Uludağ Üniversitesi Tıp Fakültesi Dergisi
Journal of Uludağ University Medical Faculty
52, 1786076, 2026
DOI: https://doi.org/10.32708/uutfd.1786076

ORIGINAL RESEARCH

Evaluation of Depression, Anxiety, Body Perception and Sexual Functions in Patients Diagnosed With Acromegaly

Rümeysa Ayşe GÜLLÜLÜ[1], Özen ÖZ GÜL[2], Yasemin AYDOĞAN ÜNSAL[3], Anıl MUŞTUCU[1], Güven ÖZKAYA[4], Selçuk KIRLI[1]

[1] Bursa Uludag University Faculty of Medicine, Department of Psychiatry, Bursa, Türkiye.
[2] Bursa Uludag University Faculty of Medicine, Department of Endocrinology and Metabolism, Bursa, Türkiye.
[3] Ankara Yıldırım Beyazıt University Yenimahalle Training and Research Hospital, Department of Endocrinology and Metabolism, Ankara, Türkiye.
[4] Bursa Uludag University Faculty of Medicine, Department of Biostatistics, Bursa, Türkiye.

ABSTRACT

Acromegaly is a chronic disease that can cause somatic disfigurement and hormonal changes. The aim of this study was to examine depression and anxiety levels, body image and sexual dysfunctions in patients with acromegaly and to compare them with those of controls. 52 patients with acromegaly who were being followed up at the Endocrinology Outpatient Clinic and 51 non-acromegalic individuals were included. The participants were evaluated cross-sectionally once and evaluated with the Beck Depression Inventory (BDI), the Beck Anxiety Inventory (BAI), the Body Image Scale (BIS) and the Golombok-Rust Inventory of Sexual Satisfaction (GRISS). The GRISS total, infrequency, dissatisfaction, impotence and premature ejaculation subdimension scores of the acromegaly patients were found to be significantly higher than those of the controls. Sexual dysfunctions were associated with older age, female sex, unemployment, menopausal status, and the presence of concomitant diabetes mellitus. No meaningful differences were detected in depression or anxiety scores between patients and controls. Body image was significantly more impaired in patients with acromegaly and was associated with higher depression and anxiety scores. There was no difference between scale scores according to disease activity. Although inverse correlations were observed between GRISS total scores and IGF-1 and free T4 levels in univariate analyses, IGF-1 was not independently associated with sexual dysfunction after adjustment for relevant clinical covariates. In conclusion, considering that patients with acromegaly are a risky group in terms of mental disorders and sexual dysfunctions, we recommend that patients should be routinely questioned in terms of psychopathology and sexual functions during their follow-up.

Keywords: Acromegaly. Depression. Anxiety. Body image. Sexuality.

Akromegali Hastalarında Depresyon, Anksiyete, Beden Algısı ve Cinsel İşlevlerin Değerlendirilmesi

ÖZET

Akromegali, somatik şekil bozukluklarına ve hormonal değişikliklere yol açabilen kronik bir hastalıktır. Bu çalışmanın amacı, akromegali tanılı hastalarda depresyon ve anksiyete düzeylerini, beden imajını ve cinsel işlev bozukluklarını incelemek ve kontrol grubuyla karşılaştırmaktır. Endokrinoloji Polikliniği'nde takip edilmekte olan 52 akromegali hastası ve 51 sağlıklı birey çalışmaya dâhil edilmiştir. Katılımcılar kesitsel olarak bir kez değerlendirilmiş; Beck Depresyon Ölçeği (BDÖ), Beck Anksiyete Ölçeği (BAÖ), Beden İmajı Ölçeği (BİÖ) ve Golombok-Rust Cinsel Doyum Ölçeği (GRCDÖ) ile ölçümler yapılmıştır. Akromegali hastalarının GRCDÖ toplam, ilişki sıklığı, tatminsizlik, empotans ve erken boşalma alt ölçek puanları kontrol grubuna göre anlamlı derecede yüksek bulunmuştur. Cinsel işlev bozuklukları ileri yaş, kadın cinsiyet, işsizlik, menopoz durumu ve eşlik eden diabetes mellitus varlığı ile ilişkili bulunmuştur. Hasta ve kontrol grupları arasında depresyon ve anksiyete düzeyleri açısından anlamlı bir fark saptanmamıştır. Akromegali hastalarında beden algısının belirgin şekilde daha bozulmuş olduğu ve bu bozulmanın daha yüksek depresyon ve anksiyete düzeyleri ile ilişkili olduğu gösterilmiştir. Ölçek puanları hastalık aktivitesine göre farklılık göstermemiştir. Tek değişkenli analizlerde GRISS toplam puanı ile IGF-1 ve serbest T4 düzeyleri arasında ters yönde ilişkiler saptanmış olmakla birlikte, çok değişkenli analizlerde IGF-1 düzeyleri cinsel işlev bozukluğu ile bağımsız olarak ilişkili bulunmamıştır. Sonuç olarak, akromegali hastalarının ruhsal bozukluklar ve cinsel işlev bozuklukları açısından riskli bir grup olduğu göz önünde bulundurularak, takip süreçlerinde bu hastaların psikopatoloji ve cinsel işlevler açısından rutin olarak sorgulanması önerilmektedir.

Anahtar Kelimeler: Akromegali. Depresyon. Anksiyete. Beden imajı. Cinsellik.

Date Received: 4.November.2025
Date Accepted: 8.February.2026

Dr. Rümeysa Ayşe GÜLLÜLÜ
Bursa Uludag University, Faculty of Medicine,
Department of Psychiatry, Görükle, 16059,
Nilüfer, Bursa, Türkiye.
E-mail: raysegullulu@gmail.com

AUTHORS' ORCID INFORMATION
Rümeysa Ayşe GÜLLÜLÜ: 0000-0001-7434-0153
Özen ÖZ GÜL: 0000-0002-1332-4165
Yasemin AYDOĞAN ÜNSAL: 0000-0002-1566-3099
Anıl MUŞTUCU: 0000-0002-2663-3661
Güven ÖZKAYA: 0000-0003-0297-846X
Selçuk KIRLI: 0000-0001-9524-5032

Acromegaly is a chronic disorder characterized by physical deformities, which are usually caused by the excessive secretion of growth hormone (GH) from a benign pituitary adenoma. Excessive GH secretion increases the secretion of insulin-like growth factor 1 (IGF-1), which exerts most of its growth-promoting effects through this hormone. Long-term elevation of both GH and IGF-1 can lead to various comorbidities, including cardiovascular complications, cerebrovascular events, gonadal dysfunction, diabetes mellitus (DM), sleep apnea, respiratory dysfunction and bone and joint diseases[1–3].

Acromegaly can negatively impact patients' quality of life and mental health through physical changes and comorbidities [4–6]. Body perception is frequently impaired in patients with acromegaly[7], and mood and anxiety disorders[8–11], neuropsychiatric disorders such as attention and cognitive dysfunction and pain syndromes are highly prevalent[7,12]. Important predictors of low quality of life and negative body image are psychopathologies such as depression and anxiety, rather than biochemical control or remission[7,8,13].

Pituitary adenomas may also cause hypogonadism by disrupting the release of sex hormones from the pituitary gland due to mass effects. Hyperprolactinemia is also present in 30% of patients with acromegaly. Consequently, decreased plasma testosterone and estradiol levels, menstrual disorders and sexual dysfunction may occur[14–16]. Furthermore, metabolic complications of acromegaly are thought to prevent regular sexual activity[2]. In patients with acromegaly, decreased desire and arousal have been observed in both sexes, alongside erectile dysfunction in men. However, it is unclear whether these decreases are directly related to hormone excess, or if they are a consequence of hypogonadism, clinical complications associated with the disease, or the resulting physical deformity and/or mental disorders[17].

It is important to recognise and combat the factors associated with the psychological and sexual symptoms of acromegaly in order to improve patients' quality of life and treatment response. The aim of this study was to evaluate patients diagnosed with acromegaly in terms of body image and sexual dysfunction, examine possible related mental and physical factors, and compare them with a control group.

Materials and Methods

Study Design and Participants

Our study included a total of 52 patients diagnosed with acromegaly and under follow-up at the Endocrinology or Mental Health and Diseases Outpatient Clinics. Inclusion criteria for the patient group were being aged 18–65 and having received a diagnosis of acromegaly. The control group consisted of 51 non-acromegalic volunteers aged 18–65 with an active sex life. Individuals with conditions hindering the administration of the scales, those with organic brain pathology, intellectual disability, psychiatric diagnosis that significantly impairs judgment and reality assessment, and having substance use disorders were excluded. The sample size was based on the availability of eligible patients meeting the inclusion criteria during the study period. Following ethical committee approval (Decision No: 2021-7/19), the study was initiated. All procedures were conducted in accordance with the Declaration of Helsinki and local laws and regulations. All participating volunteers provided informed consent, both verbally and in writing, after being informed about the purpose and procedures of the research.

Participants were evaluated cross-sectionally once and the scales were applied. The anthropometric and sociodemographic characteristics of all participants included in the study were evaluated, and their smoking habits were documented.

Psychological Measurements

Beck Depression Inventory (BDI): The BDI is a self-report questionnaire developed by Beck et al.[18] to assess the level and intensity of cognitive, emotional, physical and motivational symptoms in patients with depression. Each of the 21 symptom categories is scored on a scale ranging from 0 to 3, and the severity of depression is classified as follows: scores between 5 and 9 indicate normal condition; scores between 10 and 18 imply mild depression; scores between 19 and 29 signify moderate depression; and scores between 30 and 63 denote severe depression. The BDI was adapted into Turkish by Hisli, with a cut-off score of 17 being used to determine the presence of depression[19].

Beck Anxiety Inventory (BAI): BAI, a 21-item Likert-type self-report scale developed by Beck et al.[20], is used to determine the level, distribution and severity of anxiety symptoms. Ulusoy et al.[21] adapted the BAI into the Turkish version. Scores on the inventory range from 0 to 63. Scores ranging from 0 to 7 indicate minimal anxiety; scores ranging from 8 to 15 indicate mild anxiety; scores ranging from 16 to 25 suggest moderate anxiety; and scores ranging from 26 to 63 indicate severe anxiety symptoms.

The Golombok-Rust Inventory of Sexual Satisfaction (GRISS): The GRISS is a 28-item Likert-type scale developed by Golombok and Rust[22] to evaluate the existence and severity of sexual problems. There are two separate forms, one for men and one for women, each consisting of 28 items. The frequency of sexual intercourse, communication, satisfaction, avoidance and emotionality subscales are common to both.

However, the subscales assessing anorgasmia and vaginismus in women and impotence and premature ejaculation in men are gender-specific. High scores indicate the presence of sexual dysfunction. Tuğrul et al.[23] conducted a validity and reliability study of the scale in Turkish.

Body Image Scale (BIS): The BIS was developed by Secord and Jourard[24], and Turkish validity and reliability studies were conducted by Hovardaoğlu[25]. The scale is Likert-type, with each item relating to an organ, part, or function of the body. A higher score indicates greater body satisfaction.

Laboratory Tests

The diagnosis of acromegaly was based on compatible clinical findings and elevated age- and sex-adjusted insulin-like growth factor 1 (IGF-1) levels. Disease activity was classified as active disease or remission according to biochemical criteria. Remission was defined as normal age- and sex-adjusted IGF-1 levels together with suppressed growth hormone levels under stable treatment conditions, in line with current consensus guidelines. Patients who did not meet these criteria were considered to have active diseases. Serum IGF-1 concentrations were measured using a chemiluminescent immunoassay, with age- and sex-specific reference ranges provided by the manufacturer.

The biochemical and hormonal parameters of acromegaly patients within the last month were evaluated, and patients with impaired liver and/or kidney function were excluded from the study.

Biostatistical Analysis

The normality of the distribution of variables was assessed using the Shapiro–Wilk test. Descriptive statistics are presented as mean ± standard deviation for normally distributed quantitative variables and as median (minimum–maximum) for non-normally distributed quantitative variables. Qualitative variables are expressed as frequencies and percentages. The independent samples t-test was used to compare two groups for normally distributed data, while the Mann–Whitney U test was applied for non-normally distributed data. For comparisons involving more than two groups, one-way analysis of variance (ANOVA) was used for normally distributed variables, and the Kruskal–Wallis test was used when the normality assumption was not met. Pearson's chi-square test, Fisher–Freeman–Halton test, or Fisher's exact test were used to analyze categorical variables, as appropriate. In the case of multiple comparisons, Bonferroni correction was applied. Pearson or Spearman correlation coefficients were used to assess relationships between variables, depending on data distribution. Statistical significance was set at $\alpha=0.05$.

In addition, a prespecified multivariable linear regression model was constructed to examine factors associated with GRISS total scores. Age, sex, DM, psychotropic medication use, IGF-1 levels, and free T4 levels were entered simultaneously into the model to adjust for potential confounding. Multicollinearity was assessed using variance inflation factors (VIF). Sensitivity analyses were performed by additionally adjusting for acromegaly treatment modality to evaluate the robustness of the regression findings.

Statistical analysis of the data was performed via the statistical package program IBM SPSS23.0 *(IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).*

Results

No statistically significant differences were observed when the patient and control groups were compared in terms of sociodemographic characteristics (Table I). There were no significant differences in the body mass index (BMI) (p=0.055) or menopausal status (p=0.774) of the female participants in the two groups.

Table I. Comparison of patient and control groups in terms of sociodemographic characteristics

	Patient Group (n=52)	Control Group (n=51)	p
Age	51 (23-64) 49,69 ± 10,21	49 (25-64) 48,50 ± 10,33	0,546
Gender			
Female	25 (%48,1)	25 (%49)	
Male	27 (%51,9)	26 (%51)	0,924
Marital status			
Single	1 (%1,9)	2 (%3,9)	
Married	49 (%94,2)	46 (90,2)	-
Widow	2 (%3,8)	3 (%5,9)	
Education level			
Illiterate	4 (%7,7)	3 (%5,9)	
Primary school	18 (%34,6)	14 (%27,5)	0,916
Middle school	7 (%13,5)	7 (%13,7)	
High school	13 (%25)	15 (%29,4)	
University	10 (%19,2)	12 (%23,5)	
Working status			
Not working	26 (%50)	24 (%47,1)	0,765
Working	26 (%50)	27 (%52,9)	
Income perception			
Low	6 (%11,5)	8 (%15,7)	0,709
Mediocre	40 (%76,9)	39 (%76,5)	
High	6 (%11,5)	4 (%7,8)	
Smoking			
Never smoked	21 (%40,4)	26 (%51)	
Quit	16 (%30,8)	10 (%19,6)	0,385
Smoking	15 (%28,8)	15 (%29,4)	

The disease and treatment characteristics of patients with acromegaly are given in Table II.

Table II. Analysis of the disease and treatment characteristics of patients with acromegaly

	Patient Group (n=52)
Previous surgery	
No	2 (%3.8)
Yes	50 (%96.2)
Previous RT	
No	40 (%76.9)
Yes	12 (%23.1)
Remission status	
No	14 (%26.9)
Yes	38 (%73.1)
Pharmacotherapy	
Somatostatin analogs	25 (%48.1)
Cabergoline	5 (%9.6)
Combined treatment	8 (%15.4)
None	14 (%26.9)
Adenoma size at diagnosis	
Microadenoma	5 (%9.6)
Macroadenoma	37 (%71.1)
Unknown	10 (%19.1)
Age at diagnosis	39.5 (13-62) 38.9 ± 10.35
Follow-up duration (months)	127 (12-372) 127.53 ± 79.08
GH (ng/mL)	0.69 (0.0–12.5)
IGF-1 (µg/L)	148 (51–809)
TSH (mIU/L)	1.54 (0.01–5.50)

RT: Radiotherapy; GH: Growth Hormone; IGF-1: Insulin-like Growth Factor 1; TSH: Thyroid Stimulating Hormone. Combined treatment refers to the concomitant use of somatostatin analogs and cabergoline.

Table III shows a comparison of the patient and control groups in terms of psychiatric diagnoses and psychotropic drug use in the evaluated cross-section. Seven patients were receiving selective serotonin reuptake inhibitors (SSRIs) (two sertraline 50 mg/day, two sertraline 100 mg/day, two fluoxetine 30 mg/day and one escitalopram 10 mg/day), and one patient was receiving a serotonin–noradrenaline reuptake inhibitor (SNRI) (duloxetine 60 mg/day). Among the control group, three individuals were receiving SSRIs (two escitalopram 10 mg/day, one sertraline 50 mg/day) and two were receiving SNRIs (one venlafaxine 150 mg/day and one duloxetine 60 mg/day). All participants using psychotropic medications had been receiving the same medication at a stable dose for at least three months.

Table IV shows a comparison of the scale scores between the patient and control groups. Table V shows the relationships between the total and sub-dimension scores of the GRISS and the BDI, BAI and BIS scores of the patient and control groups.

Table III. Comparison of patients and the control group in terms of psychiatric diagnosis and psychotropic drug use

	Patient Group (n=52)	Control Group (n=51)	p
Psychiatric diagnosis			
None	38 (%73)	43 (%84,3)	0,164
Depression	11 (%21,2)	4 (%7,8)	
Anxiety disorders	3 (%5,8)	3 (%5,9)	
Obsessive compulsive disorder	0 (%0)	1 (%2)	
Psychotropic medication usage			
No	44 (%84,6)	46 (%90,2)	0,394
Yes	8 (%15,4)	5 (%9,8)	

Table IV. Comparison of the BDI, BAI, BIS and GRISS scores between the patient and control groups.

	Patient Group (n=52)	Control Group (n=51)	p
BDI	9.5 (0-38)	8 (0-32)	0.261
BAI	8 (0-62)	5 (0-39)	0.092
BIS	141 (70-197)	157 (61-199)	**0.002**
GRISS – Total	37 (11-98)	25 (7-69)	**0.010**
GRISS – Infrequency	5 (0-12)	4 (0-7)	**0.008**
GRISS – communication	3 (0-8)	3 (0-8)	0.574
GRISS – Dissatisfaction	5.5 (0-16)	4 (0-16)	**0.031**
GRISS – Avoidance	3 (0-15)	2 (0-9)	0.140
GRISS – Nonsensuality	3 (0-14)	2 (0-10)	0.132
	Patient Group Females (n=25)	**Control Group Females (n=25)**	**p**
GRISS – Vaginismus	5 (1-8)	5 (0-11)	0.156
GRISS – Anorgasmia	5.5 (0-15)	6 (0-16)	0.805
	Patient Group Males (n=27)	**Control Group Males (n=26)**	**p**
GRISS – Impotence	4.5 (0-13)	1.5 (0-7)	**0.001**
GRISS – Premature ejaculation	7 (0-14)	4 (0-11)	**0.028**

BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; BIS: Body Image Scale; GRISS: Golombok-Rust Inventory of Sexual Satisfaction

When the scale scores of the patient and control groups were compared based on the presence of a psychiatric diagnosis, patients with such a diagnosis had significantly higher scores on both the BDI and the BAI (p=0.034 for both) compared to patients without a psychiatric diagnosis. In the control group, only the BAI scores were significantly higher in participants with a psychiatric diagnosis (p=0.001).

Table V. Relationships between total and subdimension scores of the GRISS and the BDI, BAI and BIS in the patient group

Patient Group	BDI	BAI	BIS
GRISS - Total	p=0.067 r=0.256	p=0.483 r=0.099	**p<0.001** **r=-0.525**
GRISS – Infrequency	p=0.787 r=0.038	p=0.395 r=-0.121	p=0.304 r=-0.145
GRISS – Noncommunication	p=0.383 r=0.124	p=0.452 r=0.107	**p<0.001** **r=-0.504**
GRISS – Dissatisfaction	**p=0.016** **r=0.333**	p=0.266 r=0.157	**p=0.001** **r=-0.437**
GRISS – Avoidance	p=0.306 r=0.145	p=0.662 r=0.062	**p=0.017** **r=-0.330**
GRISS – Nonsensuality	**p=0.027** **r=0.307**	p=0.233 r=0.168	**p=0.005** **r=-0.384**
GRISS – Vaginismus	p=0.146 r=0.294	p=0.509 r=0.136	p=0.346 r=-0.193
GRISS – Anorgasmia	p=0.115 r=0.316	p=0.452 r=0.154	**p=0.012** **r=-0.484**
GRISS – Impotence	p=0.122 r=0.311	p=0.795 r=0.053	**p=0.003** **r=-0.552**
GRISS – Premature ejaculation	p=0.461 r=-0.151	p=0.951 r=0.013	p=0.413 r=-0.168

BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; BIS: Body Image Scale; GRISS: Golombok-Rust Inventory of Sexual Satisfaction

According to psychotropic medication use, patients receiving such treatment had significantly higher BDI and BAI scores (p=0.026 and p=0.018, respectively), while significantly lower scores were observed on the BIS and the GRISS premature ejaculation subscale (p=0.028 and p=0.037, respectively). No significant association was observed between psychotropic medication use and GRISS total scores (p=0.931).

In analyses according to sociodemographic variables, age was positively correlated with the total GRISS score (r=0.273, p=0.050) and the GRISS infrequency subscale score (r=0.344, p=0.013) in the patient group. In addition, educational level was inversely associated with the GRISS avoidance subscale scores in this group (r=−0.369, p=0.007).

In the control group, females had significantly lower scores on the BIS than males (p=0.016), whereas the total and infrequency, noncommunication, avoidance, and nonsensuality subscale scores of the GRISS were significantly higher (p<0.001; p=0.002; p=0.032; p=0.001; p=0.006, respectively). In the patient group, the total and noncommunication, avoidance and nonsensuality subscale scores of the GRISS were significantly higher in females (p=0.036; p=0.002; p<0.001; p<0.001, respectively).

According to menopausal status, no significant differences were observed in total BDI, BAI, BIS, or GRISS scores in either the patient or control groups. However, the scores for the GRISS subdimensions of infrequency, avoidance and vaginismus were significantly higher in menopausal acromegaly patients than in non-menopausal patients (p=0.036, p=0.036 and p=0.033, respectively).

No statistically significant correlation was found between the duration of follow-up from the outpatient clinic and the total BDI, BAI, BIS or GRISS scores (r=-0.167, p=0.237; r=-0.199, p=0.157; r=0.239, p=0.087; r=-0.200, p=0.156, respectively).

No significant difference was found when the effect of remission status on the scale scores was analysed (BDI: p=0.796; BAI: p=0.396; BIS: p=0.516; GRISS total: p=0.757; infrequency: p=0.307; non-communication: p=0.553; dissatisfaction: p=0.084; avoidance: p=0.909; non-sensuality: p=0.835; vaginismus: p=0.107; anorgasmia: p=0.254; impotence: p=0.534; premature ejaculation: p=0.427).

Table VI shows a comparison of scale scores applied to patient groups according to their RT history and the type of medication treatment they received for acromegaly.

Among patients with acromegaly, dyslipidemia was present in 50.0% (n=26), hypertension (HT) in 40.4% (n=21), DM in 34.6% (n=18), hypothyroidism in 25.0% (n=13), hypogonadism in 21.2% (n=11), and adrenal insufficiency in 11.5% (n = 6). In the control group, dyslipidemia was present in 15.7% (n=8), HT in 9.8% (n=5), DM in 3.9% (n=2) of the participants. When the comorbidities of both groups were analysed, DM, HT, dyslipidemia, hypothyroidism, hypogonadism and adrenal insufficiency were found to be significantly more prevalent in the patient group than in the control group (p<0.001; p<0.001; p<0.001; p<0.001; p=0.001; p=0.027, respectively).

In terms of disease specificity, no significant difference was found in the total GRISS score between patients diagnosed with and without hypogonadism (p=0.473). However, the vaginismus subscale score of the GRISS was significantly higher in patients with hypogonadism (p=0.019).

The total GRISS score of patients with a diagnosis of DM was found to be significantly higher than that of patients without a diagnosis of DM (p=0.005); no significant difference was found in the GRISS subscale scores.

Although there was no significant difference in GRISS total scores between patients with and without hypothyroidism (p=0.505), those with hypothyroidism had significantly higher premature ejaculation subscale scores (p=0.039).

A significant inverse correlation was observed between GRISS total scores and both IGF-1 (r=−0.279, p=0.045) and free T4 levels (r=−0.227, p=0.047) in patients with acromegaly. However, in the

Table VI. Relationships between scale scores of the patient group and RT history and type of drug treatment

		GRISS Total	BDI	BAI	BIS
Previous RT	**Yes**	38,5 (13-69)	11 (0-21)	8.5 (0-22)	144 (112-176)
	No	37 (11-98)	9.5 (0-38)	8 (1-62)	136.5 (70-197)
	p	0,896	0.957	0.465	0.454
Drug-free tracking	**Yes**	38.5 (15-72)	13 (1-38)	12.5 (3-62)	143 (70-197)
	No	35 (11-98)	9 (0-32)	8 (0-37)	120 (92-189)
	p	0.439	0.183	**0.033**	**0.033**
Somatostatin analogs	**Yes**	36 (12-98)	9 (0-23)	5 (0-37)	141 (105-192)
	No	37 (11-72)	13 (0-38)	13 (0-62)	135 (70-197)
	p	0.833	0.425	**0.006**	0.314
Cabergoline	**Yes**	31 (13-63)	13 (0-21)	13 (2-22)	147 (124-197)
	No	37 (11-98)	9 (0-38)	8 (0-62)	138 (70-92)
	p	0.487	0.904	0.316	0.131
Combined treatment	**Yes**	32.5 (11-66)	8 (2-32)	11 (0-19)	134.5 (70-176)
	No	37 (12-98)	10.5 (0-38)	8 (0-62)	141 (92-197)
	p	0.525	0.541	0.718	0.990

BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; BIS: Body Image Scale; GRISS: Golombok-Rust Inventory of Sexual Satisfaction; RT: Radiotherapy. Combined treatment refers to the concomitant use of somatostatin analogs and cabergoline.

Table VII. Multivariable Linear Regression Analysis of Factors Associated with GRISS Total Score

Variable	B (β)	95% CI	p
Age (years)	0.346	−0.188 to 0.879	0.198
Sex (female)	6.670	−3.109 to 16.450	0.176
Diabetes mellitus (yes)	9.301	−1.620 to 20.222	0.093
Psychotropic medication use (yes)	0.624	−12.613 to 13.860	0.925
IGF-1	0.0003	−0.0393 to 0.0399	0.988
Free T4	−26.709	−54.447 to 1.030	0.059

IGF-1: insulin-like growth factor 1. B indicates unstandardized regression coefficients. The dependent variable was the GRISS total score. No evidence of multicollinearity was observed (all variance inflation factor [VIF] values < 2.0).

prespecified multivariable linear regression model adjusting for age, sex, diabetes mellitus, psychotropic medication use, IGF-1, and free T4 levels, IGF-1 was not independently associated with GRISS total scores (p=0.988). Free T4 levels showed a borderline inverse association (p=0.059), while diabetes mellitus demonstrated a borderline p ositive association (p=0.093). The results of the prespecified multivariable linear regression analysis examining factors associated with GRISS total scores are summarized in Table VII. In sensitivity analyses additionally adjusting for acromegaly treatment modality (somatostatin analogs, cabergoline, combination therapy, or drug-free follow-up), the main findings remained unchanged, and IGF-1 levels were again not significantly associated with GRISS total scores (p=0.484). In an exploratory analysis restricted to female patients, menopausal status was additionally included in the multivariable model. In this subgroup, higher IGF-1 levels were positively associated with higher GRISS total scores.

Discussion and Conclusion

This study evaluated body perception, sexual function, depression, and anxiety in patients with acromegaly compared with matched controls and explored their associations with clinical characteristics using the GRISS, BIS, BDI, and BAI. In our study found no difference in the levels of depression or anxiety between patients with acromegaly and control subjects, regardless of having a psychiatric diagnosis or using psychotropic medications. While the remission status of patients did not affect their levels of depression, anxiety or sexual dysfunction in our study, patients who were in remission after surgery and were followed without medication had significantly lower severity of anxiety symptoms. Among patients using medication after surgery, only those using somatostatin analogs had significantly lower severity of anxiety symptoms than other forms of medication. Compared with controls, patients with

acromegaly reported a higher incidence of sexual dysfunction, particularly in areas such as infrequency, dissatisfaction, impotence and premature ejaculation. In patients with acromegaly, a negative body image is associated with sexual dysfunction.

Few studies have examined the psychiatric impact of acromegaly, and the results are inconsistent. While some reports indicate higher rates of depression, anxiety and maladaptive personality traits in patients, particularly women, our study found no significant differences in mental health outcomes between patients with acromegaly and controls. This may be due to the majority of patients being in remission, long-term follow-up at the same centre and effective disease management. Although some patients reported depressive or anxious symptoms at diagnosis, most adapted over time. Cultural and religious factors may also have contributed to lower help-seeking behaviour for psychiatric issues.

Psychological Symptoms and Remission Status

In our study, remission status was not associated with any depressive and anxiety symptoms or sexual functioning. Although this finding may initially appear unexpected, it is consistent with previous studies reporting no significant differences in mood or quality of life outcomes between patients in the active and remission phases of acromegaly[5,11,17]. *Accumulating evidence suggests that biochemical remission in acromegaly does not necessarily translate into parallel improvements in psychological well-being or quality of life. Indeed, a recent systematic review demonstrated that symptoms of depression and anxiety frequently persist despite disease control, highlighting the complex and multifactorial nature of psychological outcomes in acromegaly*[26]*. Similarly, previous studies have emphasized that depression and anxiety constitute independent therapeutic targets that are not solely driven by hormonal activity and may require specific clinical attention even during remission*[8].

Several factors may account for the lack of observable differences between remission groups in our cohort. Prolonged exposure to excess GH/IGF-1 may lead to irreversible physical changes, persistent body image disturbances, and long-standing psychosocial adaptations that do not readily resolve following biochemical control[27]. In addition, delayed diagnosis, persistence of orthopedic and cosmetic changes, ongoing comorbid conditions, and other confounding life factors may obscure potential associations. Furthermore, the unknown duration of remission limits the interpretation of its psychological impact. Finally, the relatively modest sample size may have limited the statistical power to detect small effects of remission status on psychological and sexual outcomes. Taken together, these findings suggest that remission status alone may be insufficient to capture the psychological and sexual burden of acromegaly, highlighting the need for comprehensive management strategies that extend beyond biochemical targets.

Body Image and Its Psychological Correlates

When evaluating body perception, it is important to consider cultural, social and psychological factors, as well as individual attitudes towards body shape and weight[28]. Previous studies have shown that depressive symptoms are closely associated with negative body image[13,29]. Similarly, Dimopoulou et al. reported that patients with acromegaly exhibit more negative body perception than patients with nonfunctional pituitary adenomas, independently of disease severity or biochemical control, but in a manner that is significantly related to the severity of depression[7]. Consistent with these findings, our study revealed that acromegaly patients had a more negative body image than the control group. Furthermore, increased depression and anxiety scores, as well as psychotropic medication use, were associated with poorer body perception; however, disease control status showed no significant relationship.

Our results emphasize that sexual dysfunction in acromegaly is not merely a hormonal consequence but a multifaceted phenomenon. The chronic psychological burden of living with a disfiguring disease, combined with impaired body image, creates a negative feedback loop that affects sexual desire and satisfaction. As noted in recent literature[26], body image dissatisfaction can persist even after biochemical remission is achieved. This suggests that the psychological 'scarring' of acromegaly may independently impair sexual health, regardless of current GH or IGF-1 levels. This underscores the need for integrating psychosexual counseling into the standard management of acromegaly.

Given the cross-sectional design of the study, the directionality of the observed associations cannot be determined. For example, although disturbed body image was associated with higher levels of depression and anxiety, it remains unclear whether negative body perception contributes to psychological distress or whether depressive and anxious symptoms adversely affect body image. Similarly, the temporal relationship between sexual dysfunction and psychological symptoms cannot be established, and bidirectional effects are possible.

Sexual Dysfunction: A Multifactorial Outcome

Our study revealed significantly higher GRISS scores among patients, indicating greater sexual dysfunction compared to controls. While biochemical remission is the primary goal of acromegaly management, our findings—consistent with Silvestro et al.[26]—suggest

that hormonal control alone may not suffice to resolve the psychological and sexual burden of the disease.

This study investigated the relationship between hormonal activity and sexual dysfunction in patients with acromegaly, with a particular focus on the potential role of IGF-1 levels. Although a bivariate association between IGF-1 and GRISS total scores was initially observed, this relationship did not persist after adjustment for relevant clinical confounders in multivariable analyses. These findings suggest that IGF-1 levels are not independently associated with the overall severity of sexual dysfunction when age, sex, DM, psychotropic medication use, and thyroid hormone status are taken into account.

The lack of an independent association between IGF-1 and sexual dysfunction contrasts with some previous hypotheses proposing a direct effect of GH/IGF-1 excess on sexual functioning through neuroendocrine and metabolic pathways. However, our results indicate that the observed associations in unadjusted analyses may reflect residual confounding or chance findings rather than a direct biological effect. Importantly, sensitivity analyses additionally adjusting for acromegaly treatment modality yielded consistent results, further supporting the robustness of our findings and suggesting that treatment-related factors did not substantially influence the association between IGF-1 and sexual dysfunction severity.

Sex Differences, Aging, and Sociocultural Factors

Reduced ovarian function and the consequent decline in circulating estrogen, progesterone, and testosterone levels may lead to diminished sexual desire, arousal, and satisfaction[30]. In our study, menopausal women in the patient group showed significantly higher avoidance and infrequency scores. As expected, the menopause-related reductions in sexual activity and increased avoidance observed in our cohort represent predictable physiological and psychosocial outcomes.

Regular menstruation, often perceived as a symbol of femininity and fertility, may lead some women to view menopause as a loss of femininity. Particularly among women with lower education levels, menopause has been associated with aging and reduced sexual activity[31]. A study conducted in Türkiye revealed a relationship between low educational level, unemployment, and sexual dysfunction in women[32]. Similarly, in our study, the frequency of avoiding sexual intercourse increased as educational level decreased.

Previous studies have demonstrated a positive correlation between age and sexual dysfunction in women with acromegaly[5,17]. In our study, although age was associated with a higher proportion of individuals who were not working or menopausal in both groups, a significant relationship between age and sexual dysfunction (the GRISS total score and infrequency subscale) was found only in the patient group. Furthermore, GH and IGF-1 levels decreased with age, and an inverse correlation was observed between IGF-1 and sexual dysfunction (the GRISS total score and non-communication subscale). Further studies are needed to establish whether the increase in sexual dysfunction with aging is related to decreased IGF-1 levels.

Previous studies have shown that erectile dysfunction in acromegaly patients is more prevalent among those with a longer smoking history, HT, and cardiovascular disease. However, it is not associated with psychiatric disorders, hypogonadism, or GH/IGF-1 levels[14,33]. ED appears to be primarily associated with cardiometabolic factors and vascular alterations rather than hormonal status. In female patients, Çelik et al. reported significantly lower Female Sexual Function Index (FSFI) scores in all domains compared to the control group. These scores were correlated with higher depression scores, lower AcroQoL scores and lower IGF-1 levels. Although remission status was not related to sexual dysfunction, total FSFI scores were associated with IGF-1 levels, suggesting that the effects of comorbidities persist even in biochemical remission[5]. Consistent with these findings, our study revealed significantly higher GRISS scores among patients, indicating greater sexual dysfunction. Negative body image was associated with depressive symptoms and sexual dysfunction in both groups.

Women in both groups exhibited greater sexual dysfunction, particularly in the GRISS total score, noncommunication, avoidance, and nonsensuality subscales. Sexual desire, satisfaction, and related behaviors are influenced by sociocultural factors. In conservative societies, limited sexual education, prevailing taboos, and persistent sexual myths contribute to greater sexual dysfunction in women [34]. Accordingly, the high levels of sexual dysfunction observed in women in our study are likely related to cultural factors within our population.

Impact of Medical Treatments and Radiotherapy

The psychological and sexual impact of medical treatments in acromegaly remains a subject of ongoing debate, with previous studies yielding inconsistent results. While some reports found no significant differences in depression (BDI) or quality of life (AcroQoL) scores across treatment modalities[35], others found that patients treated with lanreotide had lower scores in the mental health, appearance, and interpersonal relationships domains[36]. Short-term octreotide-LAR therapy improved only the mental health domain[37], whereas a meta-analysis concluded that lanreotide-LAR positively affects quality of life[38].

In our study, the most positive body perception and lowest anxiety levels were observed among patients

followed without medication. This may be attributed to their stable remission status, a lower cumulative disease burden, and the psychological benefit of requiring fewer clinical visits. When evaluating the impact of specific medical treatments, our results showed that patients on somatostatin analogs exhibited lower anxiety levels compared to those on other medications. The potential influence of somatostatin analogs or dopamine agonists on sexual function remains unclear. To our knowledge, no studies have specifically examined the impact of acromegaly treatments on sexual function, emphasizing the necessity for further research to optimize disease management and treatment outcomes.

Our study found no significant relationship between a history of radiotherapy (RT) and the results of the applied scale. Radiotherapy (RT) has been identified as a predictor of an increased risk of mental health disorders, which is likely to reflect a more severe and surgery-resistant disease [11]. RT has also been linked to reduced quality of life across studies, potentially via direct treatment effects or RT-induced hypopituitarism [39]. We believe that the small number of patients in our sample who received RT (n=12) and the fact that patients who developed hypopituitarism after RT were receiving hormone replacement therapy might have influenced this result.

Psychotropic medication use was not independently associated with the overall severity of sexual dysfunction in multivariable analyses (GRISS total score). This finding may be explained by the heterogeneity of psychotropic agents, variability in medication type, dosage, and treatment duration, as well as potential counterbalancing effects between symptom control and medication-related sexual side effects. Notably, patients using psychotropic medications had significantly lower scores on the premature ejaculation subscale, a finding that most likely reflects the well-established ejaculation-delaying effects of serotonergic antidepressants. Therefore, this result should be interpreted as a pharmacologically expected effect rather than an improvement in overall sexual functioning. Taken together, these findings highlight the multifactorial nature of sexual dysfunction in acromegaly, in which metabolic and hormonal factors may play a more prominent role than IGF-1 levels alone.

Comorbidities and Hormonal Determinants

Each comorbidity was analysed separately to evaluate its association with sexual function in patients with acromegaly. DM may cause sexual dysfunction through chronic vascular impairment[40]. In our study, patients with DM had significantly higher GRISS total scores than those without DM, with an average HbA1c level of 6.81%±2.29%, which exceeds the treatment target of 6%. Similarly, dyslipidemia may impair arterial blood flow due to atherosclerosis, resulting in erectile dysfunction[40]. Patients with dyslipidemia scored significantly higher on the impotence and avoidance subscales, suggesting that erectile dysfunction may lead to avoidance behaviors driven by performance anxiety and fear of failure.

In our study, the mean free T4 level was 0.99±0.17 ng/dL. Based on institutional reference ranges (0.7–1.48 ng/dL), all patients were euthyroid. Patients with hypothyroidism had significantly higher scores only in the premature ejaculation subscale of the GRISS. Although hypothyroidism is usually linked to reduced libido and erectile dysfunction, which improve with treatment[41,42], achieving euthyroidism through hormone replacement therapy could have affected this outcome. The older age of male patients with hypothyroidism (median: 56 years) likely contributed to the higher premature ejaculation scores observed. Higher free T4 levels within the normal range were associated with lower GRISS total and avoidance scores, suggesting a potential benefit that requires confirmation in larger studies.

Patients with hypogonadism showed significantly higher scores in the vaginismus subscale only. All patients were postmenopausal and on hormone replacement therapy (median age: 55 years). The elevated vaginismus scores may therefore reflect age and menopausal status. Hormone replacement therapy has been shown to improve sexual function in individuals with hypogonadism[43], and the absence of other common sexual dysfunctions, such as decreased libido or impotence, in our acromegaly cohort may be attributed to effective therapy. However, given the cross-sectional design of this study, these associations remain speculative and should be validated in prospective studies.

In conclusion, acromegaly was associated with a more negative body image and higher sexual dysfunction than in controls, although depression and anxiety levels were similar. Remission status was not related to mood or anxiety, but medication status and specific comorbidities were associated with anxiety and sexual outcomes. Management should extend beyond biochemical control to encompass psychological support, interventions to improve body image, sexual counselling and the aggressive treatment of cardiometabolic risk. Comorbidities should be considered when managing sexual dysfunction in acromegaly, as appropriate treatment may alleviate symptoms and improve sexual well-being. Future multicentre longitudinal studies should investigate the temporal relationship between hormonal control, psychosocial adaptation and sexual function, and assess whether targeted psychological and lifestyle interventions lead to long-term improvements in quality of life.

Limitations and Strengths

This study has several limitations that should be considered when interpreting the findings. First, the sample size was not based on a prespecified power analysis or sample size calculation. The number of patients included was limited to those who were under regular follow-up at a single tertiary care center, had recent laboratory data available, and were accessible during the study period. This may have reduced the ability to detect small or weak effects, particularly in subgroup and correlation analyses. Second, the cross-sectional design precludes causal or temporal inferences, and residual or unmeasured confounding cannot be fully excluded despite multivariable and sensitivity analyses. Depressive and anxiety symptom severity (BDI and BAI) were not included as covariates in the multivariable regression analyses, as they may represent intermediate variables on the causal pathway between disease burden and sexual functioning; however, their associations with sexual function were explored using correlation analyses. Third, the reliance on self-report instruments may have introduced reporting bias. Finally, the single-center design may limit the generalizability of the findings to other populations and settings.

However, strengths include the use of validated scales across multiple psychosocial domains, as well as the inclusion of clinical covariates such as remission status, treatment modality, comorbidities and hormone levels. This enables a more nuanced appraisal of psychological and sexual health in acromegaly patients.

Researcher Contribution Statement:
Idea and design: R.A.G., Ö.Ö.G.,Y.A.Ü., S.K.; Data collection and processing: A.M., R.A.G., Y.A.Ü, Ö.Ö.G.; Analysis and interpretation of data: G.Ö.; Writing of significant parts of the article: R.A.G, A.M., S.K.
Support and Acknowledgement Statement:
The authors declare that this study received no financial support.
Conflict of Interest Statement:
The authors of the article have no conflict of interest declarations.
Ethics Committee Approval Information:
Approving Committee: Bursa Uludağ University Faculty of Medicine Clinical Research Ethics Committee
Approval Date: 02.06.2021
Decision No: 2021-7/19

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