Polymyalgia rheumatica
in the 2018–2020 clinical guidelines.
Part I. At-risk groups, adjuvant therapy


Abstract. At the beginning of the Healthy Ageing Decade, a number of guidelines were published describing management of the rheumatic diseases of the elderly. The aim of the paper is to characterize and discuss the Italian Society of Rheumatology’s guideline for polymyalgia rheumatica (2020) and the European Association of Nuclear Medicine, the Society of Nuclear Medicine and Molecular Imaging, and the American Society of Nuclear Cardiology’s (2018) recommendation for positron-emission tomography/computed tomography imaging to diagnose the large vessel vasculitis and polymyalgia rheumatica. The following methods were used: original texts of recommendations, their content and methodology behind the development of both guidelines were studied by means of information analysis and compared with the recommendations for the management of polymyalgia rheumatica and giant cell arteritis elaborated in 2018–2020 by the European League Against Rheumatism, American College of Rheumatology; the German, Austrian, Swiss and British rheumatological societies; the European Headache Federation and their references. We’ve established the priority of consensus approach for the development of modern guidelines for polymyalgia rheumatica. The specific feature of the Italian guideline’s development is the search for prototypes restricted to the two evidence-based medicine databases and the grey literature as well as selection of three international guidelines for adaptation, one of them elaborated by the societies for nuclear medicine. The following issues were updated: the patient management in primary care (whose algorithm is proposed), including the consented clinical decision-making and alertness to the giant cell arteritis. Out of the first-line therapy tools, only the initial doses of glucocorticoids are evidence-based, and their reduction is allowed as an alternating regimen. The ineffectiveness of hydroxychloroquine use is justified, while both azathioprine and alternative medical drugs are not subject to discussion. It is necessary to identify the risk factors for vasculitis and its relapses, longterm glucocorticoid use and their side effects. For the first time, the use of positron-emission tomography/computed tomography is recommended for detecting of vasculitis. The recommendation for adjuvant therapy with methotrexate and abstaining from the biologic agents is found the most evidence-based, strongest and consistent; referral to a rheumatologist being the least agreed-on position. Conclusion. Solving such an urgent healthcare problem as improving the quality of polymyalgia rheumatic management suggests the medical standards being raised on the most clinically important issues, the importance of at-risk patient identification and referral to rheumatologists and ophthalmologists, and consideration of the methotrexate’s benefits.

Keywords: polymyalgia rheumatica; giant cell arteritis; complications; diagnosis; treatment; review

Introduction
Having proclaimed the 2020–2030s as the Healthy Ageing Decade, the World Health Organization (WHO) called on the national healthcare systems to establish the global evidence base and partnership networks, catering for the elderly patient needs in the long-term patient-centered healthcare, namely the primary one [1]. The universal quality-improvement tool is the international clinical recommendation-based standardization.

The inflammatory rheumatic diseases (IRDs) afflicting 2-3 % of global population is being increasingly diagnosed in the elderly people – “heterogeneous and co-morbid” risk group likely to develop the cardiovascular, oncological, infectious diseases and iatrogeniae [2]. Having recognized the polymyalgia rheumatic (PMR) as the IRD most widely-spread among the elderly patients, the international experts report the lack of factual data on morbidity and PMR treatment patterns applied at the population’s level [3-6]. These data come from the clinical trials, their reviews and evidence bases, as well as from the patient registries [3, 7].

Viewed as an exclusion diagnosis (primarily of a clinical nature, based on the acute-onset proximal muscle pain

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and stiffness in the subjects over 50), the PMR often causes consternation among the primary physicians. This fact is associated with a lack of universally accepted diagnostic criteria, weak evidence base on the laboratory diagnostic tests and medical interventions, an elevated risk of relapses which are difficult to predict, a need for the protracted (≥24 months) glucocorticoid (GC) use in 50% cases, the likely onset of atypical manifestations (20%) and their association with various oncologies, a frequent PMR association with large vessel vasculitis (in 20-30% cases) [7-11]. Despite the above-mentioned facts, the family physicians are referring fewer than 50% cases for the rheumatologic examination, and in the UK – only 17-44% cases [11-12].

In various countries across the world, the PMR prevalence among the subjects over 50 amounts to 6-8.5% [3, 13]. The morbidity rates fluctuate from 30 to 113 per 100,000 subjects of the respective age: 40 in Denmark; 50 in Minnesota, US; 96 in the UK; 112 in Norway [3, 11, 13]. The morbidity peak occurs at 75 years, however, the prevalence continues to rise until 90 years; the disease is wider-spread in the Northern Europe, among women (accounting for 70-75% cases), Caucasians and subjects of the Scandinavian descent [10-11].

It is the giant cell arteritis (GCA), a threatening condition which results in the likely irreversible blindness and aortal complications, which seems the most important PMR clinical association. The new findings obtained during 2016-2018 in the USA and Japan suggest the association existing between the PMR and inflammatory eye conditions; this association being supported by the studies of 10 scleritis and uveitis cases occurring at the PMR onset, during the PMR relapse or following the GC dose tapering [14-15].

The clinical trials held in the UK returned the controversial findings on PMR as a cardiovascular risk factor [16-17], demonstrated a possible trigger role of adjuvant flu vaccination [18] and a lack of the PMR development’s assessment with large vessel vasculitis (in 20-30% cases) [7-11].

The recent years witness a more frequent PMR detection in the Southern countries and regions [3, 20]. In 2005, the PMR prevalence among the adult population in Italy was 3.7% [21]. If 30 years ago the morbidity among the “Mediterranean population” was estimated as 12.7 per 100,000 subjects over 50 [20], at present this parameter reached 27.4, according to the monocentric clinical trial held in 2014-2016 on the basis of the preliminary European League against Rheumatism (EULAR) and American College of Rheumatology (ACR)’s classification criteria of 2012 [22]. The latter include the findings of ultrasound examination of shoulder and pelvic girdle, namely the detection of subdeltoid bursitis, tenosynovitis of biceps femoris, humeral and/or coxofemoral tenosynovitis and/or trochanteric bursitis. It is well-known that their use augments the PMR’s diagnostic precision [23]; this fact being reflected by the 2015 EULAR/ACR recommendations on the respective patient management [24]. However, due to a major fluctuation of sensitivity and specificity values this fact is not universally accepted [11]. The data obtained by the Italian rheumatologic clinic [25] demonstrated a better discriminatory capacity of the 2012 EULAR/ACR recommendation draft compared with the earlier suggested PMR diagnostic and classification criteria [8].

The further elaboration of the PMR diagnostics is associated with the publication of 2018 EULAR recommendations on imaging techniques used to diagnose the large vessel vasculitis [26], and the European Association of Nuclear Medicine (EANM) and the Society of Nuclear Medicine and Molecular Imaging (SNMMI)’s recommendation endorsed by the American Society of Nuclear Cardiology (ASNC), the EANM/SNMMI/PIG/ASNC recommendation on fluorodesoxyglucose positron emission tomography/computed tomography-angiography (FDG-PET)’s combined use with computed tomography-angiography (CTA) to diagnose large vessel vasculitides and PMR [27]. Published at the similar time, the DGRh/OR/SGR guidelines [28] by the German Society of Rheumatology (Deutsche Gesellschaft für Rheumatologie (DGRh)), Austrian Society of Rheumatology and Rehabilitation (Österreichische Gesellschaft für Rheumatologie (ÖGR)) and Swiss Society of Rheumatology (Schweizerische Gesellschaft für Rheumatologie (SGR)) were intended to overcome the existing divergences in the PMR management tactics in those countries, based on the adapted 2015 EULAR/ACR recommendations, original sources and 2.6 thousand new evidence being obtained in 2014-2016 and reviewed accordingly. The information analysis showed that over 2/3 of the DGRh/OR/SGR guidelines were based on the expert opinion and supported the importance of strengthened evidence base for the various aspects of PMR management [29].

The Italian Society of Reumatology (Società Italiana di Reumatologia (SIR))’s guideline on PMR management

Taking into account the demographic tendencies and the PMR prevalence in Italy, the above-mentioned 2015-2018 international recommendations being published, the lack of national standards and need for the improved healthcare quality provided to the elderly patients with polymyalgia syndrome [11], the Italian Society of Reumatology (Società Italiana di Reumatologia (SIR)) published its first clinical practice guideline on PMR patient management in 2020. Among its target recipients there were rheumatologists, general practitioners, internists, geriatricians, physical therapists, rehabilitologists “and other healthcare experts in charge of PMR management at the primary care level, in-patient and social care institutions”, subjects involved in the policy development and patients; target population being patients aged ≥18 years with a physician-diagnosed PMR [30].

Summing up the PMR differential diagnosis (its circle encompassing the late-onset rheumatoid arthritis (RA), GCA, calcium pyrophosphate dihydrate crystal deposition disease, remitting seronegative symmetrical synovitis with pitting edema, infections and malignant tumors), the Italian guideline authors focused their attention on the
GCA exclusion, i.e. the targeted detection of “the recently occurring headache, sudden vision disorders, jaw pain at mastication, tenderness and reduced temporal artery pulsation” in all the PMR patients [31]. This clause was developed into recommendation for the FDG-PET/CT(A) use as a diagnostic tool able to detect the large vessel vasculitis attending the PMR with a high precision [30].

The methodology of 2020 SIR guideline development primarily suggested the secondary evidence search based on the PICO (Population, Intervention, Comparator, Outcome) approach, selecting the clinical practice guidelines in two evidence-based medicine (EBM) computed databases Medline and Embase, as well as in the grey literature by means of AGREE II tool [32]. While establishing the key clinical issues, they used the PIPOH (Population, Interventions, Professionals, Outcomes, Health Settings) principle. The summarizing, ranging and adaptation of findings to “the needs and Italian healthcare context” were performed in compliance with ADAPTE guideline [33]. Out of 185 documents published during the period from January 2009 to January 2019, 14 were selected in the Medline and Embase by means of title, abstract and full-text content analysis, two clinical practice guidelines being selected in the grey literature (i.e. much fewer than while developing the 2018 DGRh/OG/SGR guidelines). The sources referred to as “grey” were the repositories of rheumatologic societies “and other information centers” available on the TRIP evidence based medicine (EBM) computed databases and the British National Institute for Health and Care Excellence (NICE), as well as the cross-references and the Google Scholar search results [30]. Most selected documents (13 out of 16) were not considered for the development of the Italian clinical practice guidelines as they turned out as “not being the clinical practice guidelines or consensuses”, duplicates, publications in the languages other than English, Italian or German, manuals of a lower standard or inconsistent with the key clinical issues and search timelines. Among them, there were the 2009 Brazilian Society of Rheumatology (Sociedade Brasileira de Reumatologia (SBR)), 2010 British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR), 2013 NICE recommendations, 2010 Dutch College of General Practitioners (Nederlands Huisartsen Genootschap (NHG)) recommendations and a range of EULAR/ACR manuals of 2014-2018.

The three remaining documents – the 2015 EULAR/ACR recommendations [26], 2018 DGRh/OG/SGR guidelines [28] and 2018 EANM/SNMMI/PIG/ASNC recommendation [27] - were endorsed by two independent experts as the initial Italian clinical practice guideline prototypes. By combining their key items and evidence bases, they developed nine recommendations in compliance with the key issues on the importance of clinical evaluation, laboratory and imaging tests prior to treatment, criteria of primary-rank patient’s referral to the specialist, drug effects and 1st line therapy regimen, types and timelines of transfer to the 2nd line therapy, non-pharmacological intervention effects, as well as the role of monitoring for the PMR remission and relapse evaluation. The evidence categories (levels) and recommendations (strength) were brought in compliance with the Oxford Centre for Evidence-Based Medicine (CEBM) (Table 1) [34]. The external manual’s evaluation and discussion of its implementation in the Italian healthcare system were performed by the multidisciplinary interest group (stakeholders) involving 22 physicians (18 rheumatologists, a general practitioner, an internist, a geriatrist and a rehabilitologist), two experts in healthcare organization and a representative of the patient society [30].

The finalized 2020 SIR guideline formulations are presented in the Table 2, each of them with the evidence base, recommendation power and stakeholder agreement level attached and ranked as a 10-point scale “as a result of concerted discussion and based on the evidence and clinical experience” [30].

Table 1. The Oxford Centre for Evidence-Based Medicine (CEBM)-suggested evidence and recommendation gradation system [34]

<table>
<thead>
<tr>
<th>Evidence</th>
<th>Source</th>
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<tbody>
<tr>
<td>1</td>
<td>RCT metaanalysis or at least one RCT</td>
</tr>
<tr>
<td>2</td>
<td>At least one non-randomized controlled trial or one cohort controlled trial</td>
</tr>
<tr>
<td>3</td>
<td>At least one controlled trial of “case-control” type</td>
</tr>
<tr>
<td>4</td>
<td>A series of cases or clinical trial of “case-control” type or cohort clinical trials</td>
</tr>
<tr>
<td>5</td>
<td>Reports of experts committees or opinion and/or clinical experience of the high-ranking managers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Sequential findings of 1st level trials</td>
</tr>
<tr>
<td>B</td>
<td>Sequential findings of 2nd or 3rd level trials or extrapolated* 1st level trials</td>
</tr>
<tr>
<td>C</td>
<td>Evidence of 4th level or extrapolated* 2nd or 3rd level controlled trials</td>
</tr>
<tr>
<td>D</td>
<td>Evidence of 5th level or inconclusive findings or unfinished trials of any level</td>
</tr>
</tbody>
</table>

Notes: RCT - randomized controlled trial, SoR - strength of recommendation, * - using data in the situation which potentially has clinically important distinctions compared to the situation of the original study.
The Table 2 demonstrates that the SIR’s four recommendations are devoted to the clinical evaluation of patients (№ 1-4), a similar number is devoted to the treatment (№ 5-8), and one recommendation is devoted to monitoring (№ 9). Most recommendations (7 out 9; 77.8%) are based on the expert opinion and thus they have the lowest, 5th level of evidence — these are recommendations № 1, 2, 4, 8, 9, partially 3 and 6.

The evidence base of the 1st category (the strongest one) supports the recommendation № 7, devoted to the 2nd line therapy, i.e. Methotrexate and abstaining from the genetic-engineering biologic agents. The contrastive analysis of the DGRh/OGR/SGR clinical practice guideline demonstrated a lack of discrepancies as to the highest level of evidence on this recommendation. The maximum agreement of the Italian stakeholders is reached on four clauses: the early initiation of GC use, individualized selection of dose and duration of therapy, abstaining from tumor necrosing factor (TNF) inhibitors and inability of genetic-engineering biologic agent recommendation.

One non-randomized and cohort controlled trial, i.e. 2nd level of evidence, supports two Italian recommendations - № 3 (in terms of high FDG-PET/CT(A) diagnostic precision) and № 6 (in terms of individualized selection of initial GC dose at a range of 12.5-25 mg per day of Prednisone). The 2018 German guidelines do not consider this diagnostic test at all, while the minimal initial recommended GC dose is 15 mg per day.

As to the 1st line therapy, the Italian recommendation № 5 on GC being used instead of non-steroidal anti-inflammatory drugs (NSAID) and analgesics is based on the 4th level of evidence (a series of cases, clinical trial of the “case-control” type and cohort trials) while in the German guidelines it is supported by the expert opinion. The expert opinion is also the foundation of the Italian recommendation on the GC therapy’s initiation right after the PMR diagnosis being made.

<table>
<thead>
<tr>
<th>№</th>
<th>Recommendation</th>
<th>LoE</th>
<th>SoR</th>
<th>LoA, median (IQR)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Clinical evaluation</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>With enough clinical data for the confirmed PMR diagnosis, one should use a</td>
<td>5</td>
<td>D</td>
<td>9 (7.75; 10)</td>
</tr>
<tr>
<td></td>
<td>safe approach excluding the PMR-mimicking and associated conditions – non-inflammatory, inflammatory (such as GCA and RA), drug-induced, endocrine, infectious, malignant. While managing the PMR patient, one should consider: - existing AH, DM, CVD, dyslipidemia, glucose tolerance disorder, peptic ulcer, osteoporosis and recent fractures, cataract, glaucoma and its risk factors, chronic and relapsing infections; - adjuvant NSAID and similar drug treatment, risk factors of GC AE. The role of relapse risk factors/ need for a protracted treatment is unclear. The primary factors associated with a higher frequency of relapses and/or a protracted treatment, according to the recent findings, are the female sex, ESR &gt;40 mm/hour and peripheral arthritis</td>
<td>5</td>
<td>D</td>
<td>9 (7.75; 25)</td>
</tr>
<tr>
<td>2</td>
<td>Laboratory test evaluation</td>
<td>5</td>
<td>D</td>
<td>9 (8; 9,25)</td>
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<tr>
<td></td>
<td>Prior to the treatment prescription, every PMR patient should be tested for a</td>
<td>5</td>
<td>D</td>
<td>9 (8; 9,25)</td>
</tr>
<tr>
<td></td>
<td>range of parameters in order to rule out the PMR-mimicking conditions and treatment monitoring: CRP and/or ESR, RF, ACCP complete blood count, glucose and creatinine blood rates, liver function test, bone samples (including calcium and AP), complete urinalysis. There may be extra tests: protein fractionation, TSH and creatine kinase (CK)</td>
<td>5</td>
<td>D</td>
<td>9 (8; 9,25)</td>
</tr>
<tr>
<td>3</td>
<td>Extra examinations</td>
<td>5*</td>
<td>2**</td>
<td>9 (7.75; 9,25)</td>
</tr>
<tr>
<td></td>
<td>On physician’s discretion,* one may undertake extra examinations, such as</td>
<td></td>
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<td></td>
<td>chest X-ray, abdominal ultrasound and densitometry. There is a high diagnostic precision associated with FDG-PET/CT(A) in PMR cases**; however, the clinical value of this test’s findings is yet unclear for the PMR management, it should be considered for the specialized centers</td>
<td></td>
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</tr>
<tr>
<td>4</td>
<td>Referral to a specialist</td>
<td>5</td>
<td>D</td>
<td>8.5 (7.5; 9.25)</td>
</tr>
<tr>
<td></td>
<td>One should refer a patient with atypical PMR manifestations (peripheral arthritis, systemic manifestations, a low rate of inflammatory markers, age up to 60 years), as well as a history or presence of risk factors of GC AE, GC refractoriness, relapse and/or a protracted PMR treatment</td>
<td>5</td>
<td>D</td>
<td>8.5 (7.5; 9.25)</td>
</tr>
<tr>
<td>5</td>
<td>1st line therapy</td>
<td>4</td>
<td>C</td>
<td>9 (8; 10)</td>
</tr>
<tr>
<td></td>
<td>The PMR patients are recommended to use GC rather than NSAID, excluding possible short-term NSAID prescriptions and/or analgesics for the pain associated with other conditions</td>
<td>4</td>
<td>C</td>
<td>9 (8; 10)</td>
</tr>
</tbody>
</table>
6 Dosage and method of 1st line drug use

GC treatment should be initiated immediately after the PMR diagnosis being made*. The initial GC dose should be determined for every individual patient and equivalent to a minimal effective daily Prednisone dose of 12.5-25 mg. The use of greater doses in the existing frameworks is possible with a high risk of relapse and low risk of AE. For the people with attendant conditions (DM, osteoporosis, glaucoma etc.) and other risk factors of GC AE, lower doses are preferable. The daily doses of ≤7.5 and >30 mg are not recommended**.

The dose tapering regimen should be selected for every individual patient, based on the disease activity monitoring, laboratory markers and AE. The initial titering target is reaching the daily dose of 10 mg for 4-8 weeks. In case the relapse occurs, the GC dose should be raised to the previous level and reduced gradually (during 4-8 weeks) to the level at which the relapse occurred. On remission being reached, the Prednisone dose should be reduced by 1 mg a week for 4 weeks (or reduced by 1.25 mg at an alternating regimen of 10/7.5 mg every two days) until the complete discontinuation if the remission persists*. The one-time internal use of a daily GC dose is to be preferred to multiple uses*.

The duration of GC treatment for PMR should be individually selected and reduced until the adequate effect is reached*.

7 2nd line therapy

An early Methotrexate addition to GC should be considered in case of a high risk of PMR relapses and/or need for a long-term treatment, as well as present risk factors of GC AE, including the attending conditions or treatment. With a further monitoring, one may consider Methotrexate prescription in case of PMR relapse and GC-dependent AE. In the clinical trials, Methotrexate is used internally at a weekly dose of 7.5-10 mg. The use of TNF inhibitor for PMR treatment is not recommended. The recommendations on other biologic agents, including Interleukin 6 (IL-6) inhibitors are not to be recommended.

8 Non-pharmacological interventions

One should consider the prescription of individualized programs of physical exercises for the muscle mass maintenance and falls risk reduction, namely for the elderly people on a protracted GC treatment as well as “fragility” patients.

9 Treatment and monitoring targets

The PMR treatment should be aimed at the best healthcare provision based on a concerted decision-making by a patient and his/her physician. The PMR management plans should be individualized. While selecting the initial GC doses and their further titering, one should consider patient plans and preferences. They should have access to the information on PMR, its treatment, predictors of its course, attending conditions, as well as recommendations on the physical exercise programs.

Every PMR patient receiving healthcare at the primary and secondary levels should be monitored in terms of GC AE evaluation and risk factors of their development, attending conditions and treatment; relapses/ protracted treatment and risk factors of their development.

Visits to the attending physician should be planned every 4-8 weeks during the 1st year of treatment, and every 8-12 weeks during the 2nd year, as well as during the relapses, dose tapering and GC discontinuation.

The patient should be guaranteed a quick and direct access to the physician or other competent healthcare provider’s counsel in case of aggravating manifestations or treatment AE developing.

Notes: ACCP - anti-cyclic citrullinated protein antibodies; AE - adverse effect; AH - arterial hypertension; AP - alkaline phosphatase; CRP - C-reactive protein; CVD - cardiovascular diseases; DM - diabetes mellitus; ESR - erythrocyte sedimentation rate; FDG-PET/CT(A) - fluorodesoxyglucose positron emission tomography/computed tomography-angiography; GC – glucocorticoids; GCA - giant cell arteritis; IQR – interquartile range; LoA – level of stakeholder agreement; LoE – level of evidence; NSAID - non-steroidal anti-inflammatory drug; PMR - polymyalgia rheumatica; RA - rheumatoid arthritis; RF - rheumatoid factor; SoR – strength of recommendation; TNF inhibitor - tumor necrosing factor inhibitor; TSH - thyroid stimulating hormone.

It is worthy of note that the lowest level of the Italian stakeholder agreement (8.5 points) was reached on the issue of PMR patient being referred to a rheumatologist (recommendation № 4). In the DGRh/OG/GR/SGR guidelines, a similar level of agreement (8.36 points) is cited for the recommendation on the early Methotrexate use.

To sum up, out of the range of the above-mentioned Italian clinical practice guideline, the recommendation on the 2nd line PMR therapy (use of Methotrexate and abstaining from genetic-engineering biologic agents) turned out the most evidence-based, strong and agreed-upon, while the recommendation on the PMR patient’s referral to a rheumatologist turned out the least concerted. The initial GC doses, as well as the FDG-PET/CT(A) test being used to detect vasculitis among the PMR patients treated at the specialized medical institutions are some-
what weaker supported; the latter being regulated by the above-mentioned medical and technical document for the first time.

Among the prototypes of the 2020 SIR clinical practice guideline, there are the respective clauses of the 2015 EULAR/ACR recommendations [24] and the 2018 DGRh/OGR/SGR guidelines [28]. While developing the recommendation on the extra diagnostic tests (№ 3), the co-authors were considering the clinical practice guidelines of 2018 EANM/SNMMI/PIG/ASNC nuclear societies [27].

The contrastive analysis of the clinical practice guideline prototypes allowed us to outline the formal discrepancies: for instance, the DGRh/OGR/SGR clinical practice guidelines contain general principles on: 1) detecting PMR as an exclusion diagnosis; 2) detecting the risk factors of adverse prognosis and examinations to precede the therapy; 3) criteria of a patient management by a rheumatologist; 4) concerted clinical decision-making with a patient; 5) order and essence of the repeat visits to a physician [28].

As to the essence, one should note the correspondence of recommendations № 1 and 2 from the Italian guidelines to the principles A and B from the guidelines intended for the German-speaking European countries. However, a range of diagnostic tests in the latter document is more extensive and includes the detection of Vitamin D level in the blood serum, anti-nuclear and anti-neutrophil cytoplasmic antibodies (ANCAs), serological tests of TB diagnostics, chest X-ray, abdominal ultrasound and densitometry [28]. In the Italian clinical practice guidelines, these examinations were referred to as “extra, and to be performed at the physician’s discretion” in recommendation № 3; it is also the first to mention the possibility of FDG-PET/CT(A) prescription; however, not by the primary care physicians [30]. One should note the concerted character of the European rheumatologic societies’ positions on a lack of “common or special recommendation on the PMR-attended tumors, which is different from universally accepted positions on the oncoscreening in the respective age groups” [28]. The above-mentioned extra diagnostic tests should be prescribed in case of clinical manifestations or symptoms being present and signaling other possible diagnoses, while “the serological tests are primarily performed at the specialized medical institutions, and densitometry is performed within the frameworks of the treatment being performed” [30].

The indications for the PMR patient’s referral to a rheumatologist are reflected in the recommendation № 4 from the Italian guidelines; they are generally consistent with principle C from the German-speaking countries [28-29] and include age under 60 years and other atypical PMR manifestations (peripheral arthritis, systemic manifestations, and a low level of inflammatory markers) as well as the detected risk factors in the medical history or patient status: risk factors of GC AE (diabetes, osteoporosis, glaucoma etc.), risk factor refractoriness to GC, risk factors of relapse development (female gender, erythrocyte sedimentation rate (ESR) > 40 mm/hour, peripheral arthritis) and risk factors of a protracted treatment. In the situations described above, as well as with a suspected GCA, the rheumatologist’s consultation is required to verify the diagnosis and determine the treatment tactics: an elevated risk of PMR relapse development requires either the GC dose increase or Methotrexate’s addition to the lower GC doses (within the range of 12.5-25 mg/day) as the steroid-maintaining drug.

The next recommendation № 5 from the Italian guidelines is devoted to the NSAID and/or analgesic withdrawal from the 1st line therapy. At this stage, the DGRh/OGR/SGR guidelines are strongly recommending to involve the patients into the decision-making: “One should strive towards the best possible healthcare being provided on the basis of a concerted decision-making by the patient and the physician, suggesting an adequate information support on the PMR outcomes and treatment” [28]. In the Italian clinical practice guidelines, this approach is relegated to “Treatment and observation targets” and reflected in the recommendation № 9 (Table 2) [30].

While comparing the recommendations № 6 and 4, one should note that the prescription of higher GC doses (maximum 30 mg/day) or lower GC doses (however, >7.5 mg/day) may be made only by a rheumatologist, as the indications cited therein coincide to a large extent. Unlike the German counterpart, the Italian clinical practice guidelines imply lower initial GC doses and an alternating regimen of dose tapering [28, 30].

The information analysis findings support the fact that the GC is consistently being considered the 1st line PMR therapy. In 2015, the EULAR/ACR recommended its clinical use to treat this condition, starting from the dose of 12.5-25 mg/day by Prednisone. It was later reflected in the 2018 DGRh/OGR/SGR guidelines (citing the rare use of 12.5 mg/day initial dose in Germany, Austria and Switzerland) and the debated Italian clinical practice guidelines of 2020. Both documents cite the possible intramuscular Methylprednisone use at an initial dose of 120 mg every 3 weeks “as an alternative to the internal use at the attending physician’s discretion”, based on the results of the double-blind clinical trial of 20 years ago. However, one rarely uses this approach in Italy, nor one divides a daily GC dose into several uses (which may be effective in case of nighttime pains arising out of Prednisone dose tapering <5 mg/day) [30].

Nevertheless, the evidence base of GC use and titering, duration of GC use to treat PMR and even initial GC dose remains weak, this fact being supported by the systematic review by Campbell A. M. et al. (2020). The search for the original sources was performed in such evidence based medicine (EBM) computed databases, as Cochrane Library, Medline, Embase, WoS, Scopus, Global Index Medicus, International Pharmaceutical Abstracts, and at the ACR website, as well as in the grey literature. The search was completed in June, 2018. The review comprised the contrastive clinical trials on various GC titering regimes, used for the treatment of rheumatic conditions within a range of 7.5 to 100 mg/day by Prednisone during ≥10 days, where at least on AE parameter was considered. Two clinical trials involving GCA and PMR patients, respectively, corresponded to these criteria; furthermore, treating PMR...
with Methylprednisone or Prednisone enabled the healthcare providers to achieve the remission at the 26th week in 100 and 89 % cases. The associations of developed AE (such as sleeping disorders and glucose tolerance disorders, infections and fractures) with the GC tapering strategies were not established. The review’s conclusion stated an absence of optimal evidence in favor of any GC tapering regimen or the need to rely on the development of recommendations based on “the expert opinion, a small series of cases and ‘trial-and-error’ principle” [35].

There is an important issue associated with the prospects of adjuvant steroid-maintaining drug use — detecting AE of a protracted GC use requirement, “typical” of PMR [3] and elevating the risk of adverse outcomes developing in the elderly people. In particular, a range of initial clinical trials and their reviews allowed the authors to detect a trend of elevating diabetes and osteoporosis risk associated with an increased Prednisone’s cumulative zone [36]. Other studies mention cataract as the key AE of GC treatment [5].

The PMR patients’ need for a protracted GC treatment is supported by Partington R. J. et al. (2018). It was “the first population-based study” recruiting the data of 42,000 patients with PMR diagnosis made during 1990-2016. The patients were receiving Prednisone on an unmitigating basis during 15.8 months (from 7.9 to 31.2). Materials of the study comprised the UK database of Clinical Practice Research Datalink, encompassing the clinical trial registries [3]. Earlier in the UK, Fardet L. et al. reported an elevated share of PMR/GCA patients with a protracted use of Prednisone in the overall structure — from 57.6 to 66.5 % during 1989-2009; however, as of 1985, 40 % cases were receiving GC treatment for over 4 years [4]. At present, at least 25 % patients are receiving GC treatment for over 3 years in Germany [37] and over 4 years in the UK [3], those facts being supported by the national registries. It is worthy of note that the GC doses recommended by the EULAR/ACR are mostly compiled with — in 75 and 92 % cases, in the UK [3] and France [6], respectively.

In the USA, by the data of Shbeeb I. et al. (2018), during 2000-2015, a mean duration of GC therapy taken for PMR treatment takes 3.95 years until its complete discontinuation, and only 19 % patients interrupted their treatment by the end of the 1st year of disease duration, 37 % - by the end of the 2nd year of disease duration, 50 % – by the end of the 5th year of disease duration. After 10 years of PMR onset, the GC treatment was completely terminated in 58 % patients [5].

According to Giollo A. et al. (2019), in Italy, 60 % PMR patients continue taking Prednisone for over 2 years. Despite the remission being reached and the GC use terminated after 20 months (from 14 to 27) in about half of the cases, 39 % patients renewed their treatment due to the PMR relapse [38].

Speaking about the PMR relapse, the US researchers are observing its higher frequency during the 1st year of treatment [5], casting a pall of doubt on the adequacy of GC doses being used, prescription of adjuvant therapy and risk factor detection in all of the outcomes.

Thus, there are a number of factors underlying the importance of adjuvant therapy of PMR. The studies made in Germany, Italy and South Korea detect an association between the addition of a range of medications required and the GC treatment duration as well as the developing relapses.

Having analyzed the data of German national patient registry and calculated the odds ratio (OR) with 95 % confidence interval (CI), Albrecht K. et al. (2018) outlined a range of risk factors behind the requirement of a protracted GC therapy among the PMR patients. Among them, there were Methotrexate use (OR=2.03; 95 % CI 1.27-3.24), Prednisone dose of >10 mg/day (1.65; 1.07-2.55), female gender (1.63; 1.09-2.43) and an elevated disease activity (1.12; 1.02-1.23). The best predictor of a protracted GC therapy requirement turned out to be an uncontrolled disease activity during the 1st year; however, as we see, the early Methotrexate use was associated with a 2-fold elevated risk of a protracted GC therapy: 256 out 1858 (13.8 %) PMR, GCA and PMR/GCA patients were taking Prednisone for over 3 years. During that time, the researchers registered an elevated rate of osteoporosis, though not diabetes or cardiovascular diseases (CVD). By the registry data, only 19 % PMR patients were taking Methotrexate; during the first 6 months of PMR, the mean daily GC dose amounted to 12.5 mg. The mean daily dose of ≤ 5 mg was reached after 13-18 months [37].

The results of retrospective analysis of 385 PMR patient data, made by Giollo A. et al (2019) in Italy, demonstrate “a frequent need for a protracted GC use” attending this disease and a possible protective effect of adjuvant aminobisphosphonate therapy; they were used by 60 % patients. The use of aminobisphosphonates was associated with the GC discontinuation irrespective of the age, initial Prednisone dose and osteoporosis presence (hazard ratio 0.66; 95 % CI 0.50-0.88) [38].

In this connection, we should refer to the strongest and most agreed-upon recommendation № 7 of the 2020 Italian clinical practice guidelines on the 2nd line PMR therapy – Methotrexate addition and abstaining from other disease modifying anti-rheumatic drugs (DMARD). This recommendation points out a lack of evidence base behind the effects of “other non-biologic DMARD, including Hydroxychloroquine” used to treat PMR. The latter turned out ineffective for the relapse prevention, based on the results of retrospective analysis of 78 patients receiving PMR therapy at the specialized medical institutions in South Korea. According to Lee J.H. et al. (2013) [39], the PMR relapses develop in almost half of all patients (46.1 %), namely during the 1st year in 38.4 %, usually half a year after the diagnosis being made. In line with the above-mentioned data [5, 37], the PMR relapses occurred mostly in women (88.9 %) on the background of higher cumulative GC doses; among the strong predictors of its development, there were a disease activity (initial C-reactive protein (CRP) rate ≥ 2.5 mg/dl (OR=6.296)) and Hydroxychloroquine use (OR=6.798). The influence of initial GC dose and of its tapering rate was not explored [39].
As we can see from the studies of the German patient registry and Korean patient cohort [37, 39], the adjuvant Methotrexate or Hydroxychloroquine therapy was associated with a 2-fold and over 6-fold increase of adverse outcome risk. However, the strongest predictor was the PMR activity per se.

As of 2020, the Italian Society of Reumatology (Società Italiana di Reumatologia (SIR)) reports “a vague role of risk factors behind the relapse development and a need for a protracted PMR therapy” [30]. According to the Japanese researchers Hattori K. et al (2020), the normalization of CRP rate during 30 days after the initiation of Prednisone use turned out to predict the remission and complete GC discontinuation by the 30th week of PMR treatment [40].

The contrastive analysis shows that the possibility of Azathioprine use is not mentioned by the Italian clinical practice guidelines of 2020 [30], unlike its prototype, the 2018 DGRh/OGR/SGR guidelines intended for the German-speaking European countries [28].

The possibility of PMR management at the primary care level was discussed by the Italian clinical practice guidelines of 2020 and other international guidelines; it is suggested “for most patients” in case of a fast and full response to GC, absence of atypical manifestations, risk factors behind the protracted GC therapy and relapses, “which may happen fairly often” [30]. However, during the 1st year of treatment up to 40 % [41] - 60 % patients [5] require a rheumatologist’s consultation. In case of no “precise recommendations” on Methotrexate prescription, its optimal doses and duration of use, Methotrexate is commonly used at a dose of 7.5-10 mg/week [41], stated by most clinical trials [30].

We should emphasize that an early Methotrexate prescription should be strongly recommended in order to achieve PMR remission and GC-maintaining effect (in particular the reduced risk of low-energy fractures), following the ruled-out paraneoplastic character of polymyalgia syndrome, confirmed PMR diagnosis and especially in conjunction with RA-mimicking disease phenotype. This recommendation arises out of 2 open retrospective studies, held in Italy during the recent years [41-42].

For instance, Quartuccio L. et al. (2018) were dealing with “detection of the PMR subgroup which had the best response to Methotrexate” [41]. Their study recruited 100 patients receiving Methotrexate either due to the relapse developing on the background of GC dose tapering (observed in 54 % cases), due to an incessant GC use ≥ 24 months, due to a need for GC use in a dose of ≥ 5 mg/day following a 4-month treatment, or due to an elevated GC AE developed or an elevated risk of its development. Those values were characteristic of younger patients and women with a higher disease activity; average duration of follow-up period was 46 months (from 12 to 185). The results demonstrated “a moderate Methotrexate efficacy”: on the background of its combination with Prednisone in a dose ≤ 2.5 mg/day, the PMR remission was achieved in 59 % cases during the 1st year of treatment and it persisted in 38 % cases after 12 months with a continued treatment. When Methotrexate was combined with Prednisone in a dose ≤ 5 mg/day, the PMR remission was achieved in 75 % cases during the 1st year of treatment. Higher initial Methotrexate doses were prescribed to the polyarthritis patients, corresponding to the number of affected joints. It is worthy of note that 34 % cases were receiving Methotrexate at an initial dose of 15-20 mg/week, while the 2020 SIR guidelines points out the doses of 7.5 -10 mg/week used in the clinical trials (see Table 2). An important outcome of this selection turns out to be a smaller number of new GC-dependent AE developing after Methotrexate prescription to treat GC AE. The absence of differences at the principal cut-off points allows the researchers to make their conclusion that Methotrexate prescription is an effective method of PMR treatment per se, including the GC resistance cases, and recognize the continued studies of subgroups as potentially useful.

The beneficial effect of Methotrexate use by the GC AE risk groups was earlier confirmed by Mazzantini M. et al. (2012). Based on the findings of cohort study involving 222 PMR patients, they found a strong association between the GC cumulative dose and low-energy fracture frequency as well as a strong association between a protracted GC use (> 2 years) with developing complications. Their findings and conclusions imply an even greater beneficial effect of Methotrexate, rather than of GC, for the elderly patients with polymyalgia if its paraneoplastic nature were ruled out: “The clinicians should not postpone the Methotrexate prescription for the patients with a high risk of GC-associated complications. Methotrexate should be strongly recommended to treat the RA-mimicking PMR phenotype” [42].

The evolution of expert opinion on the possible Methotrexate use to treat PMR is confirmed by the conclusions of Müller-Ladner U. et al. In their monograph “Methotrexate for the autoimmune diseases: the modern concepts of treatment in rheumatology, dermatology and gastroenterology” (2016), the authors do not list PMR as an indication for the Methotrexate prescription [43].

What allows us to rule out the PMR’s paraneoplastic nature and make an early Methotrexate prescription to the patient risk groups? This issue was considered by the 2018 DGRh/OGR/SGR guidelines [28] and by us [29]: among the possible risk factors of PMR’s association with an oncological disease there are: age over 75 years, male gender, present peripheral arthritis and especially polyarthritis affecting 6 or more joints, as well as the muscle and joint syndrome asymmetry, accentuated systemic manifestations in subjects under 50 years, ESR < 40 or > 100 mm/hour.

According to the 2020 SIR guidelines, an early (rheumatologist-made) Methotrexate prescription is indicated for the PMR patients with an elevated risk of relapses – i.e. attending, first and foremost, a high inflammatory activity rate, ESR >40 mm/hour, present peripheral arthritis, female rather than male gender. Methotrexate should either be added to the lower Prednisone dose (but no lower than 12.5 mg/day) – in case of present GC AE risk factors (diabetes, osteoporosis, glaucoma etc.) – or to the higher doses (but no higher than 25 mg/day) – in case of a low GC AE risk [30].
If the PMR patient has an elevated risk of relapses, the healthcare provider is facing a difficult choice: whether to prescribe higher GC doses or an early Methotrexate addition (and to which GC dose?). The content analysis of the Italian guidelines and their precursor prototypes confirms the tendency of strengthening Methotrexate’s status as a PMR treatment option, its early prescription or its prescription after the initial relapse.

This approach seems to be gaining ground. We consider it pertinent to cite the monocentral study involving rheumatologic patients with a confirmed SARS-COVID-19 diagnosis. Those findings were obtained in the Northern Italy, in 2020. All of the patients belonged to an older age group (from 55 to 76 years, mean age – 68 years; older age - 65 57 %), predominantly they were women (63 %); 4 of them had PMR, thus accounting for 6 % of the overall patient structure. Out of 12 late patients, only one patient aged 93 years was diagnosed with PMR and received Methotrexate in a dose of 5 mg/week. She did not take GC. There were no attending co-morbidities [44].

All in all, PMR is typically associated with attending co-morbidities, which may influence its course, choice of treatment tactic and its outcomes. The issue of PMR’s association with tumors remains moot [36], this fact being confirmed by 2018 Partington R. et al.’s systemic review cited by the Italian guidelines. According to the content analysis of 40 documents (selected out of 17,329 documents retrieved from 4 evidence based medicine (EBM) computed databases, there is a positive association between the PMR’s mentions and such terms as stroke, CVD, peripheral artery disease, diverticular disease and hypothyreosis. The PMR’s associations with malignant tumors “were observed in seven documents and were not confirmed by nine” [45]. According to Shibeeb I. et al. (2018), the rate of diabetes, arterial hypertension and fractures attending PMR does not exceed the one of “healthy” sex- and age-matched cohorts; however, a protracted GC therapy is likely to increase the risk of cataract [5].

The Italian guidelines determine the role of genetic-engineering biologic agents treating PMR, namely TNF inhibitors: their use is not recommended due to an absent effect of Infliximab and Etanercept, confirmed in 2007 and 2010, respectively. The 2017 preliminary findings of two clinical trials on Tozilizumab “are promising; however, they are not enough to be included in the guidelines” [30].

Methods of complementary and alternative medicine. To the same extent as the guidelines written for the German-speaking countries, their Italian counterpart does not include the 2015 EULAR/ACR-initiated recommendation on the counterindication of the traditional Chinese phytochemistry, which was first cited by Yanghe and Qi [24]. Nevertheless, there is a similarity existing between the Italian guidelines and both precursor clinical practice guidelines - EULAR/ACR (2015) and DGRh/ÖGR/SGR (2018). In the Italian clinical practice guidelines, a single recommendation № 8 emphasizes the importance of individual physical exercise programs, especially for the “fragile” PMR patients [30]. We should mention the inefficacy of our search performed 22.10.2020, using the search terms of «Polymyalgia Rheumatica» and «Tai Chi» in the main evidence databases for interventions’ effectiveness (i.e. the Cochrane Library (www.cochranelibrary.com) and the Cochrane Collaboration’s website (www.cochrane.org)). Nevertheless, based on the consensus approach, all the elderly patients receiving a protracted GC treatment are recommended to take regular exercises by EULAR/ACR (2015), DGRh/ÖGR/SGR (2018), SIR (2020) and other medical societies, in order to maintain the muscle mass and function, to reduce the fracture risk [24, 28-30].

The PMR patient management algorithm which follows the Italian Society of Reumatology (Società Italiana di Reumatologia (SIR))’s recommendations is presented in Fig. 1 [30]. Unlike the precursor clinical practice guideline prototypes, it presupposes the use of hybrid imaging technique of vasculitis diagnostics, i.e. FDG-PET/CT(A). In 2018, the FDG-PET/CT(A) use for detection of large vessel vasculitis attending the refractory PMR (either with constitutional or extracranial symptoms predominating in the clinical picture) was launched by Mayo Clinic (USA), along with CT — and MRI- angiography. Koster M. J. et al. offered a diagnostic algorithm, which took account of GCA’s clinical likelihood and such an option as ultrasonography and/or temporal artery biopsy [46-47]. The 2020 Italian clinical practice guidelines recommended the use of CT- angiography only in conjunction with FDG-PET.

Referring to the «treat to target» concept, i.e. treatment till the target is reached, used for PMR as a chronic condition, associated with elevated risks of various complications in the elderly people, we rely on the opinion by the Italian researchers and Mayo Clinic representatives, Camellino D. et al. (2019), who consider the control of inflammatory activity, functional disorders and patient health as the treatment target, as well as maintaining the life quality in general [48].

To sum up, the first Italian clinical practice guideline on PMR management was compared with its prototypes — the guidelines of the German, Austrian and Swiss rheumatologic societies of 2018 – and within the frameworks of other recently published international recommendations. The content analysis of these documents, the study of methodology underlying their creation as well as of the original sources emphasize the importance of consensus approach in case of lacking evidence (it is the background of 2/3 Italian recommendations and items of guidelines intended for the German-speaking European countries) as well as a strengthened patient and other vested interest roles – along with the “expert consensus” term used next to the “stakeholder agreement”. Specific methodology of SIR (2020) guideline elaboration consists in the search for prototypes only in two evidence based medicine (EBM) computed databases, as well as the selection of a much narrower range of documents for adaptation out of those databases and grey literature. The secondary evidence was taken from the 3 completed international clinical practice guidelines, including the nuclear medicine societies’ guidelines.
The Italian clinical practice guidelines foreground the issues of PMR diagnostics and management at the primary care level, including the customized clinical approach, concerted patient-assisted decision making and especially wariness of GCA (though not of tumors, this fact better reflected in the German-written prototype). Unlike the DGRh/OGR/SGR guidelines (2018), but in a similar way to the EULAR/ACR recommendations (2015), the Italian clinical practice guidelines do not delve into the principles, rather into the PMR management algorithm. The authors paid a lot of attention to the circumstances of healthcare provision and used the PIPOH approach to the key clinical issue formulation.

The issue of relapse risk factor, GC AE detection, need for a protracted treatment (the GC importance is considered “uncertain”, to the same extent as the clinical importance of FDG-PET/CT(A)) and vasculitis risk factors require an improved evidence base and agreement level. The 2020 Italian clinical practice guidelines on PMR recommends using this high precision imaging technique to diagnose vasculitis as an extra diagnostic test, whose results may influence the patient management only at the specialized care provision stage.

The GC status of the 1st line PMR treatment is preserved, though only initial doses are supported by evidence. An alternating regimen of GC tapering is suggested.

Recommendation on Methotrexate addition and abstaining from the biologic agents turns out the most evidence-based, strongest and agreed-upon recommendation in the Italian clinical practice guidelines, while the recommendation on rheumatologist’s referral is the most agreed-upon.

The guidelines also present the effects and advantages of an early Methotrexate prescription (in a dose up to 20 mg/week) and propose a hypothesis of relapse-preventing Aminobisphosphonate role; substantiate the lacking Hydroxychloroquine’s efficacy; avoid discussing Azathioprine treatment (unlike the 2018 DGRh/SGR guidelines) and alternative medications (unlike the 2015 EULAR/ACR recommendations).

Conclusions

Solving such an urgent healthcare problem as the improved PMR management implies elaborating the medico-technical documents at the institutional level (i.e. strengthening the evidence bases for the international recommendations and national standards); those documents dealing with clinically-important issues. On practice, one should perform a well-targeted detection of risk groups at the primary care level and recruiting rheumatologists and ophthalmologists in order to verify the diagnosis, confirm or refute the presence of vasculitis, point out the indications of Methotrexate addition or GC prescription at the high doses.

Conflicts of interests. Author declares the absence of any conflicts of interests and their own financial interest that might be construed to influence the results or interpretation of their manuscript.

References


Ревматична поліміалгія у клінічних настановах 2018–2020 років. Частина І. Групи ризику, ад’юванта терапії

Резюме. На початку Декади здорового старіння стала доступна низка клінічних настанов щодо ведення ревматичних хвороб у осіб літнього віку. *Мета* публікації — характеристики й обговорення настанови з ревматичної поліміалгії Італійського товариства ревматологів (2020) і настанови щодо застосування позитронно-емісійної томографії/ком’ютертронної томографії при вибірціх критичних ситуацій у ревматичній поліміалгії Європейської асоціації ядерної медицини та молекулярної візуалізації. Актуалізовано питання ведення пацієнтів у первинній ланці (запропоновано алгоритм), спільна комендація щодо ад’ювантної терапії метотрексатом і відмови від біологічних препаратів, найменш погодженою — позиція щодо ад’ювантної терапії засобами альтернативної медицини. Слід визнати, що засоби біологічної терапії є альтернаційними режимами їх зниження. Обґрунтовано неефективність гідроксихлорохіну, не обговорюються прийом глюкокортикоїдів і їх побічних ефектів. У першу чергу чинники ризику розвитку васкуліту, рецидивів, тривалості ефективності гідроксихлорохіну, не обговорюються прийом глюкокортикоїдів і їх побічних ефектів. У першу чергу чинники ризику розвитку васкуліту, рецидивів, тривалості ефективності гідроксихлорохіну, не обговорюються прийом глюкокортикоїдів і їх побічних ефектів.


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**Ревматична поліміалгія у клінічних настановах 2018–2020 років. Частина І. Групи ризику, ад’юванта терапії**

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Якщо ви знаходитесь в Україні, вам може захотіться звернутися до авторику О.Г. Пузанова з питаннями або відкриттями в частині ревматичного заболевання. Її робота відображає сучасність і наукову діяльність, яка важлива для здійснення як клінічних, так і наукових досліджень у области ревматології.

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Ревматическая полимиалгия в клинических рекомендациях 2018–2020 годов. Часть I. Группа риска, адъювантная терапия

Резюме. В начале Декады здорового старения стал доступен ряд клинических рекомендаций по ведению ревматических болезней у пожилых. Цель публикации — характеристика и обсуждение руководства по ревматической полимиалгии Итальянского общества ревматологов (2020) и рекомендаций по применению позитронно-эмиссионной томографии/компьютерной томографии при васкулитах крупных сосудов и ревматической полимиалгии Европейской ассоциации ядерной медицины, Общества ядерной медицины и молекулярной визуализации и Американского общества ядерной кардиологии (2018).

Материалы и методы. Содержание, первоисточники и методология разработки руководств изучены с помощью методов информационного анализа и сопоставлены с рекомендациями 2018–2020 гг. по ревматической полимиалгии и гигантоклеточному артериту Европейской антиревматической лиги, Американской коллегии ревматологов, Немецкого, Австрийского, Швейцарского, Британского обществ ревматологов, Европейской общественности ядерной медицины.

Решение такой актуальной проблемы здравоохранения, как повышение качества медицинской помощи при ревматической полимиалгии, предполагает усовершенствование медицинских стандартов по большинству клинически важных вопросов, выявление пациентов высокого риска, направление их к ревматологам и офтальмологам и рассмотрение преимуществ лечения метотрексатом.

Ключевые слова: ревматическая полимиалгия; гигантоклеточный артерит; осложнения; диагностика; лечение; метотрексат; стандарты; обзор