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ORIGINAL ARTICLE

Physical articular examination in the activity of rheumatoid arthritis: a systematic review of the literature

Systematic review of the literature regarding physical examination in rheumatoid arthritis

Yimy F. Medina[1,5] · Rafael Eduardo Ruíz-Gaviria[2,3] · Adriana Buitrago-Lopez[3,4] · Catalina Villota[4]

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Abstract
To summarize evidence concerning the articular examination needed to determine rheumatoid arthritis (RA) activity (follow-up or control) via a systematic review. A search of Medline, Embase, Lilacs, SciELO, the Web of Science, the National Technical Reports Library, and the reference lists of relevant studies through March 2017 was conducted using a systematic methodology to identify studies of patients with RA older than 18 years in which a detailed description of the physical examination or a description of the components of the articular examination was provided. Of 8322 references, 74 studies were included according to the selection criteria, and 6 references were ultimately included at the end of the review. Most of the included studies ($n = 5$) were associated with a moderate risk of bias. There was great variability among the studies and the articular examination methods used. Some studies presented the examination with a complete specification of the technique ($n = 2$), the consensus of rheumatologists ($n = 2$), or training through audiovisual materials and face-to-face courses ($n = 2$), but none of the studies explicitly showed the technique by which the physical examination was performed. Despite the importance of the clinical evaluation and physical examination of patients with RA for diagnosis, prognosis, clinimetrics, and follow-up, evidence concerning how to perform the articular examination is scarce.

Keywords Articular examination · Clinimetrics · Physical examination · Rheumatoid arthritis · Systematic review

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, multifactorial autoimmune disease [1]. RA occurs predominantly in women between the ages of 35 and 50 [2] and is characterized by inflammation and symmetrical pain in the joints, leading to limited movement and functionality [3]. In addition, RA is associated with an increased risk of death due to extra-articular and cardiovascular manifestations [4, 5].

Great advances have been made in the study of RA, such as the identification of anti-citrulline antibodies that are specific markers of the disease [6, 7]. Conventional, biological, and small-molecule disease-modifying drugs have also been identified [8, 9], and these drugs have improved the prognosis and quality of life of patients. In addition, specific treatment strategies have been studied, such as the treat-to-target approach, whose objective is to achieve low disease activity or remission [10].

In the follow-up of patients with RA, the articular examination is the cornerstone for determining disease activity and thus for measuring its severity; in this examination, the number of painful and inflamed joints is measured. However, in clinical practice, there are limitations associated with the application of this exam because of its variability and poor reproducibility [11]. The clinimetrics of RA are quantified using

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✉ Yimy F. Medina
yimy.medina@gmail.com

[1] Universidad Nacional de Colombia, Bogota, Colombia

[2] Hospital Universitario San Ignacio, Bogota, Colombia

[3] Department of Clinical Epidemiology and Biostatistics, Pontificia Universidad Javeriana, Bogota, Colombia

[4] School of Medicine, Pontificia Universidad Javeriana, Bogota, Colombia

[5] Clinical epidemiology Program, Pontificia Universidad Javeriana, Bogotá, Colombia

indices and scales that take into account the number of inflamed and painful joints; of these, the most commonly used are the DAS28 (Disease Activity Score), the CDAI (Clinical Disease Activity Index), and the SDAI (Simple Disease Activity Index) [12]. Some studies have emphasized the lack of articular counting by many rheumatologists [13] and the lack of a consensus for performing a proper articular examination; these studies recommend the development of a standardized technique that can be taught to rheumatology specialists, physicians in training, health professionals, and patients [14].

Considering this situation, it is necessary to standardize not only the physical examinations for articular pain and inflammation but also the differential diagnosis of acute, chronic, and residual synovitis and the sequence of the articular physical examination in adults. This study sought to summarize the available evidence to determine whether a standard for effective articular examination exists for treatment follow-up and prognosis determination in adult RA patients.

Materials and methods

A systematic review of the literature (SRL) was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) standards [15]. Approval of the ethics committee was not required because this review was a secondary data analysis.

Literature search

To achieve the objective of the study, a systematic search of six databases (Medline, Embase, Lilacs, SciELO, the Web of Science, and the National Technical Report Library) through August 2016 was conducted. To increase the sensitivity of the search and to identify "gray literature" references, searches were also performed using the Google Scholar search engine. The searches were updated from the date on which the first search was conducted through March 2017.

The search strategy was based on two components: RA and physical examination. The terms used were obtained from the MeSH terms, thesauri, and the keywords of the various references of the cohorts used for the development of the 2010 RA diagnostic criteria [16]. The terms were modified by the group's clinical experts and adapted to each of the databases to optimize the search strategy.

To capture studies not explicitly including the aforementioned terms in the title or abstract, general terms referring to the clinimetrics of RA and the articular examination were included. In addition, a search of the reference lists of the selected articles was performed, and the authors of the included articles were contacted about additional studies. The search strategies for each of the databases are shown in the supplementary material. The references were archived and systematized using Mendeley® bibliographic reference management software (Team, T. M. S. 2010. Mendeley Ltd., London, England. Retrieved from http://www.mendeley.com/getting-started/).

Selection criteria

The references identified using the search strategy were selected based on predefined selection criteria. Cross-sectional, observational, analytical, and experimental observational studies that described or evaluated the articular examination in patients older than 18 years with a diagnosis of RA were included. Studies including patients with diseases other than RA or pregnant women were excluded. There were no restrictions regarding language or publication date.

Study selection

After the duplicate references were removed, paired review was performed by two groups. Each group consisted of one member with experience in rheumatology (CV or YM) and another member with experience in SRL (RR or AB-L). The groups reviewed each of the titles and abstracts to determine whether they met the selection criteria. Doubts about a reference were resolved by the other pair of reviewers. The complete texts of the articles selected in the first screening, all of which were also reviewed in paired form by CV and RR, were extracted. The authors of conference presentation references were contacted for more information about their studies. When there was disagreement regarding the first screening or the second selection of articles, the decision of whether to include the article in the study was made by the most experienced clinician.

Data extraction

A database was built in Microsoft Excel® for the extraction of data. The database included the characteristics of each study (the author, the type of study, the country, and the year in which the study was performed), the characteristics of the patients with RA, the methods used for the physical examination or clinimetrics, and the techniques or measures used in training the health professionals or patients who performed the articular examination. In the constructed database, we also included the outcomes of the studies; these outcomes varied because there were no limitations on the type of study included. Therefore, correlation coefficients, concordance coefficients, sensitivity and specificity values, learning curves, changes in the assessed number of painful or inflamed joints, and scores of the scales used to evaluate RA activity (DAS-28, CDAI) were included. The data were independently extracted by two reviewers (RR and CV). When inconsistencies were

found, the data were confirmed and verified from the original sources.

Measuring the quality of the studies

Because non-randomized studies were obtained, the risk of bias in non-randomized studies of interventions (ROBINS-I) tool was used [17]. This tool evaluates the bias of non-randomized studies based on three major components (bias before intervention, bias during intervention, and post-intervention bias) using a rating ranging from a low risk of bias to a critical risk of bias.

Secondary references

A large number of studies identified in the search referred to the detailed description of the physical examination or clinimetrics in the EULAR (European League Against Rheumatism) handbook for physical examination in RA (*EULAR Handbook of Clinical Assessments in Rheumatoid Arthritis*) [18]. For this reason, the list of references in that book was reviewed in search of additional evidence.

Results

Study selection

A total of 8322 references was obtained; after excluding duplicates and performing the initial screening, 7272 of these remained. Of these remaining references, 74 articles that met the selection criteria were reviewed. No articles whose main objective was the detailed description of the articular examination in patients with RA were found. However, six articles describing some of the characteristics of the articular examination were included. The article selection process is shown in the PRISMA chart in Fig. 1 [19]. In terms of quality assessment, the included studies showed ranks between a low and moderate risk of bias, mainly due to patient selection bias, outcome reporting bias, and outcome measurement bias. The study by Cheung et al. [20] showed a low risk score for all the evaluated criteria (Table 1).

Table 2 shows the characteristics of the included studies and the study populations. The six included studies were observational; four of these were concordance studies in which the results of the articular physical examination were compared with ultrasonographic findings [22–25]. The other two studies evaluated the impact of health professional training on standardization of the articular examination of patients with RA [20, 21]. In the six studies, 381 patients ranging in age from 18 to 83 years were assessed and two to 68 joints per patient were evaluated. The studies by Naredo [24] and Kane [22] specified the type of treatment the patients received at the time of the examination. The studies by Stone [25] and Kane [22] reported that the patients evaluated had no deformities. (For additional information regarding the included studies, please consult the supplementary material.)

Evaluation of the RA articular examination

The proximal interphalangeal joints, metacarpophalangeal (MCP) joints, carpus, elbows, shoulders, and knees are the joints that are most relevant to the articular examination for RA. These are the joints that are usually involved in the disease and are relevant to the strategies used for evaluating and monitoring the patient's disease activity on several measurement scales [26].

In the identified studies, examination of the knees [22], MCP joints [25], and shoulders [23] and the combined evaluation of 58 joints [24] were described. The studies evaluating the knee and shoulder joints described the position and angle at which they were examined and the maneuvers and method used for assessing the inflammation and pain of these joints in a comprehensive and detailed manner [22, 23]. In studies evaluating the MCP joints and the 58 joints in the combined evaluation [24, 25], a prior consensus was reached among the participating rheumatologists to standardize the physical examination. Because these consensuses were not described or published, this information was requested from the authors; unfortunately, no responses were received.

The studies by Grunke [21] and Cheung [20] were performed as pedagogical interventions to improve the articular examination of patients with RA. Cheung et al. [20] trained nurses from rheumatology centers as part of the COMEDRA (Comorbidities and Education in Rheumatoid Arthritis) study, which sought to evaluate the impact of the visit of a trained nurse in the treatment of comorbidities. The results of the COMEDRA study have not been published; its ClinicalTrials.gov identifier is NCT01315652. In the first phase of the Cheung study [20], the nurses in training studied the EULAR handbook and videos available at http://www.rhumatismes.net/index.php?p=1 [27]. In the second phase, a face-to-face education session was conducted by rheumatologists at the COMEDRA study centers. In the last phase, the chief nurse and a rheumatologist at each center offered a physical examination practice exercise involving 20 patients to their nurses and, blinded to the results of the examinations, analyzed the agreement between the assessments made by the nurses and the rheumatologists.

In the study by Grunke et al. [21], a face-to-face course was offered to health workers (physicians and nurses) who were grouped according to their region (Europe, the USA, Australia, and Asia). The course covered clinimetrics and the physical examination of patients with RA. The training was based on the EULAR handbook, and the results of examinations given before and after the training were compared.

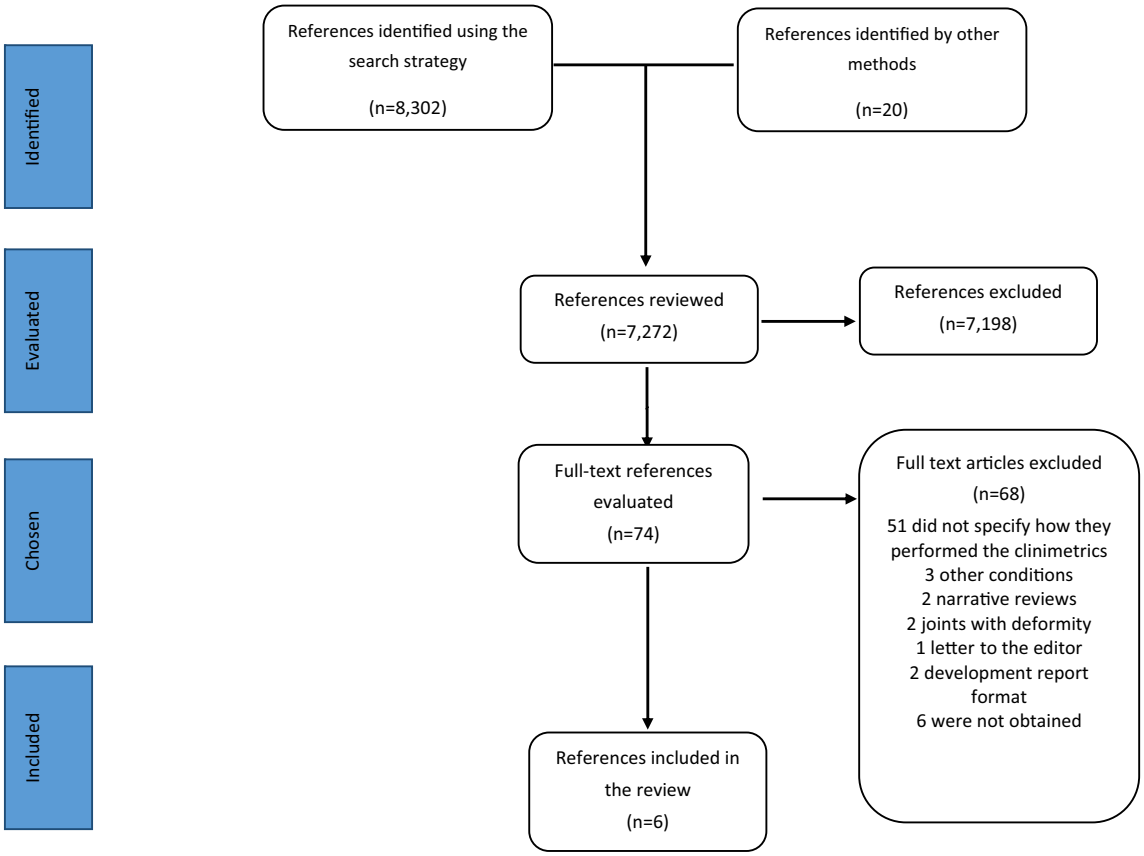

Fig. 1 PRISMA chart of the search methodology

Table 1. ROBINS-I evaluation of the included studies

ROBINS-I	Cheung 2014 [20]	Grunnke 2010 [25]	Kane 2003 [21]	Kim 2007 [23]	Naredo 2005 [24]	Stone 2009 [22]
Bias due to confounding						
Bias in selection of study participants						
Bias in classification of interventions						
Bias due to preference or modification of intervention						
Bias due to loss to follow-up						
Bias in outcome measures						
Bias in reported results						

Low risk of bias
Moderate risk of bias
High risk of bias
Critical risk of bias
Not possible to evaluate

Table 2 Summary of the characteristics of the included studies

Author	Country	Year	Objective	Patients (*n*)	Joints evaluated (*n*)	Specification of PE	Quality of evidence
Cheung PP et al. [20]	France; multicentric with 18 centers participating	2011–2014	To evaluate the learning curve of nurses in performing articular counting of patients with RA and the standardization of this evaluation	10 patients in the primary phase; 20 patients per participating center	280 joints in the primary phase	Specification and training of the PE were made through training courses, videos, and live demonstrations	Low risk
Grunke M et al. [21]	Multicentric; countries in Europe and USA	2002–2-006	To evaluate the variability of the articular PE and the impact of the implementation of training courses according to EULAR standards	1 for each group; 71 in the test group of 66/68 and 47 in the 28-joint group	17,068 in the group of 66/68 and 5488 in the 28-joint group	Training was conducted using live demonstrations, the EULAR handbook, and courses	Moderate risk
Kane D et al. [22]	United Kingdom	2003	To compare the operative characteristics of the PE with the US results to evaluate the knee articulation in patients with RA	22	44	Describes in detail the way in which the PE of the knee was performed	Moderate risk
Kim HA et al. [23]	Korea	2007	To establish the agreement of the PE and US results in evaluating shoulder articulation in patients with RA	30	60	Mentions the position in which the PE was performed as well as the maneuvers used to evaluate shoulder articulation	Moderate risk
Naredo E. et al. [24]	Spain	2004	To compare the level of inflammatory activity in patients with RA measured by physical examination versus the US gray scale	94	5640	A consensus was reached among the participating rheumatologists on how to perform the PE	Moderate risk
Stone MA et al. [25]	Canada	2009	To compare the determination of the inflammation of the MCP joints of fingers 2 to 5 between the PE and NMR	10 (5 with RA and 5 with psoriatic arthritis)	8	Specified by a live demonstration and by consensus among rheumatologists	Moderate risk

RA rheumatoid arthritis, *PE* physical examination, *EULAR* European League Against Rheumatism, *NMR* nuclear magnetic resonance; *US* ultrasonography

The number of joints evaluated varied according to the assigned group (groups of 28, 66, and 68 joints were assigned).

A large proportion of the articles excluded due to the lack of a description of the physical or articular examination cited the EULAR handbook instead [18].

Discussion

The articular examination is the cornerstone for the RA activity determination, follow-up assessment, and clinimetric evaluation, as well as for determining and implementing therapeutic strategies. It is also critical for diagnosis, as discussed in the 1987 American College of Rheumatology (ACR) criteria [28], and in the new classification criteria proposed in 2010 [16]. Despite the importance of physical and articular examination in RA, no articles were found that described detailed methods for performing the articular evaluation, probably due to assumptions that educational programs of health professionals are currently teaching them in their basic learning core because of the frequency of musculoskeletal complaints among patients [29, 30]. Another reason for the lack of a detailed description of these examination methods may be the gradual replacement of these by other diagnostic methods developed due to recent scientific advances in the evaluation of RA [31].

The articular physical examination is very important in RA, as was demonstrated in the study by Castrejon et al. who conducted a survey of rheumatologists and non-rheumatologists on the importance of vital signs, clinical history (CH), physical examination, and additional examinations in eight diseases, including RA. Fifty percent of the respondents indicated that CH and physical examination were the most important components in the diagnosis and management of RA patients [32].

Despite the importance of the physical examination in RA, there is wide variability in its implementation [33]. Cheung et al. conducted a sub-study in the context of the COMEDRA study to assess the variability of the physical examination and clinimetrics in patients with RA. The objective was to identify the variability in the physical examination among the rheumatologists of the participating centers and to reach a consensus among them with bibliographic and audiovisual material from the EULAR handbook. Poor agreement was found between newly graduated and more experienced rheumatologists, with an initial kappa of 0.28 that increased to 0.54 after the consensus and a change in the agreement of the DAS28 from 71 to 87% [34].

Despite the sensitivity of the search strategy, no primary bibliographic references were found whose main objective was improving the heterogeneity of the physical examination. Due to the absence of this information, we included studies whose primary purpose was not the articular physical examination but did present some type of physical examination description, consensus, or training of the participating health professionals. It should be emphasized that these results were indirect, as in the study by Cheung et al. [20], in which a comprehensive process of training and consensus-building was conducted among rheumatologists using audiovisual media and leaflets from the EULAR handbook.

The EULAR handbook was produced by a group of three authors led by Dr. Piet Van Riel; these authors represented the EULAR and followed the OMERACT (Outcome Measures in Rheumatoid Arthritis Clinical Trials) consensus [35], which was conducted in 1992 in Maastricht. The minimum core group of variables, the measures, and the indices of activity for monitoring RA were defined in that work. The EULAR handbook is considered the guidebook for the clinical evaluation of RA that defines the minimum set of measures to be evaluated in clinical studies and describes the rates of disease activity. The book explains some techniques for the examination of each of the joints in a detailed and concise manner and shows images that guide the practitioner in how to perform the physical examination in detail. However, these techniques were apparently not obtained through a consensus of the members of that organization. During the review process of the references in this book, we found that no studies clearly explained the clinimetrics involved in the physical examination for RA.

It is striking that of the six articles included in the present review, only two were based on or initially referenced the EULAR handbook (Cheung [20] and Grunke [21]), whereas in the other four studies, articular physical examinations were not based on this reference. This finding provides additional evidence of the heterogeneity of articular examination in RA patients and shows how this variability may limit comparisons between different publications (see the table in the supplementary material).

This review has great strength in the use of a methodology consisting of not only the synthesis and systematic compilation of the best available evidence but also a search strategy with high sensitivity that enabled the identification of articles from journals published in different regions of the world without language or chronological restrictions. In addition, the inclusion of secondary bibliographic sources and the "snowball effect" adds more power to the excellent strategy employed. The weaknesses of this review are the use of indirect results from the included references and the fact that the search was exclusively performed using electronic databases. It is possible that references related to this subject are available in physical media that are not accessible in electronic format; if so, this electronic search would lead to publication bias. However, the identification of such a bias would be difficult due to the lack of strategies that quantify this risk.

Conclusions

RA is a disease in which a physical examination and its clinical evaluation are still very useful for diagnosis, clinimetric evaluation or follow-up, and prognosis. Nevertheless, the available information on how to perform a proper and systematic articular examination is scarce and is not based on processes of consensus or proper validation. Therefore, due to the disagreement between different expert evaluators and the lack of adequate studies, the method of conducting the physical evaluation of patients with RA might be heterogeneous and non-standardized.

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Compliance with ethical standards

Disclosures None.

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Ethical standards The manuscript does not contain any clinical or patient information because of its SRL design.

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