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Update on quality of life in patients with acromegaly

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Abstract In recent years, health-related quality of life (QoL) has been considered an important outcome for clinical management of acromegaly. Poor QoL has been described in acromegalic patients with active disease as well as after endocrine cure. It is known that acromegaly determines many physical problems and psychological dysfunctions that unavoidably impact on patients' QoL. Moreover, there is evidence that factors, such as radiotherapy or post-treatment GH deficiency also impair QoL in patients diagnosed with acromegaly. Thus, including the assessment of QoL in daily clinical practice has become fundamental to understand the consequences of acromegaly and the impact on the patients' daily life.

Keywords Quality of life · Acromegaly · Quality of life questionnaires · Self-perception · Wellbeing

Introduction

Acromegaly can cause physical, psychological and social symptoms. Patients with acromegaly report impaired health-related quality of life (QoL), especially during the active phase of the disease [1]. However, QoL may not completely normalize after successful treatment [1]. Indeed, patients with long-term remission of acromegaly show more negative illness perceptions than patients with acute illness (i.e. acute pain or vestibular schwannoma) [2]. Thus, the concept of "cure" in this pituitary disease should incorporate the patients' subjective perception.

QoL should be an important outcome in clinical practice. QoL outcome gives the clinician information about the patients' point of view on their wellbeing and normal daily living. Subjects evaluate their QoL taking into account their expectations, standards and goals, as well as emotional, physical and social aspects of their daily life. Thus, QoL depends on how a particular individual feels, responds and functions in daily life.

QoL was initially measured with generic questionnaires, used for general population and any type of disease (i.e., Nottingham Health Profile—NHP-, EuroQoL which includes the EQ-5 Dimensions and a visual analogue scale, Psychological General Well-Being index—PGWBI- or Short-Form 36-SF-36-) [3–8]. More recently, QoL is measured through a disease-generated or—specific questionnaire (AcroQoL) [9]. In both, the patients should evaluate how they self-perceive their general health status through several possible ratings (i.e. excellent, very good, good, slightly bad, poor). Nevertheless, AcroQoL addresses specific issues or complaints of patients with acromegaly, and is therefore more sensitive to changes after surgery, medical treatments or radiotherapy [9]. In fact, disease duration, age, treatment with radiotherapy and presence of joint problems have been negativity correlated with AcroQoL scores [10–12].

Some subtle effects of acromegaly and its treatment on physical and psychological dimensions might go undiagnosed for years. Potential long-lasting effects of GH and IGF-1 on personality, cognition and behaviour have not been considered until recently. Novel instruments to evaluate cognitive function, psychopathological symptoms and the patient's subjective perception of QoL outcomes have

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allowed to document residual morbidity in acromegaly. In general, acromegalic patients may show reduced physical and social functioning, limitations in role functioning due to both emotional and physical problems, increased pain and decreased general well-being, as compared with healthy controls [11].

Effects of treatments on QoL

Worse QoL is usually observed in acromegaly patients during the active phase of the disease as compared with the controlled state [9, 10], although biochemical activity (e.g., high IGF-I levels) is often not found to correlate with worse QoL. Successful surgery and/or medical treatment normalize biochemical parameters (GH and IGF-1) and tend to improve general wellbeing. Nevertheless, QoL does not recover completely in most of the patients.

A systematic literature search up to 2014 of 31 papers assessing QoL in patients with acromegaly evidenced that both active and controlled acromegaly reported more impairments in QoL, than healthy controls and reference values, including depressive symptoms and sexual dysfunction (15 studies with a total of 820 patients) (15). Acromegaly and Cushing's disease had worse QoL than other pituitary adenomas. QoL generally improved after biochemical cure, although frequently normalization did not occur. Somatic factors (e.g., hypopituitarism, sleep characteristics), psychological factors (illness perceptions) and health care environment (rural vs. urban) were identified as negative influencing factors.

Neurosurgery seems to be associated with greater improvement of QoL than medical therapy alone in controlled acromegaly [13]. Although pharmacological treatment improves both acromegaly comorbidities and QoL [14], the chronic need for monthly injections of somatostatin analogs to control the disease has been related with impaired subjective perception of QoL [15]. Even so, a study has shown that adding pegvisomant (but not placebo) to somatostatin analogs in acromegalic patients with normal baseline IGF-1 improved QoL, as measured by AcroQoL and the Patient-Assessed Acromegaly Symptom Questionnaire (PASQ) score [14], suggesting that normal circulating IGF-1 is no guarantee for whole body "normalization".

Globally, however, the effects of medical therapy on QoL are conflicting; improvement after long-acting Lanreotide in active acromegaly has been reported, as well as after treatment with Pegvisomant, or combination therapy (Pegvisomant/Octreotide-LAR) in patients who reach disease control, but other reports of no change after Octreotide LAR compared to surgery, or after switching from Octreotide LAR to Lanreotide autogel have also been published (for review see 10). Furthermore, no differences were found between naïve patients treated with octreotide LAR and naïve patients treated with Pegvisomant.

Other treatments, like radiotherapy, can reduce wellbeing. Acromegaly patients treated with radiotherapy have low QoL scores, although it is unknown whether this relates to the more aggressive characteristics of the disease, which remains active after surgery and medical therapy [16]. In this prospective follow-up study over 4 years of a homogenous cohort of patients with sustained biochemical control of acromegaly, AcroQoL scores were found to subtly but progressively worsen over time, radiotherapy being the predominant indicator of this progressive impairment in QoL (16). In particular, radiotherapy may influence energy, pain and social isolation (measured by NHP); physical fatigue and reduced activity and motivation (measured by the Multidimensional Fatigue Inventory) and physical performance (measured by AcroQoL) [17].

Moreover, development of GH deficiency after treatment of acromegaly also affects QoL. In fact, the patients having the highest QoL were those who attained a normal GH after treatment (i.e., between 0.3 and 1 mcg/L after an oral glucose tolerance test), while higher than normal GH levels (consistent with active disease), or lower (suggestive of GH deficiency), were both associated with more impairment of QoL [18]. Young adult patients who became GH deficient due to prior treatment of acromegaly (with surgery and/or radiotherapy) improved their QoL after substitution therapy with rhGH, but this was not confirmed in older patients [19] (Fig. 1).

In summary, treatment with surgery and pharmacological drugs do improve QoL in acromegaly, but it doesn't normalize; being aware of this can lead to psychosocial interventions, in addition to optimal medical treatment, aimed at attaining a global improvement in patient outcome.

Effects of physical symptoms on QoL

"Cured" patients with acromegaly have a lower perceived QoL than general population in physical function dimensions on generic questionnaires like SF-36 [19]. Acromegalic patients score worse in the domains of general health, vitality, physical ability and functioning and more bodily pain than patients with non-functioning pituitary adenomas (NFPA) or prolactinomas [17, 20, 21] (Fig. 1).

On the one hand, pain due to joint complaints and musculoskeletal problems has been described in up to 90 % of acromegalic patients [12, 22, 23]. Patients with acromegaly who report bodily pain have worse AcroQoL scores than those without pain [23]. On the other hand, while the presence of headache has also been related with

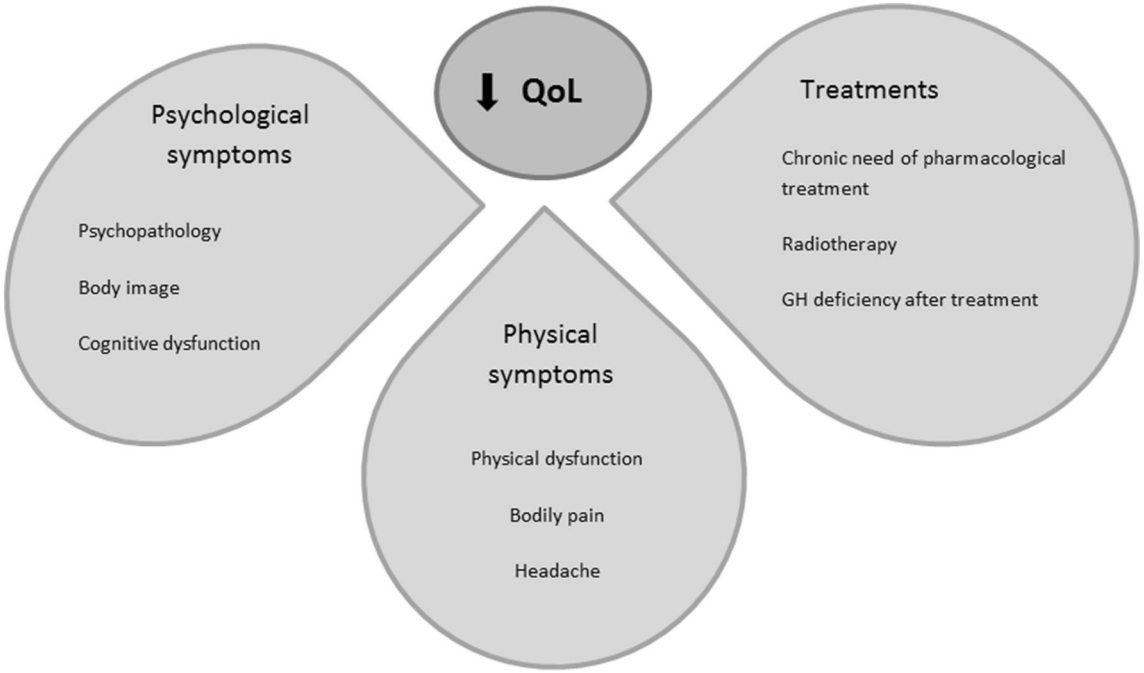

Fig. 1 Factors that can affect quality of life (QoL) in patients with acromegaly

poorer QoL [24], neuropathic pain has been associated with both worse QoL and depression [25].

Effects of psychological symptoms on QoL

Among the factors affecting QoL, psychological status is one of the most relevant. Patients with active disease show more anxiety/depression complaints compared to the other health dimensions of the EuroQoL generic questionnaire [9]. Time elapsed until the diagnosis of acromegaly has been correlated with depressive symptoms, anxiety, reduced psychological QoL, and impaired body image [26].

Body image is an important factor affecting the psychological wellbeing of acromegalic patients. Using the AcroQoL questionnaire, "appearance" has been identified as the most affected dimension [9]. Since changes in appearance persist even after long-term cure, patients with acromegaly usually report self-consciousness about social-, sexual-, bodily- and facial-appearance and show a negative self-concept which has a greater impact on their psychological status and QoL [27].

A recent study has shown that reduction of QoL is driven dominantly by psychopathology (mainly anxiety and depression) rather than other biochemical factors in acromegalic patients [28]. Increased anxiety and depression, maladaptive personality traits and less effective coping strategies have been described in patients with controlled acromegaly, which in turn may affect QoL and cognition [29–31].

Cognitive dysfunction has been identified as a comorbidity in acromegalic patients. When acromegalic patients were asked about their cognitive function, 54 % of those with controlled acromegaly and 57 % with active acromegaly expressed certain degree of cognitive dysfunction [32]. In particular, active acromegalic patients expressed more problems and more severe dysfunction for ability to learn and concentration/distractibility [32]. These cognitive problems can have a negative impact on their daily living (Fig. 1).

Conclusion

QoL measurements should be incorporated in the regular clinical follow-up of patients with acromegaly. Impaired QoL is common in acromegaly, even after successful treatment. Factors that can affect patients' wellbeing are multidimensional, including physical, psychological, social, demographic and medical dimensions. Clinicians can use QoL outcome to evaluate whether the consequences of the disease negatively impact on patients daily living, as well as to identify patients' main needs during the management of the disease. Furthermore, patients tend to appreciate being asked about issues frequently not approached in regular follow-ups.

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