

Health-related Quality of Life in Acromegaly Patients: Results from Generic and Disease-specific Questionnaires

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Abstract

Introduction: Acromegaly is associated with high morbidity, but still controversial impact on the overall quality of life (QoL). **Material and Methods:** We evaluated QoL using a generic (SF-36) and a disease-specific questionnaire (AcroQoL) in an acromegalic cohort. **Results:** Sixty-nine patients answered the questionnaires and had their records reviewed. In the SF-36 questionnaire, except for the Social Aspects domain, all others revealed a reduction in scores from 9.7 to 38.9%, when compared to the non-acromegalics. The cure was positively correlated with mental health ($P = 0.023$) and drug control was correlated with mental health ($P = 0.023$) and functional capacity ($P = 0.013$). In the AcroQoL questionnaire, the mean scores ranged from 54.7% to 72.8%. The use of antidepressants correlated with lower scores on the total AcroQoL ($P = 0.039$) and physical complaints ($P = 0.003$). The growth hormone value at diagnosis showed an inverse correlation with the total AcroQoL score ($P = 0.014$), Appearance Issues subscale ($P = 0.081$), and Personal Relations ($P = 0.002$). IGF-1 values at diagnosis and at the last visit showed no statistical correlation with any of the questionnaires. **Conclusion:** The finding of a reduction in QoL scores with both SF-36 and AcroQoL allows us to suggest this evaluation as part of the initial assessment and follow-up in acromegaly, to act globally on the individual's health condition.

Keywords: Acromegaly, quality of life, SF-36, AcroQoL

INTRODUCTION

Acromegaly is caused by excessive secretion of growth hormone (GH) and insulin-like growth factor 1 (IGF-1), generally associated with a pituitary macroadenoma.^[1] While mortality associated with acromegaly is progressively normalizing,^[2] morbidity is still high.^[3]

The quality of life (QoL) of acromegalics may be compromised especially in physical effects, psychological effects, and treatment-related effects.^[4,5] Physical effects include joint problems,^[6] the presence of obesity,^[7] headache,^[8] and neuropathic pain.^[9] Psychological effects include chronicity of the disease, hormonal hypersecretion itself, and depression.^[10]

This study aimed to consolidate the relevance of the systematic application of QoL questionnaires in the follow-up of the disease.

MATERIAL AND METHODS

The study included 69 acromegalic patients recruited between April 2017 and May 2019, from a cohort in a referral

Neuroendocrinology Center. Our study was performed following the Helsinki recommendations. The project was approved by the Institution's Research Ethics Committee and all patients signed an informed consent form.

Medical records were reviewed for clinical, laboratory, and imaging information. The diagnosis of acromegaly was established on clinical and hormonal bases (baseline and/or suppressed GH <1 ng/mL and IGF-1 above the upper limit of normality corresponding to gender and age).

The patients underwent an interview with the same physician for the Short-Form Health Survey (SF-36)^[11] and Acromegaly

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Submitted: 24-Jun-2020

Revised: 06-Aug-2020

Accepted: 04-Sep-2020

Published: 09-Nov-2020

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How to cite this article: Oliveira BdA, Araújo B, dos Santos TM, Ongaratti BR, Rech CG, Ferreira NP. *et al.* Health-related quality of life in acromegaly patients: Results from generic and disease-specific questionnaires. *Indian J Endocr Metab* 2020;24:402-5.

Access this article online

Quick Response Code:



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DOI:
10.4103/ijem.IJEM_401_20

Quality of Life Questionnaire (AcroQoL).^[12] Both questionnaires were validated and translated into Brazilian Portuguese.^[11,13] The SF-36 results were compared with the average non-acromegalic population score.^[14] AcroQoL results were assessed by the total score and the questionnaire analysis in three subscales (physical complaints, appearance issues, and personal relations) as described by Felt *et al.* (2015).^[15] At the time of the questionnaire application, two patients were awaiting drug treatment, 48 were under treatment and the others were in postoperative remission.

After analysis of descriptive parameters, for comparison between groups, the *t*-test or Mann–Whitney were used, according to the distribution of data. The comparison of categorical variables was performed by Fisher's exact test and for the correlation study the Pearson coefficient. The evaluation was performed using the *Statistical Package for Social Sciences* (SPSS), version 22.0, using $P < 0.05$ as the significance level.

RESULTS

The sample consisted of 69 patients, 43 males (62.3%), age of 50.7 ± 12.8 (24–76) years, 57 (86.4%) macroadenomas. The patients underwent pituitary surgery (61) or surgery and radiotherapy (8) and 19 (28.4%) of them were cured. Octreotide and/or cabergoline was used in 48 cases, 28 with biochemical control. Headache was reported by 33.3% of patients, 29.9% used 6 or more continuous medications, and 17.6% of the sample used antidepressant drugs.

The means of SF-36 questionnaire showed, regarding the SF-36 domains, Functional Capacity: 66.5 (10–100); Physical Functioning: 53.9 (0–100); Pain: 52.5 (0–100); General Health Status: 59.6 (15–97); Vitality: 51.8 (0–100); Social Functioning: 67.2 (0–100); Emotional Functioning: 55.5 (0–100); and Mental Health: 61.8 (4–100). These values correspond, respectively, to a decrease of 13.7, 38.9, 38.1, 32.2, 31.8, 27.6, and 9.7% of the average score of the non-acromegalic population, except for Social Functioning, which showed an increase of 11.4% in the score.

When each SF-36 domain was analyzed in relation to gender, we found more compromised values in women in the Emotional Functioning (mean 67.9 in men and 43.2 in women, $P = 0.052$) and Mental Health (mean 69.1 in men, and 57.5 in women, $P = 0.078$). The patients' age was inversely correlated with the Functional Capacity domain ($P = 0.011$) and showed a borderline correlation with the Vitality domain ($P = 0.069$). The Pain ($P = 0.011$), Vitality ($P = 0.049$), and Social Functioning ($P = 0.045$) domains were significantly reduced in patients with headache.

No relationship was found between tumor size or radiotherapy treatment, and SF-36 parameters. Similarly, the presence of hypogonadism did not determine significant impairment in QoL scores.

The number of medications used by the patient correlated with worse scores in the Pain domain ($P = 0.013$) and showed a

borderline association ($P = 0.087$) with worse scores in the Physical Functioning domain. The use of antidepressant drugs showed a statistically significant correlation with lower QoL scores on all SF-36 parameters, with significance ranging from $P = 0.001$ to 0.015.

Cured acromegaly patients, compared to uncured ones, had significantly better scores in the Mental Health domain ($P = 0.023$), which was also verified in those with biochemical acromegaly control ($P = 0.018$). In the latter, there was also a significant improvement in Functional Capacity ($P = 0.013$).

In the AcroQoL questionnaire, the values obtained were: Total Score: 61.3% (12–92%), Physical Complaints: 56.9% (6–97%), Appearance Issues: 54.7% (13.5–100%), and Personal Relations: 72.8% (10.7–100%).

The presence of headache had a significant correlation with the low score of the Physical Complaints subscale ($P = 0.019$). The use of antidepressants showed a statistically significant correlation with lower scores on the total AcroQoL score ($P = 0.039$) and the Physical Complaints subscale ($P = 0.003$).

The GH value at diagnosis showed an inverse correlation with the total AcroQoL score ($P = 0.014$), Appearance Issues ($P = 0.081$), and especially in the Personal Relations sub-item ($P = 0.002$). IGF-1 values at diagnosis and GH and IGF-1 values at the last visit showed no statistical correlation with QoL scores.

DISCUSSION

The age and the clinical characteristics at diagnosis, tumor variables, therapeutic modalities, and evolution of patients with acromegaly in the current sample are in agreement with those described in the literature, except for gender, where we find two-thirds of male patients, while in other series women predominate.^[16] Draws attention the number of medications used, especially antihypertensive drugs, oral antidiabetics, lipid-lowering agents, and antidepressants, in addition to replacement with levothyroxine, corticosteroids, and testosterone. Multipharmacy is one of the concerns expressed by Bollerslev *et al.* (2019).^[2]

Acromegaly is generally associated with decreased QoL due to the chronic nature of the disease and its comorbidities and, for some authors, there is a similarity between the results observed in acromegaly and those found in other chronic diseases, endocrinological or not.^[17,18] The scores observed in this series with SF-36 are very similar to those observed by Dantas *et al.* (2013),^[19] in Brazilian acromegalics, all below those found in the normal population,^[14] except for Social Aspects, which, as for Dantas *et al.* (2013),^[19] is rated higher than expected. A previous study using AcroQoL^[13] showed QoL impairment in acromegalics. However, the literature is conflicting regarding the factors that affect QoL, possibly due to the different study designs and the limited number of

longitudinal studies, making the evaluation time heterogeneous concerning the phase of the disease.

The average total score obtained through AcroQoL in the present study, 61.3%, is similar to that reported in a recent systematic review, including 51 publications.^[7] The authors observed that the average AcroQoL score in cross-sectional studies was 62.7%, in longitudinal studies was 61.4% and in intervention studies 58.6%.

In our study, the headache was related to worse scores in several domains of SF-36 and AcroQoL. In acromegaly, headache occurs regardless of the size of the adenoma and is, according to some authors, the second most common symptom at presentation,^[20] even more frequently than visual problems.^[21]

The use of antidepressant drugs was related to reduced scores in all SF-36 and AcroQoL items. Acromegaly is a chronic disease where a higher prevalence of mood swings and depression is expected, and even patients with biochemically controlled disease have a higher rate of depression.^[22] Depression seems to influence QoL more negatively than biochemical factors themselves.^[10]

One of the most important causes of morbidity and functional disability in acromegaly is arthropathy, with pain and joint stiffness affecting up to 94% of patients.^[23] According to Biermasz *et al.* (2005),^[6] the presence of joint problems is the main comorbidity that contributes to decreased QoL scores in patients with long-standing remission disease. The study by Wassenaar *et al.* (2010)^[23] reports that osteoarthritis is related to worse QoL with spinal pain having an important impact on the physical and psychological well-being of these patients.

The current finding that cured or drug-controlled patients obtained better scores on QoL questionnaires is consistent with some studies that describe QoL more impaired in the active phase of acromegaly.^[24,25] While a significant correlation between IGF-I levels and the AcroQoL score was demonstrated, especially in those individuals with IGF-I above 30% of the upper limit of normality,^[26] we did not observe this correlation.

In the literature, the best scenario for QoL improvement is when the acromegaly control is obtained only with neurosurgery,^[25] since QoL worsens with the addition of pharmacological treatments and radiotherapy.^[22] Although drug treatment improves comorbidities and QoL itself, the chronic need for monthly injections of somatostatin analogs has been related to worsening subjective QoL perception.^[4] Further studies are needed to establish the individual impact of different pharmacological regimens and their combination on QoL.^[5,24]

We did not find in our sample a negative effect of radiotherapy on QoL, reported by other authors.^[6,23,26] There is no consensus whether any negative effect would be due to the more aggressive characteristics of the disease, which remained active

after surgery and drug therapy, or the particular effects of this type of treatment.^[27]

One of the limitations of the current study is that acromegaly is a rare disease, frequently associated with studies of small samples, commonly biased. In this context, our results showed a reduction in QoL scores with both SF-36 and AcroQoL. The negative role of headache, the use of antidepressants, and the lack of biochemical control over QoL are relevant findings. Until the extent of QoL impairment in acromegaly is established through multicenter and longitudinal studies, the authors suggest the systematic inclusion of QoL questionnaires in the diagnosis and follow-up of these patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Dineen R, Stewart PM, Sherlock M. Acromegaly. *QJM*. 2017;110:411-20.
- Bollerslev J, Heck A, Olarescu NC. Management of endocrine disease: individualized management of acromegaly. *Eur J Endocrinol* 2019;181:R57-71.
- Melmed S, Bronstein MD, Chanson P, Klibanski A, Casanueva FF, Wass JAH, *et al.* A Consensus Statement on acromegaly therapeutic outcomes. *Nat Rev Endocrinol* 2018;14:552-61.
- Postma MR, Netea-Maier RT, van den Berg G, Homan J, Sluiter WJ, Wagenmakers MA, *et al.* Quality of life is impaired in association with the need for prolonged postoperative therapy by somatostatin analogs in patients with acromegaly. *Eur J Endocrinol* 2012;166:585-92.
- Crespo I, Valassi E, Webb SM. Update on quality of life in patients with acromegaly. *Pituitary* 2017;20:185-8.
- Biermasz NR, Pereira AM, Smit JW, Romijn JA, Roelfsema F. Morbidity after long-term remission for acromegaly: Persisting joint-related complaints cause reduced quality of life. *J Clin Endocrinol Metab* 2005;90:2731-9.
- Geraedts VJ, Andela CD, Stalla GK, Pereira AM, van Furth WR, Sievers C, *et al.* Predictors of quality of life in acromegaly: No consensus on biochemical parameters. *Front Endocrinol (Lausanne)* 2017;8:40.
- Mangupli R, Camperos P, Webb SM. Biochemical and quality of life responses to octreotide-LAR in acromegaly. *Pituitary* 2014;17:495-9.
- Dimopoulou C, Athanasoulia AP, Hanisch E, Held S, Sprenger T, Toelle TR, *et al.* Clinical characteristics of pain in patients with pituitary adenomas. *Eur J Endocrinol* 2014;171:581-91.
- Geraedts VJ, Dimopoulou C, Auer M, Schopohl J, Stalla GK, Sievers C. Health outcomes in acromegaly: Depression and anxiety are promising targets for improving reduced quality of life. *Front Endocrinol (Lausanne)* 2015;5:229.
- Ciconelli RM, Ferraz MB, Santos W, Meinão I, Quaresma MR. Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida SF-36 (Brasil SF-36). [Brazilian-Portuguese version of the SF-36. A reliable and valid quality of life outcome measure]. *Rev Bras Reumatol* 1999;39:143-50.
- Badia X, Webb SM, Prieto L, Lara N. Acromegaly quality of life questionnaire (AcroQoL). *Health Qual Life Outcomes* 2004;2:13-22.
- Webb SM, Badia X, Surinach NL. Spanish AcroQoL Study Group. Validity and clinical applicability of the acromegaly quality of life questionnaire, AcroQoL: A 6-month prospective study. *Eur J Endocrinol* 2006;155:269-77.
- Jenkinson C, Layte R, Coulter A, Wright L. Evidence for the sensitivity of the SF-36 health status measure to inequalities in health: Results from the Oxford healthy lifestyles survey. *J Epidemiol Community Health* 1996;50:377-80.
- Felt JM Jr, Depaoli SA, Pereira AM, Biermasz NR, Tiemensma J.

- Total score or subscales in scoring the acromegaly quality of life questionnaire: Using novel confirmatory methods to compare scoring options. *Eur J Endocrinol* 2015;173:37-42.
16. Mercado M, Gonzalez B, Vargas G, Ramirez C, de los Monteros AL, Sosa E, *et al.* Successful mortality reduction and control of comorbidities in patients with acromegaly followed at a highly specialized multidisciplinary clinic. *J Clin Endocrinol Metab* 2014;99:4438-46.
 17. Anagnostis P, Efstathiadou ZA, Charizopoulou M, Selalmatzidou D, Karathanasi E, Poulasouchidou M, *et al.* Psychological profile and quality of life in patients with acromegaly in Greece. Is there any difference with other chronic diseases? *Endocrine* 2014;47:564-71.
 18. Webb SM, Badia X. Quality of life in acromegaly. *Neuroendocrinology* 2016;103:106-11.
 19. Dantas RA, Passos KE, Porto LB, Zakir JC, Reis MC, Naves LA. Physical activities in daily life and functional capacity compared to disease activity control in acromegalic patients: Impact in self-reported quality of life. *Arq Bras Endocrinol Metabol* 2013;57:550-7.
 20. Lavrentaki A, Paluzzi A, Wass JA, Karavitaki N. Epidemiology of acromegaly: Review of population studies. *Pituitary* 2017;20:4-9.
 21. Giustina A, Gola M, Colao A, De Marinis L, Losa M, Siculo N, *et al.* The management of the patient with acromegaly and headache in open clinical challenge. *J Endocrinol Invest* 2008;31:919-24.
 22. Yoshida K, Fukuoka H, Matsumoto R, Bando H, Suda K, Nishizawa H, *et al.* The quality of life in acromegalic patients with biochemical remission by surgery alone is superior to that in those with pharmaceutical therapy without radiotherapy, using the newly developed Japanese version of the AcroQoL. *Pituitary* 2015;18:876-83.
 23. Wassenaar MJ, Biermasz NR, Kloppenburg M, van der Klaauw AA, Tiemensma J, Smit JW, *et al.* Clinical osteoarthritis predicts physical and psychological QoL in acromegaly patients. *Growth Horm IGF Res* 2010;20:226-33.
 24. Andela CD, Scharloo M, Pereira AM, Kaptein AA, Biermasz NR. Quality of life (QoL) impairments in patients with a pituitary adenoma: A systematic review of QoL studies. *Pituitary* 2005;18:752-76.
 25. Matta MP, Couture E, Cazals L, Vezzosi D, Bennet A, Caron P. Impaired quality of life of patients with acromegaly: Control of GH/IGF-I excess improves psychological subscale appearance. *Eur J Endocrinol* 2008;158:305-10.
 26. Van der Klaauw AA, Biermasz NR, Hoftijzer HC, Pereira AM, Romijn JA. Previous radiotherapy negatively influences quality of life during 4 years of follow-up in patients cured from acromegaly. *Clin Endocrinol (Oxf)* 2008;69:123-8.
 27. Van der Klaauw AA, Kars M, Biermasz NR, Roelfsema F, Dekkers OM, Crossmit EP, *et al.* Disease-specific impairments in quality of life during long-term follow-up of patients with different pituitary adenomas. *Clin Endocrinol (Oxf)* 2008;69:775-84.