

SUPPLEMENTARY MATERIAL

Development of an algorithm for optimizing the implementation of ultrasound in the diagnostic workflow in clinical practice: preliminary phase of the RADIAL study, a project of the US Study Group of the Italian Society for Rheumatology

Garifallia Sakellariou,^{1,2*} Antonella Adinolfi,^{3*} Joao Madruga Dias,⁴⁻⁶
Arianna Damiani,⁷ Greta Carrara,⁸ Carlo Alberto Scirè,^{8,9} Alberto Batticciotto,¹⁰
Manuela Costa,¹¹ Emilio Filippucci,¹² Francesco Porta,¹³ Marco Canzoni,¹⁴
Annamaria Iagnocco,¹⁵ Georgios Filippou¹⁶

*equal contribution

¹Department of Internal Medicine and Therapeutics, University of Pavia, Italy; ²ICS Maugeri IRCCS, Pavia, Italy; ³Rheumatology Division, Multispecialist Medical Department, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; ⁴iNOVA4Health Research Unit, Nova Medical School, Universidade Nova de Lisboa, Portugal; ⁵Comprehensive Health Research Center, Nova Medical School, Universidade Nova de Lisboa, Portugal; ⁶Médio Tejo Local Health Unit, Torres Novas, Portugal; ⁷Department of Clinical and Experimental Medicine, University of Florence, Italy; ⁸SIR Epidemiology Research Unit, Milan, Italy; ⁹School of Medicine, University of Milano Bicocca, Milan, Italy; ¹⁰Rheumatology Unit, Internal Medicine Department, ASST Sette Laghi, Ospedale di Circolo-Fondazione Macchi, Varese, Italy; ¹¹Department of Rheumatology, Centro Hospitalar de Lisboa Ocidental EPE, Lisbon, Portugal; ¹²Rheumatology Unit, Department of Clinical and Molecular Sciences, Polytechnic University of Marche, Ancona, Italy; ¹³Interdisciplinary Pain Medicine Unit, Rheumatology Section, Santa Maria Maddalena Hospital, Rovigo, Italy; ¹⁴Local Health Unit Rome-1, Rome-4 and Viterbo, Italy; ¹⁵Academic Rheumatology Center, AO Mauriziano di Torino, University of Turin, Italy; ¹⁶Department of Biomedical and Clinical Sciences, Rheumatology section, IRCCS Galeazzi - Sant'Ambrogio Hospital, University of Milan, Italy

Correspondence: Garifallia Sakellariou, ICS Maugeri IRCCS, Pavia, Italy.

Tel.: 0039 0382 5921.

E-mail: garifallia.sakellariou@icsmaugeri.it

Key words: early arthritis, rheumatoid arthritis, diagnosis, ultrasound, imaging.

Supplementary Table 1. Ranking of the variables in the surveys.

	<i>RA</i>	<i>PsA</i>	<i>PMR</i>	<i>gout</i>	<i>CPPD</i>	<i>OA</i>
	Positive RF/ACPA	Negative RF/ACPA	Age>50	Arthritis	Negative RF/ACPA	Negative RF/ACPA
	Polyarticular>oligoarticular>monoarticular	Elevated ESR and CRP	Elevated ESR and CRP	Negative RF/ACPA	Age≥50 years	Age≥50 years
	Arthritis	Polyarticular>oligoarticular>monoarticular	Polyarticular>oligoarticular>monoarticular	Monoarticular>oligoarticular>polyarticular	Arthritis	Symptom duration>3 months
	Elevated ESR and CRP	Age<50 years	Negative RF/ACPA	Elevated ESR and CRP	Monoarticular>oligoarticular>polyarticular	Polyarticular>oligoarticular>monoarticular
	Female sex	Symptom duration>3 months	Arthritis	Male sex	Elevated ESR and CRP	Female sex
	Symptom duration>3 months	Female sex	Male sex	Age≥50 years	Symptom duration>3 months	Arthritis
	Age≥50 years		Symptom duration>3 months	Symptom duration>3 months	Female sex	

RA, rheumatoid arthritis; PsA, psoriatic arthritis; PMR, polymyalgia rheumatica; CPPD, calcium pyrophosphate deposition disease; OA, osteoarthritis; RF, rheumatoid factor; ACPA, anti-cyclic citrullinated peptide antibodies; ESR, erythrocyte sedimentation rate; CRP, C reactive protein.

Supplementary Table 2. Diagnosis based on the algorithm and final diagnosis defined by the clinician.

	Final diagnosis					
Algorithm's diagnosis	CPPD	Gout	OA	PMR	PSA	RA
<i>Gout/CPPD/PsA</i>	1	1	0	0	1	1
<i>Gout/CPPD/RA/PsA</i>	0	1	0	0	0	1
<i>OA/CPPD/PsA</i>	2	1	6	0	3	0
<i>OA/CPPD/RA/PsA</i>	0	0	2	0	0	3
<i>PMR/RA/PsA</i>	1	0	3	8	4	15
<i>PsA</i>	0	0	1	0	1	0
<i>RA/PsA</i>	0	0	0	0	1	2

Results in bold represent disagreement. RA, rheumatoid arthritis; PsA, psoriatic arthritis; PMR, polymyalgia rheumatica; CPPD, calcium pyrophosphate deposition disease; OA, osteoarthritis.

Supplementary Table 3. Characteristics of the misclassified patients.

Patient	RF/ACPA	Acute phase reactants	Age> 50 yrs	Joint involvement	Algorithm diagnosis	Final diagnosis
1	-	+	+	Polyarticular	PMR/RA/PsA	CPPD
2	-	-	+	NA	OA/CPPD/PsA	Gout
3	-	+	NA	Monoarticular	Gout/CPPD/PsA	RA
4	-	+	+	Polyarticular	PMR/RA/PsA	OA
5	-	+	+	Polyarticular	PMR/RA/PsA	OA
6	-	+	+	Polyarticular	PMR/RA/PsA	OA
7	-	-	-	NA	PsA	OA

RA, rheumatoid arthritis; PsA, psoriatic arthritis; PMR, polymyalgia rheumatica; CPPD, calcium pyrophosphate deposition disease.

Supplementary Table 4. Final statements.

RA	<ul style="list-style-type: none"> ▪ The MCPs II-V and the wrists seem to be the set of joints with the best ratio of accuracy and feasibility for detecting the presence of GS synovitis and PD. ▪ A GS-synovitis and PD score > 1 at more than 2 joints of the hands is suggestive of the development of rheumatoid arthritis from an early undifferentiated arthritis. ▪ The presence of erosions at level of V MTP or the identification of an erosion $\geq 2,5$ mm at MCPs is suggestive of RA.
PsA	<ul style="list-style-type: none"> ▪ The US assessment of peritendinitis (GS+PD) on MCP (II-III) and PIP joints (central slip enthesitis + soft tissue oedema – not SLR based) is useful in confirming the diagnosis of PsA. ▪ The hand soft tissue oedema by US around flexor tendons is specific in confirming the diagnosis of PsA. ▪ The enthesal PD (< 2mm) (Achilles tendon and proximal insertion of patellar ligament) MSUS assessment can help to confirm the clinical suspicion of PsA ▪ The enthesal erosion (Achilles tendon and proximal insertion of patellar ligament) US assessment can help to confirm the clinical suspicion of PsA
PMR	<ul style="list-style-type: none"> ▪ The bilateral presence of SAD bursitis may be suggestive for PMR ▪ The unilateral presence of bursitis/arthritis/tenosynovitis of the long head of the biceps at the shoulders might suggest PMR. ▪ The evaluation of the rotator cuff conditions is useful to exclude other shoulder pathologies that could be the cause of the clinical and US findings.
Gout	<ul style="list-style-type: none"> ▪ In case of acute arthritis, the presence of the double contour at the affected joint is useful to suspect the diagnosis. The absence doesn't exclude it. ▪ In the acute arthritis of any joint, the presence of lesions suggesting the deposition of MSU crystals (double contour and/or tophi) at I MTP and knees is useful to suspect the diagnosis. ▪ In case of acute involvement of periarticular structures (bursitis, tenosynovitis), the presence of lesions suggesting the deposition of MSU crystals (double contour and/or tophi) at the level of the affected site, is useful to suspect the diagnosis. ▪ In case of a previous arthritis acute attack, the presence of double contour and/or tophi at the joint previously affected, and/or at level of I MTP and knees is useful to direct the diagnosis with high specificity.
CPPD	<ul style="list-style-type: none"> ▪ The menisci, the knee hyaline cartilage and the triangular fibrocartilage of the wrist are the sites to scan in order to confirm the presence of the typical CPP deposits. ▪ The menisci are the most accurate and reliable sites, but the absence of CPP deposits at this level doesn't exclude CPPD diagnosis.
OA	<ul style="list-style-type: none"> ▪ The absence of any US pathological findings doesn't exclude the diagnosis of OA. ▪ The presence of osteophytes is suggestive of OA at level of the scanned joint ▪ The advanced changes of the hyaline cartilage (thinning, loss, irregularities of the cartilage margins) are strongly suggestive of OA. ▪ The presence of effusion/synovitis doesn't allow to confirm or exclude the diagnosis of OA.

RA, rheumatoid arthritis; PsA, psoriatic arthritis; PMR, polymyalgia rheumatica; CPPD, calcium pyrophosphate deposition disease; OA, osteoarthritis; MCP, metacarpophalangeal; PIP, proximal interphalangeal; MTP, metatarsophalangeal; GS, grey scale; PD, power Doppler; CPP, calcium pyrophosphate; US, ultrasonography; SAD, subacromial deltoid; SLR, systematic literature review.