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Polymyalgia Rheumatica - Risk Factors, Pathogenesis, Diagnostic Methods, Treatment - New Literature Reports

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Abstract
Introduction and Aim
Polymyalgia rheumatica (PMR) is a systemic inflammatory disease predominantly affecting individuals over the age of 50, with a higher incidence among women. It is characterized by pain and stiffness in the shoulder and hip girdles, often accompanied by systemic symptoms such as fatigue, low-grade fever, and weight loss. The aim of this paper is to present a review of the current literature concerning risk factors, pathogenesis, diagnostic methods, and therapeutic options in PMR, with particular attention to recent scientific findings.
Brief Description of Current Knowledge
Although the etiology of PMR has not been fully elucidated, genetic predisposition, environmental influences, and age-related immune dysfunction are considered significant contributors. The disease often coexists with giant cell arteritis (GCA), complicating diagnosis. Glucocorticosteroids remain the cornerstone of therapy; however, recent studies emphasize the growing role of steroid-sparing agents and biologic therapies such as sarilumab and tocilizumab. Advances in imaging modalities and biomarker identification have enhanced diagnostic accuracy and facilitated earlier intervention.
Summary
Polymyalgia rheumatica continues to pose diagnostic and therapeutic challenges, particularly in patients with atypical presentations or treatment resistance. Individualized therapeutic approaches are essential to optimize outcomes. Further research is warranted to clarify the underlying pathogenesis and to refine management strategies, aiming to improve long-term prognosis and reduce treatment-associated complications.
Keywords: polymyalgia rheumatica; glucocorticoids; risk factors; biological therapy; magnetic resonance imaging

1. Introduction

Polymyalgia rheumatica (PMR) is an inflammatory disease that affects people over the age of 50. Women get the disease two to three times more often than men. It is the second most common systemic rheumatologic disease in adult patients. The etiology of the disease is not fully understood. Risk factors include female sex, age over 50, genetic factors and history of infection. It is characterized by acute or subacute onset of pain and morning stiffness in the neck, shoulder girdle, pelvic girdle and thighs. In addition to the above symptoms, elevated laboratory indicators of inflammation—CRP and ESR—are often present. Systemic symptoms (subfebrile state, fatigue, weight loss) are found in about half of patients with PMR [1].

Patients with polymyalgia rheumatica may develop or may coexist with giant cell arteritis (GCA), which has a common pathogenetic mechanism. The disease can present diagnostic difficulties, as similar symptoms can occur in other disease entities with which polymyalgia needs to be differentiated. The primary form of treatment is prednisone therapy. High hopes are also placed on glucocorticosteroid-sparing drugs and biologic drugs. We now stand at the threshold of a new chapter in PMR therapy, and treatment options are expanding significantly with the recent FDA approval of the interleukin-6 antagonist sarilumab to treat the refractory form of the disease [2].

Materials and Methods

A detailed analysis of 38 peer-reviewed scientific articles published between 2020 and 2025 from sources such as PubMed and Google Scholar focused on recent reports on polymyalgia rheumatica.

2. Risk Factors

Despite much research to date, polymyalgia is a disease whose etiology has not been fully discovered. Factors that may favor its development include age over 50, female gender, history of infection and genetic factors, among others. Although the etiology of this disease entity remains unknown, its sudden onset and significant variation in prevalence in different regions of the world suggest that one or more environmental or genetic factors may be responsible, as well as their interaction, which could lead to a seasonal distribution. However, it is important to keep in mind that many studies that have been conducted have not shown a clear seasonal trend [3].

2.1 Age

Since PMR is diagnosed practically exclusively in people over fifty years of age, it can be inferred that age has a significant impact on the development of the disease. With more years of life there is an aging of the immune system, which in turn increases susceptibility to infections and autoimmune processes. Patients with polymyalgia have also been shown to have higher values of homocysteine, which is an exponent of vascular aging and inflammatory processes [5].

2.2 Female Gender

PMR affects women more often than men. The sex ratio varies between 2:1 and 3:1. The lifetime risk of developing this disease entity is 1.7% for men and 2.4% for women [2,5].

2.3 Genetic Factors

It has been shown that the development of PMR may be favored by polymorphisms of the HLA-DRB1*04 gene. Studies have shown that alleles of this gene are associated with an abnormal immune response, which can lead to the development of inflammation in, among other things, the PMR. These changes most likely affect the frequency and severity of relapses [1,8]. IL-6 polymorphisms also appear to play an important role. There is increased expression of this pro-inflammatory cytokine in the PMR, highlighting its important role in the development of this disease [5,8].

The largest GWAS meta-analysis of polymyalgia to date identified three new loci in the IL1R1, CCDC88B, and NEK6 genes that increase the risk of its occurrence, and also confirmed the links already found with HLA-DRB1 and ANKRD55. According to recent data from 2025, exome sequencing in polymyalgia has revealed the presence of rare variants in genes linked to the inflammasome—NLRP12, NLRP3 and PLCG2. They increase susceptibility because they modulate activation of the inflammasome, which is crucial for cytokine release and triggering systemic inflammation [8]. With these discoveries, it is possible to better understand the genetic basis of polymyalgia, and thus potential methods for its prevention and treatment. Regarding epigenetic changes, data regarding the involvement of miRNAs in the development of polymyalgia are still sparse and require continued research [6,8].

2.4 Environmental Factors

Among the environmental factors that can lead to PMR are infections. It is thought that patients with a genetic predisposition may be triggered by infection with Mycoplasma pneumoniae, Chlamydia pneumoniae or paragroup viruses [5]. Some studies have also described patients with musculoskeletal symptoms matching the clinical picture of PMR after infection with COVID-19, and after analyzing the case series, it was suggested that this infection either acted as a trigger in predisposed individuals or caused an exacerbation of a pre-existing but subclinical form of PMR. The relationship between infectious agents and the onset of the disease is complex and is most likely determined by genetic predisposition, aging of the immune system, and hypothalamic-pituitary-adrenal axis dysfunction that progresses with age [1,5,8].

There are also reports of a relationship between diverticulitis and polymyalgia, by which it can be inferred that changes in the microbiota and chronic inflammatory bowel disease are involved in the immunopathogenesis of this disease entity [1].
Vitamin D plays a protective role for muscles because it affects their regeneration, but it also has anti-inflammatory properties. Deficiency of this vitamin due to inadequate UV radiation is more common in northern geographic areas. Lower levels of vitamin D may account for the onset or exacerbation of PMR. The UV rhythm is very important. Melatonin levels increase at night, while cortisol levels decrease, so there is an increase in inflammation at night, which may explain the exacerbation of morning symptoms in PMR. This has clinical implications, as it is used to optimize GC treatment with nighttime administration. This is an alternative for patients who experience significant morning stiffness due to the disease [8].
Recent reports suggest that air pollution can lead to PMR. It acts as a general inflammatory stimulus in patients with predisposition. Findings also suggest that cigarette smoking and visceral obesity are among the potentially modifiable risk factors for polymyalgia rheumatica [6,8].
An association between some vaccines and the development of PMR has also been demonstrated. Currently, the pathophysiology of vaccine-induced autoimmunity is poorly understood. It has been suggested, by their immunogenic content, preservatives, stabilizers or adjuvants that are used to enhance the immune response may contribute to the immune response. Mechanisms that may explain the relationship between vaccines and PMR include dysregulation of the immune system that progresses with age, and genetic polymorphisms that trigger an excessive immune response, resulting in the release of pro-inflammatory markers and leading to the development of disease symptoms. Vaccines, based on a review of cases, that can lead to the development of PMR include the influenza vaccine—some cases have been documented within 3 months after vaccination, and fewer such situations have been reported after hepatitis and tetanus vaccinations. In contrast, vaccination against herpes zoster contributed to the emergence of many such cases. After analysis of articles, it also appears that PMR symptoms developed in individual patients after receiving mRNA vaccination against COVID-19 [7,9,10].
It is worth citing here one example of such an illness in a 71-year-old patient after administration of Comirnaty vaccine (Pfizer-BioNTech). The woman developed such symptoms stiffness of leg muscles, joint pain, fever and general malaise, in laboratory tests elevated CRP and ESR. In HLA typing, the DRB1 allele was present. After starting steroid treatment, the patient's condition improved. The added value in this case is the confirmation of the presence of the HLA-DRB1 allele and its significant role in the development of the disease [9]. A case of a patient who showed an association between RSV vaccination and PMR was also demonstrated. The relationship between RSV vaccines and autoimmune diseases, especially polymyalgia, has not been sufficiently analyzed. In contrast, it has been suggested that there is a potential risk of autoimmune diseases with this type of vaccine [7].
ICIs, or immune checkpoint inhibitors, are used in cancer immunotherapy. They work by increasing the activation of T lymphocytes to attack cancer cells. Drugs that can initiate the disease include pembrolizumab, ipilimumab or nivolumab. In addition to the primary action, the increased immune response can lead to inflammation mimicking autoimmune diseases. Cases have been reported in the literature in which PMR-like symptoms appeared after ICI (ICIPMR)—pain and stiffness in the proximal muscles, and elevated inflammatory markers similar to classic PMR. Because of the possible development of such a syndrome, vigilant monitoring during immune checkpoint inhibitor therapy is very important [8,11].

3. Pathogenesis

The pathogenesis of PMR is not fully understood to date. This is most likely related to the fact that the studies that have been conducted have mainly involved patients with PMR and

overlapping GCA, which in turn has prevented an isolated analysis of the pathogenesis of polymyalgia. According to the study, T cells may play a special role in the pathogenesis of PMR and/or GCA. Indeed, an increase in the number of Th17 cells and memory T cells and a concomitant decrease in regulatory T cells were found. Memory T lymphocytes, due to their ability to produce significant amounts of tumor necrosis factor (TNF)-α and interferon γ, initiate the pro-inflammatory cascade in PMR. It has also been shown that patients with PMR have reduced amounts of B lymphocytes compared to healthy patients, which shows an inverse relationship with CRP and ESR levels [12,13,16].

Pro-inflammatory cytokines have been linked to the pathogenesis of PMR. In connection with the activation of Th17 lymphocytes, interleukin-17 may have a role in the development of PMR and GCA. In addition, higher interstitial levels of IL-1β, IL-1α, interleukin 1,6,8 receptor antagonists, TNF-α and serum monocyte chemotactic protein-1 have been detected in patients with muscle symptoms. Therefore, in such individuals, the etiology of the disease may be associated with elevated levels of interstitial pro-inflammatory cytokines. In addition, it has been shown that there is a correlation between higher IL-6 levels and PMR activity [13].

Of significant etiopathogenic importance is the decreased secretion of cortisol in response to inflammation in the body. Polymyalgia is a disease that develops mainly after the age of 50, and as we age, the endocrine system ages. This leads to a decrease in dehydroepiandrosterone levels, disruption of the normal functioning of the subthalamic-pituitary-gonadal axis and adrenal insufficiency, so that the body's response to inflammation is inadequate, which contributes to the development of the disease. With age, there is also a phenomenon called immunosenescence, or aging of the immune system. Both the innate and acquired immune systems are affected, although studies show that aging has a greater impact on the latter, however. This has three clinical implications: it leads to a weakening of the immune response to exogenous as well as endogenous antigens; it leads to a reduction in the effect of immune protection, making the body more susceptible to contracting cancers, for example; the response to vaccination disappears or is weakened, as the immune memory response is impaired. Referring to the increased risk of malignancies, it has been shown that skin cancers, as well as hematological malignancies, among others, multiple myeloma, acute myeloid leukemia or myeloproliferative diseases, are associated with polymyalgia rheumatica. According to studies, PMR patients have a higher incidence of cancer compared to the general population [12,16].

In patients with polymyalgia, clinical manifestations are most likely related to infiltration of immune cells in the periarticular areas and muscles. The muscles in these patients show the presence of immune complexes and increased microvascularity. PMR is also associated with synovitis. Studies have shown that the inflamed synovial tissue is dominated by macrophages and T lymphocytes, while NK cells, B lymphocytes or gamma/delta T cells are not present. In addition, significant expression of adhesion molecules such as VCAM-1 and ICAM-1 has also been detected in these patients, which may be important in recruiting some immune system elements to infiltrate the synovial membrane [12,16].

Analyzing studies on the pathophysiology of PMR, one can see that IL-6 has been an important focus of research. However, to date, it is not known why it is produced in excess and why some patients develop vasculitis and others do not. Inflammation, especially involving interleukin-6 plays a very important role, but the inflammatory mechanisms may be different in patients, which also explains the different response to treatment. Laboratory tests from peripheral blood may be atypical, so to understand immune processes more deeply, analyses of tissues involved in inflammation, such as muscle or synovial membrane, are needed. This may be important to better understand the disease and create new therapeutic options. Polymyalgia rheumatica is a disease that is most common in people over 65, but it has a clear link to aging there is little pathophysiological evidence to unequivocally support

this relationship. The aging of the immune and endocrine systems is a very promising target for research. The strong association between aging and polymyalgia rheumatica suggests that neuroendocrine disorders and immunosenescence may play a key role in the development of this disease entity and should be intensively explored in further scientific analyses [13].

4. Clinical Manifestations and Laboratory Tests in Patients with Polymyalgia Rheumatica

The primary symptom in these patients is stiffness and pain in the neck, shoulder girdle and hip girdle. These symptoms are most severe in the morning and after prolonged inactivity or rest, while they gradually decrease throughout the day. Morning stiffness usually lasts an hour or more. The onset of the discomfort is often unpredictable and usually ranges from one day (symptoms can develop overnight) to two weeks. They usually occur bilaterally, which should especially raise suspicion of the disease. Cases of pain and stiffness appearing on one side have also been described, but in such cases the symptoms also appeared on the opposite side within a few days. These symptoms make daily functioning very difficult. The pain affects sleep, awakens during the night, and therefore prevents the body from regenerating. Patients have difficulty performing basic activities such as combing their hair, getting out of bed or a chair, fastening a bra, taking a shower, etc. These discomforts are caused by inflammation within the articular and extra-articular structures, most likely within the shoulder and shoulder-blade joints, hip joints, as well as the subacromial, sub-bar and vertebral bursa of the upper extremities [1,4,5,12].

Studies conducted to date on the absence of prolonged muscle stiffness at the time of diagnosis suggest that in such patients, who are classified as polymyalgia, it is very important to rule out malignancy before a diagnosis of idiopathic PMR is made and treatment is initiated [19,20]. As an example, one study described three patients presenting with symptoms indicative of PMR, who had no prolonged stiffness (MS), atypical test results, no response to corticosteroids and no abnormalities on shoulder ultrasound. The final diagnosis was renal cell carcinoma [20]. However, further studies are needed to assess the relationship between MS and cancer [19,20].

In addition to pain and stiffness within the above locations, 25% of patients may have peripheral arthritis. It does not destructively affect the joints, does not cause deformities, erosions or contribute to the development of rheumatoid arthritis. It is most often asymmetric in the wrists and knees. Since inflammation can also involve periarticular structures, patients with PMR may develop, for example, carpal tunnel syndrome or swelling of the distal part of the limb with pitting edema, which responds quickly to treatment with corticosteroids. PMR can manifest as swollen and edematous hand syndrome, which can clinically resemble the syndrome of resolving seronegative symmetrical synovitis with pitting edema (RS3PE), in which symptoms appear suddenly [1,4,5,12].

Almost half of patients with PMR may be accompanied by general symptoms such as fatigue, weakness, lack of appetite, weight loss/anorexia, general malaise, and fever or subfebrile state. Fever is reported by only 10% of patients with polymyalgia [18]. What is important is that high body temperature is a common symptom in giant cell arteritis, which may suggest subclinical large-diameter vasculitis and overlap of PMR with GCA. This can be visualized via FDG PET. Uptake of this tracer by large vessels is observed in about 15% of polymyalgia patients. A study focused on the clinical implications of fever in patients diagnosed with PMR showed that these patients were significantly more likely to have weight loss and/or anorexia, most likely due to IL-6-induced inflammation in the body. Inflammatory parameters—ESR and CRP—were higher compared to patients without fever. Interestingly, no increased FDG uptake by the vasculature was observed, suggesting that fever in PMR patients is not associated with latent large-diameter vasculitis. The study showed that this group of patients does not need the use of more intensive treatment. There is also no increased risk of

recurrence of polymyalgia rheumatica in the first year. Patients with PMR and concomitant fever are at risk of delayed diagnostic management compared to those without this symptom, as nearly half of patients are prescribed antibiotics before they are referred to a rheumatologist. Factors, in addition to fever and other general symptoms, that may also influence delayed diagnosis include lack of knowledge about polymyalgia, inflammatory markers within normal limits, detection of rheumatoid factor-RF, osteoarthritis or behavioral disorders [17,18].

On physical examination, active movements especially in shoulder inversion may be limited. Passive movements performed by the examiner in some cases may be normal, as in a healthy person. The patient experiences widespread discomfort in the shoulder, which he or she cannot accurately localize. In addition, there is no clinically apparent swelling of the joint. Active neck and hip movements are also very often limited. On examination, there may be tenderness in the muscles of the neck, shoulders and thighs. Patients may report muscle weakness while muscle strength is usually normal. If there is muscle soreness on palpation, it is usually associated with inflammation of the joint structures or synovial bursa [5,12].

Laboratory Tests

Laboratory results are not typical. Inflammatory parameters such as ESR and CRP are usually elevated, but this is not the rule. They are among the most commonly determined serum inflammatory markers in polymyalgia patients and are one of the elements of the 2012 EULAR/ACR classification criteria for this disease entity [14]. High values of the Biernacki reaction are associated with more relapses and the need for prolonged steroid therapy. ESR is a very important indicator used both in the diagnosis and monitoring of PMR. Its values oscillate from moderate to high and often reach above 100 mm/h. Sometimes ESR is below 40 mm/h, but such patients usually have high CRP, the clinical picture is milder, there are fewer systemic symptoms and they are less severe [12]. It is worth noting that ESR values can be affected by other physiological factors such as gender, age or pregnancy, so CRP can also be used to monitor PMR activity during treatment [21].

One study showed that ESR and CRP values may be normal at the time of PMR diagnosis, making the diagnosis of this disease entity more difficult. Such patients are usually younger, the duration of symptoms is longer, but they have fewer systemic symptoms. In such patients, imaging studies can be used to make the diagnosis, but measurements of other acute phase reagents among others serum amyloid A (SAA) can also be determined [21].

Due to the presence of inflammation in the body, peripheral blood counts may show normochromic normocytic anemia (mild or moderate), thrombocytosis or leukocytosis [12].

Citrullinated protein and antinuclear antibodies are usually absent. Rheumatoid factor is also negative, although a weak positive result may occur in a small percentage of the elderly population, but this is not clinically significant. Non-specific inflammatory markers such as fibrinogen, haptoglobin, α1-antitrypsin, gamma-globulin, α1-antichotrypsin and α2 and α1-globulin may also be increased in the tests. Levels of von Willebrand factor and interleukin 6 are also elevated and show a significant decrease after treatment is initiated [12]. Levels of liver enzymes, especially alkaline phosphatase, may also increase. Lactate dehydrogenase and creatine phosphokinase values remain normal [1,12,15].

Serum levels of B-lymphocyte activating factor (BAAF) have been shown to be increased in PMR patients. However, its use as a biomarker for this disease is not possible, as elevated titers have also been observed during infection and malignancy. Patients with active PMR also showed an increase in CXCL9 and CXCL10. These biomarkers remained in elevated titers even after steroid treatment in those in remission. Therefore, they cannot be used to monitor response to treatment or relapse. Serum calprotectin has been shown to increase in PMR patients and to decrease after inclusion of glucocorticosteroids in therapy. It was thought to have potential as a marker of disease activity, but its increase has also been seen in other inflammatory rheumatic diseases, so it is not specific only to polymyalgia [14].

As mentioned earlier, GCA often coexists with PMR, which has also been the focus of research into biomarkers that could identify such cases. It was shown that the positive predictive value of subclinical GCA in polymyalgia patients was due to low serum levels of matrix metalloproteinase 3. The study also confirmed the high values of angiopoietin-2 in people with coexisting giant cell arteritis and the high ratio of angiopoietin-2 to angiopoietin-1 in people with PMR and GCA. Post-2020 studies have shown the potential for ESR to have higher values in patients with subclinical GCA compared to patients with PMR alone [14].
Joint fluid in PMR patients may show leukocytosis with values ≤20,000/mm³, neuropeptides among others VIP—a vasoactive intestinal peptide, the presence of which may not only lead to immunomodulation of joint fluid inflammation, but also initiate dangerous non-joint symptoms among others cardiac arrhythmias [12].

5. Diagnosis: Differentiation, Imaging Methods, Diagnostic Criteria

Polymyalgia rheumatica is a disease whose diagnosis is very often complex. It has many imitators, as quite a few other diseases mimic the course of PMR. In addition, the clinical picture often shows great heterogeneousness. There is no gold standard for diagnosis, and there are no specific laboratory tests to make a definite diagnosis. As with the diagnosis of other disease entities, meticulous patient evaluation, a thorough history and physical examination are important. As previously described, typical symptoms of this disease include pain and stiffness in specific locations (neck, shoulder and pelvic girdle). However, up to 50% of patients may present with peripheral musculoskeletal involvement, and thus without the typical constellation of symptoms. An example of such a disease is resolving seronegative symmetrical synovitis with pitting edema syndrome, this disease entity can coexist with PMR (10% and less of cases), being either an early or late manifestation of polymyalgia [23]. The risk of misdiagnosis is high, and thus the introduction of inappropriate treatment, perhaps unnecessary steroid therapy, which has many side effects [14].
Before making a diagnosis of PMR, a differential diagnosis of the disease should be made. Clinical features such as pain and stiffness can occur in many diseases, such as rheumatoid arthritis, fibromyalgia and osteoarthritis. It is particularly important to rule out giant cell vasculitis, as this is an entity that often coexists with PMR (40 to 60% of patients with GCA may have PMR symptoms at the time of diagnosis), and untreated GCA can lead to serious complications [12].
Inflammatory myopathies also have very similar symptomatology to PMR, which is why they are included in the differential diagnosis. The disease entities with which polymyalgia should be differentiated can be divided into rheumatologic and non-rheumatologic. The former category is divided into inflammatory and non-inflammatory. Inflammatory diseases include polymyositis, dermatomyositis, crystal arthropathies, spondyloarthropathies, rheumatoid arthritis, giant cell arteritis [12,14,22]. Non-inflammatory, on the other hand, include: rotator cone syndrome, fibromyalgia, osteoarthritis (shoulder-blade, hip-femoral), vertebrobasilar pain syndrome, subacromial/subacromial bursitis, capsulitis. The second category, i.e. non-rheumatologic diseases, can be divided into three subcategories: neoplastic—hematologic, solid, metastatic; infectious—septic arthritis, endocarditis, tuberculosis, urinary tract infections, respiratory tract infections, osteomyelitis, infectious myositis, and others—endocrine disorders (thyroid and parathyroid pathologies), drug-induced myopathies (for example, after statins), neurological disorders (e.g. Parkinson's disease), depression or vitamin D deficiency [12,14,22].

5.1 Imaging Methods Used in Diagnosis

According to the recommendations of the Norwegian Society of Rheumatology, the diagnosis can be supported by imaging studies and/or verified by classification criteria, while this is not mandatory for the diagnosis of PMR. This is dictated by the fact that many patients with polymyalgia will not have findings indicative of PMR on imaging studies. Which tests are

performed depends primarily on the clinical symptoms the patient will present with and the results of laboratory tests, which are generally nonspecific [25].

Imaging modalities that are helpful in the diagnosis of polymyalgia rheumatica include ultrasound, MRI, 18F-FDG-PET-CT, among others. Ultrasound has become a very common, valuable and useful tool used to diagnose not only PMR, but also to rule out alternative diagnoses that mimic PMR, for example, chronic osteoarthritis, rheumatoid arthritis or disease in which calcium pyrophosphate is deposited. In addition, vascular ultrasound can detect subclinical/clinical giant cell arteritis that may coexist with PMR [15,24,25].

A characteristic feature on ultrasound of temporal arteritis is the "halo sign"—defined as a hypoechoic, homogeneous thickening of the wall that is well demarcated from the lumen side, visualized in perpendicular planes. In addition, there is usually also the so-called compression sign—when a thickened wall is still visible after compressing the lumen of a vessel with active GCA with an ultrasound probe. In addition to examination of the cranial arteries, increased diagnostic accuracy in this disease entity is provided by ultrasound examination of the axillary arteries [14].

Ultrasound is a readily available, non-invasive test that allows rapid and dynamic evaluation of specific structures. However, it is a low-sensitivity examination in which imaging of deep structures can be difficult (deep synovial bursae, tendon structures of the hip and spine) and the skill of the person performing the examination is very important. Among the most commonly visualized abnormalities during the diagnosis of polymyalgia are biceps tendonitis and inflammation of the infrapatellar bursa, while less commonly detected are synovitis of the glenohumeral joint, inflammation of the ileal bursa and synovitis of the patellofemoral joint [24,25]. The results of a meta-analysis indicate that the diagnosis of PMR based on inflammation of the infrapatellar bursa is more accurate [14,15].

The 2012 EULAR/ACR classification criteria included additional criteria that award a point for at least unilateral shoulder and hip inflammation or bilateral inflammation in the shoulder rim. This increased the specificity of these criteria from 81.5 to 91.3 percent [15,25]. The diagnosis uses Power Doppler (PD) ultrasound, which, compared to conventional Doppler, allows better assessment of more intense blood flow in blood vessels. As a result, it allows detection of soft tissue inflammation [15]. The study found that a positive PD signal at the time of diagnosis correlated with a significantly increased risk of relapse. Importantly, the same study found that a positive signal was still present in more than half of the patients in clinical remission or low disease activity, which unfortunately limits the ability of ultrasound to detect disease recurrence [1,15].

MRI allows excellent visualization of inflammatory changes in deep structures especially tendon attachments, synovial membrane or synovial bursae. In addition, compared to ultrasound, it is more effective in imaging lesions of the pelvic rim and hip joint. MRI plays a very important role when it comes to identifying characteristic extra-articular lesions in polymyalgia rheumatica. This enables better diagnosis and differentiation of PMR from other musculoskeletal conditions. Studies have shown that MRI has high diagnostic accuracy and can identify characteristic patterns of PMR. These include bilateral involvement of the tendon attachments in the pelvis, enhancement of the proximal part of the rectus femoris muscle, or bilateral involvement of the adductor muscles and tendons of the pubic bone. Thanks to MRI, new areas of inflammation indicative of PMR have also been detected, including intertubercular bursitis or myofascial inflammation located mainly in the hip muscles, adductors of the pubic conjunctiva, shoulders and the pubic tubercle area. MRI shows high specificity (97.1%) and sensitivity (95.8%) in the diagnosis of PMR. As already mentioned, MRI allows differentiation of PMR from other conditions including rheumatoid arthritis. A differentiating feature is that in polymyalgia on MRI, inflammation often involves the area outside the joint capsule without involvement of the hip joint. MRI can also be useful in

predicting relapse—performing gadolinium-enhanced MRI of the shoulder increases accuracy and can predict relapse based on synovial hypertrophy and rotator cone tendonitis. In addition, MRI can act as a predictor of response to treatment—features of inflammation (extra-articular) that are detected in the examination can indicate patients who respond better to corticosteroids and show higher levels of CRP and IL-6. It has also been shown that MRI can be used as a tool to assess the effectiveness of treatment based on the resolution of inflammatory changes. Unfortunately, this test has its drawbacks, as it does not have as much accessibility as ultrasound. It is also an expensive examination. In addition, it is associated with possible side effects related to the administration of contrast [1,12,15,25].

PET/CT uses a radioactive isotope, specifically a glucose analogue—2-[fluor-18]-fluoro-2-deoxy-D-glucose. This type of imaging, in addition to being used in the diagnosis of cancer and monitoring of cancer patients, also makes it possible to visualize areas of inflamed tissue. It can detect arterial wall inflammation and changes in the lumen of extracranial arteries in the diagnosis of GCA, as well as reveal PMR lesions invisible on other tests [15].

Based on numerous studies, patterns of isotope uptake have been developed that can guide the diagnosis of PMR. The most common sites of accumulation are the shoulder-brachial, sternoclavicular, hip, intercostal bursae, greater ileum and ischial tuberosities. The characteristic pattern for polymyalgia appeared to be the letter "Y" in the intervertebral bursae. One clinical study (Sondag et al.) found that accumulation at ≥3 sites (joints, bursae, tendon attachments) has a 74% sensitivity in diagnosing PMR [15,25].

Polymyalgia rheumatica is characterized by greater involvement of periarticular structures than RA, although increased FDG uptake in the shoulder and hip joints can occur in both diseases. It was also shown that after PMR therapy, the sites with increased FDG uptake no longer showed increased uptake, raising the conclusion that this method is also very useful in terms of monitoring treatment. In addition, it was found that inflammatory pain involving the pelvic rim, lower extremities and lower back could predict a positive FDG-PET/CT result for large vessel inflammation in polymyalgia patients. This technique is difficult to access and expensive. Moreover, it exposes patients to side effects associated with higher radiation dose. It should be remembered that concomitant use of corticosteroids may affect the sensitivity of this test, so the dose should be discontinued or reduced early enough. Nonetheless, it is proving to be a useful diagnostic tool [1,15,25].

It allows a holistic assessment of the body, which is important because separate musculoskeletal findings are often insufficient to make a diagnosis of PMR. Ultrasound requires detection of lesions in both shoulders or the shoulder and hip to improve diagnostic specificity, while MRI has better resolution than ultrasound, but assesses only one musculoskeletal area at a time and does not allow simultaneous diagnosis of large vessel inflammation including GCA [26]. A major limitation of FDG-PET/CT is the lack of a standardized definition of polymyalgia rheumatica and large vessel inflammation based on tracer uptake intensity. The diagnostic value of PET-PMR results and algorithms needs further evaluation [14].

5.2 Diagnosis

Over the years, five classification criteria for PMR have been developed. The first is the Bird criteria developed in 1979, the second is the Jones and Hazleman criteria from 1981, the third is the Chuang and Hunder criteria from 1982, the fourth is the Healey criteria from 1984 and the fifth from 2012 are the provisional classification criteria of the European League for Rheumatism and the American College of Rheumatology [4,12].

Currently, none of the above classification criteria for polymyalgia rheumatica are fully validated in clinical practice. The diagnosis is made on the basis of clinical presentation, laboratory and imaging studies, and after excluding other disease entities that may mimic PMR. The 2012 classification criteria are currently the most widely used and can help make

the diagnosis. To apply them in practice, a patient must meet all prerequisites such as age over 50, bilateral shoulder rim pain and elevated, out-of-normal CRP levels and/or accelerated ESR. A clinical evaluation is then performed and a certain number of points are assigned. Clinical criteria include morning stiffness for more than 45 minutes (2 points), pain or limitation of mobility of the hip rim (1 point), absence of pain in other joints (1 point), absence of RF or anti-CCP antibodies (2 points). Additional criteria based on ultrasound images are also included: the first is at least unilateral inflammation in the shoulder rim and at least unilateral inflammation in the iliac rim (1 point), the second is bilateral inflammation of the subacromial bursa, tendon sheath of the long head of the biceps muscle or shoulder joint (1 point). To classify the disease as PMR, it is necessary to obtain at least 4 out of 6 points from the clinical criteria or 5 out of 8 possible points after taking into account additional criteria. Diagnostic difficulties arise when the clinical picture is atypical and the basic conditions for this classification are not met, e.g. unilateral shoulder girdle pain, or the absence of elevated inflammatory markers [4,5,14].

The first recommendations developed by the French Society of Rheumatology regarding the management of patients with polymyalgia rheumatica in clinical practice have recently emerged. Five general principles and nineteen groups of recommendations have been developed. In the former, special attention was paid to the potential for GCA to co-occur with PMR, to the major role of differential diagnosis in the diagnosis of the disease. The important role of rheumatology expertise in making an early diagnosis and further organizing treatment was also emphasized, as recent studies have shown that prompt referral of a patient to a rheumatology specialist increased diagnostic efficiency, reduced the use of initial doses of corticosteroids and lowered the rate of hospitalization. They also referred to PMR as a potentially treatable disease that requires an individualized approach to each patient, with therapy consisting mainly of corticosteroids. According to the developed recommendations of the French Society of Rheumatology, when starting the diagnosis, it is necessary to pay attention first of all to the symptoms accompanying the patient, whether the clinical picture is typical, whether there are any red flags or diagnostic doubts [24].

It is important to perform laboratory tests before glucocorticosteroid treatment is initiated: blood count, inflammatory markers, renal parameters: creatinine, liver parameters—ALAT, alkaline phosphatase, fasting glucose, glycated hemoglobin, calcium, ACPA, rheumatoid factor, to consider TSH, CK, protein electrophoresis and others [25]. If the clinical picture is typical, X-ray examination of those structures affected should be performed. If a patient with suspected PMR presents with worrisome symptoms, for example, fever, weight loss, headache, scalp hypersensitivity, or if pelvic girdle symptoms/sacral pain predominate, this should point to a GCA or malignancy comorbidity, and studies such as temporal artery ultrasound or 18F-FDG PET CT are indicated. In situations where the clinical picture is atypical or there are diagnostic uncertainties, studies such as vascular or joint ultrasound, MRI, 18F-FDG PET-CT may be necessary [24].

Patients who present with PMR symptoms are patients over the age of 50, often with multiple comorbidities, it is very important to know exactly what the patient suffers from and to assess risk factors for adverse effects associated with steroid therapy. The most common side effects of such treatment include gastrointestinal, metabolic, endocrine, cardiovascular or psychiatric disorders. Evaluation of disease activity should be carried out at each patient's office visit, and the PMR activity scale is used for this. The formula is as follows: CRP (mg/dl) + VAS pain according to the patient (0 to 10) + VAS activity according to the doctor (0 to 10) + duration of morning stiffness (min) × 0.1 + upper limb elevation (0 to 3). Simplifying these scales, the assessment is made as follows: low activity—if the number is below 10, intermediate between 10 and 20, and a score above 20 indicates high activity. These ranges have been shown to correctly guide therapy and identify relapse. During patient follow-up, neither ultrasound nor

18F-FDG PET-CT is recommended if the clinical response to therapy is good [24]. The first follow-up visit for patients with newly diagnosed PMR should take place, at least 2-4 weeks after starting steroids, and subsequent visits after three, six, nine and 12 months [25].

6. Treatment - Principles, New Reports

The mainstay of treatment for polymyalgia rheumatica for many years has been the oral use of glucocorticosteroids (GC). According to EULAR/ACR guidelines, the dose of prednisone used in therapy should be in the range of 12.5-25 mg, and this should be the lowest effective dose leading to remission of the disease. The selection of induction doses is individual for each patient. It is based on the severity of symptoms, comorbidities and body mass index, among other factors. The recommended initial dose averages about 15 mg/d. Smaller doses of the drug—7.5-10mg/d, can be used in patients with poorly controlled comorbidities including, for example, uncompensated diabetes with a high risk of side effects, lower body weight. Higher-than-recommended doses—20-25mg/d—can be considered in patients with severe symptoms and higher body weight [2,15].

Glucocorticosteroids, in addition to oral administration, can also be administered intrathecally by injection into the shoulders—this way, 6-methylprednisolone is administered every 4 weeks. Rapid improvement has been observed with this method, but only in half of the patients the effect persisted after six months. Another route of application is intramuscular administration of methylprednisolone acetate. It has been shown to have similar efficacy to oral administration and fewer side effects associated with this form of therapy (less weight gain or fewer fractures). In contrast, it is not commonly used in practice clinically [14].

There is no uniform, evidence-based algorithm for GC withdrawal. The approach is always individual and determined by the treating physician [14]. The goal of treatment is to resolve clinical symptoms and normalize inflammatory markers while minimizing the side effects of such therapy. Parameters usually return to normal within two to four weeks after the start of therapy, and symptoms usually resolve with them as well. If the patient does not experience improvement within two weeks of treatment, another disease entity should be considered, and the steroid dose should be increased [15].

According to the data, 29-45% of patients with polymyalgia do not respond to initial treatment, and at least half experience significant side effects of therapy. The average duration of GC treatment is usually one to two years, but as many as ¼ of patients extend this time to more than 4 years. This is due to both the clinical differences of people with PMR and the differences in treatment used in clinical practice [27]. Studies show that 43% of patients experience at least one relapse within a year of starting treatment [14]. The course of action in such a situation is to increase the steroid dose relative to the amount taken before the relapse, and then reduce over four to eight weeks to the relapse dose [27].

Steroid treatment in polymyalgia often lasts longer than recommended, despite the international consensus to limit the duration of use from one to two years. Relapse rates do not fully explain long-term therapy, suggesting that there may be other factors, not yet fully understood, that influence therapeutic decisions. Currently, there are no validated tools to predict either the risk of recurrence or the need for prolonged treatment, making it difficult to individualize therapy. Therefore, continued research is needed [28].

One study focusing on a new treatment strategy for PMR demonstrated cases in which concurrent, short-term use of corticosteroids (GCs) and tocilizumab (TCZ) can lead to rapid resolution of clinical symptoms and sustained remission of disease without the need for prolonged treatment. All of the patients studied achieved remission without further use of drugs, lasting from several months to more than two years after discontinuation of therapy, indicating the potential of this treatment strategy in PMR. A shorter duration of TCZ treatment and a lower cumulative GC dose may reduce the risk of serious side effects and improve the cost-effectiveness of therapy, which is important especially in elderly patients.

None of the described cases experienced serious side effects, which supports the safety of short-term combination therapy with TCZ and GC. Due to the small number of patients and potential limitations (low disease activity, potential for case selection), it is necessary to conduct a randomized clinical trial on a larger group to confirm the efficacy and safety of this method [29].

The list of side effects associated with steroid use is very long. It affects about 65% of patients. It is noteworthy that PMR affects people over the age of 50, where the peak age of incidence is in the 70-79 range, in whom the side effects can be even more devastating. Among the most common are fractures, osteoporosis, diabetes, hypertension, ischemic heart disease, glaucoma, cataracts or infections. That's why it's so important to limit the duration of therapy and reduce the doses of these drugs [14].

In patients with polymyalgia rheumatica, glucocorticosteroid-sparing drugs may often be necessary. This is the case when there are significant side effects of steroid therapy, relapse or refractory disease. The most commonly used drug in this group is methotrexate (MTX). It can be administered orally or intramuscularly. It is usually used at a dose of 10 to 15 mg per week. It has been studied in three randomized clinical trials with varying results, as two of them confirmed its efficacy while one showed no benefit [14].

Considering the two randomized trials showing benefit (Caporalli et al. and Ferraccioli et al.), some conclusions emerge. Both have shown that the use of methotrexate in the treatment of polymyalgia leads to a significant reduction in the cumulative dose of prednisone needed to control the symptoms of the disease and a faster achievement of remission with less use of GCS. In addition, treated patients maintained stable bone mineral density (Ferraccioli study), while patients who used prednisone alone reported a decrease in bone mineral density, suggesting that methotrexate may potentially protect against osteoporosis, which is a fairly common complication of long-term steroid treatment [30]. In a study that did not demonstrate this efficacy, low doses (less than 10 mg/week) were used, which may have accounted for the final effect [14].

Although the results of some of the studies are promising, and despite the high quality of evidence indicating the efficacy of methotrexate (MTX), the small number of participants in these studies (194) and the lack of conclusive results currently prevent a stronger recommendation for its use in the treatment of polymyalgia rheumatica [28]. According to the 2015 guidelines (EULAR/ACR), in PMR patients with a high risk of relapse or if prolonged therapy is anticipated, early implementation of MTX is recommended to be considered [27]. Early implementation of MTX is recommended in patients with PMR and comorbid glaucoma, diabetes or osteoporosis, among other conditions [5].

Leflunomide is another conventional glucocorticosteroid-sparing agent. Studies conducted to date indicate that it may be more effective than methotrexate in reducing glucocorticosteroids. In a study by Vinicki et al. where the two drugs were compared, it was shown that prednisone withdrawal time was shorter with leflunomide than with methotrexate, and that remission was more likely to be achieved with leflunomide. Therefore, this drug is promising in the treatment of PMR while it requires confirmation in randomized controlled clinical trials [30].

Azathioprine has limited efficacy and a high risk of side effects as an alternative drug for the treatment of PMR [30].

In recent years, the use of biologic drugs has become increasingly common. Thanks to groundbreaking research, interest in IL-6 antagonists has increased. As mentioned earlier, interleukin-6 plays a significant role in the pathogenesis of PMR. Its reduction in serum correlates with reduced disease activity. This is why it is a potential therapeutic option for the treatment of this condition. One of the antagonists of this interleukin is sarilumab. It is a human monoclonal antibody against the IL-6 receptor. According to the SAPHYR study, in patients with PMR using this drug, sustained remission was achieved in 28.3% of patients,

compared to a placebo group of 10.3%. This study demonstrated efficacy in the treatment of steroid-resistant polymyalgia, and contributed to the FDA's approval of sarilumab for the treatment of polymyalgia. Sarilumab shows a favorable safety profile. More common side effects include neutropenia, arthralgia, and diarrhea. It is administered subcutaneously, every 2 weeks [14].

Numerous studies have been conducted on tocilizumab—a drug that blocks the binding to the interleukin-6 receptor, thereby preventing the release of inflammatory mediators involved in the activation of B and T lymphocytes. Blocking this receptor has been shown to affect the patient's clinical picture, causing pain and stiffness to subside, and allows for a reduction in GC doses. In addition to case-control, observational, retrospective, prospective studies with positive results, RCTs were conducted where tocilizumab was administered together with GC. It has been shown that tocilizumab effectively reduces the doses of GCs used, significantly reduces disease activity and causes fewer adverse effects compared to classical therapies. It can be concluded from the studies that the use of IL-6 receptor antagonists also contributes to a decrease in the relapse rate of PMR. This improves the quality of life of polymyalgia sufferers and improves their functioning in daily life [14,31,33,34,35].

Another drug whose efficacy in treating newly diagnosed PMR has been attempted is infliximab, or anti-TNF alfa. However, a randomized trial involving forty patients showed no difference in relapse rates between the placebo group and the infliximab group. The conclusion of this study is that this biologic drug does not have positive effects in the treatment of this disease entity [14]. Another drug from this group tested in the RCT was etanercept, but its use also did not show positive effects. In view of these results, EULAR/ACR 2015 do not recommend taking anti-TNF alpha therapy in people with isolated polymyalgia rheumatica [30].

A drug that has future potential in PMR therapy is rituximab. An anti-CD20 antibody. It has been shown to be effective in GC-free disease remission when used together with glucocorticosteroids (17-week treatment). This information still needs to be confirmed by larger studies, while rituximab may be a valuable drug in the treatment of PMR to allow less exposure of patients to GC [3,31].

The use of abatacept has also been evaluated in patients with early-diagnosed polymyalgia. This is a dimeric fusion protein that prevents interactions between CD80/86, and CD28 thereby reducing T-cell activation. Despite the significant improvement in disease activity compared to placebo with this drug, it was ultimately decided that it was not a potent enough drug for further larger studies [36].

In addition to IL-6, IL-1 and IL-17 are involved in the pathophysiology of this disease entity, and two drugs targeting these inflammatory mediators, namely secukinumab—a human monoclonal antibody of the IgG1 class that attacks the interleukin IL-17A—and canakinumab—a human monoclonal IgGκ antibody that attacks IL-1β, were therefore tested. A two-week proof-of-concept study (Matteson et al.) was conducted involving 3 groups—patients treated with GC, secukinumab, and canakinumab. Patients receiving steroids showed significant pain relief, while the others showed only moderate improvement in mobility. At the end of the trial, those taking biologics did not achieve a complete response. The REPLENISH trial is also currently underway to evaluate how effective secukinumab is in reducing the need for long-term glucocorticoid use. The trial is expected to conclude in February 2026 [14,30].

Although biologic drugs such as canakinumab, secukinumab, abatacept and rituximab have treatment potential, current data are limited and their efficacy has not been conclusively proven, highlighting the need for further clinical trials in patients with isolated PMR [30].

Other drugs under investigation include JAK/STAT pathway inhibitors. The first of these is tofacitinib, which inhibits JAK3 and JAK1, suppresses the production of gamma interferon

and prevents the accumulation of T cells in the vessel wall [30]. One study showed that monotherapy with this drug showed similar benefits to GC treatment in patients with PMR. Significantly, no serious adverse events have been reported [37]. Baricitinib is also a Janus kinase inhibitor except that these are JAK1/2. According to the BACHELOR trial, a significantly higher percentage of patients achieve sustained low disease activity, improved quality of life, and a better safety profile compared to the placebo group. Full data from the trial have not yet been published, so caution should be exercised in interpretation [30]. The potential positive results of JAK inhibitors in isolated polymyalgia are yet to be determined [30].

Other innovative formulations are in the early stages of research, among them selective glucocorticoid receptor agonists and modulators (SEGRMs). Their action is to selectively activate anti-inflammatory pathways, but without triggering those that lead to the side effects of glucocorticoid therapy. This reduces the risk of side effects such as cardiovascular problems, osteoporosis and diabetes, while having a potent anti-inflammatory effect in polymyalgia patients [30,32].

Another alternative form that has potential in the future is the implementation of drug delivery systems based on liposomes. This relies on nanometer-sized particles to surround GCs and target them to inflammationally altered tissues. This reduces systemic exposure and increases local efficacy. This method has been studied in the treatment of rheumatoid arthritis, while experts suggest it may also have potential for use in GCA and PMR. Another area of research includes the use of immune checkpoint inhibitors in patients with polymyalgia. There is potential to expand knowledge by conducting studies to evaluate their efficacy in combination with existing therapies. It has been suggested that they may have a positive impact on treatment outcomes, reduce GC exposures and thereby reduce side effects, especially in PMR patients with other diseases. It is important to keep in mind that SEGRMs or immune checkpoint inhibitors are in the research stage, so their wider use will not be possible until clear trial results are available [30,38].

7. Conclusion

Older age and genetic predisposition are key non-modifiable risk factors for polymyalgia rheumatica. Genetic factors playing a role in pathogenesis include specific polymorphisms in the genes HLA-DRB1, IL-6, NEK6, IL1R1 and others, which influence an abnormal immune response and the development of inflammation. Environmental factors can lead to the development of the disease in genetically predisposed individuals. The pathogenesis of PMR has not yet been fully understood. Immunological disorders and processes related to aging of the endocrine and immune systems play an important role in its development.

Polymyalgia rheumatica is characterized by stiffness and pain in the shoulder, hip and neck, especially aggravated in the morning. These symptoms significantly impede patients' daily functioning. Their presence, especially prolonged morning stiffness, is a key diagnostic element, while the absence of prolonged stiffness may suggest other diseases, including cancer. Polymyalgia in about half of patients co-occurs with general symptoms, which can cause misdiagnosis, delay diagnosis, and thus the late inclusion of appropriate treatment. The presence of fever may suggest the coexistence of vasculitis (GCA). Inflammatory parameters such as ESR and CRP usually remain elevated, but this is not the rule—normal values do not exclude the disease, making diagnosis much more difficult. When in doubt, it is important to also consider other inflammatory markers, as well as imaging studies.

Diagnosis of PMR is difficult because there is a lack of specific diagnostic tests, the clinical picture is heterogeneous, and there are numerous diseases that have a similar course. Therefore, accurate differential diagnosis is crucial to avoid misdiagnosis and unnecessary treatment with steroids. Imaging studies, although not mandatory for the diagnosis of PMR, play an important supporting role in the diagnosis and differentiation from other diseases—

especially ultrasonography (USG), magnetic resonance imaging (MRI) and FDG-PET/CT. They enable the detection of characteristic inflammatory lesions and are helpful in confirming the diagnosis, monitoring treatment and predicting recurrence.

Glucocorticosteroids (GCs) are the mainstay of treatment, but have numerous side effects, so limiting them is important. There is a lack of clear guidelines on an algorithm for GC withdrawal, indicating the need for further research. New therapeutic strategies, including GC-sparing drugs (such as methotrexate, tocilizumab, sarilumab) and biologic therapies, show promise. In particular, IL-6 inhibitors—especially sarilumumab—approved by the FDA—may lead to faster disease remission and a reduction in prednisone doses, while also affecting treatment safety. Methotrexate also reduces the need for steroids, especially with earlier implementation. Anti-TNF biologic drugs have not demonstrated efficacy. Research is underway on new therapies (JAK inhibitors, SEGRM), which may further optimize and individualize the treatment of polymyalgia rheumatica.

9. List of Abbreviations

PMR - Polymyalgia rheumatica
CRP - C-reactive protein
ESR - Erythrocyte Sedimentation Rate
GCA - Giant Cell Arteritis
FDA - Food and Drug Administration
IL - Interleukin
HLA - Human Leukocyte Antigen
GWAS - Genome-Wide Association Study
RS3PE - Remitting Seronegative Symmetrical Synovitis with Pitting Edema
ICI - Immune Checkpoint Inhibitor
ICIPMR - Immune Checkpoint Inhibitor-Related Polymyalgia Rheumatica
TNF-α - Tumor Necrosis Factor alpha
VCAM-1 / ICAM-1 - Vascular / Intercellular Cell Adhesion Molecule-1
USG - Ultrasonography
MRI - Magnetic Resonance Imaging
FDG-PET-CT - Fluorodeoxyglucose Positron Emission Tomography - Computed Tomography
PD - Power Doppler
EULAR - European League Against Rheumatism
ACR - American College of Rheumatology
RF - Rheumatoid Factor
anti-CCP / ACPA - Anti-Cyclic Citrullinated Peptide Antibody
TSH - Thyroid Stimulating Hormone
CK - Creatine Kinase
BAAF - B-cell Activating Factor
CXCL9 / CXCL10 - Chemokines
SAA - Serum Amyloid A
VIP - Vasoactive Intestinal Peptide
ALAT - Alanine Aminotransferase
MTX - Methotrexate
TCZ - Tocilizumab
GC / GCS - Glucocorticosteroids

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