Dejaco, C; Duftner, C; Cimmino, MA; Dasgupta, B; Salvarani, C; Crowson, CS; Maradit-Kremers, H; Hutchings, A; Matteson, EL; Schirmer, M (2011) Definition of remission and relapse in polymyalgia rheumatica: data from a literature search compared with a Delphi-based expert consensus. Annals of the rheumatic diseases, 70 (3). pp. 447-453. ISSN 0003-4967 DOI: https://doi.org/10.1136/ard.2010.133850

Downloaded from: http://researchonline.lshtm.ac.uk/1106/

DOI: 10.1136/ard.2010.133850

Usage Guidelines

Please refer to usage guidelines at http://researchonline.lshtm.ac.uk/policies.html or alternatively contact researchonline@lshtm.ac.uk.

Available under license: Creative Commons Attribution Non-commercial http://creativecommons.org/licenses/by-nc/3.0/
Definition of remission and relapse in polymyalgia rheumatica: data from a literature search compared with a Delphi-based expert consensus

Christian Dejaco,¹ Christine Duftner,²,³ Marco A Cimmino,⁴ Bhaskar Dasgupta,⁵ Carlo Salvarani,⁶ Cynthia S Crowson,⁷ Hilai Maradit-Kremers,⁷ Andrew Hutchings,⁸ Eric L Matteson,⁷ Michael Schirmer,³ and members of the International Work Group for immune-mediated diseases. ⁷ – ¹⁰ However, there is no absolute definition of ‘remission’ and ‘relapse’ in PMR, with disparate use of criteria used to define these disease states in PMR treatment studies to date.

New definitions of remission and relapse have been proposed by Leeb et al.¹¹ and Binard et al.¹² respectively. Both definitions were based on the PMR activity score (PMR-AS), which was developed using predefined parameters and was not subject to a consensus finding process including a systematic literature review.¹³ ¹⁴ The validity of the PMR-AS has been supported in a number of studies.¹¹ ¹² ¹⁵ ¹⁶

This paper presents the results from a Delphi-based consensus survey involving rheumatologists (RMs) and general practitioners (GPs) identifying candidate items for new definitions of remission and relapse. We compared these parameters with currently available remission and relapse definitions retrieved from a systematic literature review.

METHODS

Literature search
A literature search was conducted in PubMed, Medline (from January 1966 to November 2003, updated June 2009), using the items ‘Polymyalgia rheumatica’, ‘PMR’, ‘Giant cell arteritis’, ‘Polymyalgia rheumatica AND Remission’ and ‘Polymyalgia rheumatica AND Relapse’ as keywords. Only studies written in English were included. All studies were screened for definitions of remission and/or relapse of PMR and parameters used to define these conditions in PMR.

Delphi exercise
We used a two-step Delphi process. Firstly, we generated a questionnaire with candidate items for definitions of remission and relapse of PMR as retrieved in a literature search. The final questionnaire included 94 items categorised into ‘history’ (n=19), ‘physical examination’ (n=14), ‘laboratory findings’ (n=54) and ‘imagining methods’ (n=7). One questionnaire each was used to assess the definition of remission on treatment medication (reflecting short-term response to corticosteroids), remission of ‘remission’ and ‘relapse’ in PMR, with disparate use of criteria used to define these disease states in PMR treatment studies to date.

New definitions of remission and relapse have been proposed by Leeb et al.¹¹ and Binard et al.¹² respectively. Both definitions were based on the PMR activity score (PMR-AS), which was developed using predefined parameters and was not subject to a consensus finding process including a systematic literature review.¹³ ¹⁴ The validity of the PMR-AS has been supported in a number of studies.¹¹ ¹² ¹⁵ ¹⁶

This paper presents the results from a Delphi-based consensus survey involving rheumatologists (RMs) and general practitioners (GPs) identifying candidate items for new definitions of remission and relapse. We compared these parameters with currently available remission and relapse definitions retrieved from a systematic literature review.

INTRODUCTION

Polymyalgia rheumatica (PMR) is a common disease in older people conventionally treated with long-term oral corticosteroids.¹ – ⁶

As corticosteroid treatment leads to rapid improvement in symptoms and returns patients to pre-morbid functional status, interventional studies in PMR usually focus on parameters such as ‘complete remission’ or ‘time in remission to relapse’, rather than on partial response criteria used in other immune-mediated diseases.⁷ – ¹⁰ However, there is still considerable uncertainty related to definitions...
importance (‘essential’, ‘less important’ or ‘not important’) and availability/practicability (‘routinely available/practicable’, ‘not always available/difficult to perform’ or ‘not available/practicable’) of diagnostic tools. Availability of diagnostic tools was examined in this round only. Experts were encouraged to add further candidate criteria to be considered for assessment and relevant comments. In addition, experts were asked to suggest cut-off points for the proposed quantitative candidate criteria items based on data from the literature review. Questionnaires were distributed to all experts via mail or e-mail. Experts were contacted by telephone and/or reminders were sent to encourage participation and return of questionnaires.

The questionnaire used in the second round was derived from that of the first round using results from the first round. Parameters considered ‘not available’ or ‘not important’ by ≥50% or ‘essential’ by <20% of experts were excluded. Items regarded as essential by ≥80% of experts for the definition of remission and/or relapse were accepted as consensus items and not further assessed. First-round results of the remaining parameters were illustrated to the experts by pie diagrams. Then, experts were asked to re-evaluate the parameters either as ‘important’ or ‘not important’ to the definition of remission and/or relapse of PMR. In addition, experts were encouraged to choose a limit for quantitative items among those proposed in the first round. All written comments were attached anonymously.

As first-round analysis of questionnaires for remission ‘on medication’ and ‘off medication’ showed almost perfect agreement, no separate assessment for remission ‘on medication’ and ‘off medication’ was performed in the second round. Only the parameter ‘patient’s assessment of pain related to neck, upper arms, shoulders and pelvic girdle by a visual analogue scale (VAS)’ revealing some disagreement was reassessed.

Experts
We invited 25 RMs from Europe (Italy (n=6), Sweden (n=1), UK (n=2), France (n=1), Austria (n=3), Spain (n=2), Germany (n=3)), Israel (n=1) and the USA (n=6) experienced in treatment and assessment, history of transient visual symptoms, fever and oedema), peripheral arthritis, patient’s and physician’s global assessment, history of transient visual symptoms, fever and physician’s pain assessment were important for >50% of RMs in the first questionnaire round and rated in the second round. After the first questionnaire round, 64 out of 94 parameters were considered ‘not important’ for defining remission, and 65/94 were considered ‘not important’ for defining relapse by the majority of RMs. The 64 parameters for remission included 6/19 from the category history, 2/14 from physical examination, 50/54 from laboratory findings, and 6/7 from imaging methods. The 65 parameters considered not important for defining relapse included 7/19 from history, 2/14 from physical examination, 50/54 from laboratory findings, and 6/7 from imaging methods.

Questionnaires related to remission ‘on medication’ and ‘off medication’ showed very high agreement (κ 0.93). Data from both questionnaires led to exclusion or consensus on the same parameters except for the parameter ‘patient’s assessment of pain related to neck, upper arms, shoulders and pelvic girdle by a VAS’, which was considered to be essential by 81.8% of RMs for ‘remission on medication’ (=consensus), and by 79.2% for ‘remission off medication’.

Availability of items for definitions of remission and relapse
Of 94 parameters from the literature, 29 were considered as routinely available/practicable by more than 80% of RMs (10/19 parameters out of the category history, 12/14 out of clinical examination, 7/54 out of laboratory findings, and 0/7 out of imaging methods) (see online supplementary tables 1a and 2a for detailed results).

Eight parameters (all blood tests for cytokines or cytokine receptors) were considered to be not available.

Results of the second questionnaire round
Tables 4 (remission) and 5 (relapse) depict those items for which RMs achieved a consensus following the two Delphi rounds. The limits for metric parameters were proposed in the first questionnaire round and rated in the second round.

Assessment of symmetric synovitis with peripheral oedema as seen in RS,PE (remitting seronegative syndrome with pitting oedema), peripheral arthritis, patient’s and physician’s global assessment, history of transient visual symptoms, fever and physician’s pain assessment were important for >50% of RMs in defining remission and relapse in both questionnaire rounds but did not reach consensus level (see online supplementary table 3a for detailed results).

Comparison of parameters resulting from Delphi exercise with previous definitions of remission and relapse of PMR
Previous definitions of remission and relapse not based on PMR-AS included the parameters patient’s assessment of pain parameters out of the category history, 12/14 out of physical examination, 50/54 from laboratory findings, and 6/7 from imaging methods.

The 64 parameters for remission included 6/19 from history, 2/14 from physical examination, 50/54 from laboratory findings, and 6/7 from imaging methods. The omission of data from GPs did not significantly alter the results of the Delphi exercise. Pooled data for RMs and GPs are shown in online supplementary tables 1b, 2b, 3b and 4.

Table 1 Definitions of remission and relapse based on the polymyalgia rheumatica activity score (PMR-AS) by Leeb and Bird

| PMR-AS = CRP (mg/dl) + patient’s pain assessment (VAS 0–10) + physician’s global assessment (VAS 0–10) + (morning stiffness (min) × 0.1) + EUL (0–3) |
|---|---|
| Remission | 0–1.5 |
| Relapse | >3.95 or a ΔPMR-AS score >6.6 |

CRP, C-reactive protein; EUL, ability to elevate the upper limbs; VAS, visual analogue scale.

Owing to the low response rate from GPs, we restricted our final analyses of both questionnaire rounds to results derived from RMs. The omission of data from GPs did not significantly alter the results of the Delphi exercise. Pooled data for RMs and GPs are shown in online supplementary tables 1b, 2b, 3b and 4.

Results of the first questionnaire round
After the first questionnaire round, 64 out of 94 parameters were considered ‘not important’ for the definition of remission, and 65/94 were considered ‘not important’ for defining relapse by the majority of RMs. The 64 parameters for remission included 6/19 from the category history, 2/14 from physical examination, 50/54 from laboratory findings, and 6/7 from imaging methods. The 65 parameters considered not important for defining relapse included 7/19 from history, 2/14 from physical examination, 50/54 from laboratory findings, and 6/7 from imaging methods.

Questionnaires related to remission ‘on medication’ and ‘off medication’ showed very high agreement (κ 0.93). Data from both questionnaires led to exclusion or consensus on the same parameters except for the parameter ‘patient’s assessment of pain related to neck, upper arms, shoulders and pelvic girdle by a VAS’, which was considered to be essential by 81.8% of RMs for ‘remission on medication’ (=consensus), and by 79.2% for ‘remission off medication’.
Table 2 Definitions of remission of polymyalgia rheumatica from the published literature

<table>
<thead>
<tr>
<th>Reference</th>
<th>History</th>
<th>Clinical examination</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behn et al(^{29})</td>
<td>ACS</td>
<td>–</td>
<td>&lt;30 – – – –</td>
</tr>
<tr>
<td>Cantini et al(^{27})</td>
<td>ACS</td>
<td>–</td>
<td>&lt;40 &lt;0.5 &lt;0.5 &lt;0.5 &lt;0.5</td>
</tr>
<tr>
<td>Catanoso et al(^{9})</td>
<td>Absence of systemic symptoms (fever, malaise, anorexia, weight loss), MS, girdles and neck pain and peripheral synovitis</td>
<td>–</td>
<td>Normal laboratory findings</td>
</tr>
<tr>
<td>Chuang et al(^{41})</td>
<td>ACS</td>
<td>–</td>
<td>&lt;20 – Hb &gt;12 g/dl</td>
</tr>
<tr>
<td>Dasgupta et al(^{42})</td>
<td>≥50% pain reduction (VAS) MS &lt;30 min</td>
<td>–</td>
<td>≤1.0 ≤1.0 ≤1.0 ≤1.0 ≤1.0</td>
</tr>
<tr>
<td>Delecroix et al(^{44})</td>
<td>ACS</td>
<td>Absence of pain on examination</td>
<td>NV – – – –</td>
</tr>
<tr>
<td>Huchings et al(^{46})</td>
<td>Absence of myalgia</td>
<td>–</td>
<td>NV NV</td>
</tr>
<tr>
<td>Kremer et al(^{11,34,35})</td>
<td>ACS</td>
<td>–</td>
<td>NV – – – – CS ≤5 mg/day</td>
</tr>
<tr>
<td>Krosgaard et al(^{17})</td>
<td>No muscular pain, no MS</td>
<td>No muscular tenderness</td>
<td>NV – – NV – – – –</td>
</tr>
<tr>
<td>Martinez-Taboada et al(^{48})</td>
<td>ACS</td>
<td>–</td>
<td>NV – – NV – – Lowest CS possible</td>
</tr>
<tr>
<td>Mertens et al(^{49})</td>
<td>ACS</td>
<td>–</td>
<td>– – – –</td>
</tr>
<tr>
<td>Proven et al(^{45})</td>
<td>ACS</td>
<td>–</td>
<td>– – – –</td>
</tr>
<tr>
<td>Salvadori et al(^{56})</td>
<td>ACS</td>
<td>≤30</td>
<td>– – – –</td>
</tr>
<tr>
<td>Salvadori et al(^{48})</td>
<td>ACS</td>
<td>≤30 &lt;0.5</td>
<td>– – – –</td>
</tr>
<tr>
<td>Van der Veen et al(^{60})</td>
<td>ACS</td>
<td>–</td>
<td>– – – –</td>
</tr>
<tr>
<td>(^{1})The upper limit of normal is 0.5 mg/dl; for the other studies, no upper limit of normal CRP levels was reported.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACS, absence of clinical symptoms (not further specified); CRP, C-reactive protein; CS, corticosteroid dose; ESR, erythrocyte sedimentation rate; Hb, haemoglobin; MS, morning stiffness; NV, normal values; VAS, measured on a visual analogue scale ranging from 0 (best) to 10 (worst) cm.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(29.4% and 21.2%, respectively), MS (23.5% and 21.2%, respectively), ESR (70.6% and 60.6%, respectively), CRP (29.4% and 30.3%, respectively) and shoulder pain/limitation on clinical examination (11.8% and 0%, respectively); and these parameters also reached consensus level in the Delphi exercise and are included in the PMR-AS (ESR may be used instead of CRP according to the original work by Leeb et al\(^{13,14}\)). Physician’s global assessment is part of the PMR-AS, but did not achieve consensus level in the Delphi exercise and was not included in the PMR-AS. In addition, we observed a high relevance (>50% agreement) of peripheral manifestations and fever compared with previous literature. Hips are involved in 50–70% of patients with PMR, and peripheral or constitutional symptoms occur in 30–50%. Assessment of these clinical features with incorporation into definitions of remission and relapse may lead to higher specificity and sensitivity of these definitions and possibly allow improved classification of those 10–50% of patients who lack shoulder symptoms. Clear improvement in, or flare of, PMR using clinical symptoms such as pain or MS was considered to be important by experts in the present survey. These parameters are included in the PMR-AS, and most proposed remission and/or relapse definitions in the current literature. However, this international PMR/GCA study group recently questioned the value of MS, as patients and clinicians may not reliably distinguish between pain and stiffness. A major concern is that pain-related items may lack specificity given the high prevalence of osteoarthritis and degenerative pain in older people. The occurrence of unilateral versus bilateral pain may be useful in this regard; however, a prospective study is needed to clarify the true value of pain and stiffness in defining remission and relapse in PMR.

DISCUSSION

This international Delphi survey among RM experts corroborated some previously proposed items for the definition of PMR remission and relapse including patient’s assessment of pain, MS, ESR, CRP, shoulder pain/limitation on clinical examination, and corticosteroid dose required to control symptoms. Many other items, such as determination of haemoglobin and fibrinogen, were considered to have little value for this purpose.

The consensus on hip involvement was unexpected, as this parameter was only considered in 2/17 and 4/33 previous studies with definitions of remission and relapse, respectively, and was not included in the PMR-AS. In addition, we observed a high relevance (>50% agreement) of peripheral manifestations and fever compared with previous literature. Hips are involved in 50–70% of patients with PMR, and peripheral or constitutional symptoms occur in 30–50%. Assessment of these clinical features with incorporation into definitions of remission and relapse may lead to higher specificity and sensitivity of these definitions and possibly allow improved classification of those 10–50% of patients who lack shoulder symptoms.

Clear improvement in, or flare of, PMR using clinical symptoms such as pain or MS was considered to be important by experts in the present survey. These parameters are included in the PMR-AS, and most proposed remission and/or relapse definitions in the current literature. However, this international PMR/GCA study group recently questioned the value of MS, as patients and clinicians may not reliably distinguish between pain and stiffness. A major concern is that pain-related items may lack specificity given the high prevalence of osteoarthritis and degenerative pain in older people. The occurrence of unilateral versus bilateral pain may be useful in this regard; however, a prospective study is needed to clarify the true value of pain and stiffness in defining remission and relapse in PMR.

The biometric limits for clinical items (eg, duration of MS) chosen by experts in the present survey were comparable to those available from a literature search and the PMR-AS. In the present Delphi survey and previous definitions of remission and relapse, cut-off values were preferred to relative changes in the parameters during follow-up. A relevant consideration in this regard is that all such measures should be zero for a PMR patient in remission. However, many older patients with arthritic/rheumatic conditions rarely consider themselves to be completely free from pain and stiffness. Therefore, several
PMR studies define remission pragmatically as absence of relapse or as duration of relapse-free survival, accepting higher (non-zero) biometric limits for patients in remission. This strategy for defining remission has the advantage of a high sensitivity, classifying all patients with PMR as either in remission or relapse. In contrast, developing separate remission and relapse criteria results in a high specificity of classification, but suggests an additional (yet undefined) disease state that is neither remission nor relapse. Sensitivity and specificity of such definitions may differ, if relevant parameters are used as a qualitative set of criteria or a composite score, such as the PMR-AS. In rheumatoid arthritis and other rheumatic diseases, composite scores are usually preferred, whereas most treatment studies in PMR to date have used qualitative sets of criteria. The question of which approach is more useful for daily clinical practice and outcome studies remains to be addressed by future studies.

In this Delphi exercise, both ESR and CRP were assumed to be routinely available and to be the most promising laboratory items for defining both remission and relapse. While CRP is a component of the PMR-AS, other published studies have preferentially used a normal ESR as a component of their remission definition. Persistently raised CRP has been suggested to correlate better with inflammation in PMR than ESR and may thus be better suited for use in definitions of remission and relapse. An important limitation of CRP and ESR is that these values have been observed in up to 27% and 14% of relapses, respectively, despite the increase in these parameters at the time of diagnosis. Indeed, normal ESR or CRP values have been observed in up to 27% and 14% of relapses, respectively, despite the increase in these parameters at the time of diagnosis.

A flare of PMR symptoms may occur in the absence of abnormal inflammatory parameters, although degenerative pain with stiffness may also mimic a flare of the disease.
A relapse of PMR can be defined even with normal CRP and/or ESR using the PMR-AS and definitions from 22 of the 33 other studies from the literature search. Notably, the PMR-EULAR response criteria that provide the basis for the PMR-AS were developed in a cohort of PMR patients who all had raised ESR and/or CRP but were not specified by RMs in the Delphi survey. Corticosteroid dose of zero defines the case of remission off medication (ie, when the patient stopped taking corticosteroids).

The corresponding proposals for limits of metric parameters and the agreement to these limits are given.

The other laboratory parameters evaluated, including blood count, markers of vascular damage/activation, hormones and cytokines/receptors, were considered less important in evaluating relapse and remission at this point in time.

Corticosteroids are the mainstay of treatment for PMR, although the optimal initial dose and tapering regimen are matters of ongoing debate.\textsuperscript{1, 30–32} Assessment of corticosteroid dose may be important to the definition of remission. A related consideration is that physicians and patients may be unwilling to accept the status of ‘remission’ if achieved at the expense of serious impairment of the patient’s general well-being due to side effects of unacceptably high corticosteroid doses.\textsuperscript{11} Maintaining a treatment-free complete clinical response after stopping treatment remains the clinical goal, which is not always achievable in PMR.\textsuperscript{11, 35}

In the present survey, >80% of experts were of the opinion that corticosteroid doses should be included in any definition of remission in PMR. While agreeing that the corticosteroid dose ‘should be as low as possible’, a specified dose limit was not agreed upon. A prospective study would be needed to clarify whether the assessment of corticosteroid doses improves the specificity of a definition of remission.

**Table 4** Parameters considered as ‘important’ for defining remission of polymyalgia rheumatica by at least 80% of rheumatologists (RMGs)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Limits</th>
<th>Agreement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning stiffness\textsuperscript{*}</td>
<td>&lt;15 min</td>
<td>94.7</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate\textsuperscript{*}</td>
<td>&lt;20 mm/1st h</td>
<td>57.9</td>
</tr>
<tr>
<td>C-reactive protein\textsuperscript{*}</td>
<td>&lt;0.5 mg/dl</td>
<td>68.4</td>
</tr>
<tr>
<td>Patient’s assessment of pain related to neck, upper arms, shoulders and pelvic girdle (VAS)</td>
<td>&lt;10 mm</td>
<td>58.8</td>
</tr>
<tr>
<td>Corticosteroid dose required to control symptoms\textsuperscript{*}</td>
<td>Limit not specified\textsuperscript{†}</td>
<td>Qualitative item</td>
</tr>
<tr>
<td>Shoulder-pain worsened by passive and active mobilisation</td>
<td>Qualitative item</td>
<td></td>
</tr>
<tr>
<td>Limitation of upper limb elevation</td>
<td>Qualitative item</td>
<td></td>
</tr>
<tr>
<td>Clinical signs of coxofemoral synovitis\textsuperscript{‡}</td>
<td>Qualitative item</td>
<td></td>
</tr>
</tbody>
</table>

The corresponding proposals for limits of metric parameters and the agreement to these limits are given.

\textsuperscript{*}Consensus on this parameter was already obtained in the first Delphi round.

\textsuperscript{†}Upper limit of a normal C-reactive protein value is 0.5 mg/dl.

\textsuperscript{‡}Coxofemoral synovitis is suggested if the patient complains about pain in the groin worsened by passive and active movements on clinical examination.

VAS, visual analogue scale with 0=no pain, 10=unbearable pain on a 10 cm scale.

**Table 5** Parameters considered as ‘important’ to define relapse of polymyalgia rheumatica by at least 80% of rheumatologists (RMGs)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Limits</th>
<th>Agreement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning stiffness\textsuperscript{*}</td>
<td>&gt;30 min</td>
<td>94.7</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate\textsuperscript{*}</td>
<td>&gt;40 mm/1st h</td>
<td>57.9</td>
</tr>
<tr>
<td>C-reactive protein\textsuperscript{*}</td>
<td>&gt;1.0 mg/dl</td>
<td>52.6</td>
</tr>
<tr>
<td>Patient’s assessment of pain related to neck, upper arms, shoulders and pelvic girdle (VAS)\textsuperscript{*}</td>
<td>&gt;20 mm</td>
<td>93.8</td>
</tr>
<tr>
<td>Corticosteroid dose required to control symptoms\textsuperscript{*}</td>
<td>Any dose</td>
<td>62.4</td>
</tr>
<tr>
<td>Shoulder pain worsened by passive and active mobilisation</td>
<td>Qualitative item</td>
<td></td>
</tr>
<tr>
<td>Limitation of upper limb elevation</td>
<td>Qualitative item</td>
<td></td>
</tr>
<tr>
<td>Clinical sign of coxofemoral synovitis\textsuperscript{‡}</td>
<td>Qualitative item</td>
<td></td>
</tr>
</tbody>
</table>

The corresponding proposals for a limit of metric parameters and the agreement to these limits are given.

\textsuperscript{*}Consensus on this parameter was already obtained in the first Delphi round.

\textsuperscript{‡}Coxofemoral synovitis is suggested if the patient complains about pain in the groin worsened by passive and active movements on clinical examination.

VAS, visual analogue scale with 0=no pain, 10=unbearable pain on a 10 cm scale.
The majority of experts thought that the need for any increment in corticosteroid dose necessary to control PMR symptoms should be included in the criteria for defining relapse. This result is in accordance with 20 studies from our literature search, which considered a flare of PMR symptoms to be a relapse if symptoms respond to an increased dose of corticosteroid.

To address possible differences related to useful parameters for assessing short-term (ie, remission when the patient is taking corticosteroids) and long-term (ie, remission after treatment withdrawal) outcomes in PMR, we used different questionnaires to define remission ‘on medication’ and ‘off medication’. The ratings of the two questionnaires showed almost perfect agreement, indicating that the same clinical parameters may be useful for defining both states of remission. However, we did not address the role of time with respect to remission, as has been reported previously.\textsuperscript{30} 31 34–37 The time in remission after withdrawal of treatment is of particular interest in distinguishing patients in ‘permanent’ remission or at low risk of relapse from those at high risk of relapse.\textsuperscript{30} 31 34–37 This issue remains to be clarified.

We invited 50 experts to participate in this Delphi exercise, recognising that no optimal number of experts for such a study exists. The reliability of results may decline rapidly with fewer than six panel members, whereas improvements in reliability are relatively small in groups larger than 15.\textsuperscript{38} 40 There is also no definition of an ‘expert’ status for a Delphi study, but, as PMR is diagnosed by RMs and GPs, we sought to consider opinions of both groups of physicians. A survey among French GPs revealed that only 36% of GPs routinely refer PMR patients to a RM for diagnosis of the disease and that only 20% of these GPs take advice from RMs for routine follow-up of PMR patients.\textsuperscript{15} Therefore we asked participating RMs to recommend one GP each in order to involve an international group of GPs with adequate experience in rheumatology. Only nine and three GPs responded to the first and second questionnaire rounds, respectively, despite recurrent telephone contacts and/or written reminders. The low response rate for GPs limits the validity of their responses, and therefore we restricted our final analysis to data derived from RMs. The omission of data from GPs, however, did not significantly alter the results.

The two rounds of questionnaires resulted in a quite limited number of parameters being accepted by the majority of experts. Many others did not achieve the predefined level of consensus. It is possible that another round addressing at least some of these items further may have resulted in them being classified as consensus items or as not important. Further rounds of questionnaires were not pursued, in part because of concern that respondent fatigue might seriously erode the value of the exercise.

The items that emerged from this Delphi-based expert consensus as important for defining relapse and remission in patients with PMR were patient’s assessment of pain related to neck, upper arms, shoulders and pelvic girdle, MS, ESR, CRP, shoulder pain/limitation on clinical examination, and corticosteroid dose. Clinical assessment of the hips turned out to be important in this survey and may further improve specificity and sensitivity of defining remission and relapse in PMR. The operating characteristics and value of the remission and relapse items derived in this exercise will require prospective evaluation.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES


APPENDIX

Participating rheumatologists of the Delphi survey and members of the International Work Group for PMR and GCA:

Kenneth Calamia, Division of Rheumatology, Mayo Clinic College of Medicine, Jacksonville, FL, USA; Roberto Caporali, University of Pavia, IRCCS S Matteo Foundation, Pavia, Italy; Marco A. Cimmino, Department of Internal Medicine, University of Genova, Genova, Italy; Bhaskar Dasgupta, Department of Rheumatology, Southend University Hospital, Essex, United Kingdom; William Docken, Brigham Orthopedics and Arthritis Center, Chestnut Hill, MA, USA; Pierre Duhaut, Department of Internal Medicine, CHU Nord, Amiens, France; Miguel A Gonzalez-Gay, Division of Rheumatology, Hospital Xeral-Calde, Lugo, Spain; Roberto Gerli, Rheumatology Unit, Department of Clinical & Experimental Medicine, University of Perugia, Perugia, Italy; Manfred Herold, Department of Internal Medicine I, Innsbruck Medical University, Innsbruck, Austria; Gery S. Hoffman, Department of Rheumatic and Immunologic Diseases, Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA; Eugene Kissin, Boston University Medical Center, Boston, MA, USA; Peter Lamprecht, Department of Rheumatology, Vascularitis Center UKSH & Clinical Center Bad Bramstedt, University of Lübeck, Lübeck, Germany; Burkhard Leeb, Lower Austrian Center for Rheumatology, Stockerau, Austria; Pierluigi Macchioni, Department of Rheumatology, Arcispedale Santa Maria Novua, Reggio Emilia, Italy; Victor Martinez-Taboada, Division of Rheumatology, Hospital Marques de Valdecilla, Santander, Spain; Eric L. Matteson, Division of Rheumatology, Mayo Clinic, Rochester, MN, USA; Peter A Merkel, Division of Rheumatology, Boston University, Boston, MA, USA; Carlo M. Montecucco, University of Pavia, IRCCS S Matteo Foundation, Pavia, Italy; Gideon Nesher, Department of Internal Medicine, Shear Zedek Medical Center, Jerusalem, Israel; Elisabeth Nordborg, Institute of Rheumatology, Huddinge University Hospital, Stockholm, Sweden; Colín Pease, Rheumatology and Rehabilitation Research Unit, University of Leeds, Leeds, UK; Carlo Salvareni, Department of Rheumatology, Arcispedale S. Maria Nuova, Reggio Emilia, Italy; Michael Schirmer, Department of Internal Medicine I, Innsbruck Medical University, Innsbruck, Austria; Wolfgang Schmidt, Department of Rheumatology, Berlin-Buch, University of Berlin, Berlin, Germany; Roberto Spierra, Beth Israel Medical Center, New York, NY, USA; Annette Wagner, Department of Rheumatology, University of Hannover, Hannover, Germany.
Definition of remission and relapse in polymyalgia rheumatica: data from a literature search compared with a Delphi-based expert consensus

Christian Dejaco, Christina Duttnner, Marco A Cimmino, Bhaskar Dasgupta, Carlo Salvarani, Cynthia S Crowson, Hilal Maradit-Kremers, Andrew Hutchings, Eric L Matteson, Michael Schirmer and members of the International Work Group for PMR and GCA

Ann Rheum Dis 2011 70: 447-453 originally published online November 19, 2010
doi: 10.1136/ard.2010.133850

Updated information and services can be found at:
http://ard.bmj.com/content/70/3/447

These include:

- Supplementary Material
  Supplementary material can be found at:
  http://ard.bmj.com/content/suppl/2010/10/21/ard.2010.133850.DC1

- References
  This article cites 60 articles, 15 of which you can access for free at:
  http://ard.bmj.com/content/70/3/447#ref-list-1

- Open Access
  This paper is freely available online under the BMJ Journals unlocked scheme, see http://ard.bmj.com/info/unlocked.dtl

- Email alerting service
  Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Articles on similar topics can be found in the following collections

- Open access (672)
- Connective tissue disease (4253)
- Musculoskeletal syndromes (4951)
- Pain (neurology) (883)
- Degenerative joint disease (4641)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/