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Evaluation of the ACR/EULAR 2022 criteria for classification of ANCA-associated vasculitis in a population-based cohort from Sweden

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Abstract

Objective: To evaluate the ACR/EULAR 2022 criteria for ANCA-associated vasculitides (AAV) classification and compare them with the European Medicines Agency (EMA) algorithm and with classification based only on ANCA serology.

Methods: In the analysis, 374 cases (47% female) were classified according to the EMA algorithm, ANCA serology and ACR/EULAR criteria. The agreement rate was calculated using the kappa (κ) statistic.

Results: Under EMA, 192 patients were classified as granulomatosis with polyangiitis (GPA), 159 as microscopic polyangiitis (MPA) and 23 as eosinophilic granulomatosis with polyangiitis (EGPA). The ACR/EULAR criteria classified 199 patients as GPA, 136 as MPA and 22 as EGPA. Four patients (1.1%) met criteria of two disease categories, and 13 (3.5%) were unclassifiable. The observed agreement between EMA and ACR/EULAR was 85% for GPA, 75% for MPA and 96% for EGPA. The unweighted κ statistic was 0.66 (95% CI: 0.60, 0.74). Of the 188 PR3-ANCA positive patients, 186 (98.9%) were classified as GPA using ACR/EULAR criteria, and 135 of 161 (83.9%) MPO-ANCA positive patients were classified as MPA. With a classification solely based on ANCA specificity, agreement with ACR/EULAR was 99% for GPA and 88% for MPA.

Conclusions: EMA and ACR/EULAR classification give similar results. A small proportion of patients cannot be classified or fall into two categories. Some patients exhibiting granuloma, a key feature of GPA, are nevertheless classified as MPA, conflicting with the current view of histopathology of AAV. There is high agreement of ANCA-based classification with that of ACR/EULAR, reflected in the considerable weight granted to ANCA in the new criteria. These crucial elements within the new criteria necessitate a consensus discussion among field experts.

Keywords: ANCA-vasculitis, classification, GPA, MPA.

Rheumatology key messages

- Classification with ACR/EULAR shows good agreement with a classification by the EMA algorithm.
- A serology-based classification produces similar results to ACR/EULAR.
- The weight granted to ANCAs in ACR/EULAR considerably impacts classification into AAV disease phenotypes.

Introduction

ANCA-associated vasculitides (AAV) are rare diseases predominantly affecting small vessels, resulting in necrotizing or granulomatous inflammation of affected tissues. AAV is further categorized according to clinicopathological characteristics as granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) [1]. ANCAs targeting either PR3 or MPO can be observed in most cases of AAV. A majority of GPA patients exhibit PR3 positivity, whereas MPO positivity is most common in MPA and, less frequently, in EGPA [1].

Classification criteria are developed to ensure the inclusion of homogeneous populations in clinical and epidemiological studies and clinical trials [2]. The American College of Rheumatology (ACR) published the first vasculitis classification criteria in 1990 [3], describing seven forms, with the aim of facilitating epidemiological research in vasculitis. Among the forms described were Wegener's granulomatosis (now GPA) [4], polyarteritis nodosa [5], and Churg–Strauss syndrome (now EGPA) [6]. Microscopic polyangiitis was not considered a separate disease under these criteria. The Chapel Hill Consensus Conference (CHCC) in 1994 and its revision

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in 2012 presented expert consensus on the nomenclature and definition of all types of primary vasculitis, introducing the term AAV and defining MPA as a separate disease entity for the first time [1, 7]. There is considerable overlap of the ACR 1990 criteria and the CHCC definitions, with some cases falling into two categories and others remaining unclassifiable [8, 9]. Watts *et al.* therefore proposed a four-step algorithm using the ACR 1990 and CHCC 1994 criteria and integrating surrogate markers and ANCA serology into the classification [10]. The algorithm does not introduce new criteria, but rather a procedure for combining earlier classification criteria and definitions. It has been widely used in AAV epidemiological research in recent years [11–13].

The latest effort in the field is the multinational Diagnostic and Classification Criteria in Vasculitis (DCVAS) project aiming to develop diagnostic and classification criteria for primary systemic vasculitides [14]. Based on the results of DCVAS, new classification criteria were adopted by ACR and the European Alliance of Associations against Rheumatism (EULAR) in 2022 for GPA, MPA and EGPA [15–17]. The new criteria are the result of a multi-year, multinational collaboration based on an impressive cohort of 6991 subjects recruited predominantly from Europe and the USA. The criteria incorporated serology and surrogate markers in addition to clinical, histological and imaging characteristics. The inclusion of ANCA specificity to discriminate GPA from MPA constitutes arguably the most significant aspect of the new criteria. Currently, ANCA analysis represents a cornerstone in clinical diagnosis of AAV, and our understanding of the role of these antibodies has improved substantially since the 1990s. The finding that MPO- and PR3-ANCA positive disease differ in genetic aspects [18], organ involvement, disease course and outcome [19] has yielded an ongoing discussion of shift from a phenotype-based approach to a serology-based approach [20–22]. The ACR/EULAR 2022 criteria acknowledge this, granting ANCAs significant weight. Elements of the new criteria are weighted, and a threshold score is required for classification (GPA and MPA $\geq$5, EGPA $\geq$6). In this study, we aimed to evaluate the ACR/EULAR 2022 criteria for classification of AAV by comparing its results with the European Medicines Agency (EMA) algorithm classification in a well-established population-based cohort of AAV cases. We also calculated agreement of the new criteria with classification based on ANCA serology.

Methods

Patients

All incident cases of AAV in the study area from 1997 through 2019 were included in this analysis. Data for PR3-ANCA and MPO-ANCA were available for all cases.

Case ascertainment and classification

Records of all potentially eligible cases were retrospectively reviewed to confirm a diagnosis of AAV. Diagnosis of small vessel vasculitis required symptoms compatible with, or typical of, vasculitis supported by histology, serology or findings strongly suggestive of vasculitis on specific investigations. In addition, no other diagnosis could account for the findings. Patients fulfilling these requirements were then classified according to the EMA algorithm [10] by the authors.

Applying the ACR/EULAR 2022 criteria

The ACR/EULAR 2022 criteria require a clinical diagnosis of small- or medium-vessel vasculitis and the exclusion of vasculitis mimickers. Eligible cases were classified by the authors according to the criteria defined in ACR/EULAR publications [15–17]. A Microsoft Excel spreadsheet with macros was designed and a unique file created for each subject. All available subject records were evaluated by the first author (J.R.). Seventy-one borderline cases were re-evaluated and classified independently by A.J.M. A final classification was applied by consensus.

Statistical analysis

Descriptive statistical analysis presented data as frequencies and percentages, mean with standard deviation, or median with interquartile range (IQR) as appropriate. To assess agreement between EMA and ACR/EULAR 2022, the kappa (κ) statistic was used. Agreement between ANCA serology-based classification and ACR/EULAR 2022 criteria is expressed as a percentage. For serology-based classification, MPO positivity was interpreted as MPA, and PR3 positivity as GPA. In an initial step, agreement was assessed for all ANCA positive cases. As most EGPA cases are ANCA-negative, and those that are ANCA positive are predominantly MPO positive, we then conducted an analysis excluding EGPA cases. Agreement with ACR/EULAR 2022 criteria was analysed using descriptive statistics. Calculations were conducted with SPSS Statistics v. 26 for Windows (IBM Corp., Armonk, NY, USA).

Ethics

The study was conducted in accordance with Declaration of Helsinki and was approved by the Regional Ethical Review Board in Lund, Sweden (2010/517). No informed consent was obtained, as this was not required by the Regional Ethical Board.

Results

Three-hundred and seventy-four subjects (47% female) with new onset AAV diagnosed 1997–2019 were included in the study. The median age at diagnosis was 67.5 (IQR 55–77). Results of ANCA analysis were available for all subjects: 188 PR3-ANCA positive, 161 MPO-ANCA positive and 25 ANCA-negative. Figure 1 shows results of EMA and ACR/EULAR classification and overlap.

Classification according to the EMA algorithm

All subjects were classified according to the EMA algorithm as exhibiting an AAV disease category (Fig. 2). Twenty-three were classified as EGPA, fulfilling the ACR 1990 criteria for EGPA (Churg–Strauss). One-hundred and ninety-two were classified as GPA. Of these, 128 fulfilled ACR 1990 criteria for GPA, 15 were classified according to histology compatible with CHCC GPA (EMA2b) and 21 exhibited histopathology compatible with CHCC MPA and GPA surrogate markers (EMA2c). In 28 cases with no histopathology, GPA surrogate markers as well as positive serology for PR3 or MPO were present (EMA2d). One-hundred and fifty-nine cases were classified as MPA. Of these, 126 showed biopsy-confirmed

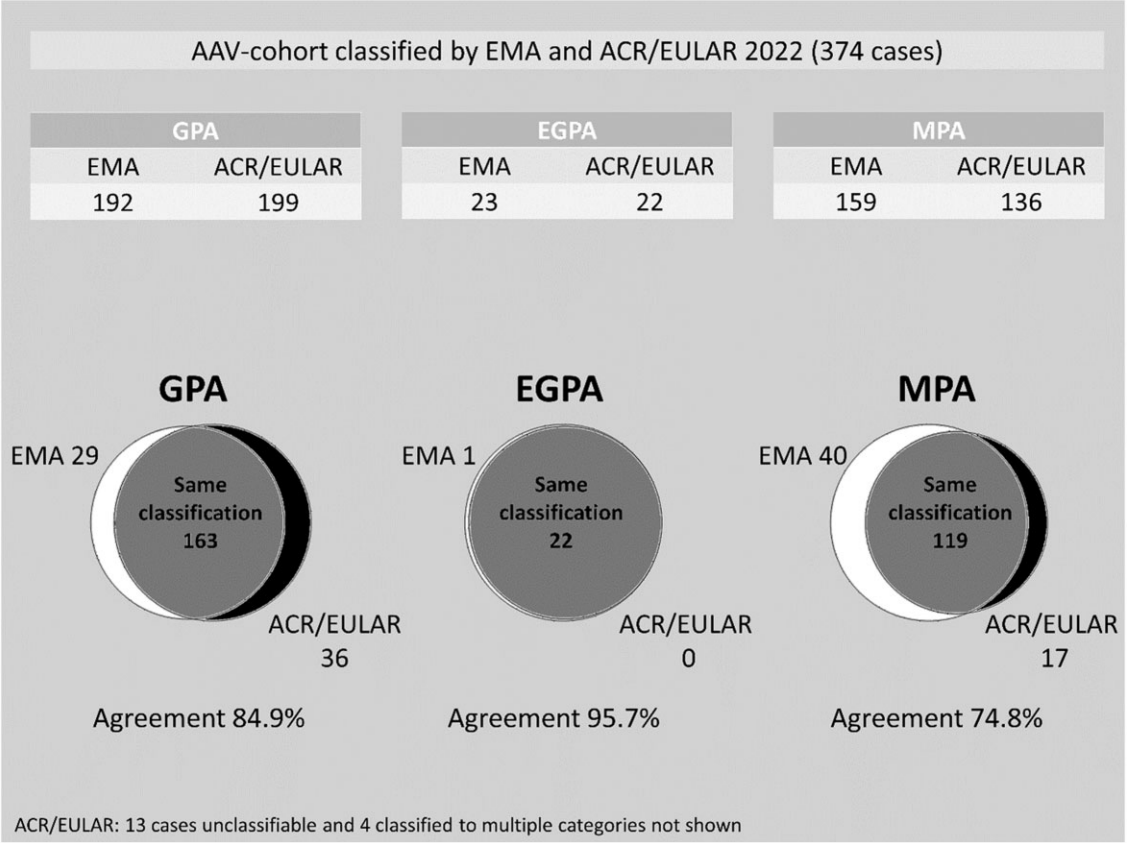

Figure 1. Classification according to EMA and ACR/EULAR. AAV: ANCA-associated vasculitides; EGPA: eosinophilic granulomatosis with polyangiitis; EMA: European Medicines Agency; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis

glomerulonephritis (GN) or small vessel vasculitis according to CHCC (EMA3a), and 33 were classified as MPA based on surrogate markers for renal vasculitis with positive ANCA. No patient was unclassified or classified into more than one disease phenotype category.

Classification according to the ACR/EULAR 2022 criteria

Under ACR/EULAR2022 criteria, 199 cases were classified as GPA, 136 as MPA and 22 as EGPA (Fig. 1). Thirteen cases were unclassifiable. Four fulfilled more than one criterion set: three for both GPA and MPA and one for GPA and EGPA. Table 1 summarizes selected findings of cases classified by ACR/EULAR criteria.

Agreement between EMA and the new ACR/EULAR 2022 criteria

The observed agreement between the EMA algorithm and the ACR/EULAR 2022 criteria is shown in Fig. 1. The unweighted κ statistic was 0.66 (95% CI: 0.60, 0.74) showing agreement of 84.9% for GPA, 74.8% for MPA and 95.7% for EGPA.

Change of classification from EMA to ACR/EULAR 2022

The ACR/EULAR 2022 assigned 51 cases to a different phenotype from that diagnosed with the EMA algorithm (Fig. 3); 16 were re-categorized from GPA to MPA and 35 from MPA to GPA.

Change of classification from MPA to GPA

Thirty-five cases classified as MPA by the EMA algorithm were assigned to GPA by ACR/EULAR 2022 criteria, based exclusively on antibody specificity. All 29 EMA3a cases re-assigned to GPA exhibited pauci-immune GN as well as haematuria but lacked other clinical features. However, they exhibited PR3 positivity and were thus classified as GPA by ACR/EULAR 2022 criteria. The remaining six cases, with EMA3b, exhibited non-specific clinical symptoms and features of acute kidney injury with no biopsy confirmation of GN (for various reasons) but surrogate markers of renal vasculitis. All were PR3-ANCA positive, and thus the ACR/EULAR 2022 classification was GPA.

Change of classification from GPA to MPA

Sixteen cases of GPA based on the EMA algorithm were re-classified as MPA according to the new ACR/EULAR criteria. All were MPO positive. Fifteen of those did not exhibit ear, nose, throat (ENT) involvement. Nine cases of EMA2a GPA (fulfilling ACR1990 criteria for GPA) were classified as MPA under the new criteria; all exhibited MPO positivity and pulmonary changes compatible with GPA (nodules or fixed infiltrates). Two cases showed granuloma on biopsy, eight had haematuria and six were diagnosed with pauci-immune GN.

Two cases of EMA2b, histologically compatible with CHCC GPA, exhibited granuloma on organ biopsy, renal failure, pauci-immune GN and MPO positivity and were thus shifted to ACR/EULAR 2022 MPA. Three cases of EMA2c, histologically compatible with CHCC MPA and

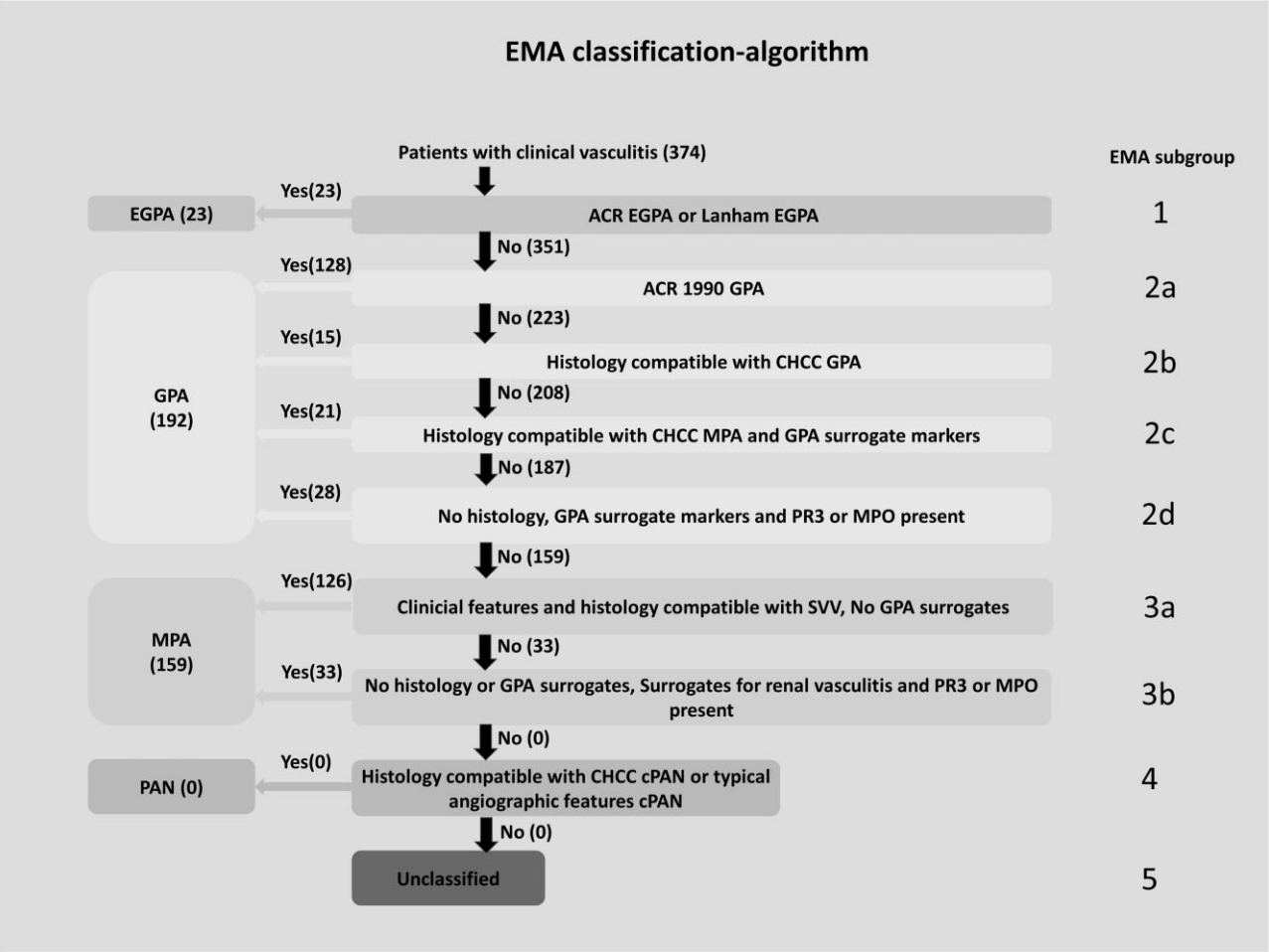

Figure 2. Categorization of 374 patients with AAV classified according to the EMA algorithm. The numbers in brackets indicate the number of patients classified in each step of the algorithm. AAV: ANCA-associated vasculitides; CHCC: Chapel Hill Consensus Conference; EGPA: eosinophilic granulomatosis with polyangiitis; EMA: European Medicines Agency; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; PAN: polyarteritis nodosa; SVV: small vessel vasculitis. Modified from Watts *et al.* [10]

Table 1. Selected clinical, laboratory and biopsy findings of AAV patients classified according to the ACR/EULAR 2022 criteria

Classification	Score, mean (range), points[a]	GN on biopsy, *n* (%)	Granuloma on biopsy[b], *n* (%)	PR3-ANCA, *n* (%)	MPO-ANCA, *n* (%)	ANCA negative, *n* (%)	ENT BVAS, *n* (%)	Chest BVAS, *n* (%)
GPA ($n = 199$)	8.82 (5–14)	81 (40.7)	52 (26.1)	186 (93.5)	8 (4)	5 (2.5)	125 (62.8)	118 (59.3)
MPA ($n = 136$)	8.33 (6–12)	98 (72.1)	4 (2.9)	1 (0.7)	135 (99.3)	0	5 (3.7)	52 (38.2)
EGPA ($n = 22$)[c]	11.5 (9–14)	1 (4.5)	0	0	8 (36.4)	14 (63.6)	15 (68.2)	17 (77.3)
Unclassifiable ($n = 13$)	NA	4 (30.8)	1 (8)	0	7 (53.8)	6 (46.2)	7 (53)	6 (46.2)
Double classification ($n = 4$)	NA	2 (50)	0	1 (25)	3 (75)	0	2 (50)	4 (100)
PR3-disease ($n = 188$)	NA	83 (44.1)	42 (22.3)	NA	NA	NA	113 (60.1)	115 (61.2)
MPO-disease ($n = 161$)	NA	100 (62.1)	11 (6.8)	NA	NA	NA	26 (16.1)	61 (37.9)

[a] Score in respective classification category ACR/EULAR 2022.
[b] Granuloma, extravascular granulomatous inflammation, or giant cells on biopsy (ACR/EULAR 2022 criteria).
[c] 21 (95%) with eosinophilia.
AAV: ANCA-associated vasculitides; BVAS: Birmingham vasculitis activity index; EGPA: eosinophilic vasculitis with polyangiitis; ENT: ear, nose and throat; GN: glomerulonephritis; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; NA: not applicable.

GPA surrogate markers, reclassified as ACR/EULAR 2022 MPA, showed haematuria and pauci-immune GN; two had fixed pulmonary infiltrates; and one showed ENT involvement. All were MPO positive.

The remaining two cases, EMA2d, i.e. no histopathology but ANCA positivity and GPA surrogate markers (pulmonary nodules), no renal or ENT involvement, but MPO positive, were classified as MPA with the new criteria.

The predominant reason for the change in classification from GPA to MPA with the new criteria was PR3 positivity. Figure 3 illustrates re-classification in disease phenotype.

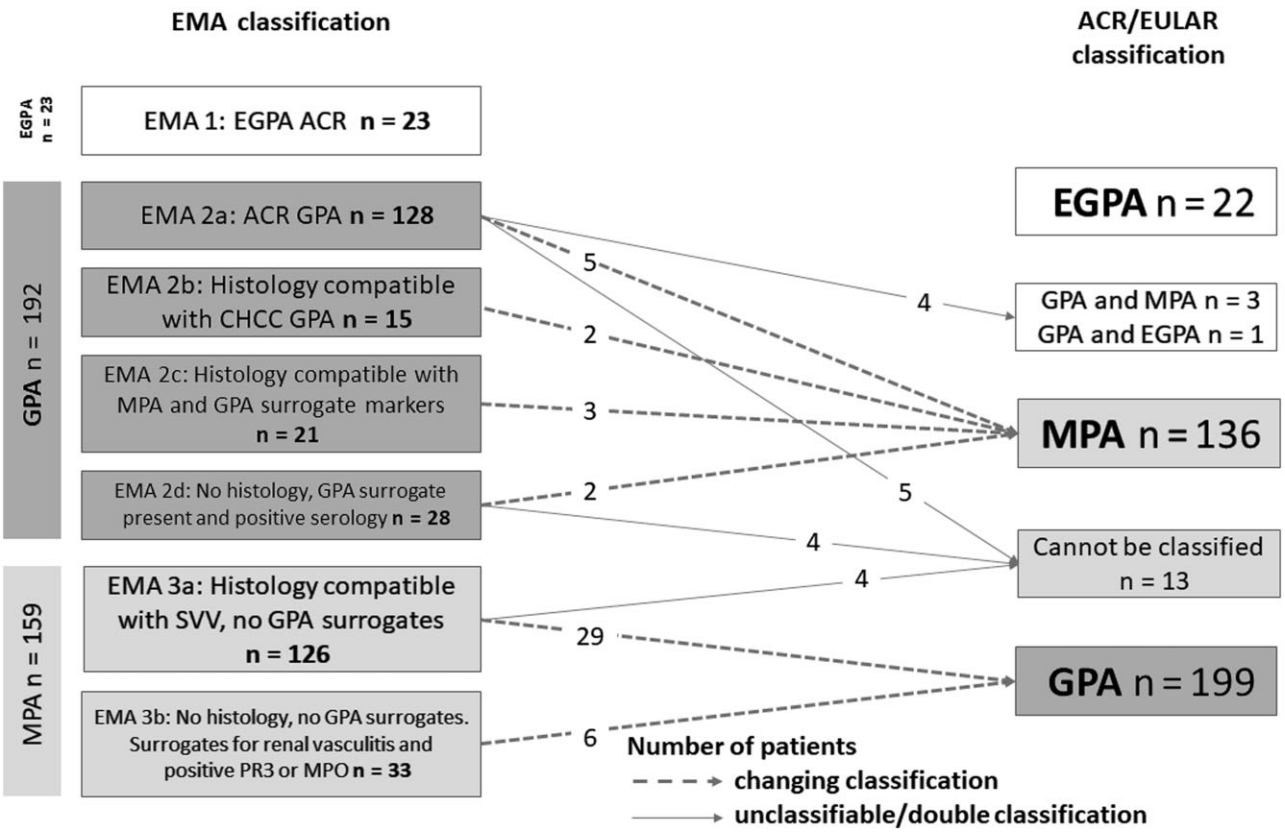

Figure 3. EMA and ACR/EULAR 2022 classification designation. CHCC: Chapel Hill Consensus Conference; EGPA: eosinophilic granulomatosis with polyangiitis; EMA: European Medicines Agency; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; SVV: small vessel vasculitis; PAN: polyarteritis nodosa

Challenges in applying the ACR/EULAR 2022 criteria

Unclassifiable cases

Thirteen cases classified by the EMA algorithm, nine GPA and four MPA, showed combinations of clinical, pathological, and serological characteristics that made fitting into a single disease category impossible according to the new criteria. Seven cases were MPO positive and the remaining six were ANCA negative. Seven patients exhibited ENT manifestations compatible with GPA, five showed nodules or fixed infiltrates on chest imaging, and in four kidney biopsy demonstrated pauci-immune GN. One case exhibited granulomatous inflammation on biopsy and two cutaneous vasculitis. All seven MPO positive patients presented nasal symptoms, three had parasinus involvement and two had hearing loss.

Overlapping classification

Four cases could be placed in more than one category using the new criteria. Three patients with GPA according to the EMA algorithm fulfilled both GPA and MPA classification under the ACR/EULAR 2022 criteria. The first exhibited pulmonary nodules, haematuria, acute renal failure, positive MPO and p-ANCA, but also tested positive for c-ANCA, resulting in classification as GPA as well as MPA. A second had bloody nasal discharge, conductive hearing loss, pulmonary nodules, MPO positivity and biopsy-confirmed pauci-immune GN, qualifying as GPA as well as MPA. The third case was diagnosed with pulmonary fibrosis years prior to diagnosis of AAV and presented with bloody nasal discharge, sinus involvement, pulmonary nodules and MPO positivity.

The fourth case, considered EGPA according to the EMA algorithm, fulfilled both GPA and EGPA diagnosis based on the ACR/EULAR 2022 criteria. The subject suffered asthma, peripheral blood eosinophilia, tissue eosinophilia, pauci-immune GN and sinunasal symptoms as well as pulmonary nodules and PR3 positivity, fulfilling both GPA and EGPA classification criteria.

Disagreement with current understanding of AAV histopathology

According to the widely accepted CHCC 2012 definitions of systemic vasculitis, granulomatous inflammation is a feature of GPA that differentiates it from MPA [1]. Granuloma is also accepted in clinical practice as a surrogate marker of GPA [10]. When we applied the new criteria, four patients with biopsy findings of granulomatous inflammation were classified as MPA. None showed ENT involvement, but one presented nodular lung disease on imaging studies. All were MPO positive.

ANCA serology-based classification

One-hundred and eighty-eight subjects positive for PR3-ANCA and 161 positive for MPO-ANCA were assumed to exhibit GPA and MPA, respectively, based on ANCA specificity. Agreement of the serology classification with the ACR/EULAR 2022 criteria for GPA was 98.9% (186/188 PR3-ANCA positive cases classified as GPA according ACR/EULAR 2022). Of the 161 cases classified MPA by serology, 135 (83.9%) were assigned MPA by ACR/EULAR

2022. PR3 positivity is rare in EGPA. In this cohort, one EGPA patient was PR3 positive, eight MPO positive and 14 ANCA-negative. Eight EGPA cases were assigned MPA by serology. We therefore excluded EGPA in the succeeding step. The above-mentioned agreement for PR3 then becomes 99.5% (186/187) and, correspondingly, 88.2% for MPO (135/153).

Discussion

We observed substantial agreement of the new ACR/EULAR classification criteria with the EMA algorithm. The agreement was highest for EGPA at almost 96%, followed by GPA and MPA with 84% and 75% agreement, respectively. However, when applying the new ACR/EULAR criteria, 3.5% of our AAV cases were unclassifiable, while 1.1% fell into two categories. PR3-ANCA and MPO-ANCA positivity as a single classification criterion would result in agreement of 99% for GPA and 88% for MPA, demonstrating the considerable weight granted to ANCA specificity in the new ACR/EULAR criteria. Nearly 14% of the subjects were classified as expressing a different disease phenotype from that determined by the EMA algorithm, mainly because of the weight the new criteria give to ANCA specificity. The difference between the ACR/EULAR 2022 criteria and a strict serological classification is so small that information provided by the new criteria may be redundant. It can be of value in ANCA negative cases. However, a substantial proportion of such cases were unclassifiable.

ACR/EULAR 2022 was the first attempt to develop classification criteria in >30 years. The ACR 1990 criteria represented an important and widely used tool [3]. However, a problem, as with many classification systems, lies in their use by physicians as diagnostic criteria. The original ACR criteria did not include microscopic polyangiitis, ANCA in small vessel vasculitis, or modern imaging studies. The next important step in facilitating epidemiological studies of vasculitis was the CHCC addressing of nomenclature of vasculitis in 1994 [7]. Although the authors of the CHCC report emphasized that the document was not intended as new classification criteria, it had a major impact on studies, as it, for first time, integrated the presence of ANCA and made a clear distinction between MPA and polyarteritis nodosa as well as between MPA and GPA, as the latter is a granulomatous disease. However, the ACR 1990 and CHCC categories showed a considerable degree of overlap, as a patient with small and medium sized vasculitis could be categorized as expressing two disease entities [10], and there was a need to develop more robust criteria for classification of systemic vasculitis. The EMA algorithm developed by Watts *et al.* in 2007 was not meant as a classification criterion but it resolved, or at least decreased, overlap between ACR 1990 and CHCC 1994.

With the new criteria, 3.5% of the cohort was unclassifiable, while 1.1% fulfilled criteria for two disease categories. Unclassifiable cases have occurred with other systems. Watts *et al.* [10] reported eight cases as unclassifiable by vasculitis experts in the original EMA study, and a Chinese validation [13] study encountered 20 such cases. Our group's earlier study of the epidemiology of AAV in southern Sweden [12] found no unclassifiable cases.

Pulmonary involvement as well as histology showing granuloma generates comparatively low scores (2 points each) in the new GPA criteria. Pauci-immune GN is given +1 point and MPO −1 point. This means a case with pulmonary nodules, granuloma on biopsy, and pauci-immune GN and MPO positivity will show a score of 4 in the GPA category and will therefore not be classified as GPA but as MPA with a score of 9 (5 needed for classification). Pyo *et al.* [23] suggested increasing the score of granuloma to 3 points, which would categorize the above-mentioned case as GPA, but classification to two phenotypes will be the consequence if no granuloma item generating a negative score in the MPA category would be introduced.

The new ACR/EULAR criteria employ a novel weighted scoring system based on a combination of organ system manifestations, serology and histopathological characteristics. For GPA classification, a minimum score of 5 is required. A score of 5 is also sufficient to classify patients as having MPA. As PR3- and MPO-ANCA are assigned the highest weight, 5 and 6, respectively, patients with small vessel vasculitis and positive serology may be classified as GPA *and* MPA, even though this is not compatible with commonly accepted definitions that include granuloma or classic ENT involvement [1]. Four of our subjects were classified as having MPA by the new criteria despite clear biopsy evidence of granulomatous inflammation. All these patients were MPO-ANCA positive. As granulomatous inflammation is one of most important features differentiating GPA from MPA, we suggest that patients with granulomatous inflammation on biopsy be classified as GPA regardless of ANCA serotype.

Studies [23–25] evaluating the ACR/EULAR criteria in patients from South Korea included 65 GPA, 117 MPA and 51 EGPA cases. The researchers report agreement of 96.6% for MPA, 73.8 for GPA and 84.9% for EGPA, compared with our corresponding findings of 74.8%, 84.9% and 95.7%. The Korean GPA cohort exhibited a considerably greater proportion (43%) of MPO positive GPA patients compared with 19% of the Swedish cohort [23]. One of the 65 GPA patients could not be classified with the new criteria, and 16 patients were re-assigned as MPA. We made similar observations with 16 (14%) of the GPA patients reclassified as MPA, primarily due to ANCA specificity. The Korean researchers report highest agreement for MPA, the category in which we observed the least agreement with the new criteria. ANCA positivity was comparable in the two cohorts (97.4% in Korea *vs* 99.3% in Sweden), Pauci-immune GN was less frequent in the Korean cohort than in ours (52.1% *vs* 71.4%). Two additional elements in the MPA category considerably impacted the score: ENT involvement (0.9% in Korea *vs* 2.9% Sweden) and lung fibrosis/interstitial lung disease (ILD) (49.6% in Korea *vs* 8% in Sweden). Approximately 50% of the Korean cases exhibited ILD on chest imaging, which might explain the high agreement in MPA compared with the Swedish cohort. Four of 17 Korean cases formerly considered MPA could not be classified under ACR/EULAR2022 criteria. We also observed four such cases as well as 35 former MPA cases now classified as GPA.

We observe almost perfect agreement for EGPA at 95.7% (an excluded double classified case would have resulted in 100%), whereas the Korean researchers report 86.3% [24]. A score of 6 is needed for EGPA classification. We did not find any score <9 in our EGPA cohort. The mean score was 11.5, whereas the Korean cohort showed a mean of 8.5 with a high number clustered around the cut-off of 6 points. With respect to ANCA distribution, we encountered one PR3

positive EGPA case, a higher number of ANCA negative, and fewer MPO positive than in the Korean study. All cases classified as EGPA with EMA were assigned the same classification with ACR/EULAR, one case was assigned EGPA and GPA by the latter, whereas 5.9% changed to MPA and 2.0% to GPA in the Korean study [23]. The same study made similar observations of cases exhibiting granulomatous inflammation on biopsy being classified as MPA, even though granuloma is traditionally regarded as a key feature of GPA [1].

A strictly ANCA-based classification system as we use it in our evaluation has limitations as ANCA specificity differs in populations globally due to genetic differences [26]. A classification system solely based on ANCA would therefore be more sensitive to genetic background than systems that even integrate clinical features and histology.

Lung fibrosis and interstitial lung disease have been described as manifestations of AAV [27, 28] and are primarily associated with MPO positivity; however, little is known about the epidemiology of ILD in AAV. A recently published study of pulmonary involvement in primary systemic vasculitis [29] based on data from the DCVAS cohort reported that 24.9% patients with MPA exhibited lung fibrosis on chest radiograph, CT or PET scan. Only six patients underwent lung biopsy, one of which showed fibrosis. Pulmonary function tests were available in 46 cases (20.6%), with results of 34.8% within normal limits. The ACR/EULAR MPA publication [15] gave considerable weight to lung fibrosis/ILD on chest imaging but provided no additional guidance for when the criteria are met. In contrast to earlier criteria and definitions, we consider this element not well defined and would welcome consensus.

The chief limitation of this study is that the data needed to apply the new criteria were collected retrospectively, with none exclusive to this study. Analyses of ANCA serology in our area have undergone modifications in the years since our cohort was established. In the earlier years, laboratories provided information on indirect immunofluorescence (IIF) analysis of ANCA; hence, data of c- or p-ANCA results were collected. In the latter half of the study period, we collected ANCA results based only on ELISA. As IIF-ANCA results are scored in the ACR/EULAR criteria, missing data may have impacted the results. The strength of this study is that, to the best of our knowledge, we used the largest cohort studied up to the present time, which covered all three disease categories of AAV.

The new ACR/EULAR criteria and the EMA algorithm show good agreement, but some important limitations apply in a small number of patients, related to overlap of disease categories, unclassifiable cases, and a variance from current understanding of histopathological features of AAV. The ANCA serology-based classification shows accuracy equivalent to the new criteria. In light of the significant issues encountered in our study when applying the new ACR/EULAR criteria of AAV, we encourage discussion and seek consensus among field experts on how to address challenges and limitations of the new criteria.

Data availability

Data are protected by the confidentiality laws in Sweden and cannot be shared. All data relevant to the study are included in the article. Please contact the corresponding author.

Contribution statement

All authors were involved in drafting the article or revising it for intellectual content, and all authors approved the final version for publication. Study conception and design: all authors. Data acquisition and analysis: J.R. and A.J.M. Statistical analysis: J.R. Data interpretation: all authors.

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