EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part I: Overall methodology and clinical characterisation

Nicolino Ruperto,[1] Seza Ozen,[2] Angela Pistorio,[3] Pavla Dolezalova,[4] Paul Brogan,[5] David A Cabral,[6] Ruben Cuttica,[7] Raju Khubchandani,[8] Daniel J Lovell,[9] Kathleen M O'Neil,[10] Pierre Quartier,[11] Angelo Ravelli,[1,12] Silvia M Iusan,[1] Giovanni Filocamo,[1] Claudia Saad Magalhães,[13] Erbil Unsal,[14] Sheila Oliveira,[15] Claudia Bracaglia,[16] Arvind Bagga,[17] Valda Stanevicha,[18] Silvia Magni Manzoni,[19] Polyxeni Pratsidou,[20] Loredana Lepore, [21] Graciela Espada,[22] Isabelle Kone Paut,[23] Francesco Zulian,[24] Patrizia Barone,[25] Zelal Bircan,[26] Maria del Rocio Maldonado,[27] Ricardo Russo,[28] Iris Vilca,[1,28] Kjell Tullus,[29] Rolando Cimaz,[30] Gerd Horneff,[31] Jordi Anton,[32] Stella Garay,[33] Susan Nielsen,[34] Giancarlo Barbano,[35] Alberto Martini[1,12]; for the Paediatric Rheumatology International Trials Organisation (PRINTO)

For numbered affiliations see end of the article

Correspondence to
Dr Nicolino Ruperto, Paediatric Rheumatology International Trials Organisation (PRINTO), IRCCS G Gaslini, Università di Genova, Pediatria II – Reumatologia, EULAR Centre of Excellence in Rheumatology 2008-2013, Largo Gaslini, 5, Genova 16147, Italy; nicolaruperto@ospedale-gaslini.ge.it

Accepted 21 December 2009

ABSTRACT

Objectives To report methodology and overall clinical, laboratory and radiographic characteristics for Henoch–Schönlein purpura (HSP), childhood polyarteritis nodosa (c-PAN), c-Wegener granulomatosis (c-WG) and c-Takayasu arteritis (c-TA) classification criteria.

Methods The preliminary Vienna 2005 consensus conference, which proposed preliminary criteria for paediatric vasculitides, was followed by a EULAR/PRINTO/PRES - supported validation project divided into three main steps. Step 1: retrospective/prospective web-data collection for HSP, c-PAN, c-WG and c-TA, with age at diagnosis ≤18 years. Step 2: blinded classification by consensus panel of a subgroup of 280 cases (128 difficult cases, 152 randomly selected) enabling expert diagnostic verification. Step 3: Ankara 2008 Consensus Conference and statistical evaluation (sensitivity, specificity, area under the curve, κ-agreement) using as 'gold standard' the final consensus classification or original treating physician diagnosis.

Results A total of 1183/1398 (85%) samples collected were available for analysis: 827 HSP, 150 c-PAN, 60 c-WG, 87 c-TA and 59 c-other. Prevalence, signs/symptoms, laboratory, biopsy and imaging reports were consistent with the clinical picture of the four c-vasculitides. A representative subgroup of 280 patients was blinded to the treating physician diagnosis and classified by a consensus panel, with a κ-agreement of 0.96 for HSP (95% CI 0.84 to 1), 0.88 for c-WG (95% CI 0.76 to 0.99), 0.84 for c-TA (95% CI 0.73 to 0.96) and 0.73 for c-PAN (95% CI 0.62 to 0.84), with an overall κ of 0.79 (95% CI 0.73 to 0.84).

Conclusion EULAR/PRINTO/PRES propose validated classification criteria for HSP, c-PAN, c-WG and c-TA, with substantial/almost perfect agreement with the final consensus classification or original treating physician diagnosis.

INTRODUCTION

The patient groups upon which the American College of Rheumatology (ACR) based the vasculitis classification criteria did not include children.[1 2] However, since then paediatricians have relied on these and other adult-based criteria[3–7] for their patients. Although children/adolescents and adults with vasculitis share many signs and symptoms of disease, they differ in the relative frequency of some clinical manifestations and concomitant diseases.[8 9] Therefore, it cannot be assumed a priori that the classification criteria developed for adults are suitable for children and adolescents.

In 2005 the vasculitis working group of the Paediatric Rheumatology European Society (PRES) proposed preliminary classification criteria, for some of the most common childhood vasculitides[10]—namely, Henoch–Schönlein purpura (HSP), childhood polyarteritis nodosa (c-PAN), c-Wegener granulomatosis (c-WG), c-Takayasu arteritis (c-TA) and Kawasaki disease. Subsequently, with support from the European League Against Rheumatism (EULAR), the Paediatric Rheumatology International Trials Organisation (PRINTO)[11] and PRES, PRINTO/PRES established a formal statistical validation process with a large-scale data collection that culminated in the final 2008 Ankara Consensus Conference.

In this first paper we describe the general methodology and overall clinical, laboratory and radiographic characteristics, while the specific details of the final classification criteria for each of the four vasculitides analysed (HSP, c-TA, c-PAN and c-WG) are reported in the accompanying paper.[12]

PATIENTS AND METHODS

Consensus formation techniques

Two well-recognised consensus formation methodologies, specifically designed to combine judgments

from a group of experts in a particular field, were used to attain the goals: the Delphi technique and nominal group technique (NGT).[13 14] The Delphi technique uses a series of well-defined mail questionnaires while NGT is a structured face-to-face meeting designed to facilitate reaching consensus, through round robin discussion.[7 15–22]

The 2005 Vienna Consensus conference

The general objective was to reach a consensus on classification criteria for childhood vasculitis, as previously described.[10] In brief, consensus (≥80%) was reached to base the general working classification for childhood vasculitides on vessel size: predominantly large-, medium- or small-vessel vasculitis (granulomatous and non-granulomatous), and other vasculitides (box 1). Preliminary classification criteria based on consensus discussion were proposed for HSP, c-PAN, c-WG, or c-TA and Kawasaki disease as reported by Ozen *et al*.[10]

Validation of the preliminary criteria

After obtaining consent from parent(s)/child and ethics committee approval (as required by the national law in each participating country), 97 PRINTO/PRES institutions in 36 countries (see complete list at the end of the paper) enrolled children with selected vasculitides, into a three-step study.

Step 1: Web-based data collection

Inclusion criteria were 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). The other rarest forms of vasculitis (cryoglobulinaemic vasculitis, Churg–Strauss syndrome) were excluded because of their low prevalence while Kawasaki syndrome was excluded because it is under evaluation by another paediatric group (personal communication).

The five-page, web-based case report form included demographic data, clinical diagnosis made by the attending physician, presence of signs/symptoms in 12 broad organs/systems (general, mucosa and skin, eye, ears/nose/throat, respiratory, cardiovascular, neurological, gastrointestinal, renal, genital, musculoskeletal, other features of active vasculitis) before or at the date of diagnosis and at least 3 months later (in this series data after diagnosis are not presented), laboratory values (antineutrophilic cytoplasmic antibody (ANCA) testing by immunofluorescence/MPO/PR3, renal features, inflammation indices, platelets), physician global assessment of disease activity on a 10 cm visual analogue scale, biopsy findings (renal, skin, upper airway, other) and imaging reports (chest x-ray, CT scan, MRI, conventional, CT or MRI angiography findings). A three-page glossary, adapted from the Birmingham Vasculitis Activity Score glossary,[23–25] provided definition of all items included in the case report forms. Data were abstracted by review of the clinical charts. Data collection was both retrospective for diagnosis before May 2007 and prospective for the remaining patients (figure 1).

Data entry was carried out online through the member area of the PRINTO website (http://www.printo.it, accessed 11 March 2010) on a secured https platform. The electronic forms contained some predefined rules to avoid errors and missing data, but were also reviewed for consistency by a dedicated PRINTO research assistant.

The aim was to collect data for approximately 150 patients with HSP, 50 with c-TA, 80 with c-PAN and 40 with c-WG using each group of vasculitis as comparator for the others.[2] These numbers were realistic projections of patient numbers required to provide reliable statistical analyses based on the relative frequencies of each disease.

Step 2: Classification by consensus panel

This step was included in order to further clean the original dataset collected, thus allowing a robust final patient dataset on which to base statistical validation of the classification criteria. Three physicians from the PRINTO international coordinating centre (NR, AP, GF) screened out all submitted cases. A total of 128 patients who did not fulfil ACR or EULAR classification criteria or were misclassified[3 10] (so called 'difficult cases') but were nevertheless diagnosed by the treating physicians as HSP, c-PAN, c-WG, c-TA or c-other were retrieved; in addition, 152 randomly selected patients were added (38 HSP, 23 c-PAN, 41 c-WG, 50 c-TA). Using three Delphi web-rounds, the representative subgroup of 280 were classified by a panel of 11 paediatric rheumatologists/nephrologists into HSP, c-PAN, c-WG, c-TA or c-other. The panel was presented with the complete time-of-diagnosis case report in web-based form, but was blinded to the original diagnosis assigned by the treating physician. A consensus ≥80% within the 11 panellists was required to establish the final classification of each difficult case. Patients for whom consensus did not reach ≥80% in the first round, were re-evaluated in the second and third rounds, where panellists were made aware of each other's evaluations and were allowed to engage in a web-based collegial discussion of the specific cases. All patients for whom consensus was not achieved (<80%) were excluded from further analysis.

We then calculated the κ level of agreement,[26 27] with 95% CI between the consensus panel classification and the

Box 1 Classification of childhood vasculitis

- Predominantly large-vessel vasculitis
  - Takayasu arteritis
- Predominantly medium-sized vessel vasculitis
  - Childhood polyarteritis nodosa (c-PAN)
  - Cutaneous polyarteritis
  - Kawasaki disease
- Predominantly small-vessel vasculitis
  - Granulomatous
  - Wegener granulomatosis
  - Churg–Strauss syndrome
  - Non-granulomatous
  - Henoch–Schönlein purpura
  - Microscopic polyangiitis
  - Microscopic polyangiitis
  - Hypocomplementaemic urticarial vasculitis
- Other vasculitides
  - Behçet disease
  - Vasculitis secondary to infection (including Hep B associated PAN), malignancies and drugs, including hypersensitivity vasculitis
  - Vasculitis associated with connective tissue diseases
  - Isolated vasculitis of the central nervous system
  - Cogan syndrome
  - Unclassified

Reproduced from Ozen *et al*.[10]

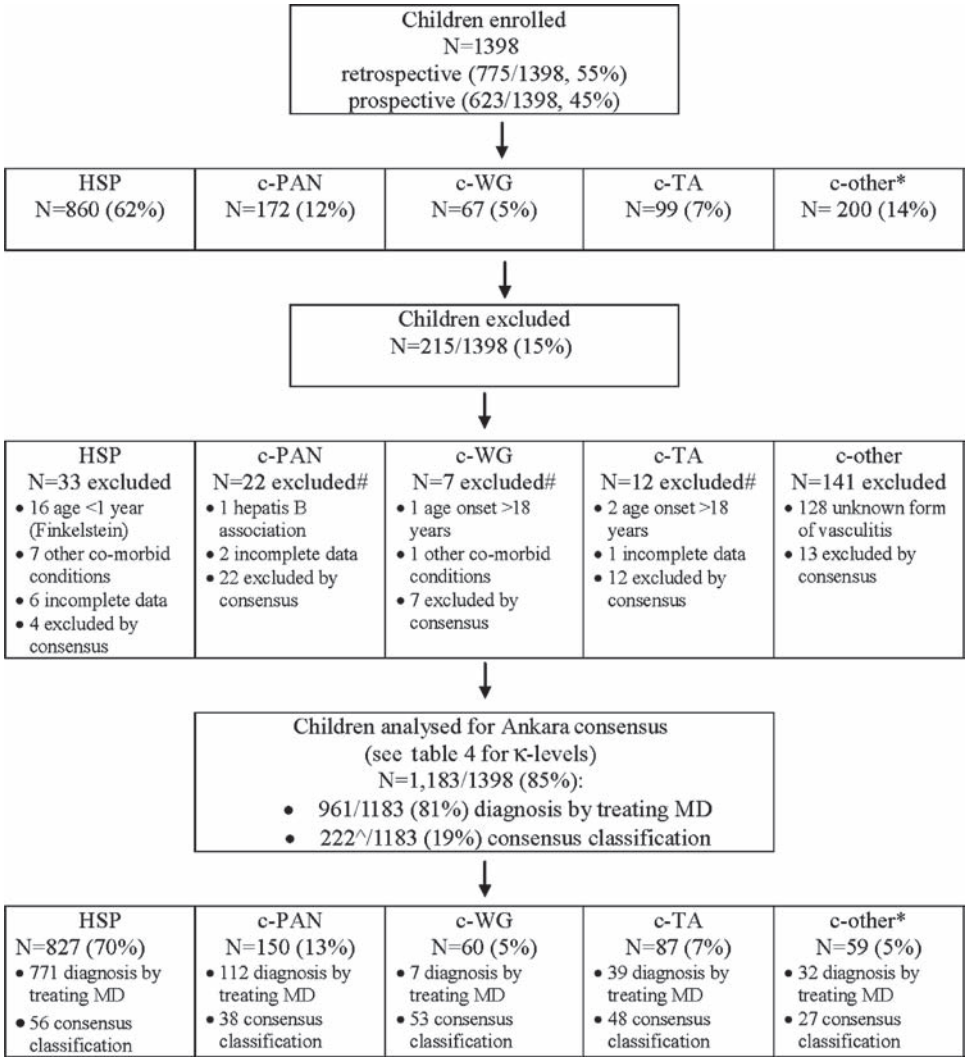

Figure 1 The final enrolment figures. #More than one reason possible for exclusion. *Includes 45 cutaneous PAN, 14 microscopic polyangiitis. ^222/280 (79%) Cases analysed by the consensus panel on which consensus was achieved (see step 2 in the "Patients and methods" and "Results" sections for further details). c-other, childhood-unknown vasculitis; c-PAN, c-polyarteritis nodosa; c-TA, c-Takayasu arteritis; c-WG, c-Wegener granulomatosis; HSP, Henoch–Schönlein purpura.

attending physician diagnosis; we expected to find a $\kappa>0.8$ (almost perfect agreement)[27] between the consensus panel and the treating physician. The expected almost perfect agreement was crucial in order to allow combination, in the third step, of both the difficult cases for whom the panellists reached classification consensus and the remaining patients diagnosed by the referring physician (see figure 1). The final diagnosis attribution for each child in the third step was given therefore by the consensus classification or by the original treating physician diagnosis.

Step 3: Statistical and consensus evaluations

An NGT consensus conference was convened in Ankara in October 2008, to discuss the statistical performance (frequency, sensitivity/specificity, area under the curve (AUC) and κ level of agreement) of clinical/laboratory findings (criteria) and of different classification criteria (about 50 for each disease) for HSP, c-TA, c-PAN and c-WG. All classification criteria tested were developed by the PRINTO international coordinating centre (NR, AP, GF) based on combinations of criteria derived from the literature (eg, ACR classification criteria, Vienna childhood criteria, etc) or created ad hoc (eg, for HSP 2/5 criteria, 3/5 criteria, etc). For the purposes of the statistical analysis, cases (eg, HSP classified by the panel or HSP diagnosed by the treating physician) were compared with the control group represented by the remaining patients with vasculitis with other diagnoses (eg, c-PAN, c-WG, c-TA, c-others). This use of other vasculitides as controls was employed in the original ACR adult vasculitis classification exercise.[1 2]

Statistics

Descriptive statistics, using the final classification criteria, were reported as means ± SD, whereas categorical variables were reported as absolute frequencies and percentages. Laboratory values were standardised based on the normal values provided by each local laboratory, as previously described.[16] Comparison of frequencies was made by the χ^2 or the Fisher exact text (post hoc with Bonferroni's correction), while comparisons of means were made by the analysis of variance (parametric or non-parametric) with post hoc comparisons (Scheffé or Dunn's test) as appropriate.

For each individual criterion/classification definition, we calculated the sensitivity (ability to recognise patients with the particular disease calculated as number of patients positive

for the criterion/definition divided by the total number of patients with the disease) and specificity (ability to exclude patients with other diseases calculated as number of patients negative for the criterion/definition divided by the total number of patients without the disease). Sensitivity and specificity for either the individual criterion (eg, purpura for HSP), reported in the accompanying paper,[12] and the classification definitions (eg, Vienna preliminary HSP criteria) were calculated using as 'gold standard' the final disease consensus classification or original treating physician diagnosis. Moreover, we evaluated in the second step, the agreement between the consensus panel classification and the diagnosis made by the treating physician, and in the third step, the agreement between the definitions tested and the final disease consensus panel or original diagnosis by the treating physician by means of the κ-coefficient,[26] with the following cut-off levels proposed by Landis and Koch[27]: 0.01–0.2 = slight; 0.21–0.4 = fair; 0.41–0.6 = moderate; 0.61–0.8 = substantial; 0.81–1 = almost perfect agreement.

Sample size calculation for the diagnostic accuracy study (study in which the main objective is to evaluate the diagnostic accuracy of clinical, laboratory and other variables for the chosen outcome—in this case classification criteria; parameters for diagnostic accuracy are sensitivity, specificity, AUC) was based on the assumption that the required minimum AUC of the receiving operating curves was 85% with standard error of 3.5% giving a sample of 60 pairs of patients (60 cases vs 60 controls) for each specific vasculitis.[28]

Data were entered in an Access XP database and analysed with Excel XP (Microsoft), XLSTAT 6.1.9 Addinsoft, Statistica 6.0 (StatSoft), and Stata 7.0 (Stata Corporation).

RESULTS

Step 1: Web-based data collection

Figure 1 shows the final enrolment figures. 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. Of the patients with HSP, c-PAN, c-WG and c-TA entered in the PRINTO web system, 74 (5%) were excluded for the following multiple reasons: 19 were beyond age limit, eight had associated co-morbid conditions, nine had incomplete data and 45 were excluded by the consensus panel classification (see step 2). Of the 200 remaining patients (c-other), 45 patients had cutaneous PAN; 14 microscopic polyangiitis; 13 were excluded by the consensus classification exercise because consensus could not be reached (k<80%); and the remaining 128 were excluded because a specific diagnosis was not given by the treating physician (unknown form of vasculitis).

Step 2: Classification by consensus panel

A total of 280/1398 (20%) children enrolled in the web-based system were classified by the consensus panel (figure 1 and table 1), blinded to the centre diagnosis. Three round robin web-based classification cycles allowed consensus ≥80% to be reached for the classification of 56 HSP, 38 c-PAN, 53 c-WG, 48 c-TA and 27 patients with c-other vasculitis. For the remaining 58 (20%) consensus was <80% and therefore these patients were discarded from further consideration (figure 1). Table 1 shows the grid of agreement for the four vasculitides, as well as the κ-coefficient between the consensus panel classification and original patient diagnosis made by the treating physician. The overall κ-agreement was 0.79 (substantial, 95% CI 0.73 to 0.84) for the 280 patients classified considered altogether. The κ-agreement was >0.8 (almost perfect agreement) for HSP, c-WG and c-TA and substantial (0.73) for c-PAN. These high levels of agreement justified the combination of either the subgroup of patients classified by the consensus panel and the remaining patients diagnosed by the treating physician into the next step.

Step 3: Statistical and consensus evaluations

For the face-to-face Ankara 2008 Consensus Conference there were therefore a total of 1183/1398 (85%) of the original patients available for the analysis (figure 1). Final disease classification for these 1183 children, was represented by the original diagnosis made by the treating physician for 961 (81%) patients (771 HSP, 112 c-PAN, 7 c-WG, 39 c-TA and 32 c-other) and the panel consensus classification for the remaining 222 (19%) (56 HSP, 38 c-PAN, 53 c-WG, 48 c-TA and 27 c-other). The 59 c-other comprised 45 patients with cutaneous PAN and 14 children with microscopic polyangiitis.

Sensitivity, specificity, AUC and κ level of agreement (measured between each definition and the final disease classification) of the final EULAR/PRINTO/PRES classification definitions and the related individual criteria for the four childhood vasculitides are reported in the accompanying paper[12] and in an online supplementary table.

Demographic and clinical characterisation according to the final EULAR/PRINTO/PRES classification criteria

As shown in table 2,children with HSP had younger age at onset, younger age at first visit and the shortest disease duration, followed sequentially by c-PAN, c-TA and c-WG. The time

Table 1 κ Level of agreement (95% CI) between the consensus panel classification (columns) and the diagnosis of the treating physician (rows).

	κ Agreement (95% CI)	HSP	c-PAN	c-WG	c-TA	c-Other or no consensus	Total
HSP	0.96 (0.84 to 1.00)	56	–	–	–	4	60
c-PAN	0.73 (0.62 to 0.84)	–	38	1	–	21	60
c-WG	0.88 (0.76 to 0.99)	–	–	51	–	9	60
c-TA	0.84 (0.73 to 0.96)	–	–	–	48	12	60
c-Other	0.53 (0.43 to 0.64)	–	–	1	–	39	40
Total	0.79 (0.73 to 0.84)	56	38	53	48	85	280

κ Statistics for agreements were computed separately for each of the c-vasculitis entities (treating physician vs consensus panel) and included also misclassified cases (c-other and no consensus); κ levels of 0.61–0.8 are substantial, >0.8 identifies an almost perfect agreement.[26 27]
c-PAN, childhood polyarteritis nodosa; c-TA, c-Takayasu arteritis; c-WG, c-Wegener granulomatosis; HSP, Henoch–Schönlein purpura.

Table 2 Baseline demographic and clinical data for the 1124 patients considered in the final analysis (see also figure 1)

	HSP (N=827)	c-PAN (N=150)	c-WG (N=60)	c-TA (N=87)	p Values
Age at onset of signs or symptoms (years)	6.9±3	8.6±3.8	11.7±3.6	10.4±3.7	<0.0001
Age at first visit (years)	7±3	9±3.7	12.5±3.3	11.6±3.8	<0.0001
Age at diagnosis (years)	7±3	9.2±3.7	12.4±3.3	11.7±3.6	<0.0001
Time to diagnosis (years)	0.1±0.3	0.5±1.3	0.7±1.2	1.3±1.6	<0.0001
Female (n (%))	408 (49)	75 (50)	41 (68)	59 (68)	0.0005
Ethnicity					<0.0001
Caucasian (n (%))	697 (84)	124 (83)	49 (82)	51 (58)	
Hispanic (n (%))	59 (7)	7 (4.5)	6 (10)	11 (13)	
Afro-American (n (%))	4 (0.5)	0 (0)	0 (0)	5 (6)	
Asian (n (%))	26 (3)	12 (8)	3 (5)	9 (10)	
Others (n (%))	40 (5)	6 (4)	2 (3)	11 (13)	
Missing (n (%))	1 (0.5)	1 (0.5)			
Physician's evaluation of disease activity (0–10 cm VAS)	4.3±2.3	7.3±1.8	8.1±1.3	7.7±1.8	<0.0001

Data for the remaining 59 patients with other c-vasculitides are not shown. Data are means ± SD unless otherwise stated. Denominators refer to the top of each column.
c-PAN, childhood polyarteritis nodosa; c-TA, c-Takayasu arteritis; c-WG, c-Wegener granulomatosis; HSP, Henoch–Schönlein purpura; VAS, visual analogue scale.

Table 3 Baseline signs/symptoms, individually or in combination, for the 1124 patients considered in the final analysis (see also figure 1)

Signs/symptoms	HSP (N=827)	c-PAN (N=150)	c-WG (N=60)	c-TA (N=87)	p Values
General					
Malaise	255 (31)	89 (59)	49 (82)	61 (70)	<0.0001
Fever	238 (29)	112 (75)	37 (62)	46 (53)	<0.0001
Mucosa and skin					
Oral/nasal ulceration	5 (0.6)	8 (5)	29 (48)	2 (2)	<0.0001
Purpura (palpable) with lower limb predominance	739 (89)	23 (15)	9 (15)	0 (0)	<0.0001
Purpura (palpable) diffuse	163 (20)	49 (33)	5 (8)	0 (0)	<0.0001
Purpura lower limb predominance/diffuse combined	*827 (100)*	*68 (45)*	*14 (23)*	*0 (0)*	<0.0001
Livedo reticularis	8 (1)	51 (34)	8 (13)	2 (2)	<0.0001
Skin nodules	9 (1)	84 (56)	9 (15)	2 (2)	<0.0001
Livedo/nodules combined	*17 (2)*	*98 (65)*	*15 (25)*	*4 (5)*	<0.0001
Superficial skin infarctions	19 (2)	19 (13)	4 (7)	2 (2)	<0.0001
Deep skin infarctions	0 (0)	16 (11)	5 (8)	1 (1)	<0.0001
Livedo/nodules/skin infarction combined	*30 (3.6)*	*104 (69)*	*18 (30)*	*7 (8)*	<0.0001
Upper airway involvement					
Nasal discharge or recurrent epistaxis/crusts/granulomata	5 (0.6)	3 (2)	42 (70)	1 (1)	<0.0001
Nasal septum perforation/saddle nose/auricular chondritis	0 (0)	0 (0)	9 (15)	0 (0)	<0.0001
Chronic or recurrent sinus nasal inflammation	3 (0.4)	1 (0.7)	35 (58)	2 (2)	<0.0001
Nasal discharge/perforation/sinus inflammation combined	*7 (0.8)*	*3 (2)*	*50 (83)*	*3 (3)*	<0.0001
Laryngo-tracheo-bronchial involvement					
Subglottic stenoses/hoarsness/stridor	0 (0)	1 (0.7)	11 (18)	0 (0)	<0.0001
Tracheal/endobronchial stenoses, obstruction	1 (0.1)	0 (0)	9 (15)	0 (0)	<0.0001
Subglottic/tracheal/bronchial stenoses combined	*1 (0.1)*	*1 (0.7)*	*13 (22)*	*0 (0)*	<0.0001
Cardiovascular					
Bruits over aorta and/or its major branches	0 (0)	1 (0.7)	(0)	50 (57)	<0.0001
Decreased peripheral artery pulse(s)	0 (0)	2 (1)	0 (0)	62 (71)	<0.0001
Claudication of extremities	1 (0.1)	7 (5)	1 (2)	33 (38)	<0.0001
Decreased pulses/claudication combined	*1 (0.1)*	*7 (5)*	*1 (2)*	*65 (75)*	<0.0001
Discrepancy on 4 limb blood pressure >10 mm Hg in any limb	0 (0)	4 (3)	0 (0)	54 (62)	<0.0001
Neurological					
Motor mononeuritis multiplex	1 (0.1)	27 (18)	0 (0)	1 (1)	<0.0001
Sensory peripheral neuropathy	1 (0.1)	31 (21)	0 (0)	0 (0)	<0.0001
Mono- or polyneuropathy combined	*1 (0.1)*	*39 (26)*	*0 (0)*	*1 (1)*	<0.0001
Gastrointestinal					
Abdominal pain	500 (60)	75 (50)	9 (15)	46 (41)	<0.0001
Genital					
Testicular pain or tenderness	68/419 (16)	15/75 (20)	0/19 (0)	0/21 (0)	0.019
Musculoskeletal					
Muscle pain or tenderness	109 (13)	108 (72)	22 (37)	27 (31)	<0.0001
Arthritis	349 (42)	65 (43)	18 (30)	10 (11)	<0.0001
Arthralgia	558 (67)	100 (67)	31 (52)	26 (30)	<0.0001
Arthritis/arthralgia combined	645 (78)	114 (76)	33 (55)	28 (32)	<0.0001

Variables in *italics* indicate combination of signs/symptoms.
Data for the remaining 59 patients with other c-vasculitides are not shown. Only data that are relevant for the proposed criteria are shown. The numbers in parentheses indicate the percentage of subjects with a particular diagnosis who had the feature in question. Denominators refer to the top of each column.
c-PAN, childhood polyarteritis nodosa; c-TA, c-Takayasu arteritis; c-WG, c-Wegener granulomatosis; HSP, Henoch–Schönlein purpura.

Table 4 Baseline laboratory, biopsy and imaging data, individually or in combination, for the 1124 patients considered in the final analysis (see also figure 1)

	HSP (N=827)	c-PAN (N=150)	c-WG (N=60)	c-TA (N=87)	p Values
Laboratory					
IF ANCA	15 (2)	15 (10)	47 (78)	3 (3)	<0.0001
MPO ANCA (or pANCA)	13 (2)	2 (1)	14 (23)	0 (0)	<0.0001
PR3 ANCA (or cANCA)	14 (2)	3 (2)	38 (63)	0 (0)	<0.0001
ANCA IF or PR3 combined	*17 (2)*	*16 (11)*	*51 (85)*	*3 (3)*	<0.0001
Any ANCA	*17 (2)*	*17 (11)*	*54 (90)*	*3 (3)*	<0.0001
ESR >20 mm/1st h	294 (36)	138 (92)	56 (93)	74 (85)	<0.0001
CRP >0.46 mg/dl	294 (36)	111 (74)	51 (85)	52 (60)	<0.0001
ESR or CRP elevation combined	*430 (52)*	*142 (95)*	*59 (98)*	*76 (87)*	<0.0001
Proteinuria >0.3 g/24 h	118 (14)	32 (21)	32 (53)	4 (5)	<0.0001
Haematuria or red blood cell casts (RBC)/hpf	250 (30)	37 (25)	37 (62)	7 (8)	<0.0001
Proteinuria/haematuria/RBC casts combined	*269 (33)*	*44 (29)*	*38 (63)*	*10 (11)*	<0.0001
Abnormal GFR (<50 normal)	31 (4)	12 (8)	19 (32)	11 (13)	<0.0001
Impaired renal function (proteinuria/haematuria/ abnormal GFR combined)	*274 (33)*	*44 (29)*	*41 (68)*	*18 (21)*	<0.0001
Hypertension	46 (6)	44 (29)	6 (10)	55 (63)	<0.0001
Biopsy reports*					
IgA deposit	83/89 (93)	2/10 (20)	1/18 (6)	0/0 (0)	<0.0001
Vessel wall granulocytes	11/12 (92)	14/19 (74)	5/7 (71)	0/1 (0)	0.19
Small-sized arteries necrotising vasculitis	0/34 (0)	28/79 (35)	3/60 (5)	0/3 (0)	<0.0001
Medium-sized arteries necrotising vasculitis	0/34 (0)	52/79 (66)	1/60 (2)	0/3 (0)	<0.0001
Small/medium sized arteries necrotising vasculitis (EULAR)	0/34 (0)	67/79 (85)	3/60 (5)	0/3 (0)	<0.0001
Granulomatous inflammation lesions	0/84 (0)	0/71 (0)	27/50 (54)	4/11 (36)	<0.0001
Necrotizing pauci-immune glomerulonephritis	0/84 (0)	9/17 (53)	24/30 (80)	0/0 (0)	<0.0001
Imaging reports*					
Chest x-ray (nodules, cavities or fixed infiltrates)	0/89 (0)	8/71 (11)	35/57 (61)	2/62 (3)	<0.0001
Chest x-ray or CT (nodules, cavities or fixed infiltrates) combined	*0/89 (0)*	*8/71 (11)*	*47/60 (78)*	*5/64 (8)*	<0.0001
Angiographic abnormalities					
Aneurysm medium/small arteries (for c-PAN)	0/0 (0)	57/79 (72)	0/2 (0)	1/87 (1)	<0.0001
Stenoses medium/small arteries (for c-PAN)	0/0 (0)	14/79 (18)	0/2 (0)	0/87 (0)	0.0002
Aneurysm/stenoses medium/small arteries combined (for c-PAN)	*0/0 (0)*	*64/79 (81)*	*0/2 (0)*	*1/87 (1)*	<0.0001
Aneurysm large arteries (for c-TA)	0/0 (0)	0/79 (0)	0/2 (0)	43/87 (49)	<0.0001
Stenoses large arteries (for c-TA)	0/0 (0)	0/79 (0)	0/2 (0)	74/87 (85)	<0.0001
Aneurysm/stenoses large arteries combined (for c-TA)	*0/0 (0)*	*0/79 (0)*	*0/2 (0)*	*87/87 (100)*	<0.0001

Variables in *italics* indicate a combination of laboratory, biopsy or imaging data.
Data for the remaining 59 patients with other c-vasculitides are not shown. Only data that are relevant for the proposed criteria are shown. The numbers in parentheses indicate the percentage of subjects with a particular diagnosis who had the feature in question. Denominators refer to the top of each column unless otherwise reported.
*Denominator refers to the number of biopsy specimens or imaging results available.
ANCA, antineutrophilic cytoplasmic antibody; c-PAN, childhood polyarteritis nodosa; CRP, C-reactive protein; c-TA, c-Takayasu arteritis; c-WG, c-Wegener granulomatosis; ESR, erythrocyte sedimentation rate; EULAR, European League Against Rheumatism; GFR, glomerular filtration rate; hpf, high power field, HSP, Henoch–Schönlein purpura; IF, immunofluorescence.

from onset of signs or symptoms to diagnosis was shortest in HSP (0.1±0.3 years), followed by c-PAN and c-WG while the longest period was observed for c-TA (1.3±1.6 years). Patients were predominantly Caucasian (82%) (p values <0.0001 for all comparisons).

In table 3 are reported the absolute frequencies, percentage frequencies and related p values (all <0.0001 except testicular pain or tenderness equal to 0.019) of the signs/symptoms (individually or in combination) for the 1124 patients included in the final analysis (data for the 59 c-other are not shown in the table). Signs/symptoms reported refer to those most frequently observed in each different form of vasculitis. General signs/symptoms (malaise or fever) were more frequently observed in the three non-HSP systemic vasculitides 245 (82%) (122 c-PAN, 53 c-WG and 70 c-TA) and were less common in HSP 386 (47%). For mucosa and skin involvement, oral/nasal ulceration were typical of c-WG, occurring in 29 (48%) cases; purpura in 827 (100%) HSP, and to a lesser extent in c-PAN 68 (45%) and c-WG 14 (23%); while specified forms of skin involvement (livedo/nodules/superficial or deep skin infarction) were observed mainly in c-PAN 104 (69%). Upper airway/laryngo-tracheo-bronchial involvement was more frequent in c-WG, occurring in 52 (87%), cardiovascular in c-TA 74 (85%) and neurological involvement in c-PAN 39 (26%). Gastrointestinal (mainly abdominal pain) and musculoskeletal complaints were evenly distributed among all four vasculitides.

Table 4 shows the absolute values, percentage frequencies and related p values (all <0.0001) of the laboratory, biopsy and imaging data. ANCA positivity was reported mainly in c-WG (any ANCA in 90%). Systemic inflammation, as measured by erythrocyte sedimentation rate or C-reactive protein, was most common in c-PAN, c-WG and c-TA 277 (combined mean 93%) as compared with patients with HSP 430 (52%). Renal involvement (haematuria/proteinuria, serum creatinine elevation, abnormal glomerular filtration rate) was most frequent in c-WG (68%), followed by HSP (33%) and c-PAN (29%). Deposition of IgA was present in 83/89 (93%) biopsies performed in HSP, small-/medium-size necrotising vasculitis 67/79 biopsies (85%) for c-PAN, while granulomatous inflammation lesions were observed in 27/50 (54%) c-WG biopsies. Similarly, abnormal chest x-ray or CT findings (nodules, cavities or fixed infiltrates) were mainly seen in 47/60

(78%) images available in c-WG. Angiography findings demonstrated that aneurysms/stenosis of medium/small arteries were present in 64/79 (81%) images in c-PAN, while in c-TA aneurysms/stenosis of large arteries were present in 87/87 (100%) of the images available.

DISCUSSION

The results of this project allow the classification of children with HSP, c-PAN, c-WG or c-TA, using different combinations of signs/symptoms, laboratory, biopsy and imaging reports. The proposed definitions robustly classify and discriminate patients with the specific type of vasculitis (sensitivity) and exclude a high proportion of patients with other diseases (specificity).

After the ACR publication in 1990 paediatric researchers had to rely on classification criteria developed for adult patients. Because of the peculiarities of childhood vasculitis and its observed differences from adult vasculitis, in 2005 the vasculitis working group of PRES decided to assess the applicability of adult-onset vasculitis classification criteria in children, with a view to determining if new or modified classification criteria should be developed for children. Indeed, it was not the intention of the PRES working group to replace existing criteria for adult patients, but rather to formally evaluate if they apply to children, and to determine if changes in classification were necessary.

The process started with a literature review and a consensus-based preliminary proposal,[10] followed by a formal validation process described in this paper. The large-scale data collection has been more successful in recruiting patient numbers than initially expected. Our validation process resembles the methodology followed by the ACR in part, since we collected a large series of paediatric cases to evaluate the sensitivity and specificity of each individual criterion and several different combinations of the most sensitive and specific items. Our process differed from the ACR methodology in that we introduced, as 'gold standard' a blinded (to the original diagnosis assigned by the treating physician) consensus classification of the most difficult cases (about 20% of the cases) by a panel of 11 experienced paediatric rheumatologists/nephrologists. The purpose of this blinded classification exercise was to confirm/exclude, with an unbiased revision, the diagnosis made by the patient's physician and to calculate the κ-agreement between the consensus panel and the treating physician. The results of the blinded evaluation showed almost perfect κ-agreement, justifying the combination into one single group of both the patients classified by the consensus panel and the patients diagnosed by the primary treating physician. The almost perfect κ was also an indirect confirmation that the diagnosis made by the treating physicians was consistent with the clinical presentation of each child as abstracted from the patients' charts.

The main advantage of this project is the large dataset sample analysed and the unique worldwide nature of the data collected, thus capturing a broad spectrum of cases and ensuring that the classification criteria can be applied universally. A possible limitation is related to the exclusion from the analysis of about 15% of the children enrolled who were, however, scattered proportionally among all vasculitides. Also, to obtain a more homogeneous sample we excluded the cases of unclassified vasculitides that will be more precisely characterised in future analysis.

In conclusion, EULAR/PRINTO/PRES propose validated definitions for the classification of HSP, c-PAN, c-WG and c-TA, each of which demonstrates high sensitivity/specificity and an almost perfect agreement with the final consensus classification or original treating physician diagnosis.

Author affiliations [1]IRCCS G Gaslini, Pediatria II, Reumatologia, PRINTO, Genova, Italy
[2]Hacettepe University Children's Hospital, Ankara, Turkey
[3]IRCCS G Gaslini, Servizio di Epidemiologia e Biostatistica, Genova, Italy
[4]Department of Paediatrics and Adolescent Medicine, 1st Faculty of Medicine and General University Hospital, Praha, Czech Republic
[5]Great Ormond St Hospital, Rheumatology, London, UK
[6]British Columbia Children's Hospital, Vancouver, Canada
[7]Rheumatology Section, Hospital General de Ninos Pedro de Elizalde, Buenos Aires, Argentina
[8]Department of Paediatrics, Jaslok Hospital and Research Centre, Mumbai, India
[9]Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, USA
[10]Children's Hospital at OUMC, University of Oklahoma, Health Sciences Center, Oklahoma City, USA
[11]Universite Paris-Descartes and Centre de reference national pour les Arthrites Juveniles. Unite d'Immunologie, Hematologie et Rhumatologie Pediatriques, Hopital Necker-Enfants Malades, Paris, France
[12]Dipartimento di Pediatria, Università degli Studi, Genova, Italy
[13]Departamento de Pediatria – UNESP, Hospital das Clínicas – Faculdade de Medicina de Botucatu, UNESP, Botucatu, Brazil
[14]Dokuz EyluL University Medical Faculty, Division of Pediatric Rheumatology–Immunology, Balcova, Izmir, Turkey
[15]Universidade Federal do Rio de Janeiro, Instituto de Puericultura e Pediatria Martagao Gesteira, Rio de Janeiro, Brazil
[16]Pediatria II/Reumatologia – IRCCS, Ospedale Pediatrico Bambino Gesù, Roma, Italia
[17]All India Institute of Medical Sciences
[18]Riga Stradins University, Pediatric, Riga, Latvia
[19]IRCCS Policlinico S Matteo, Clinica Pediatrica, Pavia, Italy
[20]Department of Pediatrics Ippokration Hospital, Aristotle University of Thessaloniki – Ippokration General Hospital, Thessaloniki, Greece
[21]Universita' degli Studi di Trieste, Scienze della Riproduzione e dello Sviluppo, Trieste, Italy
[22]Hospital de Ninos Ricardo Gutierrez, Rheumatology Section HNRG Buenos Aires University, Buenos Aires, Argentina
[23]Centre de référence national des maladies auto-inflammatoires, Service de pédiatrie générale, rhumatologie pédiatrique, Le Kremlin Bicetre (Paris), France
[24]Department of Pediatrics, University of Padua, Padua, Italy
[25]Azienda Policlinico Universita' di Catania, Clinica Pediatrica, Catania, Italy
[26]Kocaeli University Hospital, Pediatric Nephrology, Kocaeli, Turkey
[27]Hospital Infantil de Mexico, Medicina Interna y Reumatologia, Mexico City, Mexico
[28]Hospital de Pediatria Juan P Garrahan, Servicio de Inmunología/Reumatología, Buenos Aires, Argentina
[29]Great Ormond Street Hospital, Renal Unit, London, UK
[30]Dipartimento di Pediatria, Ospedale A Meyer, Firenze, Italy
[31]Zentrum für Allgemeine Paediatrie und Neonatologie, Sankt Augustin, Germany
[32]Hospital Sant Joan de Déu, Pediatric Rheumatology Unit, Universitat de Barcelona, Esplugues, Barcelona, Spain
[33]Hospital Sor Maria Ludovica, Unidad de Reumatologia, La Plata, Argentina
[34]Juliane Marie Centret, Rigshospitalet, Juliane Marie Centret, Rigshospitalet, København, Denmark
[35]IRCCS Istituto G Gaslini, Nefrologia, Genova, Italy

Acknowledgements The authors thank the EULAR/PRINTO/PRES for their financial support for the project. The authors thank Professor Ihsan Dogramacı for his support for the study. Drs Silvia M Iusan, MD, Anuela Kondi, MD, Valentin Pop, MD and Iris Vilca, MD were recipients of a EULAR training bursary. The authors thank Dr Laura Carenini and Dr Luca Villa from the PRINTO coordinating centre who managed the data collection.

Funding EULAR/PRINTO/PRES.

Competing interests None.

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 Not commissioned; externally peer reviewed.

Principal investigator: Seza Ozen, MD, Ankara, Turkey. **Project coordinator:** Nicolino Ruperto, MD, MPH, Genoa, Italy. **Vienna (Austria) Consensus Conference**[10] **Consensus moderator:** Nicolino Ruperto, MD, MPH, Genoa, Italy. **Consensus participants:** Seza Ozen, MD, Ankara, Turkey, Principal Investigator; Michael J Dillon, MD, London, UK; Arvind Bagga, MD, New Delhi, India; Karyl Barron, MD, Bethesda, MD, USA; Jean Claude Davin, MD, Amsterdam, The Netherlands; Tomisaku Kawasaki, MD, Tokio, Japan; Carol Lindsley, MD, Kansas City, KS, USA; Ross E Petty, MD, Vancouver, BC, Canada; Anne Marie Prieur, MD, Paris, France; Angelo Ravelli, MD, Genoa, Italy; Patricia Woo, MD, London, UK. **Ankara Consensus Conference: Consensus moderator:** Nicolino Ruperto, MD, MPH, Genoa, Italy. **Moderator assistant:** Giovanni Filocamo, MD, Genoa, Italy. **Consensus bio-statistician:** Angela Pistorio, MD, PhD, Genoa, Italy. **PRINTO**

analysis committee: Nicolino Ruperto, MD, MPH, Genoa, Italy; Seza Ozen, MD, Ankara, Turkey, Principal Investigator; Angela Pistorio, MD, PhD, Genoa, Italy; Angelo Ravelli MD, Genoa, Italy; Alberto Martini MD, Genoa, Italy; Silvia M Iusan, MD, Genoa, Italy; Giovanni Filocamo, MD, Genoa, Italy; Claudia Saad Magalhães, Genoa, Italy. **Consensus participants:** Paul Brogan, MD, London, UK; David A Cabral, MD, Vancouver, BC, Canada; Ruben Cuttica, MD, Buenos Aires, Argentina; Pavla Dolezalova, MD, Prague, Czech Republic; Raju Khubchandani, MD, Mumbai, India; Daniel Lovell, MD, Cincinnati, OH, USA; Alberto Martini, MD, Genoa, Italy; Kathleen M O'Neil, MD, Oklahoma City, OK, USA; Seza Ozen, MD, Ankara, Turkey, Principal Investigator; Pierre Quartier, MD, Paris, France; Angelo Ravelli, MD, Genoa, France. We are also indebted to all PRINTO/PRES members (97 centres in 36 countries) and to the families for their participation in the study: **Albania** Anuela Kondi, MD; **Argentina** Maria Teresa Apaz, MD, Esteban Rodolfo Castell, MD, Ruben Cuttica, MD, Graciela Espada, MD, Stella Maris Garay, MD, Ricardo Russo, MD, Iris Vilca, MD; **Austria** Jurgen Brunner, MD; **Brazil** Maria Odete Hilario, MD, Sheila Knupp Feitosa de Oliveira, MD, Claudia Saad Magalhães, MD, Clovis Artur Silva, MD, Flavio Sztajnbok, MD; **Bulgaria** Dimitrina Mihaylova, MD; **Chile** Benito Gonzalez, MD, Ximena Norambuena, MD; **Croatia** Lana Tambic-Bukovac, MD; **Czech Republic** Pavla Dolezalova, MD; **Denmark** Troels Herlin, MD, Susan Nielsen, MD; **El Salvador** Mauricio Alegria, MD; **Estonia** Chris Pruunsild, MD; **France** Alexandre Belot, MD, Rolando Cimaz, MD, Djamal Djeddi, MD, Michel Fischbach, MD, Erick Grouteau, MD, Isabelle Kone Paut, MD, Pierre Quartier, MD; **Georgia** Maka Ioseliani, MD, Karaman Pagava, MD; **Germany** Frank Dressler, MD, Ivan Foeldvari, MD, Dirk Foell, MD, Hermann Girschick, MD, Gerd Horneff, MD, Rolf Keitzer, MD, Rolf-Michael Kuester, MD, Hartmut Michels, MD, Ralf Trauzeddel, MD, Claudia Sengler MD; **Greece** Florence Kanakoudi-Tsakalidou, Polyxeni Pratsidou, MD, Olga Vougiouka, MD; **India** Arvind Bagga, MD, Raju Khubchandani, MD; **Iraq** Saad Alhasani, MD; **Israel** Judith Barash, MD, Yackov Berkun, MD, Riva Brik, MD, Tsvia Tauber, MD, Yosef Uziel, MD; **Italy** Maria Giannina Alpigiani, MD, Giancarlo Barbano, MD, Patrizia Barone, MD, Claudia Bracaglia, MD, Luciana Breda, MD, Antonella Buoncompagni, MD, Giuseppina Calcagno, MD, Luca Cantarini, MD, Rolando Cimaz, MD, Elisabetta Cortis, MD, Gianfranco D'Angelo, MD, Sara Garozzo, MD, Loredana Lepore, MD, Silvia Magni Manzoni, MD, Alma Nunzia Olivieri, MD, Salvatore Scarpato, MD, Achille Stabile, Donato Rigante, MD, Francesco Zulian, MD; **Latvia** Ingrida Rumba, MD, Valda Stanevicha, MD; **Libya** Halima Ben Amer, MD; **Mexico** Adriana Cespedes Cruz, MD, Maria del Rocio Maldonado, MD; **Netherlands** Esther Hoppenreijs, MD, Marion A J van Rossum, MD, Nico Wulffraat, MD; **Peru** Amparo Ibanez Estrella, MD; **Poland** Henryka Mazur-Zielinska, MD; **Romania** Nicolae Iagaru, MD, Valentin Pop, MD, Calin Lazar, MD; **Russia** Vyacheslav Chasnyk, MD; **Saudi Arabia** Sulaiman M Al-Mayouf, MD; **Serbia** Srdjan Pasic, MD, Gordana Susic, MD; **Slovakia** Richard Vesely, MD; **Slovenia** Tadej Avcin, MD; **Spain** Jordi Anton, MD, María Luz Gamir, MD, Julia Garcia Consuegra, MD, Laura Nuno, MD; **Sweden** Anders Fasth, MD; **Turkey** Nuray Aktay Ayaz MD, Esra Baskin, MD, Ilmay Bilge, MD, Zelal Bircan, MD, Faysal Gok, MD, Balahan Makay MD, Seza Ozen, MD, Erbil Unsal, MD; **UK** Paul Brogan, MD, Kjell Tullus, MD; **USA** Marisa Klein-Gitelman, MD

REFERENCES

1. **Hunder GG**, Arend WP, Bloch DA, *et al.* The American College of Rheumatology 1990 criteria for the classification of vasculitis. Introduction. *Arthritis Rheum* 1990;**33**:1065–7.
2. **Bloch DA**, Michel BA, Hunder GG, *et al.* The American College of Rheumatology 1990 criteria for the classification of vasculitis. Patients and methods. *Arthritis Rheum* 1990;**33**:1068–73.
3. **Mills JA**, Michel BA, Bloch DA, *et al.* The American College of Rheumatology 1990 criteria for the classification of Henoch-Schönlein purpura. *Arthritis Rheum* 1990;**33**:1114–21.
4. **Arend WP**, Michel BA, Bloch DA, *et al.* The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. *Arthritis Rheum* 1990;**33**:1129–34.
5. **Lightfoot RW** Jr, Michel BA, Bloch DA, *et al.* The American College of Rheumatology 1990 criteria for the classification of polyarteritis nodosa. *Arthritis Rheum* 1990;**33**:1088–93.
6. **Leavitt RY**, Fauci AS, Bloch DA, *et al.* The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. *Arthritis Rheum* 1990;**33**:1101–7.
7. **Jennette JC**, Falk RJ, Andrassy K, *et al.* Nomenclature of systemic vasculitides. Proposal of an international consensus conference. *Arthritis Rheum* 1994;**37**:187–92.
8. **Phillip R**, Luqmani R. Mortality in systemic vasculitis: a systematic review. *Clin Exp Rheumatol* 2008;**26** (Suppl 51):S94–104.
9. **Sundel R**, Szer I. Vasculitis in childhood. *Rheum Dis Clin North Am* 2002;**28**:625–54.
10. **Ozen S**, Ruperto N, Dillon MJ, *et al.* EULAR/PReS endorsed consensus criteria for the classification of childhood vasculitides. *Ann Rheum Dis* 2006;**65**:936–41.
11. **Ruperto N**, Martini A. International research networks in pediatric rheumatology: the PRINTO perspective. *Curr Opin Rheumatol* 2004;**16**:566–70.
12. **Ozen S**, Pistorio A, Iusan SM, *et al*. The EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis, and childhood Takayasu arteritis. Ankara 2008. Part II: final classification criteria. *Ann Rheum Dis* 2010;**69**:798–806.
13. **Delbecq AL**, Van de Ven AH, Gustafson DH. *Group techniques for program planning. A guide to nominal group and Delphi processes*. Glenview, IL: Scott, Foresman and Company, 1975;**1**.
14. **Ruperto N**, Meiorin S, Iusan SM, *et al.* Consensus procedures and their role in pediatric rheumatology. *Curr Rheumatol Rep* 2008;**10**:142–6.
15. **Ruperto N**, Ravelli A, Murray KJ, *et al.* Preliminary core sets of measures for disease activity and damage assessment in juvenile systemic lupus erythematosus and juvenile dermatomyositis. *Rheumatology (Oxford)* 2003;**42**:1452–9.
16. **Ruperto N**, Ravelli A, Cuttica R, *et al.* The Pediatric Rheumatology International Trials Organization criteria for the evaluation of response to therapy in juvenile systemic lupus erythematosus: prospective validation of the disease activity core set. *Arthritis Rheum* 2005;**52**:2854–64.
17. **Ruperto N**, Ravelli A, Oliveira S, *et al.* The Pediatric Rheumatology International Trials Organization/American College of Rheumatology provisional criteria for the evaluation of response to therapy in juvenile systemic lupus erythematosus: prospective validation of the definition of improvement. *Arthritis Rheum* 2006;**55**:355–63.
18. **Felson DT**, Anderson JJ, Boers M, *et al.* American College of Rheumatology. Preliminary definition of improvement in rheumatoid arthritis. *Arthritis Rheum* 1995;**38**:727–35.
19. **Giannini EH**, Ruperto N, Ravelli A, *et al.* Preliminary definition of improvement in juvenile arthritis. *Arthritis Rheum* 1997;**40**:1202–9.
20. **Ruperto N**, Ravelli A, Falcini F, *et al.* Performance of the preliminary definition of improvement in juvenile chronic arthritis patients treated with methotrexate. Italian Pediatric Rheumatology Study Group. *Ann Rheum Dis* 1998;**57**:38–41.
21. **Rider LG**, Giannini EH, Brunner HI, *et al.* International consensus on preliminary definitions of improvement in adult and juvenile myositis. *Arthritis Rheum* 2004;**50**:2281–90.
22. **Ruperto N**, Ravelli A, Pistorio A, *et al.* The provisional Paediatric Rheumatology International Trials Organisation/American College of Rheumatology/European League Against Rheumatism Disease activity core set for the evaluation of response to therapy in juvenile dermatomyositis: a prospective validation study. *Arthritis Rheum* 2008;**59**:4–13.
23. **Mukhtyar C**, Lee R, Brown D, *et al.* Modification and validation of the Birmingham Vasculitis Activity Score (version 3). *Ann Rheum Dis* 2009;**68**:1827–32.
24. **Luqmani RA**. Assessing disease activity in the systemic vasculitides. *Curr Opin Rheumatol* 2002;**14**:23–8.
25. **Luqmani RA**, Bacon PA, Moots RJ, *et al.* Birmingham Vasculitis Activity Score (BVAS) in systemic necrotizing vasculitis. *QJM* 1994;**87**:671–8.
26. **Cohen J**. A coefficient of agreement for nominal scales. *Educ Psychol Meas* 1960;**20**:37–46.
27. **Landis JR**, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;**33**:159–74.
28. **Hanley JA**, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 1982;**143**:29–36.

EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part I: Overall methodology and clinical characterisation

Nicolino Ruperto, Seza Ozen, Angela Pistorio, Pavla Dolezalova, Paul Brogan, David A Cabral, Ruben Cuttica, Raju Khubchandani, Daniel J Lovell, Kathleen M O'Neil, Pierre Quartier, Angelo Ravelli, Silvia M Iusan, Giovanni Filocamo, Claudia Saad Magalhães, Erbil Unsal, Sheila Oliveira, Claudia Bracaglia, Arvind Bagga, Valda Stanevicha, Silvia Magni Manzoni, Polyxeni Pratsidou, Loredana Lepore, Graciela Espada, Isabelle Kone Paut, Francesco Zulian, Patrizia Barone, Zelal Bircan, Maria del Rocio Maldonado, Ricardo Russo, Iris Vilca, Kjell Tullus, Rolando Cimaz, Gerd Horneff, Jordi Anton, Stella Garay, Susan Nielsen, Giancarlo Barbano, Alberto Martini and for the Paediatric Rheumatology International Trials Organisation (PRINTO)

Ann Rheum Dis 2010 69: 790-797 originally published online April 13, 2010
doi: 10.1136/ard.2009.116624

Notes

Correction

Nicolino Ruperto, Seza Ozen, Angela Pistorio, *et al*. EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part I: Overall methodology and clinical characterisation. *Ann Rheum Dis* 2010;**69**:790–797. The following authors name, Isabella Kone-Paut should have been published as Kone-Paut I.

doi:10.1136/ard.2009.116624corr1