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Polymyalgia rheumatica: concerted efforts of the European rheumatological societies

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Abstract. Population's ageing is a prerequisite for a strengthened evidence base of the specific geriatric syndromes, late-onset rheumatic diseases, and rheumatic diseases of the elderly. Among the latter, the most common is polymyalgia rheumatic whose presence and management are associated with the issues of tolerance to analgesics and anti-inflammatory medications and timely diagnosis of giant cell arteritis and malignancies. In Europe, namely in the German-speaking countries, there is a significant heterogeneity in the approaches to the polymyalgia rheumatica management persisting in the clinical practice. That is why the guidelines of the German Society of Rheumatology, the Austrian Society of Rheumatology and Rehabilitation, the Swiss Society of Rheumatology, and participating expert medical-research societies and other organizations delving in this problem, were elaborated and published in 2018. Its evidence base, overarching principles and specific recommendations are presented and discussed in the article. The guidelines are compared with the 2015 European League Against Rheumatism's and the American College of Rheumatology's recommendations for the management of polymyalgia rheumatica, and the Finnish Medical Association's guidelines recommended by the Ministry of Health of Ukraine for use in primary care as a new clinical protocol in 2016.

Keywords: polymyalgia rheumatica; treatment; standards; review

Introduction

The population's ageing emphasizes the necessity of corroborated evidence base for the specific geriatric syndromes, late-onset rheumatic diseases (RDs) and the RDs of the elderly. The international rheumatologic, internist, GP community is especially drawn to the polymyalgia rheumatica (PMR), the second wide-spread inflammatory RD after the rheumatoid arthritis (RA), developing almost exclusively after 50 years of age, most often at 70-79 years, in women twice as often as in men, and having no special diagnostic tests for its detection [1-3]. With the latter being absent, the PMR is considered to be a clinical diagnosis of exclusion, the fact consistently revealed by the contributions of the European League against Rheumatism (EULAR) and the American College of Rheumatology (ACR) of 2012 and 2015 [4-5], as well as by the guidelines of the German Society for Rheumatology (Deutsche Gesellschaft für Rheumatologie (DGRh)), the Austrian Society for Rheumatology and Rehabilitation (Österreichische Gesellschaft für Rheumatologie (ÖGR)), the Swiss Society of Rheumatology (Schweizerische Gesellschaft für Rheumatologie (SGR)) and other research medical associations and organizations in 2018 [6].

The topicality of elaborating the PMR treatment methods is due to a direct association of the acute and aggravated polymialgia syndrome, typical of this condition, and the safety issues related to the nonsteroidal anti-inflammatory drug (NSAID) use in the elderly age. One of the key PMR clinical associations requiring an urgent rheumatologist's attention and escalated glucocorticoid (GC) dose is the giant cell arteritis (GCA) and the attending risk of irreversible blindness and aortal complications developing. The issue of PMR's association with malignant tumors is moot, whether in terms of it being the risk factor (RF) of their development or in terms of a paraneoplastic syndrome [7-16].

The aim of the present paper is to make a general characteristic and to discuss the key points and evidence base

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of the recommendations (guidelines) on the PMR management by the German, Austrian and Swiss rheumatologic societies of 2018.

DGRh/ÖGR/SGR recommendations on PMR management (2018)

The guidelines under discussion [6] emphasize the lack of PMR etiology and pathogenesis studies and such possible RFs of its development as genetic, infectious, immune and vascular ageing-related factors, endocrine disorders. According to C. Dejaco and F. Muratore et al. (2016) [8, 15], there may be suggested an association between the more pronounced systemic, articular and periarticular inflammation symptoms and a history of vasculitis. The systematic review by F. Buttgereit et al. (2016) [7] reports a more common PMR clinical symptom being the bilateral shoulder pain (95 %), "other typical symptoms" being an acute or sub-acute pain in the neck and pelvic girth, as well as the morning constrain, and "possible manifestations" being arthritides and tenosynovitides of proximal (shoulder, coxofemoral) and distal (hand, knee) joints, as well as constitutional manifestations – fever, reduced appetite, weakness and/or loss of weight [8, 14]. One should stress that in reality the PMR diagnosis is made whenever there is a combination of typical clinical manifestations with an accelerated erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) rate; the diagnostic precision growing when there is subdeltoid bursitis, tenosynovitis of biceps brachii and/or synovitis of shoulder joint [7]; the circle of differential diagnostic includes a late-onset RA, GCA, chondrocalcinosis, infections and malignant tumors [8, 15].

While commending the value of EULAR/ACR recommendations of 2012 and 2015 [4-5], in 2018 the German, Austrian and Swiss experts observe a wide variety of approaches to the PMR management in the clinical practice of the German-speaking countries, Europe and the world in general. Their attention is focused on the issue of pharmacological and non-pharmacological tools being used to achieve the optimal risk-benefit ratio of the PMR treatment. The managing officers of DGRh/ÖGR/SGR define their target group as "all the adult patients with a clinical PMR suspicion". The manual was developed for all the physicians involved in the PMR management, namely rheumatologists, as well as the adjunct specialists of non-medical professional groups, possibly patients and their relatives. At the manual's center there are EULAR/ACR recommendations (2015) [5] adapted for the German-speaking countries [6].

We have earlier mentioned a great number of specialized medical societies and NGOs involved in the development, regional adaptation and implementation of clinical recommendations in Germanic [17]. The DGRh/ÖGR/SGR guidelines under discussion were co-authored by the representatives of the German Society of Gerontology and Geriatrics (Deutsche Gesellschaft für Geriatrie (DGG)), the German Rheumatism League, the German Society for the Internal Medicine (Deutsche Gesellschaft für Innere Medizin (DGIM), the German Society for Orthopaedics and Trauma (Deutsche Gesellschaft für Orthopädie und Orthopädische Chirurgie (DGOOC)), the German Society for Physical Medicine and Rehabilitation (Deutschen Gesellschaft für Physikalische Medizin und Rehabilitation (DGPMR)) and the German Society of General Practitioners and Family Physicians (Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin (DEGAM)).

The working group meetings were held in April of 2016 and February of 2017. While elaborating the general principles and special recommendations, they used the PICO (Patients, Intervention, Comparison, Outcome) mode, allowing them to formulate 12 structured questions on the interventions and 10 on the prognostication factors, as well as the GRADE (Grading of Recommendations Assessment, Development and Evaluation) and QUIPS (Quality-In-Prognosis Studies) methods in order to evaluate the quality of clinical trials (CTs), either interventional or prognosticating, respectively. The evidence base is made of 52 sources considered by the EULAR/ACR recommendations (2015) and 2663 publications found in the period 01.2014-07.2016 (out of them three were selected: one reporting the outcomes of the open monocentral CT dealing with tocilizumab use in 10 PMR patients [18], and two reporting on the RFs of adverse outcomes [16, 19]). The search terms were "the relevant names of PMR used from 1970». The search was performed in the computer databases of Cochrane Library, Medline, Embase, CINAHL, Web of Science, reinforced by the electronic and manual search in the "grey literature", namely the CT registers and proceedings of ACR, EULAR, the British Society for Rheumatology (BSR) and the international congresses on PMR, GCA and vasculitides. We've also explored the first copies of publications, and interviewed the experts on "possibility of further publications" [6].

The five general principles (A, B, C, D, E) of the PMR patient management in Germany, Austria and Switzerland were suggested by the DGRh/ÖGR/SGR working group and presented in Table 1. The authors believed that the PMR-resembling conditions were ruled out and the patients were under the rheumatologist's observation. However, the general approaches should be known by the family physicians, orthopedists, geriatricians, physiotherapists and rehabilitologists. *The rheumatologists are required to manage the patients with atypical manifestations, aggravated course or PMR relapses* reflects principle C [6].

As to the *adverse outcome predictors*, the guideline cites the findings of retrospective studies by A. T. Hancock et al. (UK, 2014) [19] and F. G. Yurdakul et al. (Turkey, 2015) [16]. In the former study, involving 3249 PMR patients of primary care and 12735 control group subjects, there is a reported association of cardiovascular events with age and male sex; the cohort of the latter study recruiting 41 patients and there was no difference of response found to GC treatment at the third week, depending on their sex and presence/absence of peripheral arthritis.

While discussing the controversial nature of evidence concerning the PMR association with the presence and risk of malignant tumor development, the authors of DGRh/ÖGR/SGR guideline are citing 6 sources (our analysis shows that only one of them was published in 2017 while others in 1993-2002). They reported *the impossibility of general and special recommendations being developed on the PMR-associated tumors*; those recommendations differed from the commonly-held opinions on oncological screening in the respective age groups [6]. The data by J. E. Naschitz et al. (1996-1997) confirm a higher likelihood of *the PMR paraneoplastic character* whenever there are more accentuated constitutional symptoms of subjects under 50, asymmetric symptoms, insufficient GC efficacy, ESR <40 or >100 mm/h and peripheral arthritis present [20-21], as well as the data by M. Bellan et al. (2017) reveal "the most powerful predictors" of paraneoplastic PMR nature being presence of ≥6 tender joints, age of ≥75 years and male sex [22]. According to Principle C (Table 1), we should note that it was the peripheral arthritis, systemic manifestations and a lower rate of inflammation markers as well as the younger age (<60 years) which were referred to as *atypical* symptoms and signs, determining the rheumatologist's management (in the EULAR/ACR recommendations – referral for consultation [5]), and thus a warning against the impending oncology.

The important prerequisite to the DGRh/ÖGR/SGR recommendations (2018) being compiled, along with the EULAR/ACR recommendations (2015) and new evidence, was a systematic review by F. Buttgereit et al. (2016), which included 20 randomized clinical trials (RCTs) of intervention effects (all in all, in 1016 patients with PMR/GCA) and 30 trials of imaging diagnostic and/or evaluation tools for the therapy effectiveness (2080 in total). As to the PMR, the survey findings prove the GC effectiveness as the first-line medication (a daily dose of 12.5-25 mg prednisone equivalent) and a beneficial effect of methotrexate addition, such as a reduced GC cumulative dose (by 20 %) and frequency of relapses (by 36 %) [7].

While comparing the five DGRh/ÖGR/SGR principles presented in Table 1 with eight principles, earlier developed by the EULAR/ACR, we should remark on the *absence of significant differences* between them and *a clear EULAR/ACR's decision to relegate some studies to the range of "additional ones"* (namely, presence of protein fractions in the blood, vitamin D, thyrotropin, creatine

Table 1. Common principles of managing the polymyalgia rheumatica patients in Germany, Austria and Switzerland [6]

Principle	Level of agreement*
A. Even with the adequate number of clinical data, one should exclude the PMR-resembling symptoms (non-inflammatory, inflammatory, treatment-induced, endocrine, infectious, oncological)	9.5
B. The rule of good clinical practice (GCP) requires performing the necessary laboratory and/or instrumental tests in every PMR patient prior to his/her treatment. With an account of the present clinical signs and symptoms and likelihood of a different diagnosis, the following tests should be made: - *laboratory:* blood tests to detect the rheumatoid factor (RF), anti-cyclic citrullinated peptide antibodies (Anti-CCP), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), parts of the blood, glucose, creatinine, calcium, alkaline phosphatase, vitamin D, serum protein electrophoresis (SPEP), liver functional tests (LFTs), urine test strips, blood tests for thyroid stimulating hormone (TSH), creatine kinase (CK) test, ANA (antinuclear antibody) test, antineutrophil cytoplasmic antibodies (ANCA) test or tuberculosis (TB) test; - *instrumental:* thoracic cavity X-ray, ultrasonography of abdominal cavity, densitometry. According to the GCP rule, the physicians should take account of *comorbidities and treatment* for every PMR patient, for instance the arterial hypertension, diabetes mellitus (DM) or reduced glucose tolerance, cardiovascular diseases (CVDs), dyslipidemia, peptic ulcer, osteoporosis, cataract, glaucoma, infections, nonsteroidal anti-inflammatory drug (NSAID) use. The significance of *adverse prognosis risk factors (RFs)* is unclear. The likely RFs of more frequent relapses and/or requirement of a more protracted treatment – female sex, ESR > 40 mm/h and present peripheral arthritis	9.63
C. Patients with *atypical manifestations and symptoms* (such as peripheral arthritis, systemic manifestations, lower inflammation rates, age < 60 years), *increased risk of development or existing side effect* treatment and/or *recurrent relapse*s and/or *more protracted treatment requirement* are often subject to the rheumatologist's observation	9.13
D. While managing the PMR, one should strive towards the best healthcare provision based on the concerted patient-physician decisions. It implies adequate awareness-raising among patients as to the PMR outcomes and its treatment	9.88
E. The follow-up visits are made every 4-8 weeks of the first year; every 8-12 weeks of the second year, as soon as the relapses occur and the PMR develops; if necessary, after the pharmacotherapy stops. At every visit, they are evaluating the following clinical and laboratory parameters: disease activity, RFs and presence of side effect treatment, comorbidities and their treatment, relapses, duration of disease	9.00

Notes: * by the scale from 0 ("no agreement") to 10 ("maximum agreement"); PMR - polymyalgia rheumatic; ANA - antinuclear antibodies; Anti-CCP - anti-cyclic citrullinated peptide antibodies; ANCA - antineutrophil cytoplasmic antibodies; CK - creatine kinase; NSAID - nonsteroidal anti-inflammatory drugs; RF - rheumatoid factor; DM - diabetes mellitus; ESR - erythrocyte sedimentation rate; CRP - C-reactive protein; CVD - cardiovascular disease; TSH - thyroid stimulating hormone; RF - risk factor.

kinase, antinuclear and anti-neutrophil cytoplasmic antibodies, tuberculosis tests, X-ray of thoracic cavity) followed by their offer to consider *a somewhat more extensive range of comorbidities* for the PMR patients (including the recent fractures, RF of glaucoma development, RF of GC-therapy's side effects). Furthermore, the customized plan of every patient's management, a personified choice of initial dose and regimen of further GC titer, importance of access to the individual program of physical exercises and fast and direct access to the healthcare providers (while the relapses are developing or the treatment is attended by the side effects) were singled out as the *separate principles* by the EULAR/ACR [1, 5].

According to the DGRh/ÖGR/SGR recommendations, the key to a successful PMR treatment is *a concerted decision-making by the physician and an especially-instructed patient*.

The Table 2 presents **the specialized DGRh/ÖGR/SGR recommendations** on the PMR management: there are five of them, and the second recommendation consists of 5 sub-clauses [6], while the earlier EULAR/ACR recommendations suggested ten of them [5]. In the German-language guidelines, their gradation corresponds to the AB0 system widely-accepted in Germany: A – strong recommendation with a formula "must" (in German: soll), B – a conditional recommendation with a formula "should, may" (in German: sollte, kann), 0 – "should not be recommended". As the Table 2 shows, there is a high agreement rate among the developers on all the clauses (as well as general principles), while 70 % clauses (7 out of 10) are based on the expert opinion rather than on the epidemiological evidence. Two recommendations (№№ 3 and 4) were corroborated by the systematic reviews; one recommendation (№ 2c) was corroborated by the RCTs, i.e. 20 and 10 % clauses, respectively.

Along with the EULAR/ACR formulated position (2015), the German-language guidelines say that the GCs have a good standing in clinical practice and *remain the first-line medication* for PMR as in most cases they bring a fast and pronounced effect. One *should not use NSAID*s

Table 2. Special recommendations of managing the polymyalgia rheumatica patients in Germany, Austria and Switzerland [6]

№	Recommendation	Level of agreement**
1	Immediately after the PMR diagnosis is made, the GC therapy should start. *Level of evidence* 5*	10.00
2	The GC dose should be selected for each PMR patient on an individual basis. One should prescribe a dose as high as necessary and as low as possible. *Level of evidence* 5*	10.00
2a	The GC mode of use: while treating PMR, they should be ingested. *Level of evidence* 5*	9.25
2b	The GC time of ingestion: while treating PMR, they should be taken once in the morning. *Level of evidence* 5*	9.00
2c	The initial GC dose: in most PMR cases, the GC-treatment should be started at a daily dose of 15-25 mg prednisone equivalent. The daily GC dose should not be ≤7.5 mg or ≥30 mg. *Level of evidence* 2*	9.00
2d	Reduction or correction of the GC dose: the GC dose should be gradually reduced, with a regular control of disease activity, laboratory test findings and developing side effects. One recommends the following principles of the GC dose reduction or correction: - at the initial reduction, one should reach an ingested dose of 10 mg prednisone equivalent for 4-8 weeks, - one should further reduce a daily ingested dose of prednisone by 1 mg every 4 weeks until the complete cessation. In case of an increased disease activity (a developing relapse), while the GC dose is reduced, one should increase a daily ingested dose of prednisone, at least by the pre-relapse rate, after which the dose should be gradually reduced for 4-8 weeks until it reaches the one used during the relapse. *Level of evidence* 5*	9.13
2e	Duration of treatment. The duration of GC treatment should be selected individually for each PMR patient. One should take it as long as necessary and as short as possible. *Level of evidence* 5*	10.00
3	The early added methotrexate should be envisaged first of all for those patients with an elevated risk of relapse and/or a more protracted GC use, as well as in those patients with the risk factors attending the disease and/or therapy, i.e. an elevated chance of the developing GC side effects. The methotrexate prescription may also be discussed in case of a developing relapse (or relapses), inadequate GC response or developing side effects. *Level of evidence* 1*	8.38
4	The PMR patients should not receive tumor necrosis factor alpha (TNFα) treatment. *Level of evidence* 1* Recommendations in terms of other biological agents, including tocilizumab, may not be made at present	10.00
5	In addition to the pharmacotherapy, the patients should be advised to adhere to the individual program of physical exercises – especially the elderly and/or frail ones. *Level of evidence* 5*	9.25

Note: *in terms of interventions, this gradation of evidence levels is accepted by the Oxford Center for Evidence Based Medicine (www.cebm.net/index.aspx?o=5653): 1 – systematic review of several randomized trials, 2 – individual randomized trial with a confirmed and pronounced effect, 3 – non-randomized trials, 4 – case-series, case-control studies, or historically controlled studies, 5 – expert opinion; ** by the scale from 0 ("no agreement") to 10 ("maximal agreement"); PMR - polymyalgia rheumatic; GC – glucocorticoids; TNF - tumor necrosis factor; RF – risk factor.

to treat PMR, for the potential risk of side effects developing exceeds the expected, often reduced therapeutic benefit. The NSAIDs and/or analgesics may be used in addition to a regular treatment: in case of pain generated by other causes. The specific recommendations on analgesic use may not be given.

The impossibility of a clearly formulated recommendation as to the *initial GC dose* is attributed to the fact that while the recommendations were made, there are few publications of a high evidence level [...] and too many patients with different clinical profiles [6]. There is a concerted *individual* decision as to the minimal effective dose, with an account of the present RFs of the GC side effects, PMR relapses and necessity of a protracted GC use, as well as comorbidities and their treatment. This consideration allows the physicians to reach the optimal "benefit-risk" ratio.

While in Germany, Austria, Switzerland and other German-speaking countries the *oral* GC prescriptions (namely to treat PMR) predominate, the authors of present recommendation point out the possibility of intramuscular methylprednisolone (MP), upon the physician's recommendation [6]. The evidence base of this alternative involves a series of successful outcomes of MP use at an initial dose of 120 mg every 3 weeks described in a double-blind contrastive study by B. Dasgupta et al. (1998) [23].

While formulating the clause of *GC use timeline*, the authors of present recommendation considered the absence of clinical trials (CTs) of this issue, relied on the clinical experience and the likelihood of developing hypothalamic-pituitary-adrenal insufficiency, circadian rhythm and sleeping disorders and opposed the daily GC dose differentiation in all the PMR. According to their opinion, it may be possible in the individual cases, such as the occurrence of nightly pains when a daily dose of <5 mg prednisone equivalent. The findings of a small CT by M. Cutolo et al. (2017) (n=62) describe the effect of modified-release prednisone used for the treatment of recently developed PMR in comparison to a regular prednisone: at the 4th week, the number of main-group patients responding to treatment exceeds the one of the controls (53.8 % vs. 40.9 %) [24]. However, this evidence does not reflect on the formulated recommendations [6].

As to the *initial GC dose*, the DGRh/ÖGR/SGR societies recommend to consider the prescription of higher doses (up to 25 mg per day prednisone equivalent) to the PMR patients with an elevated risk of the developing relapses and a low risk of the GC's developed side effects; the lower doses (about 15 mg per day) are preferred for the patients with side effects, osteoporosis, glaucoma and other RFs of the GC's developed side effects. It is well-known that *in the German-speaking European countries one does not commonly start the PMR treatment with a daily dose of 12.5 mg.* One should stress the importance of "customized" approach to the GC dose reduction while treating PMR and dose correction while the relapses are developing; it implies the consideration of RF profile and clinical-laboratory monitoring of patients, which includes the GC intolerance control [6]. Further on, the DGRh/ÖGR/SGR guidelines cite the EULAR recommendations of 2010 on the low-dose GC therapy side effect monitoring in the clinical trials and medical practice [25] and the further development of GC toxicity index (E.M. Miloslavsky et al., 2017) [26]. They reported on the principles of rapid reductions of the higher initial doses (such as 25 mg per day) in comparison to the lower ones (15 mg per day) and maintenance of "bone health" in accordance with the German research osteology societies of 2009 and 2014 [27-28].

One should pay heed to the lacking clues of the elevated GC dose advisability in case of persisting symptoms and confirmed PMR diagnosis after 2-4 weeks (which is the EULAR/ACR algorithm of 2015) in the German-language guidelines [1-2, 5].

As to the *methotrexate*, in case of a lacking typical clinical situation requiring its prescription, the authors of DGRh/ÖGR/SGR guidelines are citing the publications of 1985-2013 [29-37] and pointing out the importance of individualized use of methotrexate to treat PMR and advisability of its consideration for women, patients with a considerably elevated ESR (> 40 mm/h), presence of peripheral arthritis or comorbidities raising the GC side effect risk [6]. The listed factors are considered primary (though unconfirmed) RFs of relapses/protracted therapy requirement, while the peripheral arthritis is referred to as an atypical PMR manifestation [1, 5], as a result the methotrexate is supposed to be prescribed by a rheumatologist himself/herself.

There is a concerted decision that the additional methotrexate therapy should be considered in case of PMR relapse/relapses, inadequate response to the GCs and development of side effects. In line with the EULAR/ACR manual (2015) [5] and reviews by F. Buttgereit and C. Dejaco et al. (2016) [7-8], the guidelines intended for the German-speaking countries point out the fact that those clauses are based on the "partially contentious" findings of several randomized and one retrospective CT; moreover, they emphasize the better quality of studies confirming the methotrexate benefit in the PMR treatment (in terms of the relapse frequency, GC cumulative dose and their possible cessation) compared to others bringing the negative findings. For the patients with renal function disorders, one recommends avoiding or closely controlling the methotrexate treatment. There are reports of a weak evidence base involving the economic effects of methotrexate treatment against PMR and impossibility of the formulated recommendations on the traditional disease-modifying antirheumatic drugs (DMARDs) use, attributed to the absence of relevant CTs [6].

The Clause 4 *precluding the tumor necrosis factor (TNF) inhibitors* present in Table 2 was referred to as "confounding" [6], though earlier they did receive no approval from the EULAR/ACR [5]. The authors attribute this fact to the lack of evidence on the efficacy of these medications in the PMR treatment and extant data on an inadequate tolerance and high cost of such treatment. At the time of the DGRh/ GR/SGR guidelines (2018) publication,

following the previous EULAR/ACR manual (2015), the positive effect of *tocilizumab* was confirmed in but one open-label CT of IIa phase (L. Lally et al., 2016) [18]. While criticizing the methods and statistical force of this trial, the authors of present guidelines considered it impossible to formulate the clause on tocilizumab use in the PMR treatment. The same decision was made as to *other monoclonal antibodies*, due to a lack of published prospective CT findings on their effects [6].

Preserving muscle mass and function, falls risk reduction are considered the desired outcomes of the PMR treatment, as there are no studies confirming the benefit of *physiotherapeutic interventions* (see Table 2). However, the individually selected programs of physical exercises are considered most beneficial for the elderly and/or frail PMR patients [...] despite the lack of evidence and account being taken of an urgent wish of patients [6].

Finally, we should note the absence of any data on the contraindications of the Chinese herbal medications, the Yanghe and Biqi, mentioned by the EULAR/ACR recommendations (2015) in connection with the PMR treatment, though avoided by the German-language guidance.

In the final part, the authors of the DGRh/ÖGR/SGR guidelines (2018) make their claim as to the leading GC role in the PMR treatment, despite the weakness of evidence base on such topical issues as the initial dose, the regimen of reduction, duration of treatment, all of them attributed to the inconsistency of patient subgroups. This document, intended to support the physicians of Germany, Austria and Switzerland in their decision-making on the PMR patient management, is based on the EULAR/ACR recommendations published three years earlier and on the consensus of experts representing these countries.

We've performed our own information analysis to corroborate the high level of the DGRh/ÖGR/SGR guidance authors' agreement on all the general principles and special recommendations as well as the preponderance of expert opinion underlying their formulations (70 % of clauses). There are important specific features which make this manual distinct from its precursor – the EULAR/ACR recommendations: the increased attention drawn to the atypical PMR manifestations (peripheral arthritis, systemic signs, the younger age of patients and the lower inflammation indices) which require the rheumatologist's attention and oncological threat; a suggestion of higher initial minimal GC dose (15 rather than 12.5 mg per day); an absence of such an option as the GC dosage increase after 2-4 weeks in case of persisting symptoms and the confirmed PMR diagnosis; making a clear list of the relevant diagnostic tests as well as the primary evidence of tocilizumab's efficacy in the PMR treatment; an absence of recommendations as to the prescription of some of the Chinese folk medicines.

We should compare this manual with a clinical recommendation on "Polymyalgia Rheumatica" by the Finnish Medical Association (FMA), which is viewed as *a new clinical protocol*, un-adapted and approved by the edict of the Ministry of Healthcare of Ukraine in December of 2016 [38-39]. Both medical standards recommend an initial daily dose of prednisone of no less than 15 mg (with a simultaneously initiated prevention of osteoporosis). However, the *Finnish/Ukrainian document* requires the greatest initial daily GC dose should not exceed 20 mg, it is also noted that the greater dose is not necessary; the revision of diagnosis is recommended when there is no symptomatic improvement after 3-5 days; the dosage reduction is suggested after 2-4 weeks, "by 2.5 mg per month, and later in a slower manner". For the patients with a typical clinical picture, it is not obligatory to rule out the latent malignant tumors; among the indications of the rheumatologist's consultation, there are a suspicion of GCA, atypical clinical picture and inadequate response to the treatment; out of the above-mentioned, the suspected GCA is most thoroughly described: present headaches, tender hairy part of the head, vision problems, intermittent jaw or limb pain. "The typical clinical signs" are the age of >50 years, the ESR of>40 mm/h and "a rapid response to a daily dose of 10-20 mg prednisone for 3 days". Among the obligatory diagnostic tests, they mention only the ESR, CRP and total blood count determining the platelet rate; other assays are not numerous (alkaline phosphatase, creatine kinase, rheumatoid factor, anti-cyclic citrullinated peptide antibodies, ultrasonography of shoulder and hip joints – as a "beneficial component of the primary studies", temporal artery biopsy in case of a suspected GCA) and cited in terms of the differential diagnostics whose circle includes the RA, spondyloarthritis, vasculitis, the connective tissue disorders, polymyositis, osteoarthritis, adhesive capsulitis, fibromyalgia, hypothyroidism, viral infections, depression, myeloma diseases and other malignant tumors. In case of an aggravated PMR, the clinical practice envisages the return to the higher GC dosage. The adjuvant methotrexate therapy is suggested when there is no sufficient GC response or the developed side effects; they mention azathioprinum as its possible alternative, unlike the DGRh/GR/SGR or the EULAR/ACR recommendations. Another specific feature of the new clinical protocol is the suggested control of but a small number of parameters associated with the PMR patient management: the ESR, CRP rate, blood parts, creatinine, glucose and electrolytes [39]. Some distinctions were found between the DGRh/ÖGR/SGR recommendations and the Finnish Medical Association (FMA)'s recommendations (i.e. the new Ukrainian clinical protocol). They may be explained by their priority indication (for rheumatologists and primary care physicians, respectively) and special methods of their development, as well as their economic factors.

Conclusions

The combined recommendations by the German, Austrian and Swiss rheumatological societies and other research-medical associations and organizations (DGRh/ÖGR/SGR, 2018), which are developed in order to overcome the distinctions of approaches to the PMR patient management in those European countries and to adapt

the EULAR/ACR recommendations (2015) underlying them, to revise their sources and over 2.6 thousand new pieces of evidence, published in 2014-2016. They inspire a lot of interest due to the population ageing, medical personnel's migration and the need for the raised standards of healthcare provided for the elderly patients with polymyalgia syndrome and specifically the PMR *per se*.

The DGRh/ÖGR/SGR's general principles and special recommendations on the PMR management correspond to the overall prototype, though with their own distinctions. They deal with the initial GC doses and their correction, a list of diagnostic test and information on the tocilizumab use and the traditional Chinese medications.

The prospect of corroborated evidence base on the PMR patient management in the clinical practice is reflected by the fact that over 2/3 of DGRh/ÖGR/SGR recommendations are based on the expert opinion. However, the PMR treatment is commonly associated with the issues of comorbidities, tolerance of the analgesic and anti-inflammatory therapy, timely GCA detection (also reflected in the Ukrainian protocol) and malignant tumors (it is more clearly represented by the German guidelines).

The systemic exploration of medical and technical documents on the healthcare standardization, which are based on the evidence medicine and consensus in the developed countries, promotes their harmonization and regular renewal, opens the vista for the improvement of healthcare standards for the patients with bone-muscular disorders in Ukraine.

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Ревматична поліміалгія: об'єднуючи зусилля європейських ревматологічних товариств

Резюме. Постаріння популяції є передумовою зміцнення доказової бази специфічних геріатричних синдромів, ревматичних захворювань з пізнім дебютом і ревматичних хвороб похилого віку. Серед останніх найпоширенішою є ревматична поліміалгія, наявність і ведення якої пов'язане з проблемами переносимості знеболювальної та протизапальної терапії і вчасного виявлення гігантоклітинного артеріїту та злоякісних пухлин. В Європі, зокрема в німецькомовних країнах, зберігаються суттєві відмінності в підходах до ведення пацієнтів з ревматичною поліміалгією в клінічній практиці. Цим обумовлено створення й видання 2018 року єдиних настанов Німецького ревматологічного товариства, Австрійського товариства ревматології і реабілітації, Швейцарського ревматологічного товариства та інших науково-медичних асоціацій і організацій, присвячених даній проблемі. У статті наведено та обговорено їх доказову базу, основні принципи та спеціальні рекомендації. Розробку співставлено з настановами Європейської антиревматичної ліги та Американської колегії ревматологів 2015 року і клінічною настановою Фінської медичної асоціації, яку було схвалено Міністерством охорони здоров'я України для використання в первинній ланці як новий клінічний протокол 2016 року.
Ключові слова: ревматична поліміалгія; лікування; стандарти; огляд

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Ревматическая полимиалгия: объединяя усилия европейских ревматологических обществ

Резюме. Постарение популяции является предпосылкой усиления доказательной базы специфических гериатрических синдромов, ревматических заболеваний с поздним дебютом и ревматических болезней пожилого возраста. Среди последних наиболее распространена ревматическая полимиалгия, наличие и ведение которой сопряжено с проблемами переносимости обезболивающей и противовоспалительной терапии и своевременного выявления гигантоклеточного артериита и злокачественных опухолей. В Европе, в немецкоязычных странах в частности, сохраняются значительные различия в подходах к ведению пациентов с ревматической полимиалгией в клинической практике. Этим обусловлено создание и публикация в 2018 году единого руководства Немецкого ревматологического общества, Австрийского общества ревматологии и реабилитации, Швейцарского ревматологического общества и других научно-медицинских ассоциаций и организаций, посвященного данной проблеме. В статье представлены и обсуждены его доказательная база, основные принципы и специальные рекомендации. Разработка сопоставлена с рекомендациями Европейской антиревматической лиги и Американской коллегии ревматологов 2015 года и клинической рекомендацией Финской медицинской ассоциации, одобренной Министерством здравоохранения Украины для применения в первичном звене в качестве нового клинического протокола в 2016 году.
Ключевые слова: ревматическая полимиалгия; лечение; стандарты; обзор