"OVIDIUS" UNIVERSITY CONSTANTA
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PSORIATIC ARTHROPATHY:DIAGNOSTIC FEATURES

-THESIS ABSTRACT-

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SUMMARY

GENERAL PART

***Key words*:** Psoriatic arthropathy, seronegative spondylarthritis , psoriasis, enthesitis, dactylitis, assessment tools, radiological scores, musculoskeletal ultrasound

I. Introduction

Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease define as an inflamatory arthropathy associated with skin or nail psoriasis.

Over the past decades, psoriatic arthritis has gained increaseing importance due to increasing incidence and prevalence, with major emphasis on establishing diagnostic citeria applicable since the early stages of the disease. In the era of biological therapy, many studies have found that lack of optimal management in the early stages of inflamatory process determines the radiological progression of joint damage and functional impairment, resulting finally a dicrease in quality of life. The clinical course of psoriatic arthropathy can be insidious and nondistructive, but many patients may have severe and sometime deforming arthritis, requiring an early diagnosis.

Specialized international scientific groups have made numerous attempts to establish clear areas of evaluation in psoriatic arthropathy, some of which are proposed and validated at the meeting OMERACT 7 (Outcome Measures in rheumatoid Arthritis Clinical Trials) in 2005. A series of clinical, imaging and quality of life assessment tools have been developed within the research group of Psoriasis and Psoriatic Arthritis (The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis - GRAPPA), others tools were presented at OMERACT 8 meeting (2007) and OMERACT 9 (2009). These scores were extremely useful in monitoring therapeutic efficacy in various clinical trials , but how to apply and interpret them into clinical practice remains a niche of study. Therefore it is necessary the enuntiation of the main clinical, biological and imaging

features, used in the light of new assessment tools validated for psoriatic arthropathy, that contribiue to early diagnosis of this condition .

Based on these considerations we presented in the ***general part*** of thesis the main data from national and international literature on the state and the current vision of psoriatic arthropathy, actual knowledge about world epidemiology, the pathophysiological relationship between arthritis and psoriasis, diagnosis of psoriatic arthropathy (clinical, biological and imaging) describing the main assessment tools validated in clinical and also, physical disability in patients with psoriatic arthropathy.

Personal study had the main purpouse to establish a general profile of patients with psoriatic arthropathy, with focus on the axial asymptomatic forms, peripheral arthritis seropositive for rheumatoid factor and anti-cyclic peptide citrullinated. Also we try to determine the influence of skin and nail psoriasis on the severity and clinical expression of arthritis, assess the physical function in our patients and establish a correlation between changes in radiological clinical and ultrasound caracteristics.

Part of the results were presented at the national conference: oral presentation at the XIV edition of National Congress of Rheumatology, 2010 ("Correlation between PASI score and severity of joint disease in patients with psoriatic arthropathy"), poster in the sixteenth edition, 2012 (The particularities of axial involvement in patients with psoriatic arthropathy"), two works were published in full in journals B + (Romanian Journal of Rheumatology, Romanian Journal of Internal Medicine), and several abstracts were accepted and published abstracts Annual European Congress of Rheumatology - EULAR - Berlin (2012), Madrid (2013) (as first author or co-author).

Finally, I wish to thank Professor Dr. Maria Șuța for valuable guidance and continued support in the development of this thesis and the results achieved over the research in national and international conferences.

A valuable aid was given to me with sincerity and confidence, by dr. Ana-Maria Ramazan whose high professionalism and tenacity has been a real support for this scientific study.

II. Aims of the study

***Purpose*:** establish a profile of the patient with psoriatic arthropathy and main directions of clinical, biological and imaging evaluation, objectified by specific scoring tools have been validated in international clinical trials and elucidate the main features required diagnostic clinician in clinical practice.

***Main objectives*:**

1. Evaluation of clinical and biological characteristics of psoriatic arthropathy, time relationship between skin and joint onset, analysis of spondyloarthritis and asymptomatic forms.
2. Establishing correlations between clinical and biological parameters and scores for evidence of possible diagnostic markers useful in clinical practice.
3. Functional assessment scores correlated with osteo-articular, skin and nails diseases.
4. Assessment of quality of life in patients with PsA by correlating with the severity of skin and joints damage.

***Secondary objectives*:**

1. The clinical, imaging and evolutivity features and the significance of rheumatoid factor and anti-cyclic peptide citrullinated in patients with psoriatic arthropathy.
2. Psoriatic arthritis influence on functional status and its association with all major comorbidities described in the literature for patients studied.
3. Established prognostic factors for the development of severe forms of the disease through the new assessment tools validated in international studies.

To achieve the objectives proposed we conducted a prospective cohort study, during 2006-2012, using a sample of 88 patients with psoriatic arthropathy in the records of the Department of Rheumatology of the Medical Clinic II (Chief of Department - Prof. Dr. Șuța Maria), County Emergency Hospital "Sf. Andrei" Constanta. Patients were consecutively evaluated during hospital admission or

in the outpatient periodic medical examination (type one day hospitalization). Patients were informed about the purpose of the study and obtained their informed consent.

Patients who have been previously diagnosed according to the Moll and Wright criteria (65 patients), were reviewed using CASPAR criteria to determine the validity of the initial diagnosis. Since 2006, the diagnosis of psoriatic arthropathy was made according to CASPAR criteria. Were finally included in the study 88 patients.

For good accomplishment of research, we used a sum of methods and materials necessary for rigorous scientific foundation of the objectives pursued [functional articular index, Maastricht Ankylosing Spondylitis Enthesitis Score - MASES, The Madrid Sonographic Enthesis Index - MASEI score, radiological Sharp van der Heijde score radiological BASRI-s (Bath Ankylosing Spondylitis radiologic Index for spine), the SF-36 (Medical Outcome Survey Short Form 36)].

Statistical analysis was performed using Statistical Package for Social Sciences (Statistical Package for the Social Sciences - SPSS) version 20.0, Chicago, Illinois, USA, after completing a database of 146 variables obtained in the two evaluation visits of patients.

III. Results and Discussion

III.1. Demographic characteristics of the group

The study group had a female / male ratio of 1.44 (52/36) with a mean age of 55.53 ± 11.06 years (range between 31-80 years).

Mean articular disease duration was 12.41 ± 11.52 years (range 1 to 53 years) and mean duration of psoriasis skin was 18.7 ± 15.05 years (range 1 to 53 years).

Joint disease onset was at a mean age of 43.2 ± 13.86 years (6 to 76 years), 8 patients debuting joint disease over 60 years and 2 patients had juvenile onset (6 and 13 years) attested by medical documents.

Table 1. The main demographic characteristics of patients in study

Demographic character	**Value**
Report B: F	0,75 (36/52)
Report Caucasian: Asians	16,6 (83/5)
Report rural: urban	0,3 (20/66)
Mean age (years)	55,53±11,06
The mean age at onset of AP (years)	43,2±13,86
The mean age at onset of psoriasis (years)	37,1 + 15,51
The mean duration of joint disease (years)	12,41±11,52
The mean duration of psoriasis (years)	18,7±15,05
Currently cutaneous psoriasis (no.,%)	81 (92%)
Mean PASI score	4,8±8,57
Psoriasis of the nail (no.,%)	56 (65,1%)
R F/ anti CCP positive (no.,%)	12/12 (9 pacients was seropositives for both markers)
Titre RF / anti CCP antibodies (IU / mL)	15±19,4 / 40,7± 111,5
Spondyloarthritis (no.,%)	57 (64,8%)
Diagnosis of AS(crit NY) (no.,%)	50 (57,5%)

AS= ankylosing spondylitis, NY= New York criteria, PASI= Psoriatic Area and Severity Index

We followed changes in joints and skin for early forms (defined as duration of arthritis less than 24 months) to highlight the clinical and imaging features of disease onset. Thus, in Table 10 it is observed that local manifestations of inflammatory disease activity (swollen joint count - SJC, tender joint count -TJC) is frequently present during in the first 2 years after onset, contributing to diagnosis and classification of disease, probably also to lack of adequate background therapy. In progress, destructive joint changes are major and affects an increasing number of patients, directly related with disease duration.

Table 2. The main clinical and biological features of the PsA by disease duration

	Early PsA	**Defined PsA**		**P**
		2-5 years (n=14)	**> 5 years (n= 65)**	
The mean age (years)	53,50 ± 13,886	57,08 ± 9,652	57,08 ± 9,652	0.074
The mean duration of psoriasis (years)	12,77 ± 14,11	20,76 ± 15,08	20,76 ± 15,08	0.044
VAS (mean ±SD)	63,77 ± 27,411	53,44 ± 25,08	53,44 ± 25,08	0.215
Mean SJC no	0,77 ± 0,927	1,59 ± 2,849	1,59 ± 2,849	0.800
Mean TJC no.	8,23 ± 9,884	7,28 ± 9,044	7,28 ± 9,044	0.420
Ankylosed joints no	0,54 ± 1,050	3,08 ± 7,797	3,08 ± 7,797	0.236
Deformities no	1,38 ± 2,399	4,68 ± 8,665	4,68 ± 8,665	0.490
Xray Erosion (no.)	3	7	41	0.747
Enthesitis (patients no)	6	12	44	0.529
Sacroiliitis (patients no)	3	10	49	0.081
Cervical injury	0	4	28	0.140
Family history of psoriasis (patients no)	0	1	18	0.061
ESR (mean ±SD)	25,13 ± 30,79	22,69 ± 19,06	27,83 ± 16,06	0.135
RF positive (no.of patients)	1	1	10	0.712

III.2. Relationship at the onset and influence of skin and nail psoriasis on arthritis in patients studied

Most patients have psoriasis lesions (75%) and low frequency was recorded to palmoplantar pustular psoriasis (10%) and flexural psoriasis (8%). Borderline lesions (umbilicus) were found in one patient.

PASI score had a mean of 4.84 + 8.57, with a minimum of 0 and a maximum of 48.2; 13 patients had severe psoriasis considered when calculating PASI score was greater than 10 (15.3%), settling at these patients a moderate correlation with caucasians (p = 0.05).

Note that 7 patients had cutaneous manifestations of psoriasis (without psoriasis) at any moment in the disease course, but five of them showing signs of nail psoriasis and

one patient who declared skin psoriasis in first degree relatives.

Skin lesions preceded the onset of articular manifestation in 60.2% of patients, while joint symptoms occurred prior skin condition to 27.3% of cases. A start at the same time has been reported in 12.5% of evaluated patients (Figure 5).

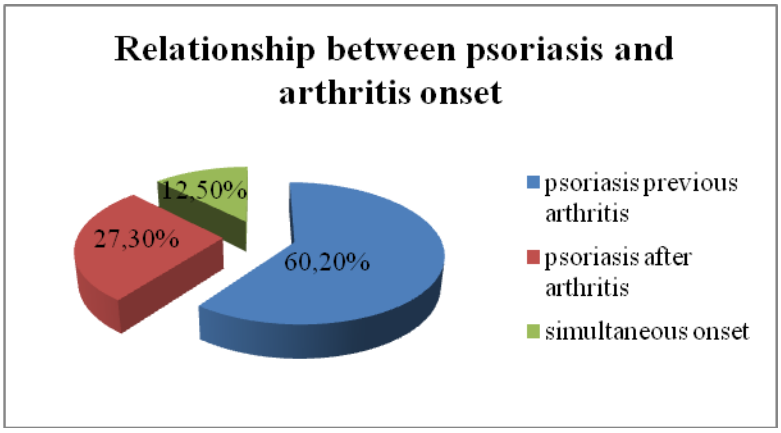

Figure 5. The relationship between psoriasis and arthritis at the onset of AP

These data are comparable with those of the literature reports, but higher percentage of psoriasis prior to arthritis onset (85%), and much lower when arthritis started before psoriasis (5-21%). Simultaneous occurrence of both psoriatic arthritis manifestations was reported in international studies between 5-10% (5-8).

Family history of psoriasis skin were recorded in 21.6% of cases (19 patients), also 13 cases of family history of spondylarthritis (14.8%), and, in particular, four patients had first or second degree relatives (ratio 3:1) with psoriasis and spondylarthritis in the same time (but without definite diagnosis of psoriatic arthritis). The influence of familial aggregation on articular severity indices, we observed that genetic predisposition for psoriasis is associated with spinal functional impairment (p= 0.09), whereas genetic predisposition for spondyloarthropathies has a direct connection to a high degree of axial activity impairment (BASDAI score = 5.29 ± 3.17 versus 5.07 ± 2.22 in patients with family history of SpA, p = 0.031).

Psoriatic nail were diagnosed by a dermatologist in a large number of patients (56 = 63.6%), the data fall into the results of international studies who have reported a

frequency between 53-86% of psoriatic nail dystrophy in patients with psoriatic arthritis (9,10). The most common nail psoriasis lesions are shown in Figure 6.

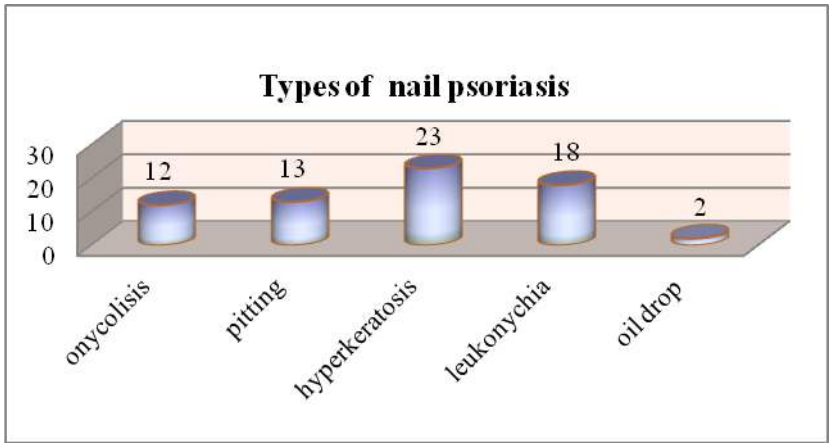

Figure 6. Types of nail psoriasis in patients from group

Analyzing the influence of nail psoriasis on articular manifestations we observed a significant relationship between parameters. Thus, psoriatic lesions of the nail matrix, particularly hyperkeratosis, were associated with a history of dactylitis ($p = 0.036$ / $p = 0.026$) and radiological changes in the cervical spine ($p = 0.060$), also with the presence of anti-CCP antibodies ($p = 0.05$). Onycholysis were correlated with ankylosing spine ($p = 0.034$), and hyperkeratosis with peripheral joint ankylosis ($p = 0.05$) and erosions of vertebral segment ($p = 0.011$). Leukonychia was associated with ankylosing peripheral joints ($p = 0.060$).

The presence of nail psoriasis in our patients with psoriatic arthritis is commonly associated with RF and anti-CCP antibodies and, especially with high titer of anti-CCP antibodies comparing with patients without nail psoriasis (43.1 ± 116.48 versus $36, 2 \pm 103.18$, $p=0.062$).

Psoriatic onychodystrophy plays a major predictor role for peripheral joint injuries potentially destructive, given the increased number of ankylosing and joint deformities found in these patients ($p = 0.020$, $p = 0.029$). We did not found a different physical disability of patients with nail involvement (average values of HAQ-DI scores were relatively equal in the two subgroups, p = NS).

A extended enthesitic process, measured by clinical MASES score is also related to pitting type nail lesions (p = 0.006) and specific osteo-erosive and osteo-proliferative structural damaged in the peripheral joints are found more frequently in patients with these extracutaneous lesions (Table 9.2).

Table 9.2. The main parameters influenced by nail psoriasis lesions and pitting

Imaging score	**Pitting average+DS;no (13patients)**	**No pitting average+DS;no (72patients)**	**P**	**Nail Psoriasis average+DS;no (56 patients)**	**No nail psoriasis average+DS;no (30 patients)**	**P**
Erosions score	12,3±15,63	10,5±10,53	0,040	9,9±10,87	13,1±13,15	0,760
Joint space narrowing score	10,8±14,28	23±24,65	0,127	17,5±19,78	27,7±29,65	0,551
Total Sharp score	23,1±29,55	33,5±31,93	0.354	27,4±25,81	40,8±41,34	0.213
BASRI	4,4±2,11	6,1±3,34	0,123	5,4±3,10	6,87±3,36	0,304
MASEI	1,83±1,94	2,87±2,97	0.289	2,4±2,67	3,3±3,6	0.288

We have also found a strong association between polyarthicular arthritis and the average age of onset of skin lesions (p = 0.011) and, to a lesser extent, between the duration of psoriasis and clinical forms at articular onset (p = 0.064). We found that skin and nail psoriasis were the most frequent in patients with oligoarthritis (27 and 32 patients), especially hyperkeratosis.

III.3. Study of psoriatic spondylarthritis in selected patients

In the literature, different definitions of psoriatic spondylarthritis have given, from isolated axial radiological changes to New York criteria for the diagnosis of ankylosing spondylitis.

Depending on the criteria used for selecting the cases, the frequency of axial involvement varies between 25-70% (11-13).

In our group of patients, we found the presence of axial involvement in a high percentage (70.45%). Of these, 71.18% (47.7% of all patients in the group) met the NY criteria to AS. Most patients had concomitant peripheral involvement (52 patients-85, 3%), including mutilating forms and only 9 patients had unique spine forms (14.51%). These results are similar to international reports, where it was established a maximum prevalence of 91.3 % for mixed forms (13). In Table 16 it can be seen the distribution of different axial regions involvement in patients studied, with almost the same percentage for the lumbar and thoracic segment.

Table 16. Distribution regions of spinal involvement

Region	Percentage
Cervical spine	54,2% (32 pacients from 59 with cervical X ray) 29 did not performed cervical Xray
Lumbar spine **(LBP and/or Schober<5cm)**	81,81%
Thoracic spine **(chest expansion<5cm)**	85,22%
Sacroiliac joints	70,5%

LBP=low back pain

A special attention has been granted both for ***asymptomatic sacroiliitis*** and/or ***spondylitis*** knowing accelerated progression of axial forms to disability. When radiological signs were present, in the absence of inflammatory low back pain, we classified patients as having asymptomatic sacroiliitis or peripheral spondylarthritis according to ASAS criteria revised in 2009 (14). Queiró et al. in his 2002 study (15) described the presence of asymptomatic sacroiliitis in 20% of patients, while another study conducted by Taylor et al in 2004 on 343 patients with PsA reported an even higher frequency of radiological lesions in the absence of axial symptoms (16).

In our study were classified as having asymptomatic sacroiliitis a number of 12 patients (13.63%), with a ratio B: F 3:1. These patients are part of a group of 28 cases who were never accused morning inflammatory pain or stiffness in the lumbar spine, resulting in a significant percentage of "silent" radiological damage (31.8%). Most

patients presented sacroiliitis grade 3 and 4 (83.3%) and 1 patient associated with aseptic osteonecrosis of the femoral head. In patients with peripheral spondylarthritis , we found a different ratio B: F (1:4), thus leading to the conclusion that women with inflammatory back pain have more frequently radiographic vertebral lesions, while men have predomonant sacroiliac involvement (Table 17).

Table 17. The main features of axial asymptomatic involvement

ASAS Criteria	***Peripheral Spondylarthritis 15patients (B:F=1:4)***	***Asimptomatic sacroiliitis 13patients (B:F=3:1)***
Arthritis • Oligoarthritis • Polyarthritis	 8(57%) 5 (35,7%)	 5(38,5%) 7 (53,8%)
Entesithis	7 (53,8%)	8(61,5%)
Dactylitis • History • Acute	 8 (57,1%) 4 (28,6%)	 9 (69,2%) 3 (23,1%)
Sindesmofite	0	4(33,3%)
Vertebral erosions	1(25%)	2 (16,7%)
Ligament calcification	11 (73,3%)	5(41,7%)
Cervical involvement	1 (25%)	5(45,5%)
Vertebral ankylosis	0	1(9,1%)
Sacroiliitis grade 2 • unilateral • bilateral	-	2(15,4%) 1 1
Sacroiliitis grade 3 • unilateral • bilateral	-	8(61,5%) 8 0
Sacroiliitis grade 4 • unilateral • bilateral	-	3 (23,1%) 2 1
AS diagnostic	0	3(23,1%)

Althought mobility and physical function was greatly influenced in this subgroup of patients, it is still superior compared to symptomatic patients. The patients in the group with inflammatory low back pain had a BASMI score 3.23 ± 3.01, respectively 1.00 ± 1.414 in those asymptomatic (p = 0.008), Shober index had an average of 3.35 ± 2.32

cm versus 4.33 ± 1.482 cm (p = 0.003), the chest expantion was 2.40 ± 1.38 cm, compare with 2,54 ± 0,964 cm in those without (p = NS), and the distance between the chin and the stenum reached the value of 3.82 ± 2.09 cm versus 2.50 ± 1.507 cm compared to asymptomatic patients (p = 0.043).

BASFI functional score generated an average of 6.29 ± 2.7, almost double comparing with asymptomatic patients (3.77 ± 2.335) (p = 0.006) and disease activity score BASDAI was increased in those patient who accused low back pain versus those without spinal pain (2.4 ± 5.91 / 4.16 ± 1.909, p = 0.028).

The most common ***radiological injuries*** were described syndesmophyte (p <0.05) and paravertebral ligamentous calcification (p = NS), certifying severe evolution of these cases. Radiological score BASRI-s resulting by summing the score for the sacroiliac joints and the cervical and lumbar spine is directly correlated to this subgroup of patients (p = 0.038), but not recorded statistically significant differences compared to group patients with low back inflammatory (5.30 ± 5.64 ± 2.263 to 3.19, p = NS). This supports the hypothesis that changes in asymptomatic radiographic severity were similar to those who accuse characteristic spinal inflammatory pain.

It seems that the absence of inflammatory spinal pain in patients with psoriatic arthropathy is not a sufficient criteria to exclude spinal damage and more, progression to disability, a hypothesis supported by other studies (17).

The main radiological changes monitored in patients with axial forms were quantified in radiologic score BASRI-s (Bath Ankylosing Spondylitis Radiographic Index for spine). The results for BASRI-s ranging from 0 to 4 points for all the components (the cervical spine, lumbar and sacroiliac joints).

For group followed BASRI - s average score was 6.31 + 4.706 , with extremes between 0 and 32. Knowing that spinal mobility is mainly influenced by structural osteo-articular changes at this level, as reflected by radiological score BASRI-s, we establish the degree of correlation between the radiological parameters and metrics. From Table

40 it can be observed a significant correlation between BASRI-s score and the main dynamic vertebral measures used in clinical practice, but also with composites scores (BASMI; p = 0.011). In addition, the data obtained confirm some international reports (18) on the relationship between radiological changes assessed by the BASRI - s score and axial mobility in all anatomical planes. It should be noted no statistically significant link between grade of sacroiliitis, classified according to New York criteria and inflammatory low back pain (p = 0.769).

Should be remarked that in patients with psoriatic spondyloarthritis, BASRI score had a strong correlation with the van der Heijde modified Sharp score (p = 0.005), calculated for radiological lesions in the peripheral joints, but also individual score for erosions (p = 0.022) and joint space narrowing (0.007), indicating ubiquitous distribution of deep structural damage. There was no significant correlation obtained with ultrasound enteseal MASEI score (p = 0.377) or clinical entheseal MASES score (p = 0.598).

Table 40. Correlation between radiological BASRI-s index and axial mobility parameters

The mobility indices (average± DS)	**BASRI-s score (P)**	**Degree of sacroiliitis (P)**
Chin-sternum (cm) (3,3 ± 2,13)	0.016	0.012
Chest expansion (cm) (2,4 ±1,37)	0.699	0.241
Modified Shober (cm) (3,5 ± 1,71)	0.001	0.003
Tragus- shoulder (cm) (11,5 ± 2,94)	0.031	0.017
BASMI (2,4 ± 2,71)	0.011	0.003
BASFI (5,3 ± 2,71)	0.404	0.047
BASDAI (5,1 ± 2,37)	0.502	0.265

Indicators of biological activity (ESR and CRP) did not affect the BASRI-s score value (p = 0.176; p = 0.265), thus allowing the assumptions of a radiological progression

even in the absence of systemic inflammation. On the other hand, we established a direct relationship between lumbar pain complaints of patients with PsA and radiologic changes composing the BASRI-s score.

Intimate correlation between the BASRI score and the major axial mobility indices and spinal pain provide a strong argument for structure-function relationship and the practical utility of these radiological scores.

III.4. The significance of the presence of rheumatoid factor and anti - cyclic peptid citrullinated antibodies in patients studied

Positive serology for RF and anti CCP antibodies is an important feature of rheumatoid arthritis, but, in recent years, has demonstrated their presence also in patients with psoriatic arthropathy: between 10-15% of patients may have anti-CCP antibodies present in the serum (19) and between 2 to 16.5% were seropositive for rheumatoid factor (20-23).

Considering that RF and anti-CCP antibodies occur particularly in patients with peripheral joint forms, I followed their presence in patients with oligoarthritis, polyarthritis and arthritis mutilans. Both biomarkers were found in 12 patients (13.6 %) , 3 patients with positive RF have associated positive serology for anti -CCP antibodies and 3 patients with anti –CCP antibodies present were negative for RF (9 patients were seropositive for both markers) so that there was a close correlation between RF and anti CCP positive patients in our study ($p < 0.001$). RF was present in significant titre mainly in women , the ratio B : F of 1:2 , with the same aspects as seen with anti-CCP antibodies (ratio of B : F = 1:1.4). All seropositive patients were Caucasian . 4 patients with positive RF had family history of psoriasis and only 2 patients reported relatives with spondylarthritis.

RF seems to affect the disease activity in peripheral joints as shown in Table 26. In these patients, there was a greater number of swollen joints ($p = 0.05$) and tender joints (p

= NS), a high level of joint pain score VAS (p = 0.03) and increased ESR and CRP (p = NS). Joint deformities were more numerous and functional HAQ score had increased in seropositive patients (p = NS) which gives us an indicator for severe joint disease and distorting .

Table 26. The relationship between activity indices and psoriatic arthropathy evolutivity presence of FR

	Positive RF (n=12)	**Absent RF (n=67)**	**p**
SJC	3±3,86	1,6±3,14	0.050
TJC	10,3±9,82	7,3±8,89	0.137
VAS	70,8±16,6	53,6±24,68	0.030
Ankylosed joint no	1,3±1,50	2,3±6,50	0.150
Deformited joint no	4,2±4,75	3,7±7,58	0.237
ESR	27,5±14,68	26,8±17,74	0.623
CRP	1,3±1,12	0,8±0,93	0.126
HAQ	1,4±0,77	1,2±0.79	0.512
BASFI	5±2,98	5,4±2,67	0.679
BASMI	0,8±1,33	2,5±2,67	0.018
MASES	4,1±3,61	3,6±3,08	0.708
MASEI	4±3,93	2,5±2,57	0.192
van der Heijde total score • **Erosions score** • **Joint space narrowing score**	41,8±19,77 14,6±8,99 27,2±12,83	29,8±34,04 10,5±12,12 19,3±25,71	0.016 0.071 0.017

From the results , we note that all activity indicators for peripheral joint disease (SJC, TJC, VAS, ESR, CRP) were elevated, but PCR titer was directly influenced by the presence of anti -CCP antibodies (p = 0.056). We found that the average number of ankylosing joints is similar in both groups of patients (p = 0.039), and functional indices for peripheral arthritis and axial involvement is at a low level in the group of RF-positive patients (p = NS) . Entheseal lesions, detected by musculoskeletal ultrasound and assessed according MASEI score were more numerous , calculating an double average score in seropositive patient group (4,7±3,67 versus 2,3±2,66, p = 0.017). Regarding the typical radiological changes for psoriatic arthropathy calculated according to van der

Heijde score, I observed the same trend towards more frequent osteo - erosive and proliferative lesions (p = NS) , similar to patients with positive RF . The same erosive elements , detected by ultrasound technique, were meet frequently in seropositive patients (58.33 %) compared to seronegatives (27.65 %) (p = 0.031) .

Table 28. Influence of anti-CCP antibodies on activity, functionality and severity of psoriatic arthritis

	antiCCP positive (n=12)	**antiCCP negative (n=47)**	**p**
SJC	2,6±3,96	1,3±1,99	0.224
TJC	8,3±10,01	7,9±9,62	0.750
VAS	63,3±25,34	53,4±25,44	0.193
Ankylosed joint no	1,3±1,50	1,3±5,36	0.039
Deformited joint no	3,1±4,15	3,4±6,13	0.803
ESR	29,7±16,94	24,5±13,46	0.351
PCR	1,2±0,93	0,8±0,93	0.056
HAQ	1,2±0,89	1,2±0,74	0.945
BASFI	4,3±3,41	5,37±2,52	0.327
BASMI	1,08±1,676	2,2±2,31	0.097
MASES	3,5±3,289	4,1±3,39	0.601
MASEI	4,7±3,67	2,3±2,66	0.017
Erosion ECHO	7(58,33%)	13(27,66%)	0.031
van der Heijde total score	38±24,41	27,9±31,90	0.108
• erosions score	14,3±11,03	8,6±8,66	0.165
• joint space narrowing score	23,6±14,68	19,3±26,20	0.150

Radiological erosive lesions were strongly associated in other studies with positive serology for RF and anti-CCP action (23,24,25). But it was not sufficiently studied the relationship between seropositivity and ultrasound changes in joints and periarticular structures, our study showing important correlations.

Calculating the predictive value of RF and anti-CCP antibodies in patients with psoriatic arthritis in the current study, we observed that anti- CCP antibodies has been shown to be a predictive factor for severe joint disease developed in both peripheral joints and axial segment, given the significant relationship with score for erosions of the van

der Heijde radiological score (p = 0.007), with the large number of erosions detected by ultrasound (p = 0.038) and the erosion of the vertebral bodies (p = 0.006). Patients with anti-CCP antibodies have frequently syndesmophytes (p = 0.036) and cervical involvement (p = 0.049). Our study noted no predictive element in relation to RF.

III.5. Characterization of imaging changes in patients of group

In particular, psoriatic arthropathy require complex imaging investigation, on the one hand to assess osteo-articular changes in the peripheral and axial joints and on the other hand for the early detection of synovial hypertrophy, tenosynovitis, enthesitis, intraarticular effusion or inflammatory synovial lesions detectable using new imaging techniques: musculoskeletal ultrasonography and magnetic resonance imaging.

For this reason, in the present study, we evaluated the articular and periarticular lesions by two different imaging techniques, namely conventional radiography and musculoskeletal ultrasound. For both techniques we applied the rules described for the calculation of scores for validated imaging psoriatic arthropathy: van der Heijde-Sharp score for radiological hand joints (26,27) BASRI-s for axial segment (28,29) and MASEI ultrasound enthesitis score (30).

Radiological changes in peripheral joints were evaluated according to van der Heijde-Sharp score. Since imaging studies performed in patients with psoriatic arthritis demonstrated that joint damage progress with the disease evolution (1,27), we evaluated joint damage in patients of group by disease duration. We found that radiological changes occur early in the disease, with rapid progression upward and a major expression in patients with a length of more than 5 years (Figure 19). Both destructive lesions and bone hyperproduction are found at onset, confirming data from the international literature that reported the presence of bone erosions and joint space narrowing from the initial stages of PsA (1,2,31), even in the absence of clinical symptoms.

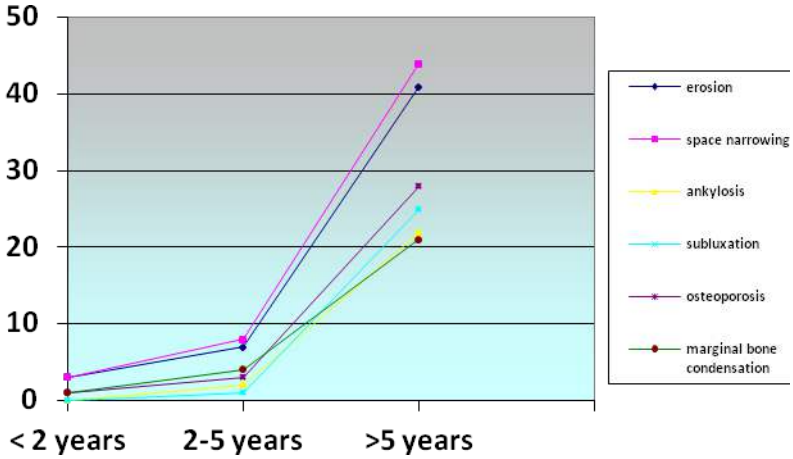

Figure 19. Evolution of the main radiological changes in the group of patients studied

Approach radiological changes depending on the clinical form showed an equal frequency of erosion ($p < 0.05$) in patients with oligoarthritis and polyarthritis. We could also demonstrate the close association between the severity of skin psoriasis calculated by PASI score, and arthritis severity, measured by the presence of osteo-destructive lesions ($p < 0.05$) and proliferative ($p < 0.01$).

Like individual radiological lesions, radiological Sharp van der Heijde score, modified for psoriatic arthropathy, recorded values increasing progressively with the disease. Sharp Van der Heijde total score was 31.44 + 31.463 average values for all patients in the group, amounted to erosion score (10.9 + 11 563) and the score for joint space narrowing (20.56 + 23.355). Except mutilating forms, the highest score was obtained from patients with radiologic spondyloarthritis, followed by polyarticular and oligoarticular pure forms. This score is associated with long joint disease duration and the patient's general impression of the disease, the number of deformed and ankylosing joints ($p < 0.001$).

Analyzing the impact of clinical manifestations of radiological progression in group of patients studied, we note that the number of swollen joints is a predictive factor for erosive disease ($p = 0.028$), while the number of tender joints is associated with the joint space narrowing ($p = 0.05$). Severe evolution of radiological changes, certified by joint ankylosis in peripheral joints, is significantly affected by joint disease duration ($p = 0.001$)

and functional status (p = 0.015). Also, joint ankylosis was identified more frequently in patients with RF and anti-CCP antibody-positive (p = 0.035, 0.005 respectively).

The data obtained are consistent with the results of recent prospective studies wich have shown that inflammation in the individual joints, expressed by the number of swollen and tender joint, can predict radiological progression to the erosion in those joints (32,33).

Table 35. Predictive factors for severe radiological progression

	Xray erosions	**Ankylosis**	**Joint space narrowing**
Sex	0.848	0.918	0.756
Age	0.632	0.706	0.431
Disease duration	0.769	0.001	0.947
Juvenile onset	0.453	0.306	0.125
SJC	0.028	0.691	0.107
TJC	0.176	0.917	0.050
HAQ	0.065	0.015	0.903
RF positive	0.365	0.035	0.286
antiCCP antibodies positives	0.620	0.005	0.911
Enthesitis	0.210	0.687	0.061

Musculoskeletal ultrasound gave accurate information on inflammatory and destructive changes in the joints, tendons and enthesis from peripheral joints, calculating also the entheseal MASEI score . Proportions of major joint and periarticular lesions visualized by this technique can be found in Figure 22, noting a high frequency of tenosynovitis , joint effusion and sonographic signs of inflammatory activity in joint.

We obtained a correlation between biological syndrome of inflammation (PrCR) and tenosynovitis (p = 0.038) and, weaker statistically, with joint effusion (p = 0.071) and Doppler signal (p = 0.065). Joint erosions are closely linked to increased ESR value at the time of evaluation (p = 0.006), but also clinically detected enthesitis (p = 0.013), rheumatoid factor (p = 0.039) and anti-cyclic peptide citrullinated (p = 0.031). There was a good correlation between erosions visualized by ultrasound and standard radiography (p = 0.05).

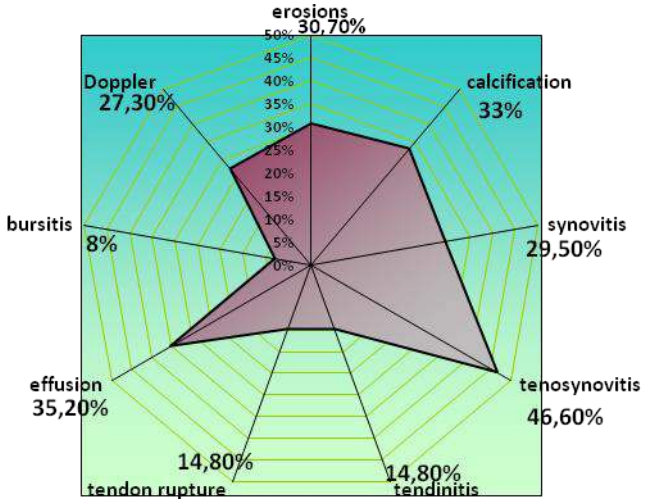

Figure 22. The main ultrasonographic changes observed in the patients studied

In our patients, ***MASEI score*** correlated well with major clinical and biological parameters of disease activity: number of swollen joints (p = 0.023), number of tender joint (p = 0.034) and ESR (p = 0.010). No correlations were obtained with functional or radiological scores, possibly due to a minimal functional impact of these injuries. Further, it has not been demonstrated a predictive role of a high MASEI score for severe osteo-cutaneous disease.

I noticed, however, that patients with ultrasound enthesitis were an increased number of erosive joints in the hand (32.6% versus 0% in those without enthesitis, p = 0.001), tenosynovitis (65.2% versus 26.1%, p = 0002), synovitis (47.8% versus 17.4%, p = 0.012) and tendinitis (20%, respectively 4.3%, p = 0.081).

On the other hand clinical entheseal MASES score correlated better with clinical parameters of joint inflammatory activity, but also functional ones (table 22).

Table 22. The relationship between entheseal indices (MASES + MASS) and joint disease activity

	MASES (p)	***MASEI(p)***
SJC	0.224	0.839
TJC	0.002	0.506
ESR	0.907	0.010
PCR	0.946	0.169
HAQ	0.004	0.684
Ankylosing joints no	0.011	0.370
BASDAI	0.001	0.969
VAS	0.008	0.763
Dactylitis	0.427	0.287

Comparing the data acquired with the 2 imaging techniques used in our study, we noticed that standard radiography detected more erosions than musculoskeletal ultrasound (58% versus 30.7%, p = 0.004), while lesions of soft such as ligament or tendon calcifications are frequently viewed by ultrasound (33% versus 26.1%, p = NS). Therefore we consider necessary the systematic use of ultrasound in current clinical investigations, together with standard radiography.

Table 44. Comparison of imaging techniques used in our study

Technique	**Erosions**	**Calcifications**
Radiography	51 (58%)	23 (26,1%)
Ultrasonography	27 (30,7%)	29 (33%)
	p=0.004	p=0.741

III.6. Aspects of functional status and quality of life of patients in group

To investigate accurately the functional impact on patients with PsA, we split our group into 3 subgroups according to the duration of joint disease. It can be seen from Table 45 that the functional indices for both peripheral joint as well as for the axial spine changes with increasing duration of joint disease (p = NS). The quality of life assessed by the SF-36, is greatly influenced early in the disease, the same aspect is observed in the case of the patient global assessment of disease (NGP).

An additional argument for the destructive and deforming character of psoriatic arthritis is the presence of ankylosis and joint deformities, since the early stages of the disease. In opposition to this feature is spinal damage, whose evolution is less severe, since vertebral ankylosing and aseptic osteonecrosis of the femoral head (AONFH) are lesions that are found in patients with established disease, especially after at least 5 years of the disease duration.

In contrast to other studies, quality of life is hampered especially in men (p = NS).

Average HAQ-DI of the entire group was 1.3 + 0.81, lower than has been reported in the REPArE study (mean = 1.5 0.56) (34), but higher than an Italian ultrasound study who reported a mean HAQ of 1.1 (35).

Quality of life, assessed using the Short-Form 36 was significantly damaged by the number of tender joints (p = 0.013), the inflammation of the spinal structures monitored by BASDAI (p <0.0001), MASES score (p = 0.012), but not the ultrasound MASEI score (p = NS).

Joint pain, whose main effect is to reduce normal daily activities and work capacity, is assessed by the patient using the visual analog scale (VAS). The severity of joint tenderness is in direct relationship with the SF-36 score (p = 0.003), recorded the same issue and if low back pain is present (p = 0.008). The same score was strongly correlated with decreased performance of daily activities objectified by HAQ - DI and BASFI (p <0.0001 for both indices), and the general mobility - BASMI (p = 0.011).

Statistical analysis determined that elements of biological syndrome of inflammation, ESR and CRP, were found in connection with the SF-36 score (p=0.022, p=0.025).

Table 45. Modification of functional indices based on disease duration

	Early AP	**Defined AP**		p
	< 2 years (nr=8)	2-5 years (nr=13)	>5 years (nr=64)	
VAS (mean±SD)	53,7±19,95	63,7±27,41	54,1±24,66	0.434
SJC(mean±SD)	3,6±6,30	0,77±0,92	1,62±2,86	0.129
TJC(mean±SD)	8,1±5,84	8,23±9,88	7,40±9,07	0.940
PASI (mean±SD)	1,9±2,45	7,9±7,58	4,5±9,12	0.007
PASI>10 (patients no,%)	-	4(30,7%)	9(14%)	0.141
HAQ (mean±SD)	1,1±0,75	1,2±0,90	1,3±0,81	0.422
BASFI (mean±SD)	4±2,07	5,8±2,67	5,46±2,77	0.143
BASMI (mean±SD)	0,75±0,70	2,2±1,86	2,5±2,88	0.074
SF-36 (mean±SD)	40±16,17	42,6±17,62	41,5±20,76	0.975
PGN (mean±SD)	58,5±17,72	53,4±32,60	59,6±23,76	0.743
Ankylosing joint no (mean±SD)	0.6±1,40	0,54±1,05	3,1±7,79	0.335
Deformed joint no (medie±SD)	2,8±4,12	1,3±2,40	4,6±8,66	0,789
Schober<2cm (pacients no,%)	0	2(15,5%)	14(21,8%)	0.300
Chin-sternum>2cm (patients no,%)	4(50%)	4(30,7%)	8(12,5%)	0.020
Tragus-shoulder >14cm (patients no,%)	1(12,5%)	3(23,%)	13(20,3%)	0.567
Vertebral ankylosing (nr. pacienți,%)	0	2(15,3%)	14(21,8%)	0.551
AONFH (patients no,%)	0	0	7(10,9%)	-

Knowing that the association of psoriatic arthritis with various ***comorbidities*** significantly decreases quality of life and increased mortality (36) among these patients, in relation to the severity of joint disease (37), we followed the presence and distribution in our group of patients, of the most important diseases that is associated with joint disease. Among our patients, was found a high prevalence of cardiovascular diseases (hypertension, ischemic coronary disease) and metabolic disorders (obesity,

dyslipidemia, diabetes), without neglected the kidney, liver or malignant, some data being similar to those reported by international studies (38-40).

Noteworthy is the presence of dyslipidemia and hypertension in most patients with severe psoriasis (90% and 80%, p = 0.012 / p = 0.027) with an increased risk of developing hypertension in patients with psoriatic arthropathy in the presence of severe skin disease (RR = 6.65).

IV. Conclusions

- Data from our study indicate the possibility of a diagnosis of psoriatic arthropathy in the absence of skin lesions, conditioned by the presence of psoriasis family history. Rigorous application of CASPAR criteria in clinical practice provides accurate and early diagnosis , on condition of a comprehensive approach to anamnesis .
- Familial aggregation of psoriasis is associated with a decrease functional status in axial region, and genetic predisposition for spondylarthropathies mainly influences the degree of activity in the spine.
- Psoriatic lesions of the nail matrix have a significant role in the development of clinical and radiological manifestations of psoriatic arthropathy. Hyperkeratosis and onycholysis were frequently correlated with severe structural damage (spondylitis, erosions), not only in the peripheral joints, but also in the spinal stuctures. In addition, the correlations obtained in the current study provides nail psoriasis, and especially pitting, a major predictive role for enthesitis assessed clinically by MASES score and by musculoskeletal ultrasound.
- Patients with psoriatic spondylarthritis had a moderate reduction of mobility of the spine.
- Asymptomatic sacroiliitis is frequent in patients with psoriatic arthropathy, mainly in men (ratio B: F = 3:1), with a major functional impact on all segments of the spine and coxo-femoral joints.

- Radiological lesions present in this subset of patients are important and extensive, showing progression to a severe impairment of spinal structures, even in the absence of symptoms.
- The presence of psoriasis skin and joint disease duration are predictors for cervical involvement.
- The presence of RF in patients with psoriatic arthritis is associated with active joint disease, demonstrated by a large number of tender and swollen joints, a high score for joint pain (VAS) and high values of biological markers of inflammation.
- RF seems to be a marker for severe and distorting joint disease, in association with a large number of deformed joints, high functional score and osteo-erosive radiological changes in peripheral joints.
- Like RF patients, anti CCP antibodies positive patients have active and severe joint disease with a high percentage of erosive joint damage detected both by ultrasound and radiography.
- The presence of anti-CCP antibodies can be considered a predictive factor for erosive joint disease in peripheral joints and axial segment (for mixed forms), as these patients had more frequent syndesmophytes , cervical involvement and erosion in vertebral bodies.
- Starting from this premise, complete serologic evaluation should include RF and anti-CCP antibodies, not only for patients with peripheral arthritis , but for those with mixed forms (spondylarthritis).
- Radiological progression is well defined by radiographic scores calculated in this study (Sharp van der Heijde and BASRI-s), whose value increases with the duration of arthritis.
- Patients with polyarticular arthritis have more aggressive evolution, being diagnosed more frequently with multiple osteolytic and erosive lesions, joint ankilosis , narrowing of the joint space and subluxations.
- Using data obtain in the study has been shown a close correlation between the severity of skin psoriasis, calculated by PASI score, and severity of peripheral

arthritis, established by the presence of osteo-destructive and proliferative changes on conventional radiographs of the hands.

- Analyzing the impact of joint symptoms on radiological progression, we found that the number of swollen joints (SJC) is a predictive factor for extended erosive joint disease.
- Spinal mobility is influenced by structural changes reflected by BASRI-s radiological score which proved useful in evaluating patients with spondylarthritis by significant correlation with vertebral dynamic indicators. It is emphasized that BASRI score correlated closely with the van der Heijde modified Sharp total score, and also, individual scores for erosions and joint space narrowing in the group of patients with mixed forms, thus supporting the hypothesis of a destructive process similar in both territories involved.
- A particular aspect was highlighted by joint ultrasound, establishing a strong relationship between bone erosions and enthesitis detected clinically, the substrate can thus be considered destructive joint lesions. An additional argument for this hypothesis is important correlation between joint erosions seen by ultrasonography and erosion score within radiological van der Heijde the Sharp score .
- Ultrasound MASEI provides an accurate assessment of joint inflammatory status, it correlates significantly with the main clinical and biological parameters of disease activity. Thus, could not demonstrate the predictive value of a high score for the severe skin and joint disease.
- Psoriatic arthropathy has an severe character since the early stages of the disease, mainly in males, which is reinforced by the presence of joint deformities and ankilosing, even during the first 2 years after onset and demonstrated by elevated functional index HAQ-DI. Also, men developed osteo-erosive joint changes more frequently than women.
- Evaluation of physical and mental SF-36 score given is an useful tool for assessing the quality of life in patients with psoriatic arthropathy by strong

correlations with spinal disease activity , clinical enthesitis score and the degree of pain in peripheral joints and lumbar. Demonstrated correlation between functional assessment (HAQ-DI, BASF), quality of life (SF-36) and clinical and biological parameters of disease activity (for the skin and the joints) reveal the importance of complex and multidirectional assessing the patient with PsA.

- Comorbidities associated with psoriatic arthropathy are important factors to reduce quality of life, in significant relationship with the cutaneous and articular disease. The risk of developing hypertension or coronary artery disease is increased in patients with severe psoriasis or genetic predisposition for psoriasis and insignificant in relation to biological parameters of inflammation.

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