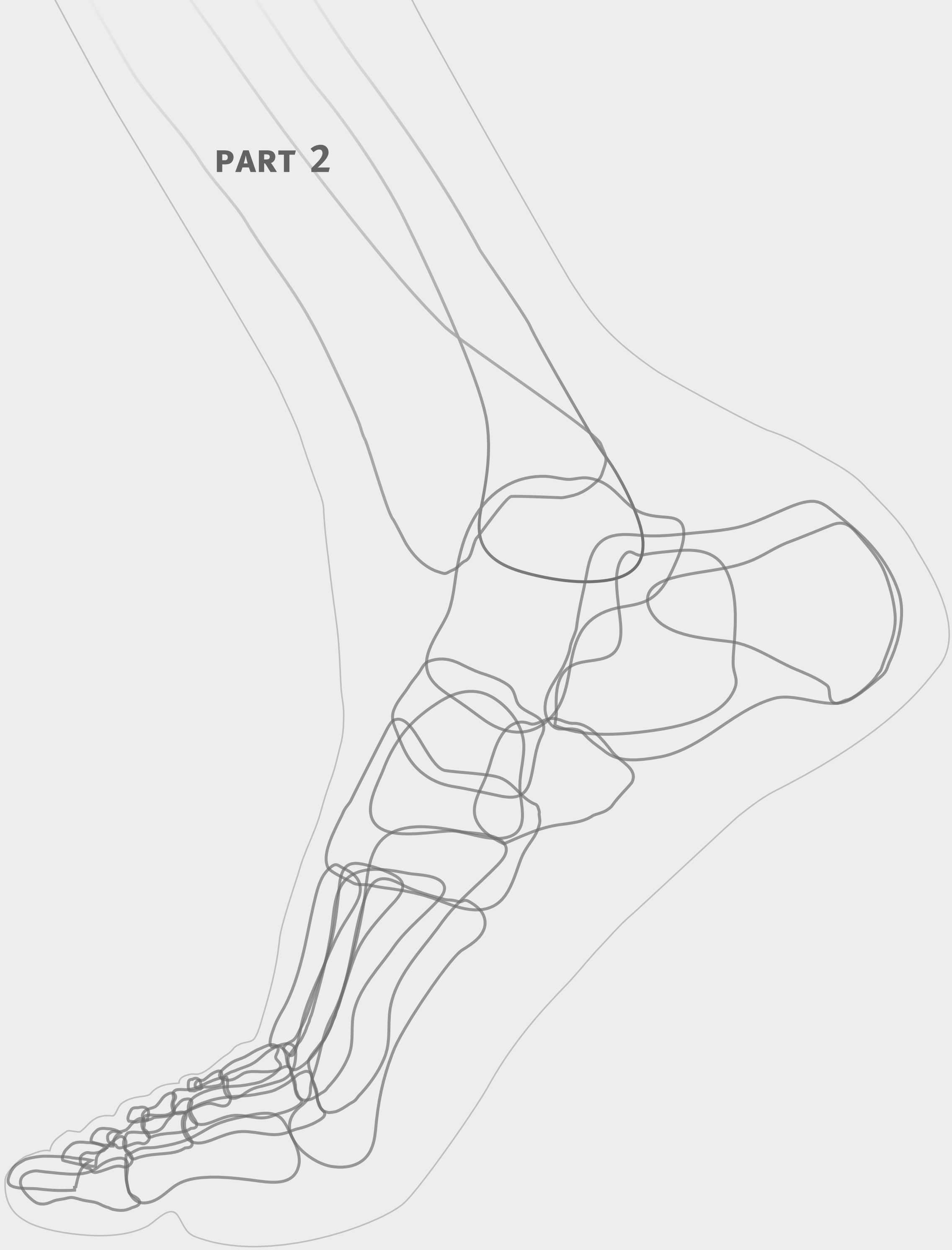
PART 2



CHAPTER 7

Forefoot pathology in relation to plantar pressure distribution in patients with rheumatoid arthritis: *A cross-sectional study in the Amsterdam Foot cohort*

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Gait & Posture. 2019;68:317-22

Abstract

Background

In patients with rheumatoid arthritis (RA), both high and low forefoot plantar pressures have been reported. Better understanding of pathology in the forefoot associated with altered pressure distribution in patients with RA could help to better formulate and specify goals for treatment with foot orthoses or therapeutic footwear.

Objectives

To investigate the association of plantar pressure with disease activity and deformity in the forefoot in patients with rheumatoid arthritis and forefoot symptoms.

Methods

A cross sectional study, using data of 172 patients with rheumatoid arthritis and forefoot symptoms, was conducted. Peak pressure (PP) and pressure time integral (PTI) in the forefoot were measured with a pressure platform. Forefoot deformity was assessed using the Platto score. Forefoot disease activity was defined as swelling and/or pain assessed by palpation of the metatarsophalangeal joints. The forefoot was divided in a medial, central and lateral region, in which the following conditions could be present: 1) no pathology, 2) disease activity, 3) deformity or 4) disease activity and deformity. A multilevel analysis was performed using condition per forefoot region as independent variable and PP or PTI in the corresponding region as dependent variable.

Results

Statistically significant higher plantar pressures were found in forefoot regions with deformities (RR 1.2, CI 1.1-1.3, $P<0.0001$), compared to forefoot regions without forefoot pathology. No significant differences in plantar pressures were found when solely forefoot disease activity was present in forefoot regions.

Significance

Forefoot deformities are related to higher plantar pressures measured in the corresponding forefoot regions. The absence of an association between local disease activity and plantar pressure might be explained by the low prevalence of metatarsophalangeal joint pain or swelling. Future research with sensitive imaging measures to detect disease activity is recommended to reveal the effect of forefoot disease activity on plantar pressure.

Introduction

Forefoot symptoms are common in patients with rheumatoid arthritis (RA). Of all patients with RA, 56-91% develop forefoot symptoms at any time during their disease [1-3]. These symptoms include pain, swelling and stiffness, which can be caused by inflammation in joints and surrounding tissue and/or forefoot joint damage [2, 4]. Also, forefoot deformities, such as subluxation of metatarsophalangeal (MTP) joints, hallux valgus and lesser toe deformities may develop [2, 4]. As a result, patients often experience limitations in daily functioning and a reduced health related quality of life [5].

Among other treatments, foot orthoses (whether or not in combination with therapeutic footwear) are used to relieve forefoot symptoms and thereby to improve daily functioning [6]. Reduction of plantar foot pressure in symptomatic areas is supposed to be one of the working mechanisms of foot orthoses [4, 7, 8]. Elevated plantar pressure might occur since the ability to adapt has decreased in deformed areas [9]. Several studies showed a significant correlation between forefoot deformities and high plantar pressure in patients with RA [7, 9-13]. However, the populations in these studies were relatively small, varying from 28 to 62 participants.

Beside elevated plantar pressure, also low plantar pressure in the forefoot has been observed in patients with RA [8]. Low forefoot pressure could be the result of a pain avoidance strategy [8, 14, 15]. To avoid regions with swelling and/or pain due to inflammation (i.e. high disease activity), offloading of these regions may occur [14]. However, the relationship between local disease activity and decreased plantar pressure is inconclusive. Only one study in RA studied this relation and showed that the presence of forefoot joint hypertrophy, measured with ultrasound, was associated with lower plantar peak pressure in the lateral forefoot region [2]. Assessment of disease activity with ultrasound is usually not used within standard care, in contrast to clinical assessment by palpation. Whether disease activity as assessed by palpation of forefoot joints is related to plantar pressure is unknown.

Better understanding of the association of pathology in the forefoot with either high or low plantar pressure in patients with RA could help to better formulate and specify goals for treatment with foot orthoses and therapeutic footwear. Previous studies investigating the relationship between forefoot pathology and plantar pressure were relatively small, mainly focused on the relation between deformities and plantar pressure, and calculated these relationships by correlational techniques. Only one study was able to provide an estimation of the effect of deformity on plantar pressure [16]. Moreover, the investigation of plantar pressure in relation to forefoot pathology by relatively easy to obtain clinical measures, of both forefoot deformities and forefoot disease activity, within one study has not been done before. This allows for comparison of plantar pressures between different forefoot conditions. The aim of the present study was to investigate and quantify the relationship of forefoot disease activity and forefoot deformity with plantar pressure in a relatively large cohort of patients with RA and forefoot symptoms.

Methods

Design & subjects

A cross-sectional study with data of the Amsterdam Foot (AMS-foot) cohort was conducted. The AMS-foot is a cohort of consecutive patients (≥18 years of age) who are referred to a rehabilitation physician or podiatrist of the multidisciplinary foot-care clinic of our outpatient rehabilitation center (Reade, Centre for Rehabilitation and Rheumatology, Amsterdam, The Netherlands). Patients who were not able to fill in questionnaires because of language difficulties were excluded from the cohort. Data were collected prior to the first visit to the rehabilitation physician or podiatrist by a trained research assistant at Reade.

For the present study patients from the AMS-foot cohort were selected who 1) were diagnosed with RA according to the revised criteria of the American Rheumatism Association [17], 2) had impairments in structure (e.g. deformities) and/or in function (e.g. pain or stiffness) of the forefoot, 3) had pressure measurement data available and 4) provided informed consent. Data collected between December 2011 and April 2017 were used. The study protocol was approved by the medical ethics committee of the Slotervaart Hospital/Reade in Amsterdam.

Measurements

Descriptive variables

The following variables were used descriptively: age, gender, body mass index (BMI), disease duration, disease activity score including a 44 joint count (DAS-44), Platto's structural index score, Foot Function Index (FFI) and Leeds Foot Impact Scale (LFIS). Length, measured with a tape measure attached to a wall, and weight, measured with a balance scale, were used to calculate BMI (in kg/m^2). Disease duration was based on the rheumatologists' reported year of diagnosis. DAS-44 and Platto score were assessed by a trained research assistant during clinical examination [18, 19]. The FFI and LFIS are self-reported questionnaires assessing the impact of foot related pain and disability on activities of daily living [20, 21].

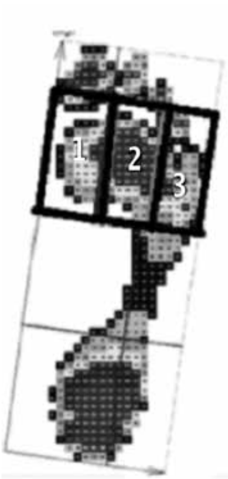

Figure 1. Division of the Emed pressure measurement into regions by a common division mask (Novel mask) (1 = medial, 2 = central, 3 = lateral, as used in the current study).

Dependent variables: forefoot peak pressure and pressure time integral

Plantar pressure in the forefoot was expressed as peak pressure (PP) and as pressure time integral (PTI). PP is defined as the highest pressure measured by a single sensor in a region [10] and is expressed as Newton per squared cm (N/cm^2). PTI is defined as the integral of pressure over time measured in the single sensor showing the PP within that region [10] and is expressed as Newton per squared cm multiplied by time in seconds ($(N/cm^2)*s$).

Plantar pressure measurements were obtained using an EMED-nt (Novel Electronics, Novel gmbh, Munich, Germany) system (4 sensors per cm^2, sample frequency of 50Hz), displaying plantar pressures of the foot when walking barefoot over a pressure measurement platform. The platform was mounted in the middle of a 3.6 meter walkway. A two-step protocol was used for pressure measurements since this was found to be the least time-consuming and least strenuous for the patient, but still a reproducible protocol [17]. In the two-step protocol the patient stands two steps away from the platform and makes contact with the platform on the second step. After familiarization with the protocol the measurement started. A measurement was considered correct when the whole foot was planted on the platform and it looked (researcher) and felt (patient) like a normal step. Incorrect measurements were immediately deleted. This protocol was repeated until both feet were correctly measured three times. The EMED software (Novel Ortho, Novel-Win) was used to analyze pressure data. See ***Figure 1*** for the division mask used. To process pressure measurement data, the mean of the three correct steps was calculated [17]. This mean was used in further analyses. Data from both feet for three forefoot regions (i.e. medial, central and lateral) were used in the analyses.

Independent variables: forefoot disease activity and forefoot deformity

Forefoot disease activity was defined as swelling and/or pain in the MTP joints, determined by palpation as part of the DAS-44 [18]. Forefoot disease activity was scored present or absent for every MTP joint.

Forefoot deformities were determined with Platto's structural index [19]. The presence of hammertoes, claw toes, subluxation of the MTP joints, hallux valgus and exostosis of MTP-5 were scored as absent or present for all digits and MTP joints.

The forefoot was divided in a medial, central and lateral region, in which the following conditions could be present: 1) no pathology, 2) disease activity, 3) deformity or 4) disease activity and deformity. See ***Table 1*** for the assignment of specific clinical findings (pain/swelling and/or forefoot deformities) to the medial, central and lateral forefoot region. The presence of one of the variables mentioned in a single cell of ***Table 1*** was considered presence of that condition in that specific region. For example, when subluxation of MTP-5 was present in the left foot, deformity in the lateral region of that foot was scored as present.

Statistical analysis

Descriptive variables were calculated and presented as mean (standard deviation [SD]) or median (interquartile range [IQR]). Percentages were calculated for stages of disease activity using cut of criteria as described by the European League Against Rheumatism (EULAR) [18].

Table 1. Division of disease activity and deformity measures into forefoot regions

Forefoot region	Disease activity	Deformity
Medial	Swelling MTP-1 and/or pain MTP-1	Hallux valgus and/or hammer- and/or claw digit 1 and/or subluxation MTP-1
Central	Swelling MTP-2 and/or 3, and/or pain MTP-2 and/or 3	Hammer- and/or claw digit 2 and/or 3 and/or subluxation MTP-2 and/or 3
Lateral	Swelling MTP-4 and/or 5, and/or pain MTP-4 and/or 5	Hammer- and/or claw digit 4 and/or 5 and/or subluxation MTP-4 and/or 5 and/or exostosis MTP-5

MTP = metatarsophalangeal

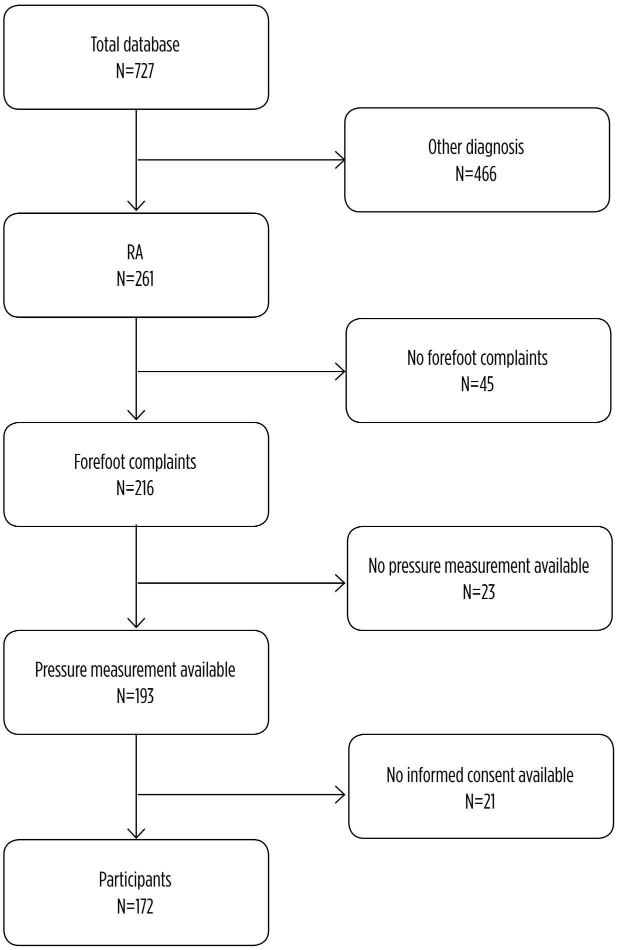

Figure 2. Flow of the patient selection

All variables were checked for normal distribution. The dependent variables PP and PTI were skewed to the right and therefore log transformed by use of a common logarithm (Log^{10}) before the analyses. All analyses were carried out on the transformed data. Regression coefficients and confidence intervals (CI) were retransformed, providing a ratio of the outcome variable between different conditions.

A multilevel analysis was performed using condition per forefoot region as the independent variable and PP or PTI in the corresponding region as the dependent variable. The independent variable was categorical, consisting of the following categories: 0) no pathology, 1) disease activity, 2) deformity, 3) disease activity and deformity. Multilevel analysis takes into account that information from multiple forefoot regions and both feet of a single participant is not independent. A three level structure was used, i.e. the three forefoot regions were clustered within the foot and the two feet were clustered within the patient. Analyses were done crude and adjusted for age, gender and BMI. Cases with missing values were excluded list wise. A significance level of $p<0.05$ was used in all analysis. PASW Statistics 18 software (v.18, SPSS Inc. Chicago, IL, USA) was used to perform the analyses.

Results

Descriptives

A total of 172 patients were included in the present study. ***Figure 2*** visualizes the patient flow. Patient characteristics are summarized in ***Table 2***. The mean age of the patients was 57.9 (± 12.9) years and most were female. A total of 97 patients were referred to podiatry (with foot orthoses as the main intervention) and 75 to the rehabilitation physician and shoe technician (with therapeutic shoes as the main intervention).

Table 3 summarizes the plantar pressure values per forefoot condition in the medial, central and lateral forefoot region. PP and PTI were highest in all regions when deformities, or a combination of deformities and disease activity, are present. Of the three forefoot regions, the lateral forefoot region showed the lowest PP and PTI in all conditions.

Association between forefoot condition and plantar pressure

Table 4 shows the results of the multilevel analyses comparing PP and PTI between the forefoot conditions. It was found that the presence of forefoot deformity in a forefoot region presented a 1.2 times higher PP and PTI ($p < 0.0001$) compared to the absence of forefoot pathology. Thus, PP and PTI were 20% higher when forefoot deformities were present, corresponding with a 15.5 N/cm^2 higher PP and a 5.2 (N/cm^2)*s higher PTI. The combination of forefoot disease activity and deformity also showed a 1.2 times higher PP and PTI ($p = 0.020$ and $p = 0.014$ respectively), corresponding to a 16.1 N/cm^2 higher PP and 8.3 (N/cm^2)*s higher PTI. Forefoot disease activity alone, i.e. the presence of pain and/or swelling of MTP joints in a forefoot region, was not significantly associated with PP and PTI. Similar results were found when local disease activity was defined as either MTP-joint pain or MTP-joint swelling.

Discussion

The results of this study showed that plantar pressure in the central, medial or lateral forefoot region was significantly higher in the presence of deformity in the corresponding forefoot region. No significant association between disease activity in a forefoot region and plantar pressure was found.

The observed association between the presence of forefoot deformities and higher plantar pressure is consistent with previous studies with smaller sample sizes [7, 9-13]. It suggests that persons with forefoot deformities are not able to avoid elevated pressure [9]. Plantar pressures were about 20% higher when deformities were present. Elevated pressure often results in hyperkeratosis and subsequent pain and discomfort in the forefoot [14, 22].

Our finding that there was no relation between the presence of disease activity in the MTP joints and plantar pressure is in contrast with the findings of Bowen et al. who found a statistically significant relationship between synovial hypertrophy in the MTP joints, as detected with ultrasound (US), and lower forefoot plantar pressure in a population of 114

Table 2. Patient characteristics (n = 172)

		% missing
Age (years) [b]	57.9 (12.9)	0%
Gender (male/female) [a]	29/143	0%
BMI (kg/m2) [b]	27.4 (5.1)	0%
Disease duration (years) [c]	7 (3;13)	0%
DAS-44 [c]	2.0 (1.3;2.7)	2.3%
- Remission (<1.6)	34.9%	
- Low disease activity (1.6 till 2.4)	27.3%	
- Moderate disease activity (2.4 till 3.7)	30.2%	
- High disease activity (≥ 3.7)	5.2%	
Platto score [c]		
- Total (range 0-38)	7.0 (4.0;12.0)	9.9%
- Forefoot (range 0-24)	5.0 (2.0;10.0)	6.4%
- Rear foot (range 0-14)	2.0 (1.0;3.0)	3.5%
FFI [c]		
- Total (range 0-100)	32.0 (16.6;49.6)	2.3%
- Pain (range 0-100)	35.7 (19.8;53.4)	7.0%
- Disability (range 0-100)	27.8 (13.9;47.2)	2.9%
LFIS [c]		
- Pain (range 0-14)	6.0 (4.0;8.6)	1.7%
- Disability (range 0-22)	7 .0 (3.0;11.0)	2.9%
PP in the forefoot (N/cm2) [c]	49.3(32.7;76.0)	0%
PTI in the forefoot ((N/cm2)*s) [c]	18.4(12.7;28.5)	0%
MTP count pain [c] (range 0-10)	3 (0;7)	5.2%
MTP count swelling [c] (range 0-10)	0 (0;2)	5.2%

Data are [a] numbers, b mean (SD) or c median (IQR). BMI = body mass index, DAS = Disease Activity Score, FFI = Foot Function Index, LFIS = Leeds Foot Impact Scale, PP = peak pressure, PTI = pressure time integral, MTP = metatarsophalangeal patients with RA (r = -0.412, p=0.046) [2]. Although the population of the present study was larger, the prevalence of disease activity in the forefoot was low in our sample. This may have led to low statistical power to detect associations. The low prevalence of forefoot disease activity could be typical for our study population since, overall, disease activity and functional limitations were low to moderate. It could also be explained by the way disease activity was assessed. In our study, palpation of MTP joints was used to detect pain and swelling. Using US to assess disease activity has been shown to be more sensitive than clinical examination and similar or even better than magnetic resonance imaging (MRI) [23, 24]. Therefore, the use of US to detect the presence of disease activity could have led to a higher percentage of regions with forefoot disease activity, possibly leading to different results. Further research using sensitive imaging measures to detect local disease activity should reveal whether or not a relation between disease activity and plantar pressure exists.

It is known that walking speed has an effect on plantar pressure and patients with greater disease activity or deformity are likely to walk slower [25]. Therefore, in addition to age, gender and BMI, walking speed was added as a covariate in a separate analysis. This did not result in

Table 3. Median (IQR) values for PP and PTI per forefoot condition

	No pathology		**Disease activity**		**Deformity**		**Disease activity and deformity**	
Region	PP *(N/cm²)*	PTI *((N/cm²)*s)*	PP *(N/cm²)*	PTI *((N/cm²)*s)*	PP *(N/cm2)*	PTI *((N/cm²)*s)*	PP *(N/cm²)*	PTI *((N/cm²)*s)*
Medial	54.8 *(38.2;72.1)*	18.5 *(14.5;26.4)*	41.3 *(27.5;54.1)*	13.1 *(11.5;19.0)*	60.8 *(41.3;90.7)*	22.9 *(16.4;35.6)*	65.8 *(60.5;75.2)*	28.3 *(21.9;31.2)*
Central	48.0 *(36.0;63.8)*	17.1 *(12.5;21.3)*	44.7 *(36.5;61.0)*	17.8 *(14.1;20.6)*	73.7 *(50.2;110.6)*	29.7 *(17.6;43.4)*	68.0 *(42.7;92.6)*	25.5 *(16.3;34.8)*
Lateral	27.5 *(21.4;36.0)*	11.2 *(9.1;14.0)*	32.9 *(28.8;39.7)*	13.9 *(11.2;21.3)*	41.5 *(27.0;72.3)*	15.7 *(11.1;26.2)*	31.0 *(25.0;50.0)*	12.7 *(10.6;21.9)*

PP = peak pressure, PTI = pressure time integral

Table 4. Results for multilevel analyses of forefoot condition with PP/PTI

	PP		**PTI**	
	Crude ratio	*Adjusted* ratio*	*Crude ratio*	*Adjusted* ratio*
No pathology	*Reference category*			
Disease activity	1.04 *CI* 0.86 – 1.25 *p* 0.714	1.03 *CI* 0.86 – 1.24 *p* 0.749	1.03 *CI* 0.85 – 1.25 *p* 0.744	1.02 *CI* 0.85 – 1.23 *p* 0.850
Deformities	1.21 *CI* 1.13 – 1.31 *p* <0.0001	1.19 *CI* 1.10 – 1.29 *p* <0.0001	1.24 *CI* 1.15 – 1.34 *p* <0.0001	1.20 *CI* 1.11 – 1.29 *p* <0.0001
Disease activity and deformities	1.25 *CI* 1.05 – 1.48 *p* 0.011	1.23 *CI* 1.03 – 1.45 *p* 0.020	1.27 *CI* 1.07 – 1.51 *p* 0.007	1.24 *CI* 1.04 – 1.46 *p* 0.014

*CI = 95% confidence interval, p = p-value, PP = peak pressure, PTI = pressure time integral. * = adjusted for age, gender and BMI* significant change of effect estimates (results not shown), indicating that walking speed did not have an impact on the associations found.

Foot pathology (here: deformities or inflammation) as well as the results of plantar pressure measurement should be considered when determining the most appropriate treatment strategy in case of forefoot symptoms. In patients with forefoot deformities and mechanical overloading, plantar pressure measurement can be used to identify the exact location of elevated pressure in order to target these areas (9, 26, 27). Using plantar pressure measurement gives a better indication of areas with elevated pressure than clinical examination (22). Treatment with custom-made foot orthoses or therapeutic footwear has been shown to decrease elevated plantar pressure and to reduce forefoot pain (26, 28). In patients with inflammatory driven forefoot symptoms, reduction of disease activity should have treatment priority. Systemic medication or local steroid injections are recommended treatment options (29). Additionally, foot orthoses could normalize forefoot loading in case of an offloading strategy, resulting in increased forefoot pressure after foot orthosis intervention (27). A multidisciplinary approach in the management of RA-related foot problems is required to align the different diagnostic and treatment options (30).

A strength of our study is the large sample size relative to other studies on the same topic. Another strength is the multilevel analysis, which enabled us to use different areas of both feet of the same participant, apart from dependency within a person. Therefore, more detailed data could be used. To our knowledge this has only been done in one other study related to the RA foot (16).

A possible limitation of the present study is the use of a common division mask (Novel mask) to divide the forefoot in three regions. It could be that the regions did not completely correlate with the anatomical location of the MTP joints. Furthermore, we only investigated the forefoot, as this is the most commonly affected area of the foot in RA. Pathology in relation to plantar pressure in other regions of the foot were beyond the scope of this study. Finally, we did not investigate a possible load shift between different foot regions. An in-depth investigation of load shifting between foot regions (both forefoot and other foot regions) in the presence of forefoot pathology could be a topic for future research.

Conclusions

The effect of forefoot disease activity and forefoot deformities on plantar pressure was investigated. Deformities in the medial, central and lateral forefoot regions are related to higher plantar pressures measured in these regions. The absence of an association between local disease activity and plantar pressure might be explained by the low prevalence of MTP pain or swelling as detected by palpation. Future research with medical imaging measures to detect disease activity is recommended to reveal the effect of forefoot disease activity on plantar pressure.

Acknowledgements

We would like to thank the research assistants of Reade for performing the measurements of this study.

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