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RESEARCH ARTICLE

Expressions and difficulty of clinical manifestations in the early diagnosis of psoriatic arthritis

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Short title: *Early manifestations of psoriatic arthritis.*

What is not known yet, about the topic

It is of particular interest to determine the early clinical manifestations of psoriatic arthritis (PsA), including variants of the onset of the disease, the relationship between its main syndromes and their specific expression.

Research hypothesis

The difficulties in the early diagnosis of PsA, the disability and the decrease in the quality of life in the first years of the disease are the reason for detailed research of the specificity of the first clinical expressions, which would allow in the future the recommendation of criteria for the classification of the early stage.

Article's added novelty on this scientific topic

In the diagnosis of PsA, the most frequently detected features were dactylitis and peripheral arthritis. These features allow the practicing dermatologist, the possibility of suspecting the presence of PsA in a patient with psoriasis. During the diagnosis of PsA, attention should be paid to the combination of psoriasis of the skin and of the nails, as well as comorbid conditions such as: diabetes mellitus, hypertension, ischemic disease and obesity of the first degree, since these patients are at an increased risk of developing PsA.

Abstract

Objectives. Study of clinical manifestations in psoriatic arthritis: enthesitis, dactylitis, peripheral arthritis, axial arthritis, skin manifestations, for early diagnosis, which would allow the establishment of an adjusted treatment and the elaboration of measures to prevent complications.

Materials and methods. The performed clinical study has an analytical-observational retrospective and included the patients who were hospitalized in the Rheumatology and Arthrology departments of the "Timofei Moşneaga" Republican Clinical Hospital during 2015-2021. The study included 103 patients with psoriasis (47 men and 56 women) with various clinical forms of psoriasis and different ages.

Results. The clinical examination of primary or referred patients with cutaneous manifestations, revealed peripheral arthritis in 15 patients (24.6%), dactylitis – in 37 (60.7%), heel pain was detected in 32 (52.5%), axial arthritis – in 30 (49.2%), enthesitis, distal interphalangeal arthritis and tendonitis were not detected. Those who primary or referred with joint manifestations, in 35 (57.4%) of patients was present peripheral arthritis, dactylitis in 40 (65.6%), enthesis of the elbow joints in 11 (18%), knee joints - in 8 (13.1%), the calcaneal region - to 25 (41%), arthritis of the distal interphalangeal joints was detected in 21 (34.4%), tendinitis - to 13 (21.3%).

Discussions. The obtained results allow us to state that one of the directions in improving the diagnosis of PsA consists in the use of ultrasound examination and MRI imaging of the joints of the hands and feet. This makes it possible to effectively identify the characteristic of enthesopathy, edema of tissues, as well as destructive changes in the joints of the hands and feet.

Conclusions. In the study group of patients with psoriasis, in 25 (24.2%) no joint damage was detected. The frequency of detection of psoriatic arthritis and other rheumatic diseases (rheumatoid arthritis, osteoarthritis, ankylosing spondylitis etc.) was 59.2% and 16.6%, respectively, 32 (52.5%) out of 61 (59.2%) patients with PsA were primarily diagnosed. The sensitivity and specificity of the mPEST (Psoriasis Epidemiology Screening Tool) questionnaire in relation to the CASPAR criteria were 77% and 69% respectively. The highest indicators of sensitivity, specificity and accuracy in the diagnosis of PsA has ultrasound and MRI: 88%, 92%, 89% and respectively, 89%, 94%, 91%

Keywords: psoriatic arthritis, early clinical manifestations.

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Introduction

Rheumatic diseases currently present themselves as chronic diseases, imposing themselves as being quite important among diseases with immune component due to the complex problems that raise them in relation to their clinical-biological individuality [1, 2]. They have come to possess a profound socio-economic impact, being responsible for 50% of absenteeism in the workplace and about 60% of the rate of permanent incapacity for work, as they largely affect people in full functional capacity. In Europe, the treatment of these diseases accounts for a quarter of the total annual expenditure on health (240 billion EUR). Also, the economic losses caused by absenteeism in the workplace amount to 650 million EUR per year. Moreover, rheumatic diseases can be disabling and often lead to early retirement [3-5].

Psoriasis (Ps) is a chronic non-infectious pathology, a disease characterized by the deterioration of the skin, caused by determined immunopathological reactions. The disease can occur at any age, but in recent years, there is a tendency towards its „rejuvenation": Ps has begun to appear at a younger age, in particular, the onset of the disease is observed in 75% patients before the age of 40 years [6].

Psoriatic arthritis (PsA) is considered as a severe form of Ps, regardless of the area of skin lesions. PsA is a chronic, inflammatory disease from the seronegative spondyloarthritis group; the clinical picture presents mainly with inflammation of the peripheral joints, enthesis and inflammation of the tendons of the fingers, hands and feet, manifested by tenosynovitis and dactylitis, but the spine (spondylitis) and sacroiliac joints (sacroiliitis) can also be affected. PsA is a severe pathology because it decreases the quality of life and functional state of patients. The aforementioned clinical forms are often manifested by erosion and deformation, change the structure and lead to disability. Particularly severe cases of PsA are more often recorded in young men [7].

According to summary data, the incidence of Ps in the general population is 2-3%, of which 13.5 to 47% of patients are diagnosed with PsA. Most often the onset of PsA is between 20 and 50 years of age. The ratio between males and females is approximately the same. In latest studies, enough data have been accumulated that prove that in 40-60% of patients with PsA, joint lesions appear in the first years of the disease [8, 9].

Obviously, the issue of treating patients with PsA is extremely relevant and no less important. The possibility of early diagnosis of the disease and the earlier start of treatment, when the structural damage to the joints is less evident, provides the chances of improving the patient's quality of life. Early PsA (lasting less than 2 years) are conditionally distinguished in a special subgroup, since the first years in the course of PsA are decisive in the development and progression of the pathological process [10], even though until recently, the early diagnosis of PsA presented difficulties associated with a variety of clinical manifestations of the disease. In the space of a long time, the international medical community and, in particular, rheumatologists have made several attempts to systematize these manifestations [11]. At the same time, the most successful classification of PsA is currently CASPAR (The ClASsification for Psoriatic Arthritis), which was developed in 2006 by a group of 30 rheumatology centers (from 13 countries). It is based on five signs of PsA, most often detected clinically, instrumentally and laboratory. The CASPAR criteria have high specificity (98.7%) and sensitivity (91.4%), including in the early stages of PsA, are based on the analysis of data from patients with an average duration of the disease of 12.5 years. To date, the CASPAR classification is generally recognized and an important diagnostic tool in the clinical practice of the rheumatologist. However, patients with Ps, due to how PsA develops, are treated in most cases by the dermatologist, and are referred to the rheumatologist at an advanced stage, which is not appropriate, due to the lack of interdisciplinary collaboration between these specialists [11, 12].

Thus, despite the availability of modern diagnostic capabilities, an algorithm for the early detection of PsA in a cohort of patients with Ps has not yet been developed, in relation to the practice of a dermatologist. Furthermore, at the moment, there is no close interaction between a dermatologist and a rheumatologist, which is extremely necessary both in relation to the primary detection of patients and in the context of further management and monitoring [13, 14].

In addition to the CASPAR criteria, in the diagnosis of PsA, especially at the early stage, a great significance has the history of the disease, the nature of clinical manifestations, the use of instrumental research methods (scintigraphy, densitometry, conventional radiography, ultrasound, magnetic resonance imaging (MRI)); laboratory data such as C-reactive protein, erythrocyte sedimentation rate, rheumatoid factor. Although it has been established that in PsA joint erosions on radiography are detected only in some patients, and at an early stage in just 20-30% of cases [15, 16].

Timely detection of PsA in patients with Ps involves early treatment and contributes to the prevention of the further development of functional disorders [17].

In this regard, it is important to optimize the methods of early diagnosis of PsA and in dermatological practice by timely detection of early clinical signs of the disease and the development of a diagnostic algorithm for early PsA [18].

The purpose of the study of our study was to study clinical manifestations in psoriatic arthritis: enthesitis, dactylitis, peripheral arthritis, axial arthritis, skin manifestations, for early diagnosis, which would allow the establishment of an adjusted treatment and the development of measures to prevent complications.

Our objectives were:

(1) Analysis of clinical aspects of patients with early manifestations in psoriatic arthritis;

(2) Highlighting of risk factors, incidence and clinical diversity of PsA;

(3) Preparation of recommendations and management plans in the early detection of clinical manifestations in psoriatic arthritis.

Material and methods

The clinical study performed has an analytical-observational retrospective character and included patients who were hospitalized in the Rheumatology and Arthrology departments at the Republican Clinical Hospital „Timofei Moşneaga", during 2015-2021. The study included 103 patients with Ps (47 men and 56 women) with various clinical forms of Ps and of different ages. The group of patients was analyzed multilaterally, according to different distribution groups that comply with the following criteria: sex, age, performing mPEST (Psoriasis Epidemiology Screening Tool) screening before establishing the diagnosis, smoking, residence environment. For all patients, the general and systemic clinical examination was performed, as well as analysis of the results of laboratory and instrumental investigations. Data presented in the study were collected from patients' medical records.

Criteria for inclusion in the study:

(1) age between 18 and 70 years;

(2) definite diagnosis of psoriatic arthritis according to CASPAR criteria (2006);

(3) assessment of the severity of the lesions and the area affected by Ps according to the PASI score (Psoriasis Area Severity Index);

(4) assessment of the total area of skin lesions according to BSA (Body Surface Area, 2007);

(5) evaluation of mPEST screening until the diagnosis has been established;

(6) highlighting and evaluation of early manifestations: enthesitis, dactylitis, peripheral arthritis, axial, cutaneous and nail manifestations in patients with PsA.

Criteria for exclusion from the study:

(1) the presence in patients of other autoimmune diseases, other skin diseases or decompensated chronic conditions such as diabetes mellitus, viral hepatitis, cirrhosis of the liver, hematological, nephrological, oncological, or cardiac diseases and other severe diseases.

(2) mismatch of diagnostic criteria for psoriatic arthritis.

Radiological examination of the hands, feet, pelvis, as well as other joints and spine was carried out in the department of radiology. The radiological stage was determined according to the Steinbroker stages. To quantify the severity of bone cartilage damage, the modified Sharp/van der Heijde method for PsA was used to calculate the total number of erosions (maximum 5 points in the hands and 10 points in the legs) and the narrowing of the intraarticular joint space of the hands and feet (maximum 4 points). The maximum score of erosion and narrowing of articular spaces in hands and feet in PsA was 518 points.

The statistical analysis of the data was performed at the statistical package Statistics 9.0 and EpiInfo, version 5 using simple descriptive statistics. For quantitative traits that have a normal distribution, the results are presented in the form of mean values and standard average deviations (M ± SD). For signs that do not correspond to the normal distribution, the median (Me) and the interquartile interval (25%; 75%) were used. To determine the reliability of differences in the average values of numerical parameters, the student's *t*-test was used, and in the absence of a normal distribution and the presence of a large data dispersion, the nonparametric method - the Mann-Whitney criterion. The analysis of the relationship between the two characteristics was carried out using non-parametric correlation analysis using the Spearman method. The statistical significance of disease risks (the evolutionary variant) was assessed using criterion X^2 and Fisher criteria. The results were considered reliable at a level of significance $p < 0,05$.

Results

The study included 103 patients with Ps (47 men and 56 women) with various clinical forms of Ps between 2019 and 2021. The age of the patients was on average 44.00 ± 13.69 years (from 18 to 70 years). The duration of Ps disease ranged from 6 months to 50 years. The average duration of Ps was 10.7 ± 1.2 years (table 1).

Table 1. *Distribution of patients according to clinical forms of Ps*

Clinical forms of Ps	Number of patients	Share (%)
Ps vulgaris	39	37.9
Ps of the scalp	24	23.3
Ps palmo-plantar	16	15.5
Ps on flexion surfaces	15	14.6
By type of erythroderma	4	3.9
Ps guttat	3	2.9
Ps pustulous	2	1.9

Note: Ps – psoriasis.

Almost a third of the patients – 39 (37.9%) had Ps vulgaris, 24 (23.3%) – Ps of the scalp, 16 (15.5%) – palmo-plantar Ps, 15 (14.6%) – Ps on the flexion surfaces, at 4 (3.9%) – the pathological process went after the type of erythroderma, 3 (2.9%) – Ps gutta, 2 (1.9%) – pustular form.

Evaluation of patients based on the mPEST questionnaire and according to CASPAR criteria

Based on the mPEST questionnaire, the diagnosis of PsA was suspected in 60 (58.2%) patients out of 103 patients. Diagnosis of PsA confirmed according to CASPAR criteria in 47 of them (45.6%). mPEST < 3 (indicating a low probability of having PsA) was observed in 43 out of 103 patients (41.7%). According to CASPAR criteria, PsA were absent at 29 (28.2%) of them.

Identification of early clinical manifestations in PsA at the first visit

Considering that the first visit of a patient with Ps can be with both cutaneous and joint manifestations, depending on what appears primarily, we evaluated the early clinical manifestations in accordance with the primary address of the patient and the detection of PsA at the initial clinical examination.

After the clinical examination, in primary or addressed patients with skin manifestations, peripheral arthritis in 15 patients (24.6%), dactylitis in 37 (60.7%), heel pain was detected in 32 (52.5%), axial arthritis in 30 (49.2%), enthesi-

tis, distal interphalangeal arthritis and tendinitis were not detected (table 2).

Table 2. Diagnosis of PsA based on the clinical manifestations of the disease

Early manifestations	Primary addressing with cutaneous manifestations	Primary address with joint manifestations
Peripheral arthritis	15 (24.6%)	35 (57.4 %)
Dactylitis	37 (60.7%)	40 (65.6%)
Axial arthritis	30 (49.2%)	-
Enthesitis of the elbow joints	-	11 (18%)
Enthesitis of the knee joints	-	8 (13.1%)
Enthesitis in the calcaneal region	32 (52.5%)	25 (41%)
Arthritis of DIP	-	21 (34.4%)
Tendinitis	-	13 (21.3%)

Note: PsA – psoriatic arthritis; DIP – distal interphalangeal joints.

Those who addressed primarily with joint manifestations, 35 (57.4%) of patients had peripheral arthritis, dactylitis – 40 (65.6%), entheses of the elbow joints – 11 (18%), knee joints – 8 (13.1%), calcaneal region – at 25 (41%), arthritis of the distal interphalangeal joints was detected in 21 (34.4%), tendinitis – 13 (21.3%).

The structure of the lesion of the osteoarticular apparatus in patients with psoriasis and the prevalence of psoriatic arthritis

Out of 103 patients with Ps, 61 had PsA (according to CASPAR criteria), which constituted 59.2%. In the remaining 42 cases (40.8%), other chronic inflammatory diseases of the joints were diagnosed. In 13 (12.6%) cases other rheumatic diseases (table 3): dermatomyositis, rheumatic polymyalgia, ankylosing spondylitis, rheumatoid arthritis, gout, etc., in 4 (4%) patients - a combination of two pathologies: PsA and gout, in 25 (24.2%) patients – no rheumatic diseases.

Table 3. The structure of the lesion of the osteoarticular apparatus in patients with Ps

Conditions	Number of patients	Share
Ps + PsA	61	59.2%
Ps without other rheumatic pathologies	25	24.2%
Ps + other rheumatic pathologies	13	12.6%
The combination of 2 rheumatic pathologies	4	4%

Note: Ps – psoriasis; PsA – psoriatic arthritis.

Identification of characteristic early clinical manifestations in psoriatic arthritis

In 61 patients of the study, the group with the presence of PsA, all the clinical features characteristic of this disease were noted: in 35 (57.4%) of patients peripheral arthritis was present, dactylitis in 40 (65.6%), enthesitis of the elbow joints in 11 (18%), knee joints – in 8 (13.1%), the calcaneal region – in 25 (41%), arthritis of the distal interphalangeal joints was detected in 21 (34.4%), tendinitis – 13 (21.3%).

Identification of patients according to the duration of PsA

It should be emphasized that from the 61 patients with PsA, in 32 (52.5%) of them the diagnosis was established for the first time at an early stage (up to 2 years). In 24 (39%) of 61 patients with PsA, the duration of the disease was less than 1 year, at 17 (28%) – from 1 to 2 years, in 11 (18%) – from 2 to 3 years, in 9 (15%) > 3 years.

Assessing the severity of Ps and PsA

BSA was determined during clinical examination in all patients and noted in the medical records, respectively. Based on the condition as a slap of the patient to the middle phalanges of the fingers corresponds to 1%.

According to the BSA index, patients were divided into 3 groups:

- BSA < 5% - Mild Ps (without affecting the patient's quality of life), in 43 patients (41.7%);
- BSA 5-20% - Moderate Ps (with impact on the patient's quality of life), in 53 patients (51.5%);
- BSA > 20% - Severe Ps, in 7 patients (6.8%).

Ps type I (the first cutaneous manifestation occurred before 25 years, in patients with a positive family history) – observed in 31 patients (30%), Ps type II (after the age of 25 years) – observed in 72 (70%) patients.

Relationship between nail Ps and PsA

Out of 103 patients, nail Ps was detected in 69 (67%) patients, and in the group of patients with PsA (n=61) – in 44 (63.7%), without PsA – 25 (36.2%). Nails Ps were not detected in 17 patients (50%) with PsA and in 17 (50%) without PsA.

When analyzing the period of manifestation of the nails in Ps, it was noticed that in most cases (47.8%), the nail lesions were detected after the cutaneous manifestations of Ps, but before PsA. This relationship may have prognostic value and may be a risk factor for the development of PsA. Therefore, in order to clarify its potential predictor, additional analysis may be necessary in some cases.

Effect of smoking on the development of PsA

We evaluated the impact of smoking as a risk factor for the development of PsA in patients with Ps. Significant difference in the frequency of detection of Ps with PsA and without PsA was not detected (26% to 37%) (Table 4).

Table 4. Effect of smoking on the development of PsA

Presence of PsA	Smokers	Nonsmokers	Total
Not	31 (73.81%)	11 (26.19%)	42
Yes	38 (62.30%)	23 (37.70%)	61
Total	69	34	103

Note: PsA – psoriatic arthritis.

Concomitant pathology in patients with Ps

Out of 103 patients examined, comorbidities were present in 77 (74.8%) of them. Among comorbidities: hypertension was observed in 23 (22.3%) patients with PsA and in 11 (10.7%) patients without PsA; diabetes mellitus – in 7 (6.8%) patients with PsA and in 4 (3.9%) without PsA; coronary heart disease – in 10 (9.7%) patients with PsA and 5 (4.9%) without PsA.

Table 5. Characteristic of patients depending on the concomitant pathology

Pathology	Patients with PsA	Patients without PsA	Total
Hypertension	23 (22.3%)	11 (10.7%)	34 (33%)
Type II DM	7 (6.8%)	4 (3.9%)	11 (10.7%)
Coronary artery disease	10 (9.7%)	5 (4.9%)	15 (14.6%)
Digestive disorders	7 (6.8%)	6 (5.8%)	13 (12.6%)
Chronic respiratory diseases	5 (4.9%)	6 (5.8%)	11 (10.7%)
Gynecological and urological diseases	7 (6.8%)	8 (7.8%)	14 (13.6%)

Note: PsA – psoriatic arthritis; DM – diabetes mellitus.

Diseases of the digestive system (gastritis, gastric and duodenal ulcers, gallstones, etc.) were observed in 13 (12.6%) patients. Chronic respiratory diseases (asthma, obstructive bronchitis, etc.) were observed in 11 (10.7%) patients. Gynecological and urological diseases (prostatitis, urolithiasis, chronic pyelonephritis, fibroids, etc.) were detected in 14 (13.6%) patients (Table 5).

Assessment of the sensitivity and specificity of instrumental diagnostic methods

One of the important components of the diagnosis of PsA is the use of instrumental methods.

In 94 patients out of 103, X-rays of the hands, feet and pelvis were performed, which totaled 91.3%. According to the results of the X-ray, the following changes were identified in patients: narrowing of the joint space in 60 patients out of 94 (63.8%), erosion of the articular surfaces in 14 (14,9%), bone proliferation (excessive growth of bone tissue at the edges of the joints) in 12 (12,8%) patients. However, in the early stages of PsA, radiological changes were not detected.

Ultrasound of the joints and entheses was performed in 53 patients out of 103 (51.5%). Following the ultrasound, the following changes were revealed: blurred contours of the articular surfaces in 38 patients out of 53 (71.7%), erosion of the ends of the bones in 18 (34%) patients, synovitis (inflammation of the synovial membrane of the joint) in 45 (85%), enthesopathy in 44 (83%), calcifications in 8 (15%).

MRI of the hands and feet was performed in 47 patients out of 103 (45.6%). MRI allows to identify numerous pathological changes in the study group of patients already at the early stage (in some cases, from 3 to 6 months): synovitis in 39 patients out of 47 (83%), tenosynovitis (inflammation of the synovial sheath of the tendon) in 40 (89.3%) patients, edema of bone tissue in 29 (61.7%) patients, erosions in 19 (40.4%) and soft tissue edema in 34 (72,3%) patients.

Discussions

This study represents a complex research on the latest discoveries in the field of detecting early manifestations of PsA. In a large group of patients with Ps, it has been shown that, in addition to PsA, this cohort of patients can develop any other rheumatic pathology: rheumatoid arthritis (RA), ankylosing spondylitis (AS), osteoarthritis (OA), reactive arthritis (ReA), gout, etc., which indicated the need for an interdisciplinary approach.

For the diagnosis of PsA there has not been identified any specific laboratory tests, however more informative for the diagnosis of inflammatory changes in the joints are radiography, USG and MRI, which have demonstrated an important significance [3-8].

In the diagnosis of PsA, the most frequently detected features were dactylitis and (less often) peripheral arthritis. These features allow the practicing dermatologist, the possibility of suspecting the presence of PsA in a patient with Ps. However, the identification of some clinical manifestations, such as enthesitis, spondylitis and tendinitis, requires additional investigations require close collaboration for the dermatologist with a rheumatologist [10, 11].

During the diagnosis of PsA, attention should be paid to the combination of Ps of the skin and Ps of the nails, as well as comorbid conditions such as: diabetes mellitus, hypertension, ischemic disease, and obesity of the first degree, since these patients are at an increased risk of developing PsA [12-15].

The results of the study provide fundamental support in the context of early diagnosis of systemic manifestations of the disease, which have an impact on the patient's quality of life. They allow diagnosing the disease in the early stages and developing treatment as quickly as possible, so that patients do not end up with destructive injuries.

The results obtained allow us to state that one of the directions in improving the diagnosis of PsA consists in the use of ultrasound examination and MRI imaging of the joints of hands and feet. This makes it possible to effectively identify the characteristic of enthesopathy, edema of tissues, as well as destructive changes in the joints of the hands and feet.

Conclusions

1. In the study group of patients with Ps, in 25 (24.2%) of them were not detected joint damage. The frequency of detection of PsA and other rheumatic diseases (RA, OA, AS, etc.) was 59.2% and 16.6%, respectively, 32 (52.5%) out of 61 (59.2%) patients with PsA were diagnosed for the first time.
2. The sensitivity and specificity of the mPEST questionnaire in relation to the CASPAR criteria were 77% and 69% respectively.
3. The highest indicators of sensitivity, specificity and accuracy in the diagnosis of PsA has ultrasound and MRI: 88%, 92%, 89% and, respectively, 89%, 94%, 91%.
4. The most frequently detected specific signs of PsA at the first address with cutaneous manifestations, it turned out to be peripheral arthritis and dactylitis - 24.6% and 60.7%. Enthesitis, spondylitis and tendinitis in people with severe skin manifestations were detected at a low rate.
5. For a better diagnosis of PsA in patients with Ps should be carried out mPEST screening. Depending on the score and the presence or absence of joint complaints, patients should be further examined. We should note the need for interdisciplinary interaction of cutaneous and joint manifestations, developing training programs for the early diagnosis of PsA, adequate therapy and improving the patient's quality of life.

Abbreviations

AS – Ankylosing Spondylitis; BSA – Body Surface Area; DIP – Distal Interphalangeal Joints, DM – Diabetes Mellitus; OA – Osteoarthritis; MRI – Magnetic Resonance Imaging, PsA – Psoriatic Arthritis; Ps – Psoriasis; RA – Rheumatoid Arthritis; USG – Ultrasonography.

Declaration of conflict of interest

Nothing to declare.

Authors' contribution

Study conception and design: ER, LG. Data acquisition: ER, LC, LD. Analysis and interpretation of data: ER, LC. Drafting of the manuscript: ER. Significant manuscript review with significant intellectual involvement: ER, LD. Approval of the „ready for print" version of the manuscript: ER, LG, LC, LD**.**

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