Pituitary diseases : long-term psychological consequences

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Chapter 3

Affected illness perceptions and the association with impaired quality of life in patients with long-term remission of acromegaly

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Abstract

Context and objective: Illness perceptions pertain to the beliefs patients develop about their illness, and these views are determinants of behavior directed at the illness. Illness perceptions are determinants of quality of life (QoL). QoL remains impaired in patients with biochemical control of acromegaly, but illness perceptions were never studied in these patients.

Aim: The aim of the current study was to explore illness perceptions and their association with QoL in patients with long-term biochemical control of acromegaly.

Design: This was a cross-sectional study.

Subjects: We included patients with long-term biochemical control of acromegaly (n=81), and compared them with Dutch reference populations: patients with acute pain (n=35) or chronic pain (n=63), Cushing's syndrome (n=52), chronic obstructive pulmonary disease (COPD; n=171), and vestibular schwannoma (n=80). Illness perceptions were evaluated using the Illness Perception Questionnaire-Revised, and QoL was assessed with the Physical Symptoms Checklist, EuroQoL-5D, and AcroQoL.

Results: Illness perceptions showed strong correlations with QoL. Patients after remission of acromegaly have a good understanding of their disease, but they experience a lack of personal control and are not likely to seek medical care compared with patients with acute disease (all $P<0.01$).

Conclusion: Illness perceptions of patients after long-term remission of acromegaly are affected and strongly related to QoL. Patients reported more negative illness perceptions than patients with acute illness, but more positive illness perceptions than patients with chronic diseases. Additional research is necessary to assess whether a self-management intervention might help in improving affected illness perceptions, and thereby improve QoL.

Introduction

Acromegaly is associated with typical signs and symptoms caused by excess of growth hormone (GH) and insulin-like growth factor 1 (IGF-1). Many of the systemic changes induced by previous excess of GH and/or IGF-I are not completely reversed upon successful biochemical treatment of active acromegaly (1). Impaired quality of life (QoL) persists despite long-term remission in acromegaly (2). Although decreased QoL may originate from persisting limitations due to irreversible effects of excessive GH and IGF-I exposure, an alternative hypothesis is that the psychological impact of suffering from this disease reduces QoL. This concept is supported by the observation that coping strategies are ineffective in patients with pituitary disease (3). Persistent, inappropriate thoughts about the disease and/or its treatment can influence general well-being. Moreover, patients and their doctors may have discrepant perceptions of the severity of the disease and the success of treatment. This concept can be studied by measuring illness perceptions.

Illness perceptions pertain to the way patients make sense of, and respond to, their illness and are conceptualized in the common sense model (CSM) of self-regulation. The CSM explains how patients generate both cognitive representations of, and emotional reactions to, their illness, integrating internal and external stimulus information with their pre-existing illness-theory (4). Leventhal *et al.* (5) designed the CSM, which starts from the premise that individuals are active problem solvers, who make sense of a threat to their health by developing a cognitive representation of the threat, which determines how the individual responds. Patients cluster these representations or ideas about the illness around five cognitive components: 1) identity: the label that is used by the individual to describe the condition and the associated symptoms, 2) cause: personal ideas about the cause of the condition, 3) time-line: expectations about the likely duration of the condition, 4) consequences: the physical, psychological, and social effects of the condition, 5) cure/control: the extent to which the condition is amenable to cure and/or control. These components form the illness representations, which determine the coping procedures of the patient (6). The sources of these perceptions are diverse. Therefore, these illness perceptions are subjective, may be partly or completely incorrect, and do not necessarily represent the actual medical status of the disease. At present, there are no studies that have evaluated illness perceptions in patients with acromegaly. Therefore, the aim of the study was to explore the illness perceptions of patients after long-term biochemical remission of acromegaly and compare these to reference groups from the literature.

Patients and Methods

Patients

We performed a clinical chart review of 156 patients with acromegaly. All were in biochemical remission at the time of the current study for at least 1yr. We invited these patients to participate in the current study. Seventy-five patients (48%) refused to participate for several reasons including old age, and/or debilitating disease. Eighty-one patients (52%) participated in the current study and completed the questionnaire on illness perceptions. Seventy-five patients also completed the QoL questionnaires.

The diagnosis of acromegaly had been established by clinical signs and symptoms and by biochemical tests, including insufficient suppression of GH during glucose tolerance test and increased IGF-1 levels for age. Biochemical control of acromegaly was defined by normal serum IGF-1 levels for age and serum GH levels below 1.9 μg/liter for all patients and, in patients without somatostatin analogue treatment, also by normal suppression of GH levels (<0.38 mcg/l) during glucose tolerance test (7). Remission was confirmed by repeating the tests at yearly intervals. Pituitary function was monitored and pituitary hormone replacement was prescribed dependent on the results of the yearly evaluation of pituitary functions. In case of corticotrope insufficiency, documented by insulin tolerance test (ITT) or CRH test, hydrocortisone was prescribed (20mg/d divided into 2-3 dosages). Evaluation of GH deficiency was performed by ITT or GHRH-arginine test, only in patients under the age of 70yr and only after at least 2yr of remission. Somatotrope insufficiency was treated with rhGH replacement, aiming at IGF-I concentrations in the normal range for age. Patients were treated with rhGH from 2005 onwards during a controlled trial of rhGH replacement (8). In addition, free T_4 and testosterone levels (in male patients) were assessed. If results were below the lower limit of the respective reference ranges, substitution with L- T_4 and/or testosterone was prescribed. In the case of amenorrhea and low estradiol levels in premenopausal women, estrogen replacement was provided.

Inclusion criteria for the current study were age over 18yr and remission defined by strict biochemical criteria for at least 1yr. The protocol was approved by the Medical Ethics Committee.

Protocol

Patients were asked to complete a questionnaire on illness perceptions and three questionnaires on QoL at home and return these in a prepaid envelope.

Illness Perception Questionnaire Revised (IPQ-R)

The IPQ-R was used to measure cognitive and emotional representations of acromegaly (9). This questionnaire was developed to assess the components of the illness representation of Leventhal's Self-Regulatory Model and is frequently used to study illness perceptions in chronic conditions (10-14). The IPQ-R is divided into three sections. The first part consists of the illness identity dimension, with a list of 14 commonly occurring symptoms and 11 symptoms commonly occurring in acromegaly. Patients are asked to rate whether or not they experienced the symptoms, and if they believe the symptom to be related to acromegaly (yes/no). The summed yes-rated items of the disease related symptoms are used in the analysis.

The second part of the questionnaire, assessing illness perception dimensions, consists of 38 statements concerning views on the illness, scored on a five-point Likert scale (from strongly disagree to strongly agree). The questions are transformed to seven dimensions: timeline acute/chronic (beliefs about the chronic nature of the condition), timeline cyclical (beliefs regarding the cyclical nature of the condition), consequences (negative consequences of the disease), emotional representations (the likelihood to seek medical care), personal control (perceived personal controllability of the disease), treatment control (perceived treatment controllability of the disease), and illness coherence (personal understanding of the disease). A higher score indicates a stronger belief in that particular dimension.

The third and final part of the questionnaire entails causal attributions. This section consists of 18 statements concerning possible causes that patients consider that contributed to their disease, scored on a five-point Likert scale (strongly disagree to strongly agree).

As recommended by the developers of the questionnaire, a principal component analysis with varimax rotation was performed on the causal items to cluster variables with shared variance (9). A principal component analysis is a technique for identifying clusters/factors in a large set of variables. Once factors have been extracted, it is possible to calculate to what degree variables load onto these factors. Factor rotation can be used to calculate this and discriminate between factors. A varimax rotation is an orthogonal rotation that attempts to maximize the dispersion of factor loadings within factors. The rotation tries to load a smaller number of variables highly onto each factor, which in turn results in more interpretable clusters of factors (15). The analysis produced four factors accounting for 73% of the total variance. The first factor labeled psychological attributions accounted for 33% of the variance and consisted of the items stress or worries, family problems or worries, emotional state, mental attitude, own behavior, overwork, ageing, personality, altered immunity, and poor medical care. The second factor labeled risk factors accounted for 25% of the variance and consisted of the items

smoking, alcohol use, accident/injury, bacteria or virus, diet or eating habits, and pollution in environment. The third factor was labeled hereditary and accounted for 9% of the variance. This factor consisted of the item hereditary. The fourth factor labeled chance accounted for 6% of the variance and consisted of the item chance or bad luck. Because the third and fourth factor included only one item, no Cronbach's alpha could be calculated. Therefore, these last two factors were excluded from further analysis. Higher scores on the first and second causal subscales indicate stronger beliefs in those attributions in causing acromegaly.

Quality of life questionnaires

Physical Symptoms Checklist (PSC): This is a checklist of 55 physical symptoms that are mentioned in the DSM-III classification (16). The symptoms cover most organ systems. There are 11 general/ neurological items, 10 autonomic items, 8 musculoskeletal/pain items, 13 gastrointestinal items, 5 genital items and 4 items about feeling hot/cold. The presence of symptoms is rated on a severity scale from 0 to 3. We excluded the gender specific items (n=4) from the analyses to rule out bias by gender. The total symptom score ranges from 0 to 153. A higher score indicates more (severe) physical symptoms in the preceding week (17).
EuroQoL-5D (EQ-5D): This QoL questionnaire measures five health dimensions; mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Scores are expressed on a 1-3 scale per dimension, with a higher score indicating a worse QoL. The questionnaire also includes a visual analogue scale (VAS) which comprises a standard vertical 20 cm scale (similar to a thermometer) for recording an individual's rating for their current health-related QoL state (18). On the VAS, a higher score indicates a better QoL.
AcroQoL: This is a disease specific QoL questionnaire designed to assess QoL in acromegaly (19). The AcroQoL consists of 22 questions on a five-point Likert scale. The response choices are divided into frequency of occurrence (ranging from 'always' to 'never') and degree of agreement with the items (ranging from 'completely agree' to 'completely disagree'). The total score ranges from 0-100, with a lower score indicating a greater impact on health-related QoL.
Six patients did not complete all QoL questionnaires.

Reference populations

We obtained reference values in patients with acute and chronic pain from the study that presented the revised version of the IPQ (9). The reference group with acute pain consisted of 35 subjects who were recruited from a private practice for physical therapy (20 men, 15 women, mean age of 36±12yr). These patients presented with a first-time peripheral painful injury that had been present for less than 6wk. The reference group of patients with chronic pain consisted of 63 sub-

jects (26 men and 37 women, with a mean age of 54±11yr) who were recruited from hospital-based chronic pain clinics. All patients experienced pain for longer than 3 months which was unexplained by medical signs alone. The reference group of patients treated for Cushing's syndrome was recruited from the Leiden University Medical Center outpatient clinic and consisted of 52 patients (7 men, 45 women, mean age of 54±11yr). Patients had been treated by transsphenoidal surgery, additional postoperative radiotherapy, or adrenal surgery. All patients were in remission with a mean duration of 16yr. Forty six patients (88%) had pituitary ACTH-dependent hypercortisolism, and six (12%) had Cushing's syndrome due to adrenal tumor. There were no significant differences between both groups of patients in the answers on the IIPQ-R (20). The fourth reference group consisted of 171 Dutch patients (112 men and 59 women, mean age 66±10yr) suffering from chronic obstructive pulmonary disease (COPD) (21). A chest physician had diagnosed all patients as suffering from emphysema and/or chronic bronchitis. We chose the reference sample of patients with COPD because COPD is a chronic illness and might therefore be comparable with respect to chronic complications of acromegaly after long-term remission. The fifth reference group consisted of 80 patients with vestibular schwannoma before treatment proposal and treatment (36 men, 43 women, and one anonymous responder). Mean age was 57yr (22). Thirty-eight percent of these patients suffered from an intracanalicular tumor. We included patients with vestibular schwannoma because these patients have to cope with the knowledge that there is a benign tumor present inside their head, which was also the case in patients with GH-secreting adenoma.

Because illness perceptions assess the perceptions of a specific disease, there are no norm values for the general population. Scores of patients with acute and chronic pain may be used instead (22).

Statistical analysis

Data were analyzed using PASW Statistics version 17.0.2 (SPSS Inc., Chicago, IL, USA). All data were presented as mean ± standard deviations, unless mentioned otherwise. Different treatment modalities of acromegaly were compared using an ANOVA with a *post hoc* analysis when appropriate, whereas patients with and without hypopituitarism were compared using a Student's t-test. The possible effect of duration of follow-up was explored by linear regression analysis. The standardized β coefficients of this analysis were reported. The level of significance for these analyses was set at $P \leq 0.05$. The primary analysis comprised the relationship between illness perceptions and QoL. Partial correlations were calculated controlling for duration of follow-up, and the level of significance was set at $P \leq 0.05$. The comparison of patients with a relatively better QoL and patients with a worse

QoL consisted of a Student's t-test with the level of significance set at P≤0.01, because of multiple comparisons.
Secondary analysis comprised the comparison of results in patients with long-term remission of acromegaly and of results in various reference groups. Means were calculated for all subscales of the IPQ and compared between groups using Student's t-test. Since multiple comparisons were used, the level of significance was set at P≤0.01.

Results

Sociodemographic and clinical characteristics

All 81 patients had long-term biochemical control of acromegaly, with a duration of follow-up of 16±10yr. Sixty-nine patients (85%) had been treated by transsphenoidal surgery and 19 patients (24%) by additional radiotherapy. Twenty-nine patients (36%) were treated with somatostatin analogues, 8 patients (10%) with pegvisomant, and 6 patients (7%) with dopamine agonists. Thirty patients (37%) were treated for some degree of pituitary insufficiency (Table 1). Figure 1 shows the self-reported symptoms of various organ systems. Most complaints involved musculoskeletal pain.

Table 1 Clinical characteristics

	Acomegaly, n=81
Gender (male/female)	47/34
Age (yrs)	60 (12)
Educational level (n)	Low: 23
	Medium: 26
	High: 32
Transsphenoidal surgery, n (%)	69 (85%)
Somatostatin analogue therapy, n (%)	29 (36%)
Pegvisomant therapy, n (%)	8 (10%)
Dopamine agonist therapy, n (%)	6 (7%)
Postoperative radiotherapy, n (%)	19 (24%)
Duration of follow-up (yrs)	16 ± 10
Hypopituitarism, n (%)	Any axis: 30 (37%)
	GH: 12 (15%)
	ACTH: 21 (26%)
	LH/FSH: 15 (19%)
	TSH: 21 (26%)
	ADH: 3 (4%)

Data are mean ± SD or number and %

Illness perceptions in acromegaly as measured with the IPQ-R

Illness identity dimension

Table 2 shows that 17-25% of the patients suffered from weight gain, sweating, back pain, snoring, and muscle pain, which they attributed solely to acromegaly. In addition, stiffness of the joints was one of the symptoms of the general illness identity dimension. This symptom was reported by 65% of the patients.

Scores of patients with long-term remission of acromegaly on various organ systems

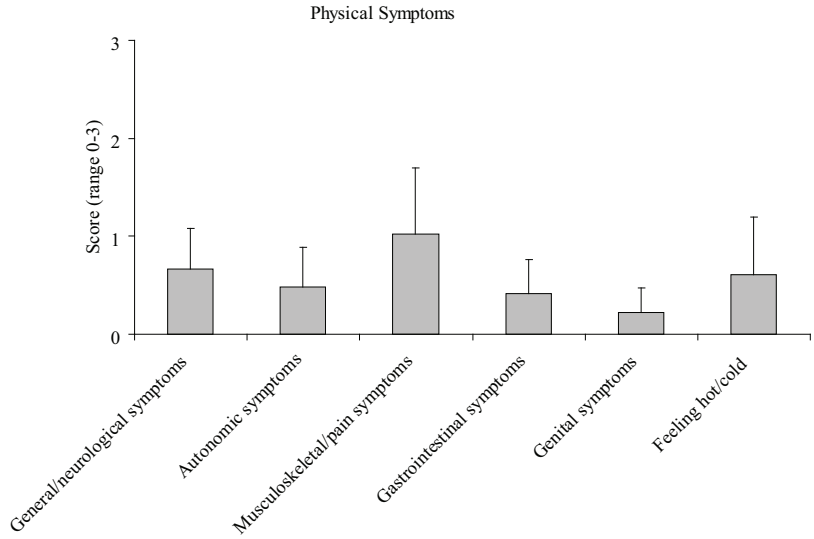

Figure 1. *Scores of patients after long-term remission of acromegaly on the various organ systems measured by the PSC. The minimal score on each scale is zero, whereas the maximum score is three.*

Causal attributions dimension

On the causal attributions dimension, patients during remission of acromegaly reported psychological attributions as the main perceived cause of acromegaly. Psychological attributions consist of stress or worries, family problems or worries, emotional state, mental attitude, own behavior, overwork, ageing, personality, altered immunity, and poor medical care as having caused acromegaly. Risk factors were also reported, but less frequently. The causal attribution risk factors consist of the items smoking, alcohol use, accident/injury, bacteria or virus, diet

Table 2 Symptoms related to acromegaly

Symptoms	Acromegaly, n=81
Gaining weight	21 (25%)
Sweating	19 (23%)
Back pain	18 (21%)
Snoring	17 (20%)
Muscle pain	17 (20%)
Hard time exercising	15 (18%)
Tingling hands	11 (13%)
Concentration problems	11 (13%)
Dental problems	11 (13%)
Memory impairment	8 (10%)
Abdomen complaints	5 (6%)

Data are n (%), symptoms commonly occurring in acromegaly of the 'illness identity' dimension of the IPQ-R

or eating habits, and pollution in environment.

Illness perception dimensions

We divided the patients in three treatment groups: 1) biochemical control by surgery, 2) biochemical control by surgery and radiotherapy and 3) biochemical control by primary or secondary medical treatment. Patients who received postoperative radiotherapy perceived more negative consequences (P=0.037) and had a worse personal understanding (P=0.041) compared with patients who had been cured by surgery alone. Additionally, patients with and without hypopituitarism were compared. Patients who were treated for some degree of pituitary insufficiency perceived less treatment control than patients who were free of pituitary insufficiency (P=0.034).

In a linear regression model, duration of follow-up was associated with perceived treatment control (β=-0.252, P=0.026) and personal understanding of the disease (β=-0.279, P=0.013).

Table 3 Quality of life in patients with acromegaly

	N=75
Physical Symptoms Checklist	
Total Score	27.6 (18)
EQ-5D	
Mobility	1.4 (1)
Self-care	1.0 (0)
Activity	1.5 (1)
Pain	1.8 (1)
Anxiety	1.4 (1)
VAS	69.4 (15)
AcroQoL	
Total Score	67.5 (15)

Data are mean (SD)

Relationship between illness perceptions and QoL

The scores of patients with acromegaly on the various QoL questionnaires are shown in Table 3. There were no significant differences in QoL between the three treatment groups. Levels of association between the IPQ-R dimensions and the QoL scales are shown in Table 4 as partial correlations, controlled for duration of follow-up.

There was a very consistent pattern of correlations between QoL and illness perceptions. A better QoL score was associated with better scores on the number of complaints attributed to acromegaly, perceived chronicity and fluctuations of acromegaly, perceived negative consequences, and the likelihood to seek medical

Table 4 Partial correlations between the IPQ-R dimensions and quality of life scales, controlling for duration of follow-up

	Physical Symptom Checklist	EQ-5D Mobility	EQ-5D Self-care	EQ-5D Activity	EQ-5D Pain	EQ-5D Anxiety	EQ-5D VAS	AcroQoL
Illness identity	.617 **	.410 **		.606 **	.462 **	.409 **	-.440 **	-.586 **
Timeline (acute/chronic)	.407 **						-.278 *	
Timeline (cyclical)	.380 **	.470 **		.356 **	.399 **		-.394 **	-.479 **
Consequences	.575 **	.405 **		.701 **	.586 **	.324 *	-.568 **	-.741 **
Emotional representations	.592 **	.392 **		.603 **	.670 **	.482 **	-.633 **	-.584 **
Personal control						-.273 *		.279 *
Treatment control	-.347 *	-.298 *		-.348 *		-.346 *		.334 *
Illness coherence	-.313 *	-.309 *				-.275 *		
Psychological attributions								
Risk factors								

Only correlations that reached statistical significance ($p<0.05$) are depicted, * $p<0.05$, ** $p<0.01$

care. A better QoL score was also associated with better scores on perceived personal and treatment control, and personal understanding of the disease.
Patients with low *versus* high scores on the various QoL questionnaires were compared, using the median value to define low versus high. Patients with high scores on the Physical Symptoms Checklist (indicating a more impaired QoL) attributed more symptoms to acromegaly (P<0.001), perceived more fluctuations (P<0.001), perceived more negative consequences (P=0.001), and were more likely to seek medical care (P<0.001) than patients with lower (and thus better) scores on this questionnaire. On the EQ-5D VAS, patients with a lower score (indicating a more impaired QoL) perceived more negative consequences (P<0.001), and were more likely to seek medical care (P<0.001) than patients with higher and better scores on the VAS scale. Patients with a lower score on the AcroQoL (indicating a more impaired acromegaly-specific QoL) attributed more symptoms to the acromegaly (P=0.001), perceived more negative consequences (P<0.001), and were more likely to seek medical care (P=0.001).

Illness perceptions in acromegaly compared with reference groups

Illness perceptions in patients after long-term cure of acromegaly compared with patients with acute or chronic pain

Compared with patients with acute pain, patients in remission of acromegaly perceived more chronicity (P<0.0001), more negative consequences (P=0.007), were less likely to seek medical care (P<0.0001), and perceived less personal control (P<0.0001), but had a better personal understanding of the disease (P<0.0001). Illness perceptions of patients with acromegaly were also compared with patients with chronic pain. Compared with those patients, patients with acromegaly were less likely to seek medical care (P<0.0001), but attributed less symptoms to their disease (P<0.0001), perceived less fluctuations (P<0.0001), perceived less negative consequences (P<0.0001), perceived more treatment control (P<0.0001), and had a better personal understanding of their disease (P<0.0001), see also Table 5 and Figure 2.

Illness perceptions in patients after long-term cure of acromegaly compared with patients treated for Cushing's syndrome

Compared with patients in long-term remission of Cushing's syndrome, patients with long-term biochemical control of acromegaly were less likely to seek medical care (P=0.001), but attributed less symptoms to their disease (P=0.007), perceived less fluctuations (P=0.01), and less negative consequences (P=0.0001), see also Table 5.

Table 5 Comparison of IPQ-R scores between acromegaly patients and other patient groups

IPQ-R	Acromegaly n=81	Acute pain n=35	Chronic pain n=63	Cushing's syndrome n=52	Chronic obstructive pulmonary disease n=171	Vestibular schwannoma n=80
Illness identity	**2.5 (2)**	2.8 (2)	6.2 (3)**	3.8 (3)*	5.6 (3)**	2.2 (2)
Timeline (acute/chronic)	**22.9 (6)**	13.4 (5)**	23.1 (4)	23.6 (7)	26.7 (4)**	20.6 (4)*
Timeline (cyclical)	**10.1 (4)**	9.4 (3)	12.9 (4)**	11.9 (4)*	12.1 (5)**	10.6 (4)
Consequences	**16.9 (5)**	14.2 (4)*	23.5 (4)**	20.4 (5)**	19.3 (6)*	16.4 (2)
Emotional representations	**12.6 (4)**	16.1 (4)**	19.8 (4)**	15.3 (5)*	14.1 (7)	15.3 (4)**
Personal control	**17.5 (5)**	22.9 (4)**	18.4 (4)	16.9 (6)	22.4 (6)**	19.1 (3)*
Treatment control	**18.1 (3)**	19.4 (3)	14.2 (3)**	16.7 (5)	14.3 (4)**	16.9 (3)
Illness coherence	**17.5 (3)**	9.3 (3)**	13.4 (5)**	17.0 (3)	NA	18.1 (4)
Psychological attributions *(score range 10-50)*	**18.2 (7)**	NA	NA	NA	NA	NA
Risk factors *(score range 6-30)*	**10.1 (4)**	NA	NA	NA	NA	NA

Data are mean (SD), * p<0.01 compared to patients with acromegaly, ** p<0.001 compared with patients with acromegaly, NA: not available or not attributable

Distribution of IPQ-R scores of patients with long-term remission of acromegaly, patients with acute pain, and patients with chronic pain

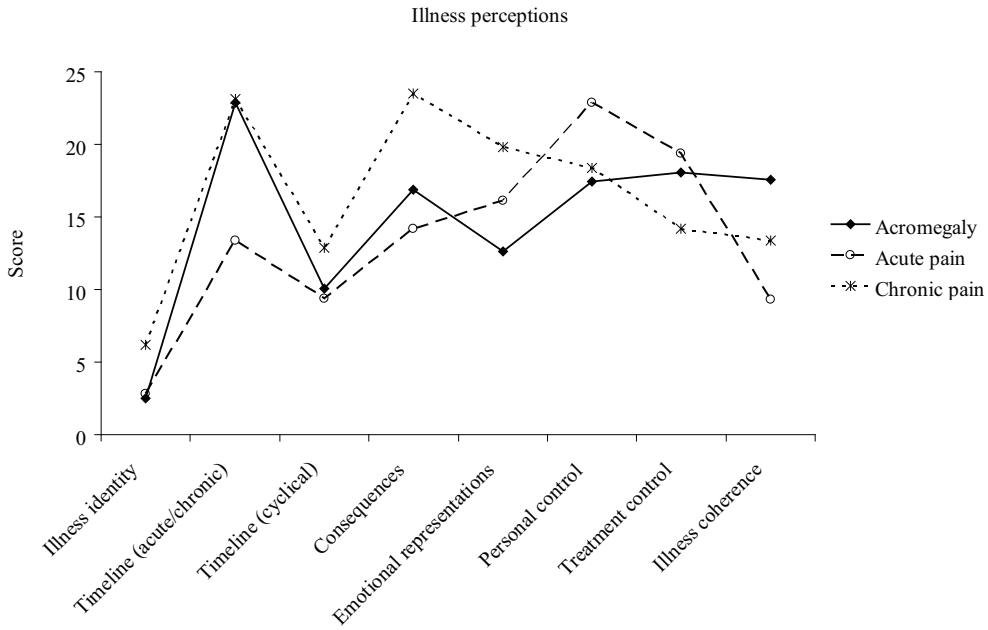

Figure 2. *Scores on the IPQ-R of patients after long-term remission of acromegaly, and patients with acute or chronic pain.*

Illness perceptions in patients after long-term cure of acromegaly compared with patients with COPD

The illness perceptions of patients in long-term remission of acromegaly were also compared with patients with COPD (Table 5). Patients with acromegaly perceived less personal control ($P<0.0001$), but attributed less symptoms to their disease ($P<0.0001$), perceived less chronicity ($P<0.0001$) and fluctuations ($P<0.001$), perceived less negative consequences ($P=0.0020$), and perceived more treatment control ($P<0.0001$).

Illness perceptions in patients after long-term cure of acromegaly compared with patients with vestibular schwannoma

Compared with patients suffering from a vestibular schwannoma, patients with acromegaly perceived more chronicity ($P=0.005$), were less likely to seek medical care ($P<0.0001$), and perceived less personal control ($P=0.006$), see also Table 5.

Discussion

This is the first study that describes illness perceptions in patients with acromegaly. In general, patients with long-term remission of acromegaly have a good understanding of their disease, but they experience a lack of personal control and are not very likely to seek medical care. Interestingly, there are clear differences between illness perceptions in acromegaly and other diseases. For example, acromegalic patients reported more negative illness perceptions than patients with acute pain or vestibular schwannoma, but more positive illness perceptions than patients with chronic conditions, like COPD. In addition, patients in long-term remission of acromegaly reported somewhat more positive illness perceptions than patients after long-term remission of Cushing's syndrome. Patients with long-term remission of acromegaly perceive impaired QoL. The illness perceptions in patients with acromegaly correlated strongly with QoL parameters, in accordance with observations in other conditions (23).

Treatment control and personal understanding of the disease were worse in patients after a longer duration of follow-up. We speculate that patients after longer duration of follow-up have less desire to have personal control over their acromegaly compared with patients with a shorter duration of follow-up. It might also be that longer follow-up of acromegaly indicated (at least for the patient) that acromegaly is a severe and chronic illness, which leads to less treatment control since patients feel the treatment they received did not cure acromegaly and also leads to less personal understanding since the doctors can not cure acromegaly and/or its (long-term) symptoms.

Illness perceptions in endocrine diseases have not been frequently studied. We documented some differences in illness perceptions between the various treatment groups of acromegalic patients. Moreover, there were also differences between patients with Cushing's syndrome and acromegaly. It is tempting to speculate that there are disease-specific characteristics in illness perceptions in addition to more general influences related to complaints or chronicity. Additional research is needed to see whether these findings can be extended to other endocrine diseases.

The reference groups all have their limitations since they differ considerably from acromegaly, but we believe that it is important to explore the illness perceptions of patients with acromegaly in reference to other illnesses since there are no data available on other hormonal illnesses. In addition, the essence of illness perception research is the perspective of the patient, independent of the medical objective of symptoms. A recent study by Figueiras and Alves (24) reported on perceptions of healthy people of serious illness with a new version of the IPQ-R for healthy people. With this questionnaire, the authors measured perceptions of

AIDS, tuberculosis, and skin cancer in a sample of 1113 healthy Portuguese subjects. The wording in the questionnaire was adapted for healthy individuals, i.e. 'this illness' instead of 'my illness'. AIDS, tuberculosis, and skin cancer are well-known illnesses and healthy individuals already have a common sense model of this illness, independent of the direct experience with this illness. However, acromegaly is a rare and not well-known disease. It is therefore not possible to ask a sample of healthy individuals about their illness perceptions concerning acromegaly without giving them information about the etiology, symptoms, and treatment of acromegaly beforehand. The provision of information about a rare and unknown disease would guide the illness perceptions in a certain direction, which in turn affects the reliability of the questionnaire. Therefore, we decided not to incorporate a group of healthy controls in the current study.

The illness perceptions of patients are based on various sources, which indicates that illness perceptions do not necessarily represent the actual medical status of the disease. This could explain, for example, why patients in long-term remission of acromegaly believe that a psychological attribution might have caused acromegaly. Psychological attribution consists of several causes i.e. stress or worries, family problems or worries, emotional state, mental attitude, own behavior, overwork, ageing, personality, altered immunity, and poor medical care. It is important for endocrinologists to explain to the patient what might have caused acromegaly, and ask the patient what their perceived cause of acromegaly is.

The current explorative study showed that there is a strong relationship between illness perceptions and QoL. More affected illness perceptions are correlated with more impaired QoL parameters. This has also been observed in patients after treatment for Cushing's syndrome (20) and in patients with various other diseases (23). This is a relevant observation, since patients with acromegaly suffer from impaired QoL even after long-term remission (2;25;26). The somatic and psychological factors that contribute to decreased QoL are not well-known, but most likely include musculoskeletal complaints (2), pituitary insufficiency (27;28) and the perception of the patients of their disease. A recent study (3) showed that patients with acromegaly use ineffective coping strategies. Additional research is necessary to establish whether, and to which extent, these illness perceptions and ineffective coping strategies can be improved which, in turn, might improve QoL.

A possible limitation of the present study is the fact that only 52% of the initially invited patients participated. We cannot exclude the possibility that the most distressed patients were more likely to participate, which might skew the results. However, this is an explorative study aiming to investigate illness perceptions in patients after long-term remission of acromegaly. We believe that the present results give a good first overview of how patients perceive acromegaly. Another limitation might be the fact that the reference samples differ in age distribution.

To date, it is unclear whether illness perceptions change with age. Although several determinants theoretically could contribute to our observations in these patients, a detailed analysis of each of these factors is not reliable considering the relatively small group of acromegaly patients. Future studies examining the differences in illness perceptions between patients with various (endocrine) disorders in larger samples should consider correcting for possible confounders like age.
In summary, in patients with long-term remission of acromegaly, illness perceptions are affected and correlate strongly with impaired QoL. Patients reported more negative illness perceptions than patients with acute illness, but more positive illness perceptions than patients with chronic diseases. We propose that a targeted self-management intervention might help in improving ineffective coping strategies and affected illness perceptions, and thereby improve QoL, at least in part, in patients with long-term remission of acromegaly.

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