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Research Article

Non-interventional observational retrospective-prospective study of health-related quality of life (EuroQoL) in patients with vasculitis associated with antineutrophil cytoplasmic antibodies undergoing treatment with rituximab

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Abstract

Working with patients with Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) requires a clear understanding of their current health status. In the scientific literature, there is not enough data on their quality of life with the different therapeutic regimens. No generic tools have been developed to assess functional indicators and health status. The aim of the study is to measure the health-related quality of life (physical, psychological and social functioning) in a Bulgarian population of patients with systemic vasculitis associated with ANCA undergoing treatment with rituximab using a common tool. Design – retrospective-prospective, observational, non- interventional, controlled study in two periods, in two rheumatology centers in Bulgaria. Treatment with rituximab leads to qualitative and quantitative improvement in all components of physical health, mental and social components. All measured parameters are within the normal range for the general population. Rituximab treatment of AAV is the best therapeutic alternative in current rheumatology practice.

Keywords

Systemic vasculitis, anti -neutrophil cytoplasmic antibody (ANCA), ANCA-associated vasculitis (AAV), EuroQol-5D-5 L, visual analog scale (VAS), rituximab (RTX)

Introduction

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are diseases with a significantly high mortality rate, with almost all patients requiring aggressive immunosuppressive treatment. The course of the disease can vary from subacute non-specific complaints to life-threatening damage to organs and systems (Hunder et al. 1990; Hochberg et al. 2019). Without treatment, mortality is >90% within up to 5 years (Lane et al. 2005). According to Chapel Hill Consensus Conferences (CHCC) (Jennette et al. 2013), there are three types of vasculitis associated with antineutrophil cytoplasmic antibodies: Microscopic polyangiitis (MPA), Granulomatosis with polyangiitis (Wegener's granulomatosis) (GPA) and Eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss Syndrome (CSS). Due to the multisystemic nature of vasculitis, a multidisciplinary approach is usually required, and patient-reported data are essential.

Several methods have been established in clinical practice for the assessment of AAV damage. The Birmingham Vasculitis Activity Score (BVAS) in adults (Luqmani et al. 1994; Stone et al. 2001; Mukhtyar et al. 2009) and the Pediatrics Vasculitis Activity Score (PVAS) (Dolezalova et al. 2013) are the main instruments (tools) for clinical assessment of disease activity in patients with AAV (Ponte et al. 2014). The two most recent forms of the BVAS – BVAS version 3 and the BVAS specific version designed for patients with GPA – were used. BVAS for GPA can also be used in other forms of vasculitis, including MPA, without further validation. Another method of measuring lasting effects in patients diagnosed with vasculitis is the Vasculitis Damage Index (VDI). (Mukhtyar et al. 2009; Suppiah et al. 2011). Other instruments such as Five-Factor Score (Guillevin et al. 2011) and Disease extent index (DEI), are also available, but are not widely used in real clinical practice.

No specific (generic) tools have been developed to assess functional indicators and health status in patients with AAV. In theory, the use of common tools combined with disease-specific tools is the optimal way to determine functional outcomes in patients with systemic vasculitis regardless of pre- or post-treatment (Asipova et al. 2018). Working with patients with AAV requires a clear understanding of their current health status. In the scientific literature, there are insufficient published data on the health-related quality of life of patients with AAV under the application of different therapeutic regimens. It is well documented that the quality of life of individuals with vasculitis who receive standard treatment is not satisfactory in terms of physical, mental and social comfort and well- being. The use of biological and biosimilar medicinal products for the treatment of vasculitis is a therapeutic innovation and is of considerable clinical interest (Parvova et al. 2014). The improvement of health-related quality of life in patients with AAV undergoing biological treatment would provide additional arguments to justify this type of treatment, against the background of the relatively high costs of drug therapy. On the other hand, this type of study will enrich the knowledge of medical professionals about the symptomatology in AAV due to the mental and social component of health, in addition to the classical somatic examination. The main goal of the diagnostic-treatment process is the identification of quantitative and qualitative parameters for accurate diagnosis, measurement of disease activity, general impairments, functional disorders, selection of a therapeutic approach, effectiveness of treatment, etc. It is essential that the process of obtaining this information takes place in a systematic, structured manner.

The primary objective of this study was to measure health-related quality of life (physical, psychological and social functioning) in a Bulgarian population of patients with systemic vasculitis associated with antineutrophil cytoplasmic antibodies (ANCA) undergoing treatment with the biologic Rituximab (RTX) (EMA 2009). A secondary objective is to evaluate the effectiveness of biologic treatment based on the quality of life data obtained. Treatment and disease effects will be measured from the patients' perspective.

Materials and methods

Design – retrospective-prospective, observational, non-interventional, controlled study in two periods, in two rheumatology centers on the territory of the city of Sofia, Bulgaria. An independent control group of patients is not planned. The selected cohort of patients is a self-controlling group, as patients self-assess their health by completing pre- and post-treatment surveys. **Study period** – January 2019 – September 2020. The main method is a "direct individual survey" with closed-ended responses. The questionnaire survey was conducted using a common instrument for measuring health status EQ-5D- 5L (EuroQol Research Foundation 2019) by completing a questionnaire in electronic format from a licensed software product. The original questionnaires are in English and have been validated by the licensor. The working version of the questionnaires has been translated into Bulgarian by a licensed translator. The questionnaires are completed independently by the patients, with the possibility of assistance from the interviewing researcher in the event of ambiguity. In this way we eliminate the possibility of "bias errors" when interviews are based on the "face to face" principle. Target number of patients – not fewer than 6, not more than 24. **The primary** endpoints of the study are measures of physical, social and behavioural functioning, mental health and patient assessment of general health.

The primary endpoints of the EQ-5D-5L were mobility, self-care, usual activities, aches and pains, anxiety and depression. A Visual Analogue Scale (VAS) was added to the tool as an additional criterion for self-report of health status. **Inclusion criteria:** 1. Signed and dated informed consent; 2. Age over 18 years; 3. Diagnosed AAV; 4. The diagnosis must be made in accordance with the EULAR criteria (Yates et al. 2016); 5. The diagnosis and decision to treat must be in accordance with the national phar-

macotherapeutic guidelines for rheumatology; 6. The patients have not been treated with a biological or biosimilar medicinal product. 7. Patients must meet criteria for treatment of systemic vasculitis with biologics. **Screening visit:** familiarization of the participants with the protocol and procedures, signing of the Informed Consent by the patient, assessment of inclusion and exclusion criteria. Patients were considered screened out if even 1 exclusion criterion was present. **Visit 1 –** takes place before starting the biological treatment. Study participants complete the EuroQol 5-Level Questionnaire (EQ-5D-5L) by answering the questions retrospectively - describing their condition at least 4 weeks ago. **Treatment duration –** includes induction of remission and maintenance treatment. The recommended dose of RTX for induction of remission in granulomatosis with polyangiitis and microscopic polyangiitis is 375 mg/m^2 body surface area administered as an intravenous infusion once a week for 4 weeks (four infusions in total). After induction of remission with RTX, maintenance treatment should be started at least 16 weeks after the last RTX infusion. **Visit 2** – Conducted 6 months after the treatment for the induction of remission with RTX.

Participants in the study completed the 5-item EQ-5D-5L questionnaire by answering the questions retrospectively – again describing their condition 4 weeks back. Once the requisite number of participants has been reached and/or the observation period has elapsed, a three-part consolidated report is prepared using the designated software product. The first part will include analysis of the primary endpoints, the second part will comprise data from the visual analogue scale, and the third will analyze the effectiveness of biologic treatment based on health-related quality of life data. Only subjects who have received prior information from a physician member of the research team about the objectives, risks and inconveniences of the trial and the conditions under which it will be conducted, as well as their right to withdraw from the trial at any time without adverse consequences to them, have given personal written informed consent to participate after being informed of the nature, meaning, consequences and possible risks of their participation. The trial was conducted according to the Declaration of Helsinki and subsequent amendments, the Law on Medicinal Products in Human Medicine (Ministry of Health 2007), the Law of Health (Ministry of Health 2004) and the Personal Data Protection Act (PDPA 2002).

Results

Only patients diagnosed with granulomatosis with polyangiitis (Wegener's granulomatosis, Wegener's disease) were included in the study. The analyzed group of patients consisted of 12 people – 10 men (83.33) and 2 women (16.67). The frequency for Bulgaria of patients with Wegener's granulomatosis is estimated as newly diagnosed cases between 14.7 – 100.80 with a median of 43.05. As previously reported in our studies and publications, no literature or official national statistics are available on the actual total number of patients with Wegener's granulomatosis for the period 2018–2021 (Delyiski 2022; Parvova et al. 2024). As an acceptable admission, we consider the presence of no more than 40 to 60 patients with this disease in Bulgaria, and of these, no more than 20 people have been diagnosed. According to data published by the NHIF for 2017, it is clear that in the first, second and third quarters of the same year, the NHIF paid for the treatment of 18, 15 and 12 patients, respectively, or an average of 15 patients per month (NHIF 2020). I.e. the study included at least 60% of all patients in Bulgaria. The mean age of the tracked men with Wegener's granulomatosis was 52.4 years, the median was 53 years, and the most common age was 51 years with a standard deviation of 13.54 years. The mean age of the women under observation was 55.5 years. The mean duration of the disease in the cohort of patients under our observation ranged from 1 to 13 years, with a median of 5 years. The time required for diagnosis following the initial presentation of symptoms is relatively short, despite the diverse and complex clinical symptoms: in 58.3% (7 patients) of the cases, the diagnosis was established within 1 month, in 3 of the cases it took up to half a year. In 2 of the cases there was a significant delay in the diagnostic process: with 1 patient it took more than 1 year and in the second – 7 years. All patients had prior conventional treatment with immunosuppressants (cyclophosphamide, azathioprine, methotrexate), systemic glucocorticoid therapy (methylprednisolone, prednisone, betamethasone), immunoglobulins (immunoglobulins, normal human). The mean duration of conventional treatment from the date of diagnosis to switching to biologic treatment was 3.5 years, with SD = 1.62. RTX treatment included 1 and/or 2 courses of treatment per study, according to the protocol. All patients after the end of the study in September 2020 continued treatment with an additional 4 to 6 courses of RTX, but the effect of this treatment was not included in the quality-of-life analyses. A BVAS version 3 clinical scorecard was completed for each patient, containing the 9 sections and 56 assessment items, the maximum achievable points for each section, and the total number of points. BVAS activity was scored using BVAS persistent points (PPs) from 0 to 33. The minimum number of BVAS persistent points is 6 and the maximum is 33, with a median of 17. The group we analysed was assessed as having moderate-severe BVAS version 3 activity (Delyiski 2022; Parvova et al. 2024).

Health status scores were measured using the EuroQol 5D-5L instrument on Visit 1 prior to initiation of biological treatment, in accordance with the EQ-5D-5L User Guide, (EuroQol Research Foundation 2019). Responses across the five main domains were collected from all respondents, with each domain including 5 possible responses ranked by severity (Table 1).

Of the 12 patients included in the study, three (25%) reported no problems with their mobility. The remaining 9 (75%) of the group have mobility problems, with the largest share occupied by patients who have moderate

Table 1. Domains of the EuroQol 5D-5L instrument – number of participants, questions and answers.

Respondents (n)	Missing answers	Unique answers
12/domain	0 (0.0%)	5 (1, 3, 4, 5 domain); 4 (2 domains)
Questions		**Number of responses**
Mobility domain		**12**
I have no problems in walking about		3
I have slight problems in walking about		1
I have moderate problems in walking about		5
I have severe problems in walking about		1
I am unable to walk about		2
Self-Care Domain		**12**
I have no problems washing or dressing myself		7
I have slight problems washing or dressing myself		2
I have moderate problems washing or dressing myself		2
I have severe problems washing or dressing myself		1
I am unable to wash or dress myself		0
Usual activities domain		**12**
I have no problems doing my usual activities		6
I have slight problems doing my usual activities		3
I have moderate problems doing my usual activities		1
I have severe problems doing my usual activities		1
I am unable to do my usual activities		1
Pain / Discomfort Domain		**12**
I have no pain or discomfort		5
I have slight pain or discomfort		2
I have moderate pain or discomfort		2
I have severe pain or discomfort		2
I have extreme pain or discomfort		1
Anxiety / Depression Domain		**12**
I am not anxious or depressed		5
I am slightly anxious or depressed		3
I am moderately anxious or depressed		2
I am severely anxious or depressed		1
I am extremely anxious or depressed		1

difficulties – 5 (41.7%). There was a correlation between disease activity assessed by BVAS version 3 and the assessment of patient mobility. A match is found in the severity score of the general condition and the score of mobility severity above 67.5%. In the Self-Care domain, 58.3% of respondents reported no problems with daily dressing and general hygiene activities. The remaining 5 (41.7%) of the group have self-maintenance problems rated as mild to moderate. Only 1 patient had serious problems and none reported a lack of self-care. The results of the third domain "Usual activities (work, study, housework, family or leisure activities)" showed that half of the participants had no difficulty with usual activities, while the other half reported difficulty of varying degrees of severity. 58.3% of patients reported pain and discomfort in their daily life, rated from mild to extremely severe in severity. 5 of the patients do not have any problems according to this criterion. In the fifth, last domain "Anxiety/Depression", 7 (58.3%) of the patients reported the presence of anxiety and/or depression during the performance of daily activities. Three have a mild form of anxiety/depression and 2 have a moderate degree. The remaining 5 or 41.7% of the group reported no problems with this indicator. Two patients fell into the most severe degree of self-assessment – a serious and extremely anxious-depressive state. Statistical evaluation of the aggregate data was based on 100% completeness of the data – all patients answered 100% of the questions asked. A five-digit number system was used to determine the individual score. Perfect health is denoted by five ones (11,111) and the worst by five fives – 55,555. Each health status can be transformed into a weighted index score using a country- or region-specific set of values. EQ-5D index values illustrate society's perceptions of health and range from – 0.590 to 1.0, where negative values correspond to poor health (conditions worse than death) and 1.0 corresponds to perfect health. Our data were compared with validated EuroQol 5D-5L index results for the general population. The comparison was performed against standardized EuroQol 5D-5L norms for the Bulgarian population (Encheva et al. 2020). The results are presented in Table 2 as relative values. Due to the small number of women, results are presented for men and women combined. The results show that health-related quality of life in patients diagnosed with granulomatosis with polyangiitis (Wegener's granulomatosis, Wegener's disease) is dramatically impaired in all five assessment domains, and the results are statistically significant – $p<0.05$.

Table 2. Comparison of the results with standardized norms EuroQol 5D-5L for the Bulgarian population.

EQ-5D-5L	Degree of severity	Norms men (n/%)	Norms women (n/%)	Results n-12 10 men/2 women
Mobility	No problem	361 (76.0%)	371 (70.0%)	**25.0%**
	Minor problems	72 (15.2%)	92 (17.3%)	**8.3%**
	Moderate problems	23 (4.8%)	46 (8.7%)	**41.7%**
	Serious problems	17 (3.6 %)	19 (3.6%)	**8.3%**
	Impossible	2 (0.4%)	2 (0.4%)	**16.7%**
Self-Care	No problem	416 (87.5%)	452 (85.3%)	**58.3%**
	Minor problems	43 (9.1 %)	54 (10.2%)	**16.7%**
	Moderate problems	14 (3.0 %)	23 (4.3%)	**16.7%**
	Serious problems	2 (0.4%)	1 (0.2%)	**8.3%**
	Inability	0 (0.0%)	0 (0.0%)	**0.0%**
Usual activities	No problem	388 (81.7%)	397 (74.9%)	**50.0%**
	Mild problems	69 (14.5%)	103 (19.4%)	**25.0%**
	Moderate problems	5 (1.1 %)	18 (3.4%)	**8.3%**
	Serious problems	12 (2.5%)	12 (2.3%)	**8.3%**
	Impossible	1 (0.2%)	0 (0.0%)	**8.3%**
Pain/Discomfort	No	314 (66.0%)	298 (56.2%)	**41.7%**
	Light	109 (2 3.0%)	152 (28.7%)	**16.7%**
	Moderate	38 (8.0%)	61 (11.5%)	**16.7%**
	Heavy	14 (3.0%)	17 (3.2%)	**16.7%**
	Extreme	0 (0.0%)	2 (0.4%)	**8.3%**
Anxiety/Depression	No	343 (72.%)	315 (59.4%)	**41.7%**
	Light	92 (19.4%)	136 (25.7%)	**25%**
	Moderate	24 (5.1%)	57 (10.8%)	**16.7%**
	Heavy	14 (3.0%)	16 (3.0%)	**8.3%**
	Extreme	2 (0.4%)	0 (0.0%)	**8.3%**

Table 3. Self-assessment data with the Visual Analogue Scale before biological treatment with Rituximab.

Total Count (N)	Missing*	Unique	Min	Max	Mean	StDev	Sum	Percentile						
								0.05	0.10	0.25	0.50 Median	0.75	0.90	0.95
12	0 (0.0%)	10	13	71	39.17	16.04	470	16.85	20.40	28.50	40	50	51.80	60.55

As mentioned in the introductory section, the Visual Analog Scale (VAS) is an integral part of the study and represents a self-assessment of status by patients. The scale resembles a thermometer and is sized from 0 to 100 points corresponding to the following questions: 0 = The best health condition you can imagine and 100 = The worst health condition you can imagine. EQ VAS data should be presented descriptively, with a measure of central tendency and a measure of dispersion being most commonly used. This may be the mean and standard deviation (SD) or, if the data are skewed, the mean and interquartile range (IQR). Our results are presented in Table 3.

The mode was calculated at 39.17 points with a standard deviation of 16.04 and a median of 40 points. No patient rated their condition as very good and/or excellent. One rated his condition as relatively good, and all others as fair to poor – the self-assessment level was 50 or below 50 points. Three patients self-rated below 25 points, a sign of critical condition. The worsened self-esteem was predominantly due to anxiety/depression, pain/discomfort and mobility. The graphical distribution is shown in Fig. 1.

Standardized EQ VAS norms for the Bulgarian population are a mean of 77.1 for women vs. a mean of 78.7 for males (Encheva et al. 2020). Our results show a fold worsening of

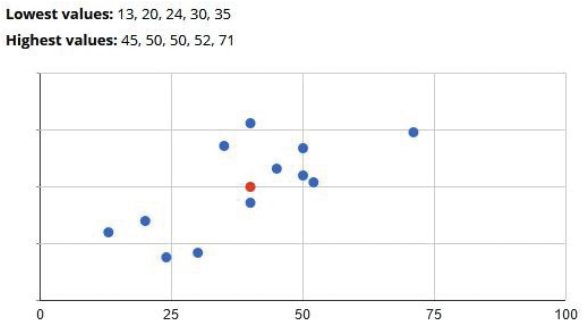

Figure 1. Self-assessment of condition using a Visual Analogue Scale.

health-related quality of life by this parameter in patients with systemic vasculitis associated with ANCA antibodies and who did not undergo biological treatment with RTX.

The assessment of health status of Visit 2 using the EuroQol 5D-5L instrument after RTX biologic treatment is presented in Table 4.

Of the patients included in the study, 73.3% reported no problems with their mobility, and 16.7% of the group reported moderate difficulties. After the RTX treatment, mobility as one of the most impaired quality-of-life

Table 4. Assessment of health status after biological treatment with Rituximab – number of participants, questions and answers.

Total number (n)	Missing answers	Unique answers	
12/domain	0 (0.0%)	3 (all domains)	
	Questions		**Number of responses**
Mobility domain			12
I have no problems in walking about			7
I have slight problems in walking about			3
I have moderate problems in walking about			2
I have severe problems in walking about			0
I am unable to walk about			0
Self-Care Domain			12
I have no problems washing or dressing myself			8
I have slight problems washing or dressing myself			3
I have moderate problems washing or dressing myself			1
I have severe problems washing or dressing myself			0
I am unable to wash or dress myself			0
Usual activities domain			12
I have no problems doing my usual activities			7
I have slight problems doing my usual activities			4
I have moderate problems doing my usual activities			1
I have severe problems doing my usual activities			0
I am unable to do my usual activities			0
Pain / Discomfort Domain			12
I have no pain or discomfort			5
I have slight pain or discomfort			4
I have moderate pain or discomfort			3
I have severe pain or discomfort			0
I have extreme pain or discomfort			0
Anxiety / Depression Domain			12
I am not anxious or depressed			8
I am slightly anxious or depressed			2
I am moderately anxious or depressed			2
I am severely anxious or depressed			0
I am extremely anxious or depressed			0

outcomes approached that of healthy individuals. In the domain "Self-Care"– only 1 patient reported moderate difficulty in self-care in daily life. Of the remaining 11 – 8 had no difficulty and 2 reported some difficulty. We can assume that in this domain after the biological treatment there is a significant improvement to complete disappearance of complaints in 91.7% of cases. In 91.7% of the participants, significant improvement was reported in performing usual daily activities such as work, study, housework, family-related activities or leisure time activities. 7 patients had no complaints and 4 had mild difficulties. Only 1 patient reported moderate difficulties. In 75% of patients, pain and discomfort in daily life were reduced to absent (5) and to mild (4). Three patients were found to have moderate pain or discomfort. Compared with the pre-treatment assessment, no patients were found to have serious or extremely severe pain or discomfort. Moderate anxiety was found in 2 patients. In 2, mild, and in 8 there was no evidence of either anxiety or depression. Compared with baseline data, when only 41.7% of all patients reported no problems on this indicator, 66.7% had no anxiety in the post-biological treatment group. If we add the two patients with a mild form, we can conclude that in 83.4% we have sustained improvement on this item.

The comparison of the results obtained for the EuroQol 5D-5L index after RTX treatment with the data for the general population is presented in Table 5 as relative values. Due to the small number of women, results are presented for men and women combined.

The results show that the health-related quality of life in patients diagnosed with granulomatosis with polyangiitis (Wegener's granulomatosis, Wegener's disease) undergoing treatment with RTX biologic is significantly improved, both compared to the baseline visit in this study and also compared to the performance of the general population. There were no severe grade and extreme grade complaints in any of the domains. The data obtained were statistically significant at $p<0.05$.

The results of the self-assessment of status with the Visual Analogue Scale after RTX biological treatment are presented in Table 6 and Graph 2. Minimum score – 40, maximum score – 100. The mode was calculated to be 70.08 points with a standard deviation of 15.63, and the median was 70 points. Almost all patients rated their condition as very good and/or excellent. Only one rated his condition as not good – the self-assessment level was 40 points. All other patients indicated a level above 56 points.

Table 5. Comparison of results with standardized EuroQol 5D-5L norms for the Bulgarian population after RTX treatment.

EQ-5D-5L	Degree of severity	Norms men (n/%)	Norms women (n/%)	Results n-12 10 men/2 women
Mobility	No problem	361 (76.0%)	371 (70.0%)	58.3%
	Mild problems	72 (15.2%)	92 (17.3%)	25.0%
	Moderate problems	23 (4.8%)	46 (8.7%)	16.7%
	Serious problems	17 (3.6%)	19 (3.6%)	0
	Impossible	2 (0.4%)	2 (0.4%)	0
Self-Care	No problem	416 (87.5%)	452 (85.3%)	66.7%
	Mild problems	43 (9.1%)	54 (10.2%)	25.0%
	Moderate problems	14 (3.0%)	23 (4.3%)	8.3%
	Serious problems	2 (0.4%)	1 (0.2%)	0
	Inability	0 (0.0%)	0 (0.0%)	0
Usual activities	No problem	388 (81.7%)	397 (74.9%)	59.3%
	Mild problems	69 (14.5%)	103 (19.4%)	33.3%
	Moderate problems	5 (1.1%)	18 (3.4%)	8.3%
	Serious problems	12 (2.5%)	12 (2.3%)	0
	Impossible	1 (0.2%)	0 (0.0%)	0
Pain/Discomfort	No	314 (66.0%)	298 (56.2%)	41.7%
	Light	109 (2 3.0%)	152 (28.7%)	33.3%
	Moderate	38 (8.0%)	61 (11.5%)	25.0%
	Heavy	14 (3.0%)	17 (3.2%)	0
	Extreme	0 (0.0%)	2 (0.4%)	0
Anxiety/Depression	No	343 (72.1%)	315 (59.4%)	66.7%
	Light	92 (19.4%)	136 (25.7%)	16.7%
	Moderate	24 (5.1%)	57 (10.8%)	16.7%
	Heavy	14 (3.0%)	16 (3.0%)	0
	Extreme	2 (0.4%)	0 (0.0%)	0

Table 6. EQ VAS after RTX treatment.

Total Count (N)	Missing*	Unique	Min	Max	Mean	StDev	Sum	Percentile						
								0.05	0.10	0.25	0.50 Median	0.75	0.90	0.95
12	0 (0.0%)	9	40	100	70.08	15.63	841	48.80	56.10	62.25	70	80	84.50	91.75

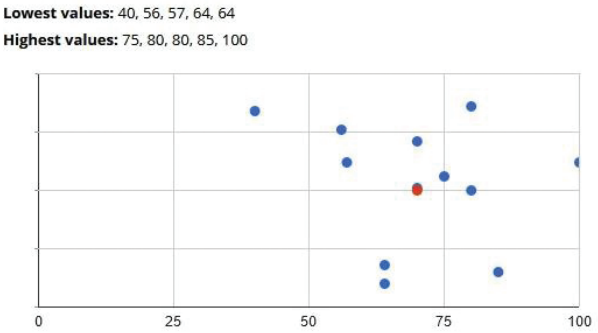

Figure 2. Self-assessment of condition by Visual Analogue Scale.

The direct comparison of the results obtained in the five domains of the EuroQol 5D-5L instrument between Visit 1 and Visit 2, before RTX incorporation and after RTX biologic treatment was administered and remission was achieved, is presented in Table 7. In the Mobility domain, a threefold improvement was found after treatment. There is a complete reversal of the results obtained – from 75% patients with moderate to severe problems, after treatment we have 85% with virtually no problems. Similar results are seen in all other domains. Table 8 presents a comparative analysis of the VAS self-assessment results between Visit 1 and Visit 2 – before and after RTX treatment.

Discussion and conclusion

We found that the time from symptom onset to diagnosis is relatively short, yet the diagnosis is made at an advanced stage of disease development – our measured disease activity in the Bulgarian population is moderate-severe BVAS version 3. Conducting conventional treatment alone does not lead to any change in the physical functioning, emotional state and perceived general health of patients. On none of the elements forming the health-related quality of life, patients undergoing conventional treatment are defined as being in normal and/or good health and do not fall into the healthy group of the general population. The health-related quality of life of patients without treatment and with standard treatment of vasculitis is significantly worse compared to the general population and does not meet current requirements. 2/3 of patients are in a severely depressed state. The use of biologics for the treatment

Table 7. Comparison of results before and after treatment with RTX.

EQ-5D-5L	Degree of severity	Exit visit	Post-treatment visit	p-value (t-test)
Mobility	No problem	25.0%	58.3%	0.008
	Mild problems	8.3%	25.0%	
	Moderate problems	41.7%	16.7%	
	Serious problems	8.3%	0	
	Impossible	16.7%	0	
Self-Care	No problem	58.3%	66.7%	0.027
	Minor problems	16.7%	25.0%	
	Moderate problems	16.7%	8.3%	
	Serious problems	8.3%	0	
	Inability	0.0%	0	
Usual activities	No problem	50.0%	59.3%	0.015
	Minor problems	25.0%	33.3%	
	Moderate problems	8.3%	8.3%	
	Serious problems	8.3%	0	
	Impossible	8.3%	0	
Pain/Discomfort	No	41.7%	41.7%	0.003
	Light	16.7%	33.3%	
	Moderate	16.7%	25.0%	
	Heavy	16.7%	0	
	Extreme	8.3%	0	
Anxiety/Depression	No	41.7%	66.7%	0.013
	Light	25%	16.7%	
	Moderate	16.7%	16.7%	
	Heavy	8.3%	0	
	Extreme	8.3%	0	

Table 8. Self-reported status with Visual Analogue Scale – comparison between Visit 1 and Visit 2 (before and after RTX treatment).

Visits	Total Count (n)	Missing	Unique	Min	Max	Mean	StDev	Sum	Percentile						
									0.05	0.10	0.25	0.50 Median	0.75	0.90	0.95
Visit 1	12	0	10	13	71	**39.17**	16.04	470	16.85	20.40	28.50	**40**	50	51.80	60.55
Visit 2	12	0	9	40	100	**70.08**	15.63	841	48.80	56.10	62.25	**70**	80	84.50	91.75

of vasculitis is a therapeutic novelty and the timely initiation of RTX treatment leads to rapid control of clinical symptomatology and entry into prolonged remission. Biologic treatment with RTX resulted in significant improvements in health-related quality of life in over 75% of patients across the two major domains of physical and mental health, compared to patients on conventional treatment where 75% of patients did not self-identify as healthy. RTX treatment resulted in qualitative and quantitative improvements in all components of physical health – on all measures, patients entered population norms. The elements forming the mental component – vitality, social functioning, emotional functioning and mental health after biological treatment are within the healthy population norm. The level of depression after RTX treatment was within the norm for the general population. The improvement in health-related quality of life in patients with AAV provides additional arguments to justify biologic therapy as the treatment of choice, despite the relatively high cost of drug therapy. Our study contributes to the knowledge of medical professionals about the symptomatology of AAV due to mental, physical and social factors. Measuring health-related quality of life in patients with AAV can be used for routine analysis of health status before and after treatment. This study shows that RTX treatment is the best therapeutic alternative in current rheumatology practice for the treatment of AAV.

Conflicts of interest

The a uthors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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