

Research Article

Quality of Life Assessment and Its Relationship with Fatigue Symptom, Demographic and Clinical Factors in Rheumatoid Arthritis Polish Patients

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Abstract

The variety of clinical symptoms occurring during rheumatoid arthritis may reduce patients' quality of life. Hence, the study aimed to assess RA patients' quality of life and determine its relationship with fatigue, demographic and clinical factors. The study group consisted of 128 RA patients diagnosed according to ACR/EULAR criteria and treated in rheumatology departments. The Arthritis Impact Measurement Scales-2 (AIMS-2) scale was used to assess the quality of life. The Functional Assessment of Chronic Illness Therapy - Fatigue Scale was used to assess the symptom of fatigue. The analyzed variables were sex, age, pharmacological treatment, arthritis pain, morning stiffness, hemoglobin, CRP, rheumatoid factor, Ritchie Articular Index, and DAS28 disease activity. In the AIMS-2 scale, the patients had the lowest quality of life in the following subscales: arthritis pain (average 6.25±2.52 points), walking and bending (average 5.63±2.71 points), and emotional tension (average 4.99±1.92 points); while patients presented the highest quality of life for the following subscales: support from family and friends (average 1.39±2.21 points) and self-care (average 2.11±2.45 points). There was a correlation between the level of quality of life and age ($r=0.24$), morning stiffness ($r=0.45$), CRP concentration ($r=0.29$), joint tenderness ($r=0.34$), and disease activity ($r=0.39$). Increasing the values of parameters such as arthritis pain, disease activity, morning stiffness, and CRP level may cause a decrease in the level of quality of life. Assessment of the quality of life should be a permanent element of assessing patients with RA.

Keywords: Quality of life; Rheumatoid arthritis; Fatigue; Clinical factors; AIMS-2 scale

Abbreviations: RA: Rheumatoid Arthritis; HRQOL: Health-Related Quality of Life; CRP: C-Reactive Protein; RF: Rheumatoid Factor; DAS28: Disease Activity; VAS: Arthritis Pain; Hgb: Hemoglobin; ACR: The American College of Rheumatology; EULAR: The European League Against Rheumatism; AIMS-2: The Arthritis Impact Measurement Scales-2; FACIT-F: The Functional Assessment of Chronic Illness Therapy – Fatigue; Avg: The Arithmetic Mean; SD: Standard Deviation; Me: Median; min: Minimum; max: Maximum

Introduction

Rheumatoid Arthritis (RA) is a connective tissue disease that affects symmetrical joints (in the course of a non-specific inflammatory process) and extra-articular tissues (e.g., kidneys, heart, lungs) and causes systemic complications [1,2]. The disease is a non-specific inflammatory-related process of unknown etiology. Inflammatory changes occur in the synovium of the joints, cartilage, and bones. The main symptoms are pain, swell-

ing, and stiffness of the joints [1-4]. Especially problems with the joints of the hands, feet and ankles make it difficult to perform everyday activities [5,6]. RA leads to disability, deformities in the limbs, invalidity, and premature death of patients [1-6].

Patients affected by this disease not only suffer from physical ailments, such as joint pain and morning stiffness, resulting

from complications of pharmacological treatment or fatigue, but they also experience consequences in the mental, economic, social, and interpersonal spheres. RA can lead to a reduction in employment and even loss of work, sometimes even poverty [2,3,5,6]. Patients are unable to perform all activities of daily living on their own. Washing, dressing, cleaning, preparing meals, going shopping in the exacerbation phase of the disease, or as a result of the progress of destructive changes, causes dependence on third parties, use of social assistance, or even resignation from them when there is no one to take care of a given person [5,6]. Their physical and mental condition makes it impossible to lead a typical family, social and cultural life. Social isolation, anxiety, and depression appear. Changing body image adversely affects self-perception, especially among women [5,6].

So far, numerous definitions of quality of life have been developed, reflecting its meaning. Their difference results from the complex nature of the issue, which has many dimensions, depending on the perspective of the subject from which it is considered [7]. The World Health Organization gave the following definition of quality of life: a person's perception of their life situation in the context of cultural conditions, value systems, and in relation to their goals, norms, and interests. And Health-Related Quality of Life (HRQOL) is defined as "a term referring to the health-related aspects of quality of life, widely regarded as reflecting the impact of disease and treatment on disability and daily functioning; it was also considered to reflect the impact of perceived health on an individual's ability to lead a fulfilling life; it is a measure of the value assigned to lifespan modified by impairments, functional states, perceptions, and abilities, influenced by disease, injury, treatment, and policy" [7-9]. Thanks to this definition, the concept of quality of life indicates its multifaceted and multifaceted nature, and thus that in medical science, its assessment cannot be based on only one paradigm but on a holistic approach. Nowadays, the clinical evaluation of the patient should take into account not only the physical condition but also its connections with other areas of life, as a consequence of, for example, the costs of health care, prolongation of life, or the possibility of choosing the method of treatment and related complications. Its dimension is subjective and objective [7-11].

Most studies on the quality of life of patients with RA focus on assessing the impact of demographic and clinical factors on the quality of life of these patients. However, our research, in addition to the variables listed above, takes into account the results of laboratory tests. The innovation of these studies is the use of multivariate analysis, which explains the share of the analyzed variables in the assessment of the quality of life of patients with RA.

The study aimed to assess the quality of life of patients with RA and to determine the relationship between the quality of life and the symptom of fatigue, as well as demographic and clinical factors, including the results of laboratory tests.

The following research questions were posed:

What is the quality of life of patients with RA?

1. Is there a relationship between the quality of life of patients with RA and demographic factors?

2. Is there a relationship between the quality of life of patients with RA, the symptom of fatigue, clinical factors and the disease's duration?

3. What clinical factors affect the quality of life of patients with RA:

a. do the clinical variables analyzed jointly: hemoglobin concentration, C-Reactive Protein (CRP), and Rheumatoid Factor (RF), influence the quality of life of the subjects?

b. do the clinical variables analyzed jointly: the type of pharmacological treatment (biological/classic) and Disease Activity (DAS28), affect the quality of life of the respondents?

c. do the clinical variables analyzed jointly: Arthritis Pain (VAS), morning stiffness (in minutes), hemoglobin (Hgb), tender joint (Ritchie Articular Index), and Disease Activity (DAS28), affect the quality of life of the subjects?

Materials and Methods

Study Design and Studied Subjects

The study group consisted of 128 patients hospitalized in Poznan's rheumatology departments (the Rheumatology Ward of the M. Dega Orthopedic and Rehabilitation Clinical Hospital of Poznan University of Medical Sciences and the Józef Struś Poznan Multidisciplinary City Hospital) from December 2016 to January 2018, see [12]. The main criterion for inclusion in the study was a diagnosis of RA according to the American College of Rheumatology (ACR) criteria and the European League Against Rheumatism (EULAR) from 2010 [13].

On the day of admission to treatment, patients received questionnaires to answer the questions included in the questionnaires. A researcher (the first author) participated in the answering process and explained any doubts about understanding the questions in the survey. In addition, the researcher checked whether all questions in the questionnaire had been answered, and if they were missing, the respondent was asked to complete the answer. Then, the physician, and rheumatologist, in the presence of the researcher (the first author), assessed the clinical status, disease activity, and pressure pain in the joints - they used the clinical tests listed later in the article.

The patients participating in the study underwent the laboratory tests listed in the other part of the article.

The exclusion criteria were people who were diagnosed with mental health-related diseases - which did not allow them to complete the questionnaires, cancer, and lack of consent or resignation during the study.

Methods

Questionnaires

The specific scale Arthritis Impact Measurement Scales-2 (AIMS-2), developed by experts from the Boston Center for Rheumatic Diseases, was used to assess the quality of life [14]. The AIMS-2 scale has been translated into many languages, and in many studies, the study group consisted of patients with RA.

The cultural and linguistic adaptation and the assessment of the psychometric properties of the Polish version of the AIMS-2 scale were prepared by a team led by Bączyk [15]. For the Polish version of the scale, Cronbach's α coefficient is 0.89 for the entire scale, while for individual subscales, the values range from 0.70 for a social activity to 0.89 for support from family and friends [15].

The AIMS -2 [14,15] scale consists of 78 questions. The first 57 questions are made up of 12 subscales, which include: mo-

bility level, walking and bending, hand and finger function, arm function, self-care, household tasks, social activities, support from family and friends, arthritis pain, work, level of tension, mood, satisfaction.

Each of these subscales contains 4 or 5 items, with a possible answer consisting of 5 alternatives: from "always" to "never" and from "all days" to "not at all - no day" [15].

The possible range of scores for individual subscales is 0 - 10, where: 0 means good functioning and good quality of life, while 10 means poor functioning and poor quality of life [14,15].

The remaining questions of the AIMS -2 scale concern the respondents' life satisfaction assessment [14].

Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) [16] Polish versions with the consent of the authors.

The FACIT-F scale allows assessing fatigue in the following domains: physical, mental, and social as part of the daily functioning of patients and their daily activities (within the last week). The scale consists of 13 questions (each question is scored from 0 to 4), with a maximum of 52 points and a minimum of 0. The questions allow you to assess whether fatigue occurs at all and the degree of its intensity in the examined area. The lower the score, the more severe the fatigue [16].

Clinical Tests

The Visual Analogue Scale (0 – 10 cm VAS Pain Scale) was used to determine the severity of joint pain; 0 cm VAS - no pain, 10 cm VAS - very severe pain [17].

The Ritchie Articular Index was used to assess joint soreness. This index determines the pain of pressing joints in points from 0 to 3:

- 0 points - the joint is not sensitive to pressure,
- 1 point - pain when pressed,
- 2 points - pain and defensive reactions to pressure,
- 3 points - violent defensive reaction to pressure.

The index value is the sum of the points for all involved joints. Its maximum value is 53 points [18].

DAS28 disease activity was assessed using a medical calculator (DAS28 CRP 3) version 1.1. [19]. the number of painful joints according to the Ritchie Articular Index and the number of swollen joints and CRP value were entered into the calculator.

A questionnaire collecting information on demographic and clinical factors as well as the results of laboratory tests

The self-designed questionnaire included the following questions: sex, age, duration of the disease, current treatment (classic Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), drugs modifying disease activity, glucocorticoids), and biological treatment (yes/no), duration of morning stiffness symptom (in minutes) and Hemoglobin Concentration (Hgb), C-Reactive Protein (CRP), and Rheumatoid Factor (RF) titers.

Ethics

The study was approved by the Ethics Committee of the Poznan University of Medical Sciences, under reference numbers 46/16 and 564/16, and was carried out in accordance with

the Declaration of Helsinki. Participants of the study received an informed consent form, where they were informed about the purpose and course of the study and that they could terminate their participation in the project at any time without incurring any consequences. All patients gave their written informed consent to participate in the study.

Statistical Analysis

Qualitative variables are described by the number (*n*) and frequency (%), and the measurable variables are characterized by the Arithmetic Mean (Avg), Standard Deviation (SD), Median (Me) and Minimum (min), and Maximum (max) values.

Due to the nature of the variables (measurable variables described on an ordinal scale and the lack of normal distribution of quantitative variables), non-parametric tests were used for statistical analyses.

The Mann-Whitney and Kruskal-Wallis U test was used to assess the relationship between quality of life and clinical, demographic, and fatigue factors. The significance level $\alpha=0.05$ was assumed (if the test probability $p>0.05$, the variables in both groups were considered to be the same).

Correlations between measurable variables were checked using Spearman's rank correlation coefficient significance test. If the test probability *p* exceeded the assumed significance level of $\alpha=0.05$, it meant that there was no correlation between the tested variables.

To assess the impact of several independent variables (clinical factors) on the level of quality of life, multiple linear regression and in-depth stepwise multiple regression were used for the most significant coefficient.

The value of $p<0.05$ was considered statistically significant.

Statistical calculations were performed using the STATISTICA 10 PL statistical package.

Results

Characteristics of the Study Group

The study group consisted of 128 patients with RA, and the fewest were men ($n=18$). The respondents were between 19 and 83 years of age; the average age for women was 53.7 ± 14.4 , and for men, 54 ± 15.6 . Only 24 patients were treated with biological drugs (19 women and 5 men). The mean duration of the disease was 11 years and the mean duration of morning stiffness was 53.3 minutes, see Table 1 and 2. More than 58% of patients had at least one comorbidity; about 37% suffered from hypertension, about 9% from type 2 diabetes, and about 7% from ischemic heart disease.

AIMS-2 Measuring Scale

The average results for individual quality of life subscales have been presented in Table 3. The normalized results of the quality of life can be compared to each other - their range is on a scale of 0-10 points.

The highest scores, and thus the lowest quality of life, were obtained by patients for the following subscales:

Arthritis pain - average 6.25 ± 2.52 points,

Walking and bending - average 5.63 ± 2.71 points,

Level of emotional tension - average 4.99 ± 1.92 points.

Table 1: General characteristics of the respondents for demographic variables.

Demographic Variables	Female n=110 (85.9%)		Male n=18 (14.1%)		Total n=128	
	n	%	n	%	n	%
Place of residence						
City	77	70.0	11	61.1	88	68.8
Country	33	30.0	7	38.9	40	31.3
Marital status						
Single	21	19.1	1	5.6	22	17.2
Married	72	65.5	15	83.3	87	68.0
Divorced	4	3.6	0	0.0	4	3.1
Widowed	13	11.8	2	11.1	15	11.7
Education						
Elementary school education	4	3.6	1	5.6	5	3.9
High school education	73	66.4	12	66.7	85	66.4
Higher education	33	30.0	5	27.8	38	29.7
Occupational status						
Professionally active	53	48.2	11	61.1	64	50.0
Unemployed	5	4.5	0	0.0	5	3.9
Retired	35	31.8	5	27.8	40	31.3
Pensioner	17	15.5	2	11.1	19	14.8
Residence status						
With someone	96	87.3	17	94.4	113	88.3
Alone	14	12.7	1	5.6	15	11.7
Biological treatment						
Yes	19	17.3	5	27.8	24	18.8
No	91	82.7	13	72.2	104	81.3
Age [years]						
Avg.±SD	53.7±14.4		54.6±15.6		53.8±14.5	
Median (min.–max.)	56.0(19–83)		57.5(23–75)		56.0(19–83)	

Abbreviations: Avg.: Average; SD: Standard Deviation; min.: Minimum Value; max.: Maximum Value.

- The lowest scores, and thus the highest quality of life, were obtained by patients for the following subscales: Support from family and friends - average 1.39±2.21 points,
- Self-care - average 2.11±2.45 points.

The average results for individual quality of life subscales for sex have been presented in Table 4. A statistically significant was negative between the AIMS-2 and sex.

Correlations between Scales

Correlations between the used scales: AIMS-2 and FACIT-F have been presented in Table 5.

A statistically significant positive correlation of moderate strength ($R_s=0.448$) occurred between the AIMS-2 and FACIT-F scales.

Correlations between Clinical Factors and the Level of Quality of Life

Statistically significant correlations occurred between AIMS-2 and:

- age - a low-strength positive correlation ($R_s=0.244$) - higher values of patients' age are accompanied by higher values of the AIMS-2 scale, which means that the overall quality of life deteriorates with age,
- VAS - positive correlation of moderate strength ($R_s=0.483$) - higher values of the AIMS-2 scale accompany high-

Table 2: General characteristics of participants in terms of their clinical data.

Clinical Variables	Total n = 128
Disease duration [years]	
Avg.±SD	11.1±8.7
Median (min.–max.)	9.5(0.2-40)
Visual Analogue Scale for pain (VAS) [cm]	
Avg.±SD	5.6±2.4
Median (min.–max.)	6.0(0-10)
Morning stiffness [min]	
Avg.±SD	53.3± 69.1
Median (min.–max.)	30.0(0-420)
Hemoglobin (Hgb) [g/dL]	
Avg.±SD	9.3±2.8
Median (min.–max.)	8.4(3.4-23.2)
C-reactive protein (CRP) [mg/L]	
Avg.±SD	11.5±15.6
Median (min.–max.)	5.9(0.1-84.4)
Rheumatoid factor (RF) [IU/mL]	
Avg.±SD	78.7±133.1
Median (min.–max.)	32.8(1-650)
Ritchie Articular Index [pts]	
Avg.±SD	24.2±17.7
Median (min.–max.)	21.5(1-53)
Disease Activity Score 28 (DAS28)	
Me±SD	3.8±0.9
Me (min. - max.)	4.0(1.8 - 5.9)
FACIT-F [pts.]	
Avg.±SD	24.1±9.1
Median (min.–max.)	44.0(7-49)

Abbreviations: Avg.: Average; SD: Standard Deviation; min.: Minimum Value; max.: Maximum Value. FACIT-F scale—a maximum of 52 points can be obtained, indicating very strong fatigue, and a minimum of 0 points, indicating no fatigue. The range of points in the question is 0–4.

er values of the VAS scale, people experiencing more pain have a worse quality of life,

- morning stiffness - positive correlation of moderate strength ($R_s=0.454$) - higher values of the AIMS-2 scale accompany higher values of morning stiffness, patients with more prolonged morning stiffness have worse quality of life,
- CRP serum concentration - low-strength positive correlation ($R_s=0.95$) - higher values of CRP concentration are accompanied by higher values of the AIMS-2 scale, people with higher CRP concentration have worse quality of life,
- Ritchie Articular Index - positive correlation of low strength ($R_s=0.339$) - higher values of the AIMS-2 scale accompany higher values of the Ritchie Articular Index, people with greater pressure pain have a worse quality of life,
- DAS28 – low-strength positive correlation ($R_s=0.390$) – higher values of the
- AIMS-2 scale accompanies higher DAS28 values, patients with higher disease activity have worse quality of life, see Table 6.

VAS Pain Intensity in Individual Subscales of AIMS-2

Statistically significant correlations occurred between pain and subscales of the AIMS-2 (Table 7):

- Mobility ($R_s=0.200$) - positive correlation of weak strength,

Table 3: Descriptive statistics of the quality of life of the respondents in individual subscales of AIMS-2 (normalized scores - scale 0 - 10 points; n=128).

Subscales AIMS-2	[pts]				
	Mean	SD	Median	Min.	Max.
Mobility level	3.24	2.52	3.00	0.0	10.0
Walking and bending	5.63	2.71	5.50	0.0	10.0
Hand and finger function	3.35	2.67	2.75	0.0	10.0
Arm function	2.78	2.36	2.50	0.0	9.5
Self-care	2.11	2.45	1.25	0.0	10.0
Household tasks	2.79	2.67	2.50	0.0	10.0
Social activities	4.34	1.91	4.50	0.0	9.5
Support from family and friends	1.39	2.21	0.00	0.0	10.0
Arthritis pain	6.25	2.52	6.50	0.0	10.0
Work	2.89	2.70	1.56	0.0	10.0
Level of tension	4.99	1.92	5.00	0.0	10.0
Mood	4.01	1.75	4.00	0.5	8.0
Satisfaction	4.38	2.21	4.60	0.0	9.2

Abbreviations: Avg.: Average; SD: Standard Deviation; min.: Minimum Value; max.: Maximum Value.

Table 4: Descriptive statistics of the quality of life of the respondents in individual subscales of AIMS-2 for sex and the results of the Mann-Whitney U test (normalized scores - scale 0 - 10 points; n=128).

Subscales AIMS-2	Sex				U Mann-Whitney test (p>0,05)	
	Women n=110		Man n=18		U	p
	Mean	SD	Mean	SD		
Mobility level	3,29	2,55	2,97	2,38	930,5	0,6859
Walking and bending	5,70	2,66	5,14	3,02	887,0	0,4823
Hand and finger function	3,40	2,70	3,03	2,53	917,5	0,6217
Arm function	2,61	2,22	3,81	2,95	758,5	0,1133
Self-care	1,98	2,40	2,92	2,65	800,5	0,1952
Household tasks	2,81	2,67	2,71	2,77	974,5	0,9181
Social activities	4,39	1,84	4,06	2,36	889,5	0,4931
Support from family and friends	1,34	2,26	1,70	1,88	804,5	0,2048
Arthritis pain	6,30	2,43	5,92	3,07	960,5	0,8424
Work	2,90	2,70	2,78	2,80	947,0	0,7708
Level of tension	5,01	1,90	4,83	2,09	890,5	0,4974
Mood	4,04	1,72	3,81	1,97	938,5	0,7267
Satisfaction	4,41	2,11	4,18	2,78	928,0	0,6734

Abbreviations: Avg.: Average; SD: Standard Deviation; p - p—Probability level for the t statistic; U - Mann-Whitney test value

Table 5: Significance test results of Spearman's rank correlation coefficient between scales.

Pair of variables	n	Rs	t(n-2)	p
AIMS-2 & FACIT-F	128	0.448	5.63	<0.0001

Abbreviations: Rs—the value of the Spearman coefficient for the number n, t—the value of the t statistic checking the significance of the Rs coefficient for the number of degrees of freedom n-2, p—probability level p for the t statistic. FACIT-F scale—a maximum of 52 points can be obtained, indicating very strong fatigue and a minimum of 0 points indicating no fatigue. The range of points in the question is 0–4.

- Walking and bending (Rs=0,346) - a low-strength positive correlation,
- Hand and finger function (Rs=0,311) - a low-strength positive correlation,
- Arm function (Rs=0,302) - a low-strength positive correlation,

Table 6: The results of the Spearman rank correlation coefficient significance test between the independent variables and the AIMS-2 scale.

Pair of Variables	AIMS-2		
	Rs	t(n-2)	p
Age [years]	0.244	2.83	0.0055
Visual Analogue Scale for pain (VAS) [cm]	0.483	6.19	0.0000
Morning stiffness [min.]	0.454	5.72	0.0000
C- Reactive Protein (CRP) [mg/l]	0.295	3.46	0.0007
Ritchie Articular Index [pts]	0.339	4.05	0.0001
Disease Activity (DAS28)	0.390	4.75	0.0000

Abbreviations: Rs—the value of the Spearman coefficient for the number n, t—the value of the t statistic checking the significance of the Rs coefficient for the number of degrees of freedom n-2, p—probability level p for the t statistic. The following clinical factors, like gender, disease duration, Hgb and RF, and the level of quality of life: were not statistically significant.

Table 7: The results of the Spearman's rank correlation test between the intensity of pain and the quality of life of the respondents in individual subscales of the AIMS-2 (normalized scores - scale 0 - 10 points; n=128).

VAS [cm] &	Rs	t(n-2)	p
Mobility level	0,200	2,30	0,0233
Walking and bending	0,346	4,14	0,0001
Hand and finger function	0,311	3,67	0,0004
Arm function	0,302	3,56	0,0005
Self-care	0,233	2,69	0,0082
Household tasks	0,142	1,61	0,1105
Social activities	0,218	2,50	0,0136
Support from family and friends	-0,009	-0,10	0,9172
Arthritis pain	0,496	6,42	<0,0001
Work	0,106	1,19	0,2346
Level of tension	0,291	3,42	0,0009
Mood	0,293	3,44	0,0008
Satisfaction	0,456	5,75	<0,0001

Abbreviations: Rs—the value of the Spearman coefficient for the number n, t—the value of the t statistic checking the significance of the Rs coefficient for the number of degrees of freedom n-2, p—probability level p for the t statistic.

- Self-care (Rs=0,233) - a low-strength positive correlation,
- Social activities (Rs=0,218) - a low-strength positive correlation,
- Arthritis pain (Rs=0,496) - positive correlation of moderate strength,
- Level of tension (Rs=0,291) - a low-strength positive correlation,
- Mood (Rs=0,293) - a low-strength positive correlation,
- Satisfaction (Rs=0,456) - positive correlation of moderate strength.

People experiencing more pain have a worse quality of life.

Multiple Regression

Table 8 presents the results of multiple regression analysis for the quality of life variable and three models of independent variables:

- Model 1 examined the combined effect of hemoglobin, CRP, and RF on quality of life,
- Model 2 examined the regression analysis for pharmacological treatment (biological/conventional drugs) and disease activity (DAS28),

Table 8: Multiple regression results for AIMS-2 variable and independent variables.

Variables	b*	The standard error for b*	b	The standard error for b	p
Model 1					
R=0.366; R2=0.134; Corrected. R2=0.113; F(3.124)=6.41; p<0.0004; Estimated standard error: 34.58*					
Hemoglobin (Hgb) [g/dl]	-0.118	0.086	-0.591	1.138	0.1727
C-Reactive Protein (CRP) [mg/l]	0.259	0.092	-0.002	0.216	0.0057
Rheumatoid Factor (RF) [IU/ml]	0.121	0.090	0.004	0.025	0.1805
R=0.330; R2=0.109; Corrected. R2=0.102; F(1.126)=15.37; p<0.0001; Estimated standard error: 34.81**					
C-Reactive Protein (CRP) [mg/l]	0.330	0.084	0.776	0.198	0.0001
Model 2					
R=0.438; R2=0.192; Corrected. R2=0.179; F(2.125)=14.84; p<0.0000; Estimated corrected error: 33.28*					
Pharmacological treatment	-0.136	0.084	-12.770	7.859	0.1067
Disease Activity (DAS28)	0.379	0.084	15.104	3.338	0.0000
R=0.418; R2=0.175; Corrected R2=0.168; F(1.126)=26.69; p<0.0000; Estimated standard error: 33.50 **					
Disease Activity (DAS28)	0.418	0.081	16.643	3.221	0.0000
Model 3					
R=0.584; R2=0.341; Corrected R2=0.325; F(3.124)=21.38; p<0.0000; Estimated standard error: 30.17 **					
Visual Analogue Scale for Pain (VAS) [cm]	0.354	0.082	5.341	1.244	0.0000
Morning stiffness [min]	0.175	0.082	0.093	0.044	0.0359
Disease Activity (DAS28)	0.221	0.081	8.809	3.241	0.0075
* multiple regression; ** progressive multiple-step regression; R—correlation coefficient; R2—correlation of determination; F—F test statistic; b — regression coefficient					

• Model 3 analyzed the effects of pain (VAS), age (in years), morning stiffness, joint tenderness (Ritchie Articular Index), and disease activity (DAS28) on quality of life.

The most significant impact on the quality of life on the AIMS-2 scale was exerted by VAS pain ($b^*=0.354\pm 0.082$), DAS28 disease activity ($b^*=0.221\pm 0.081$), and morning stiffness ($b^*=0.175\pm 0.082$).

Discussion

In Polish and foreign studies, the level of quality of life is examined using various questionnaires, the size of the study groups varies, and multiple factors are considered (e.g., clinical, demographic, psychosocial, productivity, or fatigue). These analyzes are intended to determine how the quality of life affects patients with RA and what predictors increase or decrease its level, which may translate into treatment modifications or the determination of specific socio-economic assistance.

As authors, we think the most interesting aspect of this article is multiple regression. This analysis is very rarely used to assess the impact of various factors together on the quality of life of patients with RA. In addition, on the basis of progressive stepwise multiple regression, it is theoretically possible to predict what parameters (and precisely their intensity) affect the perceived quality of life. An attempt to answer and indicate which factors together worsen the patient's condition, and thus negatively affect his quality of life, will allow for an appropriate therapeutic approach to the patient, e.g. by changing medications, incorporating additional therapies. This study analyzed almost all clinical factors specific to RA in order to identify which and to what extent negatively affect patients' quality of life.

Relationships and Correlations between Clinical and Demographic Factors and the Level of Quality of Life

In the presented study on the AIMS-2 scale, the lowest qual-

ity of life was obtained by patients in the areas of joint pain, walking and bending, and emotional tension. This may result in difficulties in performing everyday activities and professional duties, as well as absenteeism from work or social and cultural life. The highest quality of life was presented in the domains of support from family and friends and self-care. The study's authors indicated that the quality of life in RA patients correlates with pain, age, morning stiffness, disease activity, CRP levels, and joint tenderness. However, it has nothing to do with demographic factors.

In another study, Bączyk et al. [8] indicated that a better assessment of the quality of life of patients with RA in the AIMS-2 scale depended on the support received from family and friends. In contrast, lower quality of life was related to joint pain, walking, and bending. As in this study, quality of life correlated with pain, morning stiffness, and hand muscle strength but not with joint tenderness. Kaniewska K et al. [6] showed differences in the AIMS-2 scores on the "walking and bending" scale depending on the severity of RA [6].

Moreover, Roma et al. [20], assessing the quality of life of the subjects using the SF-36 scale, also showed that pain significantly impacted the quality of life, followed by general health, vitality, and physical aspects. In contrast, the subjects rated the emotional, social and mental health spheres the best. It was emphasized that categories from the physical domain significantly impacted the quality of life in patients with RA more than in the mental domain. In this study, 99 respondents rated their quality of life as low.

Matcham et al. [21] conducted a meta-analysis of 31 studies on the quality of life in patients with RA (measured with the SF-36 scale). They unequivocally indicated that the disease, RA, has a negative impact on the sense of the quality of life. Their analyses showed that the scientific literature reports that physical determinants have a much more significant impact on the

deterioration of the quality of life than mental determinants. Patients presented the lowest quality of life in the areas of role limitation due to physical health and vitality and the highest in the areas of physical functioning and mental health. Correlations between age (the higher the age, the worse the quality of life in the physical aspect), the duration of the disease, and female sex were also indicated, which in the case of the last two determinants was not confirmed in this study [21].

In randomized studies on the impact of pharmacological treatment (with the use of disease-modifying drugs; DMARDs) on the quality of life (SF-36 scale), Gerhold et al. [22] proved that it has a positive impact on the quality of life in contrast to this current study. Azevedo et al. [23] obtained similar results concerning pharmacotherapy with biological drugs.

In the study by Martiniec et al. [24], pain dominated the factors influencing the quality of life, and reducing pain perception resulted in improved in the quality of life. The pain had a negative impact on such domains of quality of life (as measured by the SF-36 scale and the World Health Organization's Quality of Life Questionnaire (WHOQOL), such as social functioning, the general perception of health, and physical functioning. In Kupcewicz et al. [25], pain also had a negative impact on the quality of life.

Abu Al-Fadl et al. [26] assessed the quality of life using the SF-36 scale. They indicated that RA negatively affects the quality of life's physical and psychological domains. Age did not correlate with the quality of life, in contrast to disease activity and gender - women presented a lower quality of life than men.

Kamisoko et al. [27] also confirmed that pain and disease activity decreases the quality of life. DAS28 significantly impacted the subjects' mental state, pain, and overall quality of life. In the Echelle de Mesure de l'Impact de la polyarthrite Rhumatoïde (EMIR), patients presented the lowest quality of life in the areas of pain and mental and the highest in the area of work.

Cruz-Castillo et al. [28] assessed the quality of life using the Spanish version of the Quality of Life Rheumatoid Arthritis (QOL-RA) tool. Patients rated their quality of life as good or moderate. The following determinants impacted the quality of life in Ecuadorian patients - functionality, disease duration, and disease activity. Aspects of support and social life were rated the highest, and pain and nervous tension the lowest.

Kumar et al. [29] found a significant correlation between the quality of life and CRP concentration.

Besides, Goma et al. [30] confirmed in their research on the Egyptian community that the quality of life is affected by pain, physical disability and limitations in this area, anxiety, depression, and social dysfunctions (such as difficult interpersonal contact).

Tański et al. [31] indicated that patients treated with biological drugs had a lower quality of life than those treated conventionally, and anxiety and depression negatively impacted their quality of life.

In their studies, Besirli et al. [32] proved that the quality of life (in the mental and physical domains of the SF-36 scale) is influenced by disease activity, anxiety, depression, and suicidal thoughts.

McBeth et al. [33], Abu Al-Fadl et al. [26], Kamisoko et al. [27], Cruz-Castillo et al. [28], Conley et al. [34] that demograph-

ic factors do not affect the quality of life in patients with RA. Bączyk et al. [8] pointed out that low education (secondary, vocational, and primary) is responsible for the low quality of life in the physical sphere, but not marital status. Lapčević et al. [35] showed that occupational qualifications impacted the sense of the quality of life; the higher and better qualifications, the better the quality of life of the respondents, and Rosa-Gonçalves et al. [36] that gender and education influenced the quality of life. Zhou et al. [37] analyzed the quality of life using the SF-36 scale. They indicated that physical functioning, in terms of quality of life, is influenced by extra-articular symptoms, joint tenderness, pain, and low income. In contrast, mental functioning is affected by low income, physical work, the number of swollen joints, and marital status.

Relationships and Correlations between Fatigue Factors and the Level of Quality of Life

The analysis showed a positive correlation of moderate strength between the level of fatigue (FACIT-F scale) and the quality of life (AIMS-2 scale). Higher values accompany higher values in the FACIT-F scale in the AIMS-2 scale, which means that people with more severe symptoms of fatigue report worse quality of life. Own research has shown that the quality of life assessed by patients in particular areas coincides with the statistical analysis within the domains positively correlated with the symptom of fatigue, i.e., walking and bending, joint pain, emotional tension level, but also mobility, hand and finger function, arm function, self-care, social activity, mood, and satisfaction.

Chang-Hee Suh et al. [38] analyzed the quality of life of Korean patients with RA in terms of the disease itself, fatigue, depression, social support, and self-efficacy. Their research confirmed that quality of life is significantly related to fatigue. Rodriguez-Muguruza et al. [39] also obtained similar results, indicating a correlation between emotional tension (examined in the AIMS 2 test) and fatigue. Albayrak Gezer et al. [40], Rongen-van Dartel et al. [41], Öncü et al. [42], and Conley et al. [34] showed in their analyzes that fatigue had the most significant impact on functional efficiency. In contrast (as in this study), fatigue did not affect household tasks. The correlation of domains in the AIMS-2 scale with the symptom of fatigue indicates a kind of functional disability (e.g., in the area of mobility, walking, bending, limb function or self-care). Similar results using other scales were obtained by Lee et al. [43], Campbell et al. [44], Diniz et al. [45], Grøn et al. [46], and Lao et al. [47]. Contrary to their research, Lapčević et al. [35] indicated that fatigue intensifies due to the use of help from third parties and numerous household duties. This discrepancy may be because in the study group analyzed in this study, as many as 118 out of 128 respondents lived with someone, had support in everyday life, and there were no patients dependent on external carers.

Multiple Regressions between Examined Factors and the Level of Quality of Life

Scientific research shows that it is difficult to isolate which factors affect the level of quality of life. It should be noted that clinical determinants may jointly affect the quality of life, lowering the perception of it or not. Regression analysis in the above studies indicated that pain, morning stiffness, disease activity, and CRP level affect the level of quality of life, where the increase in their parameters worsens the perception of quality of life.

In our study, three models of independent variables for the variable quality of life were subjected to multiple regression analysis.

Model 1 examined the combined effect of hemoglobin, CRP, and RF on quality of life. CRP was significant predictor, explaining 10.2% of the variability of the quality of life in the AIMS-2 scale. An increase in CRP concentration by one point reduced the quality of life on the AIMS-2 scale by an average of 0.776 ± 0.198 points.

In model 2, the regression analysis for pharmacological treatment (biological/conventional drugs) and Disease Activity (DAS28) revealed that DAS28 is a significant factor for life quality (AIMS-2). The regression model allows for explaining 16.8% of the variation in life quality on the AIMS-2 scale. An increase in DAS28 disease activity by one point reduced the quality of life in the AIMS-2 scale by an average of $16,643 \pm 3,221$ points.

Model 3 analyzed the effects of pain (VAS), age (in years), morning stiffness, joint tenderness (Ritchie Articular Index), and Disease Activity (DAS28) on quality of life.

Significant coefficients for quality of life (AIMS-2) were pain (VAS), morning stiffness, and DAS28. The regression model explained 32.5% of the quality of life value variability. An increase in pain perception in the VAS scale by one centimeter created the score in the AIMS-2 scale (reduced quality of life) by an average of 5.341 ± 1.244 points. An increase in morning stiffness by one minute increased the AIMS-2 score (reduced quality of life) by an average of 0.093 ± 0.044 points. In turn, an increase in DAS28 disease activity by one increased the AIMS-2 score (reduced quality of life) by an average of $8,809 \pm 3,241$ points.

The most significant impact on the quality of life on the AIMS-2 scale was exerted by VAS pain ($b^* = 0.354 \pm 0.082$), DAS28 disease activity ($b^* = 0.221 \pm 0.081$), and morning stiffness ($b^* = 0.175 \pm 0.082$).

Pain, morning stiffness, and grip strength were significant predictors of impact on quality of life also in Bączyk et al. [8]. Besides, Laric et al. [48] indicated that pain intensity, pain catastrophizing, belief in coping with pain, and alexithymia explained 54% of the variance in the physical component of Health-Related Quality of Life (HRQOL) ($p < 0.001$). Bai et al. [49] assessed the quality of life in patients with RA using the SF-36 scale, World Health Organization Quality of Life-Bref (WHOQOL-BREF), and Quality of Life Instruments for Chronic Diseases-RA (QLICD-RA). They conducted a multiple regression analysis that showed that sleep duration, psychological counseling, and C4 levels affected the quality of life, as assessed on the SF-36 scale. In the same study, information was obtained that the level of IgA and being overweight together affect the assessment of the quality of life in the WHOQOL-BREF scale.

Adequate sleep and psychological help affect the quality of life assessment in the QLICD-RA scale. Rosa-Gonçalves et al. [36] indicated in the multiple regression analysis that pain, disease activity, and education jointly affect the quality of life (measured on the SF-36 scale). Katchamart et al. [50] indicated that among Thai patients with RA, the quality of life was affected jointly by disease activity, functional disability, depression and anxiety, and pain. In Tański et al. [31], depression was the main predictor negatively affecting the quality of life, especially in the domains of perceiving the quality of life, perceiving health, and physical health (measured in the WHOQOL scale).

In Mandala et al. [51], in a multiple regression analysis, the quality of life was negatively affected by disease activity, functional disability, treatment with disease-modifying drugs, comorbidities, and extra-articular lesions.

These studies also show limitations related to the small size of the study group, the lack of repeated analyzes after changing pharmacological treatment or changes in the disease activity status, and the lack of conclusions in the area of mental condition. This creates opportunities for further research and the concept of improving the quality of life of patients with RA.

The strength of this study was the use of multiple regression analysis to assess the impact of various factors on the quality of life of patients with RA. In addition, based on progressive stepwise multiple regression, it was predicted which parameters (precisely their intensity) affect the perceived quality of life. In this study, almost all clinical factors characteristic of RA were analyzed to determine which ones and to what extent negatively affect patients' quality of life. These findings may allow a better understanding of RA patients' problems and affect the therapeutic approach.

Conclusion

Based on a progressive stepwise multiple regression, it has been shown that it is possible to predict what parameters affect the intensity of perceived quality of life. These were pain on the VAS scale, disease activity DAS28, morning stiffness, and CRP concentration (increasing their parameters will reduce the perceived quality of life).

Research on the quality of life and its assessment in individual patients is essential for the treatment itself and the patient's approach to their situation. It allows for individualized treatment and cares for the patient, meeting their needs, changing the direction of treatment, or solving problems that adversely affect the therapy process. The disease does not only affect the body but negatively affects the mind, soul, and social and professional relationships. Therefore, assessing the quality of life in patients with RA should be a permanent element of patient care.

Author Statements

Author Contributions

Conceptualization, G.B.; data curation, K.A.K.; formal analysis, K.A.K., and G.B.; investigation, K.A.K.; methodology, K.A.K., and G.B.; writing—original draft, K.A.K., G.B., and D.F; writing—review and editing, K.A.K., G.B. and D.F; supervision, G.B., and D.F. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was conducted following the Helsinki Declaration and was approved by the Ethics Committee of the Poznan University of Medical Sciences, registered under reference numbers 46/16 and 564/16.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

The data are not publicly available due to data privacy regulations. The data presented in this study are available upon request from the corresponding author.

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Conflicts of Interest

The authors declare no conflict of interest.

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