



Design of an algorithm for the diagnostic approach of patients with joint pain

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Received: 6 May 2020 / Revised: 20 July 2020 / Accepted: 4 August 2020

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Abstract

Background Rheumatic diseases are a reason for frequent consultation with primary care doctors. Unfortunately, there is a high percentage of misdiagnosis.

Objective To design an algorithm to be used by primary care physicians to improve the diagnostic approach of the patient with joint pain, and thus improve the diagnostic capacity in four rheumatic diseases.

Methods Based on the information obtained from a literature review, we identified the main symptoms, signs, and paraclinical tests related to the diagnosis of rheumatoid arthritis, spondyloarthritis with peripheral involvement, systemic lupus erythematosus with joint involvement, and osteoarthritis. We conducted 3 consultations with a group of expert rheumatologists, using the Delphi technique, to design a diagnostic algorithm that has as a starting point “joint pain” as a common symptom for the four diseases.

Results Thirty-nine rheumatologists from 18 countries of Ibero-America participated in the Delphi exercise. In the first consultation, we presented 94 items to the experts (35 symptoms, 31 signs, and 28 paraclinical tests) candidates to be part of the algorithm; 74 items (25 symptoms, 27 signs, and 22 paraclinical tests) were chosen. In the second consultation, the decision nodes of the algorithm were chosen, and in the third, its final structure was defined. The Delphi exercise lasted 8 months; 100% of the experts participated in the three consultations.

Conclusion We present an algorithm designed through an international consensus of experts, in which Delphi methodology was used, to support primary care physicians in the clinical approach to patients with joint pain.

Key Points

- We developed an algorithm with the participation of rheumatologists from 18 countries of Ibero-America, which gives a global vision of the clinical context of the patient with joint pain.
- We integrated four rheumatic diseases into one tool with one common symptom: joint pain. It is a novel tool, as it is the first algorithm that will support the primary care physician in the consideration of four different rheumatic diseases.
- It will improve the correct diagnosis and reduce the number of paraclinical tests requested by primary care physicians, in the management of patients with joint pain. This point was verified in a recently published study in the journal *Rheumatology International* (reference number 31).

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Keywords Algorithms · Arthritis · Lupus erythematosus · Osteoarthritis · Physicians · Primary care · Rheumatoid · Spondyloarthritis · Systemic

Introduction

Joint pain is one of the main symptoms and reasons for consultation in rheumatology. Most rheumatic diseases have joint pain as a common point, but it has characteristics that help to make a differential diagnosis. Four rheumatic diseases (rheumatoid arthritis, spondyloarthritis, systemic lupus erythematosus, and osteoarthritis) may have joint pain as a common semiological point, and considering that they have some individual characteristics that make it possible to differentiate them, we considered the idea of creating an algorithm for the non-rheumatologist that facilitates the approach to the patient with suspected rheumatic disease and leads to a more accurate diagnosis.

Rheumatic diseases are an important reason for consultation in outpatient and inpatient care. In general, primary care physicians are the gateway to the health systems of patients with suspected rheumatic disease. Unfortunately, in a high percentage of cases, the diagnostic approach of the patient with joint pain and suspected rheumatic diseases by primary care physicians is incorrect, as demonstrated by two studies in Colombia [1, 2] and a study conducted in Canada [3]. These studies showed that the correct diagnosis of patients with rheumatic diseases by primary care doctors does not exceed 50%. A study conducted in Chile evaluated perceptions regarding strengths, weaknesses, and confidence in the care of rheumatic patients by primary care physicians, and found weaknesses and lack of confidence in the approach of the rheumatic patient by general practitioners and specialists who are not rheumatologists [4]. Given the high frequency of error in the diagnostic approach of patients with suspected rheumatic diseases by primary care physicians, and in view of the importance of achieving an adequate diagnosis and timely referral to the rheumatologist, the idea of designing a tool to improve the diagnostic approach of joint pain by non-rheumatologists is warranted.

This research work seeks to design an algorithm that serves as a tool for the primary care physician to optimize their diagnostic approach of the patient with joint pain, and thus improve their diagnostic capacity in four rheumatic diseases.

Materials and methods

The Delphi method is an iterative process designed to combine the opinion of a group of experts within a consensus. It is

a structured methodology to systematically gather expert opinions about a problem, process the information, and finally, build a general group agreement [5]. The present study was carried out using the Delphi method as a consensus tool to construct the algorithm. In a first step, we made a literature review in order to identify the main symptoms, signs, and tests necessary to establish the diagnosis of the four diseases of interest: rheumatoid arthritis, spondyloarthritis with peripheral involvement, systemic lupus erythematosus with joint involvement, and osteoarthritis. The search focused mainly on semiology and rheumatology books, review articles on these topics, and clinical practice guidelines. The search was complemented with information from primary studies, through a search in Medline, Embase, Clinical Key, Scielo, and the Cochrane Library. The following search terms were used: “Diagnosis”; “Symptom Assessment”; “Syndrome”; “Arthritis, Rheumatoid”; “Lupus Erythematosus, Systemic”; “Spondyloarthritis”; “Osteoarthritis.” We include articles in English and Spanish published until December 31, 2018. Through this search, we identified the symptoms, signs, and paraclinical tests related to the four diseases of interest, with which we created the first questionnaire for the Delphi exercise.

Next, we describe the steps that were followed in this project, strictly applying the methodological guidelines for this type of consensus exercise [6]:

Formation of the coordinating group It was made up of three rheumatologists and an expert in the Delphi technique, with a doctorate in biomedical research methodology. The group was responsible for designing the project, making the initial review of the literature, selecting and inviting the experts, preparing the questionnaires, controlling the flow of information among the experts during the iterative consultation process, with the respective feedback, analyzing the responses of each round, preparing the subsequent questionnaires, and, finally, preparing the consensus document.

Formation of the panel of experts Rheumatologists who are members of PANLAR (Panamerican League of Associations for Rheumatology) were invited to participate. All members have at least 5 years of experience in the care area and are linked to teaching in medical training programs at the pre and postgraduate level in each of their countries.

Consultation with experts and definition of consensus Through the RedCap® information capture program, three independent consultations were carried out, and the link

generated by this program was sent to the email of each of the experts. Consultation number 1 was to define the signs, symptoms, and paraclinical tests that would make up the algorithm; consultation 2 was to establish the decision nodes and general structure of the algorithm, and consultation 3 to confirm the final structure of the algorithm.

- **Consultation 1:** The experts were asked to select from a list the signs, symptoms, and paraclinical tests that they considered related to the diagnosis of each of the four diseases. Next, they were asked to define, for the chosen items, the importance of each sign, symptom, or paraclinical test in the diagnostic process, using a Likert-type scale (very important, important, indifferent, not important, totally irrelevant). Finally, they were asked to add new signs, symptoms, or paraclinical tests (other than those presented previously), which they considered relevant in the diagnostic process, and specifically in the differential diagnosis of the four diseases of interest. As a definition of agreement, a sign, symptom, or paraclinical test was considered “accepted” for inclusion in the algorithm, if it was selected by more than 80% of the experts. Signs and symptoms that were not selected by more than 50% of the experts were removed from the consultation process. The items on which no agreement was reached (accepted by 50–80% of the experts), and therefore was not possible to define whether they were accepted or rejected as relevant in the diagnostic process, passed to a second round. The questionnaire for the second round included the items on which no agreement was reached, the answers issued by the experts (in an anonymous way), and the statistical analysis of the group answers of the previous round. From this point, the experts were asked to reevaluate their concepts, taking into account the group’s opinion, so that they could maintain or change the response given in the previous round, in the light of the new information presented.
- **Consultation 2:** This consultation questionnaire contained phrases that represented possible decision nodes for the algorithm, which were written by the coordinating group based on the results of consultation 1. The experts should indicate whether or not they agreed with each of these phrases, rating it on a Likert-type scale (totally agree, agree, disagree, strongly disagree). It was considered that an agreement was reached if more than 80% of the experts marked the phrase with “totally agree” or “agree.” As in consultation 1, the items marked by more than 50% of the experts would have marked as “totally agree” or “agree,” but without reaching the set value for consensus (> 80%), would undergo a second consultation round, providing the respective feedback on the group’s results.
- **Consultation 3:** Based on the information collected in the first two consultations, the coordinating group designed the algorithm. Following, the algorithm was presented to

the experts as an image file, and together with it a questionnaire asking for their opinion on whether the algorithm contained the signs, symptoms, and paraclinical tests necessary for an adequate approach to the patient with joint pain and suspicion of one of the four diseases of interest. In addition, they were asked if they agreed with the general structure and decision nodes of the algorithm. Each expert could reply with Likert-scale response options (completely agree, agree, disagree, completely disagree) and make general comments in a text box.

Results

The Delphi exercise included the participation of 39 rheumatologists from 18 Ibero-American countries (Argentina, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Dominican Republic, Ecuador, Guatemala, Mexico, Panama, Paraguay, Peru, Spain, USA, Uruguay, and Venezuela), all with recognition and leadership in their home rheumatology association and in PANLAR. The average time of experience as rheumatologists is 13.2 years (± 9.1), with a 100% response rate for the 3 consultations. The duration of this exercise lasted 8 months.

Consultation 1 Ninety-four items (35 symptoms, 31 signs, and 28 paraclinical tests) candidates to be included in the algorithm were presented to the experts. In the first round, 53 items (56.4%) were accepted, 11 (11.7%) were rejected, and no consensus was reached on 30 (31.9%). In the second round, 30 items were presented, 20 (66.7%) were accepted, 9 (30%) were rejected, and no consensus was reached on 1 (3.3%). The item on which no consensus was reached in the second round was “negative rheumatoid factor,” among the paraclinical exams for osteoarthritis. However, given that the acceptance score of this item in the second round was 79.5%, the coordinating group decided to consider it “accepted,” so as not to go on a third consultation round of a single item. In total, 35 symptoms, 31 signs, and 28 paraclinical tests were presented to the experts, of which 25, 26, and 23 were accepted, respectively. The average response time of the experts in this first consultation was 8.5 days (± 3.8). Tables 1 and 2 summarize the items evaluated in the two rounds of consultation 1.

Consultation 2 Fifteen phrases were presented to the experts representing possible decision nodes for the algorithm. In the first round of consultation, a consensus was reached on all phrases. Figure 1 summarizes the degree of consensus in the evaluation of each phrase. The average response time of the experts in this second consultation was 4.9 days (± 2.75).

Consultation 3 With the information collected in the two previous consultations, the coordinating group designed a

Table 1 Items evaluated by the experts in the two rounds of the first consultation for systemic lupus erythematosus with joint involvement and spondyloarthritis with peripheral involvement

Symptoms of systemic lupus erythematosus with joint involvement	Agreement round 1	Agreement round 2
Morning joint pain	89.7%	
Oral or nasal ulcers	84.6%	
Photosensitivity	82.1%	
Abundant hair loss	82.1%	
Hand pain	61.5%	89.7%
Raynaud's phenomenon	61.5%	82.1%
Osteoarticular pain that improves with movement	48.7%	
Osteoarticular pain that worsens with rest	46.2%	
Morning stiffness for more than 60 minutes	46.2%	
Evolution time less than one year	33.3%	
Signs of systemic lupus erythematosus with joint involvement		
Malar rash	84.6%	
Synovitis and/or pain in 5 or more joints	82.1%	
Oral or nasal ulcers	82.1%	
Raynaud's phenomenon	61.5%	87.2%
Symmetric involvement	56.4%	82.1%
Positive compression test	51.3%	43.6%
Difficulty gripping	48.7%	
Paraclinical tests for systemic lupus erythematosus with joint involvement		
Positive antinuclear antibodies (ANAs)	97.4%	
Positive anti-dsDNA	97.4%	
Positive anti-Smith	97.4%	
Complement consumption	97.4%	
Lymphopenia	84.6%	
Leukopenia	82.1%	
Thrombocytopenia	71.8%	97.4%
Symptoms of spondyloarthritis with peripheral involvement		
Pain that worsens with rest	94.9%	
Oligoarticular involvement	92.3%	
Morning joint pain	87.2%	
Pain that improves with movement	82.1%	
Ankle pain	74.4%	94.9%
Knee pain	74.4%	89.7%
Monoarticular involvement	59.0%	89.7%
Evolution time less than one year	38.5%	
Signs of spondyloarthritis with peripheral involvement		
Heel enthesitis	100.0%	
Dactylitis	100.0%	
Synovitis and/or pain in 1 to 4 joints (oligoarticular)	94.9%	
Uveitis	92.3%	
Asymmetric joint involvement	89.7%	
Synovitis and/or pain in ankles	89.7%	
Synovitis and/or pain in knees	79.5%	84.6%
Synovitis or pain in DIP joints in hands	71.8%	82.1%
Synovitis and/or joint pain (monoarticular)	65.8%	97.4%
Paraclinical tests for spondyloarthritis with peripheral involvement		
Increased C-reactive protein (CRP)	92.3%	
Increased erythrocyte sedimentation rate	82.1%	
Negative rheumatoid factor	76.9%	82.1%
Signs of Achilles enthesopathy in X-rays of feet	59.0%	46.2%
Juxtaarticular bone neoformation in X-rays of hands or feet	56.4%	48.7%

Scores marked in green correspond to the percentage of experts who approved the item, and with which it was included in the algorithm; those marked in yellow correspond to the percentage of experts who approved the item and with which it passed to the second round, and those marked in red, to the percentage of experts who approved the item, and with which it was decided not to include it in the algorithm. *DIP* distal interphalangeal

Table 2 Items evaluated by the experts in the two rounds of the first consultation for rheumatoid arthritis and osteoarthritis

Symptoms of rheumatoid arthritis	Agreement round 1	Agreement round 2
Symmetric joint pain	94.9%	
Morning stiffness for more than 60 minutes	94.9%	
Morning joint pain	92.3%	
Hand pain	87.2%	
Feet pain	76.9%	87.2%
Pain that worsens with rest	64.1%	89.7%
Pain that improves with movement	56.4%	46.2%
Evolution time less than one year	30.8%	
Good response to NSAIDs	25.6%	
Signs of rheumatoid arthritis		
Polyarticular involvement (synovitis and/or pain in 5 or more joints)	100.0%	
Synovitis and/or pain in wrists	100.0%	
Synovitis and/or pain in MCP joints	100.0%	
Synovitis and/or pain in PIP joints of hands	92.3%	
Symmetric involvement	89.7%	
Positive compression test	84.6%	
Difficulty gripping	66.7%	82.1%
Synovitis and/or pain in elbows	61.5%	92.3%
Synovitis and/or pain in knees	61.5%	87.2%
Synovitis and/or pain in PIP joints of the feet	61.5%	38.5%
Synovitis and/or pain in ankles	48.7%	
Synovitis and/or pain in MTP joints	43.6%	
Paraclinical tests for rheumatoid arthritis		
Positive rheumatoid factor	100.0%	
Positive anti-citrullinated protein antibody	100.0%	
Increased C-reactive protein (CRP)	100.0%	
Increased erythrocyte sedimentation rate	97.4%	
X-rays of hands with juxtaarticular erosions in MCP or PIP of hands	94.9%	
X-rays of feet with juxtaarticular erosions in MTP or PIP	89.7%	
X-rays of hands with juxtaarticular osteopenia in MCP or PIP	66.7%	46.2%
X-rays of feet with juxtaarticular osteopenia in MTP or PIP	59.0%	41.0%
Blood count with increased platelet count (thrombocytosis)	46.2%	
Symptoms of osteoarthritis		
Hand pain in first MCP	94.9%	
Knee pain	92.3%	
Pain that worsens with movement	89.7%	
Hip pain	87.2%	
Pain in DIP of hands	84.6%	
Pain that improves with rest	76.9%	100.0%
Joint pain in the evening	66.7%	48.7%
Evolution time greater than one year	64.1%	43.6%
Signs of osteoarthritis		
Heberden nodules	100.0%	
Bouchard nodules	97.4%	
Patellar rub	94.9%	
Paraclinical test for osteoarthritis		
X-rays of knees with reduction of the femorotibial joint space	100.0%	
X-rays of hands with reduction of the joint space in DIP	97.4%	
X-rays of hips with reduction of the coxofemoral joint space	97.4%	
X-rays of hands with reduction of the joint space in PIP	82.1%	
Normal C-reactive protein (CRP)	61.5%	92.3%
Normal erythrocyte sedimentation rate	53.8%	84.6%
Negative rheumatoid factor	53.8%	79.5%

Scores marked in green correspond to the percentage of experts who approved the item, and with which it was included in the algorithm; those marked in yellow, to the percentage of experts who approved the item and with which it passed to the second round, and those marked in red, to the percentage of experts who approved the item, and with which it was decided not to include it in the algorithm. *NSAIDs* non-steroidal anti-inflammatory drugs, *MCP* metacarpophalangeal, *PIP* proximal interphalangeal, *MTP* metatarsophalangeal, *DIP* distal interphalangeal

proposal for an algorithm for diagnosis and treatment of the four diseases of interest. The starting point of the algorithm is “joint pain” as a symptom, and it progressively shows semiological characteristics of pain, signs, symptoms, and paraclinical tests, which were ordered according to the importance given to them by the experts during the first consultation. The idea is to give a logical order to the approach to “joint pain,” to enable the user of the tool reaching a probable diagnosis of one of the four diseases of interest, or to take him/her to consider a different diagnosis.

The algorithm was sent to the experts along with five questions that sought to assess the degree of agreement with the structure, content, order, and decision nodes. The degree of agreement on each of the five questions exceeded 90%, so it was decided to keep the version presented to the experts as definitive (see Fig. 2). The average response time of the experts in this third consultation was 4.5 days (± 1.69).

The algorithm was designed strictly following the Delphi methodology, and complying with all the defining characteristics of this consensus technique:

- **Iterative process:** In consultation number 1, the experts issued their response or opinion on more than one occasion, through 2 rounds of questions that led to stabilize the opinions, so that the experts could reflect either reconsidering or reaffirming their opinion in the light of their own or other experts’ opinions. In consultations 2 and 3, only one consultation round was needed, since in the first round an agreement was reached.
- **Anonymity:** The experts did not know each other, and no member of the group knew to whom a particular concept or response corresponded; this prevented negative or positive influences of dominant members of the group. The coordinating group was responsible for communicating

with the experts, as direct communication between them was not allowed.

- **Feedback:** Before starting a new round, participants received information about their answers range to the items evaluated, highlighting the significant contributions of some of the experts, the discordant slants, or additional information requested by any of the participants. Consequently, before the second round of the first consultation, the experts were able to contrast their opinions with those of the rest of the group, and in this way, reconsider or reaffirm their position on the item under analysis.
- **Building a consensus:** The final purpose of the Delphi method is to obtain a general agreement of the group through the statistical processing of differences and coincidences, which was fully achieved in this exercise. Figure 3 summarizes the processes carried out in the Delphi exercise, within the framework of the 3 phases that make up this consensus technique.

Discussion

Relatively often, physicians have doubts about what is happening to the patient, which diagnostic test is the most appropriate, or what treatment will be the most effective given the presentation. As a result, uncertainty becomes a factor that constantly gravitates to the medical act. Uncertainty is part of the nature and essence of medical science [7]. Sir William Osler defined medicine as the science of uncertainty and the art of probability, and this premise is still valid today [8]. One way to reduce this uncertainty in medical practice is the use of algorithms. The word algorithm has an Arabic origin, comes

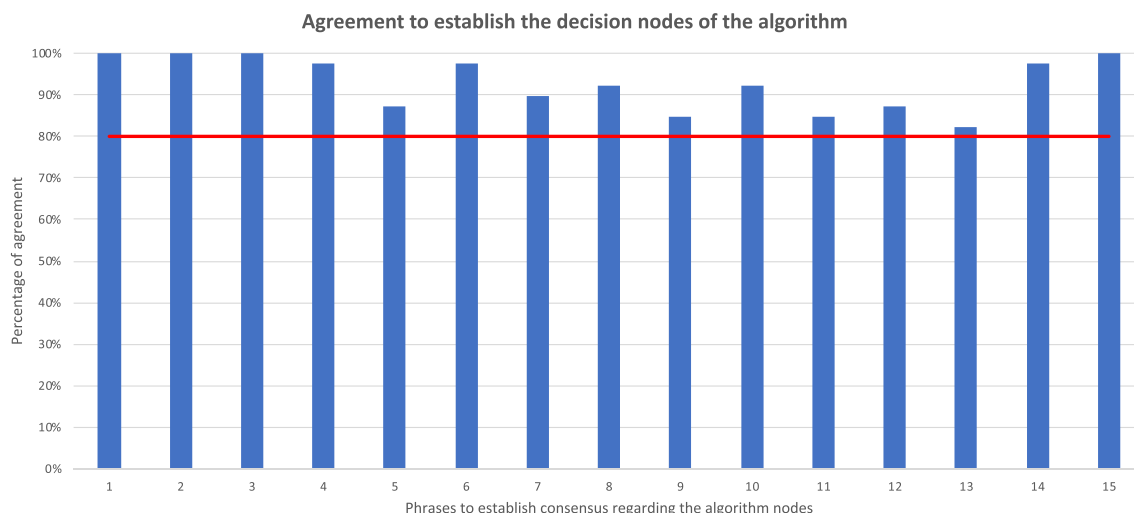
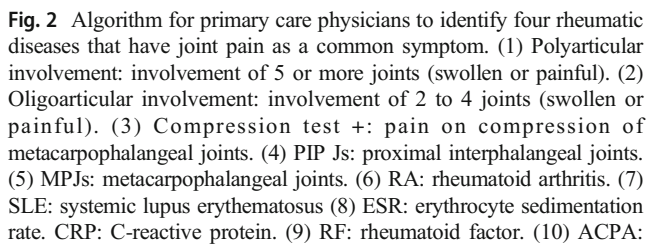
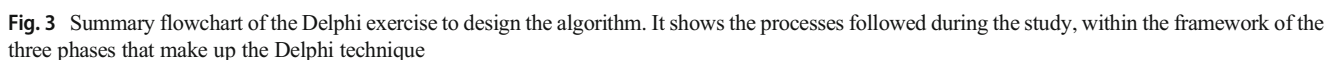


Fig. 1 Phrases presented to experts to define the algorithm nodes. The red line indicates the minimum point to define consensus: 80%



Anti-citrullinated protein antibody. (11) MTPJs: metatarsophalangeal joints. (12) ANAs: antinuclear antibodies. (13) Heel enthesitis: presence or history of spontaneous pain or swelling on examination at the place of insertion of the Achilles tendon or plantar fascia in the calcaneus. (14) DIPJs: distal interphalangeal joints. (15) Anterior uveitis: history of anterior uveitis confirmed by an ophthalmologist. (6) Inflammatory low back pain: night-predominant pain, insidious onset, improvement with exercise, does not improve with rest



from “al-Khwārizmī,” nickname of the famous mathematician and astronomer Mohamed ben Musa, born in 780 after Christ in Uzbekistan. The term al-Khwārizmī means “from Khwārizm,” the state where Ben Musa was born [9]. An algorithm is an orderly and finite series of instructions, steps, operations, or processes that allow us to find the solution to a specific problem [10]. Algorithms have been used in medicine for the diagnosis, treatment, and prognosis of different diseases [11]; its use has spread widely because they help the physician think more systematically, and although they do not resolve uncertainty, they can diminish it [12].

Algorithms have been designed in nearly all areas of medical knowledge, and rheumatology has not been an exception to this rule. In spondyloarthritis, the Berlin algorithm for low back pain is used, published in 2002 [13] and updated in 2013 [14]. In rheumatoid arthritis, the article of the 2010 classification criteria [15] includes an algorithm based on these criteria, but when searching the literature, we did not find other diagnostic algorithms for this disease. We found 3 prediction rules in rheumatoid arthritis, the most recent of EULAR [16], an outcome prediction rule for undifferentiated arthritis [17] and a prediction model for erosive arthritis [18]; these last two prediction models were evaluated in a study against the 2010 classification criteria [19]. Other rheumatology algorithms address topics such as osteoarthritis [20], Behcet’s disease [21], uveitis [22], vasculitis [23], and rheumatoid arthritis treatment [24].

Non-rheumatologists have used algorithms as a support tool in primary care [25]. These tools have become a strategy to improve education and practice in relation to rheumatic patients, furthermore, taking into account the lack of knowledge of non-rheumatologist regarding rheumatology issues, since training in this area during undergraduate medical school has been documented as insufficient [26]. Several investigations in different regions of the world have found shortcomings in undergraduate medical school in the areas of rheumatology and the musculoskeletal system, as is the case of the UK [27], North America [28–30], France [28], and Latin America [29]. In this regard, our research group proposes an algorithm that supports the non-rheumatologist in the diagnostic approach to patients with joint pain. This algorithm integrates into a single tool four rheumatic diseases with one symptom in common: joint pain. This makes it a novel algorithm, as it is the first one of its kind that will support primary care physicians in the differential diagnosis of four rheumatic diseases.

The algorithm starts with the symptom “joint pain,” and then it presents to the physician defining aspects of inflammatory joint pain; this creates different paths to follow, defined by the number and by the type of joints involved defined by the number and then by the type of joints involved. From this point, the physician using the algorithm finds boxes with signs, symptoms, or paraclinical test findings, which, according to their presence in the patient’s clinical context, will allow

the physician to move within the decision tree. In several of these boxes, it was not possible to establish minimum criteria to take into account to advance in the flowchart; for this reason, the developer group decided to present them in an open way, with the “and/or” connector, so that the physician sees in these boxes a body of knowledge that allows orientating itself in the case, and clinical context of the patient, and thus making a decision as for the need of tests or advancing until making a diagnostic approach to the case. It is important to remember that one of the best-known properties of decision trees is the representation of knowledge [30]; therefore, we decided to include these boxes in the algorithm with a group of items that would allow the physician evaluating the patient in the light of this information. The endpoints of the algorithm are four rheumatic diseases, or the option to consider another diagnosis. With the algorithm, we do not intend to replace the rheumatologist’s assessment, neither do we expect the algorithm to become a “diagnostic test”; our objective is to deliver a support tool to the non-rheumatologist to improve its clinical approach to joint pain, which allows to integrate semiological aspects and findings of paraclinical tests into clinical patterns of recognition. A point to highlight of what the algorithm will be useful for is the ability to differentiate inflammatory conditions (requiring early referral to the rheumatologist) from osteoarthritis (which usually does not require referral to the rheumatologist), which will improve the process of remission of patients from consultation of the primary care physician to the rheumatologist.

The algorithm was validated for use in clinical practice in a study recently published, in which primary care physicians analyzed clinical cases of patients with joint pain, under the methodology of a randomized clinical experiment. The diagnostic algorithm proved to be an effective tool when used by primary care physicians; the proportion of correct diagnoses increased, and the number of tests requested in the development of the cases decreased [31].

A limitation of our study is that the algorithm lacks other diseases that can occur with joint pain, such as gout and fibromyalgia. However, these were not included because they have a different clinical context and would make the algorithm more complex. Among the strengths of our study, a large group of expert rheumatologists from Ibero-America was formed, and 100% of them participated in the 3 consultations; in addition, the response times for each query were short, and finally, a consensus was reached regarding the content and design of the algorithm. Additionally, it should be noted that the methodology and concepts of the Delphi technique were strictly followed; this is of great relevance, as a recent study by our research group evidenced the lack of compliance with the methodological guidelines of the Delphi technique in rheumatology studies [32]. Another strength is that the algorithm includes simple diagnostic tools available in daily clinical practice in most countries.

In conclusion, we present an algorithm designed through an international consensus of experts, using Delphi methodology, to support primary care physicians in the clinical approach to patients with joint pain.

Authors' contributions All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Daniel Fernández-Ávila, María Ximena Rojas, Sergio Mora, Paola Varela, and Enrique Soriano. The first draft of the manuscript was written by Daniel Fernández-Ávila, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript. All co-authors take full responsibility for all aspects of the study.

Compliance with ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethical Committee of Medicine Faculty of Pontificia Universidad Javeriana (ethics approval number: 2019/011) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Disclosures None.

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