Employment, work disability and quality of life in patients with ANCA-associated vasculitides. The EXPOVAS study

L. Benarous[1], B. Terrier[1], H. Laborde-Casterot[2], A. Bérezné[1], B. Dunogué[1], P. Cohen[1], X. Puéchal[1], L. Mouthon[1], L. Bensefa-Colas[2], L. Guillevin[1], for the French Vasculitis Study Group (FVSG)

[1]*Department of Internal Medicine, National Referral Centre for Rare Autoimmune and Systemic Diseases, Cochin Hospital, Assistance Publique-Hôpitaux de Paris (AP-HP), Université Paris Descartes, Paris;*
[2]*Department of Occupational and Environmental Diseases, Cochin Hospital, AP-HP, Université Paris Descartes, Paris, France.*

*Lucas Benarous, MD**
*Benjamin Terrier, MD, PhD**
Hervé Laborde-Casterot, MD
Alice Bérezné, MD
Bertrand Dunogué, MD
Pascal Cohen, MD
Xavier Puéchal, MD
Luc Mouthon, MD, PhD
Lynda Bensefa-Colas, MD, PhD
Loïc Guillevin, MD

**These authors contributed equally to this work.*

Please address all correspondence to:
Dr Benjamin Terrier,
Internal Medicine,
Hôpital Cochin,
27 rue du Faubourg Saint-Jacques,
75679 Paris Cedex 14, France.
E-mail: benjamin.terrier@cch.aphp.fr.

Received on July 2, 2016; accepted in revised form on September 2, 2016.

Clin Exp Rheumatol 2017; 35 (Suppl. 103): S40-S46.

Key words: employment, work disability, quality of life, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, microscopic polyangiitis

Funding: this study was supported by a grant from the French Vasculitis Study Group.

Competing interests: none declared.

ABSTRACT

Objective. *Improved therapeutic strategies for ANCA-associated vasculitis (AAV) have transformed acute and life-threatening diseases into chronic ones responsible for marked morbidity that could impact employment, work disability and quality of life (QoL). We aimed to analyse work, handicaps and QoL of AAV patients and identify their determinants.*

Methods. *Patients with AAV were included in a cross-sectional study assessing employment, work disability and QoL. Specific and non-specific questionnaires, including SF-36, were sent to patients, and clinical-biological data that could affect QoL and their determinants were analysed.*

Results. *Questionnaires were completed by 189 patients. Among 94 working-age (<60 years) patients, 57% had jobs, consistent with their qualifications for 81%, 77% were stably employed; 23% of workers felt that their disease qualitatively limited the nature of their work, while 43% felt it limited the quantity of work they could do; 50% thought their disease had hindered their careers and 43% that it had led to a salary reduction. These results were comparable for the different vasculitides. QoL was significantly impaired for AAV patients compared to the general population (p<0.0001). Physical health determinants for our population were diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA), long disease duration and its neurological involvement, whereas mental health determinants tended to be ear, nose and throat and cardiovascular involvement, and unemployment.*

Conclusion. *Our findings showed that AAV patients' QoL was impaired compared to the general population, mainly for patients with EGPA and long-standing disease. In contrast, normal employment seemed to be preserved for the majority of the patients.*

Introduction

ANCA-associated vasculitides (AAV) are a group of diseases characterised by inflammation of small-sized blood vessels leading to multi-organ involvement (1). Improved therapeutic strategies have transformed most acute and life-threatening diseases into chronic ones associated with relapses, organ damage accumulation and long-term treatment toxicity (2, 3). Chronic evolution is responsible for marked morbidity that could impact employment, work capacity and quality of life (QoL), even once remission has been/is obtained (4-7). The impact of AAV on work disability and QoL are increasingly considered and should be evaluated to improve the management of patients with chronic disorders. For some authors, patients' reported outcome such as QoL should be incorporated in future composite outcome measures, in association with physician-based evaluation and serological markers to better appreciate disease evolution and response to treatments (8, 9).

Data suggest that current disease-assessment tools for disease activity, as measured by the Birmingham Vasculitis Activity Score (BVAS), and permanent organ damage, as measured by the Vasculitis Damage Index (VDI), are only partially correlated with measures and variations of QoL (9), highlighting the need for specific evaluation of the social impact of AAV. Although several studies have demonstrates a lower health-related QoL in patients with AAV (4-6, 10-12), it is crucial to confirm these data in other AAV populations and to contextualise these results to better appreciate patients' profiles.

Several factors have been previously suggested to impact on patients' QoL, including clinical manifestations (*i.e.* disease activity, pain or neurological involvement) and psychological symptoms such as fatigue (13-15). Other studies have suggested that QoL in AAV patients was affected through decreased social interactions and work disability (16). Fitness to work is a major component of life and is commonly affected in chronic autoimmune diseases (17). Furthermore, the impact of AAV on employment status has been suggested by previous studies (18, 19), but still need to be precisely described. Additional data are therefore needed to better characterise the impact of AAV on professional activities and QoL and to identify determinants of altered QoL in AAV patients, in order to develop interventions to improve patient-centered outcomes. The cross-sectional French EXPOVAS inquiry aimed to analyze employment, work disability and QoL in AAV patients and identify their determinants.

Patients and methods

Patients

We conducted a cross-sectional study between January and September 2013 in adult AAV patients followed in our National Referral Centre in Cochin Hospital, Paris, France. Patients with AAV fulfilled the American College of Rheumatology (ACR) criteria for granulomatosis with polyangiitis (GPA) and eosinophilic granulomatosis with polyangiitis (EGPA) (20), and/or the European Medicines Agency (EMA) algorithm (21) and/or Chapel Hill definitions (22) for GPA, microscopic polyangiitis (MPA) and EGPA. This observational population survey was conducted in accordance with the Declaration of Helsinki and French law and patients gave their informed consent to participate.

Data collection

Specific and non-specific self-administered questionnaires were sent to 531 unselected adult AAV patients regularly followed in our centre. In the absence of response, no recall was made. Employment and work disability were assessed using a self-administered questionnaire, performed with the collaboration of the department of Occupational and Environmental Diseases from Cochin Hospital, that recorded the demographic characteristics of the patients, their daily management of treatments, their educational level and detailed occupational status. Jobs were classified in occupational activity families according to FAP-2003 (Direction de l'Animation, de la Recherche, des Etudes et des Statistiques; Ministère du Travail; La nomenclature des Familles Professionnelles: FAP-2003 (2008)). This nomenclature, established by the French Department of Employment, groups occupations that involve common skills based on close professional practices. Work disability was defined in working-age (<60 years) patients by receiving disability living allowance or disability pension, or recognised as disabled worker status. In France, the retirement age is 60 years.

Short Form-36 (SF-36) questionnaire was used for the assessment of QoL. This questionnaire is widely used to measure QoL in inflammatory disorders, in particular AAV (9, 23, 24). The SF-36 is a generic measure containing 36 items that assess QoL in eight health dimensions: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health. Scores for each dimension range from 0 to 100, with higher scores indicating better health-related QoL. Two summary scores are derived from the eight subscales: the physical component summary (PCS) score and the mental component summary (MCS) score. Clinical-biological data that could affect QoL were recorded.

Control groups

In order to better understand and analyse the QoL of our patients, we compared our results to the French general population, patients with end-stage renal disease (ESRD) (Briançon Surveillance de la qualité de vie des sujets atteints d'insuffisance rénale chronique terminale, Institut de Veille Sanitaire, 2005), and previously reported AAV patients from the EUVAS cohort (14). Data regarding the French general population are derived from a 2002-2003 national survey conducted by the INSEE (Institut National de la Statistique et des Etudes Economiques). This study included 20574 people, with a mean age of 45 years and 53% of women. For the control group of patients with ESRD, data were taken from a study based on 773 patients under dialysis, with a mean age of 67 years and 59% of men.

Statistical analysis

Data are presented as means ± SD or as medians (range), as appropriate for continuous variables, and number (%) for qualitative variables. Fisher's exact test was used to compare qualitative variables and the non-parametric Mann-Whitney U-test to compare continuous variables. Univariate analysis was performed to identify determinants associated with altered QoL. A multivariate logistic regression was also performed to identify factors independently associated with an altered physical and mental health. We included all covariates with a p-value ≤0.10 in univariate analysis. Odds-ratios (OR) with their ninety-five percent confidence intervals (95% CI) are presented as a measure of association. $p<0.05$ defined statistical significance. Statistical analyses were computed with GraphPad Prism v. 4.0 and Instat v. 3.0 for Windows (GraphPad Software, San Diego, CA).

Results

Patient characteristics

Self-administered questionnaires were sent to 531 AAV patients. Of these patients, 189 patients (36%) completed the forms (108 women (57%), mean age 59±14 years). The causes of non-response included wrong postal addresses, lost to follow-up, unknown death and patients who were not willing to respond.

Patients' diagnoses included GPA in 132 cases (67%), EGPA in 42 cases (21%) and MPA in 24 cases (12%). Main characteristics of the patients are summarised in Table I.

Regarding marital status, 27/186 (15%) patients were single, 140/186

Table I. Characteristics of the patients.

Variables	All patients n=189
Demography	
Age, years	58.6 ± 13.9
Male gender	81 (43)
Disease duration, mo.	105.8 ± 80.8
AAV diagnosis	
GPA	126 (67)
MPA	22 (12)
EGPA	41 (21)
Baseline vasculitis involvement	
Constitutional symptoms	100/183 (55)
Myalgia	55/183 (30)
Arthralgia	75/183 (41)
Skin	50/183 (27)
Eye	41/183 (22)
ENT	140/183 (77)
Lungs	121/183 (66)
Cardiovascular	50/183 (27)
Gastrointestinal	21/183 (11)
Kidney	59/183 (32)
Nervous system	73/183 40)
ANCA status	
Positive ANCA	126/183 (69)
Anti-PR3	84
Anti-MPO	38

*Except where indicated otherwise, values are the number (%) of patients.

(75%) were married, and 19/186 (10%) were divorced or widowed. 148 out of 188 patients (79%) had children. Educational level included no diploma in 26/182 (14%), technical degree in 53/182 (29%), bachelor degree in 29/182 (16%), two-year university degree in 18/182 (10%) and master degree or more in 56/182 (31%).

Analysis of employment and work disability

The study population included 94 patients of working-age (<60 years) patients, 93 patients >60 years, and 2 students.

Among the working-age (<60 years) patients (Fig. 1), 56% worked, in accordance with their qualifications in 81%; 77% were stably employed, with 67% working full-time. Concerning AAV impact, 23% of workers felt that their disease qualitatively limited the nature of their work, while 43% felt it limited the quantity of work they could do; 77% of patients did not benefit from any workstation adaptation; 50% thought their disease had hindered their careers and 43% that it had led to a salary reduction. Employment characteristics of the working-age patients are indicated in Table II. Thirty (33%) patients did not work and did not look for work. Among them, 18 patients (60%) attributed their occupational inactivity to their health condition and 12 to other various reasons. Eight (9%) patients were unemployed but tried to find a work, and 2 (2%) were studying. Patients looking for a job thought, in half of the cases, that difficulties in obtaining a job were related to their disease and/or sequelae. Among patients aged over 60 years, 10% pursued a professional activity, while the remaining 90% of patients were retired and not working. These results were comparable for the different AAV (data not shown).

Job characteristics at diagnosis of AAV were recorded for 103 out of the 111 patients who were active workers as well as the distribution of occupational domains in the French population (Table II). In comparison with French population, AAV patients seemed to work less frequently in construction jobs (1.9% *vs*. 7.2%), and more frequently in engineering or executive industry (10.7% *vs*. 1%) and health, cultural and social activities or sports (19.4% *vs*. 10.9%). Finally, 8% percent of patients had disability living allowance, 15% had a disability pension and disabled worker status was recognised in 16% of pa-

Fig. 1. Representation of employment status of working-age AAV patients.

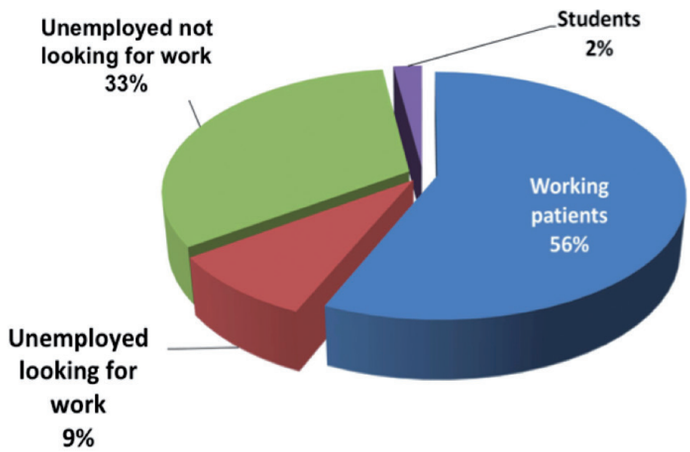

Table II. Occupational domains of employed working-age AAV patients according the FAP-2003.

Domains	Among AAV patients=103*(%)	Among French population (%)
Agriculture, navy, fishery	2 (1.9)	3.6
Construction (private and public)	2 (1.9)	7.2
Electricity, electronics	2 (1.9)	0.8
Mechanics, metallurgy	4 (3.8)	3.3
Manufacturing industry	0 (0)	3
Light industry, wood, graphics industry	3 (2.9)	1.2
Maintenance	1 (0.9)	3.2
Engineers, industry executives	11 (10.7)	1
Transport, logistics, tourism	4 (3.8)	7.3
Craftwork	1 (0.9)	0.5
Management, business administration	9 (8.7)	9.7
Data processing	3 (2.9)	2.2
Research and development	1 (0.9)	1.4
Public service, legal profession	10 (9.7)	8.4
Banking, insurance	3 (2.9)	2.9
Trade	7 (6.8)	10.6
Hotel trade, catering, food industry	3 (2.9)	4.6
Individual and community services	6 (5.8)	10.9
Communication, information, arts and entertainment	3 (2.9)	2.2
Health, social activity, cultural activity, sports	20 (19.4)	10.9
Education, teaching	6 (5.8)	4.5
Politics, religion	0 (0)	0.1

*8 patients of the 111 actives workers are employees without precision.

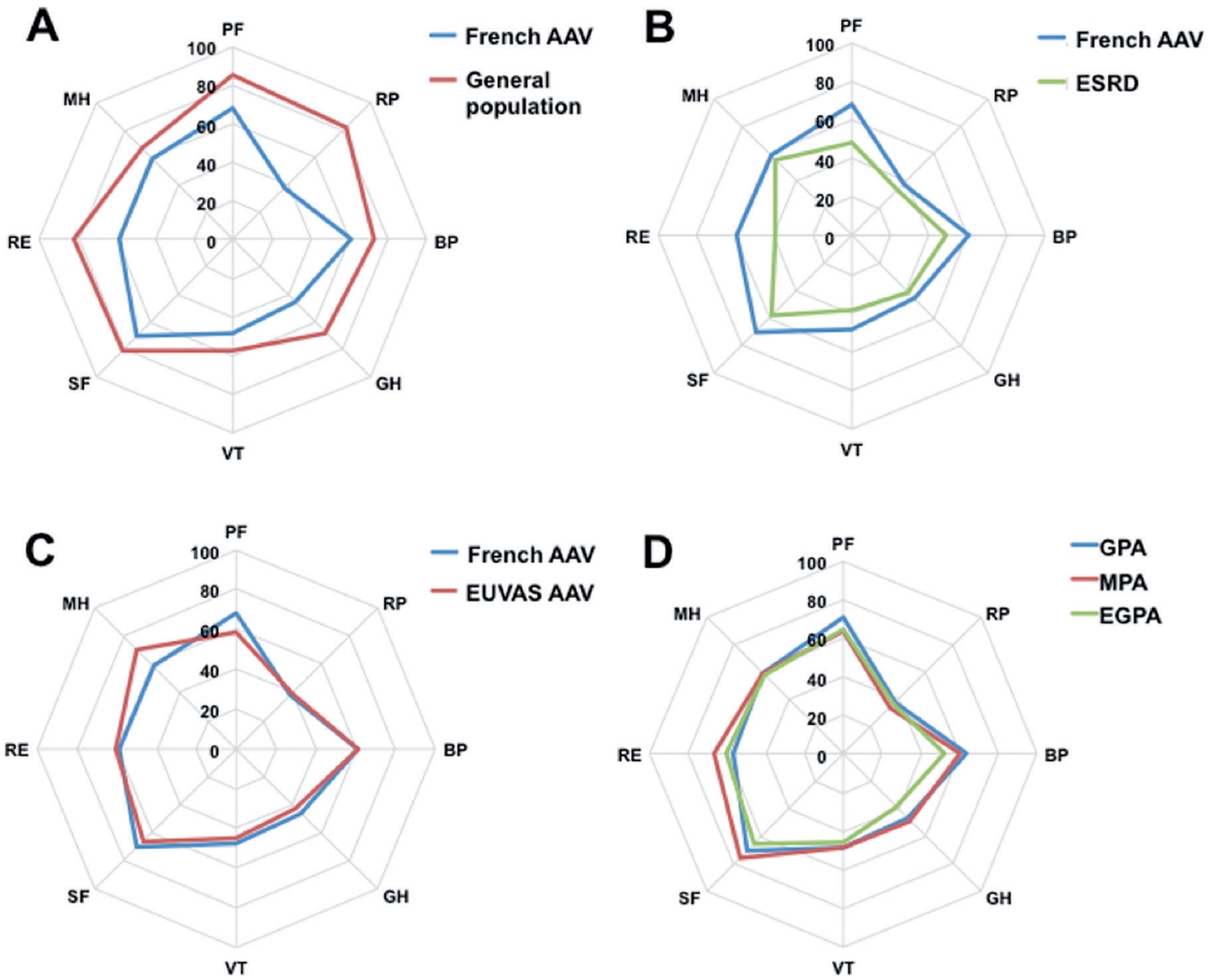

Fig. 2. Analysis of SF-36–assessed QoL of our AAV patients. (**A**) Comparison between our AAV patients and the French general population. (**B**) Comparison between our AAV patients and French patients with end-stage renal disease. (**C**) Comparison between our AAV patients and AAV patients from the EUVAS cohort. (**D**) Comparison between AAV diagnoses among our patients. PF: physical functioning, RP: role physical, BP: bodily pain, GH: general health, VT: vitality, SF: social functioning, RE: emotional role, MH: mental health.

tients. Overall, among the working-age (<60 years) patients, 35 out of 88 patients (40%) had work disability (data was lacking for 6 patients). The only variable that was significantly associated with work disability was a longer disease duration [OR 1.01 (1.00–1.02), p=0.015] (Supplementary Table).

Analysis of quality of life

Using the SF-36 to assess QoL, French general population reported better QoL than French AAV patients (p<0.0001 across all domains) (Fig. 2A). In contrast, French AAV patients reported better QoL than the French ESRD patients (p<0.0001 across all domains, except for role physical that did not differ significantly) (Fig. 2B). Our French AAV population's QoL was similar to that of the EUVAS cohort, except for our patients' physical functioning which was better in our cohort (p=0.0001), and mental health which was more impaired in French AAV (p<0.0001) (Fig. 2C). Finally, no significant difference among the health dimensions assessed by the SF-36 was noted among AAV diagnoses in our study population (Fig. 2D).

Altered physical health, defined as physical component summary score below 30, was observed in 36/189 patients (19%), whereas altered mental health, defined as MCS score below 30, was present in 27/189 patients (14%). PCS and MCS were not correlated (r=+0.03, p =0.67), indicating different determinants modulating these summary scores.

Analysis of determinants of QoL in AAV

We analysed the determinants that could affect QoL. In univariate analysis, altered physical health was significantly associated with longer disease duration (140±103 months in patients with altered physical health *vs*. 98±73 months in the others, p=0.03), more frequent EGPA diagnosis (42% *vs*. 17%, p=0.005), more frequent peripheral nervous system involvement (49% *vs*. 30%, p=0.03) and less frequent positive ANCA (49% *vs*. 74%, p=0.008),

Table III. Physical health determinants for AAV patients.

Variables	Altered physical health (n=36)	Preserved physical health (n=153)	Univariate analysis *p* value	Multivariate analysis	
				HR (95% CI)	*p* value
Demography					
Age, years	60.1 ± 14.1	58.2 ± 13.9	0.51		
Male gender, n	15 (42)	66 (43)	1.00		
Disease duration, mo.	140 ± 103	98 ± 73	**0.02**	**1.005 (1.00-1.01)**	**0.02**
AAV diagnosis			**0.005**		
GPA, n (%)	17 (47)	109 (71)		0.70 (0.20-2.39)	0.56
MPA, n (%)	4 (11)	18 (12)		1	-
EGPA, n (%)	15 (42)	26 (17)		**3.22 (1.43-7.26)**	**0.005**
Baseline vasculitis involvement					
Constitutional symptoms, n (%)	22/35 (63)	78/148 (53)	0.35		
Myalgia, n (%)	12/35 (34)	43/148 (29)	0.54		
Arthralgia, n (%)	15/35 (43)	60/148 (41)	0.85		
Skin, n (%)	9/35 (26)	41/148 (28)	1.00		
Eye, n (%)	4/35 (11)	37/148 (25)	0.11		
ENT, n (%)	26/35 (74)	114/148 (77)	0.82		
Lungs, n (%)	25/35 (71)	96/148 (65)	0.55		
Cardiovascular, n (%)	6/35 (17)	19/148 (13)	0.58		
Gastrointestinal, n (%)	5/35 (14)	16/148 (11)	0.56		
Kidney, n (%)	12/35 (34)	47/148 (32)	0.84		
Nervous system, n (%)	17/35 (49)	45/148 (30)	**0.03**	1.51 (0.65-3.55)	0.33
Positive ANCA, n (%)	17/35 (49)	109/148 (74)	**0.008**	0.60 (0.23-1.56)	0.29
Anti-PR3, n (%)	10 (29)	74 (50)	-		
Anti-MPO, n (%)	7 (20)	31 (21)	-		
Marital status			0.84		
Single	6/35 (17)	21/151 (14)			
Married	25/35 (72)	115/151 (76)			
Divorced or widowed	4/35 (11)	15/151 (10)			
Educational level			0.26		
No diploma	8/33 (24)	18/149 (12)			
Technical degree	6/33 (18)	47/149 (32)			
Bachelor degree	4/33 (12)	25/149 (17)			
Two-year university degree	3/33 (9)	15/149 (10)			
Master degree or more	12/33 (36)	44/149 (30)			
Employment status			0.80		
Students	0/33 (0)	2/146 (1)			
Employed	13/33 (39)	47/146 (32)			
Unemployed	6/33 (18)	30/146 (21)			
Inactive	14/33 (42)	67/146 (46)			

*Except where indicated otherwise, values are the number (%) of patients.

the latter being related to the diagnosis of EGPA. Other clinical measures did not significantly relate to PCS. In multivariate analysis, variables that remained significantly associated with altered physical health were a longer disease duration [OR 1.005 (1.00-1.01), *p*=0.02] and a diagnosis of EGPA [OR 3.22 (1.43-7.26), *p*=0.005] (Table III).

Altered mental health was significantly associated with more frequent ear, nose and throat (ENT) (92% in patients with altered mental health *vs*. 74% in the others, *p*=0.046) and cardiac involvement (27% *vs*. 11%, *p*=0.06), and with employment status, in particular more frequent unemployment (40% *vs*. 17%, *p*=0.06), in univariate analysis. In multivariate analysis, the only variable that remained significantly associated with altered mental health was unemployment [OR 3.28 (1.33–8.11), *p*=0.01], with a trend for more frequent ENT involvement [OR 3.89 (0.83–18.2), *p*=0.08] (Table IV).

Discussion

In the present study, we performed a global assessment of the socioprofessional impact of AAV by evaluating work disability, and aimed to contextualise the results, to compare our data between the different forms of AAV and with other AAV population, and to identify factors associated with a poor physical and mental QoL.

Work disability, defined by receiving disability living allowance or disability pension, or recognition as disabled worker status, has been mainly studied in inflammatory rheumatic diseases, in particular rheumatoid arthritis (RA) and systemic sclerosis (SSc). Work disability was found in 35% of RA patients and in 56% in SSc (17.25). In GPA, two studies reported a prevalence rate of work disability of 27% and 31% (5.18), whereas the EUVAS cohort including various AAV reported work disability in 26% of patients (19). Our results, showing a prevalence of work disability of 40%, confirm the importance of the social impact of AAV even if we show that the majority of our patients were working with a job adapted to their qualification. One third of patients had a part-time contract, without being able to know if it was directly related to their disease or not. AAV seemed to limit the nature and the quantity of work and to hinder the patients' career, leading to salary reduction in some cases. A study conducted in GPA patients suggested that disease led to a median salary reduction of 26%, one year after GPA diagnosis (18). The analysis of potential determinants of this work disability is important, even if it represents a difficult issue since work status may be influenced by many factors, including the disease, work access, social protection system and economic context of the country. Even if a causal relationship is difficult to establish, Basu *et al*. identified severe disease damage, increased body mass index, fatigue and depression as factors associated with work disability (19). In our study, disease duration was the only variable associated with work disability.

We next analysed the QoL of our patients and showed that all dimensions of the SF-36 were altered compared to the general population, revealing a significant physical and emotional impact of AAV. The most affected dimension

Table IV. Mental health determinants for AAV patients.

Variables	Altered mental health (n=27)	Preserved mental health (n=162)	Univariate analysis *p* value	Multivariate analysis	
				HR (95% CI)	*p* value
Demography					
Age, years	56.2 ± 14.6	58.9 ± 13.8	0.35		
Male gender, n	10 (37)	71 (44)	0.54		
Disease duration, mo.	89.4 ± 69.9	108.5 ± 82.3	0.49		
AAV diagnosis			0.18		
GPA, n (%)	22 (81)	104 (64)			
MPA, n (%)	1 (4)	21 (13)			
EGPA, n (%)	4 (15)	37 (23)			
Baseline vasculitis involvement					
Constitutional symptoms, n (%)	11/26 (42)	89/157 (51)	0.20		
Myalgia, n (%)	9/26 (35)	46/157 (29)	0.65		
Arthralgia, n (%)	12/26 (46)	63/157 (40)	0.67		
Skin, n (%)	7/26 (27)	43/157 (27)	1.00		
Eye, n (%)	9/26 (35)	32/157 (20)	0.13		
ENT, n (%)	24/26 (92)	116/157 (74)	**0.046**	3.89 (0.83-18.2)	0.08
Lungs, n (%)	17/26 (65)	104/157 (66)	1.00		
Cardiovascular, n (%)	7/26 (27)	18/157 (11)	**0.06**	2.22 (0.76-6.49)	0.14
Gastrointestinal, n (%)	3/26 (12)	18/157 (11)	1.00		
Kidney, n (%)	6/26 (23)	53/157 (34)	0.37		
Nervous system, n (%)	10/26 (38)	63/157 (40)	1.00		
Positive ANCA, n (%)	19/26 (73)	107/157 (68)	0.82		
Anti-PR3, n (%)	13 (50)	71 (45)	-		
Anti-MPO, n (%)	6 (23)	32 (20)	-		
Marital status			0.17		
Single	7/27 (26)	20/159 (13)			
Married	17/27 (63)	123/159 (77)			
Divorced or widowed	3/27 (11)	16/159 (10)			
Educational level			0.50		
No diploma	5/26 (19)	21/156 (13)			
Technical degree	5/26 (19)	48/156 (31)			
Bachelor degree	3/26 (12)	26/156 (17)			
Two-year university degree	2/26 (8)	16/156 (10)			
Master degree or more	11/26 (42)	45/156 (29)			
Employment status			**0.06**		
Students	0/25 (0)	2/154 (1)		-	-
Employed	7/25 (28)	53/154 (32)		1	-
Unemployed	10/25 (40)	26/154 (17)		**3.28 (1.33-8.11)**	**0.01**
Inactive	8/25 (32)	73/154 (47)		0.78 (0.27-2.40)	0.69

*Except where indicated otherwise, values are the number (%) of patients.

was the physical role underlying difficulties encounter by patients to make their activities of daily living. Others dimensions that were importantly affected were general health, vitality and mental health, which reveal the importance of psychic distress. Our results are consistent with previous studies (4) and particularly that of the EUVAS cohort (14). Koutandji *et al*. found in their cohort of patients with primary systemic vasculitides a proportion of high depressive symptoms and high anxiety symptoms of 25.5% and 43.2%, respectively (15). These results should alert clinicians about the need of rehabilitation, occupational therapy and psychological support.

In a comprehensive approach, we tried to identify determinants of altered physical and mental QoL. Previous studies suggest that disease activity and damage score, assessed by the BVAS and VDI, were insufficiently correlated with QoL (9). Along this line, we investigated the impact of clinical and socio-demographic variables in our AAV cohort. Regarding the physical component of QoL, we found that longer disease duration, diagnosis of EGPA and the presence of neurological involvement were associated with altered QoL. Our results are consistent with previous studies, in particular regarding the impact of neurological involvement being systematically associated with a poor QoL (4, 14, 15). Peripheral neuropathies and frequent sequelae in AAV commonly result in pain, sensory disturbance and functional disability (15, 26). Koutandji *et al*. reported that pain was one of the strongest determinants of QoL, explaining probably the negative impact of peripheral neuropathy on physical QoL (15). Therefore, a more aggressive approach regarding the therapeutic management of symptoms related to peripheral neuropathy could probably significantly improve physical QoL of these patients. In our cohort, two third of EGPA patients had neurological involvement, what could explain in part the association between EGPA and altered QoL. However, EGPA remained independently associated with a poor QoL, indicating that QoL of EGPA patients is probably intrinsically poorer compared to other AAV. The reason why QoL of EGPA patients is worse remain to be investigated. We could speculate that nasal polyposis and respiratory involvement which are strongly prevalent in EGPA, or peripheral neuropathy, could influence QoL of EGPA patients.

The impact of psychosocial factors on QoL was analysed by Basu *et al*., showing that fatigue, was the only factor independently associated with both physical and mental QoL (14). However, fatigue is an important part of the SF-36 vitality dimension, making this finding a quite expected result. Our study has included as a potential determinant of QoL the employment status. In multivariate analysis, we found that unemployment was the only factor associated with an altered mental QoL, whereas ENT and cardiovascular involvement had only a tendency to be associated with an altered QoL. Interestingly, Reinhold-Keller *et al*. showed that in GPA patients, work disability was associated with a lower QoL whereas clinical characteristics of the disease were comparable between patients with preserved or altered QoL

(5). Taken together, these data suggest that AAV could lead to physical disability as well as psychologic distress that impact work capacity and QoL. Nevertheless, causal inferences cannot be made with certainty. This is especially true regarding determinants of unemployment that can be the causes or the consequences of altered QoL. However, unemployment, whether it is a cause or a consequence of altered QoL, it remains an important outcome to manage in AAV patients.

Our study is limited by several bias to consider in the interpretation of data. First, cross-sectional analyses are limited to determine causal relationships, since they do not dissociate exposure and outcome during evolution. Second, we did not include in our evaluation the analysis of psychosocial factors such as depression, anxiety, copying or fatigue. These factors could influence QoL, but they are very difficult to interpret as they are influenced by many other factors independently of the disease itself.

In conclusion, our findings showed that AAV patients' QoL is impaired compared to the general population, mainly in patients with EGPA and long-standing disease. In contrast, normal employment seemed to be preserved for the majority of AAV patients although some of them would benefit a better understanding and management of work disability. Strategy aiming to improve the QoL in these patients is mandatory.

Acknowledgements

We would like to acknowledge patients from the Wegener Infos Service Association.

References

1. JENNETTE JC, FALK RJ: Small-vessel vasculitis. *N Engl J Med* 1997; 337: 1512-23.
2. MUKHTYAR C, FLOSSMANN O, HELLMICH B *et al*.: Outcomes from studies of antineutrophil cytoplasm antibody associated vasculitis: a systematic review by the European League Against Rheumatism systemic vasculitis task force. *Ann Rheum Dis* 2008; 67: 1004-10.
3. CHAIGNE B, GUILLEVIN L: Unsolved questions and concerns about treatment of anti-neutrophil cytoplasm antibody-associated vasculitides. *Clin Exp Rheumatol* 2016; 34 (Suppl. 97): S121-8.
4. WALSH M, MUKHTYAR C, MAHR A *et al*.: Health-related quality of life in patients with newly diagnosed antineutrophil cytoplasmic antibody-associated vasculitis. *Arthritis Care Res* 2011; 63: 1055-61.
5. REINHOLD-KELLER E, HERLYN K, WAGNER-BASTMEYER R *et al*.: Effect of Wegener's granulomatosis on work disability, need for medical care, and quality of life in patients younger than 40 years at diagnosis. *Arthritis Rheum* 2002; 47: 320-5.
6. CARPENTER DM, KADIS JA, DEVELLIS RF, HOGAN SL, JORDAN JM: The effect of medication-related support on the quality of life of patients with vasculitis in relapse and remission. *J Rheumatol* 2011; 38: 709-15.
7. PUGNET G, PAGNOUX C, TERRIER B *et al*.: Rituximab versus azathioprine for ANCA-associated vasculitis maintenance therapy: impact on global disability and health-related quality of life. *Clin Exp Rheumatol* 2016; 34 (Suppl. 97): S54-9.
8. HERLYN K, HELLMICH B, SEO P, MERKEL PA: Patient-reported outcome assessment in vasculitis may provide important data and a unique perspective. *Arthritis Care Res* 2010; 62: 1639-45.
9. TOMASSON G: Quality of life and outcome measures in vasculitis. *Best Pract Res Clin Rheumatol* 2013; 27: 69-77.
10. TOMASSON G, BOERS M, WALSH M *et al*.: Assessment of health-related quality of life as an outcome measure in granulomatosis with polyangiitis (Wegener's). *Arthritis Care Res* 2012; 64: 273-9.
11. CARPENTER DM, THORPE CT, LEWIS M, DEVELLIS RF, HOGAN SL: Health-related quality of life for patients with vasculitis and their spouses. *Arthritis Rheum* 2009; 61: 259-65.
12. FAURSCHOU M, SIGAARD L, BJORNER JB, BASLUND B: Impaired health-related quality of life in patients treated for Wegener's granulomatosis. *J Rheumatol* 2010; 37: 2081-5.
13. BASU N, JONES GT, FLUCK N *et al*.: Fatigue: a principal contributor to impaired quality of life in ANCA-associated vasculitis. *Rheumatology* (Oxford) 2010; 49: 1383-90.
14. BASU N, MCCLEAN A, HARPER L *et al*.: The characterisation and determinants of quality of life in ANCA associated vasculitis. *Ann Rheum Dis* 2014; 73: 207-11.
15. KOUTANTJI M, HARROLD E, LANE SE, PEARCE S, WATTS RA, SCOTT DGI: Investigation of quality of life, mood, pain, disability, and disease status in primary systemic vasculitis. *Arthritis Rheum* 2003; 49: 826-37.
16. CARPENTER DM, MEADOR AE, ELSTAD EA, HOGAN SL, DEVELLIS RF: The impact of vasculitis on patients' social participation and friendships. *Clin Exp Rheumatol* 2012; 30 (Suppl. 70): S15-21.
17. OUIMET JM, POPE JE, GUTMANIS I, KOVAL J: Work disability in scleroderma is greater than in rheumatoid arthritis and is predicted by high HAQ scores. *Open Rheumatol J* 2008; 2: 44-52.
18. HOFFMAN GS, DRUCKER Y, COTCH MF, LOCKER GA, EASLEY K, KWOH K: Wegener's granulomatosis: patient-reported effects of disease on health, function, and income. *Arthritis Rheum* 1998; 41: 2257-62.
19. BASU N, MCCLEAN A, HARPER L *et al*.: Markers for work disability in anti-neutrophil cytoplasmic antibody-associated vasculitis. *Rheumatology* (Oxford) 2014; 53: 953-6.
20. FRIES JF, HUNDER GG, BLOCH DA *et al*.: The American College of Rheumatology 1990 criteria for the classification of vasculitis. Summary. *Arthritis Rheum* 1990; 33: 1135-6.
21. WATTS R, LANE S, HANSLIK T *et al*.: Development and validation of a consensus methodology for the classification of the ANCA-associated vasculitides and polyarteritis nodosa for epidemiological studies. *Ann Rheum Dis* 2007; 66: 222-7.
22. JENNETTE JC, FALK RJ, BACON PA *et al*.: 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 2013; 65: 1-11.
23. HUSTED JA, GLADMAN DD, FAREWELL VT, LONG JA, COOK RJ: Validating the SF-36 health survey questionnaire in patients with psoriatic arthritis. *J Rheumatol* 1997; 24: 511-7.
24. KHANNA D, FURST DE, CLEMENTS PJ *et al*.: Responsiveness of the SF-36 and the Health Assessment Questionnaire Disability Index in a systemic sclerosis clinical trial. *J Rheumatol* 2005; 32: 832-40.
25. NGUYEN C, BÉREZNÉ A, BAUBET T *et al*.: Association of gender with clinical expression, quality of life, disability, and depression and anxiety in patients with systemic sclerosis. *PloS One* 2011; 6: e17551.
26. SUPPIAH R, HADDEN RDM, BATRA R *et al*.: Peripheral neuropathy in ANCA-associated vasculitis: outcomes from the European Vasculitis Study Group trials. *Rheumatology* 2011; 50: 2214-22.