Rheumatology, 2025, **64**, 6233–6240
https://doi.org/10.1093/rheumatology/keaf417
Advance access publication 8 August 2025
Original Article

British Society for Rheumatology RHEUMATOLOGY OXFORD

Clinical science

Exploration of health-related quality of life, anxiety and depression in antineutrophil cytoplasmic antibody-associated vasculitis

Annika Granath [1,2,*], Sara Brolin [3,4], Karuna Dahlberg [1], Iva Gunnarsson [3,4], Elisabet Welin [1], Susanne Pettersson [3,4]

[1]Faculty of Medicine and Health, School of Health Sciences, Örebro University, Örebro, Sweden
[2]Centre for Innovation, Research and Education, Region Västmanland, Västerås, Sweden
[3]Rheumatology Unit, Karolinska University Hospital, Stockholm, Sweden
[4]Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden

*Correspondence to: Annika Granath, Faculty of Medicine and Health, School of Health Sciences, Örebro University, 701 82 Örebro, Sweden.
E-mail: annika.granath@oru.se

Abstract

Objectives: To explore health-related quality of life (HRQoL), anxiety, depression and fatigue among persons with ANCA-associated vasculitis (AAV).

Methods: In this cross-sectional study, patients were assessed with the EuroQoL five-dimension three-level questionnaire (EQ-5D-3L) and visual analogue scale (EQ-VAS), the Hospital Anxiety and Depression Score (HADS) and the Multidimensional Assessment of Fatigue questionnaire (MAF).

Results: HRQoL measured with EQ-VAS was higher in younger patients, those with inactive disease (BVAS = 0) and those with long disease duration (≥3 years), while EQ-5D-3L only varied with disease activity. Women, patients with active disease and patients with shorter disease duration reported more anxiety, and younger persons with active disease and short disease duration reported more fatigue. In the total group, disease activity and disease duration were both associated with HRQoL, anxiety, depression and fatigue. Four clusters based on EQ-5D, EQ-5D index and HADS were identified, containing patients with various levels of HRQoL and psychological distress across the disease course.

Conclusion: In patients with AAV, HRQoL, anxiety, depression and fatigue are persistent but vary depending on disease activity, disease duration, gender and age. Associations between disease activity and duration and HRQOL, anxiety, depression and fatigue were present in all patients. Four clusters revealed the ongoing influence of AAV, emphasizing the continuous need for multiprofessional support during the disease course. In this study, EQ-VAS was better able than the EQ-5D-index to effectively distinguish subgroups with different levels of HRQoL.

Keywords: ANCA-associated vasculitis, health-related quality of life, anxiety, depression, fatigue, patient perspective, cluster analysis.

Rheumatology key messages

- HRQoL, anxiety, depression and fatigue vary by disease activity, duration, age and gender, but not subtype.
- Four patient clusters reveal varying disease burdens, with high disease activity requiring targeted support.
- EQ-VAS may be better than EQ-5D-index to distinguish subgroups with different levels of HRQoL.

Introduction

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of chronic vasculitis, characterized by inflammation predominantly in small vessels and consists of three main subtypes: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) [1]. AAV is a heterogeneous disease, characterized by systemic symptoms such as fever, joint pain and manifestations from the eyes, nervous system, kidneys, respiratory system and ear, nose and throat. It is equally distributed between men and women, and most common in older adults [2].

Both the disease itself and its treatment can cause patients to experience a multifactorial disease burden affecting several domains of health. Reduced health-related quality of life (HRQoL), fatigue and psychological distress including anxiety and depression are common among AAV patients [3–5]. Decreased HRQoL in AAV has been found to be associated

Received: 1 April 2025. **Accepted:** 29 July 2025

with several aspects of living with the disease [3, 5–9] and can persist even when the disease is in remission [10, 11].

To be able to provide the best care possible for persons with AAV, the patient perspective should be included in evaluations of how the disease affects a patient [12–14]. The overall aim of this study was therefore to explore patient-reported HRQoL, anxiety and depression among persons with AAV from different perspectives. The specific aims were:

I. To compare levels of HRQoL, anxiety, depression and disease characteristics in persons with AAV.
II. To describe associations between disease characteristics and HRQoL, anxiety and depression in persons with AAV.
III. To explore clusters of HRQoL, anxiety and depression among persons with AAV.

Methods

This was a retrospective cross-sectional study including both newly diagnosed and patients with established disease who were over 18 years of age, who had been diagnosed with either GPA, MPA or EGPA and who participated in the VASKA study at Karolinska University Hospital, Sweden, between 2008 and 2022. Patients were recruited from both rheumatology and nephrology clinics and all patients had been or were positive for ANCA. The cohort and methods of data collection have been described elsewhere [15]. During the study visit, patients were asked to complete the Swedish versions of questionnaires measuring HRQoL, fatigue, anxiety and depression. To be included in the present study, participants had to have answered at least one of the patient-reported questionnaires.

Ethical approval was granted by the Regional Ethical Review Board in Stockholm (2008/1143–31). Informed consent was obtained from all participants, and the study complied with the Declaration of Helsinki.

Patient-reported outcome measures

The EuroQoL five-dimension three-level questionnaire (EQ-5D-3L), a well-established generic questionnaire used in rheumatology [14, 16], that measures HRQoL in five dimensions – mobility, self-care, daily activities, pain/discomfort and anxiety/depression – using three levels of severity: no problems, moderate problems and severe problems. It is generally used in combination with a visual analogue scale (EQ-VAS) measuring overall health. EQ-5D-3L scores are summarized into an index score (EQ-5D index) ranging from 0 to 1, where 1 is the value for full health [17]. All five questions must be answered to accurately capture the impact on a patient's HRQoL, and so only fully completed questionnaires were included in the analysis (Supplementary Data S1, available at *Rheumatology* online).

EQ-VAS asks the patient to score their health on a scale of 0–100, where 0 represents the worst health imaginable and 100 represents the best health imaginable [17].

The Hospital Anxiety and Depression Score (HADS) is a generic questionnaire, commonly used within rheumatology [14, 16], which measures anxiety (HADS-A) and depression (HADS-D) in two dimensions, each with seven items. Each item is scored from 0 to 3, with a higher score representing a higher level of depression or anxiety. The domains are summed separately, giving a maximum possible total sum of 21 for each domain. Sum scores of 0–7 represent no anxiety or depression, 8–10 mild anxiety or depression, 11–14 moderate anxiety or depression and 15–21 severe anxiety or depression [18]. To prevent underestimation of anxiety and depression, we allowed a maximum of one missing item per dimension for analysis. Consequently, questionnaires with >1 missing item were excluded from the analysis (Supplementary Data S1, available at *Rheumatology* online).

The Multidimensional Assessment of Fatigue questionnaire (MAF), originally developed to measure fatigue in rheumatoid arthritis, and later validated for several rheumatic diseases, contains 16 items measuring four dimensions of fatigue during the previous week: severity, distress, interference in activities of daily living (ADL) and timing (in terms of frequency and change). A global fatigue index is calculated by summing the total scores from the severity and distress subscales, the average score for the degree of interference in ADL, and one timing item. The global fatigue index ranges from 1 to 50, with a higher score representing more severe fatigue, distress or impact on activities of daily living [19]. To ensure that our data accurately captured the burden of fatigue, the analysis only included patients with ≤4 missing items on the ADL subscale (Supplementary Data S1, available at *Rheumatology* online).

Disease and patient characteristics

Diagnosis of AAV, disease activity, disease duration, age, gender, prednisolone dose, body mass index (BMI) and level of education were collected by a physician during the study visit.

Disease activity was evaluated with the Birmingham Vasculitis Activity Score (BVAS), a physician-completed questionnaire that assesses disease activity in nine organs and produces a score ranging from 0 to 63 [20]. A score of zero was considered inactive disease and a score of ≥1was defined as active disease.

Disease duration was expressed in years, with ≤2 years considered short disease duration. This cut off was guided by earlier studies indicating that the first two years of disease is an intense time for patients, both medically and psychologically [21, 22].

Statistics

Descriptive statistics such as frequency distribution, median, minimum, maximum, interquartile range (IQR) and percentage were used to characterize the study cohort.

The distributions of EQ-5D index, EQ-VAS, MAF, HADS-A and HADS-D were expressed as median and IQR. To compare distributions of the EQ-5D index, EQ-VAS, MAF, HADS-A and HADS-D between groups of diagnosis, disease activity, disease duration, age, and gender, the Mann–Whitney *U* test or Kruskal–Wallis H test was performed.

Bivariate correlations between disease duration and EQ-5D index, EQ-VAS, MAF, HADS-A and HADS-D as well as disease activity and EQ-5D index, EQ-VAS, MAF, HADS-A and HADS-D were performed using Spearman's rank-order correlation. A correlation coefficient of <0.25 was considered as no association, 0.25–0.50 weak to acceptable, 0.5–0.75 moderate and 0.75–1.0 strong [23].

P-values of at least the 0.05 level were considered significant.

A hierarchical cluster analysis was performed to create clusters of individuals with AAV, based on EQ-5D index, EQ-VAS,

HADS-A and HADS-D. Cluster analysis can create homogeneous groups of attributes within a cohort of a heterogeneous population [24]. In hierarchical cluster analysis, each person starts in their own cluster, and the two most similar clusters are then merged into new clusters. The procedure of creating clusters included a hierarchical agglomerative clustering procedure using average linkage (within groups), where the average distance between cluster members is as small as possible [24, 25]. The appropriate number of clusters was determined with the guidance of coefficients, selected based on clinical relevance after discussion among the authors. For this study, four clusters were identified as the most clinically relevant solution and are described using median and IQR.

Data were analysed using version 28.0 of IBM SPSS Statistics for Windows (IBM Corp, Armonk, NY, USA).

Results

Patient characteristics

A total of 296 patients had answered at least one of the patient-reported outcomes and hence were included in the study, representing all three AAV subtypes, equally distributed between women and men, with a median age of 63 years. Their median BVAS score was 1 (range: 0–33, IQR: 0–12) and 46% had a BVAS score of zero. Median disease duration was 2 years (range: 0–31, IQR: 0–6) and 55% had a disease duration of ≤2 years. The mean current dose of prednisolone was 5 mg (range: 0–80, IQR: 0–12.5) (Table 1). EQ-5D-3L was completed by 282 patients, EQ-VAS by 271, HADS by 283 and MAF by 256 patients (Supplementary Data S1, available at *Rheumatology* online).

HRQoL, fatigue, anxiety and depression

The distributions of EQ-5D index, EQ-VAS, HADS-A, HADS-D and MAF scores were similar for all three AAV diagnoses, and no significant differences could be found ($P = 0.35$–0.69) (Supplementary Table S1, available at *Rheumatology* online).

Among all patients, HADS-A scores were higher in women than in men ($P = 0.03$), in those with active disease *vs* inactive disease ($P = 0.013$) and in those with disease duration ≤2 years *vs* ≥3 years ($P = 0.001$) (Fig. 1). No significant differences were found in HADS-D scores (Supplementary Table S1, available at *Rheumatology* online).

EQ-VAS was lower in patients with disease duration ≤2 years *vs* ≥3 years ($P = 0.005$), age ≥65 years *vs* <65 years ($P = 0.017$) and active disease *vs* inactive disease ($P = 0.006$). Moreover, patients with inactive disease had significantly higher EQ-5D-index scores in comparison to patients with active disease ($P = 0.014$) (Fig. 1), (Supplementary Table S1, available at *Rheumatology* online).

MAF scores were higher for patients with active disease *vs* inactive disease ($P = 0.005$), for patients with disease duration ≤2 years *vs* ≥3 years ($P = 0.002$) and for patients aged <65 years *vs* >65 years ($P = 0.03$) (Fig. 1), (Supplementary Table S1, available at *Rheumatology* online).

Associations

Bivariate associations were explored for the whole population as well as for the diagnostic sub-types (Table 2). In the total group, weak associations were found between disease activity and EQ-5D index, EQ-VAS, MAF, HADS-A and HADS-D ($r^2 = -0.279$–0.256), as well as between disease duration and EQ-VAS, MAF, HADS-A and HADS-D ($r^2 = -0.257$–0.286) (Table 2). However, no associations were observed for EQ-5D index and disease duration.

The small group of EGPA patients showed a moderate negative association ($r^2 = -0.736$) between disease activity and EQ-5D index, a moderate positive association ($r^2 = 0.579$) between disease duration and EQ-VAS, and a moderate

Table 1. Patient characteristics

	Total	EGPA	GPA	MPA
Diagnosis, *n* (%)	296	12 (4.1)	209 (70.6)	75 (25.3)
Age, years				
Median, range (IQR)	63, 18–90 (50–70)	59, 34–73 (41–68)	60, 18–90 (47–68)	67, 31–86 (56–73)
Age under 65 years, *n* (%)	166 (56.5)	9 (75)	127 (61)	40 (40.5)
Gender				
female, *n* (%)	157 (53)	5 (41.7)	100 (47.8)	52 (69.3)
male, *n* (%)	139 (47)	7 (58.3)	109 (52.2)	23 (30.7)
BMI				
median, range (IQR)	25.4, 16–59 (23–29.4)	24.3, 21–27 (22–26.7)	25.3, 16–59 (16–59)	25.7, 17–40 (22.6–30)
Education,[a]				
n (%)	223 (80.7)	10 (83.3)	162 (82.2)	50 (75.8)
Occupation				
employed/student, *n* (%)	133 (47.8)	8 (66.7)	102 (51.3)	23 (34.3)
retired, *n* (%)	130 (46.0)	4 (33.3)	88 (44.2)	38 (56.7)
unemployed, *n* (%)	15 (5.1)	n/a	9 (4.5)	8 (9)
Disease duration, years				
median, range (IQR)	2, 0–31 (0–6)	7, 0–19 (0–11)	2, 0–31 (2–8)	1, 0–18 (0–5)
≤2 years, *n* (%)	162 (55.3)	4 (33)	116 (56)	42 (56.8)
≥3 years, *n* (%)	131 (44.7)	8 (67)	91 (44.0)	32 (43.2)
Disease activity (BVAS)				
median, range (IQR)	1, 0–33 (0–12)	0, 0–30 (0–14)	1, 0–33 (0–12)	0, 0–31(0–14)
BVAS =0 *n* (%)	95 (46.3)	7 (70)	2 (42.8)	26 (52)
BVAS ≥1 *n* (%)	110 (53.7)	3 (30)	83 (57.2)	24 (48)
Prednisolone dose, mg				
median, range (IQR)	5, 0–80 (0–12.5)	5, 0–60 (5–7.5)	5, 0–80 (0–30)	5, 0–60 (0–10)

[a] 9 years compulsory education.
BVAS: Birmingham Vasculitis Activity Score; EGPA: eosinophilic granulomatosis with polyangiitis; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis.

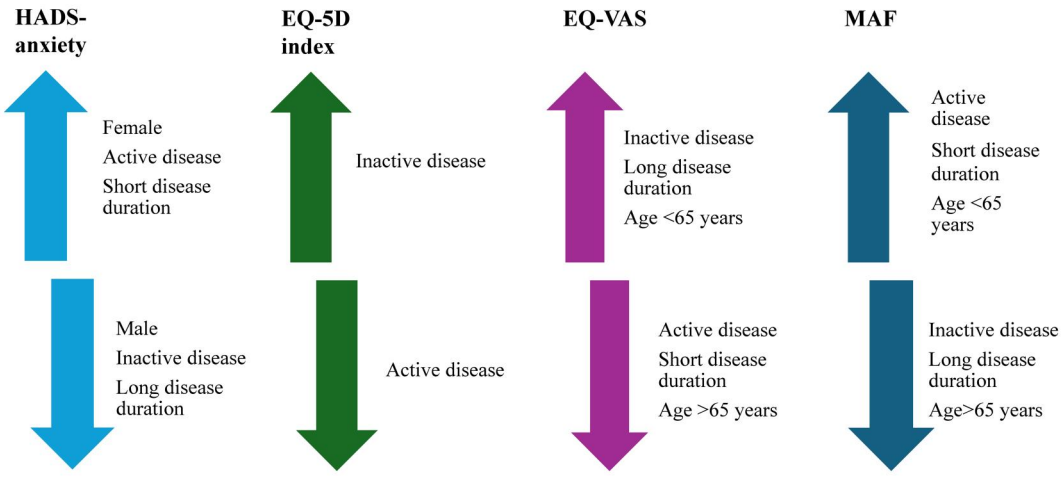

Figure 1. Differences for gender, disease activity, disease duration and age in the EQ-5D index, EQ-VAS, HADS-anxiety and MAF. Inactive disease = BVAS 0. Active disease = BVAS ≥1. Short disease duration = 2 years. Long disease duration = ≥3 years. BVAS: Birmingham Vasculitis Activity Score

Table 2. Associations between disease activity, respectively: disease duration and EQ-5D-Index, EQ-VAS, HADS-A, HADS-D, MAF

Disease activity												
	All patients	**r_s**	***P*-value**	**EGPA**	**r_s**	***P*-value**	**GPA**	**r_s**	***P*-value**	**MPA**	**r_s**	***P*-value**
EQ-5D-index	*n* = 179	**0.228**	0.002	*n* = 11	**−0.736**	0.024	*n* = 127	**−0.233**	0.008	*n* = 43	−0.155	0.322
EQ-VAS	*n* = 170	**−0.279**	<0.001	*n* = 11	−0.295	0.407	*n* = 118	**−0.337**	<0.001	*n* = 42	−0.184	0.243
HADS-A	*n* = 177	**0.221**	0.003	*n* = 10	0.045	0.901	*n* = 124	**0.209**	0.020	*n* = 43	**0.374**	0.013
HADS-D	*n* = 180	**0.189**	0.011	*n* = 10	0.225	0.532	*n* = 127	0.173	0.051	*n* = 43	0.281	0.068
MAF	*n* = 164	**0.256**	<0.001	*n* = 9	0.218	0.532	*n* = 112	**0.287**	0.002	*n* = 43	0.191	0.220
Disease duration												
EQ-5D-index	*n* = 277	0.105	0.080	*n* = 11	0.309	0.356	*n* = 207	0.106	0.139	*n* = 69	0.083	0.499
EQ-VAS	*n* = 267	**0.286**	<0.001	*n* = 12	**0.579**	0.049	*n* = 184	**0.302**	<0.001	*n* = 67	0.229	0.794
HADS-A	*n* = 274	**−0.257**	<0.001	*n* = 12	−0.348	0.267	*n* = 185	**−0.244**	<0.001	*n* = 70	**−0.336**	0.002
HADS-D	*n* = 280	**−0.164**	<0.001	*n* = 12	−0.404	0.193	*n* = 190	**−0.146**	0.040	*n* = 71	**−0.244**	0.004
MAF	*n* = 257	**−0.242**	<0.001	*n* = 10	**−0.699**	0.024	*n* = 171	**−0.307**	<0.001	*n* = 66	−0.033	0.794

Bold text indicates $P = \leq 0.05$.
EGPA: eosinophilic granulomatosis with polyangiitis; GPA: granulomatosis with polyangiitis; HADS-A: Hospital Anxiety and Depression Score – Anxiety; HADS-D: Hospital Anxiety and Depression Score – Depression; MAF: Multidimensional Assessment of Fatigue Questionnaire; MPA: microscopic polyangiitis; r_s: Spearman's rank-order correlation.

negative association ($r^2 = -0.699$) between disease duration and MAF (Table 2).

Clusters

The cluster analysis included 245 individuals. Four clusters were formed based on EQ-5D index, EQ-VAS, HADS-A and HADS-D. All four clusters had similar gender and age distributions, and all three diagnoses were represented in each of the four clusters (Supplementary Table S2, available at *Rheumatology* online). The four clusters were distinctive separated by EQ-VAS (Fig. 2).

Cluster A: High HRQoL with no anxiety or depression

Cluster A included 65 individuals with high EQ-5D index (median: 0.848, IQR: 0.796–1) and EQ-VAS (median: 85, IQR: 80–90). They showed no signs of depression (median: 2, IQR: 0–3) or anxiety (median: 3, IQR: 1–5.5). In comparison to the other three clusters, this group had a longer disease duration (median: 4, IQR: 1–11), low BVAS (median: 0, IQR: 0–1), was less affected by fatigue (median: 19.6, IQR: 14–30) and used a lower prednisolone dose (median: 3, IQR: 0–5). One patient had EGPA (1.5%), 44 (67.7%) had GPA and 20 (30.8%) had MPA.

Cluster B: Moderate to high HRQoL with mild to no anxiety and no depression

Cluster B included 96 individuals with moderate to high EQ-5D index (median: 0.724, IQR: 0.689–0.796) and EQ-VAS (median: 70, IQR: 60–70). They showed no signs of depression (median: 4, IQR: 2–6) and mild to no anxiety (median: 5, IQR: 3–9). The group had short disease duration (median: 2, IQR: 0–6) and lower BVAS score (median: 0, IQR: 0–6.5) and was somewhat affected by fatigue (median: 28.6, IQR: 22.1–33.7). Patients in this group used moderate doses of prednisolone (median: 5, IQR: 0–12.5). Five had EGPA (5.2%), 68 (70.8%) had GPA and 23 (24%) had MPA.

Cluster C: Moderate HRQoL with mild to no anxiety and no depression

Cluster C included 44 individuals with moderate EQ-5D index (median: 0.725, IQR: 0.3–0.791) and EQ-VAS (median: 50, IQR: 45–50). They showed no signs of depression (median: 6, IQR: 3.3–8.8) and mild to no anxiety (median: 4.5, IQR: 2.3–10). This group had shorter disease duration than cluster B (median: 2, IQR 0–7) and lower BVAS than cluster A (median: 2.5, IQR: 0–11.5). Patients in this group were somewhat affected by fatigue (median: 30.9, IQR: 23.3–

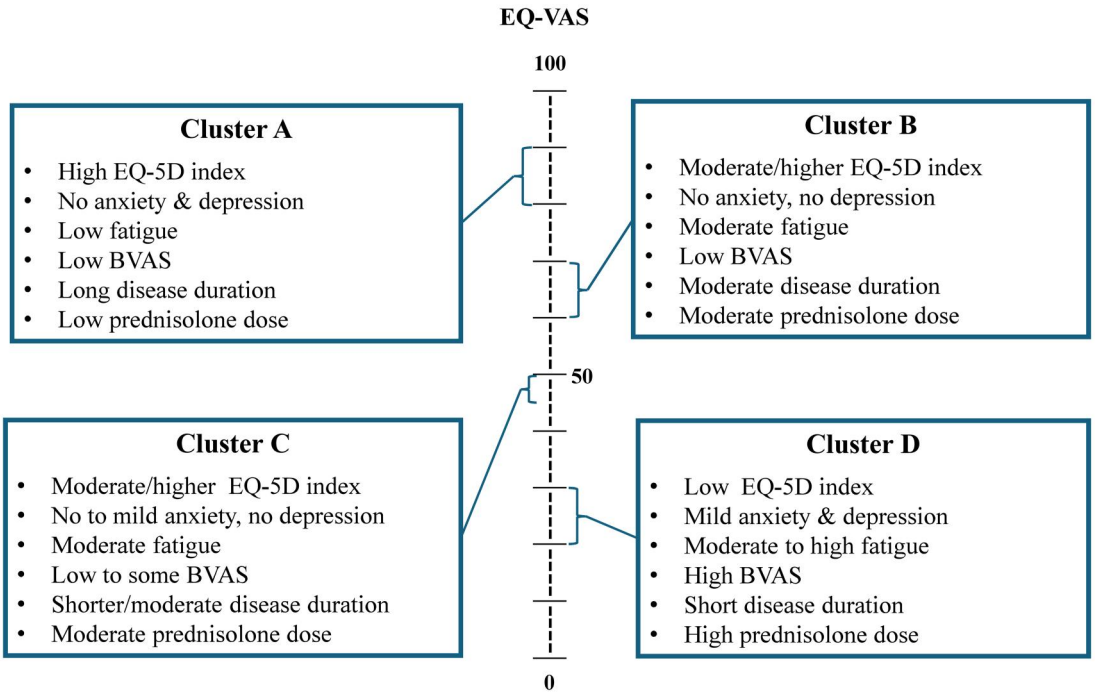

Figure 2. Interquartile range ({) on the EQ-VAS scale for clusters A–D

34.2) and were treated with a moderate dose of prednisolone (median: 5, IQR: 2–10.5). Four (9.1%) had EGPA, 32 (72.7%) had GPA and eight (18.2%) had MPA.

Cluster D: Low HRQoL with mild anxiety or depression

Cluster D included 40 individuals with lower EQ-5D index (median: 0.293, IQR: 0.1–0.62) and lower EQ-VAS (median: 30, IQR: 20–30) than clusters B, C and D. Further, they had signs of mild depression (median: 7.5, IQR: 4–11) and anxiety (median: 8, IQR: 5–11.8). In comparison to the other three clusters, this group had shorter disease duration (median: 0, IQR: 0–3), higher BVAS (median: 11, IQR: 0–19), was more affected by fatigue (median: 36.8, IQR: 32.3–40.9) and used a higher prednisolone dose (median: 15, IQR: 2–53). One patient (2.5%) had EGPA, 28 (70%) had GPA and 11 (27.5%) had MPA.

Discussion

This study evaluated the impact of AAV on HRQoL, psychological well-being and fatigue in a large patient cohort. Our findings demonstrate that these aspects vary significantly with disease activity, disease duration, sex and age, but not with AAV subtype. The cluster analysis indicated that the burden of AAV persists even in patients with low disease activity and long disease duration, reinforcing the need for continuous support.

Compared with the Swedish general population [26], and in concordance with earlier research [27], HRQoL was impaired for all of our patients, including those with low disease activity, longer disease duration and younger age. Measured by EQ-VAS, HRQoL was lower in older patients, those with shorter disease duration and those with active disease, whereas EQ-5D index only varied with disease activity. Approximately one-third of patients reported anxiety symptoms (HADS-A >7), particularly women and those with active disease or shorter disease duration. Depressive symptoms (HADS-D >7) were reported by one-fifth of patients, but no significant subgroup differences were observed. Fatigue was more prevalent in patients with active disease, shorter disease duration and younger age, aligning with previous studies that highlight the multifactorial nature of fatigue [28, 29]. Our results emphasize the ongoing impact of AAV and the importance of addressing psychological distress and fatigue in patient care [4].

Unlike previous findings [30, 31], we did not confirm an association between BMI and HRQoL, psychological well-being or fatigue, possibly due to the majority of our cohort having a normal BMI range.

Associations between disease activity, disease duration, HRQoL (primarily measured with EQ-VAS), anxiety, depression and fatigue were found among all patients. This might be explained by the ongoing inflammation, causing decreased HRQoL with worse psychosocial wellbeing and more fatigue. Though our findings are consistent with some previous studies [32–34], our associations were predominantly weaker and cannot be interpreted as evidence of a causal relationship. Interestingly, stronger associations were found in the EGPA group, but those findings must be interpreted as exploratory and not adequate powered due to the small number of patients. Due to the cross-sectional approach of this study and the multifactorial cause of disease burden in patients with chronic systemic diseases [34–37], causality cannot be determined.

The cluster analysis, based on HRQoL, anxiety and depression identified four clinically relevant clusters which distinguished different levels of disease burden across the disease course. All three subtypes of AAV were represented in all four clusters. Notably, EGPA patients were predominantly found in clusters with moderate HRQoL and minimal psychological distress, suggesting a comparatively lower burden of anxiety and depression, but might be caused by random

variation due to the small number of patients. The cluster with the lowest HRQoL (D) was characterized by higher disease activity, shorter disease duration and higher corticosteroid use, highlighting a subgroup that requires targeted support. Conversely, the cluster with the highest HRQoL (A) included patients with low disease activity, long disease duration and minimal psychological distress, indicating a lower need for intervention. The intermediate clusters (B and C) further confirmed the progressive consequences of AAV, with fatigue present in all groups. Our findings underscore the need for continuous tailored support from healthcare providers beyond the early disease phase, as patients remain vulnerable even after the initial years.

A holistic approach from healthcare providers may promote self-management and strengthen patients in various ways, allowing them to maintain psychological well-being throughout the disease course [38–40]. The importance of non-pharmacological interventions such as psychological and educational support has been emphasized in previous studies and should be a key focus in AAV care [4, 34, 41, 42].

Methodological considerations

Incorporating the patient's own perspective is an essential part of care while living with a chronic disease such as AAV [14, 43]. The present study included well-known and within rheumatology widely used generic questionnaires [14, 16–19]. Although this has the benefit of allowing comparison with other patient groups, these questionnaires lack the ability to capture the disease-specific burden of AAV. Use of disease- and treatment-specific questionnaires, such as the AAV-PRO [44], might capture the disease-specific aspects for patients living with AAV, and future studies should ideally include such instruments. Furthermore, performing qualitative studies could uncover additional knowledge and lead to improvement in AAV care [14, 45, 46]. To prevent overestimation or underestimation of the levels of distress among our patients, some individuals with incomplete or missing questionnaires were excluded from the analytical part of this study [47] (Supplementary Data S1, available at *Rheumatology* online).

Cluster analysis enables grouping of individuals where the data objects are similar to each other within the group but dissimilar to each of the other groups [24]. This was determined to be a suitable method to explore the impact of AAV, based on HRQoL and HADS. To our knowledge, this is the first study to evaluate the consequences of AAV with a cluster approach. However, different clustering methods and decisions during the clustering process may provide different results [24, 25], which must be taken into consideration while interpreting the present findings. With the aim to find patterns among our patients and determine the most clinically relevant number of clusters, the results of several different cluster solutions were discussed among the authors. Four clusters were considered relevant, in order for the groups to be fairly equal in size and to achieve clinically relevant information on how AVV affected the patients. These results provide understanding into the continuous influence of AAV on patients during the disease course. Fewer clusters prevented conclusions to be drawn due to lack of nuances and the similarity of the groups, whereas more than four clusters created smaller groups of patients, which limits the clinical adaptation.

In this study, HRQoL was measured using EQ-5D-3L, although the Short Form-36 (SF-36) questionnaire is more commonly used in vasculitis research [14, 27]. The SF-36 has both a physical score component and a mental score component, and so the use of SF-36 might have provided additional information on these dimensions of HRQoL, as well as allowing for comparison of results between studies. On the other hand, discrepancies in levels of psychological distress between SF-36 and HADS have been suggested [3] and HADS might be favoured over SF-36 in providing a deeper understanding of psychological distress.

In line with earlier research [48, 49], we found that EQ-VAS was better able than the EQ-5D index to distinguish between different levels of HRQoL. In addition, EQ-VAS scores could discriminate between patients with inactive *vs* active disease, long and short disease duration and different age categories, whereas differences in EQ-5D index scores were only found between inactive and active disease. Moreover, EQ-VAS was the only instrument with no overlapping IQRs in the cluster analysis. One tentative explanation for our findings could be that the EQ-VAS has the advantage of allowing a patient's individual interpretation of 'full health' to guide the evaluation, rather than being limited by the five dimensions in EQ-5D: mobility, self-care, daily activities, pain/discomfort and anxiety/depression [50].

A key strength of this study is its large cohort size, providing robust insights into the impact of AAV. However, limitations include the long sampling period, which was necessary due to AAV's low incidence as well as the cross-sectional design, which precludes causal conclusions. The use of EQ-5D-3L instead of SF-36, or other questionnaires, may have limited the ability to capture certain aspects of HRQoL, although EQ-VAS appeared to provide a more sensitive measure of disease burden. Notably, EQ-VAS distinguished between different patient subgroups more effectively than the EQ-5D index, suggesting its potential superiority in capturing HRQoL variations. This warrants further investigation.

Conclusion

This study highlights the persistent burden of AAV on HRQoL, psychological well-being and fatigue, with variations by disease activity, duration, age and gender. Cluster analysis revealed distinct patient subgroups requiring tailored care strategies throughout the disease course. EQ-VAS emerged as a potentially superior tool for assessing HRQoL variations, which should be explored in future research. These findings reinforce the need for comprehensive multidisciplinary care to support AAV patients beyond the early disease stages.

Supplementary material

Supplementary material is available at *Rheumatology* online.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Funding

This work was supported by the Swedish Rheumatism Association [ST-202111 to A.G.] [R-1025817 to I.G]. Stockholm County Council Regional Council (ALF) [FoUI

–985152 to I.G]. The King Gustaf V 80-year Foundation [FAI 2023–0958 to I.G].

Disclosure statement: Susanne Pettersson: Speaker: AstraZeneca (2024), Research grant: Novartis (2022), Pfizer (2024), CSL Vifor (2024). Sara Brolin: Consultant: CSL Vifor (2023, 2024), Research grant: Novartis (2019), CSL Vifor (2024).

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Rheumatology, 2025, 64, 6233–6240
https://doi.org/10.1093/rheumatology/keaf417
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