could explain the relatively high prevalence of onychomycosis.

Finally, we also observed that patients with abnormal nail findings and nail disease were more frequently concerned about their nail health status and rated lower in their nail-related health VAS. These findings were also observed in patients with concomitant onychomycosis. Nail disorders may cause pain and affect patient functionality. They may also interfere with daily activities, such as walking and the picking up of fine objects, and interfere with tactile sensation and protective functions (48). The functional effects of nail disorders magnify in RA patients, in whom they appear to have an additive effect on the functional limitation that is already present due to erosive damage and additional comorbid conditions (30).

The present study has some limitations. First, the study was conducted in a single tertiary-care level center and the population consisted of Hispanic patients, who are known to have particular characteristics regarding the rheumatic diagnosis (16, 20), which limits the generalisation of the results. Second, it was performed within an observational cohort and therefore has the limitations of such cohorts, particularly follow-up losses, which may be due to a more aggressive disease. Therefore, the prevalence of nail findings may have been underestimated. Also, we did not use any scoring validated method to quantify structural damage. Finally, because of the cross-sectional nature of our study, although we found a significant association between HAQ and nail diseases, it is not possible to establish causality.

In conclusion, nail abnormalities are frequent findings in patients with RA. They are very diverse, are associated with age and radiographic damage and have a linear impact on disability. Greater knowledge of the causes of nail abnormalities and disease in RA patients will enable more effective preventive measures, as well as an adequate treatment, and may eventually help to reduce disability. Patients with RA may benefit from nail hygiene, proper nails cut, adequate (orthopaedic) shoes, orthopaedic devices and even a referral to podiatrist.

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