Rheumatology International (2023) 43:933–940
https://doi.org/10.1007/s00296-023-05288-4

Rheumatology
INTERNATIONAL

OBSERVATIONAL RESEARCH

Patient-reported outcomes in ANCA-associated vasculitis: a cross-sectional study to explore the interactions between patients' and physicians' perspectives

José Joel Hurtado-Arias[1] · Isabela Ramírez-Mulhern[1] · Carlos Gonzalez-Martínez[2] · Javier Merayo-Chalico[1] · Ana Barrera-Vargas[1] · Andrea Hinojosa-Azaola[1]

Received: 4 November 2022 / Accepted: 15 February 2023 / Published online: 22 February 2023

Abstract

To evaluate associations between the domains of the ANCA-associated vasculitis patient-reported outcome (AAV-PRO) instrument and clinical variables. Patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA), or renal-limited vasculitis (RLV) were recruited from a tertiary care center in Mexico City. Demographic, clinical, serological, and treatment-related data were retrieved. Disease activity, damage, patient and physician global assessments (PtGA and PhGA) were evaluated. All patients completed the AAV-PRO questionnaire, male patients also completed the International Index of Erectile Function (IIEF-5) questionnaire. Seventy patients (44 women and 26 men) were included, with a median age of 53.5 years (43–61), and a disease duration of 82 months (34–135). Moderate correlations were identified between the PtGA and the AAV-PRO domains: social and emotional impact, treatment side effects, organ-specific symptoms, and physical function. The PhGA correlated with the PtGA and prednisone doses. Subanalyses of the AAV-PRO domains according to sex, age, and disease duration showed significant differences in the treatment side effects domain, with higher scores in women, in patients < 50 years, and in patients with disease duration < 5 years. The domain of concerns about the future showed a higher score in patients with disease duration < 5 years. A total of 17/24 (70.8%) of men who completed the IIEF-5 questionnaire were classified as having some degree of erectile dysfunction. The domains of AAV-PRO correlated with other outcome measures, while differences were found between some of the domains according to sex, age, and disease duration.

Keywords ANCA-associated vasculitis · Patient-reported outcomes · Sexual function · Outcome measures · Physician global assessment · Patient global assessment

Introduction

The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are a group of complex chronic diseases that result in morbidity, accumulated organ damage, treatment burden, and risk of relapses. The advent of current immunosuppressive regimens has transformed these conditions from fatal to chronic diseases characterized by a relapse and remission cycle. Compared to the general population, patients with AAV are more likely to report poor health-related quality of life (HRQoL) and high levels of fatigue, with important impairments in physical functioning and bio-psychosocial factors [1–3].

Nowadays, patients actively participate in the shared decision-making process, transforming outcome measures into relevant and understandable aspects of the disease. A key aspect of outcome measures is the incorporation of the patients' views or illness perceptions to determine the impact of the disease. These subjective complementary experiences may differ from the clinicians' views and are important determinants of health-related behavior, treatment adherence, and functional recovery [4].

✉ Andrea Hinojosa-Azaola
andreaha@yahoo.com

[1] Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Vasco de Quiroga No. 15, Colonia Sección XVI, Tlalpan, 14080 Mexico City, Mexico

[2] Department of Urology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

The Outcome Measures in Rheumatology Vasculitis Working Group (OMERACT) has defined a core domain set of outcome measures for AAV, covering the spectrum of disease activity, damage, patient-reported outcomes (PRO), and mortality [5]. Generic instruments, such as the Survey Short-Form 36 Questionnaire (SF-36), the Health Assessment Questionnaire (HAQ), the EuroQol 5D, and the Hospital Anxiety and Depression Scale (HADS), are typically used to measure HRQoL, disability, depression and anxiety in vasculitis patients; however, important aspects specific to vasculitis and the patient's perspective of the burden of disease have not been adequately captured by these tools [6–8].

To address this unmet need, a new disease-specific, patient-based instrument, AAV-PRO, was designed and validated in 626 patients with AAV from the UK, US, and Canada. It is a 29-item questionnaire comprising six subscales or domains: "organ-specific symptoms," "systemic symptoms," "treatment side effects," "social and emotional impact," "concerns about the future," and "physical function" [9]. This instrument has shown strong psychometric properties, provides a profile of the impact of AAV and its treatment, and has now been validated for inclusion in clinical trials [10, 11].

Chronic diseases and their treatment are associated with poor sexual function [12]. However, the impact of AAV on sexuality has not yet been fully explored. In a validation study of the AAV-PRO, the concerns about difficulties with sexual activity or desire were addressed; however, the percentage of missing responses hindered the inclusion of this item in the final version [9].

Previous studies have reported a delay in diagnosis, early organic damage, increased risk of severe infections, and impaired HRQoL in Mexican AAV patients [13]. Therefore, the aim of this study was to evaluate the association between the domains of the AAV-PRO instrument and clinical variables as well as other outcome measures in a cohort of ambulatory Mexican patients with AAV diagnosis. In addition, this study explored the impact of AAV on male sexual function using a specific instrument to assess erectile dysfunction.

Patients and methods

Study population

We conducted a cross-sectional study and included patients aged > 18 years with an established diagnosis of granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA), or renal-limited vasculitis (RLV), according to the definitions of the 2012 Chapel Hill Consensus Nomenclature and/or the 1990 American College of Rheumatology Classification Criteria [14–16], who attended the outpatient clinic of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, a tertiary care center in Mexico City, during the period comprised from July 2021 to April 2022. Patients with AAV diagnosed with other autoimmune diseases in overlap were excluded.

Data collection and measures

All patients underwent complete rheumatologic evaluation. Information regarding demographics, current comorbidities, and clinical variables, including disease duration, clinical manifestations throughout the disease course, and the clinicopathological phenotypes were retrieved. ANCA positivity at AAV diagnosis was determined by immunofluorescence microscopy (IF), and by enzyme-linked immunosorbent assays (PR3-ANCA and MPO-ANCA). The current treatment, including the cumulative dose of glucocorticoids, was also considered. Laboratory parameters assessed on the day of the evaluation included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum creatinine, estimated glomerular filtration rate (eGFR, calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula, and serum hemoglobin. Disease activity and damage were evaluated using the Birmingham Vasculitis Activity Score for GPA (BVAS/WG) and the Vasculitis Damage Index (VDI), respectively [17, 18]. Patient and physician global assessments (PtGA and PhGA, respectively) on a 0–100 scale were also evaluated. All the patients completed the certificated Spanish translation version of the AAV-PRO questionnaire (VF247424-AAV PRO questionnaire-guide to scoring_July2017-v1-Spanish-Spain). The six domains of the AAV-PRO questionnaire are reported as mean values ranging from 0 to 100, with higher scores representing a higher intensity of the symptoms [9]. Moreover, sexual function in male patients was assessed using the International Index of Erectile Function (IIEF-5) questionnaire, which consists of 5 domains and a score ranging from 5 to 25, with a score ≤ 22 indicating some degree of erectile dysfunction [19].

Statistical analysis

Descriptive statistics included the number, percentage, mean with standard deviation, and median with the 25th and 75th percentiles. Correlation analyses were performed using the Pearson correlation coefficient (r), or the Spearman correlation coefficient (rho), depending on the type and distribution of the variables. The Bonferroni correction was applied for multiple comparisons. The correlation cut-off values were considered as follows [20]: 0.00–0.10 (negligible correlation), 0.10–0.39 (weak correlation), 0.40–0.69 (moderate correlation), 0.70–0.89 (strong correlation), 0.90–1.00

(very strong correlation). Normality was assessed using the Shapiro-Wilk test. Differences in the AAV-PRO domains between groups according to sex, age, disease duration, and damage accrued were analyzed using the Mann–Whitney *U* test after testing for normality. Differences between men with and without erectile dysfunction were analyzed using the Student *t* test or Mann–Whitney *U* test for continuous variables, and Chi-square or Fisher's exact test for categorical variables. Exact *p*-values are reported with a two-sided *p*-value < 0.05 considered statistically significant. All analyses were conducted using Stata software (Stata Corp, College Station, TX, USA), version 14.0.

The study was approved by the hospital's institutional review board (Comité de Investigación y Comité de Ética en Investigación) on July 2021 (Reference 3811). All procedures performed followed the ethical standards of the Declaration of Helsinki, and written informed consent was obtained from all the participants. Permission for the academic use of the AAV-PRO instrument was granted from the AAV-PRO team.

Results

Clinical and demographic characteristics

A total of 70 AAV patients were included: 44 (63%) women and 26 (37%) men, with a median age of 53.5 years (43–61) and a disease duration of 82 months (34–135). The most frequent clinical diagnosis was GPA (58 patients, 83%), followed by EGPA and RLV (5 patients each, 7%), and MPA (2 patients, 3%). Most of the patients (93%) were ANCA-positive at the time of diagnosis. The most frequent comorbidity was arterial hypertension (33 patients, 47%), followed by dyslipidemia (29 patients, 41%), and obesity (24 patients, 34%).

Information on the level of formal education was available for 51 patients. Of these, 51.5% had attained primary school, 38.5% had secondary school, and 37.1% had tertiary education.

The most frequent clinical phenotypes were severe MPO-ANCA in 30 patients (43%), and severe PR3-ANCA in 22 patients (31%), whereas 18 (26%) were non-severe. Predominantly granulomatous manifestations in the ear, nose, and throat (ENT) were present in 53 (76%), whereas lung granulomatous manifestations were present in 25 (36%). Vasculitic manifestations involving eyes/mucous membranes were present in 38 (54%), kidneys in 34 (49%), and nervous system in 27 (39%) patients.

At the time of the assessment, 49 patients (70%) were receiving prednisone, with a median dose of 2.5 mg (0–5), and a cumulative glucocorticoid dose since AAV diagnosis of 17.9 g (11.9–26.5); 22 (31%) were receiving azathioprine, 16 (23%) were receiving rituximab, 10 (14%) were receiving methotrexate, and 10 patients were receiving other immunosuppressants.

Disease activity, damage, and global assessments

At the time of recruitment, the patients presented with low disease activity, with a median BVAS/WG score of 1 point (0–2), an ESR of 2 mm/h (2–5), and CRP levels of 0.3 mg/dL (0.1–0.9). The most frequent clinical manifestations included ENT involvement in 21 patients (30%), constitutional symptoms in 10 (14%), and involvement of lung and nervous system in 7 (10%) patients. PhGA and PtGA showed medians of 5 mm (2–11) and 17.5 mm (7–32), respectively.

Concerning the damage assessment, the median VDI score was 3 points (2–4), with damage accrued mainly in the following organs: ENT, 43 patients (61%); kidneys, 31 (44%); and cardiovascular, 28 patients (40%).

Associations between patient-reported outcomes and other clinical variables

All the patients completed the AAV-PRO questionnaire. The subscales that reported the higher scores were: concerns about the future, with a mean score (SD) of 46 (28.7), followed by the social and emotional impact, with a mean score of 40.8 (25.8), and systemic symptoms, with a mean score of 37.7 (26.2). The treatment side effects domain had a mean score of 31.8 (21.7), the organ-specific symptoms domain of 29.5 (23.8), and the physical function of 24.7 (21.6).

The correlation analysis included the following variables: gender, age, disease duration, clinical phenotype, current prednisone dose, cumulative prednisone dose, ESR, CRP, serum creatinine, serum hemoglobin, eGFR, the PhGA, the PtGA, the BVAS/WG score and its specific items, the VDI score and its specific items, the six domains of the AAV-PRO instrument, and the IIEF-5 score.

Moderate positive correlations were identified between the PhGA and the following variables: PtGA ($r = 0.61$, $p = 0.001$), the BVAS/WG score ($r = 0.54$, $p < 0.0001$), and the current prednisone dose ($r = 0.40$, $p < 0.0001$). Moreover, the PtGA showed moderate positive correlations with the following domains of the AAV-PRO: organic-specific symptoms ($r = 0.40$, $p = 0.001$), treatment side effects ($r = 0.40$, $p = 0.001$), and physical function ($r = 0.49$, $p < 0.0001$). The organic-specific symptoms domain of the AAV-PRO and the VDI score also showed a moderate positive correlation ($r = 0.40$, $p = 0.001$). No other significant correlations were found between the AAV-PRO domains and the variables of disease duration, current or cumulative doses of prednisone, the BVAS/WG score, or the inflammatory markers. The results of the correlation analyses between the clinical variables, outcome measures, and domains of the AAV-PRO

Table 1 Associations between the PhGA and other variables

Variables	Correlation coefficient	*p*-value
PhGA and PtGA	0.61	0.001
PhGA and BVAS/WG	0.54	< 0.0001
PhGA and current prednisone dose	0.40	< 0.0001
PhGA and clinical phenotype	− 0.07	1.00
PhGA and cumulative prednisone dose	0.39	0.46
PhGA and VDI	0.34	1.00
AAV-PRO domains		
Organ-specific symptoms	0.22	0.07
Systemic symptoms	0.20	0.10
Treatment side effects	0.34	0.005
Social and emotional impact	0.30	0.015
Concerns about the future	0.15	0.22
Physical function	0.39	0.001

PhGA physician global assessment, *VDI* vasculitis damage index, *PtGA* patient global assessment, *BVAS/WG* Birmingham vasculitis activity score for granulomatosis with polyangiitis

Table 2 Associations between the PtGA and other variables

Variables	Correlation coefficient	*p*-value
PtGA and disease duration	− 0.07	0.57
PtGA and current prednisone dose	0.20	0.10
PtGA and cumulative prednisone dose	0.30	0.01
PtGA and ESR mm/h	− 0.03	0.77
PtGA and CRP mg/dL	0.007	0.95
PtGA and BVAS/WG	0.32	0.01
PtGA and VDI	0.29	0.01
AAV-PRO domains		
Organ-specific symptoms	0.40	0.001
Systemic symptoms	0.37	0.002
Treatment side effects	0.40	0.001
Social and emotional impact	0.41	0.0006
Concerns about the future	0.34	0.005
Physical function	0.49	< 0.0001

PtGA patient global assessment, *VDI* vasculitis damage index, *BVAS/WG* Birmingham vasculitis activity score for granulomatosis with polyangiitis

are shown in Tables 1, 2 and 3, in Fig. 1 and in Supplementary Material 1.

Subgroup analysis of patient-reported outcomes

Subgroup analyses were performed to evaluate the impact of sex, age, and disease duration on the AAV-PRO domains. Women scored higher (i.e., worse) than men in the treatment side effects domain (35 (17.5–50) vs. 20 (10–35), respectively, $p = 0.04$) (Supplementary Material 2), whereas patients < 50 years old also scored higher in this domain compared with patients > 50 years old (40 (25–55) vs. 20 (10–40), respectively, $p = 0.005$), and in the concerns about the future domain (55 (45–85) vs. 35 (10–70), respectively, $p = 0.02$) (Supplementary Material 3). Regarding disease duration, patients with < 5 years scored higher than those with a disease duration > 5 years in the treatment side effects subscale (40 (25–50) vs. 20 (10–45), respectively, $p = 0.03$) (Supplementary Material 4).

Additional analysis to evaluate the impact of damage accrual on the AAV-PRO domains was performed by comparing patients with a VDI score of ≤ 3 points and those with a score of > 4 points. No significant differences were found between the groups (Supplementary Material 5).

Sexual function

Twenty-four of the 26 male patients (92%) completed the IIEF-5 questionnaire. Overall, the median score was 20 (12–23). According to the cutoff values, 17 (70.8%) of men had some degree of erectile dysfunction (in 12 of them it was mild to moderate and in 5 it was severe). No correlations were observed between the IIEF-5 score and the clinical variables, AAV-PRO domains, disease activity, or damage scores (data not shown). Moreover, no differences were found between male patients with and without erectile dysfunction with respect to age, disease duration, clinical phenotype, comorbidities, treatment, serologic tests, disease activity, or damage (Supplementary Material 6).

Discussion

This study examined the association between the domains of the AAV-PRO instrument, other outcome measures, and clinical variables in 70 patients with AAV from Mexico. Preliminary studies have validated the AAV-PRO instrument in other populations [21]. Table 4 summarizes the results of the present study and the validation studies of the AAV-PRO.

Fatigue was rated highly in this cohort. It is a common and poorly understood manifestation of vasculitis, and it usually does not correlate with measures of disease activity [4]. Previous studies have suggested that AAV-related fatigue is complex and multifactorial in origin and that sleep disturbance, pain, and elevated CRP are associated determinants [22].

Patients in the current study ranked the more "subjective" domains of the AAV-PRO (i.e., concerns about the future and social and emotional impact) higher than the "objective" domains (i.e., organ-specific and systemic symptoms). This suggests that patients' perceptions emphasize the psychological and social aspects of the disease [23]. The PhGA correlated with the PtGA, with disease activity, and with

Table 3 Associations between the AAV-PRO domains and other variables

Domain	Disease duration	Current PDN dose	Cumulative PDN dose	BVAS/WG	ESR	CRP	VDI
OS	0.14 (0.25)	− 0.06 (0.60)	0.26 (0.03)	0.20 (0.11)	− 0.04 (0.71)	− 0.003 (0.97)	0.40 (0.001)
SS	− 0.06 (0.59)	0.16 (0.20)	0.19 (0.13)	0.23 (0.06)	− 0.11 (0.36)	0.02 (0.86)	0.06 (0.59)
TSE	− 0.27 (0.03)	0.17 (0.16)	0.06 (0.62)	0.21 (0.09)	− 0.11 (0.37)	0.05 (0.67)	0.02 (0.81)
SEI	− 0.21 (0.08)	0.12 (0.33)	0.17 (0.15)	0.09 (0.47)	− 0.10 (0.41)	0.23 (0.06)	0.10 (0.43)
FC	− 0.16 (0.18)	0.22 (0.07)	0.17 (0.16)	0.06 (0.60)	− 0.11 (0.37)	0.20 (0.10)	0.003 (0.97)
PF	− 0.03 (0.78)	0.08 (0.49)	0.15 (0.22)	0.22 (0.08)	− 0.03 (0.80)	0.01 (0.91)	0.14 (0.26)

Data are presented as correlation coefficients (*p* value)

OS organ-specific symptoms, *SS* systemic symptoms, *TSE* treatment side effects, *SEI* social and emotional impact, *FC* concerns about the future, *PF* physical function, *PDN* prednisone, *VDI* vasculitis damage index, *BVAS/WG* Birmingham vasculitis activity score for granulomatosis with polyangiitis, *ESR* erythrosedimentation rate, *CRP* C-reactive protein

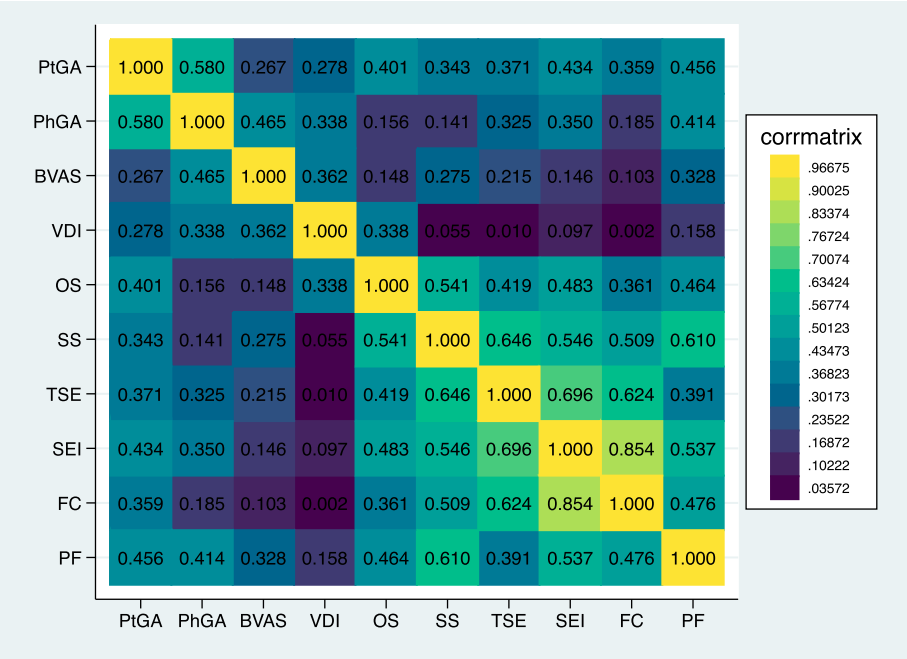

Fig. 1 Correlation heat plot of the AAV-PRO domains and other outcome measures

OS, organ-specific symptoms; SS, systemic symptoms; TSE, treatment side effects; SEI, social and emotional impact; FC, concerns about the future; PF, physical function; VDI, vasculitis damage index; BVAS, Birmingham vasculitis activity score.

the current prednisone dose, whereas the PtGA correlated with most of the domains of the AAV-PRO. Despite this, the PtGA and PhGA measurements were discordant, as shown by a difference of > 5 mm between the assessments. This emphasizes the notion that the perception of the disease differs between patients and physicians [24].

A validation study of the AAV-PRO indicated that the instrument discriminated among disease states [9]. In the present study, however, no significant associations were found between the BVAS/WG and the AAV-PRO domains. A possible explanation is that most patients had very low disease activity at the time of recruitment. In this regard, previous studies in patients with GPA have shown decreased self-perceived HRQoL measured with the SF-36 survey even in phases of clinical remission and no correlation with the extent of organ damage [25]. Additional longitudinal studies in AAV patients using generic measures of HRQoL such as the "Routine Assessment of Patient Index Data 3" (RAPID3) have reported strong associations between this tool and disease activity as measured by BVAS [26].

In the AAV-PRO validation study, women scored higher (i.e., worse) in all six domains [9]. However, in the present study, women scored higher than men only in the treatment side effects domain. Substantial differences in the way men and women cope with chronic illnesses, including autoimmune diseases, have been previously been described [27].

Table 4 Comparison of the main studies that have evaluated the AAV-PRO

Variables	Robson 2018 [9] *n* = 626	Treppo 2022 [21] *n* = 229	Present study *n* = 70
Country	UK, USA, Canada	Italy	Mexico
Age, years, mean (SD) or median (IQR)	60.4 (13.2)	61 (51–72)	52.3 (14)
Women/men, n (%)	397 (64)/229 (36)	129 (56)/100 (44)	44 (63)/26 (37)
Disease duration, years	9.3	5.5	7.5
Predominant AAV	GPA 69.5%	GPA 57.2%	GPA 83%
Disease activity, median (IQR)	Active (self-reported) 28.5%	BVAS = 0 (0–3)	BVAS/WG = 1 (0–2)
Influence of damage (VDI)	NA	Positive correlation with the SS domain	Positive correlation with the OS domain
AAV-PRO domains with highest scores	1. SS 2. SEI	1. SS 2. FC	1. FC 2. SEI
Role of gender on AAV-PRO domains	Women scored worse on all AAV-PRO domains	Women scored worse on SEI impact domain	Women scored worse on TSE domain
Influence of age on AAV-PRO domains	< 65 years-old scored worse on SEI domain	≥ 65 years scored worse on PF domain	< 50 years-old scored worse on TSE and FC domains
Impact of disease duration on AAV-PRO domains	No correlations were observed	NA	< 5 years scored worse on TSE domain

AAV ANCA-associated vasculitis, *GPA* granulomatosis with polyangiitis, *BVAS* Birmingham vasculitis activity score, *VDI* vasculitis damage index, *NA* not available, *AAV-PRO* ANCA-associated vasculitis patient reported outcomes, *OS* organ-specific symptoms, *SS* systemic symptoms, *TSE* treatment side effects, *SEI* social and emotional impact, *FC* concerns about the future, *PF* physical function

Patients aged < 50 years showed significantly higher scores on the treatment side effects and concerns about the future subscales of the AAV-PRO. Similarly, in a validation study by Robson et al., younger people (defined as < 65 years) scored higher on the social and emotional impact subscales [9]. Moreover, in a study of 692 patients with vasculitis, younger age was a risk factor for negative illness perceptions [4]. In contrast, a meta-analysis of patients with newly diagnosed AAV found that older age at baseline was associated with lower SF-36 scores, suggesting differences in the meaning of health problems at different stages of life [28].

A striking result of the present study was the high percentage (70.8%) of men who were classified with some degree of erectile dysfunction according to the IIEF-5 questionnaire. Previous studies have described 18% of self-reported sexual dysfunction in men with systemic lupus erythematosus, in association with comorbidities such as diabetes and thrombosis [29]. Additional studies evaluating sexual function in rheumatic diseases in comparison with healthy controls using the IIEF-5 have also reported a high prevalence of erectile dysfunction (80%) in patients with spondyloarthritis and rheumatoid arthritis. An association of erectile dysfunction in these patients was found with variables such as a lower sexual desire, but not with specific disease parameters, as in the present study [30]. Moreover, in another study, androgen deficiency was found in 47% of male AAV patients in remission, in association with worse scores on the subscales of general health perception, physical functioning, and reduced activity compared to men with normal androgen levels [31]. These findings support the notion that impaired sexual health is prevalent in men with rheumatic diseases, and that the extent of impairment varies according to the disease.

It is important to contextualize that the present study was conducted during the SARS-CoV-2 pandemic, which severely impacted Mexico as the rest of the world, resulting in an increased frequency of depressive disorders, limitations in daily life, and socioeconomic difficulties. Recent data have shown that outcome measurements in AAV patients, such as the BVAS score, were predictors of current depressive disorders during the pandemic, unlike those before the pandemic [32]. Therefore, it would be interesting to assess the AAV-PRO questionnaire and disease activity in the future to assess the variability in illness perceptions over time.

This study has some potential limitations. These include the lack of repeated AAV-PRO measurements to assess changes in illness perceptions and the impact of relapses over time. In addition, work productivity (absenteeism and presenteeism), which has been shown to impact HRQoL in patients with AAV, was not evaluated in the present study. Moreover, the generalizability of the findings is limited because the study population may not be representative of patients with active disease or newly diagnosed AAV.

The important strengths of this study include the in-person evaluation of all patients, as opposed to other online studies assessing PROs, allowing the direct comparison of

patient-reported measures with physician-derived measures. Moreover, to our knowledge, the present study is the first to provide information on sexual function in men with AAV. The impact of AAV on sexuality in women remains unexplored and deserves attention in future studies.

In conclusion, in this cohort of AAV patients with low disease activity, correlations were found between the specific domains of the AAV-PRO and other outcome measures. Differences were found between some of the AAV-PRO domains according to sex, age, and disease duration. It is essential to capture and understand patient-centered outcomes, needs, and perspectives in the clinical care of AAV.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00296-023-05288-4.

Acknowledgements The authors thank Joanna Robson, PhD, MRCP (University of the West England) and the AAV-PRO team for granting the permission to use the AAV-PRO instrument, and Dr. María Cinta Cid Xutgla (Hospital Clínic Barcelona) for kindly providing the Spanish translated version of the AAV-PRO questionnaire. The results of this study were presented as an abstract during the American College of Rheumatology Annual Meeting in November 2022.

Author contributions Conception and design: JJHA, IRM, CGM, JMCH, ABV, AHA. Material preparation and data collection: JJHA, IRM, CGM, JMCH, ABV, AHA. First draft of the manuscript: JJHA, IRM, CGM, JMCH, ABV, AHA. All authors commented on previous versions of the manuscript, read and approved the final version, and take full responsibility for the integrity and accuracy of all aspects of the work.

Funding No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Data availability The data underlying this article is available in the article and will be shared on reasonable request to the corresponding author.

Declarations

Conflict of interest JJHA, IRM, CGM, JMCH, ABV, AHA declare that they have no conflict of interest.

References

1. Basu N, McClean A, Harper L, Amft EN, Dhaun N, Luqmani RA et al (2014) The characterisation and determinants of quality of life in ANCA associated vasculitis. Ann Rheum Dis 73:207–211. https://doi.org/10.1136/annrheumdis-2012-202750
2. Carpenter DM, Meador AE, Elstad EA, Hogan SL, DeVellis RF (2012) The impact of vasculitis on patients' social participation and friendships. Clin Exp Rheumatol 30(1 Suppl 70):S15–S21
3. Robson JC, Jayne D, Merkel PA, Dawson J (2019) Systemic vasculitis and patient-reported outcomes: how the assessment of patient preferences and perspectives could improve outcomes. Patient Relat Outcome Meas 10:37–42. https://doi.org/10.2147/PROM.S163601
4. Grayson PC, Amudala NA, Mcalear CA, Leduc RL, Shereff D, Richesson R et al (2013) Illness perceptions and fatigue in systemic vasculitis: fatigue and illness perceptions in vasculitis. Arthritis Care Res (Hoboken) 65:1835–1843. https://doi.org/10.1002/acr.22069
5. Merkel PA, Aydin SZ, Boers M, Direskeneli H, Herlyn K, Seo P et al (2011) The OMERACT core set of outcome measures for use in clinical trials of ANCA-associated vasculitis. J Rheumatol 38:1480–1486. https://doi.org/10.3899/jrheum.110276
6. Merkel PA, Herlyn K, Mahr AD, Neogi T, Seo P, Walsh M et al (2009) Progress towards a core set of outcome measures in small-vessel vasculitis. Report from OMERACT 9. J Rheumatol 36:2362–2368. https://doi.org/10.3899/jrheum.090373
7. Ponte C, Sznajd J, O'Neill L, Luqmani RA (2014) Optimisation of vasculitis disease assessments in clinical trials, clinical care and long-term databases. Clin Exp Rheumatol 32(5 Suppl 85):S118–S125. https://doi.org/10.1007/s10067-006-0216-3
8. Suppiah R, Robson J, Luqmani R (2010) Outcome measures in ANCA-associated vasculitis. Rheum Dis Clin North Am 36:587–607. https://doi.org/10.1016/j.rdc.2010.04.001
9. Robson JC, Dawson J, Doll H, Cronholm PF, Milman N, Kellom K et al (2018) Validation of the ANCA-associated vasculitis patient-reported outcomes (AAV-PRO) questionnaire. Ann Rheum Dis 77:1157–1164. https://doi.org/10.1136/annrheumdis-2017-212713
10. Austin K, Janagan S, Wells M, Crawshaw H, McAdoo S, Robson JC (2022) ANCA associated vasculitis subtypes: Recent insights and future perspectives. J Inflamm Res 15:2567–2582. https://doi.org/10.2147/JIR.S284768
11. Berti A, Boleto G, Merkel PA, Tómasson G, Monti S, Quinn KA et al (2022) Psychometric properties of outcome measurement instruments for ANCA-associated vasculitis: a systematic literature review. Rheumatology (Oxford). https://doi.org/10.1093/rheumatology/keac175
12. Merghati-Khoei E, Pirak A, Yazdkhasti M, Rezasoltani P (2016) Sexuality and elderly with chronic diseases: a review of the existing literature. J Res Med Sci 21:136. https://doi.org/10.4103/1735-1995.196618
13. Hinojosa-Azaola A, Mejía Vilet JM (2022) Comment on the review article: ANCA-associated vasculitis in Latin America. A systematic literature review: about their epidemiology and their clinical features by Victor R. Pimentel-Quiroz et al. J Clin Rheumatol 28:e682–e683. https://doi.org/10.1097/RHU.0000000000001848
14. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F et al (2013) 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheumatol 65:1–11. https://doi.org/10.1002/art.37715
15. Masi AT, Hunder GG, Lie JT, Michel BA, Bloch DA, Arend WP et al (1990) The American College of Rheumatology 1990 criteria for the classification of Churg–Strauss syndrome (allergic granulomatosis and angiitis). Arthritis Rheumatol 33:1094–1100. https://doi.org/10.1002/art.1780330806
16. Leavitt RY, Fauci AS, Bloch DA, Michel BA, Hunder GG, Arend WP et al (1990) The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. Arthritis Rheumatol 33:1101–1107. https://doi.org/10.1002/art.1780330807
17. Stone JH, Hoffman GS, Merkel PA, Min YI, Uhlfelder ML, Hellmann DB et al (2001) A disease-specific activity index for Wegener's granulomatosis: modification of the Birmingham Vasculitis Activity Score. International Network for the Study of the Systemic Vasculitides (INSSYS). Arthritis Rheumatol 44:912–290. https://doi.org/10.1002/1529-0131(200104)44:4%3c912::AID-ANR148%3e3.0.CO;2-5
18. Exley AR, Bacon PA, Luqmani RA, Kitas GD, Gordon C, Savage CO et al (1997) Development and initial validation of the Vasculitis Damage Index for the standardized clinical assessment

of damage in the systemic vasculitides. Arthritis Rheumatol 40:371–380. https://doi.org/10.1002/art.1780400222
19. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A (1997) The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology 49:822–830. https://doi.org/10.1016/s0090-4295(97)00238-0
20. Schober P, Boer C, Schwarte LA (2018) Correlation coefficients: appropriate use and interpretation. Anesth Analg 126:1763–1768. https://doi.org/10.1213/ANE.0000000000002864
21. Treppo E, Isola M, De Martino M, Padoan R, Urban ML, Monti S et al (2022) AB0627 Evaluation of internal consistency, feasibility, and reliability of the Italian version of ANCA-associated vasculitis patient-reported outcome (AAV-PRO_ita) questionnaire: preliminary results from a multicenter study on a large cohort of Italian patients. Ann Rheum Dis 81:1440. https://doi.org/10.1136/annrheumdis-2017-212713
22. Basu N, McClean A, Harper L, Amft EN, Dhaun N, Luqmani RA et al (2013) Explaining fatigue in ANCA-associated vasculitis. Rheumatology (Oxford) 52:1680–1685. https://doi.org/10.1093/rheumatology/ket191
23. Herlyn K, Hellmich B, Seo P, Merkel PA (2010) Patient-reported outcome assessment in vasculitis may provide important data and a unique perspective. Arthritis Care Res (Hoboken) 62:1639–1645. https://doi.org/10.1002/acr.20276
24. van Tuyl LHD, Boers M (2012) Patient's global assessment of disease activity: what are we measuring? Arthritis Rheumatol 64:2811–2813. https://doi.org/10.1002/art.34540
25. Faurschou M, Sigaard L, Bjorner JB, Baslund B (2010) Impaired health-related quality of life in patients treated for Wegener's granulomatosis. J Rheumatol 37:2081–2085. https://doi.org/10.3899/jrheum.100167
26. Annapureddy N, Elsallabi O, Baker J, Sreih AG (2016) Patient-reported outcomes in ANCA-associated vasculitis. A comparison between Birmingham Vasculitis Activity Score and routine assessment of patient index data 3. Clin Rheumatol 35:395–400. https://doi.org/10.1007/s10067-015-2921-2
27. Carpenter DM, Kadis JA, Devellis RF, Hogan SL, Jordan JM (2011) The effect of medication-related support on the quality of life of patients with vasculitis in relapse and remission. J Rheumatol 38:709–715. https://doi.org/10.3899/jrheum.100808
28. Walsh M, Mukhtyar C, Mahr A, Herlyn K, Luqmani R, Merkel PA et al (2011) Health-related quality of life in patients with newly diagnosed antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis Care Res (Hoboken) 63:1055–1061. https://doi.org/10.1002/acr.20471
29. Merayo-Chalico J, Barrera-Vargas A, Morales-Padilla S, Reyna-De la Garza R, Vázquez-Rodríguez R, Campos-Guzmán J et al (2019) Epidemiologic profile of erectile dysfunction in patients with systemic lupus erythematosus: the Latin American landscape. J Rheumatol 46:397–404. https://doi.org/10.3899/jrheum.180292
30. Fazaa A, Rouached L, Mourad Dali K, Miladi S, Ouenniche K, Souabni L et al (2020) Comparison of sexual function in men with spondyloarthritis and rheumatoid arthritis. Egypt Rheumatol 42:275–279. https://doi.org/10.1016/j.ejr.2020.07.004
31. Tuin J, Sanders J-SF, Buhl BM, van Beek AP, Stegeman CA (2013) Androgen deficiency in male patients diagnosed with ANCA-associated vasculitis: a cause of fatigue and reduced health-related quality of life? Arthritis Res Ther 15:R117. https://doi.org/10.1186/ar4297
32. Yun JD, Lee JH, Pyo JY, Ahn SS, Song JJ, Park YB et al (2022) Birmingham vasculitis activity score and the short form 36-item health survey predict current depressive disorders in patients with antineutrophil cytoplasmic antibody-associated vasculitis during the SARS-CoV-2 pandemic. Z Rheumatol 24:1–8. https://doi.org/10.1007/s00393-022-01233-1