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Original Article

Association between Pain, Arthropathy and Health-Related Quality of Life in Patients Suffering from Acromegaly. A Cross-Sectional Study

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Abstract

Introduction: Despite successful therapy, acromegalic patients have reduced health-related quality of life (HRQoL) compared to healthy controls. Finding predictors of poor HRQoL can be crucial to improving these patients' global health state.

Aim: The primary objective of the study was to find out predictors of HRQoL. Secondary objectives were: (I) to determine correlations with AcroQoL subscales, and (II) to identify predictors for subscales.

Materials and methods: In this cross-sectional study conducted in 2019 at the Messina Policlinic Hospital, 45 acromegalic patients were assessed at the Physical and Rehabilitative Medicine Ambulatory. During routine outpatient clinic attendances, the following questionnaires were administered: Acromegaly Quality of Life Questionnaire (AcroQoL), Patient-Assessed Acromegaly Symptom Questionnaire (PASQ), and Western Ontario and McMaster Universities Arthritis Index (WOMAC). We furthermore included the following variables obtained by medical record review: age, BMI, disease duration, previous surgery (Yes/No), previous radiotherapy (Yes/No), use of GH lowering medications (Yes/No), hypertension (Yes/No), diabetes mellitus (Yes/No), and biochemical control of the disease (Yes/No): immunoradiometric assays were employed to serum GH and IGF-1 measurements to identify biochemical control of the disease. Correlation between outcome measures and AcroQoL has been performed. Pearson's *r* was calculated for continuous data following normal distribution (AcroQoL, PASQ, AcroQoL-B, AcroQoL-R, WOMAC-P), while Spearman's rank order correlation was calculated for non-normally distributed data (WOMAC, WOMAC-F, WOMAC-S, AcroQoL-P) and point-biserial correlation for binary variables (biochemically controlled disease, use of GH lowering medications, radiotherapy, surgery).

The same correlation analysis was performed for the AcroQoL subscales.

Multiple linear regression with backwards, stepwise analysis was used to assess the influence on AcroQoL of correlated variables.

Results: AcroQoL was strongly negatively correlated with PASQ (r=−0.700, p<0.001) and negatively correlated with WOMAC [r_s (43)=−0.530, p<0.001] and among WOMAC subscales with WOMAC-Physical fitness [r_s (43)=−0.518, p<0.001] WOMAC-Pain [r (43)=−0.428, p=0.003], WOMAC-Stiffness [r_s (43)=−0.393, p=0.007], and radiotherapy [r (43) =−0.314, p=0.035].

After univariate stepwise regression, PASQ was the strongest independent predictor of AcroQoL, with R^2 of 0.392 [F (1,43)=27.695, p<0.001].

Conclusions: This study shows that the severity of painful symptoms is the most important predictor of HRQoL in patients with acromegaly; at the same time, acromegalic arthropathy leads to pain and to a variable amount of functional impairment, exerting great impact on the patient's perception of his health status. Measure of the progression of arthropathy and symptomatic management could lead to a great HRQoL benefit.

Keywords

acromegaly, arthropathy, quality of life, biochemical control, PASQ

INTRODUCTION

Acromegaly is a rare chronic disease with an estimated global prevalence of 40-130 cases/million and an incidence of 3-4 cases/million[1]: in approximately 95% of the cases, this disease is determined by a GH-secreting pituitary adenoma, leading to growth hormone (GH) overproduction[2]. GH overproduction stimulates the liver to produce an excess of insulin-like growth factor-1 (IGF-1), thus determining a complex multi-systemic syndrome, with the main signs being peculiar changes in physical appearance. Symptoms can include musculoskeletal and joint pain, increased sweating, headaches, and paresthesias.[2] GH and IGF-1 elevated serum levels are also correlated with increased incidence of diabetes mellitus, hypertension, obesity, obstructive sleep apnea syndrome, and heart disease.[3]

The observation of typical abnormalities during clinical examination is often the first step of diagnosis. Depending on age at disease onset, the patient usually develops several typical signs of the disease like acral overgrowth (hands or feet), facial dysmorphia, prognathism, and soft tissue hypertrophies with appreciable thickening of lips and facial cartilages. Acromegaly frequently begins as a silent disease and is usually diagnosed up to 10-15 years after the first symptoms appear.[4] Measurement of plasma IGF-1 levels is recommended as a first-line diagnostic test in patients showing or reporting typical manifestations of acromegaly.[5]

According to the World Health Organization, reducing mortality and morbidity, and improving quality of life (QoL) are the main objectives of chronic disease management[6]: as concerns mortality and morbidity, the evolution of treatment strategies has led to remarkable prevention/management of metabolic, cardiovascular, and musculoskeletal comorbidities, mainly by normalization of IGF-1 (age-normalized serum IGF-1 values) and GH nadir levels (GH<1.0 ng/mL random or after oral glucose tolerance test).[5] Recently, surgical, radiotherapic, and pharmacological approaches have shown to be effective in normalizing GH and IGF-1 levels and/or in reducing hormonal dysregulations.[7] So, while the initial focus on reducing mortality and improving morbidity has achieved successful results, in recent decades, the assessment of health-related quality of life (HRQoL) has been a popular research topic as concerns acromegaly. Several studies showed lower HRQoL in acromegalic patients compared to healthy subjects, determined by the loss of physical and social functioning, emotional and physical problems, increased pain, reduced perception of wellness, and possible presence of complications.[2,8-11]

To date, there is still no agreement on the predictors of HRQoL in acromegaly.[9]

In addition, the use of general GH-lowering medications was not associated with better HRQoL according to a recent systematic review: speculatively, QoL during/after therapy could be treatment-specific.[2]

Until now, biochemical control or treatment of acromegaly appeared to be insufficient to predict HRQOL. There is broad consensus suggesting that patient-oriented outcomes, monitoring not only the biochemical control per se but also the disease burden on patient's HRQoL, should be included in the clinical evaluation.[2,9] Specifically, the Acromegaly Quality of Life Questionnaire (AcroQoL) is a well-validated acromegaly-specific outcome, which allows assessment of self-perceived impact of acromegaly on HRQoL. Studies including generic measures of QoL allowed comparison of HRQoL in acromegaly with healthy status or different chronic diseases[24], highlighting that despite adequate treatment, acromegalic patients suffer from severe QoL impairment. Several authors suggest that the correlation between clinical severity and impact of disease on patient's lives could be weak.[12-15] Symptom severity can be assessed using a disease-specific questionnaire, the Patient-Assessed Acromegaly Symptom Questionnaire (PASQ), developed specifically for this purpose and extensively adopted in research.[1] Although not disease-specific, Western Ontario and McMaster Universities OsteoArthritis Index (WOMAC) is a commonly adopted questionnaire (composed of three scales evaluating articular pain, stiffness, and functionality) to study diseases determining arthropathy, such as acromegaly. The adoption of PASQ and WOMAC can give insights into the level of pain and disability suffered by the acromegalic patient.[1,16]

AIM

The primary objective of the study was to find predictors of HRQoL (measured with AcroQoL) in acromegalic patients.

Secondary objectives were: (I) to determine correlations with AcroQoL subscales, and (II) to identify predictors of subscales.

MATERIALS AND METHODS

Participants and study design

This descriptive, cross-sectional study was conducted at the Physical Medicine and Rehabilitation Department of Policlinic Gaetano Martino, Messina, in collaboration with the Department of Endocrinology. We selected acromegalic patients treated and currently followed in this center. All acromegalic patients treated in the center in 2019 were invited to participate in the QoL assessment study and informed of the inclusion of the data in the study protocol. Data were collected in our structure at the first visit after patient's agreement to participate.

The inclusion criteria for research participants of this study were as follows: diagnosis of acromegaly according to the Clinical Practice Guidelines from the Endocrine Society[17]; age ≥18 years; and ability to give informed consent. To ensure an adequate sample size, a priori power analysis was performed for linear regression model with an alpha level of 0.05 and a beta level of 0.95 showing that a sample size of 45 research participants was more than adequate to determine regression coefficient (variance explained = 0.3; R^2 deviation = 0.3). Of 47 patients, 45 accepted to participate in the study (response rate 95.7%). Written consent was obtained from all participants in the study. The study protocol was approved by the Institutional Review Board/Ethics Committee (Comitato Etico di Messina).

Clinical data collection

Data analyzed in this study were collected by administration of questionnaires, by medical record reviews (chart review of the medical history of participants), and clinical examination. We administered 3 questionnaires to every patient, to evaluate the following disease dimensions: quality of life, joint pain, function and stiffness, and general acromegaly symptoms.

Furthermore, the patients' records were reviewed, and clinical data examined to include the following variables: age, BMI, disease duration, biochemical control of the disease (Yes/No), previous surgery (Yes/No), previous radiotherapy (Yes/No), use of GH lowering medications (Yes/No), hypertension (Yes/No), and diabetes mellitus (Yes/No).

AcroQoL, PASQ, and WOMAC were administered during routine outpatient clinic attendances.

Acromegaly Quality of Life Assessment

AcroQoL was the Italian translation of the original questionnaire.[15,18] The AcroQoL questionnaires take approximately 5 to 10 minutes to complete, which makes them suitable for routine use in clinical setting: AcroQoL is essential in assessing QoL at the moment of clinical visit and in particular to monitor changes in evaluation of pharmacological treatments or after surgery.[18]

Assessment of acromegaly clinical manifestations

PASQ is a disease specific questionnaire composed of 7 items, commonly adopted and translated in several languages, including the Italian translation adopted in this study.[19,20] The first 6 items evaluate presence and severity of signs and symptoms (headache, excessive sweating, joint pain, fatigue, soft tissue swelling, and numbness or tingling of the extremities) and the seventh item concerns general perceived health state: score goes from 1 (excellent) to 8 (very bad) for the first six questions, and from 1 to 10 for the seventh question. Total score range goes from 7 to 58 with higher scores reflecting worse symptoms.[19]

Assessment of osteoarthritis index

The Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index is a validated self-reported questionnaire widely used in lower limb osteoarthritis: the Italian version was adopted.[16,21,22] WOMAC breaks down into 3 subscales investigating pain, stiffness, and disability. WOMAC can be completed in about 12 minutes. Here follows an explanation of the scoring system: WOMAC-pain (WOMAC-P) is composed of 5 items exploring pain both during activity and at rest; WOMAC-stiffness (WOMAC-S) consists of two items; WOMAC physical function (WOMAC-F) is composed of 17 items regarding impairment in different activities of daily life: any of the 24 items regards a different symptom, and can be scored from 0 to 4, corresponding to the intensity of the symptom (none = 0, mild = 1, moderate = 2, severe = 3, and extreme = 4). Final score can range from 0 (absence of symptoms) to 96 (any of the symptoms has extreme intensity).

Serum GH and IGF-1 levels

Immunoradiometric assays were employed to perform serum GH and IGF-1 measurements (Immulite 1000 Immunoassay System, Siemens).[23] The sensitivity thresholds for the GH and IGF-1 values were 0.04 ng/ml and 6 ng/ml with coefficients of variation <5% and <10%, respectively. The normal values for serum IGF-1, within the following ranges of age 21–35, 36–50, and 51–75 years, were 115–358 ng/ml, 94–284 ng/ml, and 64–238 ng/ml, respectively. Serum IGF-1 levels are expressed in ng/ml and as upper limit of normality (×ULN). Disease was considered adequately controlled when IGF-1 levels were ≤1.0 ×ULN and random GH <1.0 ng/ml.[5]

Statistical analysis

Values are presented as mean±SD (median; min-max) for continuous variables and as numbers (percentages) for categorical data. Normality of data distribution was evaluated by Shapiro-Wilk test. Correlation between outcome measures and AcroQoL was performed. Pearson's *r* was cal-

culated for continuous data following normal distribution (AcroQoL, PASQ, AcroQoL-B, AcroQoL-R, WOMAC-P), while Spearman's rank order correlation was calculated for non-normally distributed data (WOMAC, WOMAC-F, WOMAC-S, AcroQoL-P) and point-biserial correlation for binary variables (biochemically controlled disease, use of GH lowering medications, radiotherapy, surgery).

The same correlation analysis was performed for the AcroQoL subscales.

Multiple linear regression with backwards, stepwise analysis was used to assess the influence on AcroQoL of correlated variables. Significance level was set up at $p<0.05$. Power analysis was performed using G*Power[24], all the other analyses were performed using SPSS for Windows version 22.0 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.).

RESULTS

As concerns general characteristics of patients with acromegaly: results for descriptive statistics are reported in **Table 1**.

The patient reported outcomes are summarized in **Table 2**.

Correlation analysis

AcroQoL was strongly negatively correlated with PASQ ($r=-0.700$, $p<0.001$); AcroQoL presented a moderate negative correlation with WOMAC [$r_s(43)=-0.530$, $p<0.001$]. Among WOMAC subscales, AcroQoL showed a moderate, negative correlation with WOMAC-F [$r_s(43)=-0.518$, $p<0.001$], and WOMAC-P [$r(43)=-0.428$, $p=0.003$], and a weak negative correlation with WOMAC-S [$r_s(43)=-0.393$, $p=0.007$], and radiotherapy [$r(43)=-0.314$, $p=0.035$].

Table 3 is a summary of all significant correlation coefficients for AcroQoL and AcroQoL subscales.

AcroQoL-P had a moderate negative correlation with PASQ [$r_s(43)=-0.564$, $p<0.001$], WOMAC [$r_s(43)=-0.469$, $p=0.001$], WOMAC-F [$r_s(43)=-0.485$, $p=0.001$] and a weak negative correlation with WOMAC-S [$r_s(43)=-0.372$, $p=0.012$] and WOMAC-P [$r_s(43)=-0.303$, $p=0.043$].

AcroQoL-B was negatively associated with PASQ [$r(43)=-0.390$, $p=0.008$], to biochemical controlled disease [$r(43)=+0.353$, $p=0.018$], and to GH lowering medications

Table 1. General characteristics and epidemiological data of 45 acromegalic patients

Variable	Mean value ± SD Number (%)		Variable	Mean value ± SD Number (%)
Sex			Biochemical data	
Male (M)	15/45 (33.3%)		GH (ng/mL)	1.54 (0.2-14.8)*
Female (F)	30/45 (66.6%)		IGF-1 (ng/mL)	196.0 (115-425)*
Age	62.42±13.06			
Years from diagnosis	24.3±11.24		Biochemical controlled disease	28/45 (62.2%)
BMI (kg/m^2)				
All patients	29.42± 4.82		Comorbidities	
Normal weight	2 M	4 F	Hypertension	35/45 (77.8%)
	24 (±1.41)	23.6 (±1.02)		
Overweight	5 M	15 F	Diabetes mellitus	20/45 (44.4%)
	27.40 (±1.40)	27.27 (±1.03)		
Obese	8 M	11 F		
	36.38 (±8.31)	34.27 (±5.04)		
Previous treatment			Current treatment	
Surgery	25/45 (55.5%)		SSA	27/45 (60%)
Radiotherapy	8/45 (17.7%)		Pegvisomant	5/45 (11.1%)
Surgery+radiotherapy	--		Combination of two agents	6/45 (13.3%)
None	12/45 (26.6%)		None	7/45 (15.5%)

Continuous variables are expressed as mean ± standard deviation (M±SD). As shown in this table, most of the patients in this study are females; on average, participants were diagnosed with acromegaly more than 20 years before the study and most of them (28/45) had a biochemically controlled disease. Only 6 patients out of 45 had a normal body weight, and the most frequent comorbidity was hypertension (35/45). Over half of the patients underwent surgical treatment in the past (25/45), and 60% (27/45) of the patients were currently treated with somatostatin analogues. *: range of values; GH: growth hormone; IGF-1: insulin-like growth factor type 1; SSA: somatostatin analogues; HT: hypertension; DM: diabetes mellitus.

Table 2. Functional and Quality of life assessment

Evaluation scales					
AcroQoL		**WOMAC**		**PASQ**	
	Mean value ± SD		**Mean value ± SD**		**Mean value ± SD**
Global	29.16 (±16.44)	WOMAC tot	36.49 (±22.14)	PASQ	26.80 (±10.59)
Physical	21.62 (±6.68)	WOMAC-P	7.56 (±4.41)		
Body image	21.16 (±7.02)	WOMAC-S	2.91 (±2.16)		
Personal relationships	26.38 (±5.59)	WOMAC-F	25.82 (±16.98)		

Results are presented as mean ± standard deviation. On average, patients showed a reduced quality of life with presence of physical impairment, stiffness and pain derived by arthritis and other painful symptoms. AcroQoL: acromegaly quality of life questionnaire; PASQ: patient-assessed acromegaly symptom questionnaire; WOMAC: Western Ontario and McMaster Universities osteoarthritis index; WOMAC-P: WOMAC-pain; WOMAC-S: WOMAC-stiffness; WOMAC-F: WOMAC physical function.

[$r(43)=-0.340$, $p=0.022$] with a weak correlation.

AcroQoL-R had a moderate negative correlation with WOMAC, [$r_s(43)=-0.469$, $p=0.001$], WOMAC-F [$r_s(43)=-0.485$, $p=0.001$] and a weak negative correlation with PASQ [$r(43)=-0.375$, $p=0.011$], WOMAC-S [$r_s(43)=-0.372$, $p=0.012$], and WOMAC-P [$r(43)=-0.346$, $p=0.020$], surgery [$r(43) =-0.336$, $p=0.024$], and radiotherapy [$r(43)=-0.305$, $p=0.041$].

Any other correlation between AcroQoL, its subscales and other outcome measured was not significant.

Regression analysis

Linear regression analysis was performed in a model including the significantly correlated variables (PASQ, WOMAC, WOMAC-F, WOMAC-P, WOMAC-S, Radiotherapy) as independent variables and the AcroQoL total score as dependent variable to study factors predicting AcroQoL: this regression model was significant [$F(6,38)=6.189$, $p<0.001$] with an R^2 of 0.703, and individual analysis indicated that PASQ ($p<0.001$) and WOMAC-P ($p=0.047$) were the only significant predictors in the model.

After univariate stepwise regression, PASQ was the strongest independent predictor of AcroQoL, with R^2 of 0.392 [$F(1,43)=27.695$, $p<0.001$].

The same method was then applied for AcroQoL subscales: the results of regression are summarized in **Table 4.**

DISCUSSION

The analysis in this study of the relation between HRQoL and demographical, biochemical, and clinical data showed that PASQ, WOMAC and subscales, as well as radiotherapy, surgery, biochemical control, and GH-lowering medications, are correlated with AcroQoL scores.

The main result of our statistical analysis is that PASQ, a commonly adopted, patient-reported measure of painful symptoms in acromegaly, is the most accurate predictor of HRQoL among the ones included. To predict AcroQoL, PASQ is more reliable than the assessment of biochemical control. As a secondary result, joint stiffness, pain, and disability (measured with WOMAC), as well as previous surgery, negatively affected the personal relationships perception of study participants, reduced joint function determined a reduction of perceived physical function, and on the other hand, biochemical control had a positive effect on perceived body image.

This was a cross-sectional study. Acromegaly was diagnosed on average 24.3 years before evaluation of the pa-

Table 3. Results of correlation analysis

AcroQoL	**PASQ**	**WOMAC tot**	**WOMAC-F**	**WOMAC-P**	**WOMAC-S**	**Radiotherapy**	
-Global	−0.70**	−0.53**	−0.52**	−0.43*	−0.39*	−0.31	
AcroQoL	PASQ	WOMAC tot	WOMAC-F	WOMAC-P	WOMAC-S		
-Physical	−0.56**	−0.47**	−0.48**	−0.30	−0.37*		
AcroQoL	PASQ	BC	GH-LM				
-Body Image	−0.39*	+0.35	−0.34				
AcroQoL	PASQ	WOMAC tot	WOMAC-F	WOMAC-S	WOMAC-P	Surgery	Radiotherapy
-Personal relationships	−0.37*	−0.47**	−0.48**	−0.37*	−0.35*	−0.34	−0.30

The data shown are the significant correlation coefficients following the analysis reported in the methods section, approximated to two decimal digits. *p-value <0.05; **p-value <0.01; BC: biochemical control; GH-LM: GH lowering medications.

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Table 4. Univariate stepwise regression analysis: data shown are the standardized B of independent predictive factors for sub-scales, approximated to two decimal digits

AcroQoL scale	PASQ	WOMAC tot	WOMAC-F	Biochem. Control	Surgery
Global	−0.55**	//	//	//	//
Physical	−0.34*	//	−0.33*	//	//
Body image	−0.37*	//	//	+0.33*	//
Personal relationships	//	-0.45**	//	//	-0.35**

*p-value <0.05; **p-value<0.01; //= regression not significant= not a predictor.

tient; even though GH and IGF-1 levels were within target in 62.2% of the patients, this is seemingly not sufficient to determine optimal HRQoL. Conversely, as highlighted by our results, PASQ, a self-reported measure of painful or annoying symptoms (headache, excessive sweating, joint pain, fatigue, soft tissue swelling, and numbness or tingling of the extremities) has a direct relationship with AcroQoL scores **(Fig. 1)**.

The connection between PASQ score and HRQoL is not surprising, as the score of this questionnaire is higher when there is coexistence of different symptoms in a single patient.[16] Interestingly, PASQ appeared to be the main element correlated with HRQoL. We could suggest that periodical collection of PASQ or similar patient-reported outcomes could determine a better perception of the specific needs of the patient, with the final aim of addressing the most burdening symptoms and achieve QoL improvement.

In the other hand, a 2017 systematic review outlined that GH and IGF-1 values (although being a crucial target of therapy), are not correlated with QoL: our results are consistent with this observation.[9] Nevertheless, among AcroQoL subscales, we observed that biochemical control has a positive predictive value for AcroQoL-B: although this could appear surprising, two previous works by Biermasz et al. obtained a similar result.[3,25] The reason of the observed relationship between GH/IGF-1 and cognition, mood, and body image in patients suffering from acromegaly could still be considered an unsolved question.[3,26,27] Lower AcroQoL-B scores in patients with absence of biochemical control could be exclusively determined by the consequences of acromegaly (often invalidating) and the psychological burden of living with a chronic disease.[25] However, it is believed that GH/IGF-1 could influence psychological function per se. In humans, low levels of IGF-1 in women and high in men have been identified as a predictor of the incidence of depressive disorders after 5 years.[27] There is general agreement that higher levels of peripheral IGF-1 are typical of patients suffering from depressive disorders[26,28,29] and anxiety[27], but to date, the nature of a possible causative relationship between this hormone and emotional and cognitive disturbances has not been clearly described: only a limited amount of studies are available, often showing discrepant results[26]. On the other hand, we evidenced no correlation between biochemical control and any other measure of AcroQoL: this result just adds to the evidence that there is no marked relationship between overall HRQoL in acromegaly and biochemical control: in fact, other factors (i.e. severity of symptoms and depression) are consistently associated, and could justify lower HRQoL.[9]

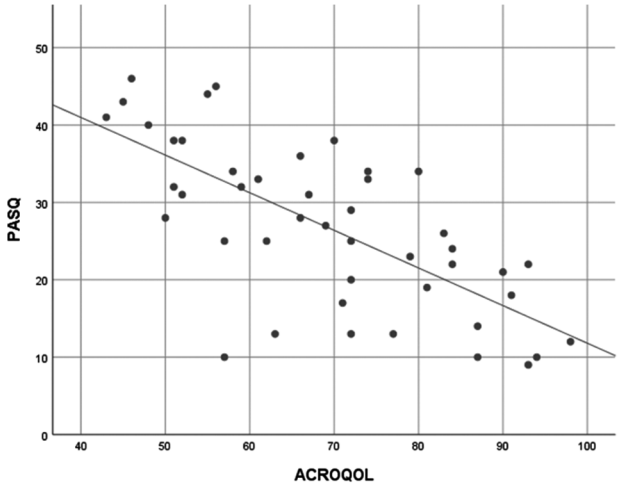

Figure 1. Scatter plot showing the correlation between PASQ and AcroQoL scores.

Finally, we observed a negative correlation of general AcroQoL and radiotherapy: nevertheless, radiotherapy is not a predictor of low AcroQoL. Radiotherapy is considered a third line management option: therefore, a likely explanation for the observed correlation is that patients usually treated with radiotherapy are those with larger and more aggressive tumors, they could be affected by a more invalidating disease.[2,30]

Also, WOMAC (total score and subscales) were correlated with HRQoL in patients in exam. Specifically, WOMAC-F and total score were predictors of AcroQoL and AcroQoL-R. The direct relationship between measures of arthropathy (as concerns physical function and activities of daily living) can be easily explained, as motor disability in acromegaly is mainly accounted for by arthropathy.[16] The pathogenesis of the joint disease is divided into two separate phases: as a first step elevated serum levels of GH and IGF-1 lead to hypertrophy of cartilages and periarticular ligaments with laxity and limited range of motion; subsequently, over time, joints geometrical alterations and repetitive micro-traumas that result in chronic inflammatory processes, scars and osteophyte formation. Although

the first phase can be potentially treated, the latter is less responsive to treatment.[31-33] Surprisingly, as reported by Claessen and colleagues, cartilage defects are usually higher after achievement of disease remission, although in the cited study the controlled patients were on average older than the patients with active disease.[34] We also observed absence of correlation between articular impairment and time elapsed from diagnosis, in line with previous works.[16] Therefore, even if symptoms could be improved by therapy (e.g. somatostatine analogues), our results are consistent with the idea that disease activity is not correlated with self-reported joint complaints. Among the questionnaires tested in acromegaly, we suggest the use of PASQ and WOMAC, since they proved to be a simple tool quantifying dimensions of acromegalic disease strongly associated to loss of QoL (as well as several other aspects, e.g. work productivity). Furthermore, in daily clinical practice these questionnaires may possibly help to screen patients for symptomatic therapy and physiatric-orthopedic management of arthropathy, taking in consideration non-surgical approaches[33,35-37], especially if validated for this specific disease in the future.

Limitations

This work aimed to identify possible predictors for AcroQoL and its subscales within demographic, biochemical and clinical measures: the effects of medical treatment on painful symptoms and articular impairment could not be adequately addressed in our study, as a perspective observation can better describe the effect of therapy on HRQoL, compared with a cross-sectional observation which can include the use of GH-lowering medications only as a binary outcome (treatment: Yes/No). A long-term evaluation of patients could be important to compare the effect of several variables in exam, progression of symptoms and arthropathy, and differences between patients with controlled and uncontrolled disease and surgically cured and therapy-controlled patients.

Our study is limited by the analysis of a restricted number of patients: we aimed to describe quality of life in the patients treated in our facility at the time; nevertheless, the limited sample in analysis did not allow us to study specific subsets of patients. A limited amount of self-reported measures has been included, describing mainly the pain and function dimension: other than PASQ and WOMAC, other measures could be integrated in future analysis to specifically investigate the impact of social and psychological factors.

CONCLUSIONS

Identification of predictors of HRQoL is crucial to improving the management of acromegaly. Our results suggest that severity of painful symptoms of acromegaly is the most important predictor of HRQoL; acromegalic arthropathy is also (according to our results) correlated with HRQoL. Arthropathy leads to pain and to a variable amount of functional impairment, exerting great impact on the patient's perception of his health status. A measure of the progression of arthropathy and symptomatic management of symptoms could lead to a great HRQoL benefit and should therefore be considered in the routine assessment of the patients. Evidence is still required to improve our knowledge about acromegalic patients' QoL and to explore the need of new clinical rating scales. Further studies with a wider casuistry could take specifically in exam subsets of patients, selected by BMI, age range, age of first diagnosis. To address the limitations of this work, a study with progressive assessment would be effective to confirm that a modification of the predictors results in an improvement of HRQoL after a certain time point. To deal with another mentioned limitation, a similar study including an evaluation of psychological and social data would add up to our knowledge of the predictors of low QoL. In conclusion, further research could address whether periodic collection of PASQ and WOMAC may lead to an adaptation of the management of the patient with acromegaly to achieve better QoL.

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Связь между болью, артропатией и качеством жизни, связанным со здоровьем, у пациентов, страдающих акромегалией. Поперечное исследование

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Резюме

Введение: Несмотря на успешную терапию, у пациентов с акромегалией снижается качество жизни, связанное со здоровьем (HRQoL), по сравнению со здоровыми людьми из контрольной группы. Поиск предикторов плохого HRQoL может иметь решающее значение для улучшения общего состояния здоровья этих пациентов.

Цель: Основная цель исследования состояла в том, чтобы выяснить предикторы HRQoL. Второстепенными целями были: (i) определить корреляции с субшкалами AcroQoL и (ii) определить предикторы для субшкал.

Материалы и методы: В этом поперечном исследовании, проведённом в 2019 году в поликлинической больнице Мессины, 45 пациентов с акромегалией были обследованы в Амбулатории физической и реабилитационной медицины. Во время обычных посещений амбулаторных клиник применялись следующие опросники: опросник качества жизни при акромегалии (AcroQoL), опросник по симптомам акромегалии по оценке пациента (PASQ) и индекс артрита университетов Западного Онтарио и Макмастера (WOMAC). Кроме того, мы включили следующие переменные, полученные при просмотре медицинской документации: возраст, ИМТ, продолжительность заболевания, предыдущее хирургическое вмешательство (Да/Нет), предыдущую лучевую терапию (Да/Нет), использование средств для снижения уровня pH (Да/Нет), артериальную гипертензию (Да/Нет), сахарный диабет (Да/Нет) и биохимический контроль заболевания (Да/Нет): иммунорадиометрические анализы применялись для измерения сывороточного pH и IGF-1 для определения биохимического контроля заболевания. Была проведена корреляция между показателями результатов и AcroQoL. Коэффициент Пирсона был рассчитан для непрерывных данных, следующих за нормальным распределением (AcroQoL, PASQ, AcroQoL-B, AcroQoL-R, WOMAC-P), тогда как ранговая корреляция Спирмена была рассчитана для данных с ненормальным распределением (WOMAC, WOMAC- F, WOMAC- S, AcroQoL- P) и точечно-бисериальная корреляция для бинарных переменных (биохимически контролируемое заболевание, использование средств для снижения уровня гормона роста, лучевая терапия, хирургическое вмешательство).

Такой же корреляционный анализ был проведён для подшкал AcroQoL.

Множественная линейная регрессия с обратным пошаговым анализом использовалась для оценки влияния коррелированных переменных на AcroQoL.

Результаты: AcroQoL сильно отрицательно коррелировал с PASQ (r=-0.700, $p < 0.001$) и отрицательно коррелировал с WOMAC [r_s(43)=-0.530, p<0.001] и среди подшкал WOMAC с WOMAC – физическая подготовка [r_s(43)=-0.518, p<0.001] WOMAC -боль [r(43)=-0.428, p=0.003], WOMAC – скованность [r_s(43)=-0.393, p=0.007] и лучевая терапия [r(43)=-0.314, p=0.035].

После одномерной ступенчатой регрессии PASQ был самым сильным независимым предиктором AcroQoL с R2 0.392 [F (1,43) = 27.695, p<0.001].

Заключение: Это исследование показывает, что тяжесть болевых симптомов является наиболее важным предиктором качества жизни HRQoL у пациентов с акромегалией; в то же время акромегалическая артропатия приводит к болям и различным функциональным нарушениям, оказывая большое влияние на восприятие пациентом состояния своего здоровья. Измерение прогрессирования артропатии и симптоматическое лечение могут привести к значительному улучшению качества жизни HRQoL.

Ключевые слова

акромегалия, артропатия, качество жизни, биохимический контроль, PASQ