ROAD (mean 4.3 vs. 3.0; F-ratio 17.37; p < 0.001) and higher Kihon score (mean 9.1 vs. 5.7; F-ratio 29.88; p < 0.001).

Conclusion: CS is strongly related to patient-reported disease activity, functional disability and frailty in patients with RA independently from other patient-and disease-related aspects. CS is an important determinant of functional disability in patients with chronic inflammatory arthritides. Therefore, special attention should be paid to RA patients, in whom the concomitant diagnosis of CS should be routinely ruled out.

REFERENCES:

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Precision medicine in SLE: where are we?

OP0013
APPLYING STANDARD CLASSIFICATION CRITERIA EXCLUDES UP TO A HALF OF ALL PATIENTS FROM CONNECTIVE TISSUE DISEASES (CTD) CLINICAL TRIALS

Keywords: Sjögren syndrome, Systemic sclerosis, Systemic lupus erythematosus
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Background: Classification criteria aim to identify a homogeneous population of patients with a high specificity for clinical research.

Objectives: To determine how connective tissue disease (CTD) phase III trials utilise classification criteria within their inclusion and exclusion criteria. We then applied the most commonly used classification criteria to a large cohort of patients with an existing CTD diagnosis to explore which patients would be included and excluded from trials.

Methods: A comprehensive review of all major published phase III trials in CTDs was performed using clinicaltrials.gov (Nov 22). We included trials of biological or DMARD therapy, and excluded open label trials and long-term extensions. Adult patients (May 14 - July 22) were recruited from five rheumatology centres in North West England into the LEAP cohort. Patients were eligible for inclusion if they had ≥1 clinical feature of a CTD and ≥1 antibody within the AANA spectrum. The (rheumatologist) diagnostic time at recruitment was used as the primary classifier of patients. Classification criteria utilised in the majority of clinical trials were systematically applied to this cohort, irrespective of clinical diagnosis.

Results: There were 49 trials in CTDs identified from 1909 records: systemic lupus erythematosus (SLE)=29, systemic sclerosis (SSc)=7, idiopathic inflammatory myopathy (IIM)=7 and primary Sjögren’s syndrome (pSS)=6. There were no trials in MCTD or UCTD. The majority of trials (N=47, 95.9%) required patients to meet classification criteria for their respective disease. The ACR-1997 for SLE, 2002 American European Consensus Criteria (AECG) criteria for pSS, ACR criteria for SSc 1980, and Bohan and Peter for IIM were the most commonly employed criteria. The majority of pSS (N=5=83.3%) and SSc (N=4=57.1%) trials excluded patients with other overlapping CTDs, whereas only a minority of IIM (N=1, 14.3%) and SLE (N=2, 6.9%) trials mandated this. A further 2 (28.6%) IIM and 2 (6.9%) SLE trials excluded CTD patients with specific overlapping features, e.g. SSc with significant pulmonary hypertension. 15 trials (30.6%) allowed exclusion of significant coexisting diseases at the investigators’ discretion and 18 (36.7%) made no reference. 391 patients were recruited to the LEAP cohort (Female: 352 [90.0%], median [IQR] age: 52 [40-59] years, median [IQR] disease duration: 6.1 [2.9-13.2] years). 254 (65.0%) patients met classification criteria for at least one CTD (Table 1). 222 (74.0%) patients with pSS, SLE, SSc or IIM, met the classification criteria for their respective diagnosis. Of these, 26/222 (6.7%) met criteria for >1 CTD. In total, 196/391 (50.1%) would be eligible, 195/391 (49.9%) ineligible for recruitment to a phase III trial, based upon their physician diagnosis, and trial eligibility criteria. Patients eligible to participate were similar in age (p=0.822), gender (p=0.607) and ethnic background (p=0.822) but had longer median disease duration (7.5 vs 5.2 years, p=0.024) to those ineligible.

Table 1. The proportion of patients meeting classification criteria utilised in clinical trials, by physician diagnosis

<table>
<thead>
<tr>
<th>SLE</th>
<th>pSS</th>
<th>UCTD</th>
<th>SSc</th>
<th>MCTD</th>
<th>IIM</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=164</td>
<td>N=77</td>
<td>N=61</td>
<td>N=37</td>
<td>N=30</td>
<td>N=22</td>
<td>N=391</td>
</tr>
<tr>
<td>Bohan and Peter for IIM</td>
<td>2 (1.2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>3 (8.1)</td>
<td>2 (6.7)</td>
<td>9 (40.9)</td>
</tr>
<tr>
<td>ACR/EULAR Systemic sclerosis 2013</td>
<td>1 (0.6)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>30 (81.1)</td>
<td>8 (26.7)</td>
<td>4 (18.2)</td>
</tr>
<tr>
<td>AECG Sjögren’s</td>
<td>10 (6.1)</td>
<td>45 (58.4)</td>
<td>0 (0)</td>
<td>1 (3.3)</td>
<td>1 (4.5)</td>
<td>57 (14.6)</td>
</tr>
<tr>
<td>ACR SLE 1997</td>
<td>138 (84.1)</td>
<td>14 (82.3)</td>
<td>0 (0)</td>
<td>2 (5.4)</td>
<td>14 (46.7)</td>
<td>5 (22.7)</td>
</tr>
</tbody>
</table>

Conclusion: Clinical trial recruitment is challenging, in part due to due to stringent eligibility criteria. In an unselected, real-world cohort of CTD patients, up to a half would be excluded due to classification criteria, overlapping features or a lack of trials within their disease. Directly targeting molecular pathology in biomarker driven basket trials could potentially revolutionise drug development by benefitting those with an undifferentiated or overlap condition who would be traditionally excluded from clinical trials.

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