2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for granulomatosis with polyangiitis

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ABSTRACT

Objective To develop and validate revised classification criteria for granulomatosis with polyangiitis (GPA).

Methods Patients with vasculitis or comparator diseases were recruited into an international cohort. The study proceeded in five phases: (1) identification of candidate criteria items using consensus methodology, (2) prospective collection of candidate items present at the time of diagnosis, (3) data-driven reduction of the number of candidate items, (4) expert panel review of cases to define the reference diagnosis and (5) derivation of a points-based risk score for disease classification in a development set using least absolute shrinkage and selection operator logistic regression, with subsequent validation of performance characteristics in an independent set of cases and comparators.

Results The development set for GPA consisted of 578 cases of GPA and 652 comparators. The validation set consisted of an additional 146 cases of GPA and 161 comparators. From 91 candidate items, regression analysis identified 26 items for GPA, 10 of which were retained. The final criteria and their weights were as follows: bloody nasal discharge, nasal crusting or sino-nasal congestion (+3); cartilaginous involvement (+2); conductive or sensorineural hearing loss (+1); cytoplasmic antineutrophil cytoplasmic antibody (ANCA) or anti-proteinase 3 ANCA positivity (+5); pulmonary nodules, mass or cavitation on chest imaging (+2); granuloma or giant cells on biopsy (+2); inflammation or consolidation of the nasal/paranasal sinuses on imaging (+1); pauci-immune glomerulonephritis (+1); perinuclear ANCA or antimyeloperoxidase ANCA positivity (−1); and eosinophil count ≥1×10^9/L (−4). After excluding mimics of vasculitis, a patient with a diagnosis of small- or medium-vessel vasculitis could be classified as having GPA if the cumulative score was ≥5 points. When these criteria were tested in the validation data set, the sensitivity was 93% (95% CI 87% to 96%) and the specificity was 94% (95% CI 89% to 97%).

Conclusion The 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for GPA demonstrate strong performance characteristics and are validated for use in research.

INTRODUCTION

The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) are multisystem disorders involving inflammation of the small blood vessels and include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA).[1] GPA is characterised by necrotising granulomatous inflammation involving the ears, nose and upper and lower respiratory tracts, and necrotising vasculitis affecting predominantly small- to medium-sized vessels, often including necrotising glomerulonephritis.[1]

Unlike diagnostic criteria, the purpose of classification criteria is to ensure that a homogeneous population is selected for inclusion in clinical trials and other research studies of GPA. In 1990, the American College of Rheumatology (ACR) published criteria for the classification of GPA (then named Wegener's granulomatosis).[2–4] The 1990 criteria were effective and widely accepted, facilitating coordinated approaches to international randomised controlled trials.[5 6] In 2011 it was proposed to change the name 'Wegener's granulomatosis' to 'granulomatosis with polyangiitis' with subsequent wide adoption of the new terminology.[7–9] The 1994 and 2012 publications of the International Chapel Hill Consensus Conference (CHCC) nomenclature for vasculitis clarified and standardised the nomenclature of the systemic vasculitides.[1 10] The CHCC is a nomenclature system based on expert consensus rather than a classification system.[1]

There are several important reasons for the development of revised classification criteria for the vasculitides, including a decline in the sensitivity of the 1990 ACR classification criteria, particularly for AAV[11]; a consensus that any such criteria must now incorporate testing for ANCA; increased and widespread use, since 1990, of cross-sectional diagnostic imaging tools, including MRI and CT[12 13]; and the introduction and adoption of the classification of patients with MPA, a term not in use in the 1990 ACR classification criteria.

There have been methodological advances in the derivation of classification criteria, moving from the 'number of criteria' rule, as used in the ACR 1990 criteria,[3] toward weighted criteria with threshold scores, as demonstrated in the 2010 classification criteria for rheumatoid arthritis.[14] Weighted criteria improve measurement properties of classification

criteria because certain items within a criteria list may be more discriminative. The previous 1990 criteria for vasculitis collected retrospective data from patient files, without specification of which items were relevant at the time of diagnosis compared with those that were important later in the disease process. Criteria based on prospectively collected data sets from newly diagnosed patients should have higher face validity as inclusion criteria for future clinical trials of early-stage disease. This article outlines the development and validation of the revised ACR/European Alliance of Associations for Rheumatology (EULAR)—endorsed classification criteria for GPA.

METHODS

A detailed and complete description of the methods involved in the development and validation of the classification criteria for GPA is provided in online supplemental appendix 1. Briefly, an international Steering Committee comprising clinician investigators with expertise in vasculitis, statisticians, and data managers was established to oversee the overall Diagnostic and Classification Criteria in Vasculitis (DCVAS) project.[15] The Steering Committee established a 5-stage plan using data-driven and consensus methodology to develop the criteria for each of six forms of vasculitis.

Stage 1: generation of candidate classification items for the systemic vasculitides

Candidate classification items were generated by expert opinion and reviewed by a group of vasculitis experts across a range of specialties using a nominal group technique.

Stage 2: DCVAS prospective observational study

A prospective, international, multisite observational study was conducted (see collaborators for study investigators and sites). Consecutive patients representing the full spectrum of disease were recruited from academic and community practices. Patients were included if they were 18 years or older and had a diagnosis of vasculitis or a condition that mimics vasculitis. Patients with AAV could only be enrolled within 2 years of diagnosis. Only data present at diagnosis were recorded.

Stage 3: refinement of candidate items specifically for AAV

The Steering Committee conducted a data-driven process to reduce the number of candidate items of relevance to cases and comparators for AAV. Items were selected for exclusion if they had a prevalence of <5% within the data set and/or they were not clinically relevant for classification criteria (eg, related to infection, malignancy or demographic characteristics). Low-frequency items of clinical importance could be combined, when appropriate.

Stage 4: expert review to derive a gold standard—defined set of cases of AAV

Experts in vasculitis from a wide range of geographic locations and specialties reviewed all submitted cases of vasculitis and a random selection of mimics of vasculitis. Each reviewer was asked to review ~50 submitted cases to confirm the diagnosis and to specify the certainty of their diagnosis as follows: very certain, moderately certain, uncertain or very uncertain. Only cases agreed on with at least moderate certainty were retained for further analysis.

Stage 5: derivation and validation of the final classification criteria for GPA

The DCVAS AAV data set was randomly split into development (80%) and validation (20%) sets. Comparisons were performed between cases of GPA confirmed by expert review and a comparator group randomly selected from the DCVAS cohort in the following proportions: another type of AAV (including MPA and EGPA), 64%; another form of small-vessel vasculitis (eg, cryoglobulinaemic vasculitis) or medium-vessel vasculitis (eg, polyarteritis nodosa), 36%. Least absolute shrinkage and selection operator (lasso) logistic regression was used to identify items from the data set and create a parsimonious model including only the most important items. The final items in the model were formulated into a clinical risk-scoring tool with each factor assigned a weight based on its respective regression coefficient. A threshold that best balanced sensitivity and specificity was identified for classification.

In sensitivity analyses, the final classification criteria were applied to an unselected population of cases and comparators from the DCVAS data set based on the submitting physician diagnosis. Comparison was also made between the measurement properties of the new classification criteria for GPA and the 1990 ACR classification criteria for GPA using pooled data from the development and validation sets.

RESULTS

Generation of candidate classification items for the systemic vasculitides

The Steering Committee identified >1000 candidate items for the DCVAS case report form (see online supplemental appendix 2.

DCVAS prospective observational study

Between January 2011 and December 2017, the DCVAS study recruited 6991 participants from 136 sites in 32 countries. Information on the DCVAS sites, investigators and study participants is listed in online supplemental appendices 3–5.

Refinement of candidate items specifically for AAV

Following a data-driven and expert consensus process, 91 items from the DCVAS case report form were retained for regression analysis, including 45 clinical (14 composite), 18 laboratory (2 composite), 12 imaging (all composite) and 16 biopsy (1 composite) items. Some clinical items were removed in favour of similar but more specific pathophysiological descriptors. Online supplemental appendix 6, lists the final candidate items used in the derivation of the classification criteria for GPA, MPA and EGPA.

Expert review to derive a gold standard—defined final set of cases of AAV

Fifty-five independent experts reviewed vignettes derived from the case report forms for 2871 cases submitted with a diagnosis of either small-vessel vasculitis (90% of case report forms) or another type of vasculitis or a mimic of vasculitis (10% of case report forms). The characteristics of the expert reviewers are shown in online supplemental appendix 7. A flow chart showing the results of the expert review process is shown in online supplemental appendix 8. A total of 2072 cases (72%) passed the process and were designated as cases of vasculitis; these cases were used for the stage 5 analyses.

After expert review, 724 of 843 cases retained a reference diagnosis of GPA. There were 813 comparators randomly selected

Table 1 Demographic and disease features of cases of GPA and comparators*

	GPA (n=724)	Comparators (n=813)*	P value
Age, mean±SD years	53.6±16.2	56.4±17.1	0.001
Sex, no. (%) female	340 (47.0)	424 (52.2)	0.048
Maximum serum creatinine, mean			0.077
μmoles/L	168.3	185.2	
mg/dL	1.9	2.1	
cANCA positive, no. (%)	531 (73.3)	40 (4.9)	<0.001
pANCA positive, no. (%)	71 (9.8)	342 (42.1)	<0.001
Anti-PR3-ANCA positive, no. (%)	595 (82.2)	21 (2.6)	<0.001
Anti-MPO-ANCA positive, no. (%)	59 (8.1)	399 (49.1)	<0.001
Maximum eosinophil count ≥1×10^9/L, no. (%)	196 (27)	366 (45)	<0.001

*Diagnoses of comparators for the classification criteria for granulomatosis with polyangiitis (GPA) included microscopic polyangiitis (n=291), eosinophilic granulomatosis with polyangiitis (n=226), polyarteritis nodosa (n=51), non-ANCA-associated small-vessel vasculitis that could not be subtyped (n=51), Behçet's disease (n=50), IgA vasculitis (n=50), cryoglobulinaemic vasculitis (n=34), ANCA-associated vasculitis that could not be subtyped (n=25), primary central nervous system vasculitis (n=19) and antiglomerular basement membrane disease (n=16). ANCA, antineutrophil cytoplasmic antibody; anti-MPO-ANCA, anti-myeloperoxidase-ANCA; anti-PR3-ANCA, anti-proteinase 3-ANCA; cANCA, cytoplasmic antineutrophil cytoplasmic antibody; GPA, granulomatosis with polyangiitis; pANCA, perinuclear ANCA.

for analysis. Table 1 shows the demographic and disease features of the 1537 cases included in this analysis (724 patients with GPA and 813 comparators), of which 1230 (80%; 578 patients with GPA and 652 comparators) were in the development set, and 307 (20%; 146 patients with GPA and 161 comparators) were in the validation set.

Derivation and validation of the final classification criteria for GPA

Lasso logistic regression analysis using all 91 items resulted in a model of 26 independent items (see online supplemental appendix 9B). The variables 'positive test for cytoplasmic ANCA (cANCA)' and 'positive test for anti-proteinase 3 (anti-PR3) antibody' and the variables 'positive test for perinuclear ANCA (pANCA)' and 'positive test for antimyeloperoxidase (anti-MPO) antibody' were strongly colinear and were combined within the model as 'positive test for cANCA or positive test for anti-PR3 antibody' and 'positive test for pANCA or positive test for anti-MPO antibody', respectively. Each item was scrutinised for inclusion based on statistical significance, clinical relevance and specificity to GPA, resulting in 10 final items. Weighting of an individual criterion was based on logistic regression fitted to the 10 selected items (see online supplemental appendix 10B).

Model performance

Use of a cut-off of ≥5 for total risk score (see online supplemental appendix 11B, for different cut points) yielded a sensitivity of 92.5% (95% CI 86.9% to 96.2%) and a specificity of 93.8% (95% CI 88.9% to 97.0%) in the validation set. The area under the curve (AUC) for the model was 0.98 (95% CI 0.98 to 0.99) in the development set and 0.99 (95% CI 0.98 to 1.00) in the validation set (online supplemental appendix 12B). The final classification criteria for GPA are shown in figure 1 (for the slide presentation version, see online supplemental figure 1).

Sensitivity analyses

The classification criteria for GPA were applied to 2511 patients randomly selected from the DCVAS database using the original physician-submitted diagnosis (n=483 GPA and 2028 comparators). Use of the same cut point of ≥5 points for the classification of GPA yielded a similar specificity of 94.6% but a lower sensitivity of 83.8%. This upheld the a priori hypothesis that specificity would remain unchanged but sensitivity would be reduced in a population with fewer clear-cut diagnoses of GPA (ie, cases that did not pass expert review).

When the 1990 ACR classification criteria for GPA were applied to the DCVAS data set, the criteria performed poorly due to low sensitivity (69.3%) and moderate specificity (75.8%), with an AUC of 0.73 (95% CI 0.70 to 0.75).

DISCUSSION

Presented here are the final 2022 ACR/EULAR GPA classification criteria. A 5-stage approach has been used, underpinned by data from the multinational prospective DCVAS study and informed by expert review and consensus at each stage. The comparator group for developing and validating the criteria were other forms of AAV and other small- and medium-vessel vasculitides, the clinical entities where discrimination from GPA is difficult, but important. The new criteria for GPA have excellent sensitivity and specificity and incorporate ANCA testing and modern imaging techniques. The criteria were designed to have face and content validity for use in clinical trials and other research studies.

These criteria are validated and intended for the purpose of *classification* of vasculitis and are not appropriate for use in establishing a *diagnosis* of vasculitis. The aim of the classification criteria is to differentiate cases of GPA from similar types of vasculitis in research settings. Therefore, the criteria should only be applied when a diagnosis of small- or medium-vessel vasculitis has been made and all potential 'vasculitis mimics' have been excluded. The exclusion of mimics is a key aspect of many classification criteria, including those for Sjögren's syndrome[16] and rheumatoid arthritis.[14] The 1990 ACR classification criteria for vasculitis perform poorly when used for diagnosis (ie, when used to differentiate between cases of vasculitis vs mimics without vasculitis),[17] and it is expected that the 2022 criteria would also perform poorly if used inappropriately as diagnostic criteria in people in whom alternative diagnoses, such as infection or other non-vasculitis inflammatory diseases, are still being considered. The relatively low weight assigned to glomerulonephritis in these classification criteria highlights the distinction between classification and diagnostic criteria. While detection of kidney disease is important to diagnose GPA, glomerulonephritis is common among patients with either GPA or MPA and thus does not function as a strong classifier between these conditions.

These criteria differ from the previous 1990 ACR criteria in that they have been developed using cases presenting prospectively at the start of their disease process. This approach is different from the methods used to generate the 1990 ACR criteria, in which prevalent case records were used, potentially including items related to irreversible damage accrued over time. Inclusion of newly diagnosed cases in these criteria should improve their accuracy within the context of early intervention trials as well as refractory disease. The comparators used for these new criteria are also more appropriate and are closer mimics of GPA; for example, comparators with predominantly small-vessel vasculitis rather than predominantly giant cell arteritis were included. The new criteria perform better than previous criteria within this

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CLASSIFICATION CRITERIA FOR GRANULOMATOSIS WITH POLYANGIITIS

CONSIDERATIONS WHEN APPLYING THESE CRITERIA

- **These classification criteria should be applied to classify a patient as having granulomatosis with polyangiitis when a diagnosis of small- or medium-vessel vasculitis has been made**
- **Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria**

CLINICAL CRITERIA

Nasal involvement: bloody discharge, ulcers, crusting, congestion, blockage, or septal defect / perforation	+3
Cartilaginous involvement (inflammation of ear or nose cartilage, hoarse voice or stridor, endobronchial involvement, or saddle nose deformity)	+2
Conductive or sensorineural hearing loss	+1

LABORATORY, IMAGING, AND BIOPSY CRITERIA

Positive test for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) or antiproteinase 3 (anti-PR3) antibodies	+5
Pulmonary nodules, mass, or cavitation on chest imaging	+2
Granuloma, extravascular granulomatous inflammation, or giant cells on biopsy	+2
Inflammation, consolidation, or effusion of the nasal/paranasal sinuses, or mastoiditis on imaging	+1
Pauci-immune glomerulonephritis on biopsy	+1
Positive test for perinuclear antineutrophil cytoplasmic antibodies (pANCA) or antimyeloperoxidase (anti-MPO) antibodies	-1
Blood eosinophil count ≥ 1 x10^9/liter	-4

Sum the scores for 10 items, if present. A score of ≥ 5 is needed for classification of GRANULOMATOSIS WITH POLYANGIITIS.

Figure 1 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for granulomatosis with polyangiitis.

data set.[11] ANCA is a major discriminator within these criteria, although patients can be classified as having GPA without having a positive test result for ANCA if they have a sufficient number of other features. These new criteria were validated in an independent data set and are weighted with threshold scores[14 16] to maximise predictive ability.

There are some study limitations to consider. Although this was the largest international study ever conducted in vasculitis, most patients were recruited from Europe, Asia and North America. The performance characteristics of the criteria should be further tested in African and South American populations, which may have different clinical presentations of vasculitis. These criteria were developed using data collected from adult patients with vasculitis. Although the clinical characteristics of GPA and the other vasculitides which these criteria were tested against are not known to differ substantially between adults and children, these criteria should be applied to children with some caution. The scope of the criteria is intentionally narrow and applies only to patients who have been diagnosed as having vasculitis. Diagnostic criteria are not specified. The criteria are intended to identify homogeneous populations of disease and, therefore, may not be appropriate for studies focused on the full spectrum of clinical heterogeneity in these conditions. To maximise relevance and face validity of the new criteria, study sites and expert reviewers were recruited from a broad range of countries and different medical specialties. Nonetheless, the majority of patients were recruited from academic rheumatology or nephrology units, which could have introduced referral bias.

A key strength of this study is the use of an independent expert review process to confirm cases of GPA and comparators to avoid the circularity of using predefined criteria to define the gold standard. Approximately one-quarter of cases were excluded via this process, due to either a lack of consensus on exact diagnosis or insufficient data available to make the diagnosis. A limitation of this approach, however, could be the exclusion of true, but less clearcut cases submitted by the original physicians. It is important that cases are classified accurately for inclusion in clinical trials; therefore, some loss of sensitivity

may be appropriate. Importantly, this study also demonstrated that applying the new criteria for GPA to the whole unselected DCVAS data set resulted in a reduction in sensitivity while maintaining specificity. Thus, the criteria should also be useful in a more generalised, 'real-world' population.

The 2022 ACR/EULAR classification criteria for GPA are the product of a rigorous methodological process that used an extensive data set generated by the work of a remarkable international group of collaborators. These criteria have been endorsed by the ACR and EULAR and are now ready for use to differentiate one type of vasculitis from another to define populations in research studies.

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SUPPLEMENTARY MATERIAL

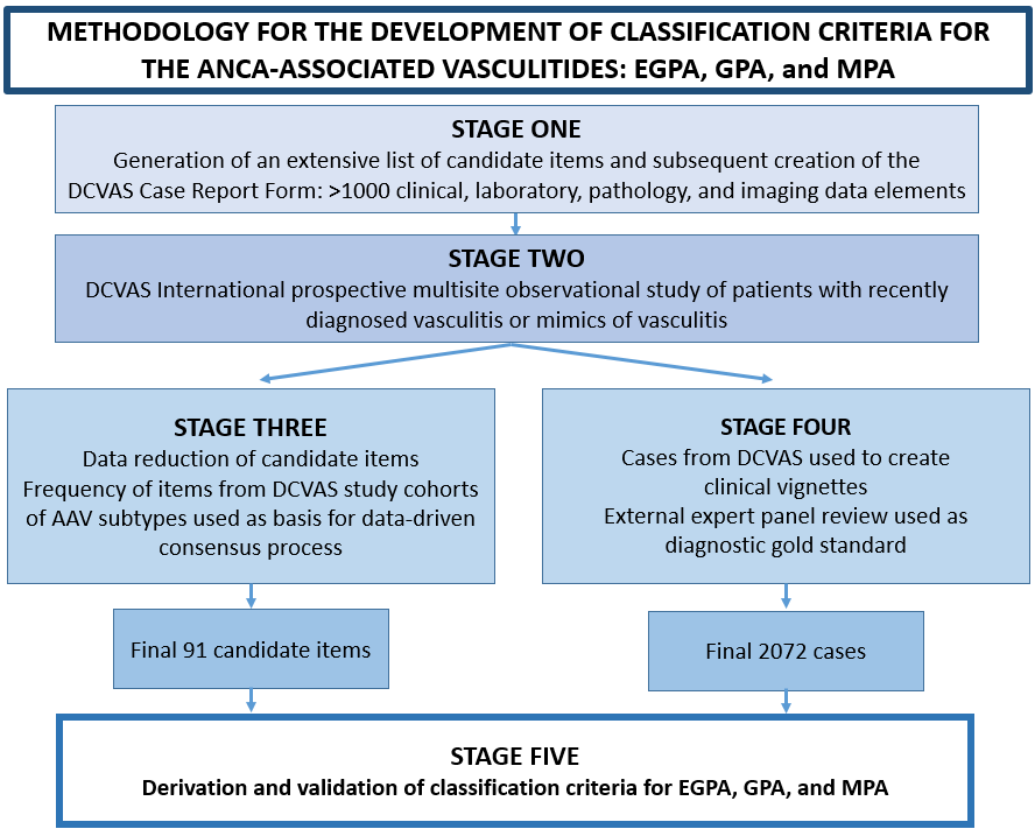
AMERICAN COLLEGE OF RHEUMATOLOGY AND EUROPEAN LEAGUE AGAINST RHEUMATISM 2021 CLASSIFICATION CRITERIA FOR ANCA-ASSOCIATED VASCULITIS [GRANULOMATOSIS WITH POLYANGIITIS, MICROSCOPIC POLYANGIITIS, AND EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS]

1. **Detailed description of the research methods for the development of classification criteria for eosinophilic granulomatosis with polyangiitis, granulomatosis with polyangiitis, and microscopic polyangiitis**
2. **Diagnosis and Classification of Vasculitis Study Case Report Form**
3. **Diagnosis and Classification of Vasculitis Study Sites and Investigators**
4. **Diagnosis and Classification of Vasculitis Study Sites/Investigators Characteristics**
5. **Study Participant Details**
6. **Final candidate items used within each regression analysis to derive classification criteria for granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis**
7. **Expert reviewer characteristics**
8. **Flow chart of expert review process to create the Diagnosis and Classification of Vasculitis Study dataset for ANCA-associated vasculitis**
9. **Results of regression analysis for each type of ANCA-associated vasculitis**
10. **Data-driven and clinically-selected models for each type of ANCA-associated vasculitis with associated risk scored based off beta coefficient weighting**
11. **Performance characteristics of a points-based risk score for each type of ANCA-associated vasculitis with different thresholds**
12. **Discrimination curves for the classification criteria for each type of ANCA-associated vasculitis**

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 1. Detailed description of the research methods for the development of classification criteria for eosinophilic granulomatosis with polyangiitis, granulomatosis with polyangiitis, and microscopic polyangiitis

An international Steering Committee comprised of clinician investigators with expertise in vasculitis, statisticians, and data managers was established to oversee the overall DCVAS project. A five-stage process was used to derive each of the classification criteria for granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), and microscopic polyangiitis (MPA). An overview of each stage of the methodology is presented in the figure below.



EGPA: eosinophilic granulomatosis with polyangiitis; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis

Full details of each stage in the process are described below.

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Stage One: Generation of candidate classification items for the systemic vasculitides

Candidate items were generated by expert opinion including items from the 1990 ACR Classification Criteria, the 2012 Chapel Hill Nomenclature, and the major disease activity and damage indices for AAV (1-5). Items were categorized as demographic, symptoms, physician-observed findings, laboratory tests, diagnostic radiology, and biopsy results. Candidate items were reviewed and discussed at a major international vasculitis conference, and nominal group technique was used to modify the potential list of items with input from vasculitis experts across a range of specialties. The full list of items was then reviewed by the Steering Committee to address potential omissions or redundancy in the list with appropriate revisions made. A list of data elements was finalized by the Steering Committee for use in prospective data collection in Stage Two. The resulting DCVAS case report form (CRF) is shown in **Supplementary Materials 2**.

Stage Two: DCVAS prospective observational study

The DCVAS study is an international prospective multisite observational study of patients recently-diagnosed with vasculitis or mimics of vasculitis (6).

The University of Oxford sponsored the study, and ethics approval was given by the UK Berkshire Research Ethics Committee (reference 10/H0505/19) on May 7, 2010. The study was performed in accordance with the 1964 Declaration of Helsinki, ethical approval was obtained by national and local ethics committees in accordance with national legislation.

Site Selection

A wide range of sites were targeted for inclusion to ensure representation from different geographical regions, clinical specialties, and types of sites (including both academic and non-academic clinical practices). To increase the number and types of study sites, the DCVAS study was promoted through national and international presentations, and the DCVAS website (**Supplementary Materials 3 & 4**).

Patient Recruitment

Inclusion criteria for the DCVAS study:

1) Patients aged ≥18 years; 2) Ability to give informed consent or consent via an appropriate surrogate; 3) i) Diagnosis as made by the submitting clinician within the previous two years of GPA, MPA, EGPA, other AAV, giant cell arteritis, anti-glomerular basement membrane disease, cryoglobulinemic vasculitis, Behçet's disease, primary central nervous system vasculitis, IgA vasculitis, isolated aortitis, other large-vessel vasculitis, or a diagnosis within the previous five years of polyarteritis nodosa or Takayasu's arteritis; OR ii) Diagnosis as made by the submitting clinician within the previous two years of a condition which mimics systemic vasculitis, e.g., infection, tumor, other inflammatory conditions (see **Supplementary Materials 5** for the complete details of physician-submitted diagnoses). For patients enrolled six months after diagnosis, only patients for whom the submitting physician had complete records detailing symptoms present at the time of diagnosis were eligible for study inclusion.

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Exclusion criteria:
1) Patients < 18 years of age; 2) Inability to provide informed consent.

Submitting-Physician Diagnosis
For patients with vasculitis who were enrolled in the DCVAS study within six months of the initial diagnosis, the submitting physician was asked to confirm the accuracy of the diagnosis at the six-month time point in a separate study form.

Data Collection
Paper and web-based versions of the CRF were used **(Supplementary Materials 2)**. Data from patients with a working diagnosis of systemic vasculitis or mimics of systemic vasculitis were entered. The diagnosis and level of certainty for diagnosis was requested from the submitting physician at time of diagnosis and six months later. Data from all study participants was reviewed at a central location for completeness. Local investigators were contacted to resolve any data discrepancies.

Stage Three: Refinement of candidate items specifically for ANCA-associated vasculitis

The DCVAS CRF included > 1000 data elements. The final statistical analysis to create classification criteria for all subtypes of AAV, including GPA, required approximately 100 predictors to avoid over-fitting of the final model during regression analysis (7).

A data-driven process of reduction of the DCVAS initial items was used to retain candidate items of relevance to cases and comparators for AAV. Seven members of the DCVAS Steering Committee (PG, RL, PM, CP, RS, JR, RW) were split into groups of two to each review a different category of items in terms of frequency across all AAV subtypes, and assess clinical relevance: clinical features, laboratory results, pathology results, and imaging. Data on frequency of items was prepared for review from cases of GPA, MPA and EGPA (physician diagnosis) from the DCVAS dataset. Items were selected for exclusion if they had i) prevalence of <5% within the data set and/or ii) they were non-clinically relevant for classification criteria (e.g., related to infection, malignancy, or demography). Low-frequency items of clinical importance could be combined, when appropriate (for example the items for “fever”, “night sweats”, and “rigors”, see **Supplementary Materials 6** for single and composite items). Consensus was reached between the two independent Steering Committee members, who then presented and discussed the items for exclusion to reach agreement across the wider steering committee over the course of four teleconferences.

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Stage Four: Expert panel methodology to derive a gold standard-defined set of cases of ANCA-associated vasculitis

An online independent Expert Review Process was used to avoid the circularity of applying a previously derived gold standard such as the 1990 ACR Criteria (8). Experts in vasculitis from a wide range of geographical locations and specialties reviewed all cases of vasculitis submitted (see **Supplementary Materials 7** for the expert reviewer characteristics). Fifty-five external expert reviewers reviewed approximately 50 cases each. Reviewers were blinded to the submitting physician's diagnosis**.**

Clinical vignettes of each case, including clinical, laboratory, imaging, and biopsy results were produced using data from the CRFs and presented in a standard clinical vignette form**.** All cases labeled GPA, MPA, EGPA, or a different form of small vessel vasculitis by the submitting physician were reviewed. To ensure a rigorous process, 10% of cases with a submitting physician diagnosis of polyarteritis nodosa, other small-vessel vasculitis, large-vessel vasculitis, or a condition mimicking vasculitis were also randomly included for expert review.

For each case vignette, the expert reviewer indicated:

(i) whether or not the diagnosis was vasculitis
(ii) which category of vasculitis was present, based on vessel size (small, medium, large, or not categorizable)
(iii) if a type of vasculitis was chosen in (ii) then which subtype of vasculitis was present (for example, if AAV was selected, then a choice of GPA, MPA, EGPA, or uncertain sub-type was provided).

Reviewers were asked about their certainty for each of (i)-(iii) as follows: very certain, moderately certain, uncertain, or very uncertain.

A case was considered to be agreed in full if the Expert Reviewer's assessment matched the submitting physician's assessment at each level, with at least moderate certainty. Cases that were not agreed on expert review were submitted for a blinded second review by a member of the Steering Committee. If the Steering Committee member agreed with either the submitting physician's assessment or the initial expert reviewer with moderate certainty, then the case was agreed upon in full. Cases that were not agreed upon in full were rejected from further analysis. The panel review process was conducted in 2016 using all available data to date. Since study enrollment continued through 2017, additional cases of AAV were submitted to the DCVAS cohort that were not used for analysis.

A flow diagram depicting the results from the expert review process is provided in **Supplementary Materials 8**.

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Stage Five: Derivation and validation of the final classification criteria for the ANCA-associated vasculitides

A similar process for the derivation of each of the three final classification criteria for GPA, MPA and EGPA was followed. There were two methodological differences between the three criteria due to a higher proportion of GPA cases available for analysis than the other two types of AAV (as expected in line with known prevalence of the individual subtypes of AAV).

All cases with small or medium vessel vasculitis agreed by the expert review process in Stage 4 were included within the derivation of the GPA classification criteria as either cases (GPA) or comparators (See Table 1 GPA manuscript for subdivision of comparators). For the derivation of the MPA and EGPA criteria, only a proportion of the available GPA cases were included within the comparator groups. This was to avoid over-representation of GPA cases within each comparator group due to higher overall prevalence in the DCVAS dataset. GPA cases were chosen randomly for inclusion as comparators for EGPA and MPA. Exact numbers are shown in Table 1 of each manuscript.

For the GPA criteria, due to a high availability of GPA cases, the development and validation sets were derived from the DCVAS dataset of approved cases (Stage 4) on an 80:20 basis in order to maximize descriptive power of the resultant criteria. In contrast, the derivation of the MPA and EGPA sets split the DCVAS dataset into development and validation sets on a 50:50 basis.

For each criteria, the cases were comprised of one of either GPA, EGPA or MPA cases depending on the criteria, and the comparators made up of the two other forms of AAV plus other small and medium vessel vasculitides (exact numbers given in Table 1 of each manuscript). This process resulted in the generation of a binary outcome (AAV type or comparators) and the following steps were then followed for each criteria using the same 91 candidate item predictors identified from Stage Three.

The candidate predictors from Stage Three were included in a logistic regression model. Fractional polynomial regression modeling was used to assess evidence of linearity with outcome for continuous predictor variables (9). Multiple imputation was used to overcome potential bias from missing data (10). Lasso (least absolute shrinkage and selection operator) logistic regression was used to identify predictors from the dataset and create a parsimonious model including only the most important predictors (7,11,12). To extract the non-zero coefficients and, therefore, the significant predictors, a single model was fitted and adjusted for all potential variables with a 10-fold cross-validation and the minimum average mean-squared error (**Supplementary Materials 9**).

For each criterion, an iterative process within the Steering Committee was followed, with the clinician researchers and expert biostatisticians working collaboratively, to ensure face and content validity and acceptability of the resultant criteria. Most items were excluded because they were not significant predictors within the final model, i.e they did not differentiate between cases and comparators (for example for GPA, “presence of cutaneous infarcts or purpura”, or “maximum ESR”). Some predictors were statistically significant (i.e.

p<0.05) but were either redundant to other items in the final model or thought to be of low clinical significance (for example for GPA, "morning stiffness for >1 hour", or "unspecified tissue inflammation on biopsy"). These items were then removed from the model with the reduced item model tested in turn for discrimination, area under the curve (AUC) sensitivity and specificity to check there was no reduction in predictive value of the model. In this way, the final criteria were based on the most parsimonious models available including only the most important predictors.

The final items in the model were formulated into a clinical risk-scoring tool with each factor assigned a weight based on its respective regression coefficient (13) (**Supplementary Materials 10**). A threshold was identified for classification, which best balanced sensitivity and specificity (**Supplementary Materials 11 & 12**).

Sensitivity Analyses:
Since the expert review could have resulted in the exclusion of cases which were less clear-cut to classify, the final classification criteria were applied to an unselected population of cases and comparators from the DCVAS dataset based on the submitting physician diagnosis. The *a priori* hypothesis of these analyses was that if the final criteria were fit for purpose, specificity should be unchanged but sensitivity should be reduced within the unselected population. Comparators used for the unselected population analysis were as follows:

- *Comparators for GPA analysis*: MPA (404, 19.9%), EGPA (315, 15.5%), AAV that could not be subtyped (59, 2.9%), non-AAV small-vessel vasculitis that could not be subtyped (171, 8.4%), anti-glomerular basement membrane disease (14, 0.6%), cryoglobulinemic vasculitis (46, 2.3%), IgA vasculitis (240, 11.8%), Behçet's disease (151, 7.4%), primary central nervous system vasculitis (39, 1.9%), other forms of vasculitis that could not be subtyped (23, 1.1%), polyarteritis nodosa (130, 6.4%), giant cell arteritis (92, 4.5%), Takayasu's arteritis (91,4.5%), idiopathic aortitis (22, 1.1%), large-vessel vasculitis that could not be subtyped (52, 2.6%), and vasculitis mimics (179, 8.8%).
- *Comparators for EGPA analysis*: MPA (404, 15.8%), GPA (843, 33.0%), AAV that could not be subtyped (59, 2.3%), non-AAV small-vessel vasculitis that could not be subtyped (171, 6.7%), anti-glomerular basement membrane disease (14, 0.6%), CV (46, 1.8%), IgA vasculitis (240, 9.4%), Behçet's disease (151, 5.9%), primary central nervous system vasculitis (39, 1.5%), other form of vasculitis that could not be subtyped (23, 0.9%), polyarteritis nodosa (130, 5.1%), giant cell arteritis (92, 3.6%) Takayasu's arteritis (91, 3.6%), isolated aortitis (22, 0.9%), large-vessel vasculitis that could not be subtyped (52, 2.0%), and vasculitis mimics (179, 7.0%).
- *Comparators for MPA analysis*: EGPA (315, 12.7%), GPA (843, 34.2%), AAV that could not be subtyped (59, 2.40%), non-AAV small-vessel vasculitis that could not be subtyped (171, 6.9%), anti-glomerular basement membrane disease (14, 0.6%), cryoglobulinemic vasculitis (46, 1.9%), IgA vasculitis (240, 9.7%), Behçet's disease (151, 6.1%), primary central nervous system vasculitis (39, 1.6%), other form of vasculitis that could not be subtyped (23, 0.9%), polyarteritis nodosa (130, 5.3%), giant cell arteritis (92, 3.7%) Takayasu's arteritis (91, 3.7%), isolated aortitis (22, 0.9%), large-vessel vasculitis that could not be subtyped (52, 2.1%), and vasculitis mimics (179, 7.3%).

Comparisons were also made between the measurement properties of the new classification criteria for GPA and EGPA and the respective 1990 ACR Classification Criteria for GPA and EGPA using pooled data from the development and validation sets. These comparisons were not performed for MPA as there are no pre-existing classification criteria for this disease.

Additional Acknowledgements:

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Supplementary Materials 2. DCVAS Case Report Form

See separate PDF file titled "DCVAS Case Report Form"

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 3: Diagnosis and Classification of Vasculitis Study (DCVAS) Sites and Investigators

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Australia	Paul Gatenby	ANU Medical Centre, Canberra
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Canada	Lillian Barra	Lawson Health Research Institute, London, Ontario
Canada	Simon Carette/ Christian Pagnoux	Mount Sinai Hospital, Toronto
Canada	Navjot Dhindsa	University of Manitoba, Winnipeg
Canada	Aurore Fifi-Mah	University of Calgary, Alberta
Canada	Nader Khalidi	St Joseph's Healthcare Hamilton, Ontario
Canada	Patrick Liang	Sherbrooke University Hospital Centre
Canada	Nataliya Milman	University of Ottawa
Canada	Christian Pineau	McGill University
China	Xinping Tian	Peking Union Medical College Hospital, Beijing
China	Guochun Wang	China-Japan Friendship Hospital, Beijing
China	Tian Wang	Anzhen Hospital, Capital Medical University
China	Ming-hui Zhao	Peking University First Hospital
Czech Republic	Vladimir Tesar	General University Hospital, Prague
Denmark	Bo Baslund	University Hospital, Copenhagen (Rigshospitalet)
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Egypt	Amira Shahin	Cairo University
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ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

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Japan	Yoshihiro Arimura	Kyorin University Hospital
Japan	Hiroaki Dobashi	Kagawa University Hospital
Japan	Shouichi Fujimoto	Miyazaki University Hospital (HUB)
Japan	Masayoshi Harigai/Fumio Hirano	Tokyo Medical and Dental University Hospital
Japan	Junichi Hirahashi	University Tokyo Hospital
Japan	Sakae Honma	Toho University Hospital
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Japan	Hajime Kono	Teikyo University
Japan	Hirofumi Makino	Okayama University Hospital
Japan	Kazuo Matsui	Kameda Medical Centre, Kamogawa
Japan	Eri Muso	Kitano Hospital
Japan	Kazuo Suzuki/Kei Ikeda	Chiba University Hospital
Japan	Tsutomu Takeuchi	Keio University Hospital
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United Kingdom	Neil Basu	NHS Grampian, Aberdeen Royal Infirmary
United Kingdom	Iain Bruce	Manchester University Hospitals NHS Foundation Trust
United Kingdom	Kuntal Chakravarty	Barking, Havering and Redbridge University Hospitals NHS Trust
United Kingdom	Bhaskar Dasgupta	Southend University Hospital NHS Foundation Trust
United Kingdom	Oliver Flossmann	Royal Berkshire NHS Foundation Trust
United Kingdom	Nagui Gendi	Basildon and Thurrock University Hospitals NHS Foundation Trust
United Kingdom	Alaa Hassan	North Cumbria University Hospitals
United Kingdom	Rachel Hoyles	Oxford University Hospitals NHS Foundation Trust
United Kingdom	David Jayne	Cambridge University Hospitals NHS Foundation Trust
United Kingdom	Colin Jones	York Teaching Hospitals NHS Foundation Trust
United Kingdom	Rainer Klocke	The Dudley Group NHS Foundation Trust
United Kingdom	Peter Lanyon	Nottingham University Hospitals NHS Trust
United Kingdom	Cathy Laversuch	Taunton & Somerset NHS Foundation Trust, Musgrove Park Hospital
United Kingdom	Raashid Luqmani/ Joanna Robson	Nuffield Orthopaedic Centre, Oxford
United Kingdom	Malgorzata Magliano	Buckinghamshire Healthcare NHS Trust

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Country	Investigator	Participating Center
United Kingdom	Justin Mason	Imperial College Healthcare NHS Trust
United Kingdom	Win Win Maw	Mid Essex Hospital Services NHS Trust
United Kingdom	Iain McInnes	NHS Greater Glasgow & Clyde, Gartnavel Hospital & GRI
United Kingdom	John Mclaren	NHS Fife, Whyteman's Brae Hospital
United Kingdom	Matthew Morgan	University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital
United Kingdom	Ann Morgan	Leeds Teaching Hospitals NHS Trust
United Kingdom	Chetan Mukhtyar	Norfolk and Norwich University Hospitals NHS Foundation Trust
United Kingdom	Edmond O'Riordan	Salford Royal NHS Foundation Trust
United Kingdom	Sanjeev Patel	Epsom and St Helier University Hospitals NHS Trust
United Kingdom	Adrian Peall	Wye Valley NHS Trust, Hereford County Hospital
United Kingdom	Joanna Robson	University Hospitals Bristol NHS Foundation Trust
United Kingdom	Srinivasan Venkatachalam	The Royal Wolverhampton NHS Trust
United Kingdom	Erin Vermaak / Ajit Menon	Staffordshire & Stoke on Trent Partnership NHS Trust, Haywood Hospital
United Kingdom	Richard Watts	East Suffolk and North Essex NHS Foundation Trust
United Kingdom	Chee-Seng Yee	Doncaster and Bassetlaw Hospitals NHS Foundation Trust
United States	Daniel Albert	Dartmouth-Hichcock Medical Center
United States	Leonard Calabrese	Cleveland Clinic Foundation
United States	Sharon Chung	University of California, San Francisco
United States	Lindsy Forbess	Cedars-Sinai Medical Center
United States	Angelo Gaffo	University of Alabama at Birmingham
United States	Ora Gewurz-Singer	University of Michigan
United States	Peter Grayson	Boston University School of Medicine
United States	Kimberly Liang	University of Pittsburgh
United States	Eric Matteson	Mayo Clinic
United States	Peter A. Merkel	University of Pennsylvania
United States	Jason Springer	University of Kansas Medical Center Research Institute
United States	Antoine Sreih	Rush University Medical Center

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 4. Diagnosis and Classification of Vasculitis Study Sites and Investigators' Characteristics

Characteristics	**N=136**	**Characteristics**	**N=136**	**Characteristics**	**N=136 (%)**
Country		**Country**		**Specialty**	
Australia	3	Mexico	2	Rheumatology	99 (72.8)
Austria	1	Netherlands	2	Nephrology	21 (15.4)
Belgium	1	New Zealand	4	Neurology	5 (3.7)
Canada	8	Norway	2	Internal Medicine	4 (2.9)
China	4	Poland	1	Immunology	4 (2.9)
Czech Republic	1	Portugal	4	Dermatology	2 (1.5)
Denmark	1	Republic of Korea	1	Respiratory	1 (0.7)
Egypt	2	Russia	1		
Finland	2	Slovenia	1	**Number of patients with ANCA-associated vasculitis seen annually**	
Germany	6	Spain	2		
Hungary	1	Sri Lanka	1	0-10	1 (0.7)
India	6	Sweden	3	11-20	3 (2.2)
Ireland	2	Switzerland	1	21-50	20 (14.7)
Italy	4	Turkey	5	51-100	22 (16.2)
Japan	20	United Kingdom	31	>100	60 (44.1)
Malaysia	1	United States of America	12	Unknown	30 (22.1)
Background	**N (%)**	**Sex of primary investigator**	**N (%)**	**Years within specialty**	**N (%)**
Academic hospital/ Medical school	89 (65.4)	Male	99 (72.8)	0-5	0
		Female	37 (27.2)	6-10	15 (11.0)
Non-academic hospital	17 (12.5)			11-15	22 (16.2)
Unknown	30 (22.1)			16-20	21 (15.4)
				>20	48 (35.3)
				Unknown	30 (22.1)

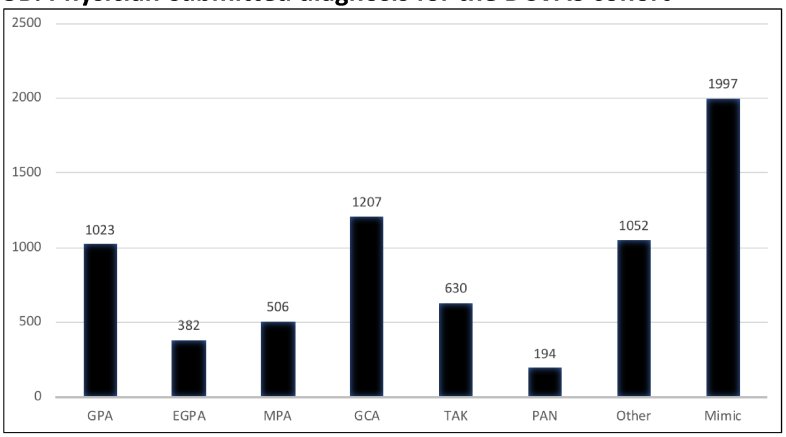
ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 5. Study Participant Details

5a. Patient recruitment by region

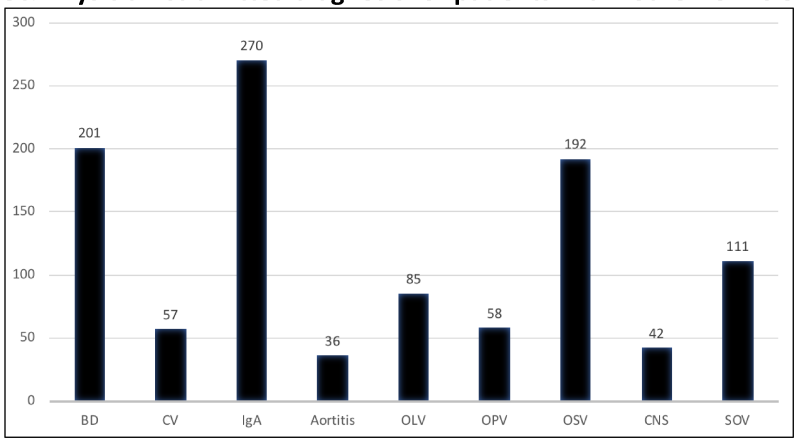
	Total Sites	Total Patients Recruited	% Patients Recruited
Europe	71	4107	59%
North America	22	1497	21%
Other Regions	43	1387	20%
TOTAL	136	6991	

5B. Physician-submitted diagnosis for the DCVAS cohort



GPA = granulomatosis with polyangiitis
EGPA = eosinophilic granulomatosis with polyangiitis
MPA = microscopic polyangiitis
GCA = giant cell arteritis
TAK = Takayasu's arteritis
PAN = polyarteritis nodosa
Other = other form of vasculitis
Mimic = other condition that mimics vasculitis

5c. Physician-submitted diagnosis for patients with "other forms of vasculitis"



BD = Behcet's disease
CV = cryoglobulinemic vasculitis
IgA = IgA vasculitis
Aortitis = isolated aortitis
OLV = other form of large-vessel vasculitis
OPV = other form of primary vasculitis
OSV = other form of small-vessel vasculitisi
CNS = primary central nervous system vasculitis
SOV = single organ vasculitis

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 6. Final candidate items used within each regression analysis to derive classification criteria for granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis

Significant differences in frequencies of item between the specific types of ANCA-associated vasculitis [granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis] and comparators: *p<0.05, **p<0.01

Item	Description	Composite Items	GPA N= 724	MPA N=291	EGPA N=226
Sex	Sex (female)		340 (47.0)*	164 (56.4)*	113 (50.0)
Age	Age (years)		56.6 (16.2)*	65.5 (13.2)**	52.9 (14.4)*
Smoke1	Smoking status (current)		77 (10.6)	29 (10.0)	4 (1.8)**
CLINICAL					
Bron3	Bronchitic changes or mucosal injury		52 (7.2)	6 (2.1)	16 (7.1)*
Bron6	Blood stained bronchoalveolar lavage		32 (4.4)*	13 (4.5)	3 (1.3)
CPCF2	Crackles / râles on auscultation		109 (15.1)	87 (29.9)**	36 (15.9)
CPCF4	Respiratory compromise requiring oxygen		58 (8.0)	39 (13.4)*	23 (10.2)
CPSym1	Dyspnea / Shortness of Breath		317 (43.8)*	124 (42.6)	155 (68.6)**
CPSym2	Non-productive cough		169 (23.3)*	64 (22.0)	75 (33.2)**
CPSym3	Productive cough with purulent sputum		83 (11.5)	39 (13.4)	43 (19.0)**
CPSym4	Minor hemoptysis		135 (18.6)**	39 (13.4)	18 (8.0)
CVCF5	Arrhythmia		10 (1.4)	5 (1.7)	14 (6.2)**
CVSym1	Angina / ischemic cardiac pain		7 (1.0)*	4 (1.4)	16 (7.1)**
entcf3entcf4	Conductive hearing loss/sensorineural hearing loss	Y	172 (23.8)	12 (4.1)**	21 (9.3)
ENTCF5	Nasal polyps		35 (4.8)**	4 (1.4)**	84 (37.2)**
ENTSym5	Non-blood stained nasal discharge		139 (19.2)**	17 (5.8)*	45 (19.9)**
ENTSym7	Loss of smell (anosmia)		74 (10.2)**	1 (0.3)	32 (14.2)**
EyeCF3	Conjunctivitis		47 (6.5)**	4 (1.4)	2 (0.9)
GenSym3	Fatigue		411 (56.8)	208 (71.5)**	139 (61.5)*
GeUrSym1	Macroscopic hematuria (blood visible in urine)		25 (3.5)*	31 (10.7)**	2 (0.9)*
GISym1	Abdominal pain (any)		64 (8.8)**	27 (9.3)*	42 (18.6)

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Item	Description	Composite Items	GPA N= 724	MPA N=291	EGPA N=226
Lung4	Reduced DLCO or KCO		40 (5.5)	33 (11.3)**	15 (6.6)
MskCF2	Muscle tenderness		36 (5.0)	20 (6.9)	23 (10.2)*
MskCF3	Muscle weakness		36 (5.0)*	32 (11.0)*	30 (13.3)*
MskSym6	Myalgia (muscle pain) or muscle cramps		177 (24.4)	65 (22.3)	72 (31.9)*
SknCF3	Maculopapular or papular rash		48 (6.6)*	18 (6.2)	30 (13.3)*
SknCF10	Ulcer		32 (4.4)*	4 (1.4)**	8 (3.5)
SknSym2	Painful skin lesions of any type		63 (8.7)*	11 (3.8)**	23 (10.2)
VMDMeds6	Leukotriene antagonist		2 (0.3)**	0 (0)*	29 (12.8)**
Bron5CPSym5Lung5	Evidence of alveolar hemorrhage/major hemoptysis/increased KCO	Y	88 (12.2)**	35 (12.0)*	4 (1.8)**
bron8entcf1entcf8entcf2	Endobronchial involvement/inflamed ear or nose cartilage/hoarse voice stridor/saddle nose deformity	Y	157 (21.7)**	6 (2.1)**	13 (5.8)
CVCF2CVCF3	Congestive cardiac failure/cardiomyopathy	Y	7 (1.0)**	13 (4.5)	38 (16.8)**
entcf6entsym6entsym4entCF7	Bloody nasal discharge/nasal ulcers, mucosal abnormalities, crusting/sino nasal congestion or blockage/nasal septal defect, perforation	Y	527 (72.8)**	32 (11.0)**	124 (54.9)**
eyecf5eyecf6eyecf7	Keratitis (inflammation of the cornea)/scleritis or episcleritis/uveitis	Y	103 (14.2)**	6 (2.1)**	2 (0.9)**
gencf6gensym4gensym5	Fever ≥ 38^{o}C (≥ 100.4F)/night sweats/rigors	Y	355 (49.0)**	116 (39.9)	85 (36.3)
GenCFWt2or3	Weight loss 2 -5kg/weight loss ≥5 Kg	Y	271 (37.4)*	114 (39.2)*	82 (36.3)
lung3cpcf3	Obstructive airways disease/wheeze	Y	67 (9.3)**	18 (6.2)**	148 (65.5)**
mskcf1msksym1	Swollen or inflamed joint(s)/arthralgia	Y	406 (56.1)**	82 (28.2)**	82 (36.3)
msksym2msksym3msksym4msksym5	Morning stiffness ≥ 1 hour in any of neck/torso/shoulders/arms/hips/thighs	Y	127 (17.5)**	25 (8.60)	15 (6.6)
NeurCF10	Sensory neuropathy (not due to radiculopathy)		96 (13.3)**	50 (17.2)	84 (37.2)**
neurcf6neurcf8	Mononeuritis multiplex/motor neuropathy (not due to radiculopathy)	Y	79 (10.9)**	44 (15.1)*	108 (47.8)**
SknCF1SknCF2SknCF9	Cutaneous infarct/petechiae or purpura/splinter hemorrhage	Y	130 (18.0)*	26 (8.9)**	53 (23.5)
gisym3gisym6	Diarrhea/bloody diarrhea	Y	33 (4.6)**	26 (8.9)**	26 (11.5)

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Item	Description	Composite Items	GPA N= 724	MPA N=291	EGPA N=226
LABORATORY					
TstHaem8_cat	Maximum eosinophil count (x10^9/L) category >=1		0.08 (0.27)**	15 (5.2)**	206 (91.2)**
TstChem1dn	Maximum CRP (mg/L) (range)		97.6 (103.5)**	94.6 (151.6)*	67.0 (69.3)*
TstChem6dn	Maximum creatinine - µmol/L (range)		168.3 (185.2)	336.7 (302.7)**	85.3 (53.6)**
Tsthaem9dn	Maximum ESR (mm/hr) (range)		66.3 (35.0)**	74.4 (36.5)**	47.1 (30.2)**
TstHaem1	Significant anemia (Hb <10g/dL)		250 (34.5)	187 (64.3)**	27 (11.9)**
TstHaem3	Significant thrombocythemia (platelets > 500 x 10^9/L)		170 (23.5)**	42 (14.4)	34 (15.0)
TstHaem5	Significant elevation of WBC (total WBC > 15 x 10^9/L)		180 (24.9)	65 (22.3)	115 (50.9)**
TstHaem7	Significant neutrophilia (PMN > 10 x 10^9/L)		200 (27.6)*	80 (27.5)*	52 (23.0)
TstChem3	AST(SGOT) or ALT(SGPT)>2 upper limit normal		48 (6.6)	8 (2.7)*	21 (9.3)*
TstChem4	Alkaline phosphatase >2x upper limit of normal		44 (6.1)	14 (4.8)	17 (7.5)
TstChem8	Albumin below 30g/L		168 (23.2)	125 (43.0)**	35 (15.5)*
tstur1tstur5	Protein on urine dipstick* or 24 hour protein		418 (57.7)*	240 (82.5)**	60 (26.5)**
TstUr2	Blood on urine dipstick*		436 (60.2)**	252 (86.6)**	54 (23.9)**
TstUr3	Leucocytes or nitrites on urine dipstick*		161 (85.1)	103 (35.4)**	26 (11.5)**
TstUr4	Red cell casts in urine		136 (18.8)	99 (34.0)**	10 (4.4)**
TstCC1	Serum cryoglobulins present		3 (0.4)**	7 (2.4)*	8 (3.5)
TstAA1=1	cANCA on immunofluorescence present		531 (73.3)**	11 (3.8)**	17 (7.5) **
TstAA3=1	PR3 ANCA (ELISA) present		595 (82.2)**	6 (2.1)**	7 (3.1)**
TstAA2=1	pANCA on immunofluorescence present		71 (9.8)**	236 (81.1)**	83 (36.7)
TstAA4=1	MPO ANCA (ELISA) present		59 (8.1)**	279 (95.9)**	98 (43.3)
TstAA5	Other ANCA by immunofluorescence		13 (1.8)	3 (1.0)	6 (2.7)
TstAA7	Rheumatoid factor present		161 (22.2)	60 (20.6)	62 (27.4)*
ancagrp6	cANCA or PR3 (composite to replace individual items TstAA1 and TstAA3)	Y	616 (85.1)**	12 (4.1)**	21 (9.3)**
ancagrp7	pANCA or MPO (composite item to replace individual items TstAA2 and TstAA4)	Y	84 (11.6)**	284 (97.6)**	107 (47.2)*

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Item	Description	Composite Items	GPA N= 724	MPA N=291	EGPA N=226
IMAGING					
imag1	Imaging of the chest/lungs with nodules OR mass/tumor OR cavitation	Y	263 (36.3)**	31 (10.7)*	31 (13.7)
imag2p1	Imaging of the chest/lungs with hemorrhage OR infiltrates OR consolidation OR ground glass changes	Y	203 (28.0)**	67 (23.0)	73 (32.3)**
imag2p3	Imaging of the chest/lungs with hemorrhage	Y	59 (8.1)**	22 (7.6)*	1 (0.4)*
imag3	Imaging of the pleura/chest with effusion	Y	68 (9.4)	38 (13.1)	27 (11.9)
imag4	Imaging of the chest/lungs with fibrosis OR ILD	Y	15 (2.1)**	67 (23.0)**	16 (7.1)
imag5	Imaging of the trachea/epiglottis with stenosis OR inflammation OR ulceration	Y	9 (1.2)	0 (0)	0 (0)
imag6	Imaging of the nasal/paranasal sinuses with inflammation OR effusion OR consolidation OR wall thickness OR mastoiditis	Y	212 (29.3)**	5 (1.7)**	64 (28.3)**
imag7	Imaging of the nasal/paranasal sinuses with (deviated septum OR bony destruction OR septal perforation)	Y	41 (5.7)**	0 (0)*	2 (0.9)
imag8	Imaging of the nasal/paranasal sinuses with polyps	Y	17 (2.3)	0 (0.0)*	14 (6.2)**
imag9	Imaging of the orbital wall with mass/tumor OR inflammation	Y	13 (1.8)*	1 (0.3)	2 (0.9)
imag10	Imaging of the heart/cardiac muscle with EF<50% OR myocarditis OR myocardiopathy OR cardiomyopathy OR hypokinesis OR akinesis OR MRI of the heart/cardiac muscle with inflammation	Y	7 (1.0)**	6 (2.10	38 (16.8)**

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Item	Description	Composite Items	GPA N= 724	MPA N=291	EGPA N=226
BIOPSY					
biop1	Pauci-immune glomerulonephritis		201 (27.8)*	141 (48.5)**	11 (4.9)**
biop2	Necrotizing arteritis +/- fibrinoid necrosis	Y	82 (11.3)	40 (13.7)	15 (6.6)*
biop3	Perivascular infiltrates or perivascular inflammation (combined item)	Y	17 (2.3)	6 (2.1)	10 (4.4)
biop4	Prominent neutrophils in vasculitis		26 (3.6)	3 (1.0)***	3 (1.3)*
biop5	Absence or paucity of immune complex deposition vessels other than glomeruli		16 (2.2)	16 (5.5)***	5 (2.2)
biop7	Prominent eosinophils in vasculitis		5 (0.7)**	1 (0.3)**	42 (18.6)**
biop8	Predominant mononuclear leucocytes in vasculitis		11 (1.5)	10 (3.4)	2 (0.9)
biop9	Anti-GBM staining on immunofluorescence		0 (0)	0 (0)	0 (0)
biop10	Immune complex glomerulonephritis		3 (0.4)	4 (1.4)	0 (0)
biop12	Immune complex deposition in vessels other than glomeruli with prominent IgA/IgA dominant immune complex glomerulonephritis	Y	6 (0.8)**	1 (0.3)**	0 (0)
biop13	Necrotizing or leucocytoclastic arteriolitis/venulitis/leucocytoclastic vasculitis	Y	48 (6.6)*	11 (3.8)**	17 (7.5)
biop14	Extravascular eosinophil predominant inflammation/increased eosinophils in bone marrow	Y	9 (1.2)**	1 (0.3)**	47 (20.8)**
biop6biop15	Granuloma/extravascular granulomatous inflammation/giant cells	Y	160 (22.1)**	7 (2.4)**	13 (5.8)
biop16	Unspecified tissue inflammation/extravascular non-granulomatous inflammation	Y	147 (20.3)**	20 (6.9)*	34 (15.0)

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 7A. Expert Reviewer Characteristics

Characteristics	N=55 (%)	Characteristics	N=55 (%)
Country		**Specialty**	
Australia	1 (1.8)	Rheumatology	33 (60.0)
Canada	3 (5.5)	Nephrology	11 (20.0)
Czech Republic	2 (3.6)	Internal Medicine	4 (7.3)
Denmark	1 (1.8)	Immunology	3 (5.5)
Egypt	1 (1.8)	Dermatology	2 (3.6)
France	1 (1.8)	Neurology	1 (1.8)
Germany	7 (12.7)	Pathology	1(1.8)
India	2 (3.6)		
Ireland	2 (3.6)	**Number of patients with AAV seen at site per year**	
Italy	3 (5.5)		
Japan	2 (3.6)	>50	32 (58.2)
Mexico	2 (3.6)	21-50	11 (20.0)
Netherlands	2 (3.6)	6-20	11 (20.0)
New Zealand	1 (1.8)	Unknown	1
Portugal	2 (3.6)		
Russia	2 (3.6)	**Years in specialty**	
Slovenia	1 (1.8)	0-5	2 (3.6)
Spain	1 (1.8)	6-10	11 (20.0)
Switzerland	2 (3.6)	11-15	13 (23.6)
Turkey	2 (3.6)	16-20	9 (16.4)
United Kingdom	6 (10.9)	>20	19 (34.5)
United States of America	9 (16.4)	Unknown	1
Background		**Sex**	
Clinician	11 (20.0)	Male	38 (69.1)
Clinician and researcher	44 (80.0)	Female	17 (30.9)

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

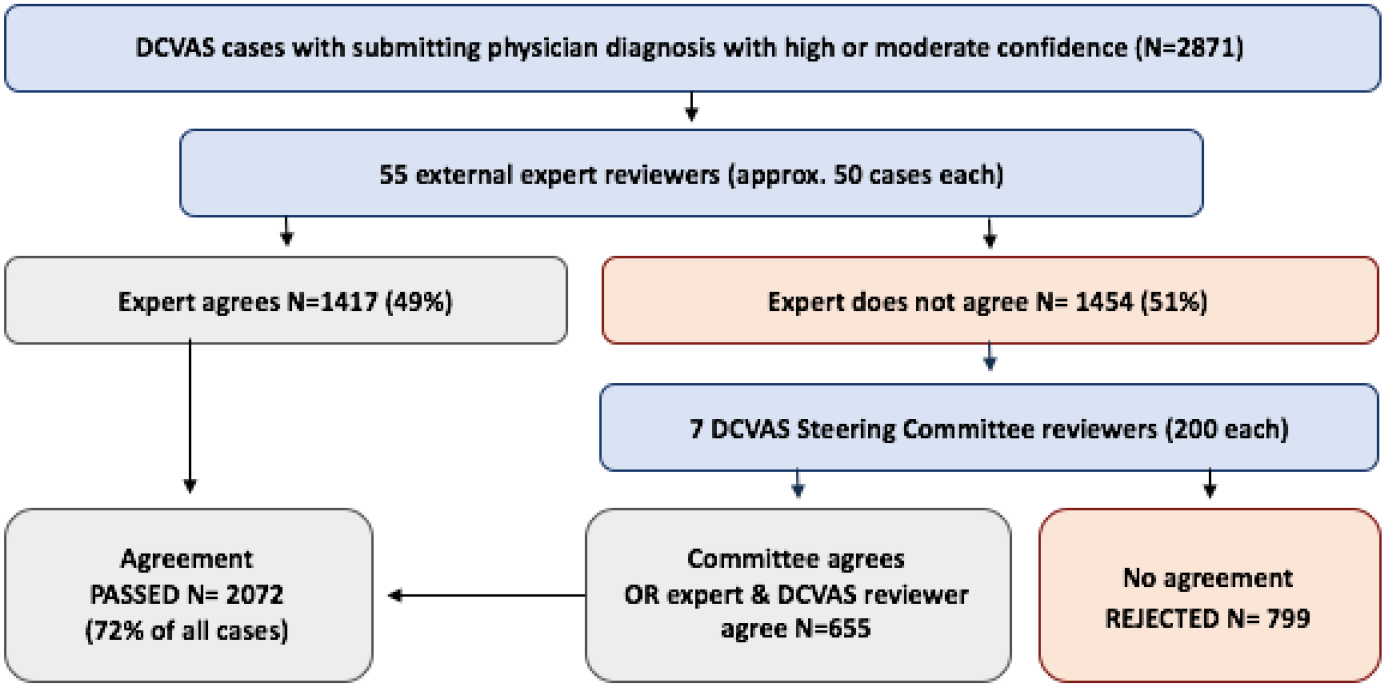
Supplementary Materials 7B. Names of the Expert Reviewers

Alba, Marco
Barra, Lillian
Baslund, Bo
Basu, Neil
Brown, Nina
Cid, Maria
Daikeler, Thomas
Direskeneli, Haner
Emmi, Giamoco
Flores-Suárez, Luis Felipe
Fujimoto, Shouichi
Gatenby, Paul
Geetha, Duvuru
Geraldes, Ruth
Gewurz-Singer, Ora
Guillevin, Loïc
Hammam, Nevin
Hauser, Thomas
Hellmich, Bernhard
Henes, Jörg
Hinojosa, Andrea
Hočevar, Alojzija
Holle, Julia
Hruskova, Zdenka
Jayne, David
Jennette, Charles
Kallenberg, Cees
Karadağ, Ömer
Khalidi, Nader
Lamprecht, Peter
Langford, Carol
Little, Mark
Macieira, Carla
Matsui, Kazuo
Matteson, Eric
Micheletti, Robert
Milman, Nataliya
Moiseev, Sergey
Molloy, Eamonn
Monach, Paul
Neumann, Thomas
Novikov, Pavel
Quincey, Vicki
Rajasekhar, Liza
Salama, Alan
Salvarani, Carlo
Schmidt, Wolfgang
Sharma, Aman
Smith, Rona
Springer, Jason
Sunderkötter, Cord
Sznajd, Jan
Teng, Yko
Tesar, Vladimir
Vaglio, Augusto

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 8. Flow chart of expert review process to create the Diagnosis and Classification of Vasculitis Study dataset for ANCA-associated vasculitis.

Cases passed by the expert review process were used to derive classification criteria for granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis.



ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 9A. Results of regression analysis (n=91 candidate items) for eosinophilic granulomatosis with polyangiitis. Top ten strongest independent variables

Predictor Variables	Odds Ratio (95% CI)	P-value
Serum eosinophil count >1x10^9/L	122.88 (34, 596)	<0.001
Nasal polyps	21.56 (3.84, 156.37)	<0.001
Evidence of obstructive airway disease	17.3 (4.15, 83.65)	<0.001
cANCA or anti-PR3-ANCA	0.03 (0, 0.15)	<0.001
Pauci-immune glomerulonephritis	0.02 (0, 0.27)	0.01
Extravascular eosinophil inflammation	15.72 (1.71, 172.54)	0.02
Non-productive cough	6.07 (1.46, 28.97)	0.02
Mononeuritis multiplex or motor neuropathy	3.75 (1.05, 13.73)	0.04
Hematuria	0.26 (0.06, 0.94)	0.05
Dyspnea	2.98 (10.77, 12.48)	0.12
Maximum value of serum creatinine	1.00 (1.00, 1.00)	0.97

ANCA: anti-neutrophil cytoplasmic antibody; cANCA: cytoplasmic anti-neutrophil cytoplasmic antibody; PR3: proteinase 3

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 9B. Results of regression analysis (n=91 candidate items) for granulomatosis with polyangiitis. Top ten strongest independent variables

Predictor Variables	Odds Ratio (95% CI)	P-value
cANCA or anti-PR3 ANCA positive	142.3 (65.9, 335.0)	<0.001
Nasal bloody discharge, ulcers, crusting, or sinonasal congestion/blockage	28.1 (14.1, 59.4)	<0.001
Eosinophil count (x10^9/L) (≥1 vs. <1)	0.03 (0.01, 0.09)	<0.001
Granuloma or giant cells on biopsy	13.3 (4.29, 44.8)	<0.001
Pulmonary nodules, mass, or cavitation on chest imaging	7.65 (3.59, 17.0)	<0.001
Cartilaginous involvement (cartilage inflammation of the ear or nose, hoarse voice or stridor, endobronchial involvement, or saddle nose deformity)	9.48 (3.51, 27.9)	<0.001
pANCA or anti-MPO ANCA positive	0.30 (0.15, 0.60)	<0.001
Nasal polyps	0.16 (0.04, 0.53)	<0.001
Abdominal pain	0.21 (0.08, 0.51)	<0.001
Inflammation, consolidation, or effusion of the nasal/paranasal sinuses on imaging	3.13 (1.38, 7.37)	<0.001

ANCA: anti-neutrophil cytoplasmic antibody; cANCA: cytoplasmic anti-neutrophil cytoplasmic antibody; PR3: proteinase 3; pANCA: perinuclear anti-neutrophil cytoplasmic antibody; MPO: myeloperoxidase

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 9C. Results of regression analysis (n=91 candidate items) for microscopic polyangiitis. Top ten strongest independent variables

Predictor Variables	Odds Ratio (95% CI)	P-value
pANCA or anti-MPO ANCA positive	251.22 (64.78, 1587.65)	<0.01
Maximum serum eosinophil count ≥1 x10^9/L	0.02 (0.004, 0.10)	<0.01
Nasal bloody discharge, ulcers, crusting, or sinonasal congestion or blockage, or nasal septal defect /perforation	0.09 (0.03, 0.26)	<0.01
Pauci-immune glomerulonephritis on biopsy	10.73 (3.73, 36.09)	<0.01
Fibrosis or interstitial lung disease on chest imaging	16.23 (4.00, 85.26)	<0.01
Significant anemia (Hb <10g/dL)	3.61 (1.30, 10.71)	0.02
Microscopic hematuria	1.83 (0.69, 4.87)	0.22
cANCA or anti-PR3 ANCA positive	0.25 (0.07, 0.89)	0.03
Maximum value of serum creatinine	1.06 (0.87, 1.35)	0.61

ANCA: anti-neutrophil cytoplasmic antibody; cANCA: cytoplasmic anti-neutrophil cytoplasmic antibody; MPO: myeloperoxidase; pANCA: perinuclear anti-neutrophil cytoplasmic antibody; PR3: proteinase 3; Hb: hemoglobin

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Table 10A. Data-driven and clinically-selected seven-item model for classification of eosinophilic granulomatosis with polyangiitis with associated risk score based off beta coefficient weighting.

Predictor Variables	Odds Ratio (95% CI)	Beta Coefficient	Risk Score
Eosinophil count >1x10^9/L	109.57 (36.05, 410.43)	4.70	+5
Nasal polyps	14.44 (3.64, 66.45)	2.89	+3
Evidence of obstructive airway disease	19.75 (5.91, 60.31)	-3.27	+3
cANCA or anti-PR3-ANCA	0.04 (0.01, 0.15)	2.67	-3
Extravascular eosinophil inflammation	10.68 (1.59, 97.24)	2.37	+2
Mononeuritis multiplex or motor neuropathy	3.19 (1.07, 9.62)	1.16	+1
Hematuria	0.23 (0.07, 0.67)	-1.48	-1

ANCA: anti-neutrophil cytoplasmic antibody; cANCA: cytoplasmic anti-neutrophil cytoplasmic antibody; PR3: proteinase 3

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 10B: Data-driven and clinically-selected ten-item model for classification of granulomatosis with polyangiitis with associated risk scored based off beta coefficient weighting

Predictor Variables	Odds Ratio (95% CI)	Beta Coefficient	Risk Score
cANCA or anti-PR3 ANCA positive	100.0 (53.8, 196.2)	4.61	+5
Nasal bloody discharge, ulcers, crusting, or sinonasal congestion	16.9 (9.38, 31.6)	2.83	+3
Granuloma, or giant cells, extravascular granulomatous inflammation on biopsy	8.94 (3.59, 22.7)	2.19	+2
Pulmonary nodules, mass, or cavitation on chest imaging	6.40 (3.31, 12.66)	1.86	+2
Cartilaginous involvement (cartilage inflammation of the ear or nose, hoarse voice or stridor, endobronchial involvement, or saddle nose deformity)	6.84 (2.92, 16.7)	1.92	+2
Hearing loss (conductive or sensorineural)	3.22 (1.35, 7.91)	1.17	+1
Pauci-immune glomerulonephritis	2.17 (1.19, 4.01)	0.75	+1
Inflammation, consolidation, or effusion of the nasal/ paranasal sinuses or mastoiditis on imaging	2.11 (1.07, 4.23)	0.75	+1
pANCA- or anti-MPO ANCA-positive	0.30 (0.16, 0.53)	-1.21	-1
Maximum serum eosinophil count ($x10^9$/L) (≥1 vs. <1)	0.03 (0.01, 0.06)	-3.58	-4

ANCA: anti-neutrophil cytoplasmic antibody; cANCA: cytoplasmic ANCA; MPO: myeloperoxidase; pANCA: perinuclear ANCA; PR3: proteinase 3

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Table 10C. Data-driven and clinically-selected six-item model for classification of microscopic polyangiitis with associated risk scored based off beta coefficient weighting

Predictor Variables	Odds Ratio (95% CI)	Beta Coefficient	Risk Score
pANCA- or anti-MPO ANCA-positive	284.7 (83.7, 1481.2)	5.65	+6
Pauci-immune glomerulonephritis	15.5 (5.71, 49.2)	2.74	+3
Fibrosis or interstitial lung disease on chest imaging	13.2 (3.7, 57.2)	2.58	+3
Serum eosinophil count ≥ 1 $x10^9$/L	0.03 (0.01, 0.09)	-3.68	-4
Nasal bloody discharge, ulcers, crusting or sinonasal congestion	0.07 (0.02, 0.19)	-2.71	-3
cANCA- or anti-PR3 ANCA-positive	0.25 (0.06, 0.88)	-1.39	-1

ANCA: anti-neutrophil cytoplasmic antibody; cANCA: cytoplasmic ANCA; MPO: myeloperoxidase; pANCA: perinuclear ANCA; PR3: proteinase 3.

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 11A: Performance characteristics of a points-based risk score for eosinophilic granulomatosis with polyangiitis with different thresholds in the development set

Threshold Score	Sensitivity (%)	Specificity (%)
1	99.2	55.1
2	95.8	83.5
3	95.8	89.0
4	92.4	95.2
5	89.1	97.5
6	84.9	99.1
7	76.5	99.3
8	68.1	100.0

A total score of ≥6 was considered the best cut-point to provide high enough specificity for purposes of enrolling patients into clinical trials without compromising sensitivity. If a higher total score is chosen, specificity increases but there is a corresponding disproportionate drop in sensitivity. When scoring an individual patient, the higher the score, the higher the specificity for eosinophilic granulomatosis with polyangiitis.

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 11B: Performance characteristics of a points-based risk score for granulomatosis with polyangiitis with different thresholds in the development set

Threshold Score	Sensitivity (%)	Specificity (%)
3	97.3	90.7
4	94.5	92.5
5	92.5	93.8
6	84.2	98.1

A total score of ≥ 5 was considered the best cut-point to provide high enough specificity for purposes of enrolling patients into clinical trials without compromising sensitivity. If a higher total score is chosen, specificity increases but there is a corresponding disproportionate drop in sensitivity. When scoring an individual patient, the higher the score, the higher the specificity for granulomatosis with polyangiitis.

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 11C: Performance characteristics of a points-based risk score for microscopic polyangiitis with different thresholds in the development set

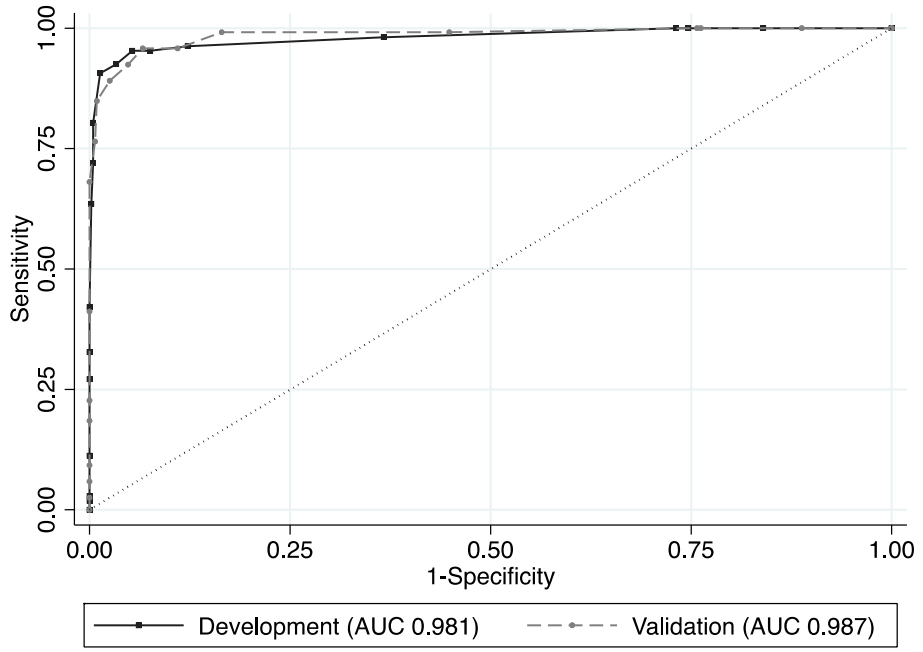
Threshold Score	Sensitivity (%)	Specificity (%)
1	98.6	82.1
2	98.6	82.6
3	94.3	90.6
4	90.8	94.0
5	90.8	94.2
6	86.6	95.7
7	50.7	98.1

A total score of ≥ 5 was considered the best cut-point to provide high enough specificity for purposes of enrolling patients into clinical trials without compromising sensitivity. If a higher total score is chosen, specificity increases but there is a corresponding disproportionate drop in sensitivity. When scoring an individual patient, the higher the score, the higher the specificity for microscopic polyangiitis.

ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 12A. Discrimination curves for the classification criteria for eosinophilic granulomatosis with polyangiitis.

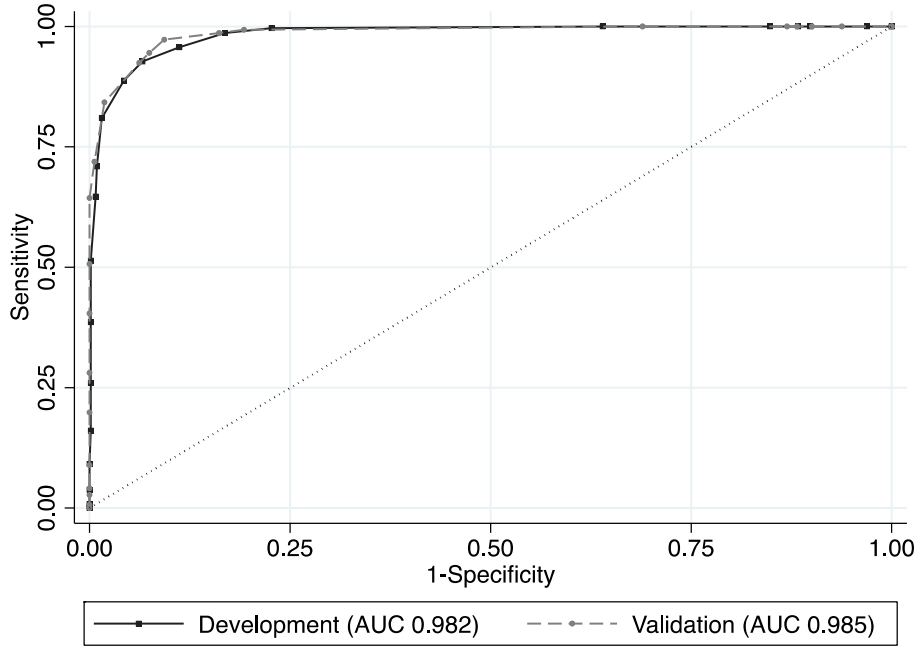
Classification criteria applied to 1,113 cases confirmed by Expert Review, 226 with EGPA and 887 comparators divided into a development set (50%) and validation set (50%). The Area Under Curve (AUC) for the development set is shown (solid line) and the AUV for the validation set is shown (dotted line).



ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 12B. Discrimination curves for the classification criteria for granulomatosis with polyangiitis.

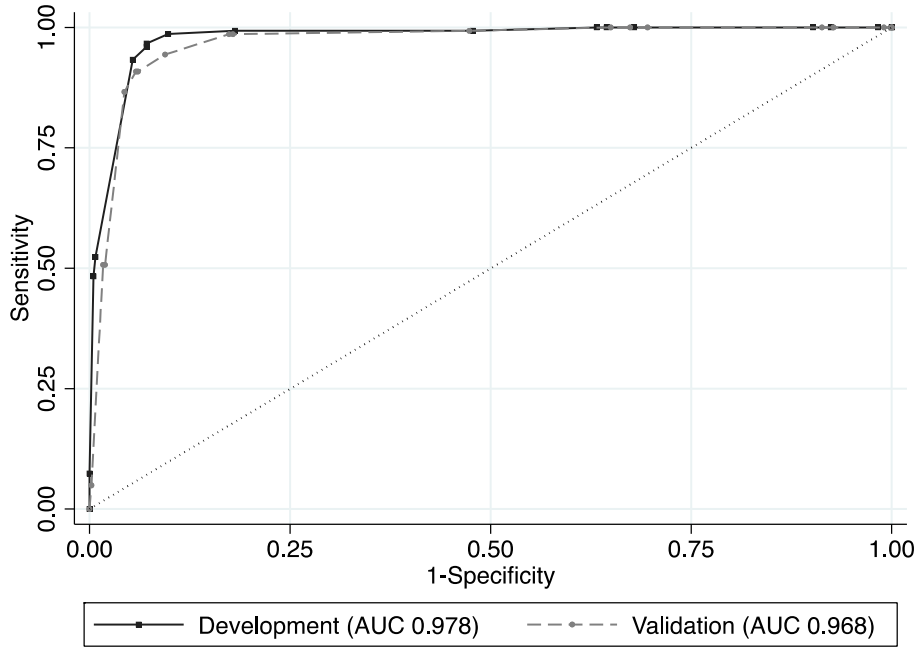
Classification criteria applied to 1537 cases confirmed by Expert Review (N= 1537), 724 with GPA (47.1%) and 813 (52.9%) comparators divided into a development set (80%) and validation set (20%). The Area Under Curve (AUC) for the development set is shown (solid line) and the AUC for the validation set is shown (dotted line).

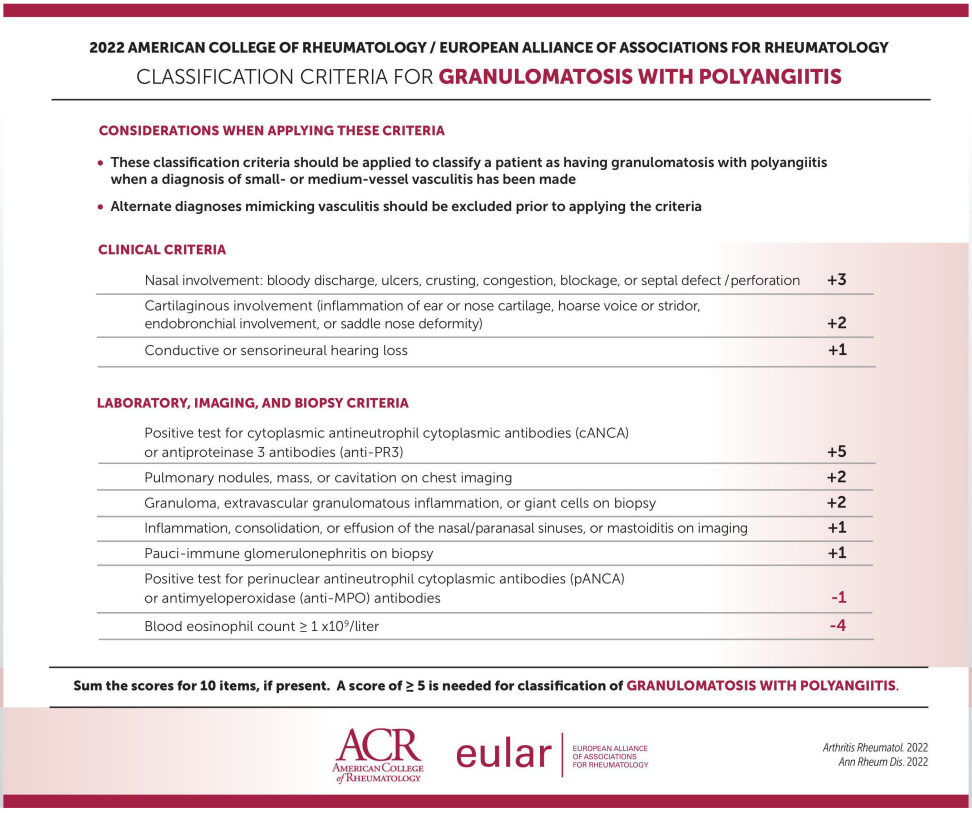


ACR-EULAR Classification Criteria for ANCA-Associated Vasculitis

Supplementary Materials 12C. Discrimination curves for the classification criteria for microscopic polyangiitis.

Classification criteria applied to 1,113 cases confirmed by Expert Review, 291 with MPA and 822 comparators divided into a development set (50%) and validation set (50%). The Area Under Curve (AUC) for the development set is shown (solid line) and the AUV for the validation set is shown (dotted line).





2022 AMERICAN COLLEGE OF RHEUMATOLOGY / EUROPEAN ALLIANCE OF ASSOCIATIONS FOR RHEUMATOLOGY

CLASSIFICATION CRITERIA FOR **GRANULOMATOSIS WITH POLYANGIITIS**

CONSIDERATIONS WHEN APPLYING THESE CRITERIA

- **These classification criteria should be applied to classify a patient as having granulomatosis with polyangiitis when a diagnosis of small- or medium-vessel vasculitis has been made**
- **Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria**

CLINICAL CRITERIA

Nasal involvement: bloody discharge, ulcers, crusting, congestion, blockage, or septal defect / perforation	+3
Cartilaginous involvement (inflammation of ear or nose cartilage, hoarse voice or stridor, endobronchial involvement, or saddle nose deformity)	+2
Conductive or sensorineural hearing loss	+1

LABORATORY, IMAGING, AND BIOPSY CRITERIA

Positive test for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) or antiproteinase 3 antibodies (anti-PR3)	+5
Pulmonary nodules, mass, or cavitation on chest imaging	+2
Granuloma, extravascular granulomatous inflammation, or giant cells on biopsy	+2
Inflammation, consolidation, or effusion of the nasal/paranasal sinuses, or mastoiditis on imaging	+1
Pauci-immune glomerulonephritis on biopsy	+1
Positive test for perinuclear antineutrophil cytoplasmic antibodies (pANCA) or antimyeloperoxidase (anti-MPO) antibodies	-1
Blood eosinophil count ≥ 1 x10^9/liter	-4

Sum the scores for 10 items, if present. A score of ≥ 5 is needed for classification of GRANULOMATOSIS WITH POLYANGIITIS.

ACR American College of Rheumatology eular European Alliance of Associations for Rheumatology

Arthritis Rheumatol. 2022
Ann Rheum Dis. 2022

APPENDIX A: THE DCVAS INVESTIGATORS
<<hd1>>**APPENDIX A: THE DCVAS INVESTIGATORS**
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