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ABSTRACT

Objectives To validate the previously proposed classification criteria for Henoch–Schönlein purpura (HSP), childhood polyarteritis nodosa (c-PAN), c-Wegener granulomatosis (c-WG) and c-Takayasu arteritis (c-TA).

Methods Step 1: retrospective/prospective web-data collection for 827 children with HSP, c-PAN, c-WG and c-TA with age at diagnosis ≤20 years. Step 2: blinded classification by consensus panel of a representative sample of 280 cases. Step 3: statistical (sensitivity, specificity, area under the curve and κ-agreement) and nominal group technique consensus evaluations.

Results 827 patients with HSP, 150 with c-PAN, 60 with c-WG, 87 with c-TA and 52 with c-other were compared with each other. A patient was classified as HSP in the presence of purpura or petechiae (mandatory) with lower limb predominance plus one of four criteria: (1) abdominal pain; (2) histopathology (IgA); (3) arthritis or arthralgia; (4) renal involvement. Classification of c-PAN required a systemic inflammatory disease with evidence of necrotising vasculitis OR angiographic abnormalities of medium-/small-sized arteries (mandatory criterion) plus one of five criteria: (1) skin involvement; (2) myalgia/muscle tenderness; (3) hypertension; (4) peripheral neuropathy; (5) renal involvement. Classification of c-WG required three of six criteria: (1) histopathological evidence of granulomatous inflammation; (2) upper airway involvement; (3) laryngo-tracheo-brachial involvement; (4) pulmonary involvement (x-ray/CT); (5) antineutrophilic cytoplasmic antibody positivity; (6) renal involvement. Classification of c-TA required typical angiographic abnormalities of the aorta or its main branches and pulmonary arteries (mandatory criterion) plus one of five criteria: (1) pulse deficit or claudication; (2) blood pressure discrepancy in any limb; (3) bruits; (4) hypertension; (5) elevated acute phase reactant.

Conclusion European League Against Rheumatism/ Paediatric Rheumatology European Society propose validated classification criteria for HSP, c-PAN, c-WG and c-TA with high sensitivity/specifity.

INTRODUCTION

In 1990 the American College of Rheumatology (ACR) proposed classification criteria for patients with vasculitides1–5 by analysing 807 adults patients with different form of vasculitis: 85 with Henoch–Schönlein purpura (HSP), 118 with polyarteritis nodosa (PAN), 85 with Wegener granulomatosis (WG), 63 with Takayasu arteritis (TA) and 456 with other vasculitides (Churg–Strauss, hypersensitivity, giant cell arteritis and other un especific forms).6 Patients with each specific vasculitis were compared with all the remaining diseases grouped into a single control category.

The ACR criteria for HSP (sensitivity 87.1%, specificity 87.7%) require the presence of at least two of the following: (1) age ≤20 years at disease onset; (2) palpable purpura; (3) acute abdominal pain; (4) biopsy showing granulocytes in the walls of small arterioles/venules.1

The ACR criteria for PAN (sensitivity 82.2%, specificity 86.6%) require at least three of the 10 following criteria: (1) granulocyte or mixed leucocyte infiltrate in an arterial wall on biopsy; (2) arteriographic abnormalities; (3) lvedo reticularis; (4) myalgia; (5) diastolic blood pressure (BP) >90 mm Hg; (6) mono- or polyneuropathy; (7) elevated blood urea nitrogen or creatinine; (8) testicular pain/tenderness; (9) hepatitis B reactants; (10) weight loss >4 kg.3,5

The ACR criteria for WG (sensitivity 88.2%, specificity 92%) require at least two of the following: (1) abnormal urinary sediment (red cell casts or >5 red blood cells per high power field);
European League Against Rheumatism (EULAR). However, the Rheumatology European Society (PRES) proposed new ACR criteria were derived by comparing 63 patients with adult graphic and clinical characterisation are reported in the accompanying EULAR-endorsed criteria for paediatric vasculitides. The project culminated finally at the 2008 Ankara Consensus Conference which had, as its primary objective, the validation of the aforementioned EULAR-endorsed criteria for paediatric vasculitides.

With this second paper we describe the final classification criteria for each of the four vasculitides analysed (HSP, c-TA, c-PAN and c-WG) while the general methodology and overall demographic and clinical characterisation are reported in the accompanying paper.

PATIENTS AND METHODS
The methodology used is described in detail in the accompanying introduction and methods paper. In brief, after obtaining consent from parent(s)/child and ethics committee approval as appropriate, 97 PRINTO/PRES institutions in 36 countries, enrolled children with vasculitides, into a three-step retrospective/prospective study.

Step 1: Web-based data collection
Children with age at diagnosis ≤18 years, diagnosed by their treating physician, as HSP, c-PAN, c-WG, c-TA or other c-primary systemic vasculitis (c-other) were included. Data collected included demographic, diagnosis, signs/symptoms (glossary provided) before/or at the date of diagnosis and at least 3 months after, laboratory, histopathological and imaging reports.

Step 2: Classification by consensus panel
Using three Delphi technique web-rounds, a subgroup of 280 cases were classified (blinded to original diagnosis by the treating physician), by a panel of 11 paediatric rheumatologists/ nephrologists into HSP, c-PAN, c-WG, c-TA or c-other. The main purpose of the classification exercise was to evaluate the κ level of agreement with 95% CI between the consensus panel classification and the attending physician diagnosis.

Step 3: Statistical and consensus evaluations
A nominal group technique consensus conference was convened in Ankara in October 2008 to discuss the statistical performance (frequency, sensitivity, specificity, area under the curve (AUC) and κ) of clinical/laboratory findings (criteria) and of 56 HSP, 29 c-PAN, 62 c-WG and 25 c-TA definitions. For the purposes of the statistical analysis all cases of specific vasculitis (eg, HSP classified by the consensus panel or diagnosed by the treating physician) were compared with the control group represented by the remaining cases of childhood vasculitides (eg, c-PAN, c-WG, c-TA, c-other).

RESULTS
Of the 1398 children enrolled, 860 (62%) were diagnosed by the treating physician as HSP, 172 (12%) as c-PAN, 67 (5%) as c-WG, 99 (7%) as c-TA and 200 (14%) as c-other.

Henoch–Schönlein purpura
Step 1: Web-based data collection
From the 860/1398 (62%) children with HSP available in the database, 29 patients were excluded from the analysis for the following reasons: 16 patients because they were diagnosed with infantile haemorrhagic oedema/Finkelstein purpura (all aged <1 year), seven because of other co-morbid conditions and six for missing data.

Step 2: Classification by consensus panel
Sixty patients (22 difficult cases and 38 randomly selected) were blinded for the referring centre diagnosis and classified by the consensus panel: 56 were confirmed as HSP while four were excluded (in three patients consensus not achieved and one was unclassifiable). The κ-agreement between the consensus panel and treating physician was 0.96 (95% CI 0.84 to 1), therefore justifying the inclusion of all 827 patients with HSP in the next step.

Step 3: Statistical and consensus evaluations
The 827/1183 (70%) patients with HSP (771 diagnosed by the treating physician and 56 by the consensus panel) were included in the final analysis and compared with the remaining 356 patients with another form of vasculitides who were used as a control group (c-PAN 150, c-WG 60, c-TA 87, c-other 59 patients).

All patients had purpura (lower limb predominance or diffuse combined) while the characteristic palpable purpura, commonly in crops, with lower limb predominance was seen in 89% of the patients with HSP and in 15% of those with c-PAN and c-WG. Diffuse abdominal pain was present in 60% of children with HSP, arthritis/arthralgia in 78%, proteinuria/haematuria combined in 33%. IgA deposition was observed in 83/827 (10%) of the HSP cases but only 125 patients (39 HSP and 36 controls) had biopsies available. There were no other signs and symptoms, laboratory/ biopsy/imaging reports that were more frequently seen in patients with HSP than in the other vasculitides (see accompanying paper for further details and online supplementary figure 1A web).

Figure 1A shows the sensitivities/specificities of patients with HSP versus the other c-vasculitides. Purpura with lower limb predominance and IgA deposition had both sensitivities/specificities >80%; vessel wall granulocyes (ACR criterion) had a low specificity (26%). Abdominal pain had sensitivities/specificities >60%, arthritis/arthralgia was sensitive (78%) but less specific and proteinuria/haematuria was specific (70%) but less sensitive.

Table 1 provides a glossary of definitions, sensitivity/specificity/AUC for each HSP criterion and the final EULAR/PRINTO/ PRES definition. The sensitivities/specificities/AUC and κ-agreement (between the consensus panel and specific definition) of the final HSP EULAR/PRINTO/ PRES classification definition was 100%/87%/93.5%, respectively, with an almost perfect κ-agreement of 0.90 (95% CI 0.84 to 0.96) compared with 100%/69% of the preliminary EULAR HSP proposal. The sensitivity/specificity of the original HSP
Criteria

ACR criteria were 100%/2%/51% (κ=0.04), which rose to 100%/75%/87.5% (κ=0.81) when the age criterion (≤20 years) was not considered.

**Childhood polyarteritis nodosa**

**Step 1: Web-based data collection**
A total of 172/1398 (12%) children with c-PAN were available in the database.

**Step 2: Classification of difficult cases by consensus panel**
Sixty patients (37 difficult cases and 23 randomly selected) were blinded for the referring centre diagnosis and classified by the consensus panel: 38 as c-PAN while 22 were excluded (more than one reason possible: one because of hepatitis B association, two because of incomplete data, 12 because consensus was not achieved and 10 because they were unclassifiable). The κ-agreement between the consensus panel and treating physician was 0.73 (95% CI 0.62 to 0.84), therefore justifying the inclusion of all 150 patients with c-PAN into the next step.

**Step 3: Statistical and consensus evaluations**
The 150/1124 (13%) patients with c-PAN (112 diagnosed by the treating physician and 38 by the consensus panel) were included in the final analysis and compared with the remaining 974 patients (HSP 827, c-WG 60, c-TA 87).

Small- or medium-sized artery necrotising vasculitis was documented in 28 (19%) and 52 (35%) patients, respectively (small or medium in 67 patients, 45%). Angiographic abnormalities were present in 64 patients (43%), with 14 (9%) having stenoses of medium/small arteries and 57 (38%) aneurysms. The presence of necrotising vasculitis or angiographic abnormalities was seen in 116 (77%) of the patients. Among the others signs/symptoms the most common was myalgia reported by 108 (72%) patients. The second clinical characteristic was skin involvement observed in 104 (69%) patients with c-PAN versus 18 (30%) with c-WG; 51 (34%) with livedo reticularis, 84 (56%) with skin nodules, 19 (13%) with superficial skin infarction

45 patients with cutaneous PAN and 14 with microscopic polyangiitis were also excluded from the analysis.

**Figure 1**
(A) Sensitivity and specificity values seen in the 827 patients with HSP versus the other forms of childhood vasculitides (c-PAN 150, c-WG 60, c-TA 87). (B) Sensitivity and specificity values seen in the 150 patients with c-PAN versus the other forms of childhood vasculitides (HSP 827, c-WG 60, c-TA 87). c-PAN, childhood polyarteritis nodosa; c-TA, c-Takayasu arteritis; c-WG, Wegener granulomatosis; HSP, Henoch–Schönlein purpura.
and 16 (11%) with deep skin infarction. Hypertension was documented in 44 (29%) patients with c-PAN and in 55 (63%) with c-TA. Peripheral neuropathy (mono- or polyneuropathy) in 39 (26%) and renal involvement (proteinuria, haematuria or red blood cell casts) in 44 (29%). Finally, testicular pain or tenderness was present in 15/75 male children (20%) and signs/symptoms suggesting vasculitis of any other major organ system (pulmonary, gastrointestinal, cardiovascular, or central nervous system) were reported in 113 (75%). There were no other signs and symptoms that were more frequently observed in patients with c-WG than in the other vasculitides (see accompanying paper for further details and online supplementary figure 1B).

Figure 1B shows the sensitivities/specificities of patients with c-PAN versus the other c-vasculitides. Specificity was >99.5% for the mandatory criteria with sensitivity being higher for aneurysm (72%), followed by medium- and small-size artery necrotising vasculitis and stenoses. Sensitivity/specificity for histopathological changes or angiographic abnormalities combined were 90.6%/99.6% in this population. Specificity of the remaining signs/symptoms were >80% with the exception of renal involvement (37%), while sensitivity was >70% only for skin involvement and myalgia.

Table 2 provides a glossary of definitions, sensitivity/specificity/AUC for each c-PAN criterion and the final EULAR/PRINTO/PRES definition. The sensitivities/specificities/AUC and κ-agreement (between the consensus panel and specific definition) of the final EULAR/PRINTO/PRES c-PAN classification definition was 89.6%/99.6%/94.6%, respectively, with an almost perfect κ-agreement of 0.92 (95% CI 0.86 to 0.98) compared with 86.3%/99.6%/93% of the preliminary EULAR c-PAN proposal. The sensitivity/specificity for the original adult PAN ACR criteria were 94.7%/95.2%/95% (κ=0.77) in this paediatric population.

Childhood Wegener granulomatosis

Step 1: Web-based data collection
A total of 67/1398 (5%) children with c-WG were available in the database.

Step 2: Classification of difficult cases by consensus panel
Sixty patients (19 difficult cases and 41 randomly selected) were blinded for the referring centre diagnosis and classified by the consensus panel: 51 were confirmed as c-WG (plus one was originally diagnosed as c-PAN and one as another form of c-vasculitis) while nine were excluded (multiple reasons possible: one because age at onset >18 years, one because of other co-morbid conditions, five because consensus was not achieved and four because they were classified as c-other). The κ-agreement between consensus panel and treating physician was 0.88 (95% CI 0.76 to 0.99), therefore justifying the inclusion of all 60 patients with c-WG in the next step.

Step 3: Statistical and consensus evaluations
The 60/1185 (5%) patients with c-WG (seven diagnosed by the treating physician and 53 by the consensus panel) were included in the final analysis and compared with the remaining 1123 patients (HSP 827, c-PAN 150, c-TA 87, c-other 59 patients).

Granulomatous inflammation lesions were present in 27/50 patients (54%) (13 in the upper airways, seven kidney, four orbital mass, three others). More than 70% of the patients had upper airway involvement (either nasal discharge or septum perforation or sinus inflammation), chest x-ray or CT signs (47/60 patients, 78%), versus <10% in the other vasculitides. Immunofluorescence antineutrophilic cytoplasmic antibody (ANCA) was positive in 47 (78%) patients, MPO/pANCA in 14 (23%) and PR3/cANCA in 38 (63%) (any ANCA positivity in 54, 90%) while the frequency of any ANCA positivity was 11% in c-PAN and <5% in the other vasculitides. Renal involvement was observed in 39 (65%) of the patients with c-WG versus the other c-vasculitides (see accompanying paper for further details and online supplementary figure 2A).

Figure 2A shows the sensitivities/specificities of patients with c-WG versus the other c-vasculitides. Sensitivities/specificities were >75% for upper airway involvement, pulmonary

Table 1 Final EULAR/PRINTO/PRES HSP criteria (with glossary) and classification definition (sample 973)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Glossary</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>AUC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purpura (mandatory criterion)</td>
<td>Purpura (commonly palpable and in crops) or petechiae, with lower limb predominance, * not related to thrombocytopenia</td>
<td>89</td>
<td>86</td>
<td>87.5</td>
</tr>
<tr>
<td>1. Abdominal pain</td>
<td>Diffuse abdominal colicky pain with acute onset assessed by history and physical examination. May include intussusception and gastrointestinal bleeding</td>
<td>61</td>
<td>64</td>
<td>62.2</td>
</tr>
<tr>
<td>2. Histopathology</td>
<td>Typically leucocytoclastic vasculitis with predominant IgA deposit or proliferative glomerulonephritis with predominant IgA deposit</td>
<td>93</td>
<td>89</td>
<td>91.1</td>
</tr>
<tr>
<td>3. Arthritis or arthralgias</td>
<td>Arthritis of acute onset defined as joint swelling or joint pain with limitation on motion Arthralgia of acute onset defined as joint pain without joint swelling or limitation on motion</td>
<td>78</td>
<td>42</td>
<td>59.9</td>
</tr>
<tr>
<td>4. Renal involvement</td>
<td>Proteinuria &gt;0.3 g/24 h or &gt;30 mmol/mg of urine albumin/creatinine ratio on a spot morning sample Haematuria or red blood cell casts: &gt;5 red blood cells/high power field or red blood cells casts in the urinary sediment or &gt;2+ on dipstick</td>
<td>33</td>
<td>70</td>
<td>51.4</td>
</tr>
<tr>
<td>HSP EULAR/PRINTO/PRES</td>
<td>Purpura or petechiae (mandatory) with lower limb predominance* and at least one of the four following criteria:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankara 2008 classification definition: κ &gt; 0.90 (95% CI 0.84 to 0.96)</td>
<td>Abdominal pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histopathology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis or arthralgia</td>
<td></td>
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<td></td>
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<tr>
<td>Renal involvement</td>
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</tr>
</tbody>
</table>

* For purpura with atypical distribution a demonstration of an IgA deposit in a biopsy is required.
involvement on chest x-ray or CT and ANCA (sensitivities/specificities immunofluorescence 84%/91%, MPO 26%/94%, PR3 69%/96%).

Table 3 provides the glossary of definitions, sensitivity/specificity/AUC for each c-WG criterion and the final EULAR/PRINTO/PRES definition. The sensitivities/specificities of the final 2009 EULAR/PRINTO/PRES classification definition were 93.3%/99.2%/96.3%, respectively, with an almost perfect κ-agreement of 0.90 (95% CI 0.84 to 0.97) compared with 88%/100%/94% for the preliminary EULAR c-WG proposal. The sensitivities/specificities of the original adult WG ACR criteria were 83%/98%/90.5% (κ=0.77) in this paediatric population.

### Childhood Takayasu arteritis

**Step 1: Web-based data collection**
A total of 99/1598 (7%) children with c-TA were available in the database.

**Step 2: Classification of difficult cases by consensus panel**
Sixty patients (10 difficult cases and 50 randomly selected) were blinded for the referring centre diagnosis and classified by the consensus panel: 48 as c-TA while 12 were excluded (multiple reasons possible: two because age at onset was >18 years, one because of incomplete data, nine because consensus was not achieved and three because they were unclassifiable). The κ-agreement between consensus panel and treating physician was 0.84 (95% CI 0.73 to 0.96) therefore justifying the inclusion of all 87 patients with c-TA in the next step.

**Step 3: Statistical and consensus evaluations**
The 87/1183 (7%) patients with c-TA (39 diagnosed by the treating physician and 48 by the consensus panel) were included in the final analysis and compared with the remaining 1096 patients with other form of vasculitides (HSP 827, c-PAN 150, c-WG 60, other forms 59 patients).

All 87 patients had angiographic abnormalities (100%) (for three patients stenoses were documented by MR or CT), of whom 74 (85%) had stenoses and 43 (49%) aneurysms. Decreased peripheral artery pulse(s) were observed in 62 (71%) and claudication of extremities in 33 (38%) (either signs in 65 patients, 75%). Discrepancy of four limb BP >10 mm Hg, bruits over aorta and/ or its major branches were reported in 54 (62%) and 50 (57%) patients, respectively. Also, hypertension was present in 55 (63%) children as compared with the 44 (29%) patients with c-PAN and six (10%) with WG. Abnormal acute phase reactants (erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)) were observed, at the time of diagnosis, in 76 (87%), similar to c-PAN and c-WG. There were no other signs and symptoms that were more frequently observed in patients with c-TA than in the other vasculitides (see accompanying paper for further details and online supplementary figure 2B).
Figure 2B shows the sensitivities/specificities of patients with c-TA versus the other c-vasculitides. Stenoses had higher sensitivities/specificities (85%/100%) than aneurysms (49%/99.9%). The other four features showed a specificity of ≥90%, while sensitivity was >70% only for pulse deficit/claudication. Sensitivities/specificities of abnormal acute phase reactants (ESR<20 or CRP elevated) were 95%/14%.

Table 4 provides a glossary of definitions, sensitivity/specificity/AUC for each c-TA criterion and the final EULAR/PRINTO/PRES definition. The sensitivity/specificity/AUC of the final EULAR/PRINTO/PRES classification definition was 100%/99.9%/99.95%, respectively, with an almost perfect κ-agreement of 0.99 (95% CI 0.93 to 1) compared with 94.3%/99.9%/97.1% of the preliminary EULAR c-TA proposal. The sensitivities/specificities for the original adult TA ACR criteria were 85.1%/99.6%/92.4% (κ=0.89) in this paediatric population with a decrease in sensitivity if the age criterion (<40 years) was removed.

Further results on sensitivities, specificities, AUC and κ-agreement

In order to control for potential skewing of data we repeated the analysis with a random sample of 120 patients with HSP instead of the full 827 sample. Sensitivities, specificities, AUC and κ-agreement of the final classification criteria, as well as of the individual criterion for HSP, c-PAN, c-WG and c-TA did not change when a random sample of 120 patients with HSP was used instead of the full 827 HSP sample (data not shown).

DISCUSSION

The diagnosis of classic HSP is commonly made by paediatricians. However, validated classification criteria did not exist. This is crucial for future collaborative studies, which require standardised criteria. While there are some similarities between the original ACR criteria and the new criteria (eg, purpura and abdominal pain), some changes were also considered. The ACR criteria required biopsy showing granulocytes in the walls of arterioles or venules; however, this criterion had a very low sensitivity and specificity.
The major change to the original 2005 EULAR/PRES c-WG criteria was the removal of the requirement for age in the definition. For the 2008 classification, the age criterion was already mandatory in the 2005 EULAR/PRES criteria. Also, the specific definition had a slight increase in specificity compared with the preliminary 2005 EULAR-endorsed c-WG criteria. The addition of chest CT scan results, the inclusion of ANCA positivity, and the use of more specific items for upper and lower respiratory involvement were thought to be important since c-WG has some features such as more frequent subglottic stenosis that differentiate it from the adult form. Very minor changes were made to the original 2005 EULAR/PRES c-WG criteria that includes any detected ANCA (immunofluorescence/MPO/PR3/c ANCA) with a substantial $\kappa$-agreement with the blinded evaluation of difficult cases by the consensus panel. Although the sensitivity and specificity of the ACR was greater than 97% in the subjects analysed in the original paper, the specificity dropped dramatically in our sample because all patients had, by inclusion criteria, an age < 18 years; indeed, the specificity rose to 75% when the age criterion was removed.

For the diagnosis of c-PAN, histopathological and angiographic findings are crucial and for this reason this combined criterion was already mandatory in the 2005 EULAR/PRES c-WG criteria. During the discussion there was a specific concern about the imaging modalities to be used in children owing to the recent advances in these techniques. Although conventional angiogram remains the current ‘gold standard’, it is an invasive technique especially in young children where the problem of radiation should also be considered. The group is aware that imaging modalities are advancing rapidly. Future studies may establish a place for non-invasive angiographic techniques. The major change to the original 2005 EULAR/PRES c-WG criteria was the removal of the criteria for the signs and symptoms for vasculitis in specific organ systems and testicular pain or tenderness; this change led to an increase of the specificity and to a simplification of the final criteria. A special challenge in the classification of PAN is the lack of consensus on the borders of cutaneous PAN, which constitutes a large group in paediatric practice. We have not included in the analysis microscopic polyangiitis and cutaneous c-PAN since data related to these two subgroups of the disease were few and since they were empirically defined in the 2005 EULAR/PRES criteria.

For c-WG the main differences from the ACR criteria were the addition of chest CT scan results, the inclusion of ANCA positivity, and more specific items for upper and lower respiratory involvement. These additions were thought to be important since c-WG has some features such as more frequent subglottic stenosis that differentiate it from the adult form. Very minor changes were made to the original 2005 EULAR/PRES c-WG criteria that includes any detected ANCA (immunofluorescence/MPO/PR3/c ANCA) with a substantial $\kappa$-agreement with the blinded evaluation of difficult cases by the consensus panel. Although the sensitivity and specificity of the ACR was greater than 97% in the subjects analysed in the original paper, the specificity dropped dramatically in our sample because all patients had, by inclusion criteria, an age < 18 years; indeed, the specificity rose to 75% when the age criterion was removed.

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in 41% of the children and this figure rose to 100% when we considered all imaging modalities. During the consensus discussion special emphasis was placed on the differential diagnosis of non-inflammatory conditions such as fibromuscular dysplasia or mid-aortic syndrome for which future imaging technologies may be of help. Other differences from the ACR were the combination of pulse deficit and claudication, which were both very frequent (75%) and highly specific, the addition of hypertension (more frequent than in the other c-vasculitides) and the removal of the age limit criterion. Moreover, the addition of increased acute phase reactants as an extra criterion, led us to properly classify all cases in which this laboratory sign, associated with acute phase reactants as an extra criterion, led us to properly classify all cases in which this laboratory sign, associated with
ing multi-centre studies similar to those carried out by EUVAS, and gathering our expertise and knowledge so that we can serve

Table 4 Final EULAR/PRINTO/PRES c-TA criteria (with glossary) and classification definition (sample 1056)

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Glossary</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>AUC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic abnormality (mandatory criterion)</td>
<td>Angiography (conventional, CT, or MRI) of the aorta or its main branches and pulmonary arteries showing aneurysm/dilatation, narrowing, occlusion or thickened arterial wall not due to fibromuscular dysplasia, or similar causes; changes usually focal or segmental</td>
<td>100</td>
<td>99.9</td>
<td>99.9</td>
</tr>
<tr>
<td>1. Pulse deficit or claudication</td>
<td>Loss/decreased/unequal peripheral artery pulse(s) Claudication: focal muscle pain induced by physical activity</td>
<td>74.7</td>
<td>99.1</td>
<td>86.9</td>
</tr>
<tr>
<td>2. Blood pressure (BP) discrepancy</td>
<td>Discrepancy of four limb systolic BP &gt;10 mm Hg difference in any limb.</td>
<td>63.5</td>
<td>99.6</td>
<td>81.6</td>
</tr>
<tr>
<td>4. Bruits</td>
<td>Audible murmurs or palpable thrills over large arteries</td>
<td>58.8</td>
<td>99.8</td>
<td>79.3</td>
</tr>
<tr>
<td>5. Hypertension</td>
<td>Systolic/diastolic BP greater than 95th centile for height</td>
<td>63.2</td>
<td>90.5</td>
<td>76.8</td>
</tr>
<tr>
<td>6. Acute phase reactant</td>
<td>Erythrocyte sedimentation rate &gt;20 mm per first hour or CRP any value above normal (according to the local laboratory)</td>
<td>95.0</td>
<td>14.1</td>
<td>54.6</td>
</tr>
<tr>
<td>c-TA EULAR/PRINTO/PRES Ankara 2008 classification definition: $\kappa$ 0.99 (95% CI 0.93 to 1.00)</td>
<td>Angiographic abnormalities of the aorta or its main branches and pulmonary arteries showing aneurysm/dilatation (mandatory criterion) plus one of the five following criteria: Pulse deficit or claudication Four limbs BP discrepancy Bruits Hypertension Acute phase reactant</td>
<td>100</td>
<td>99.9</td>
<td>99.9</td>
</tr>
</tbody>
</table>

AUC, area under the curve; CRP, C-reactive protein; c-TA, c-Takayasu arteritis; EULAR, European League Against Rheumatism; PRES, Paediatric Rheumatology European Society; PRINTO, Paediatric Rheumatology International Trials Organisation.

in 41% of the children and this figure rose to 100% when we considered all imaging modalities. During the consensus discussion special emphasis was placed on the differential diagnosis of non-inflammatory conditions such as fibromuscular dysplasia or mid-aortic syndrome for which future imaging technologies may be of help. Other differences from the ACR were the combination of pulse deficit and claudication, which were both very frequent (75%) and highly specific, the addition of hypertension (more frequent than in the other c-vasculitides) and the removal of the age limit criterion. Moreover, the addition of increased acute phase reactants as an extra criterion, led us to properly classify all cases in which this laboratory sign, associated with acute phase reactants as an extra criterion, led us to properly classify all cases in which this laboratory sign, associated with

### Acknowledgements

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### Competing interests

None.

### Funding

EULAR/PRINTO/PRES.

### Ethics approval

This study was conducted with the approval of all participating centres if required by the national laws of the specific country.

### Provenance and peer review

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**Table 4** Final EULAR/PRINTO/PRES c-TA criteria (with glossary) and classification definition (sample 1056)

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Glossary</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>AUC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic abnormality (mandatory criterion)</td>
<td>Angiography (conventional, CT, or MRI) of the aorta or its main branches and pulmonary arteries showing aneurysm/dilatation, narrowing, occlusion or thickened arterial wall not due to fibromuscular dysplasia, or similar causes; changes usually focal or segmental</td>
<td>100</td>
<td>99.9</td>
<td>99.9</td>
</tr>
<tr>
<td>1. Pulse deficit or claudication</td>
<td>Loss/decreased/unequal peripheral artery pulse(s) Claudication: focal muscle pain induced by physical activity</td>
<td>74.7</td>
<td>99.1</td>
<td>86.9</td>
</tr>
<tr>
<td>2. Blood pressure (BP) discrepancy</td>
<td>Discrepancy of four limb systolic BP &gt;10 mm Hg difference in any limb.</td>
<td>63.5</td>
<td>99.6</td>
<td>81.6</td>
</tr>
<tr>
<td>4. Bruits</td>
<td>Audible murmurs or palpable thrills over large arteries</td>
<td>58.8</td>
<td>99.8</td>
<td>79.3</td>
</tr>
<tr>
<td>5. Hypertension</td>
<td>Systolic/diastolic BP greater than 95th centile for height</td>
<td>63.2</td>
<td>90.5</td>
<td>76.8</td>
</tr>
<tr>
<td>6. Acute phase reactant</td>
<td>Erythrocyte sedimentation rate &gt;20 mm per first hour or CRP any value above normal (according to the local laboratory)</td>
<td>95.0</td>
<td>14.1</td>
<td>54.6</td>
</tr>
<tr>
<td>c-TA EULAR/PRINTO/PRES Ankara 2008 classification definition: $\kappa$ 0.99 (95% CI 0.93 to 1.00)</td>
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