CAN WE EXPLAIN GAIT CHANGES IN RHEUMATOID ARTHRITIS

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CAN WE EXPLAIN GAIT CHANGES IN RHEUMATOID ARTHRITIS

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Introduction

Rheumatoid Arthritis (RA) is an inflammatory joint disease and results frequently in substantial joint destruction and disability. Involvement of the lower limb either by inflammation or destruction can result in abnormal walking. This involvement is potentially irreversible and may lead to substantial disability. (1)
When measuring disease activity, structural joint damage, or function, the applied instruments like X-ray, MRI, laboratory tests and questionnaires are static. The obtained information is used for intervention management and outcome evaluation. By definition they fail to give information on dynamic function and do not always explain the variability in walking disability. With clinical gait analysis, a dynamic instrument is within reach. With the measurement of "gait" parameters, compilation into a database and the systematic interpretation of it, it is potentially possible to describe normal walking patterns and distinguish them from pathological patterns. Advancing computer technology and software facilitate the investigator in gathering, adapting and interpreting the gait data.
Up to present, gait analysis was mostly applied to children with cerebral palsy. In these cases, gait analysis is used for planning and evaluating therapies like surgery. Other areas of application are degenerative or inflammatory joint disease, neuromuscular disease and traumatic brain injury. (2) The evaluation of RA could also benefit from this instrument. Consequently, there is increasing attention for gait analysis as a tool for measuring joint function in RA.(1, 3) (4-12)
In this chapter, we will give a comprehensive introduction to human motion analysis and give an overview of the history and development of gait analysis.

Human motion analysis.
Human motion analysis or gait analysis is the science that describes, analyses and assesses human movement/gait. Humans have always been interested in their walking. Earliest literary evidence dates from Aristotle (384-322BC) in "De motu animalium" and addresses among other things the up and down movement of the head, when walking.(13)

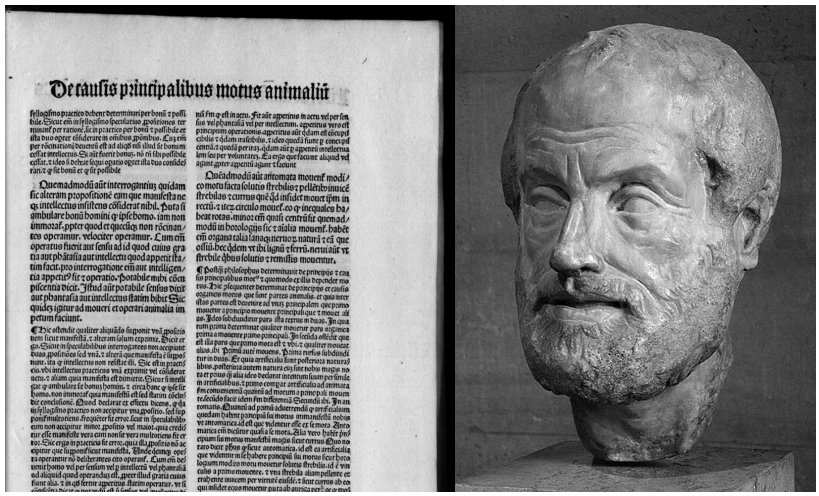

Figure 1. A part of Aristotle's De Motu Animalium in an edition from the Bayerische Staatsbibliothek 1498, Köln.

Motion can be described and analysed from the perspective of classical mechanics: position in three dimensions, direction of movement, forces and resistance. Variables used in the description of movement are: **kinematics, kinetics, muscle mechanics** and **Electromyography** (EMG).

Kinematic variables address motion, independent of the forces that cause the movement. Linear and angular displacements and velocities of the joint as well as of whole body mass are measured. The description of the movement includes the spatial reference system, which is either relative (related to an anatomical coordinate system that varies with each segment, for example joint angles) or absolute (related to an external spatial reference that is fixed). The latter is most frequently used in kinematic data. The development of several marker- and tracking systems, in combination with the appropriate software, facilitates the measuring and interpretation. The foot models applied in gait analysis of RA patients are usually based on the protocol of Carson or a variation. (14) Reflective markers are attached to the skin in a standardized manner (see fig 2) and patients are asked to walk several times a certain distance up and down at a self-selected speed.

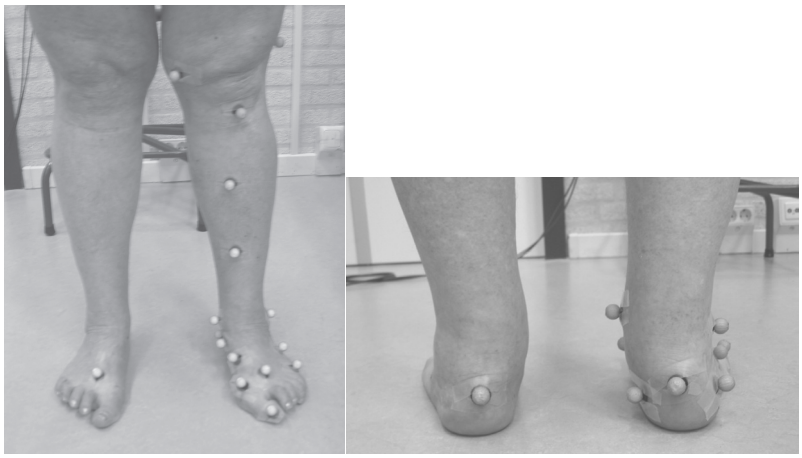

Figure 2. RA patient with reflective markers, gait protocol as described by Simon et al.

Several cameras record the course of the markers (raw data) and afterwards inter-segment and joint angles are calculated with the help of special software. Then post processing is performed for averaging, normalisation of the data to the gait cycle, graphical representation and temporospatial calculations.

Kinetics is the term that describes the forces that cause the movement. Force is what can cause an object with mass to change its velocity. Forces can be internal, from muscles or ligaments, or external: every force from outside like ground forces, the wind and so on. Other terms dealing with kinetics are: moments (the turning effect of a force about a point), power (the rate at which work is done) and energy (the amount of work that can be performed by a force). Kinetic variables are important in gait analysis, because they give information on what causes the movement of the joint or the limb, movement strategies and neural compensation. (15)

Muscle mechanics describes the variation in mechanical properties and characteristics of the muscles. How they vary in length and tension with every action, and how neural recruitment affects this. It also defines joint characteristics like centre of rotation.

EMG (electromyography) is the registration of the neural control of the muscle; it is the primary signal to describe the input to the muscular system. EMG shows a non-linear relationship with muscle tension. Sometimes there is significant neural activation, without a single muscle movement. Therefore, EMG covers more then the resulting movement of the muscle. This has especially been useful in the assessment and treatment of cerebral palsy and has lead to new operation techniques and better planning of surgical procedures. (16)

All the above-mentioned variables are part of the description of movement and their individual development contribute to the improvement of gait analysis. The past two decades have delivered faster (computerized) systems and consequently more and higher quality data. Measurement protocols have been refined, so that data collection is more reliable and practical. All these improvements influence the interpretation process positively and lead to better understanding of (pathological) gait.

History of gait analysis

Accurate measurement of motion is most important in scientific methods of gait analysis, and started already in the 17th century (although earliest mentioning of interest in gait comes from Aristotle as already mentioned). Notables such as Galvani, Newton, Descartes, Galileo and his student Borelli, and Duchenne founded a solid base for later understanding of human motion.
It is clear from history that most progression was made in the analysis of gait, when scientists from different sections met and worked together.
In the middle of the nineteenth century Marey, a French physiologist who has to be regarded as a pioneer, developed photography as a tool in studying human and animal motion. He worked together with Muybridge, a famous American photographer, and in fact the founder of the moving cine, competing with the brothers Lumière. The latter claimed to be the inventors of the cinema, and were regarded as such, but this was mainly due to the fact that Marey was not interested in 3D-registration of motion or cinema.

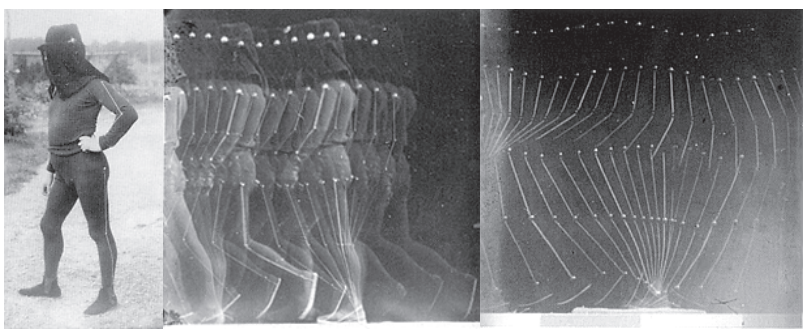

Figure 3. Marey: the black suit, outlined with white strips.

Marey and Muybridge were a source of inspiration for various artists, and some of the work (see fig 4 and 5) of Muybridge lead directly to paintings such as Nude Descending a Staircase (Marcel Duchamps, 1912, Philadelphia Museum of Art in Philadelphia), and Paralytic child (Francis Bacon, 1961, Gemeentemuseum, Den Haag). A selection of the first films of Marey and Muybridge can be watched on YouTube now (http://www.youtube.com/watch?v=b7MxdhI7FLY&feature=related) and recently there has been an interesting overview of Muybridge's work in the Tate gallery London.

Figure 4. Muybridge, Nude descending

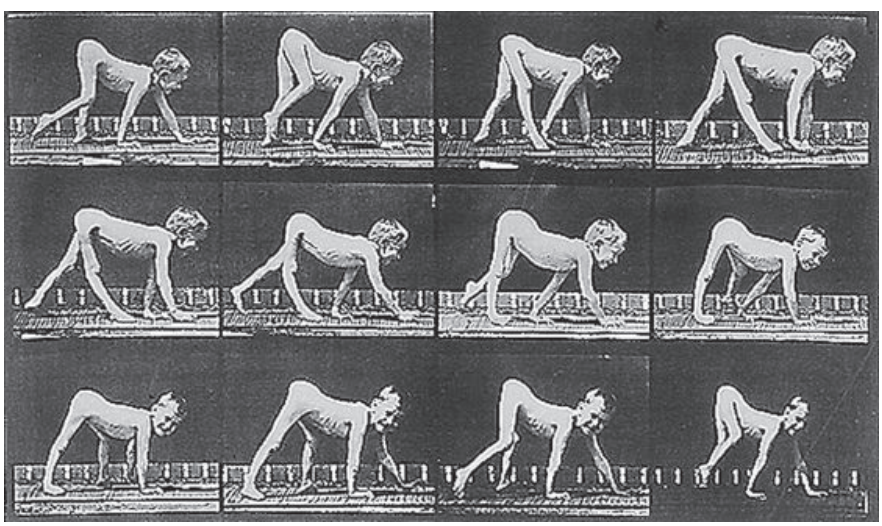

Figure 5. Muybridge, Paralytic child

Approximately at the same time in Germany, Braune and Fischer analysed measurement of joint angular rotations and whole body mass, now recognized to be essential. They used Geissler tubes, applied to the extremities and interrupted by tuning forks at regular intervals. These tubes, invented and created by the gas blower Geissler, are filled with gas, usually neon or argon. Under current, the gas reacts with other gasses and forms ions, which can be seen as colour, depending on the kind of gas. The subject to whom the tubes were attached, was asked to walk in darkness while photographs were taken from different angles at the same moment. Halfway through the twentieth century, Eberhardt (an engineer) and Inman (a surgeon) also used interrupted light. The main problem with these methods was the laboriousness, which made them suitable only for research reasons. Later, in Milwaukee, Wisconsin, Murray (a physical therapist) combined strobe light with reflective strips to measure motion. This proved to be unsatisfactory because of the roughness of the method. Another drawback was, that it did not provide joint rotations in the transversal plane.

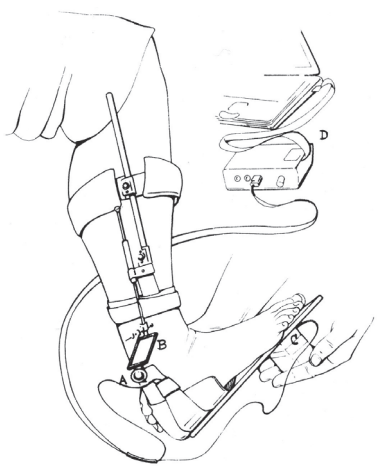

Figure 6. An electrogoniometer.

Afterwards the electrogoniometer has been developed, fig 6 .

A useful tool but not widely adopted because of some drawbacks: necessity for matching concerning the size of the goniometer and the size of the patient, the offset of the device to the side of the limbs segments and the inability to obtain simultaneous measurements.

Finally, video and movie, in combination with EMG-data, lead to the development of VICON (video converter) 3-D system. Sutherland a student of Inman was one of the pioneers, together with bio-engineers and industries. (17)

From the early forties, EMG was developed to gain more insight in the electric activity of the muscles and their individual contribution to normal and pathological gait. These first attempts were rather primitive: two needle electrodes were used, measuring only one muscle at a time. Walking with the electrodes was painful and thus not very suitable, esp. not for children. Besides, the results were loaded with noise and interference. As computers did not yet exist, the synchronizing of the EMG-signal with gait movie was difficult. However, with improving technique, computer-assisted interpretation of the raw data, surface electrodes (in stead of needle), EMG now is a very useful tool, particularly in combination with kinematic and kinetic data. Important attributors to the development of EMG were Perry and Sutherland. They both were students of Inman. Perry kept concentrating on EMG as well as on clinical observation of gait, Sutherland moved to the digitalisation of film data.

First scientific attempts to measure kinetic ground forces came from French investigators, again Marey and his pupils Carlet and Demeny. They developed systems to measure in-shoe-pressure. It was however Amar, who developed the precursor of a force plate including all three force components. This plate measures the ground reaction forces of human foot contact. Through the years, a further development lead in the end to a (commercial) ground force plate that is routinely used in a wide variety of gait labs. These plates offer the opportunity to utilize force vectors derived from the ground reaction forces, in order to study external factors and moments leading to joint movements. The difficulty, at least in the beginning was, that all moments calculations etc. had to be done by hand, and thus meant a lot of work. Davis and Winter are among the pioneers, who put a great effort in developing and stressing the importance of assessing kinetic data and the clinical application of these. These clinical applications are important as one may realise that a part of orthopaedic interventions is to lengthen or transfer muscles.

Others (Cavagna, Burdett, and Ralston) measured external mechanical work, oxygen consumption and oxygen cost. This has proven to be important in understanding and improving pathological gait with orthoses that require the lowest oxygen cost, for example in children with myelodysplasia and cerebral palsy. (18)

These above mentioned developments cover the different fields of gait analysis, and lead step by step to where we are today: a technology to analyse human motion, serving scientific purposes as well as daily clinical questions. A beautiful and comprehensive overview of the developments in the precomputer-era is given by Baker (19).

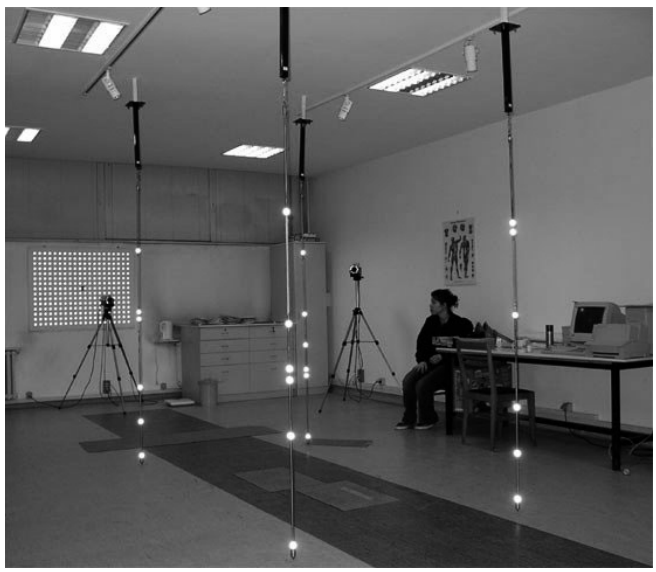

Figure 7. Example of a modern gait lab, with 3D vicon and a forceplate.

Gait analysis in patients with rheumatoid arthritis.

Data on gait analysis of the hip and knee in rheumatoid arthritis (RA) is scarce; most of the work has been done on the development of foot and ankle models. There is a fair amount of gait studies of the knee, but they are mainly limited to osteoarthritis (OA) of the knee. Although there is some similarity, we think OA is substantially different from arthritis in RA. Most patients with knee arthritis (RA) are not able to extend the knee and experience more limitation of flexion. The range of motion in knee RA is smaller and foot /ankle and/or hip affection may influence knee joint stance more in RA then in OA.
The earliest hip or knee gait studies in RA date from the seventies and discuss the impact of knee involvement in both inflammatory and degenerative joint disease (20-22). These studies are mainly limited to the measurement of kinetic data like floor reaction patterns and step, cadence and stride length. Protocols, target population, subjects and aim vary widely.

Afterwards, authors developed kinematic models, describing the motion of foot and/or ankle. They were firstly concerned with the way of collecting data, calibration, collection and interpretation. (7, 23-25)
Kadaba tried to set a standard for performing gait analysis of the lower extremity in studies as well as in daily clinical practice. He described a marker system for measuring the lower extremity, including a detailed description of the axes and planes about which the rotations take place, as well as a method to reconstruct these axes and planes. He strongly recommends the use of a uniform method for data acquisition, as this will contribute to the comparability of the different studies. (26)
Carson also tried to develop a standard multi-segment (3 segments) foot model. In their study, they performed a repeatability analysis (between-day and between-tester), analysing confidence intervals (CI) for the comparison of inter segment angles. He found that the shape of the curves did not vary, but that the absolute value of the inter-segment angles showed a remarkable shift, mainly due to marker placement variations, as was found, among others, by Leardini et al. (27, 28)
These attempts to develop a uniform system of gathering and interpreting gait data did however not result in general following. There is still a large heterogeneity in the choice of model, methodology, data processing and interpretation of the data.
The foot and ankle studies in RA show a development from kinetic towards kinematic data. With time, the models are getting more detailed as the description of even 9 or 10-segmented models demonstrates. Also the scientific questions become more refined. Rankine gives an enlightening review of the consecutive models, and where they differ with regard to description of the movement. (29)

Till present, gait analysis in RA patients is rarely used in clinical practice as a diagnostic tool, but merely in studies for measuring the mobility associated with disease activity and structural damage, and its relationship with other clinical or functional variables. Furthermore, it provides information to help describe treatment and better assess its outcome. (30, 31)
However, gait analysis is becoming a more common tool in evaluating joint function in RA. (4-12, 32-34) The timeline shows that the consecutive marker models in RA show a development into more segmented and refined models and provide us with more detailed information on function, impairment and disability.(8, 11, 34) (35, 36)

Yet, there remain some drawbacks. First (practical): gait analysis is expensive (due to personal costs) and it might therefore not be regarded as a routine instrument. Simon proposes that gait analysis should therefore be done by health technicians rather than by highly skilled professionals, in order to reduce the personal costs. (37)

Interpretation of the gait analysis data is sometimes difficult to understand for clinicians; the gait data supplied for interpretation can be counterintuitive and may be discarded as inaccurate, unless the team has sufficient confidence in the data collection and data reduction process. (2) The most important drawback in gait analysis research is however the variability: errors/variations/uncertainties occurring in the collection of the data due to marker placement artefacts and to the natural variability in gait parameters. Moreover variability due to the specific nature of RA, i.e. inhomogeneous patient cohorts, multiple joint involvement, and patients with multiple orthopaedic surgical procedures makes interpretation difficult. Furthermore, data reduction techniques and interpretation vary strongly among the several models and are not standardized. This compromises the repeatability and reliability of the models, and makes mutual comparison difficult. The variability problem is not solved easily, but there are a few publications, recommending certain measurements and steps in order to unify data collection, reduction and interpretation. (2, 17, 37-40)

To understand the gait of specific RA conditions, one should strive for homogenous patient populations in gait analysis studies. The description of movement of all joints should be standardized; global and relative orientation should be defined and maintained, in order to increase the accuracy of joint and moment calculations. Simon recommends among others, the use of neural networks or knowledge-based artificial intelligence systems, to improve interpretation of the data. He advocates that data and analytical methods should be shared among gait laboratories, enhancing knowledge. When these recommendations are followed, the comparability of the different studies will certainly improve, which may lead to more refined and coordinated investigations, that will benefit the RA patient with gait abnormalities due to destruction or inflammation of the lower limb joints.

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2

Gait analysis of the lower limb in patients with Rheumatoid Arthritis, a systematic review

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Abstract

Introduction: In rheumatoid arthritis (RA), signs and symptoms of feet and ankle are common. In order to evaluate the dynamic function of feet and ankles, namely walking, a variety of gait studies have been published. In this systematic review, we provide a systematic overview of the available gait studies in RA, give a clinimetrical assignment and review the general conclusions regarding gait in RA.

Methods: A systematic literature search within the databases Pubmed, CINAHL, sportdiscus, Embase and Scopus was described and performed, and delivered 78 original gait studies that were included for further data extraction.

Results: The clinimetrical quality of the 78 included RA gait studies measured according a tailored QUADAS item list and proposed clinimetrical criteria by Terwee et al. is moderate. General conclusions regarding the walking abnormalities of RA patients point to: a slower walk, longer double support time and avoidance of extreme positions. Frequently found static features in RA are: hallux valgus, pes planovalgus and hind foot abnormalities.

Conclusions: Gait studies in RA patients show moderate clinimetrical properties, but are a challenging way of expressing walking disability. Future gait research should focus on more uniformity in methodology. When this need is satisfied, more clinical applicable conclusions can be drawn.

Introduction

In rheumatic conditions, especially rheumatoid arthritis (RA), signs and symptoms of the feet are prevalent. The majority of the RA patients present with arthritis of the feet and 20% of them have radiographic damage at the time of diagnosis. (1) Prevalence of radiographic damage of the feet increases over time up to 80% at a disease duration of 5 years. (2) Obviously, other involvement of the lower limb such as involvement of the ankle can additionally result in substantial disability(3).

When measuring disease activity, damage or function of the foot, the applied instruments like X-ray, MRI, laboratory tests and questionnaires are static. The obtained information is used for decisions on intervention, follow-up and outcome evaluation. These methods fail however by definition to give information on dynamic function. With the development of clinical gait analysis (esp. 3D kinetics and kinematics), a dynamic instrument is within reach, and it is possible to describe normal walking patterns and distinguish them from pathological patterns. Advancing computer technology and software facilitate the investigator in gathering, adapting and interpreting the gait data, and have since lead to an increasing interest for gait analysis as a tool for measuring joint function in RA, in particular of the foot and ankle.(4, 5) (6-14)

A variety of gait studies have been published since. These studies are heterogeneous. The lack of uniformity in methodology and gait models often prevents comparison. A systematic review on foot and ankle instruments has been published earlier (15), but this review included other functional outcome measures then gait alone, like self reported questionnaires and a variety of pain and function related scoring systems. Moreover, it was mainly focused on the clinimetrical properties of the studies, and did not include the knee and hip. Another review by Rankine et al describes multisegmental foot models, but this was not a systematic review, and focuses solely on kinematic foot models.(16)

In the present study, we systematically reviewed all gait studies involving adult RA patients. All studies reporting kinetic, kinematic, plantar pressure data, muscle mechanics and electromyographic data were investigated.

Kinematic variables address motion, independent of the forces that cause the movement. Linear and angular displacements and velocities of the joint as well as of whole body mass are measured. For example, the foot models used in gait analysis

of RA patients are based on the protocol of Carson or a variation, like the protocol developed by the Heidelberg group. [17, 18] Reflective markers are attached to the skin in a standardized manner and patients are asked to walk several times a certain distance up and down at a self-selected speed. Several cameras record the course of the markers (raw data) and afterwards inter-segment and joint angles are calculated using special software. Then post processing is performed for averaging, normalisation of the data to the gait cycle, graphical representation and temporospatial calculations.

Kinetics is the term that describes the forces that cause the movement. Force is that which can cause an object with **mass** to change its acceleration and consequently its position. Forces can be internal (from muscles, ligaments) or external (gravity). Kinetic variables are important in gait analysis, because they give information on what causes the movement of the joint or the limb, movement strategies and neural compensation.

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In the present study, we aim to give a systematic overview of gait analysis in rheumatoid arthritis. The first goal of this study is to provide a complete overview of gait studies in rheumatoid arthritis patients and to review the clinimetrical properties of them. The second goal is to outline the main results and conclusions regarding the aberrant walking pattern of RA patients.

Methods

All studies included in this systematic review were original articles addressing gait in rheumatoid arthritis patients. The selected studies used kinematic, kinetic, muscle mechanics and EMG data as outcome measure. We searched the electronic databases PubMed, CINAHL, Embase, Scopus and Sportdiscus. Pertinent narrative review articles and reference lists of key articles were searched for further relevant publications. Two authors (HB and RD) independently screened articles for inclusion in the full text review by an initial screen of all titles and abstracts retrieved from the search strategy. Articles were included if they reported data from an original study in which RA patients or at least a subcohort, were subjected to gait analysis. Any articles identified from the first screen by either reviewer as possibly relevant to the study question were brought forward to the full text review. Full text review was undertaken as the next step. Articles were included in the systematic review if they reported original data on 1) RA patients > 17 years 2) the language was English, Dutch or German. 3) foot/ankle, knee or hip gait analysis. Moreover, abstracts, books, theses, and conference proceedings were not included. Finally, all articles references were searched manually for additional eligible studies. A description of the aim and methodology was extracted from the selected articles, including used measures, study population, aim and, when applicable, intervention.
For the purpose of clinimetrical assignment, we used a tailored QUADAS item list, as proposed by the QUADAS study group. The following QUADAS items were used as criteria and each QUADAS item was scored yes, no or unclear.

QUADAS 1 item: Was the spectrum of patients representative of the patients who will receive the test in practice? Addresses the generalizability.
QUADAS 2 item: Were selection criteria clearly described? Concerns all relevant information regarding how participants were selected for inclusion in the study.
QUADAS 8 item: Was the execution of the index test described in sufficient detail to permit replication of the test? Addresses whether a study reports a sufficient detailed description of the execution of test method to permit replication of the test.
QUADAS 10 item: Were the index test results interpreted without knowledge of the results of the reference standard? Checks if the study clearly states that the test results were interpreted blind to the results of the other tests.
QUADAS 12 item: Were the same clinical data available when test results were interpreted as would be available when the test is used in practice? Addresses the availability of clinical data during interpretation of test results that may affect estimates of test performance.

QUADAS 13 item: Were uninterpretable/ intermediate test results reported? A diagnostic test can produce an uninterpretable/indeterminate/intermediate result with varying frequency depending on the test. These problems are often not reported in diagnostic accuracy studies with the uninterpretable results simply removed from the analysis. This may lead to the biased assessment of the test.
QUADAS 14: Were withdrawals from the study explained? If patients lost to follow-up differ systematically from those who remain, for whatever reason, then estimates of test performance may be biased.

Moreover, according to the proposed quality criteria on clinimetric properties by Terwee (17) the following items were assessed: internal consistency, agreement, reliability, construct validity, responsiveness, interpretability.

Internal consistency: The extent to which items in a (sub)scale are intercorrelated, thus measuring the same construct. Scoring:

+ factor analyses performed on adequate sample size (7 x no of items) AND Cronbach's alpha(s) calculated per dimension in a sample size of at least 50 patients AND Cronbach's alpha(s) > 0.70.
? no factor analysis OR doubtful design or method OR sample size too small.
- Cronbach's alpha(s) <0.70, despite adequate design and method.
0 no information found on internal consistency.

Agreement: The extent to which the scores on repeated measures are close to each other (absolute measurement error). Scoring:

+ (minimal important change(MIC) OR 0.5 x standard deviation(SD)) >smallest detectable change (SDC) OR (MIC OR 0.5 SD) outside the limits of agreement(LOA) AND SDC and MIC both determined in a sample size of at least 50 patients.
? doubtful design or method or sample size <50.
- (MIC OR 0.5 x SD) < SDC OR (MIC OR 0.5 SD) inside LOA, despite adequate design.
0 no information found on agreement.

Reliability: The extent to which patients can be distinguished from each other, despite measurement errors. Scoring:

+ intraclass correlation coefficient (ICC) or kappa >0.70 with the lower limit of the confidence interval >0.60 or a sample size of at least 50 patients.
? doubtful design or method (e.g. time interval not mentioned, Pearson correlation) OR ICC or kappa >0.70 with the lower limit of the confidence interval 0.60 or sample size <50.
- ICC or kappa <0.70, despite adequate design and method.
0 No information found on reliability.

Construct validity: The extent to which scores on a particular instrument relate to other measures in a manner that is consistent with theoretically derived hypotheses concerning the concepts that are being measured. Scoring:

+ specific hypotheses were formulated AND at least 75% of the results are in accordance with these hypotheses in a sample of at least 50 patients.
? doubtful design or method OR sample size <50.
- less than 75% of the hypotheses were confirmed despite adequate design and methods.
0 no information found on construct validity.

Responsiveness: The instruments ability to detect important change over time in the concept being measured. Scoring:

+ specific hypotheses were formulated AND at least 75% of the results are in accordance with these hypotheses in a sample of at least 50 patients.
? doubtful design or method OR sample size <50.
- less than 75% of the hypotheses were confirmed despite adequate design and methods.
0 no information found on responsiveness.

Interpretability: The degree to which one can assign qualitative meaning to quantitative scores. Scoring:

+ mean and SD scores presented of at least 2 relevant subgroups of patients in a sample size of at least 50 patients.
? doubtful design or method OR less than 2 subgroups OR sample size < 50.
0 no information found on interpretation.

Results

On Nov the 17th 2010, we conducted the search of PubMed, EMBASE. CINAHL and Scopus according to the methodology described. We searched for publications in English, German or Dutch language on the following search terms: rheumatoid arthritis AND foot OR ankle OR rear foot OR hind foot OR hip OR knee AND gait OR kinematics OR kinetics OR plantar pressure. For the complete search strategy we refer to the appendix. We obtained the following number of abstracts from the searches: 565 in Pubmed, 117 in Embase, 172 in CINAHL, and 473 in Scopus. After screening abstracts, 249 studies seemed eligible for full text review. Completing full text reading, 73 studies remained eligible for review and data extraction. After checking the references of the included studies, another 5 articles were added, resulting in 78 full text articles.

The included studies all fulfilled the listed criteria and reported original gait data on RA patients, the language was English, Dutch or German, and foot/ankle, knee or hip gait analysis studies were included.

The selected studies were classified according to their measurement concept and method to the following categories:

- plantar pressure measurement with the EMED system
- plantar pressure measurement using F-scan
- other or not specified plantar pressure measurement methods
- studies reporting temporospatial data
- 3-D gait studies
- EMG-studies
- a mixed group with: studies of range of motion (ROM), kinetic data, nerve conduction and röntgen stereogammetry.

Forty-seven of the 78 publications reported on plantar pressure measurement data; 18 used EMED, 6 F-scan and there was a miscellaneous group. Thirty-five of the 78 studies reported data regarding temporospatial variables. Only 16 studies reported on three-dimensional variables, 2 used EMG, 1 Rontgen stereophotogammetry, 6 range of motion (ROM), 3 reported on kinetic data, and finally 1 article, in which nerve conduction was studied.

For the results of the description of the studies concerning the methodology, measurement concept, study population, aim and intervention, we refer to table 1, see addendum, page 119 in which a complete overview is given.

In table 2, page 139, we present the results of the scoring of the tailored QUADAS list. The first QUADAS item (Was the spectrum of patients representative of the patients who will receive the test in practice?) was nearly always scored as yes. In three studies, the studied population was not described adequately. The second QUADAS item (Were selection criteria described?) was present in 59 of the 78 studies. QUADAS item 8 (Was sufficient description of the index test reported) was met in 68 of the 78 studies. QUADAS item 10 (Were the test results interpreted without knowledge of the results of the reference standard?), was positive in 24 of the studies, most of them scored NA. QUADAS Item 12 (Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?) was scored as a yes in 74 of the studies. QUADAS item 13 (Were uninterpretable/ intermediate test results reported) was scored in 47 studies, and QUADAS item 14 (Were withdrawals from the study explained?) was only mentioned in 14 of the 78 studies.

The clinimetric properties are shown in table 3, page 148. None of the studies reported on all items. Only 18 of the 78 (23%) studies fulfilled (positive or indeterminate) more then one of the criteria. The studies that scored positive (+) or indeterminate (?) on one or more items are summarised in table 2. The item internal consistency was in only 2 studies given an indeterminate score. The item agreement was given 13 times indeterminate and once a positive score. Reliability was 21 times scored as indeterminate and 4 times as positive. Construct validity was 35 times scored as indeterminate and 3 times given positive score. Responsiveness was 15 times indeterminate and 2 times positive. Interpretability was the most frequently met criterion; 52 times it was assessed as indeterminate and 15 times as positive.

The second goal of our review was, to summarise the results and the findings of the studies, regarding the gait of RA patients. That what is traditionally known as the "rheumatoid shuffle", can be more meticulously defined. Some plantar measurement studies revealed that plantar pressures in RA patients are higher, esp. the static plantar pressure.(19, 20) This may not be true for early RA patients. (21) Some investigators found higher pressures under the first and second ray of the metatarsals (22, 23), others report that especially on the outer metatarsals, the pressure was higher (24). There are however studies that could not confirm a higher plantar pressure in RA patients. (25, 26) When higher plantar pressure was found in

RA patients, it was in most studies, but not in all, associated with clinical variables like pain and erosions. Exact reasons for high pressures in RA are not given, but it has been suggested that antalgic walking patterns, in order to avoid pain under the forefoot while walking, may lead to higher pressures elsewhere. Hallux valgus, lesser toe deformities and severe hindfoot disease also cause higher forefoot pressures. (27) When corrective measures were applied (i.e. orthoses or corrective surgery), both plantar pressure distribution and clinical signs and symptoms can improve, but are not necessarily correlated. (28-31)

With respect to temporospatial parameters, RA patients tend to walk slower, with a longer gait cycle, a shorter step length, a longer double support time and a lower cadence (when compared with similar walking speed in healthy subjects). (32-35) Definite conclusions have to be drawn with care, because speed-dependent gait variables are affected when controlling for the effect of speed in subjects with RA. (36)The reduction in walking speed can be related to an increase in MTP 1 stiffness(37). Furthermore it was suggested that reduced speed may be caused by antalgic walking patterns, the need for "pain control", and muscle weakness.(38)

Regarding kinematic features, smaller ranges of motion combined with reduced joint moments and power of the hip flexion/extension, the hip abduction/adduction, the knee flexion/extension and the ankle plantar flexion occur in RA, and influence the HAQ (Health Assessment Questionnaire) as a measure of functional disability (39) There is an increased internal rotation of the tibia, a delayed heel rise, a decreased plantar flexion at toe-off and an abnormal eversion of the rear foot. Often a reduction of MTP-1 dorsiflexion is observed and an increased abduction of the forefoot. Aforementioned features can cause a considerable loss of normal rocker function. (38, 40-44).

Static features are hallux valgus, an exaggerated valgus heel posture and collapse of the medial longitudinal arch with decreased navicular height. Abnormalities of the hind foot more then of the forefoot, seem to affect gait in RA. Greater levels of foot-related disability and a greater number of abnormal kinematic features were found in patients if the hindfoot was severely deformed, compared to those with severe forefoot deformity. (27) Whether static hindfoot deviations were caused by insufficiency of the tibialis posterior is still the subject of debate. Another association with stance abnormalities of the hind foot is increased muscle activity of the gastrocnemius and the soleus (45), to compensate for increasing valgus.

For the full tables, see addendum thesis, page 119.

Discussion

Combining the 78 gait studies in rheumatoid arthritis patients our data show that measurement and clinimetrical properties can be improved. However, consistently the studies reveal a slower walk, longer double support time and avoidance of extreme positions during walking of RA patients.

None of the 78 included studies has been tested for all measurement properties. Part of the moderate results regarding the measurement properties of the selected studies, can be explained by the fact that we did not select on clinimetrical properties, to avoid selection bias. The limitation of using the QUADAS criteria lies in the fact that the QUADAS is a list that is meant for assessing the quality of diagnostic tests. Most of the used methods or measurement concepts in our selected studies were not compared with a golden standard or a more validated test, simply because there is none. The criteria list proposed by Terwee et al that we used for measurement properties performed equally moderate. The majority of the items could not be scored positive, but only indeterminate, because of the small sample size or non-optimal methodology and analysis. We do acknowledge that this is a very strict set of criteria, but this was predominantly done so, to avoid drawing conclusions from underpowered studies. There is however no standard set of criteria applicable to the elaboration and the rating of gait analysis. It would be very helpful if the professional association or the experts came up with one. Agreement and reliability can improve by standardly reporting results of between-day, between-trial, between-subject and between-clinician repeatability. Construct validity and interpretability may improve, when gait parameters are compared with clinically meaningful outcome measures (i.e. of function or damage). More practical conclusions and recommendations can make a translation to daily practice easier and might benefit the patient directly. To facilitate the comparability between studies and centers, it would help if there were a larger uniformity in methodology. Within the group of the 3D studies, 4 up to 11-segmented models are used, based on functional or either anatomical segments. The labour intensive methods of gathering and processing the data vary widely, which makes a proper comparison difficult. Also the lack of normative data for normal as well as pathological subjects is counteracting in the interpretation of the findings. Furthermore, especially in RA, it would be helpful to have more longitudinal data to investigate the natural course of rheumatoid arthritis or to measure the effect of targeted interventions. Future research should focus on more uniformity of measurement methodology and terminology, for a proper validation of the motion analysis system, and strive for a

more thorough clinical translation and interpretation, leading eventually to better understanding and treatment of gait problems in RA. Despite varying methods of research, there is a deal of consensus on the interpretation of gait abnormalities in RA in these 78 studies. Static features frequently encountered are hallux valgus or lesser toe deformities, more often a pes planovalgus, sometimes associated with severe stance abnormalities of the hind foot. This results among others in the following kinematic features: the RA patient walks slower, with a longer double support time. There is a tendency to avoid extreme positions of the joints. These gait abnormalities are caused by structural damage like erosions or stance deviations, or by active inflammation of the joints as the hallmark of rheumatoid disease. For another part, gait in the RA patient is determined by avoiding pain. The RA patient tends therefore to walk slower in order to control the speed of heel strike and toe-off.

In conclusion, gait studies in RA patients show moderate clinimetrical properties, but are a challenging way of expressing walking disability. Future gait research should focus on more uniformity in methodology. When this need is satisfied, more clinical applicable conclusions can be drawn, which eventually benefits the treatment of walking problems in RA patients.

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Appendix

Search terms

("arthritis, rheumatoid"[MeSH Terms] OR ("arthritis"[All Fields] AND "rheumatoid"[All Fields]) OR "rheumatoid arthritis"[All Fields] OR ("rheumatoid"[All Fields] AND "arthritis"[All Fields])) AND (("biomechanics"[MeSH Terms] OR "biomechanics"[All Fields]) OR ("gait"[MeSH Terms] OR "gait"[All Fields]) OR (pedobarogr*) OR mechanical[All Fields] OR ("biomechanics"[MeSH Terms] OR "biomechanics"[All Fields] OR "kinematics"[All Fields]) OR "kinetics"[MeSH Terms]) OR (plantar[All Fields] AND ("pressure"[MeSH Terms] OR "pressure"[All Fields]))) AND (("foot"[MeSH Terms] OR "foot"[All Fields]) OR ("ankle"[MeSH Terms] OR "ankle"[All Fields] OR "ankle joint"[MeSH Terms] OR ("ankle"[All Fields] AND "joint"[All Fields]) OR "ankle joint"[All Fields]) OR (hind[All Fields] AND ("foot"[MeSH Terms] OR "foot"[All Fields])) OR (rear[All Fields] AND ("foot"[MeSH Terms] OR "foot"[All Fields])) OR ("knee"[MeSH Terms] OR "knee"[All Fields] OR "knee joint"[MeSH Terms] OR ("knee"[All Fields] AND "joint"[All Fields]) OR "knee joint"[All Fields]) OR ("hip"[MeSH Terms] OR "hip"[All Fields]) OR ("lower extremity"[MeSH Terms] OR ("lower"[All Fields] AND "extremity"[All Fields]) OR "lower extremity"[All Fields] OR ("lower"[All Fields] AND "limb"[All Fields]) OR "lower limb"[All Fields]) OR ("lower extremity"[MeSH Terms] OR ("lower"[All Fields] AND "extremity"[All Fields]) OR "lower extremity"[All Fields])) AND (English[la] OR German[la] OR Dutch[la] OR French[la]) NOT ("animals"[MeSH Terms:noexp] OR animals[All Fields])

3

Flexor Hallucis Longus tendon rupture in RA-patients is associated with MTP 1 damage and pes planus

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Abstract

Background: To assess the prevalence of and relation between rupture or tenosynovitis of the Flexor Hallucis Longus (FHL) tendon and range of motion, deformities and joint damage of the forefoot in RA patients with foot complaints.

Methods: Thirty RA patients with painful feet were analysed, their feet were examined clinically for the presence of pes planus and range of motion (ROM), radiographs were scored looking for the presence of forefoot damage, and ultrasound examination was performed, examining the presence of tenosynovitis or rupture of the FHL at the level of the medial malleolus. The correlation between the presence or absence of the FHL and ROM, forefoot damage and pes planus was calculated.

Results: In 11/60(18%) of the feet, a rupture of the FHL was found. This was associated with a limited motion of the MTP1-joint, measured on the JAM ($\chi 2$ = 10.4, p = 0.034), a higher prevalence of pes planus ($\chi 2$ = 5.77, p = 0.016) and a higher prevalence of erosions proximal at the MTP-1 joint ($\chi 2$ = 12.3, p = 0.016), and joint space narrowing of the MTP1 joint ($\chi 2$ = 12.7, p = 0.013).

Conclusion: Rupture of the flexor hallucis longus tendon in RA-patients is associated with limited range of hallux motion, more erosions and joint space narrowing of the MTP-1-joint, as well as with pes planus.

Background

In rheumatoid arthritis (RA), synovial inflammation affects the joints as well as periarticular structures such as tendons. It is well recognized that the inflammatory tissue in rheumatoid arthritis has a local destructive potency. Inflammation and the resulting damage both cause functional limitations [1]. Tenosynovitis or rupture of the tendon of the tibialis posterior is considered prevalent and important in the development of foot deformities in the feet of RA patients [2,3]. Rupture or tenosynovitis of the flexor hallucis longus (FHL) is rarely recognized by clinical examination in RA. This may be due to underestimation, since in clinical assessment of the painful hind foot, swelling is often interpreted as synovitis of the ankle [4].
Imaging has shown to be more sensitive in detecting tenosynovitis than physical examination [2,4,5]. MRI-studies in RA-patients with hind foot pain showed a FHL-teno- synovitis prevalence of approximately 20% [2,4]. Ultra- sound studies (US) in RA patients showed a higher prevalence of FHL tenosynovitis then anticipated clinically [5,6]. To the best of our knowledge, FHL rupture is never reported in RA-patients.

Considering its function, damage of the flexor hallucis longus (FHL) as a possible consequence of tenosynovitis might be relevant. The FHL not only flexes the great toe but it contributes, together with plantar fascia, to the distribution of forces at the plantar side of the forefoot and maintenance of the longitudinal arch of the foot [7]. Loss of the tendon and its loading capability of the longitudinal arch, esp. at the level of the first ray, can lead to a pes planus [8].
Tenosynovitis (or rupture) of this tendon can also result in a (functional) hallux rigidis and tightening of the FHL tendon. The subsequent dorsal compression in the first MTP-joint can in turn lead to the forming of osteophytes, further mechanical impingement, limitation and damage of the MTP1 [9].
The relation between FHL tenosynovitis or rupture and aforementioned abnormalities of the foot in RA patients has to be determined.
In our study we aim to assess the prevalence of FHL tenosynovitis or rupture and the relation between FHL rupture or tenosynovitis and the range of motion, joint damage and pes planus in symptomatic feet of RA-patients.

Methods

We included 30 consecutive RA patients with at least one painful forefoot and or hind foot who visited the outpatient rheumatology clinic of the Medisch Spectrum Enschede in September 2005. In 60 feet we measured the range of motion of the first metatarsophalangeal joint using the joint alignment motion scale (JAM) [10]. A normal range of motion (ROM) of MTP is scored 0. A ROM limitation to 65–70 degrees is scored 1, to 55–65 degrees as 2, to 20– 55 degrees as 3 and a range of motion less then 20 degrees is scored as 4. Spiegel et al described the JAM scale and this shows good inter reader reliability as well as a good relation with disease activity and function [10,11].

The feet were examined clinically for the presence or absence of a pes planus.

Radiographs were made of all feet. The MTP and IP joints were each scored for joint erosions (range 0–10) and joint space narrowing (0–4) per joint according to Sharp/van der Heijde [12].

Erosion score of the proximal surface of MTP1 (0–5) was scored separately, as FHL tendon problems can lead to a hallux rigidis with a higher prevalence of dorsal erosions of the first metatarsal head [9].

One licensed and qualified rheumatologist, using a Logiq 7 General Electrics, 7–13 MHz linear transducer, performed ultrasound investigation. If present, the FHL tendon cross section was measured and the tendon assessed for signs of tenosynovitis (fluid around the tendon or presence of Power Doppler signs). This was performed at the level of the medial malleolus and extended 6 cm proximal to 6 cm distal of this point. Rupture of the FHL tendon was defined as absence of this tendon at the level of the medial malleolus. This tendon is difficult to visualise. If it could not be found at first sight, the great toe was flexed, causing motion of the tendon. If no motion was detected, the FHL tendon was finally judged to be absent.

Ultrasound is regarded as a reliable tool for detecting tendon abnormalities. Naredo et al observed an overall agreement of 88.5% in detecting tenosynovitis and 92% in tendon lesions of the ankle and foot, although these findings were not limited to the tendon of the FHL. Scheel et al observed an excellent κ value of 1 for the detection of tendon tears and a moderate κ value of 0.49 in detecting tenosynovitis, but this was calculated for tendons in general and not specified for the tendons of the ankle or the FHL [13,14].

Differences between groups, regarding the rupture of the FHL, and the correlation with the ROM, Sharp/van der Heijde score and presence of pes planus were tested, using Pearson's chi squared test. Ethical approval was obtained from the ethics committee from The Medical Spectrum Twente; all patients gave their written consent.

Results

Table 1 shows the demographic characteristics of the studied RA patients, showing a wide range of age, disease duration and damage.
The median and the range of the JAM score are provided in Table 1.
Forty-two feet (70%) were scored as a pes planus. Results of the radiograph scores are presented in Table 1.
Ultrasonography revealed that the tendon of the FHL was ruptured in 11/60(18%) of the feet Figure 2.

Table 1. Mean values of the demographic, radiographic and joint mobility characteristics.

	TOTAL N=60	FHL TENDON absenT n=11	FHL TENDON present n=49
Age (years)	54	57,6	53,1
Disease duration (years)	11,6	11,2	11,7
JAM score MTP-1 motion (0-4)	2,1	3,09	1,84
SHS erosion proximal MTP 1 (0-5)	1,0	2,18	0,74
SHS narrowing MTP 1 (0-4)	1,62	2,55	1,4
Total SHS feet (0-84)	29.7	47,1	25,6

JAM= joint alignment motion scale, SHS=Sharp van der Heijde score, FHL=flexor hallucis longus

FHL tendon rupture was associated with a limited range of motion of MTP1, measured as a significant higher score of the JAM motion MTP1 ($\chi 2 = 10.4$, $p = 0.034$.)
In only one foot, a tenosynovitis was diagnosed, based on fluid around the tendon. No tendon tears were found.
A pes planus was found in all of the feet with a ruptured FHL, and only in 31 of the 49 remaining feet ($\chi 2 = 5.77$, $p = 0.016$.)
There was a significant relation between rupture of the FHL and erosions proximal at the MTP 1 joint ($\chi 2 = 12.3$, $p = 0.016$.), and joint space narrowing of the MTP 1 joint. ($\chi 2 = 12.7$, $p = 0.013$.)

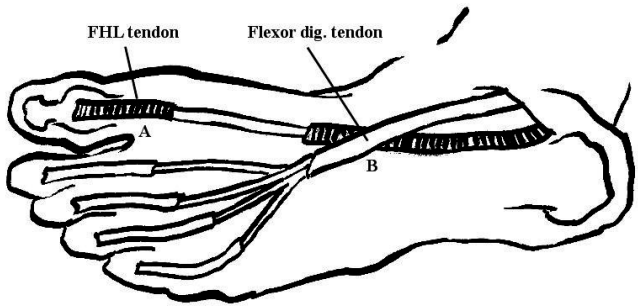

Figure 1a. Medioplantar aspect of the foot.

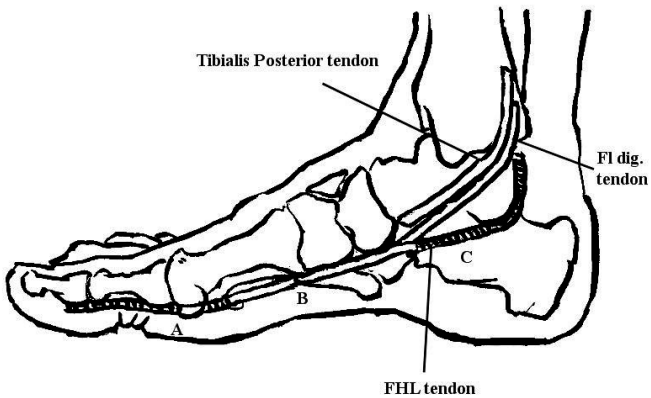

Figure 1b. Medial aspect of the foot.

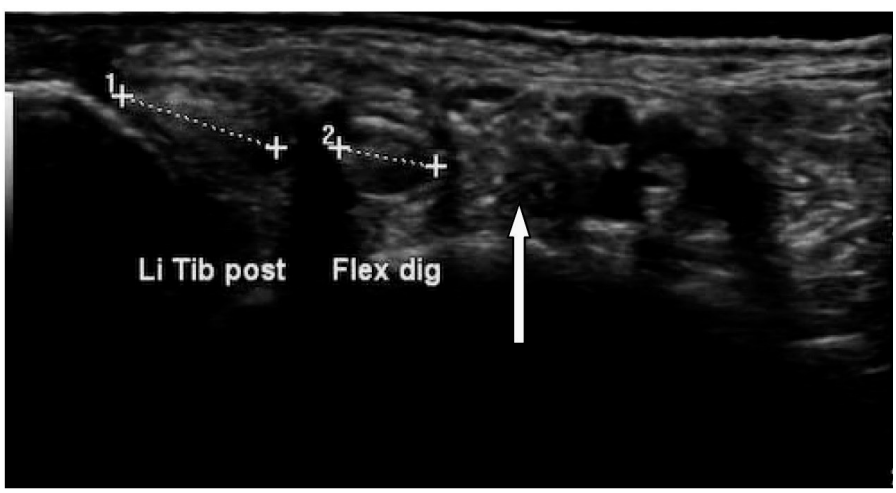

Figure 2. Left medial ankle of a 57-year-old patient with RA, missing the FHL tendon (arrowhead).

Discussion

This study shows that in RA patients, rupture of the flexor hallucis longus tendon is associated with limited range of hallux motion, erosions and joint space narrowing of the MTP-1 joint and pes planus.
The observed prevalence of FHL rupture seems high in this study. We must stress that this is not representative for the RA population since we included only patients with a painful foot. However, the reported prevalence of FHL tenosynovitis in the study of Maillefert et al is also rather high, 3/17 feet (18%) [4]. As far as we know, there are no reports on the prevalence of ruptured FHL in RA patients.
FHL rupture (following tenosynovitis) might be provoked by rheumatoid inflammation. As stated earlier, RA can affect tendons as well as joints. This can occur at the level A and C in the Figures 1a and 1b. Early damage of the great toe joint might lead to limited joint motion and subsequent chronic underuse of the FHL, contributing to atrophy of its tendon [15].
Mechanical reasons for inflammation or rupture of the tendon are deformity or anatomical variations of the foot at the level B or C, Figure 1, as can be seen in calcaneus fractures or bony abnormalities like a prominent os trigonum, or overuse of the tendon in runners, dancers and athletes [16].

Although nothing can be concluded regarding causality, we hypothesize that following rheumatoid inflammation, rupture of the FHL tendon takes place. This can occur unnoticed, as the associated pain and swelling of the ankle are often erroneously contributed to synovitis of the ankle [4]. During tenosynovitis, damage of the MTP 1 joint may arise, according to the mechanism described by Michelson et al [9].
The association with a pes planus can be explained by the loss of the FHL in its supporting role of distributing the forces (together with the fascia plantaris) under the foot and maintenance of the longitudinal arch, as described by Hamel et al [7].
We hypothesize that early recognition and timely adequate treatment of tenosynovitis of the FHL (for example by local ultrasound guided steroid injections) might become important to prevent damage.
A larger prospective follow-up study however, demonstrating the causal relationship between tenosynovitis or rupture of the FHL and deformities in the rheumatoid foot is warranted to draw definite conclusions.

Conclusion

Rupture of the flexor hallucis longus tendon in RA- patients is associated with limited range of hallux motion, more erosions and joint space narrowing of the MTP-1- joint, as well as with pes planus.

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4

Ultrasound findings in rheumatoid wrist arthritis highly correlate with function

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Abstract

Purpose: The wrist is almost invariably affected in rheumatoid arthritis (RA) and inflammation of the wrist can lead to impaired function and eventually to severe destruction.
Classical signs of inflammation, pain, swelling and heat may often be observed in clinical examination of wrist arthritis and in ultrasound (US) investigation.
We described the relation between clinical and ultrasound parameters of wrist arthritis and secondly their relation to function.

Patients and methods: In 33 RA patients with wrist arthritis, clinical and US parameters were measured. Function was evaluated with the SODA-S (Sequential Occupational Dexterity Assessment-Short) and the DASH-DLV (Disabilities of the Arm, Shoulder and Hand-Dutch Language Version). Correlation coefficients were calculated and factor analysis was performed to describe the relation between the aforementioned measures.

Results: Correlation coefficients between clinical and ultrasound parameters of RA wrist inflammation in this study were fair to moderate. We found a good correlation between ultrasound and observed function. Conclusion. The classical signs of inflammation (pain, swelling, redness, heat and impaired function) seem to reflect different aspects of arthritis. Ultrasound correlates well with function, thus can give paramount information on wrist function, and might therefore be a valuable complementary tool in measuring wrist arthritis in RA.

Introduction

The wrist is almost invariably affected in rheumatoid arthritis (RA) and inflammation of the wrist can lead to impaired function and eventually to severe destruction [1,2]. Inflammation is, classically described by Celsus in De Medicina, the presence of 'rubor et tumor cum calore et dolore' (redness and swelling with heat and pain). Two centuries later, Galen completed this with the fifth sign: functio laesa, impaired function. From those initial four classical signs of inflammation, pain, swelling and heat may often be observed as clinical signs of the rheumatoid joint and in ultrasound (US) investigation. Yet, 'rubor' or red- ness, the result of increased blood flow (vasodilatation) in the affected joint, is not a common clinical finding in an inflamed wrist. However, an increased blood flow can be demonstrated by ultrasound investigation with Power Doppler ultrasound (PDUS). Indeed, Newman et al. [1] concluded that PDUS reflects hyperemia in an inflamed joint.

The fifth classical sign of inflammation, functio laesa, is derived from the other four. The relation between pain, inflammation and function is complex and determined by many factors. It is demonstrated that other aspects, as socio-economic status, age, general perception of health, personal motivation and other 'external' or non-medical factors do influence functional status [2,3].

In this descriptive cross-sectional study, we aimed to address firstly the relation between clinical and ultrasound parameters of wrist arthritis and secondly their relation to function in RA patients with wrist arthritis.

Patients and methods

For this study, we used data from a randomized clinical trial, in which the effect of a wrist-working splint in active wrist arthritis was evaluated [4]. Thirty-three patients with RA, meeting the 1987 ACR criteria, were included. To be included, wrist arthritis according to the attending rheumatologist and wrist pain of 30 mm scored on a VAS scale 0–100 over the past week were needed. Written informed consent was obtained.

At baseline, demographic variables were collected: age, sex and disease activity (DAS 28).

Patients were randomly allocated to intervention (wrist working splint) or control group.

At baseline and after 4 weeks (end of the study) the following items were measured.

Clinical measures

Pain in the wrist measured on a numeric rating scale (NRS) from 0 to 10, pain Ritchie Articular Index (RAI): assessment of pain at palpation from 0 to 3, swelling wrist (RAI), scored as absent or present.

Functional measures

Grip strength (Vigorimeter, kPa). A SODA-S (Sequential Occupational Dexterity Assessment-Short) was performed. The SODA-S is designed to measure bimanual hand function in RA. The SODA-S consists of six standardized hand-related daily activities (three unilateral, three bilateral) performed under controlled conditions without splint. The total score, which is a combination of these two scores, was computed, ranging from 0 (low dexterity) to 48 (high dexterity). The SODA-S pain score was computed by counting the number of activities that caused pain (range: 0–6) [5,6]. Furthermore, we used the DASH-DLV (Disabilities of the Arm, Shoulder and Hand-Dutch Language Version), a self-administered scale measuring patients' perception of symptoms and functional status of upper arm disability [5,7,8].

Ultrasound parameters

The dorsal side of the wrist was scanned from side to side in the longitudinal plane. In the evaluation of the wrist, the radio carpal joint and the ulno carpal joint, the midcarpal joints and the extensor tendons were scanned. We measured synovitis as grey scale synovial hypertrophy (0–3), effusion (0–3), Power Doppler (PDUS) signals (0–3). As for simplifying the analysis, a total PDUS score was calculated, as were a total synovitis and total effusion score (see Figure 1).

Szkudlarek et al. [9] described the scoring method we used. Two experienced rheumatologists, who carried out a consensus on joint assessment before the study performed the ultrasound investigation, on a Logic 9 (GE) with a 9–13 linear probe. To describe the relation between variables within patients, the observations at baseline and at 4 weeks were merged, resulting in 66 observations, eligible for cross-sectional analysis. The data were not analysed longitudinally in this study, as this has already been done [4]. The correlation between the inflammation signs, ultrasound parameters and function were calculated using Spearman's correlation. Thereafter, the main variables were entered in a factor analysis (principal component analysis), a multivariate technique to identify whether the correlation between the variables stem from their relation with underlying, latent variables (factors). Data analysis was performed using the Statistical Package for the Social Sciences (SPSS 12.0.1).

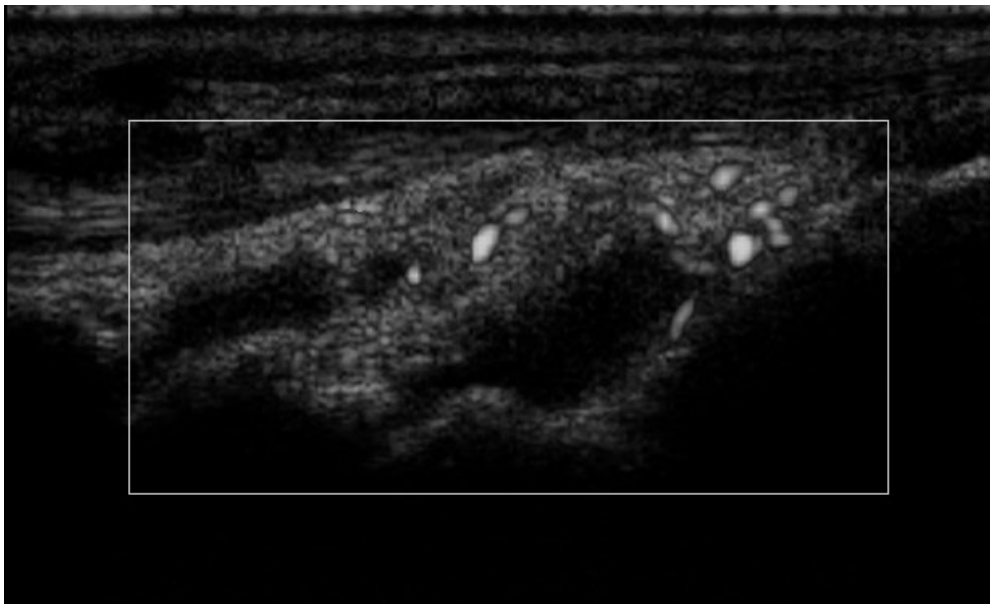

Figure 1: Longitudinal view of a wrist, with synovitis, effusion and increased Power Doppler signals.

Results

The demographics of the study population are shown in Table 1. Thirty-three patients were eligible, 30% men and 70% women. The mean age was 58 years. All patients had wrist arthritis. The mean VAS pain was 54. Spearman's correlations between the ultrasound parameters, the clinical variables and function (SODA-S, DASH-DLV and grip strength) are presented in Table 2.

Table 1. Demographics.

Sex F: M	**23:10 (70% F)**
Age (years, mean and SD)	58 ± 12,0
SJC (#, mean and SD)	7 ± 4,2
DAS 28 (score, mean and SD)	4,35 ± 1,15
ESR (mmHg, mean and SD)	21 ± 19
VAS pain at inclusion (mean and SD)	54,2 ± 16,4

SJC= Swollen Joint Count, DAS 28 = Disease Activity Score, measured on 28 joints, ESR= erythrocyte sedimentation rate, VAS= Visual Analogue Scale

Table 2. Spearman's correlation coefficients between the main clinical, ultrasound and functional variables.

	DASH tot	Pain wrist nrs	Total score SODA-S	Total pain score SODA-S	SYN TOT	EFF TOT	PDUS TOT	Sw wrist RAI	Pain wrist RAI	Grip strength
DASH tot	1,000	0,502**	-0,354**	0,318*	0,192	0,120	0,211	0.088	0.329**	-0.213
Pain wrist nrs		1,000	-0.213	0,350**	0,213	0,178	0,171	0.100	0.541**	-0,060
Total score SODA-S			1,000	-0,247*	-0,380**	-0,474**	-0,557**	-0.049	-0.153	0.011
Total pain score SODA-S				1,000	0,054	0,177	0,123	0,086	0,310*	-0,250*
SYN TOT					1,000	0,647**	0,720**	0,210	0.241*	0.119
EFF TOT						1,000	0,714**	0.397**	0.342**	0.194
PDUS TOT							1,000	0.350**	0.311*	0,189
Sw wrist RAI								1.000	0.359**	0.042
Pain wrist RAI									1.000	0.097
Grip strength										1,000

* = 2-tailed significant correlation at the 0.05 level, ** = 2-tailed significant correlation at the 0.01 level. DASH= disabilities of the Arm, Shoulder and Hand Questionnaire, NRS=numeric rating scale, SODA-S= Sequential occupational dexterity assessment-short, PDUS = Power Doppler ultrasound signals measured on a scale 0 – 3, SYN = synovitis, measured with ultrasound on a scale 0 – 3, EFF = effusion, measured with ultrasound on a scale of 0 – 3, grip strength = the mean grip strength 3 times measured on a Vigorimeter (kPa).

The correlation between clinical and ultrasound parameters of wrist inflammation is fair to moderate. Self-reported pain (NRS) did not correlate with any of the ultrasound parameters. Pain of the wrist, measured as within the RAI, showed a correlation of $r_s = 0.342$ with effusion and $r_s = 0.311$ with PDUS. Swelling of the wrist also correlated moderately, both with effusion ($r_s = 0.397$) and with PDUS ($r_s = 0.350$).

The DASH correlated with pain ($r_s = 0.502$, $p < 0.01$ for the NRS and $r_s = 0.329$, $p < 0.01$ for pain RAI), SODA-S total ($r_s = 0.354$, $p < 0.01$) and SODA-Spain ($r_s = 0.318$, $p < 0.05$). The DASH showed no correlation with any of the ultrasound parameters.

The total SODA-S score correlated highly with all ultrasound parameters. From these ultrasound parameters, PDUS showed the highest correlation with the SODA-S ($r_s = 0.557$, $p < 0.01$).

Factor analysis was performed (principal component extraction with oblique rotation and Kaiser normalisation), searching for underlying, latent factors that could explain the variance.

In the factor analysis, four components were extracted, with loading of the 'functional' variable grip strength onto factor 2, pain and self-reported function onto factor 3 and observed function together with pain separate onto factor 4 (see Table 3).

The ultrasound variables, together with observed function (SODA-S) loaded onto factor 1.

Table 3. Factor analysis.

	Component			
	1	2	3	4
Pain wrist RAI			.901	
Pain NRS			.853	
DASH total score		-.446	.506	
Grip strength		-.936		
Total pain score SODA-S				.882
Total score SODA-S	.556			.545
Syn	.904			
Eff	.933			
PDUS	.903			

RAI= Ritchie Articular Index, NRS=numeric rating scale, DASH= disabilities of the Arm, Shoulder and Hand Questionnaire, SODA-S= Sequential occupational dexterity assessment-short, grip strength = the mean grip strength 3 times measured on a Vigorimeter (kPa) SYN = synovitis, measured with ultrasound on a scale 0 – 3, EFF = effusion, measured with ultrasound on a scale of 0 – 3, PDUS = Power Doppler ultrasound signals measured on a scale 0 – 3.

Discussion

In our study, ultrasound parameters and clinical signs and symptoms of wrist inflammation are dissociated, suggesting inflammation is not one-dimensional. We found a good correlation between ultrasound and functional outcomes. Ultrasound parameters in this study correlated only moderate with the clinical findings like swelling and pain. This is consistent with earlier findings; dependent on the joint the correlation coefficients between clinical findings and ultrasound measurement vary from poor to moderate. A clinical swollen joint evaluated with ultrasound often turns out to be something else, like tenosynovitis or soft tissue swelling [10–12]. This was moreover confirmed in our factor analysis, which showed, that the ultrasound variables (together with the total SODA-S) did not load onto the pain factor, but seem to cover an additional part of inflammation, not measured by clinical findings. Ribbens, who found no correlation at all between the US and the clinical findings, described this phenomenon earlier. He stated: 'US yields additional information about joint inflammation and is a complement to clinical examination, the current standard of reference' [13].

Function, measured with the DASH, a self- administered scale of perception of disability and symptoms, correlated highly with the other functional measure, the total SODA-S. Adams et al. [14] reported a correlation between the DASH and therapist-rated hand ability using the Grip Ability Test (Dellhag and Bjelle, 1995) and hand impairment in an early RA patient cohort. Correlation between DASH and grip strength was also confirmed in a study with patients with psoriatic arthritis. [15] We found a high correlation between the DASH and wrist pain. This is not surprising. At least five items of the DASH questionnaire deal with pain or a closely related item like tingling sensations. There- fore, in our study, the DASH gives not only a reflection of function but seems to be a pain scale as well, as was well demonstrated in our factor analysis (Table 3). Apparently, patients value their function better if the pain is less.

Observed function, measured with the total SODA-S was highly correlated with al ultrasound parameters of inflammation. This finding suggests that dexterity in daily tasks as measured with the total SODA-S might be influenced more by inflammation of the wrist measured with ultrasound, than by clinical symptoms like pain and swelling. The only study that compared disease activity directly with the total SODA-S is that of van Lankveld et al. [16]. They demonstrated that disease activity was not correlated to the total SODA-S. Change in disease activity more than 1 year, however, was significantly correlated to change on the SODA-S. They furthermore convincingly demonstrated that the wrist is major for dexterity, as is

shown by the good correlation between wrist range of motion (ROM), wrist pain and total SODA-S in their study [16].

To our knowledge, this is the first time the relation between US measurement and function has been addressed. There are some limitations: this study was not very large. It was a cross-sectional study and the results have to be confirmed in a longitudinal study.

In conclusion, we found that wrist inflammation has many aspects, already described in the antiquity. Of the clinical signs, only pain shows a good correlation with function. The ultrasound parameters also correlate well with function. For clinical practice, this means that examination should not be limited to clinical signs and symptoms, but that additional ultrasound examination might be valuable in the evaluation and treatment of rheumatoid wrist arthritis, especially in impaired function.

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5

Magnetic Resonance Imaging of the rheumatic foot according to the RAMRIS system is reliable

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Abstract

Objective: In rheumatology, magnetic resonance imaging (MRI) is predominantly applied in the assessment and outcome measurement of rheumatoid arthritis (RA) in hands and wrists, leading to the development of the RAMRIS (RA-MRI-Scoring) system. The Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) initiated it. The RAMRIS system has not been applied widely in the measurement of feet. We investigated the interreader and intrareader agreement of the RAMRIS scoring system in the assessment of feet in RA.

Methods: Twenty-nine patients with RA who had radiological damage and/or arthritis underwent MRI. Two experienced readers independently read both complete sets. One reader read 6 random sets after the initial session, in order to assess the intrareader agreement. For evaluation of the intrareader and interreader reliability, quadratic-weighted κ scores were calculated per joint and lesion.

Results: For the forefeet, interreader scores were excellent, ranging from 0.77 (bone edema) to 0.95 (bone erosion). Hindfoot interreader agreement scores were highest for erosion (0.90) and synovitis global score (0.88), but edema and synovial thickness agreement were also acceptable (0.83 and 0.86). Intrareader scores were on the whole slightly lower, but excellent.

Conclusion: Reliability (interreader and intrareader agreement) in the assessment of the rheumatoid foot according to the RAMRIS method is excellent.

Introduction

There is increasing interest in the use of magnetic resonance imaging (MRI) in the diagnosis and monitoring of rheumatoid arthritis (RA)[1,2,3]. The advantages of MRI over radiography, apart from the absence of ionizing radiation, are the superior imaging of the tissues involved in RA, such as synovial tissue, tendons, sheaths, ligaments, bone, and cartilage [4,5,6,7]. MRI has proven to be a sensitive and reliable instrument for the detection of inflammatory and destructive changes in RA. Synovial enhancement on MRI closely correlates with the histopathological findings of synovitis [8,9] and bone marrow edema represents inflammatory infiltrates or osteitis [10,11]. In rheumatology, MRI is predominantly applied in the assessments and outcome measurement of RA in hands and wrists, because of their frequent involvement in RA (including early RA) and the fact that these joints are included in traditional clinical and radiological scoring systems in RA [12]. This has led to the development of the RAMRIS (RA-MRI-Scoring) system, initiated by OMERACT (Outcome Measures in Rheumatoid Arthritis Clinical Trials), and allowing semiquantitative, standardized assessments of inflammatory and destructive changes in RA[12-16]. There have been some interesting studies in the field of foot MRI in RA [17,18] especially the study by Mundwiler, *et al*, who calculated the predictive value of MRI lesions on the occurrence of radiological damage [19]. Ostendorf, *et al* applied the RAMRIS system to the feet [18]. We examined the interreader and intrareader agreement of the RAMRIS system in the assessment of feet in RA, which to our knowledge has not been done yet.

Materials and methods

Twenty-nine patients with RA from the Arthritis Centre Twente, meeting the 1987 American College of Rheumatology criteria, participated in our study. To be included, patients had foot complaints attributed to arthritis and/or structural damage as a consequence of RA. MRI was performed in both feet and ankles. The ethics committee approved our study and written informed consent was obtained from each patient.

Two readers experienced in the field of musculoskeletal MRI did the scoring. They independently read both complete sets of images after 2 combined sessions of practicing the RAMRIS system on MRI that were not included in our study. One reader read 6 random sets after the initial session, in order to assess the intrareader agreement. MRI was obtained from a 1.5 Tesla MR scanner (Phillips Medical Systems,

Best, The Netherlands) with a 4-element synergy body coil, providing enough coverage for imaging both feet in 1 acquisition. The imaging protocol comprised an axial (short axis) 3-D T1-weighted gradient echo [2 mm slice thickness, 1 mm inplane, TR (relaxation time) 17 ms; TE (echo time) 4.6 ms; flip angle 25], a sagittal T1-weighted SE (spin echo) sequence [3.5 mm slice thickness, gap 0.3 mm; TR 609 ms; TE 19 ms; 3 NSA (number of signal averages)] and a sagittal fat-saturated T2 TSE (3.5 mm slice thickness, gap 0.3 mm; TR 4785 ms; TE 150 ms; 4 NSA). After administration of 15 ml contrast (gadodiamide, 0.5 mmol/ml), a sagittal fat-satu- rated T1-weighted SE sequence (3.5 mm slice thickness, gap 0.3 mm; TR 609 ms; TE 19 ms; 3 NSA) and an axial (short axis) fat-saturated T1 SE sequence (3.0 mm slice thickness, gap 0.3 mm; TR 609 ms; TE 19 ms; 3 NSA) were acquired. In all sequences, the field of view was 10–14, matrix 256 × 217. Decent images were obtained in all 29 cases.

The MRI sets were scored according to the OMERACT method, a semiquantitative method described by Østergaard *et al* [12]. Bone erosion was defined as a bone defect with sharp margins, visible in 2 planes (when 2 planes were available) with a cortical break seen in at least 1 plane. Bone erosion lesion was scored from 0 to 10 by the volume of the erosion as a proportion of the "assessed bone volume" by 10% increments judged on all available images. For the tarsal bones, the "assessed bone volume" was the whole bone. For long bones, the "assessed bone volume" was from the cortex of the articular surface (or its best estimated position if absent) to a depth of 1 cm. Bone edema was defined as a lesion with ill-defined margins that was neither erosion nor defect and had high signal intensity on T2- weighted sequences. Each bone was scored separately (as for erosions). The scale is 0–3 based on the proportion of bone with edema, as follows: 0, no edema; 1, 1%–33% of bone edematous; 2, 34%–66% of bone edematous; and 3, 67%–100%. This judgment was made on the basis of the pre- eroded bone, so that maximum erosion scores could not limit the bone edema score. Synovitis was the area in the synovial compartment that shows enhancement of a thickness greater than the width of the joint capsule after gadolinium. Synovitis global score was assessed in the joints of the hindfoot: the tibiotalar joint, the subtalar joint, the talonavicular joint, the calcaneocuboid joint, the tarsometatarsal joint, and the cuneonavicular joint, and in each metatarsophalangeal (MTP) joint. The scale is 0–3. Score 0 is normal, and 1–3 (mild, moderate, severe) are by thirds of the presumed maximum volume of enhancing tissue in the synovial compartment. Synovial thickness was also measured and expressed in exact mm. This was not described in the RAMRIS protocol. The synovial thickness was measured, using electronic calipers, on the point where the enhanced synovium was maximal, in 2 directions, and then averaged.

All MTP joints and joints of the hindfoot were then judged for erosion and edema. For the MTP joints, erosion and edema were scored separately in the distal and proximal part of the joint. The 5 metatarsal bones were scored at the bases for erosion and edema, as were the following tarsal bones: navicular, cuboid, the 3 cuneiforms, talus, and calcaneus. All items per joint were added, and then the interreader and intrareader agreements per joint were calculated.

The data were analyzed individually by joint and lesion to determine how agreement differed by joint and by lesion, and as aggregated scores. Descriptive statistics of each lesion (mean, minimum, maximum, SD, median, 25th and 75th percentiles) for individual joints and aggregated scores were calculated by reader and across both readers. For evaluation of the intrareader and interreader reliability, quadratic-weighted κ scores were calculated per joint and lesion.

The statistical programs used were SPSS 17.0, Analyse-it, and Graphpad Prism.

Results

Demographics and patient characteristics are given in Table 1. Descriptive statistics of the items, including the maximum possible scores as well as the maximum scored range, as scored by each reader, are given in Table 2. Mean and range were presented for both readers. The summed scores of both feet were scored in the full range only for the synovitis global scores. Scores for bone edema were in the lower segment of the range (floor effect).

Table 1. Demographics and patient characteristics.

Age (years)[1]	55 (16,1)
Sex (F/M)	5/25
Disease duration (months) [2]	100.00 (60.00, 206.00)
Rheumatoid factor positivity	66.6 %
Pain ankle	35 %
Swelling ankle	40 %
Pain forefoot	48%
Total number of swollen MTP's[1]	1.47 (1.51)
SvdH total score feet[2]	4.00 (1.0, 12.5)
Larsen score hindfoot[2]	1.00 (0.00, 3.00)

1. Mean (standard deviation) 2. Median (lower, upper quartiles), SvdH = Sharp van der Heijde, Larsen score = radiological damage scoring system, according to Larsen (20)

Synovitis scores and synovial thickness were highest in MTP 1, then in MTP 5 (Figure 1). Both synovitis and synovial thickness were lowest in MTP 4. Bone erosion, both proximal and distal, followed the same patterns. Proximal bone edema was again highest in MTP 1. Distal bone edema was equally distributed between all MTP. Erosion and edema scores were highest in the proximal part of the MTP joint. In the hindfoot, synovitis global score and synovial thickness were highest in the tarsometatarsal joint, followed in descending order by the subtalar joint, the tibiotalar joint, the talonavicular joint, the calcaneocuboid joint, and the cuneonavicular joint. Erosion scores in the hindfoot were highest in the navicular bone and the cuneiform bones, and lowest in the talus and calcaneus (Figure 2). Edema scores in the same region were highest in the talus and calcaneus as well as the cuneiform bones, and lowest in the cuboid bone (Figure 3). Metatarsal erosion scores were highest in MT 2, followed by MT 1, 3, 4, and 5. The bone marrow edema scores were the opposite, with highest scores in MT 5 and 4 and lowest scores in MT 2.

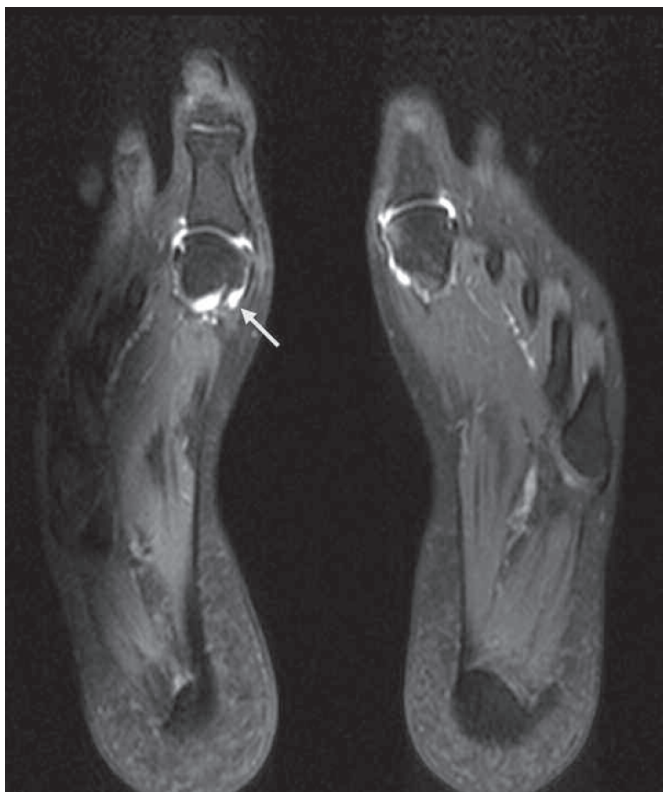

Figure 1: Transversal image showing post gadolinium enhanced synovitis of the metatarsophalangeal joint 1 (arrow).

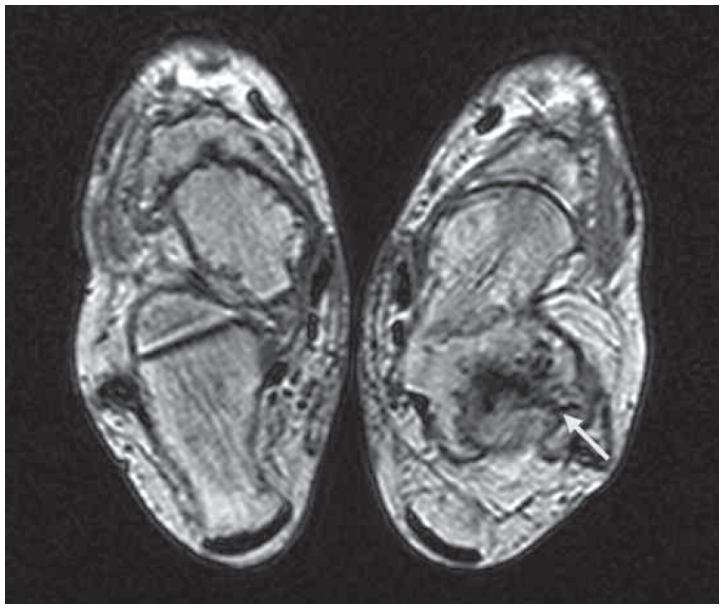

Figure 2: T1-weighted axial image showing extensive erosions in the right ankle (arrow).

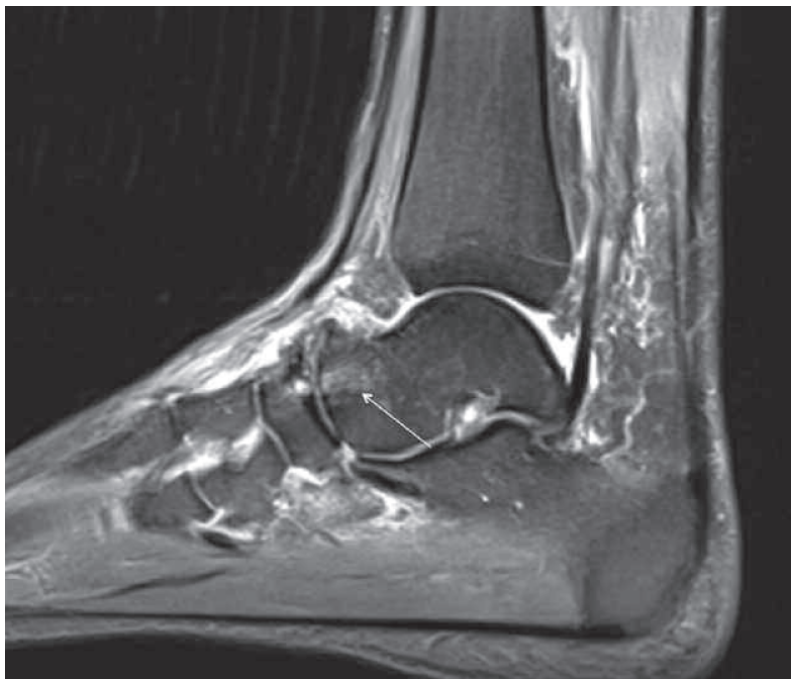

Figure 3: T2-weighted sagittal slice showing bone marrow edema of the navicular bone (arrow).

Table 2. Mean (range) scores of MTPs, metatarsal bases, tarsal bones and hind foot joints, left and right summed per joint.

	Synovitis global score (0-30)		Synovial thickness mm		Bone erosion prox (0-100)		Bone erosion dist (0-100)		Bone edema prox (0-30)		Bone edema dist (0-30)	
	R 1	R 2	R 1	R 2	R 1	R 2	R 1	R 2	R 1	R 2	R 1	R 2
MTP's												
MTP 1	3,6 (0-6)	3,3(0-6)	6,2(0-20)	4,9(0-12)	7,4(0-17)	7,0(0-17)	5,2(0-15)	4,1(0-15)	0,77(0-3)	1,0(0-3)	0,61(0-5)	0,61(0-3)
MTP 2	2,3 (0-6)	2,1(0-6)	3,9(0-13)	3,4(0-12)	5,4(0-18)	5,1(0-17)	3,6(0-16)	3,3(0-16)	0,44(0-3)	0,55(0-3)	0,53(0-5)	0,61(0-3)
MTP 3	2,0 (0-6)	1,9(0-6)	3,6(0-10)	3,0(0-10)	5,6(0-17)	5,5(0-16)	4,1(0-16)	3,5(0-16)	0,55(0-4)	0,55(0-3)	0,47(0-5)	0,39(0-3)
MTP 4	1,9 (0-6)	1,7(0-6)	2,9(0-9)	2,4(0-9)	4,7(0-17)	4,3(0-18)	3,2(0-15)	2,9(0-15)	0,44(0-2)	0,66(0-3)	0,41(0-4)	0,50(0-3)
MTP 5	2,5 (0-6)	2,4(0-6)	4,0(0-11)	3,4(0-9)	7,6(0-19)	7,3(0-19)	4,4(0-16)	4,2(0-15)	0,50(0-2)	0,83(0-2)	0,65(0-5)	0,50(0-3)
	Bone erosion (0-100)		**Bone edema (0-30)**									
	R 1	R 2	R 1	R 2								
METATARSAL BONES, bases												
MT 1	2,3(0-11)	1,6(0-10)	0,2(0-3)	0,15(0-2)								
MT 2	2,9(0-10)	1,6(0-8)	0,0(0)	0,15(0-2)								
MT 3	2,4(0-10)	1,3(0-7)	0,2(0-3)	0,19(0-2)								
MT 4	2,1(0-10)	1,6(0-11)	0,1(0-2)	0,19(0-3)								
MT 5	1,8(0-14)	1,3(0-14)	0,33(0-5)	0,34(0-4)								
	Bone erosion (0-100)		**Bone edema (0-30)**									
	R 1	R 2	R 1	R 2								
TARSAL BONES												
Navicular bone	4,4(0-14)	4,3(0-15)	1,0(0-6)	0,96(0-6)								
Cuboid bone	3,1(0-12)	3,3(0-15)	0,73(0-6)	0,74(0-6)								
Med cuneiform	3,1(0-14)	3,1(0-15)	0,53(0-4)	0,74(0-4)								
Int cuneiform	3,3(0-19)	3,1(0-18)	0,92(0-5)	0,77(0-5)								
Lat cuneiform	3,1(0-15)	3,2(0-15)	0,73(0-8)	0,48(0-3)								
Talus	3,0(0-11)	3,4(0-20)	0,96(0-8)	0,66(0-3)								
Calcaneus	2,3(0-10)	2,6(0-17)	0,80(0-4)	0,74(0-4)								

JOINTS HINDFOOT	Synovitis global score (0-30)		Synovial thickness mm	
	R 1	R 2	R 1	R 2
TT	1,9(0-6)	1,8(0-6)	3,7(0-13)	2,9(0-11)
ST	1,9(0-6)	1,9(0-6)	3,8(0-13)	3,2(0-11)
TN	1,8(0-6)	1,8(0-6)	3,2(0-14)	3,0(0-12)
CC	1,4(0-6)	1,6(0-6)	2,2(0-16)	2,4(0-10)
TMT	1,9(0-6)	1,9(0-6)	3,3(0-12)	2,8(0-9)
CN	1,6(0-6)	1,7(0-6)	2,5(0-11)	2,5(0-10)

R1=reader1 (JA), R2=reader2 (RB), MTP=metatarsophalangeal, MT=metatarsal, TT=tibiotalar, ST= subtalar, TN=talonavicular, CC=calcaneocuboid, TMT=tarsometatarsal, CN=cuneonavicular.

Table 3 shows the interreader and intrareader weighted κ scores of synovitis, synovial thickness, bone erosion, and bone edema, in both the forefeet and hindfeet areas. The interreader scores ranged from 0.77 (bone edema) to 0.95 (bone erosion). The intrareader scores ranged from 0.67 for bone edema to 0.90 for bone erosion. The weighted κ scores for synovitis were higher in the forefeet than in the hindfeet, for both interreader and intrareader agreement. For synovial thickness, on the other hand, agreement was comparable for forefeet and hindfeet, but on the whole lower than the synovitis semiquantitative scores.

Table 3. Inter-reader and intra-reader quadratic weighted k scores (CI) per item, aggregated.

	Inter-reader	Intra-reader
MTP's (1-5)		
Synovitis global score	0,94 (0,91-0,97)	0,85 (0,77-0,92)
Synovial thickness mm	0,87 (0,82-0,92)	0,74 (0,62-0,92)
Bone erosion prox	0,95 (0,92-0,98)	0,89 (0,84-0,94)
Bone erosion dist	0,95 (0,93-0,96)	0,90 (0,83-0,97)
Bone edema prox	0,78 (0,68-0,89)	0,67 (0,38-0,96)
Bone edema dist	0,77 (0,68-0,87)	0,73 (0,47-0,99)
METATARSAL BONES, bases (1-5)		
Bone erosion	0,83 (0,77-0,89)	0,81 (0,69-0,92)
Bone edema	0,83 (0,70-0,95)	0,89 (0,80-0,99)
TARSAL BONES and JOINTS HINDFOOT		
Bone erosion	0,90 (0,83-0,96)	0,86 (0,77-0,95)
Bone edema	0,83 (0,70-0,95)	0,68 (0,51-0,86)
Synovitis global score	0,88 (0,83-0,92)	0,87 (0,80-0,93)
Synovial thickness mm	0,86 (0,81-0,90)	0,75 (0,61-0,88)

Discussion

Our study revealed a good to excellent interreader as well as intrareader reliability for MRI of the rheumatic foot using the RAMRIS system. In the forefoot, synovitis global score and bone erosion showed excellent weighted κ scores (0.94 and 0.95, respectively), while bone edema κ scores were 0.77 and 0.78. The smaller range of these scores might partially cause the slightly lower κ values for edema. Hindfoot interreader agreement scores were again highest for erosion (0.90) and synovitis global score (0.88), but edema and synovial thick- ness agreement was also excellent (0.83 and 0.86). As an alternative to the synovial global score, we measured synovial thickness as well. The agreement of this item was in both the foot and the hindfoot joints slightly inferior to the synovial global score. This confirms earlier findings of

Lassere, *et al*, who also found a marginally inferior inter- class correlation coefficient (ICC) score for synovial thickness [21]. This might be due to the fact that the margins of measurement are not always easy to determine, and in our study, the lack of precise agreement on the plane/view in which to measure.

Moreover, gadolinium-containing contrast agents are such small molecules that they leak rapidly out of synovial capillaries and into the adjacent synovial fluid, obscuring the synovium-effusion interface. In small joints such as the MTP, equilibration can occur in as little as 1 minute post-injection. Thus, synovial thickness measurements are not very accurate. Exact knowledge of synovial thickness is not necessary. For the metatarsal bones, erosion and edema interreader weighted κ scores were lower, but still excellent (0.83).

For the intrareader agreement, all weighted κ values were slightly lower, but the trend was the same. The only items with a weighted κ below 0.7 were bone edema of the MTP and bone edema of the tarsal bones. The other κ values lay between 0.73 and 0.90, which is acceptable. The reason for the lower intrareader values compared to the interreader values might be explained by the fact that there was a substantial delay of about 14 months between the first and the second reading, for personal reasons. As well, only 6 sets were scored for the second time, leading to lower ranges, which could affect the κ values. Still, these intrareader weighted κ values are acceptable. As there are no previous studies on the intrareader and interreader agreement of the RAMRIS in feet, a direct comparison is not possible. However, there is considerable documentation regarding the RAMRIS in the hands and wrists, thanks to the OMERACT MRI working group [16,21-25]. Østergaard, *et al* [26] described the first multicenter session, without previous training, and found ICC varying from 0.44 to 0.68 for the synovitis global score of the metacarpophalangeal (MCP joints). Bone erosion proximal ICC of the MCP joints varied between 0.39 and 0.80. Among the synovitis scores of the wrist joints, ICC showed a range from 0.50 to 0.64. Østergaard, *et al* found that joint space narrowing could not be scored reliably, and was thus abandoned in further scoring [26]. After partial adoption of the scoring system and thorough training of the readers, Lassere *et al* showed in RAMRIS exercise 3 that the interreader agreement significantly improved [21]. Average ICC value in the metacarpal regions increased to 0.95 for synovitis global score. In the wrist region, the ICC values were very high for synovitis, erosion, and edema (0.90–0.94). Our study showed comparable quadratic-weighted κ values, especially for synovitis and erosion. Further comparison between hand and foot scoring is limited by the specific differences. The changes in MTP 1 are often degenerative, and not a

disease-specific feature; erosive changes in the hindfoot might also be degenerative and a consequence of weight-bearing function.

The good results of our cross-sectional study are promising, but do not guarantee good results in longitudinal data. This needs to be confirmed in follow-up studies. One limitation of our study is the small number of subjects.

Our study shows that the reliability of interreader and intrareader agreement in the assessment of the rheumatoid foot, according to the RAMRIS method, is highly accept- able. The forefoot especially showed excellent reliability. It is a common subject of study and can easily be compared with other imaging techniques.

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6

We should not forget the foot: relations between signs and symptoms, damage, and function in rheumatoid arthritis

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Abstract

We studied rheumatoid arthritis (RA) patients with foot complaints to address the associations between clinical signs and symptoms, radiographic changes, and function in connection with disease duration. Secondly, we describe the contribution of several foot segments to the clinical presentation and function. In 30 RA patients with complaints of their feet, attributed to either signs of arthritis and/or radiographic damage, we compared radiographic, ultrasound, clinical, and functional parameters of the feet and ankle. Pain and swelling of the ankle were correlated weakly but statistically significantly with limitation and disability (0.273 to 0.293) as measured on the 5-Foot Function Index (FFI). The clinical signs of the forefoot joints did not influence any of the functional outcome measures. Radiographic scores for both forefeet (SvdH) and hindfeet (Larsen) were correlated with the total Health Assessment Questionnaire Disability Index (HAQ DI) and the 5-FFI-limitation subscale. Pain and disease duration, more than radiographic damage, influence the total HAQ DI significantly. With the progression of time, structural damage and function of the rheumatic foot worsen in RA patients. Pain and swelling of the ankle contribute more to disability than radiographic damage of the foot and ankle.

Introduction

In rheumatic conditions, especially rheumatoid arthritis (RA), signs and symptoms of the feet are common. The majority of RA patients present with arthritis of the feet and 20% of them have radiographic damage at the time of diagnosis [1]. In RA, both forefoot and hindfoot involvement is associated with disease duration and lead to severe impairment and disability [2, 3]. After 6 years of disease duration, up to 50% of the patients have considerable radiographic damage in the ankle and the tarsus [4]. Despite the extent of the problem, the rheumatoid foot is neglected. Although in the last few years some scientific interest has arisen, there is still limited interest in the foot in RA in the clinic possibly causing undertreatment [1]. In this study, we examined patients suffering from RA and common foot complaints to investigate the associations between clinical signs and symptoms, structural damage, and function in connection with disease duration. Secondly, we explored the contribution of several foot segments to the clinical presentation and function.

Patients and methods

We performed a cross-sectional observational study. Thirty consecutive RA patients of the outpatient clinic of the Arthritis Centre Twente were recruited. To be included, patients had signs or symptoms of arthritis and/or radio- graphic damage of the feet or ankles due to RA. They had to meet the 1987 ACR criteria for RA. The local ethical committee approved this study and a written informed consent was obtained from each patient.

The following demographic and clinical variables were collected: age, sex, disease duration, total number of used DMARDS, rheumatoid factor DAS 28 [5], and painful or swollen joints in the foot.

All patients underwent ultrasound investigation of the feet and ankles to measure synovitis (0 to 3), effusion (0 to 3), and power Doppler (PDUS) signals (0 to 3) according to the method described by Szkudlarek [6]. The following joints were examined: the tibiotalar joint, the subtalar joint, the talonavicular joint, and the five metatarsophalangeals (MTPs). An experienced rheumatologist, who had undertaken specific postgraduate training in ultrasonography, performed the ultrasound investigation on a Logic 9 (GE) with a 9–13 MHz linear probe. To simplify the analysis, a total PDUS score was calculated for the MTPs as well as for the hindfoot joints by adding up the PDUS of the individual joints. This was also done for total synovitis, total effusion, and total erosion score.

To assess radiological structural damage, two experienced readers (WD, HB) read the radiographs of the feet. According to the method, Sharp/van der Heijde, each side of the MTP or IP joint was scored for erosions from 0 to 5 with a maximum of 10 for both sides of the joint, and for joint space narrowing from 0 to 4 with a maximum of 4 per joint. For the total Sharp/van der Heijde score, the erosions and joint space narrowing scores were added. The maximum total score for both feet adds up to 168 [7].

In addition, we read the tibiotalar joint, the subtalar joint, and the talonavicular joint following the Larsen method, in which erosions and joint space narrowing as well as other signs of inflammation are expressed in one score with a range from 0 (normal) to 5 (total mutilation of the joint). The scoring is based on the comparison with the standard film series as described by Larsen [8].

In each patient, we measured the Joint Alignment and Motion (JAM) scale of feet and ankle according to the description of Spiegel et al. [9]. It consists of a five-point scale for each joint. A score of 0 represents a normal range of motion (ROM) and alignment, a score of 1, a 0% to 5% decrease in ROM or malalignment, a score of 2, a 6% to 25% decrease in ROM or mild malalignment, a score of 3, a 26% to75% decrease in ROM or joint subluxation, and a score of 4, a 76% to 100% decrease in ROM or joint fusion or joint dislocation. The JAM score for an individual joint represents the most severe or limiting aspect of either motion or alignment.

Function was measured by the following variables: Health Assessment Questionnaire (HAQ), Arthritis Impact Measurement Scales (AIMS), and 5-Foot Function Index (5-FFI). The HAQ has been developed by Fries et al. and was adapted for the Dutch population [10]. The questionnaire consists of eight categories, which represent the activities of daily living, and for each category, there are two to four questions. The responses are scored on a four- point scale: 0 without difficulty; 1 with some difficulty; 2 with difficulty; and 3 impossible. The questionnaire has a final column in which respondents can indicate the use of any aid or device. The use of any of these devices is scored by at least a 2. The highest score for each of the eight categories is taken as the score for that category. The final score of the questionnaire is the averaged score of all the categories and ranges between 0 and 3.

The AIMS score is a widely used instrument and has been adapted and validated for the Dutch language and culture [11]. The score consists of 77 items divided into 12 scales. These 12 scales can be combined into five components: physical health, psychological health, symptoms, social interaction, and work. The scales vary from 0 (good health) to 10 (bad health). The components for psychological health and social interaction and work were used to describe psychosocial functioning.

The 5-FFI is a self-administered index consisting of 23 items divided into three scales (Limitation, Pain, and Disability). We used the validated five-point Dutch language version [12]. The items of the FFI-5pt are identical to those of the FFI but are rated on a five-point visual rating scale ranging from "never" (0) to "always" [4] on the Limitation scale, "no pain" (0) to "intense pain" [4] on the Pain scale, and "no difficulty" (0) to "impossible" [4] on the Disability scale. To calculate the definitive scale scores, the item scores are summed, divided by the maximum possible sum of the item scores, and then multiplied by 100. The total score is the mean of the three scale scores [12].

Statistical analysis

The association between the signs, symptoms, damage, and function parameters were calculated using Spearman's correlation. Afterwards, we performed regression analysis in order to assess the most important variables that predict the functional outcome (HAQ) in our model. For the data analysis, we used the Statistical Package for the Social Sciences (SPSS 16.0).

Results

Thirty patients were included, of whom 25 were female. The mean age was 54 years, and median disease duration was 8 years. Twenty had a positive rheumatoid factor. The median HAQ DI was 1.18, and Larsen and Sharp/van der Heijde scores were 1.0 and 4.0, respectively.

Table 1 presents Spearman's correlation coefficients of the correlation between clinical signs and function. Clinical signs were the presence of either swelling or pain as a sign of joint inflammation. Pain and swelling of the ankle showed weak but statistically significant correlation coefficients between 0.273 and 0.293 with limitation and disability, measured on the 5-FFI, as well as with the HAQ and the mobility subscale of the AIMS. The clinical signs of the forefoot joints did not correlate with any of the functional outcome measures. Of the ultrasound (US) parameters, only PDUS of the hindfoot showed a weak but statistically significant correlation with the HAQ walking.

Table 1. Spearman's correlations coefficients (p-value) between clinical signs/symptoms and function.

	Pain ankle	Swelling ae	Pain MTP's/ toes	Swelling MTP's	US PD MTP's	US PD hind foot
5-FFI limitation	0.273 (0.034)	0.290 (0.025)	-0.200 (0.126)	-0.166 (0,206)	-0.045 (0.734)	0.127 (0.334)
5-FFI pain	0.095 (0.470)	0.010 (0.940)	-0.049 (0.710)	-0.027 (0.836)	0.176 (0.178)	0.025 (0.851)
5-FFI disability	0.293 (0.023)	0.278 (0.032)	-0,248 (0.056)	-0,168 (0.200)	0.019 (0.885)	0.023 (0.860)
HAQ walking	0.098 (0.455)	0.104 (0.428)	-0.234 (0.071)	-0,189 (0.147)	0.167 (0.203)	0.374 (0.003)
Total HAQ	0.053 (0.689)	0.353 (0.006)	-0.133 (0.309)	-0.073 (0.579)	0.169 (0.196)	0.112 (0.396)
AIMS mobility level	0.257 (0.047)	0.286 (0.027)	-0.02 (0.882)	-0.029 (0.824)	0.005 (0.967)	0.142 (0.280)

5-FFI= 5 foot function index, HAQ=health assessment questionnaire, AIMS= Arthritis Impact Measurement Scales, US PD= Ultrasound power Doppler.

In Table 2, we present the Spearman's correlation coefficients between structural damage and function. Both the Larsen and the Sharp/van der Heijde showed a statistically significant correlation (r_s = 0.263 and 0.277, respectively) with the total HAQ DI. Further, the Larsen score correlated with the 5-FFI-limitation subscale (r_s = 0.282). There was a moderate negative correlation between the JAM and 5-FFI pain (r_s = –0.325). The JAM did not correlate significantly with any of the other functional measures. Swelling of the MTPs showed a negative correlation (r_s = –0.516) with disease duration. All measures of structural damage as well as the total HAQ DI correlated moderate with disease duration: JAM (r_s = –0.584), SvdH (r_s = 0.660), (Larsen r_s = 0.470), and HAQ DI (r_s = 0.470). None of the 5FFI subscales correlated with disease duration.

Table 2. Spearman's correlations coefficients (p-value) between radiographic damage/ limitation and function.

	SvdH	Larsen	JAM feet	US er HF	US er FF
5-FFI limitation	0.190 (0.154)	0,282 (0.032)	0.163 (0.212)	0.135(0.303)	0.263(0.046)
5-FFI pain	-0.054 (0.689)	0,051 (0.702)	-0.325 (0.011)	-0.149(0.255)	-0.164(0.210)
5-FFI disability	0.002 (0.991)	0.195 (0,142)	-0.080 (0.541)	0.106(0.422)	-0.033(0.801)
HAQ walking	0.001 (0.993)	0.242 (0.067)	0.047 (0.724)	0.137(0.295)	0.177(0.175)
Total HAQ	0.277 (0.035)	0.263 (0.046)	0.194 (0,138)	0.073(0.582)	0.165(0.208)
AIMS mobility level	0.134 (0.314)	0.162 (0.226)	-0.06 (0.648)	0.072(0.587)	0.173(0.187)

5-FFI= 5 foot function index, HAQ=health assessment questionnaire, AIMS= Arthritis Impact Measurement Scales, SvdH=Sharp van der Heijde, JAM=Joint Alignment Motion Scale, US er HF= Ultrasound erosion score hindfeet, US er FF= Ultrasound erosion score forefeet.

Regression model

We searched for the variables explaining the variance in the total HAQ DI. The following variables were entered: disease duration, 5-FFI total pain score, swelling ankle, US synovitis total score, and the SvdH score. These variables were entered on basis of their correlation coefficient (>0.3) or they were judged as important predictors of the HAQ in earlier studies [13]. Using the enter method, a significant model emerged ($F = 21.316$, $p < 0.001$). Sixty-four percent of the variance in HAQ DI score is explained by the following variables: disease duration, 5- FFI pain subscale, and swelling of the ankle. The regression coefficients with the 95% CI are presented in Table 3.

Table 3. Regression analyses with HAQ DI as the dependent variable.

Model	Regression coefficients	95% CI of the regression Coefficient		p-value
		Lower bound	Upper bound	
(Constant)		-.401	.310	.798
Disease duration	.478	.001	.003	.000
FFI 5 total pain score	.545	.012	.023	.000
Swelling ankle	.281	.140	.521	.001
US synovitis total score	.118	-.013	.071	.176
SvdH total score	.068	-.005	.011	.428

Standardized coefficients (b) and their CI, adjusted R^2 0.64 FFI Foot Function Index, US ultrasound, SvdH Sharp/van der Heijde, CI confidence interval.

Discussion

In this study, we explored associations between clinical signs and symptoms, structural damage, and function in connection with disease duration and the contribution of the individual foot segments.

Our data suggest that impaired foot function is associated more with signs and symptoms of the ankle than with forefoot complaints. Function of the foot is only weakly associated with overall radiological damage but again with a larger impact of the hindfoot. Finally, disease duration influences damage and function as well.

When regarding clinical signs in relation to function, we found that the results of our observational cross-sectional study are partially in line with earlier studies. In our study, pain and swelling of the ankle correlated weakly but statistically significantly with function, whereas forefoot symptoms did not. These findings confirm earlier studies suggesting that subjective pain of the forefoot does not correlate with

function [14] and that patients considered their ankle complaints more impactful than forefoot complaints [1]. The ultimate function of the feet, walking, is severely and more impaired by rear foot disease than by forefoot involvement [15].

Regarding the relation between radiological damage and function, we found that both the Larsen and the Sharp/van der Heijde score correlated weakly with the HAQ DI but fell out of the regression model. The Larsen score correlated with the 5-FFI-limitation subscale, this is in line with preceding studies, which showed that general joint damage is correlated with loss of function [4, 13, 16]. Furthermore, there was a weak correlation between the Larsen score (ankle, talonavicular, and subtalar joint) and the 5-FFI-limitation subscale, which may reflect the seriousness of destruction of the hindfoot and ankle.

With disease duration, function (HAQ) also worsened. The triangle of increasing radiological damage, worsening function with longer disease duration has been described by many others, varying from stable progression rate [17] to a steeper worsening, but earlier plateau [18]. Belt et al. concluded that after 20 years of follow-up, the subtalar joint and ankle were affected in 24 of the 103 patients but leading to severe impairment [19]. The JAM, presented as a measure of joint deformity, also correlates with disease duration in our rather established RA cohort. In an early RA population, one might imagine that the JAM predominantly reflects disease activity and would not show a relationship with disease duration. Swelling of the MTPs correlated negatively with disease duration. This might reflect the treatment effect and among others is shown in the study of Welsing et al. [20].

In the regression analysis, we found that disease duration, pain, and swelling of the ankle were the only significant predictors of the HAQ DI. This is in line with other studies, which report pain as one of the most important predictors of the HAQ DI followed by disease activity and radiographic damage [21, 22]. Most large cohort studies report a significant predictive value for radiographic damage on the HAQ DI. The lack of significance in our cohort might possibly be explained by the fact that we only used the Sharp/van der Heijde and Larsen scores of the foot and ankle, scores of the hands and large joints were not included. In most studies, the Sharp/ van der Heijde score is not specified. Hulsmans et al. demonstrated that approximately half of the Sharp/van der Heijde score could be attributed to the damage of the feet. Extrapolating this to our current data, one might assume that the correlations regarding radiographic damage would have been larger [17]. Moreover, the total number of patients in this study was only small.

Although lately more interest in the foot in RA arises, we still think that the subject is somewhat neglected. It is illustrative that in the DAS 28, the most widely used instrument to measure disease activity in RA, the feet are not included, sometimes

leading to an invalid definition of remission in individuals [23]. This may not only lead to insensitive scoring on population level (in the case of research) but also to the neglect of foot inflammation or damage, especially where we sense a tendency towards more strategy (DAS 28) driven care [24–26]. Within the rheumatic foot, most attention is focused on the joints of the forefoot. However, our study supports the idea that involvement of the hindfoot and ankle may contribute to impairment and disability in the same way as the forefoot as has been suggested earlier [1, 15]. A limitation of this study is the small number of patients studied, which limits the ability to find strong correlations, but despite the small number and weak correlations, we found some significant correlations indicating the existence of true relationships. Another drawback is that the cross- sectional design obstructs conclusions regarding time relations. However, cross-sectional studies including patients with a broad range of disease durations, seem to provide fairly reliable estimates of the course of health outcomes [27]. Future research should focus longitudinally on the relation between clinical signs and structural damage of the foot and especially the ankle. In conclusion, we suggest that in RA patients, pain and swelling of the ankle contribute more to disability than forefoot signs. In daily clinical practice and clinical research, rheumatologists should pay attention to the ankle and hindfoot as well, as they contribute to disability.

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7

Foot and ankle kinematics in rheumatoid arthritis: the influence of foot and ankle joint and leg tendon pathologies

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Abstract

Introduction: From early onset of the disease, patients with rheumatoid arthritis (RA) suffer from walking impairments. RA gait characteristics such as reduced walking speed and altered joint kinematics have been observed compared to healthy subjects. Clinically, pathologic effects of RA on foot and ankle structures have been studied, but little is know how they relate to kinematic changes during gait. The aim of this study was to analyse the relationship between clinically observed pathologies of foot and ankle joints and leg tendons and the corresponding gait kinematics.

Methodology: Gait of 25 subjects with varying stages of RA disease was recorded. Maximum first metatarso-phalangeal (MTP I) dorsiflexion, midfoot pronation range of motion and subtalar eversion range of motion were assessed. Magnetic resonance imaging was performed of each subject: MTP I, midfoot and hindfoot synovitis and erosion scores and leg tendon involvement were determined. Subtalar alignment and passive motion as well as MTP I passive motion, were included as representatives of daily clinical assessment. Spearman correlation tests were used to analyse the relationships between the clinical and kinematic parameters ($p<0.05$).

Results: Maximum MTP I dorsiflexion at pre-swing was related to reduced MTP I passive motion (correlation coefficient, CC -0.50), MTP I synovitis (CC -0.63) and erosion (CC -0.69), midfoot synovitis (CC -0.40) and erosion (CC -0.54) and hindfoot erosion (CC -0.40). Midfoot pronation range of motion during single-stance was related to subtalar alignment (CC -0.51) and Achilles tendon involvement (CC +0.42). Subtalar eversion range of motion during single-stance was related to subtalar alignment (CC -0.55) and peroneus longus tendon involvement (CC -0.41).

Conclusions: Significant relationships were observed between foot and ankle gait kinematics and structural pathologies.

Introduction

At the onset of the disease, 60% of the patients with rheumatoid arthritis (RA) suffer from walking impairments while this percentage is 40% later on in the disease [1]. These impairments have been related to the effects of RA on, among others, walking speed and foot and ankle structures. Metatarsal pain, global foot pain, disease activity, swollen joint count of foot and hindfoot deformity all affect and impair walking at some point during the disease process [2-5]. Several studies have analysed foot and ankle joint kinematics in subjects with RA during walking at comfortable speed to attain insight in gait differences compared to healthy subjects [6-9]. However, little is known about the effects of local structural pathologies on foot and ankle joint kinematics in RA subjects.

Turner analysed the effects of predominantly forefoot, hindfoot or combined deformation in RA subjects on foot and ankle kinematics and observed changes in both fore foot and hindfoot kinematics [10]. Laroche studied the effect of metatarso-phalangeal (MTP) stiffness on gait parameters in RA subjects [11]. MTP stiffness was significantly related to walking speed, knee flexion and foot angle at toe-off, though the effects on foot and ankle joint kinematics were not analysed. The effects on foot and ankle kinematics of other frequently reported structural impairments such as tibialis posterior tendon involvement and ankle arthritis have been studied, but not in a RA population [12-15].

A better understanding of the effects of foot and ankle structural pathologies on foot and ankle kinematics during gait may support clinical decisions in both conservative and surgical treatment for this complex disease [10,15-17]. In addition, for daily clinical practice a better understanding between easy assessable clinical scores and gait kinematics, if existing, would be of use. Assessment of structural pathologies usually requires technologies such as X-ray or magnetic resonance imaging (MRI), but a clinical score like the joint alignment of motion (JAM) [18] can be easily, quickly and frequently determined and has already been related to foot function impairments [2,19].

The aim of this study was to analyse the relationship between clinical foot and ankle assessment (JAM), structural inflammation and damage and joint kinematics of the foot and ankle during gait of subjects with varying degrees of RA.

Methodology

Subjects

Twenty-five RA patients (out-patient clinic) with varying foot and ankle affections and disease duration participated in this study. An informed consent was obtained from all subjects prior to participation. All subjects met the 1987-ACR criteria for rheumatoid arthritis and had not undergone orthopedic surgery on their feet and ankles. The subjects, 3 male and 22 female, had a mean age of 51 years (range 23 to 78 years) and mean disease duration of 9 years (range 0.5 to 23 years). This study received ethical approval from the local medical ethics committee.

Protocol

Gait analysis was performed, with subjects walking at comfortable walking speed, using a 6 infra-red video camera based (1.3 megapixel, 100 Hz) motion analysis system (Vicon Nexus, Vicon Motion Systems, Oxford Metrics Group, UK). Nineteen infra-red reflective markers were attached to the lower limbs of the subject according to the method described by Simon [20] (figure 1). Both feet were measured according to the above protocol, but only the foot causing most discomfort was used in the analysis. During each session, 8 to 10 trials were recorded to obtain sufficient usable steps in the analysis.

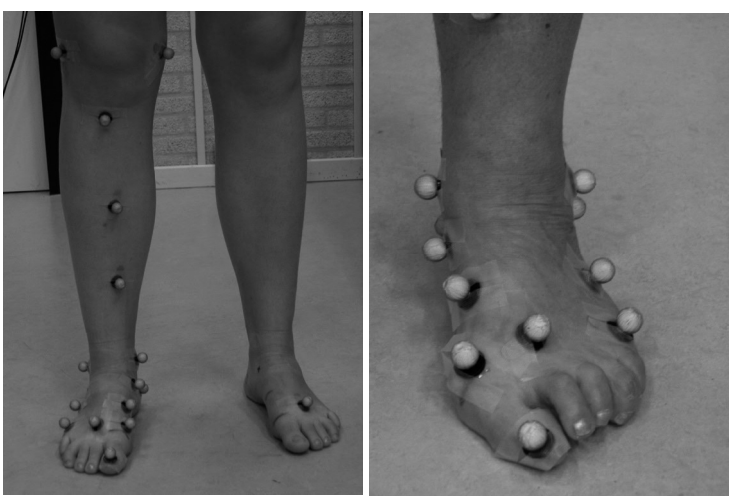

Figure 1: a. Leg, foot and ankle marker placement according to Simon [20]; b. Foot and ankle marker placement of more severe deformed foot.

Data analysis

The temporal parameters walking speed, step length, stride length, stride width, stride time and double stance phase were assessed for each subject from the marker co-ordinate recordings in a special LabVIEW script (V7.2, National Instruments). This script was also used to normalise the data to the stance phase using the specified initial contact and toe-off indications in Vicon Nexus (Vicon Motion Systems). The method developed by Simon was applied to assess foot and ankle kinematics and their joint kinematic definitions and nomenclature will be used.

For each subject, the mean value of the joint angles motion, as function of the percent stance phase, was assessed using 6 to 7 trials. The stance phase was subdivided into three parts: foot-loading, single-stance, and pre-swing. Foot-loading was defined from initial heel contact to opposite foot toe-off (first double-stance), single-stance was defined from opposite foot toe-off to opposite foot heel contact, and pre-swing was defined from opposite foot heel contact to foot toe-off (second double-stance). For each subject the maximum, the minimum and the range of motion (ROM) values were calculated for each joint and each part of the stance phase. ROM was defined as the maximum minus minimum angle. In further analyses, the maximum first metatarsal-phalangeal (MTP I) dorsi flexion at pre-swing, the midfoot supination-pronation ROM at single-stance and the subtalar everion-inversion ROM at single-stance were evaluated. These foot motions were identified as being influenced by the RA disease as an independent factor in addition to the corresponding, often reduced, walking speed [21].

The three kinematic parameters were correlated with clinical parameters assessed by an experienced radiologist and rheumatologist. Synovitis and bone erosions of the MTP I, the midfoot and hindfoot were assessed by means of MRI [16,22]. The exact MRI protocol and reliability of the method have been described in a recent publication [23]. Bone erosion was scored from 0-10 and synovitis from 0-3. The MRI bone erosions of the proximal and distal part of the MTP I joint were combined as the MTP I erosion. Midfoot erosion was defined as the sum of the MRI bone erosion scores of the proximal metatarsals, the cuneiforme, the cuboid and the navicular bone. Hindfoot erosion was defined as the sum of the MRI bone erosion scores of the calcaneal and talar bone. MTP I synovitis was obtained directly from the MRI synovitis score for the MTP I joint. The MRI joint synovitis of the tarsometataral and cuneonavicular joint formed the midfoot synovitis. The MRI joint synovitis of the tibiotalar, talo(calcaneo)navicular, calcaneotalar and calcanealcuboid joint formed the hindfoot synovitis. An overview of the definition of the clinical erosion and synovitis parameters is given in table 1. Furthermore, involvement of the tibialis posterior, peronei, triceps surae and flexor hallucis longus tendons were assessed

from MRI. The tendon involvement scores were calculated by adding the MRI tendon scores (0-1) for inhomogeneity, fluid (collection), thickening, enhanced signal intensity and tearing, as a sign of tenosynovitis or damage of the tendons. The joint alignment and motion (JAM)[18] was assessed and the sub-scores subtalar alignment and passive motion and MTP I passive motion were analysed as individual parameters. Involvement of the MTP 2-5 joints and flexor digitorum longus was not taken into account as the MTP 2-5 were not represented in the computer model.

Statistical analysis

Statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). The gait and clinical parameters were not normally distributed, hence Spearman correlation tests were used to analyse the relationship between the different gait and clinical parameters. The level of significance was set to 0.05.

Results

Table 1. Definition of the clinical erosion and synovitis parameters.

Clinical parameter	MRI bone erosion or joint synovitis scores
Erosion MTP I	Bone erosion of proximal and distal MTP I
Synovitis MTP I	Synovitis of MTP I joint
Erosion midfoot	Bone erosion of proximal metatarsals, cuneiforme, cuboid and navicular bone
Synovitis midfoot	Synovitis of tarsometataral and cuneonavicular joints
Erosion hindfoot	Bone erosion of calcaneal and talar bone
Synovitis hindfoot	Synovitis of tibiotalar, talo(calcaneo)navicular, calcaneotalar and calcanealcuboid joints

Table 2. Results of the Spearman correlation tests between clinical and kinematic parameters: the correlation coefficient (CC) and significance level (p). In bold, the assessed significant relationships.

Spearman correlation test	MTP I max. dorsiflexion pre-swing		Midfoot pronation ROM at single-stance		Hindfoot erversion ROM at single-stance	
	CC	p	CC	p	CC	p
Subtalar pas. motion JAM	-0.35	-0.09	-0.22	0.29	-0.20	0.33
MTP I pas. motion JAM	**-0.50**	**0.01**	-0.23	0.28	-0.26	0.20
Subtalar alignment JAM	-0.38	0.06	**-0.51**	**0.01**	**-0.55**	**0.01**
Synovtis MTP I MRI	**-0.63**	**0.00**	-0.01	-0.96	-0.36	0.09
Erosion MTP I MRI	**-0.69**	**0.00**	-0.34	0.10	-0.22	0.30
Synovitis Midfoot MRI	**-0.40**	**0.05**	-0.21	0.33	0.00	0.99
Erosion Midfoot MRI	**-0.54**	**0.01**	-0.29	0.17	-0.19	0.93
Synovitis Hindfoot MRI	-0.31	0.15	-0.38	0.06	0.07	0.73
Erosion Hindfoot MRI	**-0.40**	**0.05**	-0.30	0.16	-0.13	0.53
Tib. pos. tendon involv. MRI	-0.02	0.91	0.05	0.83	-0.06	0.80
Fl. hlx. l. tendon involv MRI	-0.12	0.58	0.03	0.87	0.08	0.72
Peron. tendon involv. MRI	-0.26	0.22	-0.21	0.33	**-0.47**	**0.02**
Achiilles tendon involv. MRI	-0.04	0.86	**0.42**	**0.04**	0.14	0.51

The maximum MTP I dorsiflexion at pre-swing was significantly influenced by local pathologies of the MTP I: high negative correlation coefficients (CC) of -0.63 and -0.69 were assessed for the correlation with synovitis and erosion of the MTP I, respectively. A negative CC indicates that more MTP I erosion and inflammation resulted in less MTP I dorsiflexion at pre-swing. Furthermore, erosions of the midfoot and hindfoot and the MTP I passive motion measured clinically in the JAM

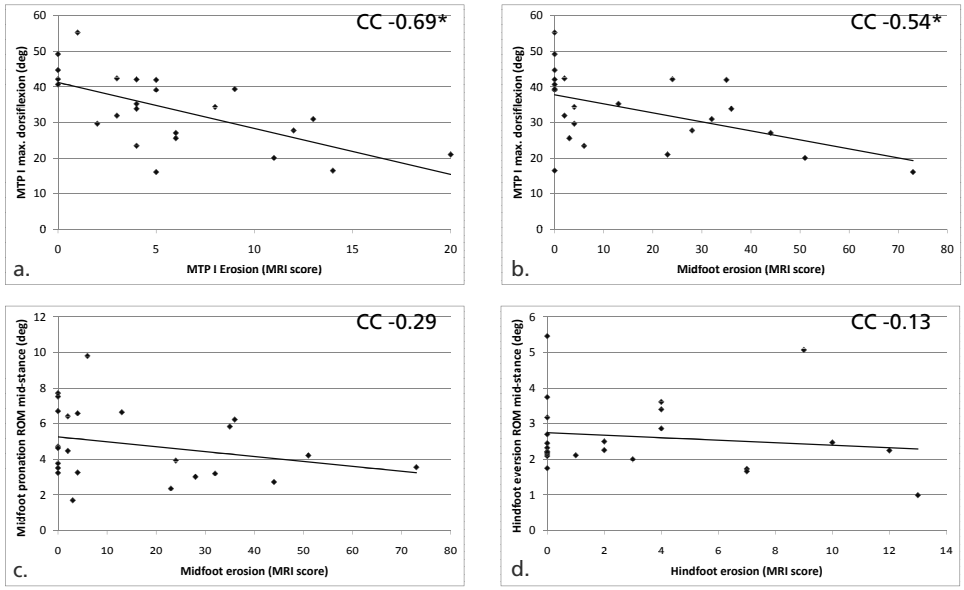

Figure 2: Individual effects of joint erosion on joint motion with corresponding linear regression line and Spearmans correlation coefficient (CC, * statistically significant): a, b. Maximum MTP I dorsiflexion as function of MTP I and midfoot erosion, respectively; c. Midfoot pronation ROM as function of midfoot erosion; d. Hindfoot eversion ROM as function of hindfoot erosion.

Midfoot pronation and hindfoot eversion ROM during single-stance were not significantly influenced by local erosions or inflammations, but only by the alignment of the subtalar joint as measured in the JAM and tendon involvement (table 2, figure 2). Midfoot pronation motion was significantly influenced by pathologic changes of the Achilles tendon (CC +0.42) and more severe Achilles tendon involvement was related to more midfoot pronation motion. More severe involvement of the peroneus longus tendon resulted in significantly less hindfoot eversion motion at single-stance (CC -0.46). No significant effect was observed for involvement of the tibialis posterior tendon on midfoot or hindfoot motion (figure 3).

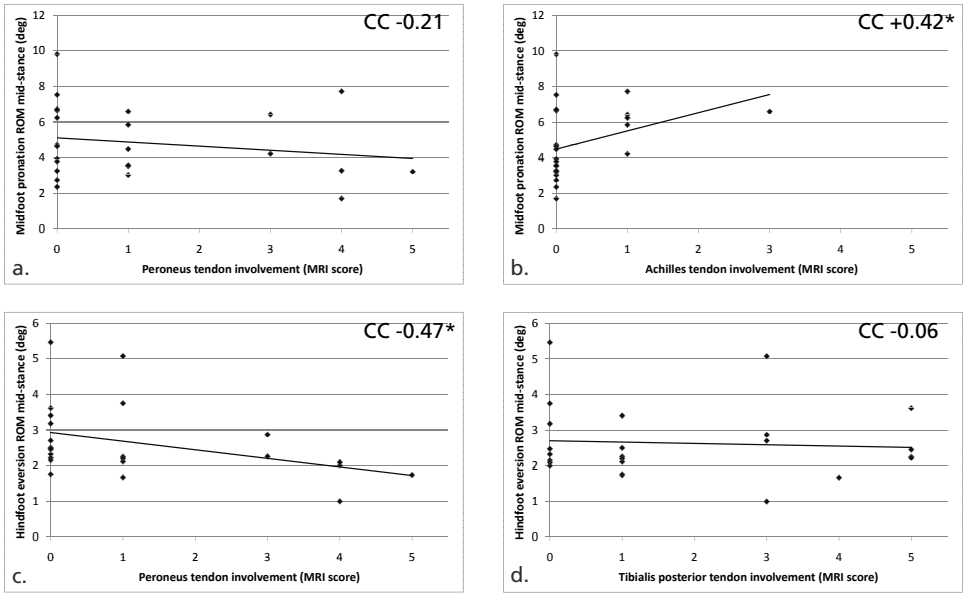

Figure 3: Individual effects of tendon involvement on midfoot (a, b) and hindfoot (c, d) kinematics with corresponding linear regression line and Spearman's correlation coefficient (CC, * statistically significant).

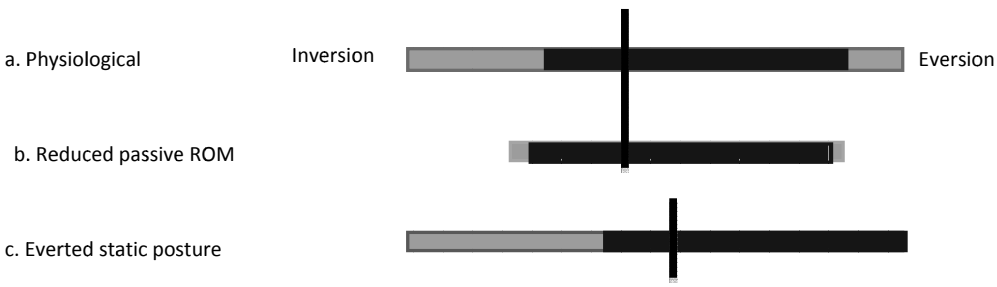

Figure 4: Hindfoot in/eversion motion with active ROM (dark) required during gait, available passive ROM (light) and posture of the hindfoot in the frontal plane (black line). a. Physiological situation: The active ROM required during gait is less than the available ROM. b. The required ROM during gait is still possible even though the available ROM is reduced as a consequence of joint stiffness. c. Due to an initial everted hindfoot posture the joint reaches it's maximum eversion value during the required active ROM.

Discussion

The aim of this study was to analyse the relationship between clinically observed pathological changes in the joints and tendons of the foot in RA subjects and their corresponding MTP I, midfoot and hindfoot motion during gait. In addition, the relationship between sub-scores of the JAM and joint kinematics were analysed. Although RA is a complex disease with multiple impairments to the foot and ankle, relationships between clinical and kinematic parameters were found in our cross-sectional cohort.

Joint involvement

The maximum MTP I dorsiflexion at pre-swing was significantly influenced by MTP I mobility and by joint pathologies in the whole foot and ankle. Synovitis and erosion of the MTP I joint result in pain and or stiffness of the joint. MTP I pain may result in the desire to unload the pressure applied to the forefoot and reduce the range of MTP I motion during gait. This can be achieved, among others, by reducing the walking speed, which has already been observed in RA subjects with forefoot pain [4]. In healthy subjects, lower walking speed resulted in lower peak pressures under MTP I [24], required less MTP I dorsiflexion and ankle range of motion at pre-swing [24], which were both related to peak pressure under MTP I and hallux [26]. To further unload their MTP I, RA subjects increase their cadence and reduce their stride length [27] so, for similar walking speeds, an even lower MTP I dorsiflexion at pre-swing can be achieved. Nevertheless, in RA subjects an increased peak pressure under the MTP I was observed compared to healthy subjects and was related to damage to the forefoot in RA subjects [28]. MTP I stiffness directly limits the maximum attainable MTP I dorsiflexion during gait: Canseco reported a significant reduction of MTP I maximum dorsiflexion in subjects with hallux rigidus compared to healthy subjects [29] and furthermore, in RA subjects, MTP I stiffness was related to walking speed [11]. Joint erosions of the midfoot and hindfoot resulted in less MTP I dorsiflexion at pre-swing. These hindfoot findings confirm earlier studies that observed effects of hindfoot arthrosis (in a general population) [14] or hindfoot deformities (in a RA population) [4,10], on MTP I motion pre-swing and stride length. No studies were found that studied the effects of mid-foot erosion on gait parameters.

Midfoot supination-pronation and hindfoot eversion-inversion motion during the single-stance phase were related to hindfoot alignment but not to midfoot or hindfoot erosion or synovitis. Only for the more severe cases of hindfoot erosion, reduced midfoot pronation and hindfoot eversion motion were observed. The latter corresponds to similar findings reported by Turner who only observed significant

changes in hindfoot and fore foot kinematics in a group of RA subjects with severe hindfoot deformations and not in a group with mostly fore foot deformations [10]. Also in subjects with severe ankle arthrosis changes in hindfoot kinematics were observed [14]. This may be explained by the fact that during gait, only a limited amount of hindfoot motion is required in the frontal plane (Figure 4a). The data suggest, that only a more advanced stadium of hindfoot pathologies with severe stiffness may influence and impair midfoot and hindfoot kinematics (Figure 4b). Foot posture, however, shifts the required motion with regards to the available motion (Figure 4c) and a pronated foot type was related to maximum hindfoot eversion during gait in healthy and in RA subjects [30,31]. Hence, in our study the increased hindfoot alignment of RA subjects with a more everted static posture of the hindfoot may result in less available eversion motion during single-stance.

Tendon involvement

Statistical significant relationships were observed between tendon involvements and midfoot and hindfoot motion during gait. Achilles tendon involvement was related to an increased pronation motion of the midfoot. Several studies have reported that tensioning of the Achilles tendon results in reduced inclination of the calcaneus, flattening of the medial arch and tensioning of the plantar fascia [32-35]. Consequently, damage to the Achilles tendon may reduce the pre-tensioning capacity to the foot structures and result in more midfoot motion during mid-stance. The studies including Achilles tensioning did not report on its effect on midfoot and hindfoot motion in the frontal plane.

More severe involvement of the peroneus longus tendon was related to less hindfoot eversion motion during single stance. In this study, involvement of the peroneus longus tendon was strongly related to the subtalar alignment sub-score of the JAM and to hindfoot synovitis and erosion. Hindfoot joint synovitis can lead to destruction of the ankle ligaments. Both have been associated with peroneus longus tendon involvement [38], but also with changes in passive ankle joint ROM and alignment [32,39,40]. As subtalar alignment also significantly influences midfoot motion it is not clear at present, if the peroneus longus involvement and reduced midfoot motion have a causal relationship.

Tibialis posterior tendon involvement was related to the subtalar passive motion sub-score of the JAM, but did not influence the midfoot supination or the hindfoot eversion motion during mid stance. Eight of our RA subjects did not have pathological involvement of their tibialis posterior tendon and another seven only had inhomogeneities. However, also for those RA subjects with more severe involvement of the tibialis posterior tendon, no reduction of midfoot and hindfoot

motion during mid stance was observed in our study. Other studies did report a statistically significant effect of tibialis posterior tendon dysfunction on fore foot and hindfoot kinematics in subjects with severe tibialis posterior tendon pathologies [13]. It must be noted though, that in these studies the subjects also had a flatfoot or significant hindfoot eversion posture, which was not always the case in our study. So possibly, the observed effects in the other studies might be attributed mostly to foot alignment. As described previously, the foot alignment was found to significantly influence hindfoot eversion and midfoot pronation motion in our study.

Limitations

The RA disease process results in multiple pathologies to foot and ankle structures and in this study a cross-sectional cohort of RA subjects, with various stages of the disease and corresponding pathologies was included. Due to the complexity of the disease, inhomogeneity of the study population and a limited number of subjects, the analysis of relationships between clinical and gait parameters may have resulted in the assessment of strong relationships only. In future, it is suggested to study the effects of pathologies on kinematics in a more homogeneous study population and preferably, in a long-term study.

Furthermore, due to limitations of the used foot and ankle model, the lateral fore foot (MTP 2-5) was not taken into account in this study. As these structures are frequently impaired in RA subjects, future kinematic analysis studies should consider taking the motion of the MTP 2-5 joints or the lateral forefoot into account.

Clinical relevance

Significant effects of joint and tendon pathologies on foot and ankle kinematics were observed from the onset of the pathologies. As these pathologies deteriorate from the beginning of the disease, subtalar alignment, MTP I passive motion, foot and ankle joint synovitis and erosions and Achilles and peroneus longus tendon involvement should be monitored and treated carefully. The JAM sub-scores, MTP I passive motion and subtalar alignment, are easily measured in daily clinical practice without burden to the patient. Large JAM sub-score variability was observed between subjects. However, long-term individual monitoring may provide an easy measure to estimate foot and ankle function during gait. Furthermore, the JAM score and its sub-scores have already been related to functional scores [2,19], so JAM monitoring would provide insight in foot and ankle function during gait and in daily life.

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8

Summary and conclusions

The main theme of this thesis is foot and ankle complaints in patients with RA. This choice results from the practical observations that often as clinical routine, the disease activity is determined by means of computing a DAS 28. That means that the feet and or ankles don't have to be examined during the visit. There are other reasons to avoid the feet. For patients, it is often laborious to take off their shoes, especially when it concerns customized shoes, or when due to hand damage, unlacing and taking off the shoes lasts minutes. Feet often smell more or less, which is annoying for the rheumatologist and uncomfortable for the patient. The neglect of feet in clinical practice prevents targeted treatment and may lead to untimely referral to podiatrist or orthopaedic surgeon, or to late dose adjustment of the DMARD therapy. Unnecessary inflammation and or damage can be the result. In order to form hypothesis on the nature of and the sequences of events in foot involvement, we conducted a pilot study with thirty outpatient clinic RA patients. All patients underwent clinical examination, then additional imaging studies were performed (ultrasound, X-ray and MRI) and patients filled in questionnaires. Afterwards, gait analysis was performed in all patients. The obtained data could not be presented in one publication, hence the result of our study that was meant to create hypotheses. The results of gait analysis are published in separate PhD thesis of engineer, Mrs. R.Dubbeldam.

In **chapter 1** of this thesis, we give an overview of the history of gait analysis. At first, the different parts of gait (kinetics, kinematics, muscle mechanics and EMG) and how they can work together are explained. There has been a long tradition of interest in biomechanics of the body, dating from Aristotle. He wrote a book called "De Motu Animalium" - On the Movement of Animals, in which his fascination with anatomy and structure of living things is proven. Many other scientists after him shared their interest for biomechanics with him, especially during the renaissance. In the 19th century, biomechanics' history got a new boost with the moving picture inventions of Marey, Muybridge and Lumiere, eventually leading to an early precursor of movie. Another major breakthrough is the invention of the computer, and hence the facilitation of data acquisition post processing and interpretation. The use of gait analysis was initially mainly applied in the diagnostics and treatment planning of cerebral palsy. Only last decades, gait analysis is applied in other areas like RA.

In **chapter 2** a systematic literature search was performed, in order to give an overview on the existing gait studies in RA, their main conclusions and the clinimetrical properties. After an in detail described literature search, 78 original gait studies were included for further data extraction. The clinimetrical quality

of the 78 included studies measures (according a tailored QUADAS item list and proposed clinimetrical criteria by Terwee et al.) was moderate. General conclusions regarding the walking abnormalities of RA patients were described: the RA patient walks slower, with a longer gait cycle, a shorter step length, a longer double support time and a lower cadence. The reduced speed may be caused by antalgic walking patterns and muscle weakness. Plantar pressure is often abnormal, can be higher or lower as a sign of damage or to avoid pain. Kinematic changes are: decreased ranges of motion combined with reduced joint moments and power. There is a delayed heel rise, a decreased plantar flexion and an abnormal eversion of the rear foot. Future gait research should focus on more uniformity in methodology. When this need is satisfied, more clinical applicable conclusions can be drawn, which eventually benefits the treatment of walking problems in RA patients.

In **chapter 3**, we describe the prevalence of and relation between rupture or tenosynovitis of the Flexor Hallucis Longus (FHL) tendon and range of motion, deformities and joint damage of the forefoot in our cohort RA patients with foot complaints.
Our patients were examined clinically for the presence of pes planus and range of motion (ROM), radiographs were scored looking for the presence of forefoot damage, and ultrasound examination was performed, examining the presence of tenosynovitis or rupture of the FHL at the level of the medial malleolus. The correlation between the presence or absence of the FHL and ROM, forefoot damage and pes planus was calculated.
In 11/60(18%) of the feet, a rupture of the FHL was found. This was associated with a limited motion of the MTP1-joint, measured on the JAM ($\chi 2 = 10.4$, $p = 0.034$), a higher prevalence of pes planus ($\chi 2 = 5.77$, $p = 0.016$) and a higher prevalence of erosions proximal at the MTP-1 joint ($\chi 2 = 12.3$, $p = 0.016$), and joint space narrowing of the MTP1 joint ($\chi 2 = 12.7$, $p = 0.013$).
Thus, it has to be concluded that rupture of the flexor hallucis longus tendon in RA-patients is associated with limited range of hallux motion, more erosions and joint space narrowing of the MTP-1-joint, as well as with pes planus.

In **chapter 4**, we described the relation between clinical and ultrasound parameters of wrist arthritis and secondly their relation to function.
In 33 RA patients with clinically observed wrist arthritis, clinical and US parameters were measured. Function was evaluated with the SODA-S (Sequential Occupational Dexterity Assessment-Short) and the DASH-DLV (Disabilities of the Arm, Shoulder and Hand-Dutch Language Version).

Correlation coefficients between clinical and ultrasound parameters of RA wrist inflammation in this study were fair to moderate. Of the clinical signs, only pain shows a good correlation with function. The ultrasound parameters also correlate well with function. For clinical practice, this means that examination should not be limited to clinical signs and symptoms, but that additional ultrasound examination might be valuable in the evaluation and treatment of rheumatoid wrist arthritis, especially in impaired function.

In **chapter 5**, we present the results of the first interreader and intrareader agreement of the RAMRIS scoring system in the assessment of feet in RA. In rheumatology, magnetic resonance imaging (MRI) is predominantly applied in the assessment and outcome measurement of RA in hands and wrists, leading to the development of the RAMRIS (RA-MRI-Scoring) system, initiated by the Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT). Twenty-nine patients with RA who had radiological damage and/or arthritis underwent MRI. Two experienced readers independently read both complete sets, according to the RAMRIS recommendations. One reader read 6 random sets after the initial session, in order to assess the intrareader agreement. For evaluation of the intrareader and interreader reliability, quadratic-weighted κ scores were calculated per joint and lesion. For the forefeet, interreader scores were excellent, ranging from 0.77 (bone edema) to 0.95 (bone erosion). Hindfoot interreader agreement scores were highest for erosion (0.90) and synovitis global score (0.88), but edema and synovial thickness agreement were also acceptable (0.83 and 0.86). Intrareader scores were on the whole slightly lower. We concluded that the reliability (interreader and intrareader agreement) in the assessment of the rheumatoid foot according to the RAMRIS method is excellent.

In **chapter 6**, we addressed the associations between clinical signs and symptoms, radiographic changes, and function in connection with disease duration. Secondly, we described the contribution of several foot segments to the clinical presentation and function. We compared radiographic, ultrasound, clinical, and functional parameters of the feet and ankle. Pain and swelling of the ankle were correlated with limitation and disability (0.273 to 0.293) as measured on the 5-Foot Function Index (FFI). The clinical signs of the forefoot joints did not influence any of the functional outcome measures. Radiographic scores for both forefeet (SvdH) and hindfeet (Larsen) were correlated with the total Health Assessment Questionnaire Disability Index (HAQ DI) and the 5-FFI-limitation subscale. Pain and disease duration, more than radiographic damage, influence the total HAQ DI significantly. With the progression of time, structural damage and function of the rheumatic foot worsen

in RA patients. Pain and swelling of the ankle contribute more to disability than radiographic damage of the foot and ankle.

In **chapter 7** we describe the relationship between clinically observed pathologies of foot and ankle joints and leg tendons and the corresponding kinematics in the gait of 25 subjects with RA. Maximum metatarsophalangeal I (MTP I) dorsiflexion, mid foot pronation range of motion and subtalar eversion range of motion were assessed. Magnetic resonance imaging was performed of each subject: MTP I, mid foot and hind foot synovitis and erosion scores and leg tendon involvement were determined. Subtalar alignment and passive motion and MTP I passive motion, were included as representatives of daily clinical assessment, according to the JAM (joint alignment motion scale). Maximum MTP I dorsiflexion was related to MTP I passive motion (correlation coefficient, CC -0.50), MTP I synovitis (CC -0.63) and erosion (CC -0.69), mid foot synovitis (CC -0.40) and erosion (CC -0.54) and hind foot erosion (CC -0.40). Mid foot pronation range of motion was related to subtalar alignment (CC -0.51) and Achilles tendon involvement (CC +0.42). Subtalar eversion range of motion was related to subtalar alignment (CC -0.55) and Peroneus longus tendon involvement (CC -0.41). As these pathologies deteriorate from the beginning of the disease, subtalar alignment, MTP I passive motion, foot and ankle joint synovitis and erosions and Achilles and Peroneus longus tendon involvement should be monitored and treated carefully. The JAM sub-scores, MTP I passive motion and subtalar alignment, are easily measured in daily clinical practice without burden to the patient. Large JAM sub-score variability was observed between subjects. However, long-term individual monitoring may provide an easy measure to estimate foot and ankle function during gait.

Discussion

Structural damage and inflammation do influence kinematic parameters of gait, as we demonstrated in chapter 7, but there is a lot that we still don't know. Correlations were found, but the exact sequence of events is unknown. We could not confirm the often-mentioned insufficiency of the posterior tibial tendon that supposedly would cause collapse of the medial arch and subsequent stance deviations of the hindfoot and forefoot abduction. However, other tendons like the flexor hallucis longus and the peroneal tendons, were of importance in stance and kinematic abnormalities in RA in our study.

The main insight of this thesis is that problems of the foot and ankle in rheumatoid arthritis are not limited to the forefoot but that hindfoot and the soft tissues are also significantly involved. These conclusions should at least lead to an adaptation of daily clinical practice. Instead of a DAS 28 as clinical routine, a complete DAS (of 44 joints) should be done, to avoid neglect of the feet. Additionally, the JAM could be of use: it is an easy way of assessing damage and inflammation in the rheumatoid joint, not for comparing patients as there is a wide inter-subject variation, but as a longitudinal tool. When deterioration is noted by simple clinical assessment, additional investigation should be prompted. I would advocate MRI. We demonstrated that this is a reliable instrument in the assessment of damage and inflammation. It does not only provide data on erosive bony changes, but gives a thorough insight in the soft tissues. In our cohort for example, deviations of tendons were present in about 70% of the patients. After careful diagnosis, targeted treatment or subsequent steps can be initiated, like local injection therapy, adaptation of DMARD treatment or timely referral to a podiatrist or orthopaedic surgeon. We do realise that the efficacy of these treatment modalities still has to be proven, but given the underlying mechanisms we think this is likely. To determine the exact sequence of events in rheumatoid foot and ankle involvement, and their consequences for gait, a longitudinal study is necessary. The outcome of our study can function as a guide to formulate hypotheses, as cross-sectional studies in the past have been proven to provide reliable indications of health assessment outcome in chronic diseases. Patients with and without foot and ankle complaints should be included at the start of disease and a full gait analysis should be carried out, in combination with clinical examination and additional imaging. Such research however is costly and will only lead to treatment hypotheses, which again must be tested. The path of gait analysis research in RA has not yet been walked to the end, but many steps will have to follow. And that will benefit the RA patient.

9

Samenvatting en conclusie

Het belangrijkste onderwerp van dit proefschrift is voet- en enkel klachten bij patiënten met RA. De keuze voor dit onderwerp komt voort uit de praktische observatie dat in de klinische praktijk het voetonderzoek niet voorop staat. De ziekte activiteit en schade worden in de klinische praktijk meestal vastgelegd door middel van een DAS 28 scoring. Dat betekent dat de voeten en/of enkels niet hoeven te worden onderzocht tijdens het consult. Er zijn nog andere redenen om het onderzoek van de voeten en de enkels te vermijden. Voor patiënten is het vaak lastig hun schoenen uit te trekken, vooral wanneer het gaat om othopedisch schoeisel, of wanneer door handdeformaties, losmaken van de veters en uitdoen van de schoenen soms minuten duurt. Voeten ruiken nogal eens minder fris, dat is vervelend voor de reumatoloog en ongemakkelijk voor de patiënt. De verwaarlozing van het voetonderzoek in de klinische praktijk kan leiden tot te late verwijzing naar een podotherapeut of orthopedisch chirurg, of te late dosisaanpassing van DMARD therapie. Onnodige ontsteking en/of schade kan optreden. Om hypothesen te vormen over hoe, wanneer en in welke volgorde voetproblemen optreden bij RA patiënten, voerden we een studie uit met dertig poliklinische RA patiënten. Alle patiënten ondergingen klinisch onderzoek; aanvullend werd beeldvormend onderzoek gedaan (echografie, röntgenfoto's en MRI), en patiënten vulden vragenlijsten in. Daarna werd bij alle patiënten gangbeeldanalyse uitgevoerd. Dit onderzoek is opgezet als hypothesevormend. Uiteindelijk bleek dat de hoeveelheid data niet kon worden verwerkt in één publicatie; het uiteindelijke resultaat is dit proefschrift. De resultaten van de gangbeeldanalyse worden afzonderlijk gepubliceerd in het proefschrift van mw ir. R. Dubbeldam.

In **hoofdstuk 1** van dit proefschrift wordt een overzicht gegeven van de geschiedenis van gangbeeldanalyse. Eerst worden de verschillende onderdelen van de gangbeeldanalyse uitgelegd: kinetica, spier mechanica, kinematica en EMG. Er is een lange traditie van interesse in de biomechanica van het lichaam, al daterend van Aristoteles. Hij schreef een boek genaamd "De motu animalium" - over de beweging van dieren, waarin veel van zijn fascinatie voor anatomie en structuur van levende wezens teruggevonden wordt. Veel andere wetenschappers na hem deelden hun belangstelling voor biomechanica met hem, vooral tijdens de renaissance. In de 19e eeuw kreeg de geschiedenis van de biomechanica een nieuwe impuls met de uitvinding van het "bewegende beeld" door Marey, Muybridge en Lumière, die uiteindelijk zou leiden tot een vroege voorloper van de hedendaagse film. Een andere belangrijke doorbraak is de uitvinding van de computer, en daardoor de snellere verwerking en interpretatie van de data. Het gebruik van gangbeeldanalyse werd aanvankelijk voornamelijk toegepast in de diagnostiek en behandelplanning

van cerebrale parese. De laatste decennia wordt gangbeeldanalyse meer en meer toegepast bij reumatoïde artritispatiënten.

In **hoofdstuk 2** werd een systematische literatuurstudie uitgevoerd, waarin een overzicht wordt gegeven van de bestaande gangbeeld studies bij RA, de voornaamste conclusies en de klinimetrische eigenschappen. Een systematisch literatuur onderzoek in de databases Pubmed, CINAHL, sportdiscus, Embase en Scopus werd beschreven en uitgevoerd, en 78 oorspronkelijke gangbeeld studies werden geïncludeerd voor verdere gegevensextractie. De kwaliteit van de klinimetrische eigenschappen van de 78 studies werd beoordeeld aan de hand van een verkorte QUADAS itemlijst en de door Terwee voorgestelde klinimetrische criteria. Algemene conclusies met betrekking tot gangbeeldafwijkingen bij RA patiënten werden beschreven: de RA patiënt loopt langzamer, met een langere gang cyclus, een kortere staplengte, een langere "double support" tijd en een lagere cadans. De lagere snelheid kan worden veroorzaakt door een antalgisch looppatroon en door spierzwakte. Afwijkende plantaire druk komt vaak voor en kan hoger of lager zijn, als een gevolg van schade of om pijn te vermijden. Kinematische veranderingen zijn: verminderde beweeglijkheid van de gewrichten, gecombineerd met verminderde kracht. Er is een vertraagd omhoog komen van de hiel, een verminderde plantaire flexie en een abnormale eversie van de achterzijde voet. De kwaliteit van de klinimetrische eigenschappen is vatbaar voor verbetering. Toekomstig gangbeeldonderzoek moet zich richten op meer uniformiteit in de methodologie. Als aan deze behoefte wordt voldaan, kunnen meer valide conclusies worden getrokken, die uiteindelijk de behandeling van loopproblemen bij RA patiënten ten goede komt.

In **hoofdstuk 3** beschrijven we de prevalentie van schade en/of ruptuur van de pees van de musculus Flexor Hallucis Longus (FHL) en de relatie met de beweeglijkheid, deformiteit en schade van de voorvoet in ons cohort RA patiënten met voetklachten. De patiënten met pijnlijke voeten werden klinisch onderzocht op de aanwezigheid van pes planus en de beweeglijkheid van de gewrichten (ROM) werd vastgesteld; röntgenfoto's werden gescoord op schade van de voorvoet en met echografisch onderzoek werd gekeken naar de aanwezigheid van tenosynovitis of ruptuur van de FHL op het niveau van de mediale malleolus. De correlatiecoëfficiënten tussen de aanwezigheid of afwezigheid van de FHL, ROM, voorvoetschade en pes planus werden berekend. In 11/60(18%) van de voeten, werd een ruptuur van de FHL gevonden. Dit was geassocieerd met een beperkte beweging van het MTP1-gewricht, gemeten op de JAM ($\chi 2 = 10.4$, $p = 0.034$), een hogere prevalentie van pes planus ($\chi 2 = 5.77$, $p = 0.016$) en een hogere prevalentie van proximale erosies van MTP 1 ($\chi 2 = 12.3$, $p =$

0.016), en gewrichtsspleetversmalling van het MTP1 gewricht ($\chi 2 = 12.7$, $p = 0.013$). Concluderend is er bij de RA-patiënten uit ons cohort sprake van een associatie tussen een ruptuur van de pees van de musculus flexor hallucis longus enerzijds en bewegingsbeperking van de hallux, meer erosies en gewrichtsspleetvernauwing van het MTP-1-gewricht anderzijds, alsook met pes planus.

In **hoofdstuk 4**, beschrijven we de relatie tussen klinische en echografische parameters van pols-artritis en hun relatie met functie. In 33 RA patiënten met een klinisch vastgestelde polsartritis werden klinische en echografische parameters gemeten. Functie werd geëvalueerd met de SODA-S (Sequential Occupational Dexterity Assessment-Short) en de DASH-DLV (Disabilities of the Arm, Shoulder and Hand-Dutch Language Version). Correlatiecoëfficiënten tussen klinische en echografie parameters van reumatoïde pols-artritis in deze studie waren zwak tot matig. Van de klinische verschijnselen toonde alleen pijn een goede correlatie met functie. De echografische parameters correleerden goed met functie. Voor de klinische praktijk, betekent dit dat onderzoek niet beperkt moet blijven tot klinische tekenen en symptomen, maar dat extra echografisch onderzoek waardevol zou kunnen zijn in de beoordeling en behandeling van reumatoïde pols-artritis, met name bij verminderde polsfunctie.

In **hoofdstuk 5** presenteren wij de resultaten van de inter- en intrareader beoordelingsbetrouwbaarheid van het RAMRIS scoresysteem in voeten en enkels bij RA. In de reumatologie wordt magnetische resonantie beeldvorming (MRI) voornamelijk toegepast voor hand- en pols afwijkingen bij RA, wat geleid heeft tot de ontwikkeling van het systeem van de RAMRIS (RA-MRI-score), geïnitieerd door de OMERACT-werkgroep. Het RAMRIS-systeem wordt niet algemeen toegepast bij de beoordeling van de voeten. Negenentwintig RA-patiënten ondergingen MRI. Twee ervaren radiologen beoordeelden onafhankelijk beide complete sets, volgens de RAMRIS-methodologie. Voor de intrareader-betrouwbaarheid, las één van de radiologen 6 willekeurig gekozen MRI's voor de tweede keer. Voor evaluatie van de intra- en interreader betrouwbaarheid, werden gewogen kwadratische kappa (κ) scores berekend per gewricht en per laesie. De interreader κ scores voor de voorvoeten waren uitstekend, variërend van 0.77 (bot oedeem) tot 0.95 (bot erosie). Achtervoet interreader κ scores waren het hoogst voor erosie (0.90) en synovitis globale score (0.88); de κ-scores voor oedeem en synoviale dikte overeenkomst waren 0.83 en 0.86 resp. Intrareader κ scores waren over het algemeen iets lager, maar ook goed. Wij concluderen dat de inter- en intrareader betrouwbaarheid bij de beoordeling van voeten en enkels bij RA volgens de RAMRIS methode uitstekend is.

In **hoofdstuk 6** onderzochten we de associaties tussen klinische symptomen, radiologische veranderingen en functie in relatie tot de ziekteduur. Daarnaast beschreven we de bijdrage van de verschillende segmenten van de voet aan de klinische presentatie en functie. We vergeleken radiologische, echografische, klinische, en functionele parameters van de voeten en enkels. Pijn en zwelling van de enkels was zwak maar statistisch significant (0.273-0.293) gecorreleerd met de subschalen "beperking" en "handicap", gemeten met de 5-Foot Function Index (FFI). De klinische symptomen van de voorvoeten toonden geen correlatie met een van de functiematen. Radiologische scores voor zowel voorvoeten (SharpvdHeijden) en achtervoeten (Larsen) waren gecorreleerd met de HAQ DI(Health Assessment Questionnaire Disability Index) en de 5-FFI-beperking. Meer dan radiologische schade beïnvloeden pijn en ziekteduur de totale HAQ DI. In de loop van de tijd verergeren schade en functiebeperking van de reumatische voet bij RA patiënten. Pijn en zwelling van de enkels dragen meer bij aan handicap dan radiologische schade aan voet en enkel.

In **hoofdstuk 7** beschrijven we de relatie tussen klinische afwijkingen van voet- en enkelgewrichten en pezen en de bijbehorende kinematica in het gangbeeld van 25 RA-patiënten. Maximale metatarsofalangeale 1(MTP 1) dorsiflexie, pronatie (ROM) van de middenvoet en subtalaire eversie ROM werden beoordeeld. MRI werd verricht om synovitis- en erosiescores voor MTP 1, middenvoet en achtervoet, alsmede betrokkenheid van pezen te objectiveren. Subtalaire stand en passieve ROM en MTP 1 passieve ROM werden vastgelegd aan de hand van de JAM (Joint Alignment Motion scale). Maximale MTP 1 dorsiflexie was gerelateerd aan MTP I passieve ROM (correlatiecoëfficiënt, CC-0.50), MTP 1 synovitis (CC-0.63) en erosie (CC-0.69), middenvoet synovitis (CC-0.40) en erosie (CC-0.54) en achtervoet erosie (CC-0.40). In de middenvoet was pronatie ROM gerelateerd aan subtalaire stand (CC-0.51) en afwijkingen aan de achilles pees (CC +0.42). Subtalaire eversie ROM was gerelateerd aan subtalaire stand (CC-0.55) en afwijkingen aan de peroneus longus pees (CC-0.41). Bovengenoemde afwijkingen kunnen verslechteren in de loop van de ziekte. De JAM, MTP 1 ROM en subtalaire stand kunnen gemakkelijk worden vastgelegd in de dagelijkse klinische praktijk zonder veel last voor de patiënt. Grote variabiliteit van de JAM scores word waargenomen tussen patiënten. Echter, longitudinale individuele monitoring van de JAM is een eenvoudige manier om de voet- en enkelfunctie en de verandering hierin vast te stellen.

Discussie

Structurele schade en ontsteking hebben invloed op de kinematische parameters van het gangbeeld, zoals we hebben aangetoond in hoofdstuk 7, maar er is nog veel onbekend. Correlaties werden gevonden, maar de exacte volgorde van de gebeurtenissen in het ontstaan van RA gerelateerde voet- en enkelafwijkingen zijn onbekend. Zo kunnen wij de vaak genoemde insufficiëntie van de pees van de tibialis posterior die verondersteld wordt te leiden tot inzakken van de mediale boog en latere standsafwijkingen van achtervoet en voorvoet niet bevestigen. Andere pezen echter, zoals die van de musculus flexor hallucis longus en van de peroneï, zijn van belang bij stands- en kinematische afwijkingen bij RA.
Het belangrijkste inzicht, voortkomend uit dit proefschrift, is dat de problemen bij reumatoïde artritis niet beperkt zijn tot de voorvoet maar dat achtervoet en de weke delen ook aanzienlijk zijn betrokken. Deze conclusie moet op zijn minst leiden tot een aanpassing van de dagelijkse klinische praktijk. In plaats van een DAS 28 als klinische routine, moet een volledige DAS (van 44 gewrichten) gedaan worden, om verwaarlozing van de voeten te voorkomen. Bovendien zou aanvullend de JAM vastgelegd kunnen worden: het is een gemakkelijke manier om de gevolgen van schade en ontsteking in het reumatoïde gewricht te beoordelen, niet zozeer voor het vergelijken van patiënten, want er is een brede interindividuele variatie, maar als longitudinaal instrument. Wanneer verslechtering wordt geconstateerd, moet extra onderzoek worden gevraagd. Ik pleit hier voor vaker inzetten van MRI. Wij bevestigden dat het hier gaat om een betrouwbaar instrument bij de beoordeling van de schade en ontsteking door RA. Het voorziet niet alleen in gegevens over erosieve botafwijkingen, maar geeft tevens een goed inzicht in afwijkingen van de weke delen. In onze studie bijvoorbeeld waren afwijkingen van pezen aanwezig in ongeveer 70% van de patiënten. Na zorgvuldige diagnose moet gerichte behandeling volgen, zoals lokale injectie therapie, aanpassing van de DMARD behandeling of tijdige verwijzing naar een podotherapeut of orthopedisch chirurg. Wij realiseren ons dat de effectiviteit van deze interventies nog bewezen dient te worden, maar gezien het onderliggende mechanisme achten wij dit zeer waarschijnlijk. Om de exacte volgorde van gebeurtenissen bij schade aan voet en enkel bij RA te bepalen, en de gevolgen daarvan voor het lopen, is longitudinale studie nodig. De resultaten van onze studie zouden kunnen functioneren als een leidraad voor het formuleren van hypothesen, daar cross-sectionele studies in het verleden hebben bewezen betrouwbare hypothesen te kunnen genereren voor het longitudinaal vastleggen van “health assessment outcome” bij chronische ziekten. Patiënten met en zonder voet- en enkel klachten zouden dan moeten worden geïncludeerd aan het begin van

de ziekte en een volledige gangbeeldanalyse moet plaatsvinden, in combinatie met klinisch onderzoek en aanvullend beeldvormend onderzoek. Dergelijk onderzoek is echter kostbaar en zal slechts leiden tot behandelhypothesen, die wederom in volgend interventie-onderzoek getoetst moeten worden. Kortom, de weg voor gangbeeldanalyse-onderzoek in RA is nog lang niet ten einde bewandeld en vele stappen zullen nog moeten worden gezet. Waarvan de RA patiënt beter wordt.

Tables 1- 3, Addendum to Chapter 2.

Table 1. Description of the studies.

Method/Measurement concept	Year of publication	Target population	Study population	Study number	Measure(s)	AIM	Intervention/ treatment
Plantar pressure EMED (1-20)							
Bitzan (1)	1997	RA patients	26 feet in 16 patients after forefoot surgery	16	Plantar pressure	To evaluate resection of all MT heads in RA pts	Forefoot surgery. Resection of metatarsal heads
Davys (3)	2005	RA	RA pts	38	Plantar pressure	To compare forefoot pain, pressure and function before and after normal and sham callus treatment in RA	Prescription of insoles for pts with painful rheumatic foot deformities
Giacomozzi (4)	2009	RA, selection on basis of the HAQ	RA and healthy subjects	112 RA patients; 30 healthy	Pressure, peak force, pressure time integral, force time integral, PPC, and NFC	To detect gait alterations in RA patients using peak pressure curves (PPC) and normalized force curves (NFC) in comparison wit the HAQ	None
Hodge (5)	1999	RA	RA with forefoot pain	12	Plantar pressure gait velocity	To investigate the effectiveness of foot orthoses in the management of plantar pressure and pain in subjects with rheumatoid arthritis	Four styles of foot orthosis were compared
Mulcahy (6)	2003	RA pts after forefoot surgery	RA pts after forefoot surgery	100 feet in 61 pts	Area of contact (cm2), pressure time integral (PTI; Ns/cm2), and peak pressures (N/cm2)	To compare the functional, radiographic, and pedobarographic results of different reconstructive methods for severe rheumatoid forefoot deformities.	2 types of reconstructive forefoot surgery were compared:
Philipson (7)	1994	Inflammatory arthritis	11 RA, 1 SLE, 3 non-specific foot deformities	15	Plantar pressure, peak pressure. PTI. Contact areas	To determine how effective forefoot arthroplasty is at reducing the pressures under the forefoot	Forefoot arthroplasty

Method/Measurement concept	Year of publication	Target population	Study population	Study number	Measure(s)	AIM	Intervention/ treatment
Rosenbaum (8)	2006	RA	25 RA patients, 21 healthy controls	46	Dynamic plantar pressure. Plantar sensitivity	to investigate the tactile sensitivity of the plantar surface in rheumatoid feet and its relationship to walking pain and plantar foot loading characteristics	none
Samnegard (9)	1990	RA	10 RA pts, post surgery feet	10 RA pts, 10 healthy controls	Plantar pressures	Examination of ten RA patients with an EMED gait analysis system in a mean four years after foot surgery and compared that with ten normal subjects.	4 years after forefoot surgery. No pre-operative measurement
Schmiegel (10)	2008	RA	RA pts and healthy controls	112	Pedobarography	To evaluate the use of pedobarographic measurements for detecting changes in plantar loading characteristics and their relationship to foot pain in RA	None
Schmiegel (11)	2008	RA	RA pts and healthy controls	16 RA pts, 21 healthy controls	Pedobarography	To compare RA patients' clinical, radiographic and pedographic status in order to investigate the relationship between mechanical damage and plantar pressure distribution under the forefoot	None
Semple (12)	2007	RA	RA pts and healthy controls	74 RA, 53 matched controls	Pedobarography	To undertake a comparison of the regionalized duration and velocity of the centre of pressure between rheumatoid arthritis patients with foot impairments and healthy able-bodied adults	None
Tastekin (13)	2009	RA	RA and heel valgus	50 RA pts	Plantar pressure	To document the plantar pressure distribution changes in RA patients with heel valgus and to compare results in those without valgus.	None
Tuna (14)	2005	RA	RA	50 RA pts, 50 healthy controls	Plantar pressure	To assess probable plantar pressure alterations in RA patients compared with normals and the probable relation between pressure and radiologic foot erosion score	None

Turner 2006 (15)	2006	RA	RA with foot problems	12 RA pts, 12 controls	Temporospatial data, plantar pressure. Gait analysis	To compare clinical disease activity, impairment, disability, and foot function in normal and early RA	None
Turner 2008 (16)	2008	RA	RA	74 RA pts, 54 controls	Temporospatial data, plantar pressure. Gait analysis	To evaluate biomechanical foot function and determine factors associated with localised disease burden in patients with this disease.	None
Turner 2008 (17)	2008	RA	RA with forefoot/ hindfoot or combined problems	28 RA pts, 50 healthy controls	Temporospatial data, plantar pressure. Gait analysis	To describe the clinical and biomechanical characteristics of patients with severe rearfoot, forefoot or combined deformities and determine localised disease impact	None
Van der Leeden (18)	2004	RA	RA	20 pts with inflammatory disease, 15 RA, 1 SpA, 1 JIA, 2 PsA	Plantar pressure	To compare the reproducibility of measurements among one-step, two-step, and three-step protocols for data collection in patients with arthritis.	None
Van der Leeden (19)	2006	RA	RA	62 RA pts with foot complaints	Plantar pressure	To assess the relationship between forefoot joint damage and foot function, pain, and disability in patients with foot complaints secondary to RA	None
Woodburn (20)	2000	RA	RA	8 RA pts with 14 callosities	Plantar pressure	To determine the effect of expert debridement of foot callosities on forefoot pain and plantar pressure distribution in rheumatoid arthritis (RA)	Debridement of callosities
Plantar pressure F-scan (21-26)							
Grondal (21)	2006	RA pts	RA pts	14 plantar pressure, 12 gait data.	Stride data, plantar pressure	To study the effect of the difference between the Mayo resection vs. arthrodesis in RA forefoot reconstruction	Forefoot surgery in RA patients
Jackson (22)	2004	RA	RA pts, 9 female, 1 male	10	Plantar pressure	To determine which design could better manage high forefoot plantar pressures in patients with RA	Two prefab insoles

Method/Measurement concept	Year of publication	Target population	Study population	Study number	Measure(s)	AIM	Intervention/ treatment
Li (23)	2000	RA	RA	12 RA pts, 8 healthy controls	Plantar pressure	To compare the foot pressures and loading forces during gait in RA patients and healthy subjects, and evaluate the effects of foot orthoses in RA	Prescription of foot orthoses
Novak (24)	2009	RA pts	RA pts	12	Plantar pressure	To compare foot orthoses and unshaped orthotic material on plantar pressure, pain reduction and walking ability in RA.	Foot orthosis (functional or unshaped)
Vidmar (25)	2009	RA	RA pts with forefoot complaints	12 RA	Plantar pressure	To assess reliability of the F-Scan plantar pressure measurement system in rheumatoid arthritis patients	None
Woodburn (26)	1996	RA	Ra and healthy controls	104 RA, 42 controls	Plantar pressure	To investigate the relation between the position of the rearfoot and the distribution of forefoot plantar pressures and skin callosities in rheumatoid arthritis.	None
Plantar pressure otherwise or not specified (27-49)							
Andriacchi (27)	1977	Patients with knee disability	Patients with knee disability. 11 OA, 5 RA. 17 healthy normals	16	Temporospatial parameters, plantar pressure	To examine two types of gait parameters (temporal and ground reaction force) obtained from normal subjects and patients with knee joint disabilities.	None
Barrett (28)	1976	RA patients	RA pts with callosities at the MTP's	25	Plantar pressure points	To discuss the role of shoe-wear in the treatment of painful metatarsalgia in RA patients and to evaluate a special sandal developed for this purpose	Treatment of metatarsalgia with special sandal

Beauchamp (29)	1984	RA pts	RA patients who underwent forefoot surgery	37	Plantar pressure	To compare joint fusion MTP 1 with excision of the MTP1	To compare 2 types of forefoot arthroplasty (MTP1 fusion or excision)
Betts (30)	1988	RA pts	RA PTS PRE- AND POST Kates Kessel	60 feet in 35 RA patients, 18 feet in 10 controls	Plantar pressure	To assess the results of forefoot arthroplasty in both a prospective study group of 60 feet and in a retrospective study group of 18 feet	Forefoot surgery (Kates Kessel)
Carl(2)		RA	20 RA patients with painful foot deformities who were provided with insoles	20	Plantar pressure	To examine the clinical effectiveness of insoles and to establish pedobarography as a means of quality control for orthotic management of the rheumatic foot.	Insoles
Collis (31)	1972	RA	RA patients	10 healthy feet, 10 rheumatoid feet	Plantar pressure	To measure the pressures under the different parts of the foot and describe the pressure pattern for normal feet and some of the changes that occur in rheumatoid arthritis	None
Dereymaeker (32)	1997	RA	RA pts, who underwent forefoot reconstruction	38	Plantar pressure	To evaluate the results after forefoot reconstruction	Forefoot reconstruction
Firth (33)	2007	RA pts	RA	10	Plantar pressure	Validity and reliability of PressureStat in patients with RA	None
Godfrey (34)	1967	RA	RA? And volunteers	?	Plantar pressure	To introduce a new method of pressure measurement during walking	None
Hamilton(48)	2001	RA	24 early RA pts	24 early RA	Plantar pressure, stride data	To assess the clinical usefulness of a prototype walkmat system in patients with early RA	None

Method/Measurement concept	Year of publication	Target population	Study population	Study number	Measure(s)	AIM	Intervention/ treatment
Harris(49)	1997	RA	RA pts who underwent forefoot surgery	35	Plantar pressure	To present a prospective 10-16 year clinical and pedobarographic evaluation of a modification to the Kates et al forefoot arthroplasty	Kates forefoot arthroplasty
Henessy (35)	2007	RA	RA with forefoot pain	20	Plantar pressures and pressure time integral	To evaluate the effect of running footwear as an alternative to off-the-shelf orthopaedic footwear on plantar pressure	Running shoes vs. orthopaedic footwear
Masson (36)	1989	RA,DM	RA and diabetes pts	37 RA pts, 38 diabetic pts	Plantar pressure, nerve conduction velocity.	To examine the relationship between high foot pressure, neurological abnormalities, and ulceration in RA and DM	None
Minns (37)	1984	RA/normals	RA patients and healthy controls	124 RA, 67 normal subjects	Plantar pressure	To compare static and dynamic forces in a large cohort	None
Otter (39)	2004	RA	RA pts	25 EARLY RA. 25 controls	Plantar pressure	To investigate the magnitude and duration of peak forefoot plantar pressures in rheumatoid arthritis	None
Rome (40)	2009	RA	Ra pts	19 RA, 21 healthy controls	Gait data, centre of pressure	To evaluate postural stability in rheumatoid arthritis patients	None
Sharma (41)	1979	RA	RA pts and controls	27 RA pts, 30 volunteers	Plantar pressure	To quantify the force distribution under the feet of patients and controls of similar age and weight.	None
Siegel (42)	1995	RA	6: 4 RA, 1 excessive pronation, 1 healthy subject	6: 4 RA, 1 excessive pronation, 1 healthy subject	Gait variables, plantar pressure	A technique to measure foot function during the stance phase of gait is described. Advantages of the method include its three-dimensional approach with anatomically based segment coordinate systems..	None

Simkin (43)	1981	RA	RA	18 RA. 20 controls	Stride parameters, vertical + local forces	Measuring the dynamic force distribution under the foot in RA and normals	None
Stauffer (44)	1977	KNEE diseased, OA and RA	OA and RA	65 OA (108knees) and 30 RA (54 knees). 29 healthy volunteers	Stride parameters, vertical forces	Biomechanical parameters of knee joint function for 95 patients (162 knees) with RA and degenerative joint disease were studied and compared with those for 29 normal subjects.	None
Stockley (45)	1989	RA	RA after surgery	35 pts	Pressure under forefoot	The modified Kates et al. metatarsal head resection arthroplasty has been evaluated in RA	A modified Kates procedure
Stockley (46)	1990	RA	RA	47 feet in 28 RA patients	Pressure under forefoot	To assess the relationship between hindfoot deformity and forefoot pressure in 28 RA after forefoot	Forefoot reconstruction Kates. Kessel. Kay (1967)
Turner 2003 (47)	2003	RA	RA pts with pes planovalgus	23 RA pts 23 age-matched controls	Temporospatial data, Joint angles, plantar pressures	To compare gait and foot function between RA patients with painful pes planovalgus deformity and healthy age- and sex-matched adults.	None
Temporospatial data (4, 5, 14-17, 21, 27, 43, 44, 47, 48, 50-72)							
Giacomozzi (4)	2009	RA, selection on basis of the HAQ	RA and healthy subjects	112 RA patients; 30 healthy	Pressure, peak force, pressure time integral, force time integral, PPC, and NFC	To detect gait alterations in RA patients using peak pressure curves (PPC) and normalized force curves (NFC) in comparison wit the HAQ	None
Hamilton(48)	2001	RA	24 early RA pts	24 early RA	Plantar pressure. Stride data	To assess the clinical usefulness of a prototype walkmat system in patients with early RA	None
Hodge (5)	1999	RA	RA with forefoot pain	12	Plantar pressure gait velocity	To investigate the effectiveness of foot orthoses in the management of plantar pressure and pain in RA	Four styles of foot orthosis were compared

Method/Measurement concept	Year of publication	Target population	Study population	Study number	Measure(s)	AIM	Intervention/ treatment
Tuna (14)	2005	RA	RA	50 RA pts, 50 healthy controls	Plantar pressure	To assess plantar pressure alterations in RA patients compared with normal and in relation with erosion scores	None
Turner (15)	2006	RA	RA with foot problems	12 RA pts, 12 controls	Temporospatial data, plantar pressure. Gait analysis	To compare clinical disease activity, impairment, disability, and foot function in normal and early RA	None
Turner (16)	2008	RA	RA	74 RA pts, 54 controls	Temporospatial data, plantar pressure. Gait analysis	To evaluate biomechanical foot function and determine factors associated with localised disease burden in patients with this disease.	None
Turner (17)	2008	RA	RA with forefoot/ hindfoot/ combined problems	28 RA pts, 50 healthy controls	Temporospatial data, plantar pressure. Gait analysis	To describe the clinical and biomechanical characteristics of patients with severe rearfoot, forefoot or combined deformities and determine localised disease impact	None
Grondal (21)	2006	RA pts	RA pts	14 plantar pressure, 12 gait data.	Stride data, plantar pressure	To study the effect of the difference between the Mayo resection vs. arthrodesis in RA forefoot reconstruction	Forefoot surgery in RA patients
Andriacchi (27)	1977	Patients with knee disability	Patients with knee disability. 11 OA, 5 RA. 17 healthy normals	16	Temporospatial parameters, plantar pressure	To examine two types of gait parameters (temporal and ground reaction force) obtained from normal subjects and patients with knee joint disabilities.	None
Simkin (43)	1981	RA	RA	18 RA. 20 controls	Stride parameters, vertical + local forces	Measuring the dynamic force distribution under the foot in RA and normals	None
Stauffer (44)	1977	KNEE diseased, OA and RA	OA and RA	65 OA and 30 RA,. 29 normals	Stride parameters, vertical forces,	To compare biomechanical parameters of knee joint function for 95 patients (162 knees) with RA and normal subjects.	None

Turner 2003 (47)	2003	RA	RA pts with pes planovalgus	23 RA pts 23 age-matched controls	Temporospatial data, Joint angles, plantar pressures	To compare gait and foot function between RA patients with painful pes planovalgus deformity and healthy age- and sex-matched adults.	None
Brinkmann (50)	1985	Pts with arthritis of the knee	RA/OA	72 healthy adults, 69 RA and 20 OA	Gait velocity, range of motion	To determine the relationship between gait velocity and rate and ROM knee, during ambulation, for healthy and arthritic subjects	Total knee replacement
Eastlack (51)	1991	RA pts	RA pts with abnormal gait	3	Videotaped observational gait-analysis (VOGA)	To determine the interrater reliability of videotaped observational gait-analysis (VOGA) assessments	None
Eppeland (52)	2009	RA pts	Asymptomatic RA pts	17	Gait parameters	To investigate the characteristics of gait in RA vs. controls.	None
Fransen (53)	1997	RA pts	RA pts	30	Gait variables	To assess the effectiveness of off-the shelf orthopedic footwear in RA	Prescription of orthopedic footwear
Fransen (54)	1999	RA pts	RA pts	31	Gait variables	To assess the reliability and responsiveness of gait speed, cadence and stride length at two self-selected speeds (SSS) in RA	None
Fransen (55)	1994	RA pts	RA pts and normal subjects	113 RA pts, 104 normal subjects	Gait/stride parameters	Differences in the gait parameters at three different self selected speeds between 113 subjects with rheumatoid arthritis and 104 normal controls	None
Gyory (56)	1976	Knee patients	RA, OA and healthy controls	65 OA, 29 healthy, 30 RA pts	Gait variables, motion of the knee	To study functional performance of the knee joints of 29 normal volunteers, 65 OA patients and 30 RA pts	None
Isacson (57)	1988	RA	Female RA pts < 50 years	17	ROM, gait velocity stride parameters	Detecting early aberrations of gait in rheumatoid arthritis 17 women suffering from that disease were examined.	None
Kavlak (58)	2003	RA	RA pts	18	Physiologic cost index (PCI), stride data, VAS pain	To determine the effect of foot orthoses on pain, gait, and energy expenditure in patients with RA.	Different orthotic interventions

Method/Measurement concept	Year of publication	Target population	Study population	Study number	Measure(s)	AIM	Intervention/ treatment
Keenan (59)	1991	RA	RA pts	20	Electromyography, gait/stride data, ROM	To investigate the cause of valgus hindfoot in RA and to characterize the effects of the deformity on gait.	None
Kettelkamp (60)	1972	RA	RA pts with knee problem?	27	Stride data, floor reaction force	To correlate various clinical characteristics to gait abnormalities in the rheumatoid knee	None
Khazzam (61)	2007	RA	RA pts,	22 RA pts, 29 feet	Temporospatial parameters.	To examine specific changes in segmental foot motion in patients with RA as compared to normals subjects	None
Laroche (62)	2007	RA with forefoot damage	RA pts	9 RA pts with malalignment of the forefeet, 7 controls	Stride parameters, duration, kinematic data	To investigate the modifications of gait parameters in RA To extract the mechanisms used to compensate for these impairments	None
Laroche (63)	2005	RA with forefoot damage	RA pts	9 RA pts with malalignment of the forefeet, 7 controls	Walking frequency, walking velocity, stride length, duration	To evaluate the effects of loss of ROM of the MTP joint on the kinematic parameters of walking in RA	None
Locke (64)	1984	RA with ankle and subtalar	25 RA pts, 20 healthy subjects	25 RA pts, 20 healthy subjects	ROM, stride data	To document ankle and subtalar motion during gait in 20 healthy subjects and in 25 RA patients, to determine stride characteristics with and without the use of an extended orthosis in RA patients.	Use of an extended University of California Biomechanics Laboratory orthosis
Long (65)	2003	RA pts	RA pts before + after surgery	10 RA	Temporospatial, kinematic	A new series of ten RA patients are evaluated before and after surgical intervention	Forefoot surgery, not specified
MacSween (66)	1999	RA pts	RA pts with and without orthoses	8 RA pts	Temporospatial parameters	To study the effect of custom moulded EVA foot orthoses on walking ability in RA.	Use of a custom moulded foot orthosis

Marshall (67)	1980	RA pts	RA pts with subtalar involvement	6 RA pts with subtalar involvement	Temporospatial, kinematic	To describe changes in the orientation of ankle and subtalar axes in RA	None
Mejjad (68)	2004	RA	RA pts with metatarsalgia	16	Spatiotemporal gait variables	To assess the efficacy of foot orthoses in RA patients with pain and if improvement of pain was related to an improvement in gait	Cross over design: orthotics of 10mm semiflexible mat
Murray (69)	1975	Total hip pts	Total hip pts	30 pts with total Hip, of which 4 RA pts	ROM, muscle strength, CoP, stride parameters. Forces cane/crutch	To measure function before and at six and twenty-four months after 100 McKee-Farrar total hip replacements in eighty-three patients	McKee-Farrar total hip replacement
Platto (70)	1991	RA	RA pts	31	Stride data	We evaluated the relationships among pain, structural deformity of the foot, 4 variables of gait, and an index of function in 31 RA patients.	None
Weiss (71)	2007	RA + ankle surgery	RA	14 RA pts, 14 matched controls	3D gait analysis, kinetic and time distance parameters	To evaluate the effects of ankle/ hindfoot arthrodesis in RA on gait pattern of the knee and hip	Ankle joint surgery
Woodburn (72)	2004	RA	RA	11 RA, 5 healthy volunteers	3D kinematics, temporospatial parameters	To test a multisegment foot model for kinematic analysis during walking in RA patients with foot impairments.	None
3D gait (14-17, 38, 42, 47, 51, 57, 65, 67, 71-75)							
Tuna (14)	2005	RA	RA	50 RA pts, 50 healthy controls	Plantar pressure	To assess plantar pressure alterations in RA patients compared with normal and in relation with erosion scores	None
Turner (15)	2006	RA	RA with foot problems	12 RA pts, 12 controls	Temporospatial data, plantar pressure. Gait analysis	To compare clinical disease activity, impairment, disability, and foot function in normal and early RA	None
Turner (16)	2008	RA	RA	74 RA pts, 54 controls	Temporospatial data, plantar pressure. Gait analysis	to evaluate biomechanical foot function and determine factors associated with localised disease burden in patients with this disease.	None

Method/Measurement concept	Year of publication	Target population	Study population	Study number	Measure(s)	AIM	Intervention/ treatment
Turner (17)	2008	RA	RA with forefoot/ hindfoot or combined problems	28 RA pts, 50 healthy controls	Temporospatial data, plantar pressure. Gait analysis	To describe the clinical and biomechanical characteristics of patients with severe rearfoot, forefoot or combined deformities and determine localised disease impact	None
O Connell (38)	1998	RA	10 RA, 7 healthy subjects	17	Plantar pressure, ankle ROM	To evaluate how painful metatarsal arthritis affects foot and ankle mechanics and mobility	None
Siegel (42)	1995	RA	6: 4 RA, 1 excessive pronation, 1 healthy subject	6: 4 RA, 1 excessive pronation, 1 healthy subject	Gait variables, plantar pressure	A technique to measure foot function during the stance phase of gait is described. Advantages of the method include its three-dimensional approach with anatomically based segment coordinate systems.	None
Turner (47)	2003	RA	RA pts with pes planovalgus	23 RA pts 23 age-matched controls	Temporospatial data, Joint angles, plantar pressures	To compare gait and foot function between RA patients with painful pes planovalgus deformity and healthy age- and sex-matched adults.	None
Eastlack (51)	1991	RA pts	RA pts with abnormal gait	3	Videotaped observational gait-analysis (VOGA)	To determine the interrater reliability of videotaped observational gait-analysis (VOGA) assessments	None
Isacson (57)	1988	RA	Female RA pts < 50 years	17	ROM, gait velocity stride parameters	Detecting early aberrations of gait in rheumatoid arthritis 17 women suffering from that disease were examined.	None
Long (65)	2003	RA pts	RA pts before + after surgery	10 RA	Temporospatial, kinematic	A new series of ten RA patients are evaluated before and after surgical intervention	Forefoot surgery, not specified
Marshall (67)	1980	RA pts	RA pts with subtalar involvement	6 RA pts with subtalar involvement	Temporospatial, kinematic	To describe changes in the orientation of ankle and subtalar axes in RA	None

Weiss (71)	2007	RA + ankle surgery	RA	14 RA pts, 14 matched controls	3D gait analysis, kinetic and time distance parameters	To evaluate the effects of ankle/ hindfoot arthrodesis in RA on gait pattern of the knee and hip	Ankle joint surgery
Woodburn (72)	2004	RA	RA	11 RA, 5 healthy volunteers	3D kinematics, temporospatial parameters	To test a multisegment foot model for kinematic analysis during walking in RA patients with foot impairments.	None
Weiss (73)	2008	RA	RA and controls	50 RA, 37 healthy subjects	3D gait analysis, ground reaction forces	To analyse kinematic and kinetic gait changes in RA in comparison to healthy controls and to examine whether HAQ-scores were associated with gait parameters.	None
Woodburn (74)	2002	RA	RA	50RA+ orthosis, 48 RA controls and 45 controls	3D kinematics of the AJC	To evaluate the efficacy of custom foot orthoses for the management of painful rearfoot in RA	Prescription of custom foot orthoses
Woodburn (75)	1999	RA	RA and healthy	10 RA, 10 controls	3D kinematics of the AJC	To determine the feasibility of using electromagnetic tracking (EMT) for quantifying 3D kinematics at the ankle joint complex (AJC)	Footwear/ orthotic intervention in 10 RA
EMG (59, 76)							
Keenan (59)	1991	RA	RA pts	20	Electromyography, gait/stride data, ROM	To investigate the cause of valgus hindfoot in RA and to characterize the effects of the deformity on gait.	None
Garling (76)	2005	RA with TKA	RA with TKA	7	EMG	To assess the differences in muscle activity (surface EMG) between 2 types of TKA in RA	TKA
Other: **Rontgen stereophotogammetry** (77)**ROM** (38, 52, 56, 57, 64, 69) **Kinetic data** (71, 73, 78) **Nerve conduction** (36)							

Method/Measurement concept	Year of publication	Target population	Study population	Study number	Measure(s)	AIM	Intervention/ treatment
Rontgen stereophotogammetry							
Eberhardt (77)	1986	RA pts	RA pts with knee damage	4	Roentgen stereo photogrammetry	To demonstrate the usefulness of röntgen stereophotogammetry, to locate the axis of rotation.	None
ROM							
O Connell (38)	1998	RA	10 RA, 7 healthy subjects	17	Plantar pressure, ankle ROM	To evaluate how painful metatarsal arthritis affects foot and ankle mechanics and mobility	None
Eppeland (52)	2009	RA pts	Asymptomatic RA pts	17	Gait parameters	To investigate the characteristics of gait in RA vs. controls.	None
Gyori (56)	1976	Knee patients	RA, OA and healthy controls	65 OA, 29 healthy, 30 RA pts	Gait variables, motion of the knee	To study functional performance of the knee joints of 29 normal volunteers, 65 OA patients and 30 RA pts	None
Isacson (57)	1988	RA	Female RA pts < 50 years	17	ROM, gait velocity stride parameters	Detecting early aberrations of gait in rheumatoid arthritis 17 women suffering from that disease were examined.	None
Locke (64)	1984	RA with ankle and subtalar	25 RA pts, 20 healthy subjects	25 RA pts, 20 healthy subjects	ROM, stride data	To document ankle and subtalar motion during gait in 20 healthy subjects and in 25 RA patients, to determine stride characteristics with and without the use of an extended orthosis in RA patients.	Use of an extended University of California Biomechanics Laboratory orthosis
Murray (69)	1975	Total hip pts	Total hip pts	30 pts with total Hip, of which 4 RA pts	ROM, muscle strength, CoP, stride parameters. Forces cane/crutch	To measure function before and at six and twenty-four months after 100 McKee-Farrar total hip replacements in eighty-three patients	McKee-Farrar total hip replacement

Kinetic data							
Weiss (71)	2007	RA + ankle surgery	RA	14 RA pts, 14 matched controls	3D gait analysis, kinetic and time distance parameters	To evaluate the effects of ankle/ hindfoot arthrodesis in RA on gait pattern of the knee and hip	Ankle joint surgery
Weiss (73)	2008	RA	RA and controls	50 RA, 37 healthy subjects	3D gait analysis, ground reaction forces	To analyse kinematic and kinetic gait changes in RA in comparison to healthy controls and to examine whether HAQ-scores were associated with gait parameters.	None
Sakauchi (78)	2001	RA	RA patients with knee problems	14 RA pts, 7 healthy subjects	Angular changes were analysed by an EM tracking instrument	To analyse abnormal gait patterns in patients with rheumatoid arthritis involving the knee joint.	None
Nerve conduction							
Masson (36)	1989	RA, DM	RA and diabetes pts	37 RA pts, 38 diabetic pts	Plantar pressure, nerve conduction velocity.	To examine the relationship between high foot pressure, neurological abnormalities, and ulceration in RA and DM	None

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Table 2. Results of scoring of selected QUADAS items.

Method	QUADAS 1	QUADAS 2	QUADAS 8	QUADAS 10	QUADAS 12	QQUADAS 13	QUADAS 14
Plantar pressure EMED (1-20)							
Bitzan (1)	Yes	Yes	Yes	NA	Yes	No	Yes
Davys (3)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Giacomozzi (4)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Hodge (5)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Mulcahy (6)	Yes	Yes	Yes	NA	Yes	Yes	Yes
Philipson (7)	Yes	Yes	Yes	NA	Yes	Yes	NA
Samnegard (9)	Yes	No	Yes	NA	Yes	No	NA
Schmiegel (10)	Yes	Yes	Yes	NA	Yes	Yes	NA
Schmiegel (11)	Yes	Yes	Yes	NA	Yes	No	NA
Semple (12)	Yes	Yes	Yes	NA	Yes	Yes	NA
Tastekin (13)	Yes	Yes	Yes	NA	Yes	Yes	NA
Tuna (14)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner 2006 (15)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner 2008 (16)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner 2008 (17)	Yes	Yes	Yes	NA	Yes	Yes	NA
Van de Leeden (18)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Van de Leeden (19)	Yes	Yes	Yes	NA	Yes	Yes	NA
Woodburn (20)	Yes	No	Yes	NA	Yes	Yes	Yes
Plantar pressure F-scan (21-26)							
Grondal (21)	Yes	Yes	Yes	Yes	Yes	No	Yes
Jackson (22)	Yes	Yes	Yes	NA	Yes	No	Yes
Li (23)	Yes	Yes	Yes	NA	Yes	Yes	NA
Novak (24)	Yes	Yes	Yes	NA	NA	No	NA
Vidmar (25)	Yes	No	Yes	Yes	Yes	No	NA
Woodburn (26)	Yes	No	Yes	NA	Yes	Yes	NA
Plantar pressure otherwise or not specified (27-49)							
Andriacchi (27)	Yes	No	Yes	NA	Yes	Yes	No
Barrett (28)	Yes	Yes	Yes	NA	Yes	No	No
Beauchamp (29)	Yes	No	No	NA	Yes	No	No

Method	QUADAS 1	QUADAS 2	QUADAS 8	QUADAS 10	QUADAS 12	QQUADAS 13	QUADAS 14
Betts (30)	Yes	No	Yes, in other study	NA	Yes	Yes	No
Carl(2)	Yes	Yes	Yes	NA	Yes	Yes	No
Collis (31)	Yes	No	Yes	NA	Yes	No	No
Dereymaeker (32)	Yes	No	Yes	No	Yes	Yes	Yes
Firth (33)	Yes	No	Yes	Yes	Yes	Yes	NA
Godfrey (34)	No	No	No	Yes	Yes	No	No
Henessy (35)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Hamilton(48)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Harris(49)	Yes	No	No	NA	Yes	No	Yes
Masson (36)	Yes	Yes	earlier study	NA	Yes	Yes	NA
Minns (37)	Yes	Yes	Yes	MA	Yes	No	NA
Otter (39)	Yes	Yes	Yes	NA	Yes	Yes	Yes
Rome (40)	Yes	Yes	Yes	NA	Yes	No	NA
Sharma (41)	Yes	No	No	NA	Yes	No	NA
Siegel (42)	Yes	Yes	Yes	NA	Yes	Yes	NA
Simkin (43)	Yes	No	1, in another study	NA	Yes	No	NA
Stauffer (44)	Yes	Yes	Yes	NA	Yes	Yes	NA
Stockley (45)	Yes	No	No	NA	No	No	No
Stockley (46)	Yes	No	No	NA	Yes	No	No
Turner 2003 (47)	Yes	Yes	Yes	NA	Yes	Yes	NA
Temporospatial data (4, 5, 14-17, 21, 27, 43, 44, 47, 48, 50-72)							
Giacomozzi (4)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Hamilton(48)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hodge (5)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Tuna (14)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (15)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (16)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (17)	Yes	Yes	Yes	NA	Yes	Yes	NA
Grondal (21)	Yes	Yes	Yes	Yes	Yes	No	Yes

Andriacchi (27)	Yes	No	Yes	NA	Yes	Yes	No
Simkin (43)	Yes	No	Yes, in another study	NA	Yes	No	NA
Stauffer (44)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner 2003 (47)	Yes	Yes	Yes	NA	Yes	Yes	NA
Brinkmann (50)	Yes	Yes	Yes	NA	Yes	No	No
Eastlack (51)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Eppeland (52)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Fransen (53)	Yes	Yes	Yes	No	Yes	Yes	Yes
Fransen (54)	Yes	Yes	Yes	Yes	Yes	No	NA
Fransen (55)	Yes	Yes	Yes	NA	Yes	Yes	NA
Gyory (56)	Yes	Yes	Yes	Yes	Yes	No	NA
Isacson (57)	No	Yes	No	NA	Yes	No	No
Kavlak (58)	Yes	Yes	Yes	Yes	Yes	No	No
Keenan (59)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Kettelkamp (60)	Yes	No	No	Yes	Yes	No	NA
Khazzam (61)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laroche (62)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Laroche (63)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Locke (64)	Yes	Yes	Yes	NA	Yes	Yes	NA
Long (65)	Yes	No	Yes	NA	Yes	No	No
MacSween (66)	Yes	Yes	Yes	NA	Yes	Yes	NA
Marshall (67)	Yes	Yes	No	NA	Yes	No	NA
Mejjad (68)	Yes	Yes	Yes	NA	Yes	No	NA
Murray (69)	Yes	Yes	No	NA	No	No	No
Platto (70)	Yes	Yes	Yes	NA	Yes	Yes	NA
Weiss (71)	Yes	Yes	Yes	NA	Yes	Yes	Yes
Woodburn (72)	Yes	Yes	Yes	NA	Yes	Yes	NA
3D gait (14-17, 38, 42, 47, 51, 57, 65, 67, 71-75)	Yes	Yes	Yes		Yes	Yes	
Tuna (14)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (15)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (16)	Yes	Yes	Yes	NA	Yes	Yes	NA

Method	QUADAS 1	QUADAS 2	QUADAS 8	QUADAS 10	QUADAS 12	QQUADAS 13	QUADAS 14
Turner (17)	Yes	Yes	Yes	NA	Yes	Yes	NA
O Connell (38)	Yes	Yes	Yes	NA	NA	No	NA
Siegel (42)	Yes	Yes	Yes	NA	Yes	Yes	NA
Turner (47)	Yes	Yes	Yes	NA	Yes	Yes	NA
Eastlack (51)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Isacson (57)	No	Yes	No	NA	Yes	No	No
Long (65)	Yes	No	Yes	NA	Yes	No	No
Marshall (67)	Yes	Yes	No	NA	Yes	No	NA
Weiss (71)	Yes	Yes	Yes	NA	Yes	Yes	Yes
Woodburn (72)	Yes	Yes	Yes	NA	Yes	Yes	NA
Weiss (73)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Woodburn (74)	Yes	Yes	Yes	Yes	Yes	Yes	No
Woodburn (75)	Yes	No	Yes	NA	Yes	Yes	NA
EMG (59, 76)							
Keenan (59)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Garling (76)	No	Yes	Yes	NA	Yes	Yes	NA
Other: **Rontgen stereophotogammetry (77)** **ROM (38, 52, 56, 57, 64, 69)** **Kinetic data (71, 73, 78)** **Nerve conduction (36)**							
Rontgen stereophotogammetry							
Eberhardt (77)	Yes	Yes	Yes	Yes	Yes	No	NA
ROM							
O Connell (38)	Yes	Yes	Yes	NA	NA	No	NA
Eppeland (52)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gyori (56)	Yes	Yes	Yes	Yes	Yes	No	NA
Isacson (57)	No	Yes	No	NA	Yes	No	No
Locke (64)	Yes	Yes	Yes	NA	Yes	Yes	NA
Murray (69)	Yes	Yes	No	NA	No	No	No
Kinetic data							
Weiss (71)	Yes	Yes	Yes	NA	Yes	Yes	Yes
Weiss (73)	Yes	Yes	Yes	Yes	Yes	Yes	NA
Sakauchi (78)	Yes	Yes	Yes	NA	Yes	No	NA
Nerve conduction	Yes	Yes			Yes		
Masson (36)	Yes	Yes	Earlier study	NA	Yes	Yes	NA

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Table 3. Summary of the evaluation of the clinimetric measures.

Method	Internal consistency	Agreement	Reliability	Construct validity	Responsiveness	Interpretability
Plantar pressure EMED						
Semple (1)	0	? CoV 3.5% to 14.3% control 5.7% to 19.3%	0	0	0	+
Tastekin (2)	0	0	0	?	0	+
Tuna (3)	0	0	0	0	0	+
Turner 2008 (4)	0	0	0	?	0	+
Van de Leeden (5)	0	0	?, max Pearson's CC 0,352	+	0	+
Plantar pressure F-scan						
Woodburn (6)	0	0	0	+	0	+
Plantar pressure otherwise or not specified						
Hamilton(7)	?	?, CoV < 4 % kinematic parameters, < 7% kinetic parameters	? in another study	? (sample size < 50)	? (sample size < 50)	? (sample size < 50)
Masson (8)	0	0	0	? differences DM/RA (statistic method NS) p <0,01	0	+
Minns (9)	0	0	?	?	0	+
Temporospatial data						
Hamilton(7)	?	?, CoV < 4 % kinematic parameters, < 7% kinetic parameters	? in another study	? (sample size < 50)	? (sample size < 50)	? (sample size < 50)
Tuna (3)	0	0	0	0	0	+
Turner (4)	0	0	0	? sample size < 50	0	? sample size < 50
Fransen (10)	0	? Sample size 31 ICC CI 0,60-0,96	0	? Sample size < 50	0	? Sample size < 50
Fransen (11)	0	0	? MWU, p>0,001 for differences in fast stride data	0	0	+

Gyory (12)	0	0	?, statistical method ?, sign differences between RA and normals	0	0	+
Keenan (13)	0	0	? no differences between the 2 groups	?	0	? sample size < 50
MacSween (14)	0	? ICC 0,91-0,96 in 22 normal controls	? small sample size(8), only sign difference in velocity	0	0	? sample size 8
Woodburn (15)	0	? MC 0.677 to 0.982 in healthy, 0.830 to 0.981 in RA	? sample size 11	0	0	? sample size 11
3D gait						
Tuna (3)	0	0	0	0	0	+
Turner (4)	0	0	0	? sample size < 50	0	? sample size < 50
Woodburn (15)	0	? CoMC 0.677 to 0.982 in healthy, 0.830 to 0.981 in RA	? sample size 11	0	0	? sample size 11
Weiss (16)	0	0	? sign. mean differences with 95% CI	-	0	+
Woodburn (17)	0	CoMC 0.97 to 0.77 in former study	? sample size 45	? sample size 45	? sample size 45	? sample size 45
Woodburn (18)	0	? CoMC 0,81 to0,97	? sample size 20	? sample size 20	? sample size 20	? sample size 20
EMG						
Keenan (13)	0	0	? no differences between the 2 groups	?	0	? sample size < 50
Other: ROM						
Gyory (12)	0	0	?, statistical method ?, sign differences between RA and normals	0	0	+
Kinetic data						
Weiss (16)	0	0	? sign. mean differences with 95% CI	-	0	+
Sakauchi (19)	0	0	? sample size 21	? sample size 21	0	? sample size 21
Nerve conduction						
Masson (8)	0	0	0	? differences DM/RA (statistic method NS) p <0,01	0	+

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Curriculum Vitae

De auteur van dit proefschrift is geboren in Rijssen, en ging daar naar de lagere school. De middelbare school volgde zij aan het College Noetsele in Nijverdal. Vanaf 1985 tot 1990 was zij in opleiding tot en werkzaam als operatie-assistente, in het Twenteborgziekenhuis te Almelo, zowel differentiatie chirurgie als anaesthesiologie. In 1990 begon ze haar studie geneeskunde aan de VU in Amsterdam. Tijdens haar studie deed ze een jaar musicologie aan de UvA, waar ze nog elke dag plezier van beleeft. Ook werkte ze daar als operatie-assistente in het Andreasziekenhuis en de Jan van Goyenkliniek. Na haar studie begon ze als AGNIO en vervolgens AGIO op de afdeling interne geneeskunde in de ZGT Almelo bij opleider dr. L. Van Bergeijk. Haar vervolgopleiding reumatologie vond plaats in Enschede, bij prof. MAFJ van de Laar. Inmiddels werkt ze sinds 2006 met veel plezier als reumatoloog in de ZGT. Ze is gehuwd en heeft 1 zoon.