Medical Ultrasonography
2010, Vol. 12, no. 4, 300-305

Gray scale and power Doppler ultrasonography in evaluation of early rheumatoid arthritis

Carolina Botar-Jid[1], Sorana Bolboacă[2], Daniela Fodor[3], Corina Bocşa[4], Maria Magdalena Tamaş[5], Mihaela Micu[6], Sorin M. Dudea[1], Dan Vasilescu[1], Radu Badea[7]

[1] Radiology Department, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, Romania
[2] Department of Biostatistics and Medical Informatics, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, Romania
[3] 2nd Internal Medicine, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, Romania
[4] University Medical Center Interservisan, Cluj-Napoca, Romania
[5] Rheumatology Department, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, Romania
[6] Rheumatology Department, Rehabilitation Hospital Cluj-Napoca, Romania
[7] Imagistic Department, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, Romania

Abstract

Introduction: Ultrasonography provides information regarding synovial membrane proliferation and its vascularization. **The aim** of our study was to evaluate the role of gray scale and power Doppler ultrasonography in assessing early rheumatoid arthritis by analyzing the scores determined by the evaluation of synovial proliferation, joint effusion, erosion or soft tissue swelling. **Material and methods:** The study was prospective comprising 34 patients (31 female, 3 men), mean age 45.68 years, with clinical changes and biochemical early rheumatoid arthritis. Bilateral wrist, II-V metacarpophalangeal, and proximal interphalangeal joints were evaluated by dorsal and palmar scans. **Results:** The mean duration from the onset of symptoms was 3.46 months. Based on the clinical, biochemical and US scores the patients from our study presented early stages of RA. Also, statistically significant correlations were observed between the time elapsed from the onset, the changes highlighted by ultrasound and the stage of the disease (stage 0 or 1). **Conclusions:** Our study confirms that US evaluation of changes in the joints of the hand offers useful information for staging the diagnosis of RA.

Keywords: gray scale ultrasound, Doppler ultrasound, rheumatoid arthritis, synovitis

Rezumat

Introducere: Examinarea ultrasonografică oferă informaţii asupra modificărilor ţesuturilor moi, evidenţiind foarte bine proliferarea membranei sinoviale şi a gradului de vascularizatie a acesteia. **Obiectivul** studiului a fost evaluarea rolului ecografiei bidimensionale si Doppler în stabilirea diagnosticului şi aprecierea severităţii poliartritei reumatoide prin analiza scorurilor stabilite prin ecografie. **Material şi metodă:** Studiul, de tip prospectiv (aprilie 2009 – august 2010), a cuprins 34 de pacienţi cu modificări clinice şi biochimice de poliartrită reumatoidă. Examinarea ecografică a fost efectuată cu un echipament Hitachi EUB 8500 cu transductor liniar cu frecvenţă variabilă 6,5-13 MHz. **Rezultate:** Din cei 34 de pacienţi incluşi în studiu, 31 au fost femei şi 3 bărbaţi, cu vârsta medie 45.68 ani. Durata medie de la debutul simptomatologiei şi prezentarea la medic a fost de 3.46 luni. Pe baza scorurilor clinice, biochimice şi ecografice, au fost stabilite stadiile evolutive. De asemenea, au fost observate corelaţii statistic semnificative între intervalul de timp scurs de la debutul bolii, modificările evidenţiate ecografic şi stadiul evolutiv al bolii. **Concluzii:** Studiul nostru confirmă faptul că evaluarea ecografică a modificărilor de la nivelul articulaţiilor mici ale mâinii oferă informaţii utile pentru stadializarea poliartritei reuamtoide.

Cuvinte cheie: ecografie bidimensională, ecografie Doppler, poliartrită reumatoidă, sinovită

Received 04.09.2010 Accepted 27.09.2010
Med Ultrason
2010, Vol. 12, No 4, 300-305
Address for correspondence: Carolina Botar-Jid
Radiology Department, University of Medicine and Pharmacy "Iuliu Haţieganu"
3-5 Clinicilor str. Cluj-Napoca, Romania

Introduction

Rheumatoid arthritis (RA) is a chronic and progressive systemic disease, characterized by inflammation of multiple joints. The disease has a prevalence of about 1% in the general population [1-5]. RA occurs two to three

times more often in women. The incidence is largely consistent racially and geographically, and the peak age of onset lies between 30 and 50 years of age [1,3,6].

The American Rheumatology Association (ARA) criteria established in 1987, are universally accepted for a positive diagnosis [1,7,8]. The early diagnosis and a proper therapy is crucial for managing patients with RA [5,9,10].

Conventional radiography remains the mainstay for evaluation RA patients in daily practice. In the early stages of the disease there may be no changes, or the X-ray may demonstrate juxta-articular osteopenia, soft tissue swelling and loss of joint space. As the disease advances, bony erosions and subluxation can be demonstrated [3,7,9,11-13].

Because the X-ray shows late signs of disease activity and destruction of cartilage or bone other medical imaging techniques such as ultrasound (US) and magnetic resonance imaging (MRI) are used in RA in order to assess the earlier signs.

Information provided by US is comparable to the MRI findings, with the advantage of accessibility, speed, lower cost and lack of ionizing radiation. High-frequency transducers (10 MHz or higher) have improved the spatial resolution of US images; these images can depict 20% more erosions than conventional radiography. Also, color Doppler and power Doppler ultrasound (PD US), which show vascular signals of active synovitis depending on the degree of inflammation, are useful in assessing synovial inflammation. This is important, since in the early stages of rheumatoid arthritis, the synovium is primarily affected, and synovitis seems to be the best predictive marker of future joint damage [5,14-21]. PDUS has proved to be a feasible and a promising tool for short-term monitoring of changes in synovial perfusion induced by disease-modifying anti-rheumatic drugs and biological agents in patients with rheumatoid arthritis [22,23], but more studies are required to achieve a proper standardization.

MRI is considered to be the best method for detecting joint inflammation, bone edema and bone erosions, but it is time-consuming, expensive and has limited availability [3,24-27].

Our study's objective was to analyze the contribution of US (gray scale and power Doppler) in assessing patients with early RA, in order to improve their management.

Material and method

In this prospective study 34 patients were included, examined in the Radiology and Imaging Laboratory of the Cluj Emergency Clinical Hospital for inflammatory joint disease between April 2009 - August 2010. The study was approved by the university Ethical Committee. The study included patients with swelling in at least two of the more small joints of the hand with a maximum duration of 2-6 weeks without any previous anti-rheumatic treatment. The patients were referred to the US by the rheumatologist after clinical evaluation and laboratory investigations. The rheumatologic diagnosis was of early RA based on the definition of early RA accepted in literature [1,7]. X-ray examination of the hands was performed on all patients.

US was performed using a 8500 Hitachi EUB machine and a 6.5-13 MHz variable-frequency linear transducer, in real time for all examined regions. The transducer was placed in the wrist region, II-V metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints on the dorsal and palmar view, billateralery. All the joints were assessed in transversal and longitudinal scans. The averaged time required for examination of the 22 joints was 15 minutes. The following pathological findings were noted: intraarticular fluid, synovial hypertrophy, erosions, and swelling of the adjacent soft tissues. Intraarticular fluid appears as an abnormal hypoechoic or anechoic (relative to subdermal fat, but sometimes may be isoechoic or hyperechoic) intra-articular material that is displaceable and compressible and does not exhibit a Doppler signal [28,29]. The synovial hypertrophy (synovitis) represents an abnormal hypoechoic (relative to subdermal fat, but sometimes may be isoechoic or hyperechoic) intra-articular tissue that is nondisplaceable and poorly compressible; may exhibit Doppler signal [28,29]. Bone erosions are seen as intraarticular discontinuities of the bone surface in two perpendicular planes [14,15,29].

We scored the US changes, using modified scores from literature, applied for the most affected joint [14]:

- synovial proliferation: 0 = absent, 1 = slight, 2 = moderate, 3 = intense;
- joint effusion: 0 = absent, 1 = present;
- erosions: 0 = absent, 1 = 2 erosions; 2 = more than 2 erosions;
- small parts swelling: 0 = absent, 1 = mild, 2 = moderate.

Doppler mode examination was performed in the same windows and sections with gray scale US. For a correct examination a lower PRF and greater color gain settings were applied. To avoid artifacts, the color gain setting was selected on a level slightly higher than noise.

The presence of blood flow in the synovial proliferation, was encoded by PD score: 0 = absence of Doppler signal, 1= reduced signal visible in a single vessel, 2 = moderate signal of vessels visible at the confluence, 3 =

intense Doppler signal present in more than half of intra-articular surface [14,19].

The US changes were compared with the serum level of 1 hour erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and rheumatoid factor (RF) scored as:

- ESR: 0 = normal values (0-10 mm), 1 = slow increased (10-20 mm), 2 = moderate increased (20-40 mm), 3 = very increased (> 40 mm)
- CRP: 0 = normal values (< 0.6 mg/dL), 1 = increased values (> 0.6 mg/dl)
- RF: 0 = absent, 1 = present

US changes were evaluated in stages, taking into account the time elapsed from symptom onset.

Processing and summarizing the results of statistical analysis was performed with SPSS 16.0 and Microsoft Excel.

Results

Of the 34 patients included in the study with mean age 45.68 years, 31 were female (91.18%. X-rays examination of the hands was normal in 29 patients. In 5 patients juxta-articular osteopenia and soft tissue swelling was detected.

The distribution of patients, according to the US, encountered changes and assigned scores are presented in table I (fig 1-4).

In order to study the correlation between the grade of synovitis and inflammatory blood tests, the relationship between synovitis score, PD scores and serum ESR, CRP and RF was evaluated. The results are presented in table II.

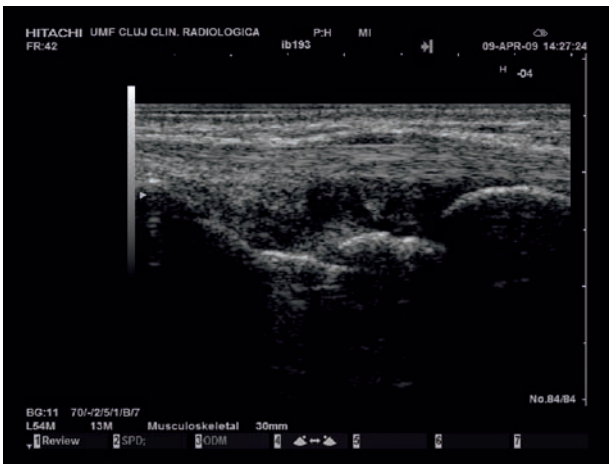

Fig 1. 2D US: F, 35 years, thickening of the synovial membrane in the right ulnocarpal joint

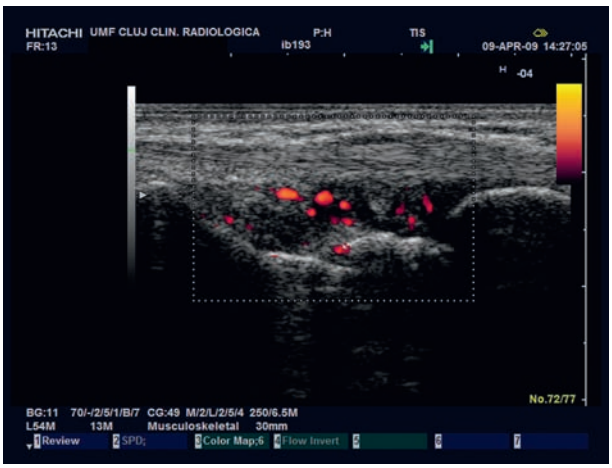

Fig 2. Power Doppler US: F, 35 years, proliferated synovial vascularity in the right ulnocarpal joint, score 2

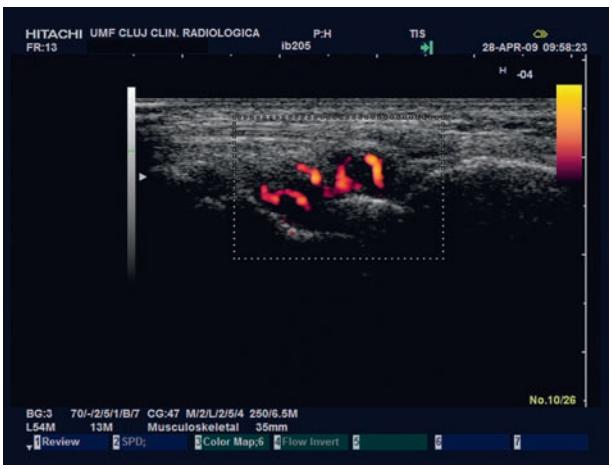

Fig 3. Power Doppler US: F, 42 years, proliferated synovial vascularity in the left third MCP joint, score 3

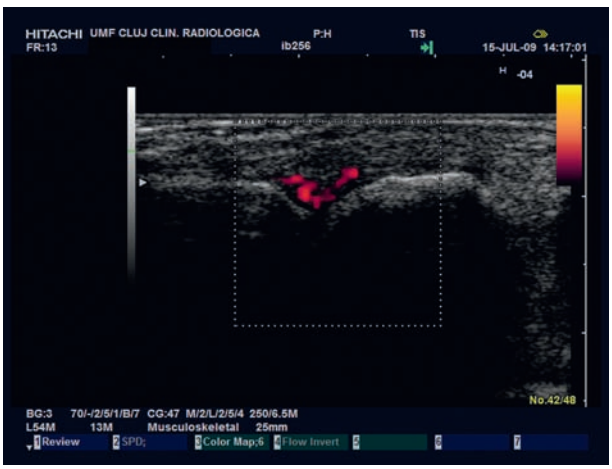

Fig 4. Power Doppler US: F, 45 years, proliferated synovial vascularity in the right second MCP joint, score 3

Table I. Distribution of patients according to US scores (total number of patients- 34)

Synovitis		Power Doppler vascularization		Joint effusion		Small parts swelling		Erosions	
score	n	score	n	score	n	score	n	score	n
0	5	0	5	0	29	0	5	0	31
1	12	1	22	1	5	1	24	1	3
2	15	2	4			2	5	2	0
3	2	3	3						

n- number of patients

Table II. Relationship between synovitis, power Doppler scores and serum ESR, CRP and RF scores

Synovitis score	Power Doppler score	ESR score	CRP score	RF score
0	0	0	0	0
1	1	1	0	0
2	2	2	1	1
3	3	3	1	1

Based on the clinical, biochemical and US scores, the patients from our study presented early stages of RA. Thus, 12 patients (35.30%) were included in stage 0, while 22 cases (64.70%) presented stage 1 of RA.

Average time elapsed from symptom onset and at diagnosis was 3.46 months. Therefore, to verify the assumption that there is a statistically significant correlation between the onset of RA, the pathological stage of disease and the US changes, the correlation coefficient of rank Spearman was calculated. Thus, we found that the stage of RA statistical depends on the time interval from symptoms' onset ($p = 1.53 \cdot 10^{-7}$). Also, the synovitis score and PD score are statistically correlated with the time interval from onset of the disease ($p = 2.47 \cdot 10^{-5}$, respectively $p = 1.3 \cdot 10^{-5}$). Statistically significant correlations between synovitis scores and stage of RA ($p = 2.81 \cdot 10^{-9}$), and between the PD score and stage of disease ($p = 7.7 \cdot 10^{-5}$) have been found. Also, power Doppler score has an interdependent relationship with the synovitis score ($p = 7.6 \cdot 10^{-6}$).

Discussions

The assessment of RA activity is of great importance regarding the accurate diagnosis and adequate therapy. The classic diagnosis is based on clinical examination, blood tests and radiological changes. Because conventional radiography shows only the late changes the evaluation by other imaging methods for emphasizing the early signs of joint damage has become increasingly important. 2D US has been proven to visualize synovial hypertrophy very well, which represents an earlier sign of the disease and produces the cascade of changes in the pathophysiology of RA [22]. PD has increased the sensitivity of US examination, by revealin the vessels inside the synovitis, the increased vascularity being associated with active joint inflammation [5,11,15].

At clinical examination the patients presented swelling of the articular/periarticular tissue. Frequently it is difficult for the clinician to identify the cause of this swelling but US identifies the intraarticular fluid or synovitis responsible for the joint swelling.

In our study findings revealed by US were included in low established scores. Synovitis was observed in most of the patients (29 patients); only in a small number of cases was it absent (5 patients). In the 5 patients with clinical soft tissue swelling, US revealed joint effusion, showing that inflammation intensity is very incipient.

In 10 cases with grade 1 of synovitis, we observed a greater PD US score, which probably means that the disease is more active than was suspected after examination using 2D US. On the other hand, in 11 patients the synovitis score was greater when compared with the PD US score. This observation can be explained by a lower grade of disease activity in these patients, even if it was marked synovial proliferation [5,11].

In 5 patients the joint effusion was detected without synovial proliferation. This fact can be explained by the observation that intraarticular fluid is not specific for RA, while synovitis represents the most characteristic sign of joint alteration in RA [5,11,13,15].

The erosions were present only in 3 patients of our group, a fact which confirmed that our patients were in the early stages of disease [9,15]. This is due to the selection criteria of patients included in the study. In spite of symptoms that fit the definition of early RA, there are some cases with advanced disease, which bone erosions show the long subclinical evolution. In these cases, radiological examination revealed no bone lesions, so that in such cases, US evaluation is important to view changes and to establish more accurate staging.

There was a direct concordance between the degree of synovial proliferation and its vascularization and

ESR values. This is explicable due to the fact that ESR is a marker of inflammation, its values increasing with the degree of inflammation. CRP values were normal in cases with low synovitis and PD US score (CRP is better correlated with the degree of inflammation in RA). RF values were negative in cases with a low degree of synovitis and positive in cases with a stage grade of disease, but with no statistical significant correlation with the activity of disease.

Patients in our study were included only in stages 0 and 1 of PR by Rx evaluation, most being in stage 1. This presents an important factor for the patients' management; in these stages applying an optimal therapy can prevent disease progression and joint destruction. Detection of early RA findings is crucial for subsequent assessment and management of the disease. Follow-up of these patients will reveal the evolution under the treatment.

Analyzing the correlation between the onset of RA, pathological stage of disease and US changes, it can be seen that the evolution stage of RA is dependent on the time elapsed from symptom onset. It also significantly correlates with the evolutionary stage of synovitis ultrasound score and the degree of vascularization of proliferated synovial membrane. These observations confirm that US evaluation of synovial inflammation and degree of vascularization is important for diagnosis and staging of patients with RA [5,11,18].

There are certain limitations of the present study. One limitation is the lack of interobserver and intraobserver variability in US evaluation, this exploration being generally recognized as operator dependent. Another limitation is that the group was limited in the number of patients; a larger group of patients would probably have strengthened the results.

Conclusions

Our study confirms that US evaluation of changes in the joints of the hand offers useful information for staging diagnosis of RA. However, standardization of US is required to ensure accurate diagnosis, reproductibility and reliability.

Conflict of interest: absence of conflict of interest

References

1. Guidelines for the management of rheumatoid arthritis. American College of Rheumatology ad hoc Committee on Clinical Guidelines. Arthritis Rheum 1996; 39: 713–722.
2. Gabriel SE. The epidemiology of rheumatoid arthritis. Rheum Dis Clin North Am 2001; 27: 269–281.
3. Sommer OJ, Kladosek A, Weiler V, Czembirek H, Boeck M, Stiskal M. Rheumatoid arthritis: a practical guide to state-of-the-art imaging, image interpretation, and clinical implications. Radiographics 2005; 25: 381–398.
4. Alamanos Y, Voulgari PV, Drosos AA. Incidence and prevalence of rheumatoid arthritis, based on the 1987 American College of Rheumatology criteria: a systematic review. Semin. Arthritis Rheum 2006; 36: 182–188.
5. Farrant JM, O'Connor PJ, Grainger AJ. Advanced imaging in rheumatoid arthritis Part 1: synovitis. Skeletal Radiol 2007; 36: 269–279.
6. Majithia V, Geraci SA. Rheumatoid arthritis: diagnosis and management. Am J Med 2007: 120: 936–939.
7. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines: Guidelines for the management of rheumatoid arthritis: 2002 update. Arthritis Rheum 2002; 46: 328-346.
8. Arnett F, Edworthy S, Bloch D, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988; 31: 315–324.
9. Wakefield RJ, Gibbon WW, Conaghan PG, et al. The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis: a comparison with conventional radiography. Arthritis Rheum 2000; 43: 2762-2770.
10. Landewe RB. The benefits of early treatment in rheumatoid arthritis: confounding by indication, and the issue of timing. Arthritis Rheum 2003; 48: 1-5.
11. Weidekamm C, Koeller M, Weber M, Kainberger F. Diagnostic value of high-resolution B-mode and power sonography for imaging of hand and finger joints in rheumatoid arthritis. Arthritis Rheum 2003: 48: 325-333.
12. Lopez-Ben R, Bernreuter WK, Moreland LW, Alarcon GS. Ultrasound detection of bone erosions in rheumatoid arthritis: a comparison to routine radiographs of the hands and feet. Skeletal Radiol 2004; 33: 80–84.
13. Luukkainen R, Sanila MT, Luukkainen P. Poor relationship between joint swelling detected on physical examination and effusion diagnosed by ultrasonography in glenohumeral joints in patients with rheumatoid arthritis. Clin Rheumatol 2007; 26: 865-867.
14. Boutry N, Morel M, Flipo RM, Demondion1X, Cotten A. Early Rheumatoid Arthritis: A Review of MRI and Sonographic Findings. AJR Am J Roentgenol 2007; 189: 1502–1509.
15. Rednic N. Poliartrita reumotaoidă. In: Fodor D. Ecografie clinică şi musculoscheletală. Editura Medicală Bucureşti 2009; 286-300.
16. Schueller-Weidekamm C. Modern ultrasound methods yield stronger arthritis work-up. Diagnostic Imaging May 2010: 20-22.
17. Bajaj S, Lopez-Ben R, Oster R, Alarcón GS. Ultrasound detects rapid progression of erosive disease in early rheumatoid arthritis: a prospective longitudinal study. Skeletal Radiol 2007; 36: 123–128.
18. Farrant JM, O'Connor PJ, Grainger AJ. Advanced imaging in rheumatoid arthritis Part 1: Synovitis. Skeletal Radiol 2007; 36: 381-389.

19. Kamishima T, Sagawa A, Tanimura K, et al. Semi-quantitative analysis of rheumatoid finger joint synovitis using power Doppler ultrasonography: when to perform follow-up study after treatment consisting mainly of antitumor necrosis factor alpha agent. Skeletal Radiol 2010; 39: 457–465.
20. Reynolds PP, Heron C, Pilcher J, Kiely PD. Prediction of erosion progression using ultrasound in established rheumatoid arthritis: a 2-year follow-up study. Skeletal Radiol 2009; 38: 473–478.
21. Seymour M, Taylor PC. Articular ultrasonography in rheumatoid arthritis. Int J Clin Rheumatol 2009; 4: 583-595.
22. Ribbens C, Andre B, Marcelis S, et al. Rheumatoid hand joint synovitis: gray-scale and power Doppler US quantifications following anti-tumor necrosis factor alpha treatment: pilot study. Radiology 2003; 229: 562–569.
23. Taylor PC, Steuer A, Gruber J, et al. Comparison of ultrasonographic assessment of synovitis and joint vascularity with radiographic evaluation in a randomized, placebo-controlled study of infliximab therapy in early rheumatoid arthritis. Arthritis Rheum 2004; 50: 1107–1116.
24. Backhaus M, Burmester GR, Sandrock D, et al. Prospective two year follow up study comparing novel and conventional imaging procedures in patients with arthritic finger joints. Ann Rheum Dis 2002; 61: 895-904.
25. Bergin D, Schweitzer ME. Indirect magnetic resonance artrography. Skeletal Radiol. 2003; 32: 551-558.
26. Stewart NR, Crabbe JP, McQueen FM. Magnetic resonance imaging of the wrist in rheumatoid arthritis: demonstration of progression between 1 and 6 years. Skeletal Radiol 2004; 33: 704–711.
27. Østergaard M, Duer A, Hørslev-Petersen. Can magnetic resonance imaging differentiate undifferentiated arthritis? Arthritis Res Ther 2005; 7: 243-245.
28. Fodor D. Joints. In: Fodor D. Ecografie clinică şi musculoscheletală; Editura Medicală Bucureşti 2009; 50-63.
29. Wakefield RJ, Balint PV, Szkudlarek M, et al. Musculoskeletal ultrasound including definitions for ultrasonographic pathology. J Rheumatol 2005; 32: 2485-2487.