



Assessment of the condition of the salivary glands using ultrasound in patients with acromegaly

Emir Efendiyev*

Postgraduate Student

M.F. Vladimirsky Moscow Regional Research and Clinical Institute
129110, 61/2 Shchepkina Str., Moscow, Russian Federation
<https://orcid.org/0000-0002-5276-3873>

Malkan Amkhadova

Doctor of Medical Sciences, Professor

M.F. Vladimirsky Moscow Regional Research and Clinical Institute
129110, 61/2 Shchepkina Str., Moscow, Russian Federation
<https://orcid.org/0000-0002-9105-0796>

Anna Sizova

PhD in Medical Sciences, Assistant

Federal State Budgetary Educational Institution of Higher Education
"Russian University of Medicine"
of the Ministry of Health of the Russian Federation
127006, 4 Dolgorukovskaya Str., Moscow, Russian Federation
<https://orcid.org/0000-0002-1592-7584>

Abstract. Acromegaly is a chronic neuroendocrine disease caused by prolonged hypersecretion of growth hormone and insulin-like growth factor-1 and leading to systemic soft tissue hypertrophy, while the condition of the salivary glands has not been sufficiently explored. The purpose of the study was to compare the size of the submandibular salivary glands according to ultrasound data in patients with active acromegaly and in healthy individuals of comparable age and gender, and to identify clinical and biochemical factors associated with the volume of the glands. A prospective comparative study included 27 patients with active acromegaly and 26 healthy volunteers. All underwent an ultrasound examination of the submandibular glands, measuring the length, width, and thickness of each gland and calculating the volume. The age, duration of symptoms, index of insulin-like growth factor-1, and presence of hyperprolactinaemia and echostructure of parenchyma were additionally assessed in patients. In patients with acromegaly, the median volume of the right gland was higher than in healthy subjects (10.0 versus 6.3 cm³), as was the volume of the left (8.8 versus 7.0 cm³; $p < 0.01$ for both), with a significant increase in length and width and no differences in thickness. Gland volume was negatively associated with age and duration of symptoms, was higher in men, and tended to decrease in hyperprolactinaemia; male gender, and duration of symptoms turned out to be independent predictors of volume. Acromegaly was accompanied by marked hypertrophy of the submandibular salivary glands, mainly due to an increase in length and width, which allows considering ultrasound evaluation of these glands as an additional non-invasive marker of the tissue response in acromegaly

Keywords: submandibular salivary glands; ultrasound examination; salivary gland volume; insulin-like growth factor-1; hyperprolactinaemia

Introduction

Acromegaly is a chronic neuroendocrine disease caused by prolonged hypersecretion of growth hormone (GH) by pituitary adenoma, followed by an increase in the level of insulin-like growth factor-1 (IGF-1) and activation

of the GH/IGF-1 axis [1-3]. Excessive secretion of GH/IGF-1 leads to progressive hypertrophy of soft tissues, enlargement of internal organs and bone remodelling with the appearance of systemic complications [2,3].

Efendiyev E, Amkhadova M, Sizova A. Assessment of the condition of the salivary glands using ultrasound in patients with acromegaly. Eurasian Health J. 2026;18(1):93-108. DOI: 10.54890/1694-8882-2026-1-93

*Corresponding author (efendiev_199@mail.ru)



Copyright © The Author(s). This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (<https://creativecommons.org/licenses/by/4.0/>)

The disease is characterised by thickening of the soft tissues of the face (rough features), enlargement of the lower jaw (prognathism), expansion of the interdental spaces and malocclusion, enlargement of the tongue (macroglossia), enlargement of the hands and feet [4]. These changes develop gradually and often remain unrecognised for many years, which causes a delay in diagnosis by an average of 5-8 years from the onset of the first symptoms [3]. Doctors of other specialities, including dentists, can play an important role in the early detection of acromegaly: cases of primary diagnosis of the disease at a dental appointment due to progressive malocclusion and an increase in interdental spaces are described. According to the literature, up to a third of acromegaly patients report dental complaints related to maxillofacial changes and dental manifestations of the disease for the first time [5]. Craniofacial changes in acromegaly can be considered as morphological markers of the disease, complementing biochemical parameters (levels of GH and IGF-1) [3]. Chronic hyperproduction of GH and IGF-1 causes not only bone-soft tissue changes, but also generalised enlargement of internal organs. Acromegaly is associated with cardiomegaly, hepatosplenomegaly, nephromegaly, and thyroid hyperplasia [3,6]. The manifestations of organomegaly in the head and neck include enlargement of the tongue (macroglossia) [7] and enlargement of a number of glandular organs. Retrospective data indicate that more than half of patients with acromegaly have obstructive sleep apnoea syndrome, the development of which is facilitated by the growth of cranial bones and soft tissues, including hypertrophy of the root of the tongue and epiglottis [3]. These changes determine the contribution of head and neck organomegaly to the clinical picture of acromegaly. The issue of enlarged salivary glands in acromegaly remains poorly understood. Human salivary glands (parotid, submandibular, and sublingual) belong to the large exocrine glands of the head and neck. Their function is regulated by the autonomic nervous system and depends on the influence of systemic hormones and growth factors. It has been shown that the size and secretory activity of salivary glands can be influenced by sex hormones and other hormonal factors [8]. Prolactin binding is detected in human salivary gland tissue, which indirectly confirms the hormonal sensitivity of this system [9]. In a number of conditions, particularly Sjögren's syndrome, changes associated with prolactin-associated proteins in the epithelial cells of the salivary glands have been reported [10]. In addition to hormonal influences, local factors can affect the salivary glands; in particular, prolonged increased functional load (hypersalivation) is theoretically capable of leading to compensatory enlargement of the parenchyma.

The clinical significance of evaluating salivary glands in acromegaly is related not only to the fact of a possible increase in their size, but also to potential

functional consequences for the oral cavity and upper respiratory tract. Changes in the tissues of the face and neck in chronic hormonal hypersecretion can be accompanied by subjective complaints that affect the quality of life, and create additional difficulties in dental treatment, including planning surgical interventions and conducting anaesthesia. Simultaneously, an objective assessment of salivary glands in routine practice is often limited to a clinical examination, which may not be sensitive enough to moderate volume changes and does not allow quantifying the dynamics. Ultrasound is an accessible, non-invasive and repeatable imaging method that allows evaluating both morphometric parameters and the overall echostructure of glandular tissue. In this context, quantitative ultrasound assessment of the submandibular salivary glands can be considered as an additional tool for complex characterisation of tissue manifestations of acromegaly and substantiation of an interdisciplinary approach to patient management. The purpose of the study was to evaluate the size of the submandibular salivary glands in patients with active acromegaly using ultrasound diagnostics and to determine clinical and laboratory factors affecting the volume of salivary glands.

Materials and Methods

A single-centre comparative study was conducted in two groups: patients with acromegaly and conditionally healthy individuals. Inclusion criteria: confirmed diagnosis of active acromegaly and age over 18 years. The acromegaly group included 27 patients (10 men and 17 women) aged 27-62 years (median 44 (40-51) years). The diagnosis of acromegaly was established based on clinical manifestations and biochemical criteria and was confirmed by pituitary neuroimaging data [6]. At the time of inclusion, all patients retained the activity of the disease: the IGF-1 level exceeded the age norm by an average of 2.1 times, and the GH level during the oral glucose tolerance test was 1.6-40 mcg/l (median 11 mcg/l). In 19 patients, acromegaly was detected for the first time; in 8, the previously established diagnosis was accompanied by insufficient compensation against the background of ongoing therapy (IGF-1 remained elevated). The duration of the disease (according to patients, from the onset of the first symptoms) was a median of 5 (3-9) years. Concomitant hyperprolactinaemia (a moderate increase in prolactin levels) was detected in 9 patients (33%) and was associated with mixed somatotrophic pituitary adenoma. The control group consisted of 26 conditionally healthy adults (11 men and 15 women) without signs of endocrine pathology and without complaints at the time of examination. Exclusion criteria: for both groups: the presence of salivary gland disorders (tumours, Sjögren's syndrome, recurrent sialadenitis, etc.), a history of radiotherapy to the head and neck, severe obesity, and serious systemic conditions that make it difficult to perform an

ultrasound scan. For patients with acromegaly, remission of the disease was an additional exclusion criterion.

Ultrasound examination was performed for all included study participants ($n=53$) in the absence of contraindications and technical limitations. A GE LOGIQ P9 device and a linear sensor with a frequency of 7-12 MHz were used; the patient was in a supine position with a slight extension of the head. Scanning was performed in the longitudinal and transverse planes. For each gland, three linear dimensions were recorded – anteroposterior, craniocaudal, and mediolateral – in centimetres. Each size was recorded with two repeated measurements, after which the average value was calculated for statistical analysis. The volume was calculated using the ellipsoid equation $V = (\text{length} \times \text{width} \times \text{thickness}) \times \pi/6$ with the result presented in cm^3 . For analytical tasks, derived indicators were calculated, including the average volume, defined as the arithmetic mean of the volumes of the right and left glands; this indicator was used in correlation and regression analysis. The upper conditional limit of the norm for the calculated volume was defined as the maximum volume value in the control group. The echostructure was evaluated qualitatively and belonged to one of two categories: without structural changes or with the presence of structural changes; heterogeneity of the parenchyma and/or diffuse or focal changes in echogenicity were considered a sign of changes.

Statistical processing was performed using the Statistica 13 package (TIBCO Software Inc.). Since the distribution of most quantitative indicators was significantly different from normal (Shapiro-Wilk $p < 0.05$), non-parametric criteria were used. The Mann-Whitney U-test and the accurate χ^2 test were used to compare the groups. To identify correlations, the Spearman coefficient (ρ) and the point-biserial coefficient r_{pb} were calculated. The influence of several factors on the volume of the salivary gland was analysed by multiple linear regression. The data was presented as a median and interquartile range (Q1-Q3). The critical

significance level – 0.05. For regression analysis, the average volume of the submandibular glands (the arithmetic mean of the volumes of the right and left glands) was used as a dependent variable, since this indicator reduces the influence of random asymmetry and reflects the overall level of sialomegaly. Demographic and clinical and laboratory parameters were considered as potential predictors, which were pre-selected based on the pathophysiology of the disease and its clinical significance. Categorical variables (for example, gender and the presence of hyperprolactinaemia) were introduced into the model as binary indicators. The regression results were evaluated based on the coefficients of the model and the level of statistical significance, interpreting the identified relationships as associations rather than causal relationships. Additionally, the correctness of data entry and the presence of omissions were monitored; in the absence of a value for a particular indicator, the corresponding observations were excluded from the analysis of a specific relationship (pairwise exclusion), without removing the patient from all calculations. The median and interquartile range were used to describe the distributions, which is conditioned by the likely deviation of many clinical and biochemical parameters from the normal distribution in clinical samples. For comparability of results between groups, a unified approach to data presentation and a critical significance level of $p < 0.05$ were applied. All participants in the study gave written informed consent to participate and publish anonymised data. The study protocol was approved by the local ethics committee of MONIKI and was conducted in accordance with the Declaration of Helsinki.

Results

Characteristics of the examined groups and ultrasound parameters. Comparative data on age and ultrasound parameters of the submandibular salivary glands in the acromegaly group and the control group are presented in Table 1.

Table 1. Age and ultrasound parameters of submandibular salivary glands (median (IQR))

Indicator	Acromegaly (median (IQR))	Control (median (IQR))
Age, years	44 (40-51)	46 (43-55)
Length of the right gland, cm	3.90 (3.62-4.30)	3.60 (3.42-3.80)
Width of the right gland, cm	2.90 (2.20-3.02)	1.90 (1.71-2.10)
Thickness of the right gland, cm	1.69 (1.42-2.00)	1.85 (1.62-2.00)
Volume of the right gland, cm^3	10.00 (5.90-12.35)	6.30 (5.70-7.20)
Length of the left gland, cm	3.90 (3.64-4.32)	3.60 (3.31-3.70)
Width of the left gland, cm	2.70 (2.39-3.05)	2.00 (1.90-2.12)
Thickness of the left gland, cm	1.70 (1.50-1.90)	1.87 (1.65-2.08)
Volume of the left gland, cm^3	8.80 (7.25-11.80)	6.98 (5.46-7.72)

Source: compiled by the authors

The size of salivary glands in patients with acromegaly and in control. Ultrasound examination confirmed an increase in the submandibular glands in

patients with acromegaly compared with the control group (Fig. 1, Table 1). The volume of the right gland in patients was 10.00 (5.90-12.35) cm^3 , while in healthy

individuals it was 6.30 (5.70-7.20) cm³ ($p < 0.0001$). The volume of the left gland in the acromegaly group (8.80 (7.25-11.80) cm³) also exceeded the control values (6.98 (5.46-7.72) cm³; $p = 0.006$). The total volume of the two submandibular glands in a patient with acromegaly was 18.8 (17.2-21.4) cm³ versus 13.3 (11.7-14.8) cm³ in the control group (the difference was ~41%). In 25 out of 27 patients (93%), the volume of at least one gland exceeded the upper limit, conventionally defined as the maximum value in the control group. There was no significant asymmetry between the right and left glands in the control group (the median relative difference in volume was 4%; $p = 0.37$). In the acromegaly group, volume asymmetry > 10% was detected in 8 patients (30%); the predominance of the right or left gland was multidirectional, and there was no statistically significant trend towards lateralisation ($p = 0.65$). The linear dimensions of the submandibular glands in patients with acromegaly were also larger. The length of the right gland was 3.90 (3.62-4.30) cm versus 3.60 (3.42-3.80) cm in the control group, the width was 2.90 (2.20-3.02) cm versus 1.90 (1.71-2.10) cm; for the left gland, the length was 3.90 (3.64-4.32) cm versus 3.60 (3.31-3.70) width – 2.70 (2.39-3.05) cm versus 2.00 (1.90-2.12) cm. The thickness of the glands in the groups was comparable (Table 1). Thus, an increase in the volume of salivary glands in acromegaly is mainly associated with an increase in length and width while maintaining a comparable thickness.

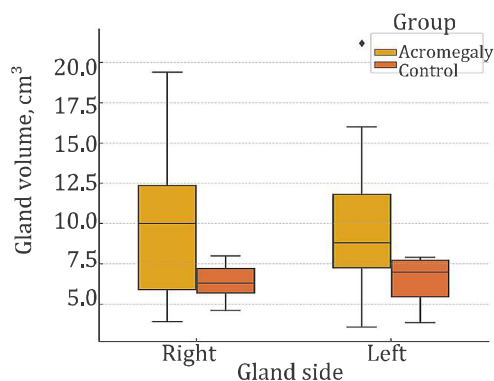


Figure 1. Comparison of the distribution of the volume of the submandibular glands in patients with acromegaly and in control individuals (span diagrams)
Source: compiled by the authors

The parenchyma of all the glands under study had a typical fine-grained echostructure; no pathological inclusions (stones, cysts, nodes) were observed. In 21 out of 27 patients (78%), the echogenicity of the salivary gland was slightly reduced relative to the conditional norm, in the rest it was isoechogenic; in the examined control group, echogenicity was usually normal. An example of an ultrasound image of the submandibular glands in a patient with acromegaly (with echostructural changes) is shown in Figure 2.

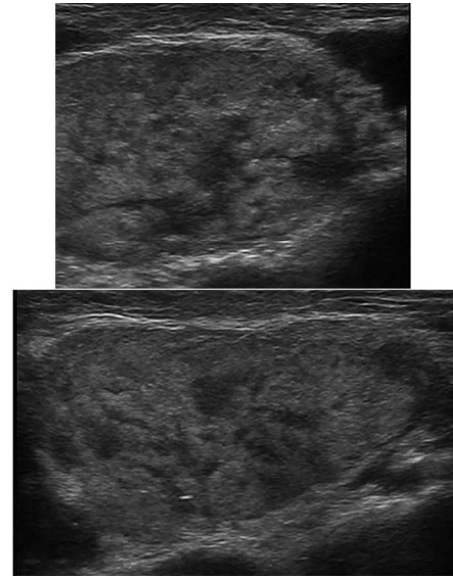


Figure 2. Example of an ultrasound image of the submandibular glands in a patient with acromegaly (with echostructural changes)
Source: compiled by the authors

Factors associated with salivary gland volume in acromegaly. The relationship between the size of the salivary glands and the main clinical and biochemical parameters in patients with acromegaly was evaluated. In men, the volume of the mandibular glands was greater than in women: the total volume of the two mandibular glands was 20.4 (19.3-22.0) cm³ versus 16.8 (15.7-18.5) cm³, respectively (difference ~21%; $p = 0.0005$). In the control group, there were practically no sex differences in volume (13.9 cm³ in men and 12.8 cm³ in women; $p = 0.12$). The sexual and age-related features of acromegaly are described in the literature [13]. Age showed an inverse correlation with salivary gland volume ($\rho = -0.46$; $p = 0.015$): younger patients had more gland volume. A similar negative relationship was found between the duration of acromegaly and gland volume ($\rho = -0.42$; $p = 0.03$). It has also been shown that in adult patients with untreated acromegaly, the rate of unstimulated salivation is higher than in healthy patients, but it progressively decreases with increasing age. The data obtained are consistent with this observation: in younger patients, the volume of salivary glands is larger; which may reflect a more pronounced trophic tissue response to chronic excess of GH/IGF-1. The IGF-1 index (ratio to the upper limit of the age norm) ranged from 1.2 to 5.7 (median 2.1), but there was no statistically significant correlation between the IGF-1 index and salivary gland volume ($\rho = 0.21$; $p = 0.28$). Similarly, there was no relationship between GH levels and gland volume ($\rho = 0.09$; $p = 0.64$).

The presence of moderate hyperprolactinaemia in some patients allowed assessing its possible effect on the size of the salivary glands. In 9 patients with elevated

prolactin levels, the volume of the submandibular glands was slightly lower on average (9.0 cm³) compared with patients without hyperprolactinaemia (10.1 cm³), but the difference did not reach statistical significance ($p = 0.09$). Considering the data on hormonal sensitivity of the salivary glands [9,10], this issue requires further study. For a comprehensive assessment of the factors, a multiple linear regression model was built, including gender, age, duration of the disease, IGF-1 index and hyperprolactinaemia. Independent predictors of salivary gland volume in acromegaly were male gender ($\beta = +0.45$; 95% CI: 0.12-0.79; $p = 0.010$) and shorter duration of the disease ($\beta = -0.39$; 95% CI: -0.72...-0.06; $p = 0.028$). According to observations by L. Manetti *et al.*, even in patients in biochemical remission after treatment, the volume of the submandibular glands remains increased compared to healthy ones [13].

For clarity, the results obtained can be summarised in the form of several key observations. In patients with acromegaly, compared with the control group, a statistically significant increase in the individual linear dimensions and estimated volume of the submandibular salivary glands was revealed, which confirmed the presence of sialomegaly as one of the morphological manifestations of the disease. In addition, the differences between the groups were more related to the length and width of the glands, while the changes in thickness were less pronounced, which may reflect anatomical limitations and the varying sensitivity of individual measurements to tissue changes. A qualitative assessment of the echostructure showed that structural changes in the parenchyma were detected in some patients, while in others the glands retained a homogeneous echocartin, which indicates a heterogeneity of morphological changes even in the active form of the disease. Correlation and regression analyses revealed a relationship between the average gland volume and a number of clinical characteristics, including gender and duration of the disease, which allows identifying factors potentially associated with the severity of changes. Thus, the results are presented not only as intergroup differences, but also as a set of relationships between morphometric parameters and clinical and biochemical characteristics, which creates the basis for their clinical interpretation.

Discussion

The present study confirmed that acromegaly is accompanied by an enlargement of the submandibular salivary glands. Against the background of a chronic increase in growth hormone and insulin-like growth factor-1, a generalised increase is formed not only in the internal organs, but also in the exocrine glands of the head and neck. Similar changes have been demonstrated in relation to the lacrimal glands: in patients with acromegaly, the volume of the lacrimal glands is

increased according to magnetic resonance imaging, regardless of the status of the disease activity [12-14]. In the study by L. Manetti *et al.* [13], there were also no differences in the size of the submandibular glands between patients with active acromegaly, patients on therapy with somatostatin analogues and patients in surgical remission: in all subgroups, the volume of glands remained elevated and differed mainly from the control. Taken together, these observations suggest that hypertrophy of the salivary (and lacrimal) glands develops in the early stages of the disease and may persist for a long time, including after achieving biochemical remission. Similar stability is characteristic of a number of bone changes: despite partial regression of soft tissue manifestations after treatment of acromegaly, many skeletal deformities (malocclusion, enlargement of the lower jaw, hyperostosis) they persist even years after normalisation of insulin-like growth factor-1. From a practical standpoint, this means that enlargement of the salivary glands can be detected in patients with acromegaly, regardless of the current status of the disease activity. Data on the condition of the salivary glands in acromegaly are limited. Rare clinical cases of enlargement of the parotid glands in patients with acromegaly have been described [11]. In a study using magnetic resonance imaging of the orbits, it was shown that in patients with acromegaly, the volume of lacrimal glands is statistically higher than in healthy people and positively correlates with IGF-1 levels [12]. These observations support the hypothesis of diffuse hypertrophy of the glandular organs of the head and neck with a chronic excess of GH/IGF-1, although clinically such changes may remain unnoticeable. Enlargement of the salivary glands, in particular the submandibular glands, is often difficult to assess on physical examination due to their anatomical location. In this regard, an objective assessment of the size of the salivary glands in patients with acromegaly is of interest to clarify the spectrum of morphological changes in this disease. L. Manetti *et al.* [13] compared the volume of the submandibular salivary glands in patients with acromegaly and healthy individuals using ultrasound imaging and showed that in patients with acromegaly, the volume of the glands is about 1.5-2 times higher than normal values. Simultaneously, the factors associated with the severity of hypertrophy were not analysed in this study, and the question of the relationship between the size of the glands and the activity of acromegaly remained open.

Ultrasound is an accessible and informative method for evaluating large salivary glands. Ultrasound allows measuring the linear dimensions and volume of the parotid and submandibular glands, detecting structural changes (nodules, cysts, diffuse heterogeneity of the parenchyma) and assessing the condition of the ducts [15]. The method is safe, non-invasive and suitable for dynamic monitoring. In endocrinological practice, ultrasound is widely used to evaluate other glands

(thyroid, parathyroid, adrenal glands), while salivary glands usually remain outside the area of routine evaluation. It is assumed that ultrasound of the salivary glands in patients with acromegaly will allow quantifying the presence of their hypertrophy and identifying possible predictors of this condition. This study is aimed at expanding the understanding of organomegaly in acromegaly and evaluating the possibility of using ultrasound biometry of the salivary glands as an additional marker of the tissue response to excess GH/IGF-1 [16].

It should be noted that hypertrophy of the submandibular glands in acromegaly has unequal severity along the anatomical axes: length and width increase, while thickness does not change significantly. This pattern of size change is consistent with anatomical limitations: the submandibular gland is located in the submandibular triangle of the neck, bounded by the mandible and fascial structures, which makes it difficult for it to significantly thicken in the antero-posterior area. Parenchymal hyperplasia is mainly realised in the areas of lesser mechanical limitation, which leads to elongation and lateral expansion of the organ while maintaining a relatively flattened shape. A similar phenomenon has been described for macroglossia in acromegaly: the tongue increases mainly in length and width, which may contribute to a violation of the closure of the dentition, while the thickness is limited by the space of the oral cavity and varies to a lesser extent [16]. It is advisable to take these morphometric features into account when assessing the dynamics during treatment. For the salivary glands, the reverse development of hyperplasia after therapy has not been sufficiently investigated; however, it can be assumed that there are similar limitations to regression in conditions of a fixed anatomical space.

The present study identifies factors associated with the severity of salivary gland hypertrophy in acromegaly. It was shown that the volume of the submandibular glands in men with acromegaly is greater than in women, in the absence of significant sex differences in the control group. This is consistent with clinical observations, according to which the disease is often more severe in men and remains unrecognised for longer, which may be conditioned by more pronounced morphological manifestations at the time of diagnosis. Additionally, the role of sex hormones as possible modifiers of the tissue response to excess growth hormone and insulin-like growth factor-1 is discussed. It was previously noted that in postmenopausal women, the disease may be accompanied by less pronounced acromegaloid changes, which is associated with a change in the modulation of the somatotrophic axis. However, the absence of statistically significant sex differences in salivary gland volume in the control group indicates a minimal effect of sex hormones on the size of salivary glands under physiological conditions. Consequently, the revealed sex

differences are manifested mainly in conditions of pathology against the background of a chronic excess of growth hormone. There is also information in the literature about more frequent hyperprolactinaemia and larger pituitary adenomas in men with acromegaly, which may indirectly affect the severity of peripheral changes. In general, gender can be considered as one of the markers of the degree of tissue response in acromegaly, including from the salivary glands.

Another factor associated with the volume of salivary glands was the duration of the disease. It has been shown that with a shorter period from the onset of acromegaly, hypertrophy of the salivary glands is more pronounced, whereas with a prolonged course of the disease, the volume of the glands is somewhat smaller. This may reflect the dynamics of tissue changes: in the early stages, glandular tissue is actively hypertrophied under the influence of a chronic excess of growth hormone and insulin-like growth factor-1, whereas as the disease progresses, partial involution and an increase in the proportion of connective tissue are possible. With prolonged acromegaly, fibrous changes develop in various organs, including the myocardium, thyroid gland, and skin; similar processes cannot be excluded in the salivary glands. An additional explanation may be that patients with a long-term course of the disease are more likely to receive treatment that partially affects peripheral manifestations. The results obtained are consistent with the understanding of the clinical dynamics of acromegaly, according to which, as the disease develops, external stigmas become less dynamic, complications come to the fore, and active soft tissue growth stabilises. Therefore, early diagnosis and treatment of acromegaly are important not only for the prevention of complications, but also for limiting the degree of irreversible morphological changes, including changes in the salivary glands.

The lack of correlation of salivary gland volume with current levels of insulin-like growth factor-1 and growth hormone in patients in the active phase of the disease also deserves attention. With a relatively high and relatively uniform excess of insulin-like growth factor-1 in the sample, the variability of hormonal parameters could not have a significant effect on the already formed increased volume of glands. Similarly, it was noted in the literature that the severity of organomegaly and soft tissue manifestations is not always directly proportional to the concentrations of growth hormone and insulin-like growth factor-1, especially in the range of high values; more significant determinants may be the duration of hypersecretion, individual tissue sensitivity, and sexual and genetic factors. The factors considered in the analysis (gender, duration of the disease, hyperprolactinaemia) explain about half of the interindividual variation in salivary gland volume, which indicates the role of additional, probably individual, determinants.

The results obtained are of practical importance. It has been shown that ultrasound can be used to detect and quantify salivary gland enlargement in acromegaly. Ultrasound biometrics of the salivary glands can potentially be included in the complex examination of patients, including for dynamic monitoring of the soft tissue response to treatment. In addition, the revealed relationship between gland volume and sex and duration of the disease underscores the need for an individualised approach to clinical observation, primarily in men and patients with a relatively short period of disease manifestation. In addition, the data obtained complement the arguments in favour of early treatment of acromegaly. It is known that effective therapy of acromegaly leads to an improvement in symptoms and a reduction in mortality [1-3], and may also contribute to partial regression of external manifestations. However, the reverse development of salivary gland hypertrophy has not been sufficiently investigated; further studies, including repeated ultrasound measurements after surgical and drug treatment, seem appropriate.

Ultimately, the results are of interest not only to endocrinologists, but also to dentists, maxillofacial surgeons, and otorhinolaryngologists. Diffuse enlargement of the salivary glands is more often considered in the context of autoimmune diseases, sialolithiasis and tumour processes, and less often as a manifestation of endocrine pathology. Patients with acromegaly show significant hyperplasia of the salivary glands, which should be considered in the differential diagnosis of sialomegaly. Functional changes in salivation in acromegaly (increased salivation and/or changes in saliva composition) can affect the condition of the oral cavity [16]. According to the literature, periodontal diseases occur in patients with acromegaly; an enlargement of the gingival papillae associated with hypertrophy of the connective tissue structures of the periodontium has been described [17,18]. This complicates the management of dental patients and highlights the need for interaction between endocrinologists and dentists. Otolaryngologists should consider the possibility of asymptomatic enlargement of the salivary glands and soft tissues of the pharynx in patients with acromegaly, which may contribute to snoring and obstructive sleep apnoea [19,20]. The data obtained complement the understanding of orofacial changes in acromegaly, including changes in the salivary glands.

The interpretation of the revealed patterns requires considering the features of the tissue response in acromegaly. An increase in the linear size and volume of the submandibular salivary glands may reflect a combination of parenchymal hyperplasia, an increase in the interstitial component, and changes in microcirculation due to chronic hormonal stimulation. Simultaneously, the uneven dynamics of individual sizes (for example, more pronounced changes in length and

width compared to thickness) may be associated with anatomical limitations of the gland bed and the peculiarities of parenchymal distribution in the fascial spaces of the submandibular region. The obtained relationship between gland volume and gender may reflect both differences in hormonal levels and soft tissue composition, and potential differences in the thresholds of clinical manifestation of acromegaly, when tissue changes in men become more noticeable with a shorter duration of the disease. The association with the duration of the disease, in turn, is not necessarily linear: in the early stages, a faster increasing tissue reaction is possible, whereas with a prolonged course relatively stable morphological changes are formed, and the contribution of concomitant factors (age, therapy, comorbidity) may increase. A qualitative assessment of the echostructure, where some patients showed structural changes, may reflect the heterogeneity of the process, from predominantly diffuse hypertrophy to a combination of hypertrophy with parenchymal remodelling sites. From a practical standpoint, this emphasises the need to interpret the ultrasound picture in a clinical context and avoid unambiguous conclusions based on a single feature, based on a combination of morphometric and qualitative characteristics.

The study had a number of limitations. The study was performed in one centre and included a relatively small sample, which limited the external validity of the results. The design was cross-sectional, so the identified connections should be interpreted as associations rather than causal relationships. Ultrasound assessment of the salivary glands is an operator-dependent technique; no separate quantitative assessment of the reproducibility of measurements was carried out in the framework of this work. In addition, the analysis focused on morphometric parameters and qualitative echostructure without evaluating the functional parameters of salivation, which limits the interpretation of the clinical consequences of the identified changes.

Conclusions

Acromegaly, accompanied by a chronic excess of growth hormone, leads to multiple morphological changes, including generalised organomegaly and maxillofacial manifestations. The present study shows that in patients with active acromegaly, the submandibular salivary glands are larger in volume than in healthy individuals of comparable gender and age (by about 40%). The increase in the volume of the glands is mainly due to an increase in length and width while maintaining a comparable thickness, which reflects the anatomical limitations of growth in the confined space of the bottom of the oral cavity. The volume of salivary glands is associated with the gender and duration of the disease: in men and with a shorter duration of the disease, the increase is more pronounced, whereas in women and with a prolonged course, the degree of hypertrophy

is somewhat lower. There was a tendency to a smaller salivary gland volume in patients with concomitant hyperprolactinaemia, which may be conditioned by the specifics of the hormonal profile in somatotrophic adenomas. In the range of values of active acromegaly, there was no direct relationship between the size of the salivary glands and the levels of growth hormone and insulin-like growth factor-1, which indicates a possible threshold effect and the role of individual characteristics of the tissue response.

The results obtained expand the understanding of the systemic manifestations of acromegaly, complementing the list of changes that form the phenotype of the disease, hypertrophy of the salivary and lacrimal glands. Ultrasound assessment of the size of salivary glands can be considered as an additional method for quantifying morphological changes and dynamic monitoring of patients with acromegaly. Further research is required to assess the reversibility of salivary gland

hyperplasia following long-term effective treatment and to investigate the functional consequences of changes in gland volume on salivation and oral health. Interdisciplinary collaboration between endocrinologists and dental specialists remains an important prerequisite for early diagnosis and comprehensive management of patients with acromegaly.

Acknowledgements

The authors would like to thank their colleagues from the Endocrinology Department at MONIKA for their assistance in recruiting patients.

Funding

None.

Conflict of Interest

None.

References

- [1] Dedov II, Mel'nichenko GA, eds. [Endocrinology. Russian clinical guidelines](#). Moscow: GEOTAR-Media; 2021. 1112 P.
- [2] Melmed S. Acromegaly pathogenesis and treatment. *J Clin Invest*. 2009;119(11):3189–202. [DOI: 10.1172/JCI39375](#)
- [3] Colao A, Grasso LFS, Giustina A, Melmed S, Chanson P, Pereira AM, et al. Acromegaly. *Nat Rev Dis Primers*. 2019;5(1):20. [DOI: 10.1038/s41572-019-0071-6](#)
- [4] Ribeiro-Oliveira A, Barkan A. The changing face of acromegaly – advances in diagnosis and treatment. *Nat Rev Endocrinol*. 2012;8(10):605–11. [DOI: 10.1038/nrendo.2012.101](#).
- [5] Petrossians P, Daly AF, Natchev E, Maione L, Blijdorp K, Sahnoun-Fathallah M, et al. Acromegaly at diagnosis in 3173 patients from the Liège Acromegaly Survey (LAS) database. *Endocr Relat Cancer*. 2017;24(10):505–18. [DOI: 10.1530/ERC-17-0253](#)
- [6] Katznelson L, Laws ER Jr, Melmed S, Molitch ME, Murad MH, Utz A, et al. Endocrine Society. Acromegaly: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(11):3933–51. [doi:10.1210/jc.2014-2700](#)
- [7] Kutti Sridharan G, Rokkam VR. Macroglossia. In: [StatPearls \[Internet\]](#). Treasure Island: StatPearls Publishing.
- [8] Afanas'ev VV, Zairat'yants OV, Kalinchenko SYu, Stepanenko RS. [Correlation of salivary and genital glands. An experimental study](#). *Stomatologiya (Mosk)*. 2012;91(6):12–5.
- [9] Abbey LM, Witorsch RJ. Prolactin binding in normal human minor salivary gland tissue: An immunohistochemical study. *Oral Surg Oral Med Oral Pathol*. 1984;58(6):682–7. [DOI: 10.1016/0030-4220\(84\)90034-3](#)
- [10] Steinfeld S, Rommes S, François C, Decaestecker C, Maho A, Appelboom T, et al. Big prolactin 60 kDa is overexpressed in salivary glandular epithelial cells from patients with Sjögren's syndrome. *Lab Invest*. 2000;80(2):239–47. [DOI: 10.1038/labinvest.3780027](#)
- [11] Mandel L, Zeng Q, Silberthau KR. Parotid gland enlargement in acromegaly: A case report of this rare finding. *J Oral Maxillofac Surg*. 2020;78(4):564–7. [DOI: 10.1016/j.joms.2019.12.001](#)
- [12] Mergen B, Arici C, Kizilkilic O, Tanriover N, Kadioglu P. Lacrimal gland enlargement and tear film changes in acromegaly patients: A controlled study. *Growth Horm IGF Res*. 2021;59:101397. [DOI: 10.1016/j.ghir.2021.101397](#)
- [13] Manetti L, Bogazzi F, Brogioni S, Grasso L, Lupi I, Genovesi M, et al. Submandibular salivary gland volume is increased in patients with acromegaly. *Clin Endocrinol (Oxf)*. 2002;57(1):97–100. [DOI: 10.1046/j.1365-2265.2002.01576.x](#)
- [14] Zajkowski P, Ochal-Choińska A. Standards for the assessment of salivary glands – an update. *J Ultrason*. 2016;16(65):175–90. [DOI: 10.15557/jou.2016.0019](#)
- [15] Bogusławska A, Gilis-Januszevska A, Godlewska M, Nowak A, Starzyk J, Hubalewska-Dydejczyk A. Sex and age differences among patients with acromegaly. *Pol Arch Intern Med*. 2022;132(6):16232. [DOI: 10.20452/pamw.16232](#)
- [16] Campelo RC, Benatti BB, de Sousa JAB, Nascimento GC, Azulay SS, dos Faria MS, et al. Clinical factors associated with salivary flow rate in adults with acromegaly. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2024;138(6):735–44. [DOI: 10.1016/j.oooo.2024.08.009](#)
- [17] Başçıl S, Turhan İyidir Ö, Bayraktar N, Ertörer ME, Başçıl Tütüncü N. Severe chronic periodontitis is not common in acromegaly: Potential protective role of gingival BMP-2. *Turk J Med Sci*. 2021;51(3):1172–8. [DOI: 10.3906/sag-2006-93](#)
- [18] De Stefani A, Dassie F, Wennberg A, Preo G, Muneratto A, Fabris R, et al. Oral manifestations and maxillo-facial features in the acromegalic patient: A literature review. *J Clin Med*. 2022;11(4):1092. [DOI: 10.3390/JCM11041092](#)

- [19] Wiśniewska B, Piekarski K, Spychała S, Golusińska-Kardach E, Stelmachowska-Banaś M, Wyganowska-Świątkowska M. Collaboration between endocrinologists and dentists in the care of patients with acromegaly – a narrative review. J Clin Med. 2025;14(15):5511. DOI: 10.3390/jcm14155511
- [20] Preo G, De Stefani A, Dassie F, Wennberg A, Vettor R, Maffei P, et al. The role of the dentist and orthodontist in recognizing oro-facial manifestations of acromegaly: A questionnaire-based study. Pituitary. 2022;25(1):159–66. DOI: 10.1007/s11102-021-01183-y

Оценка состояния слюнных желез методом ультразвуковой диагностики у больных акромегалией

Эмир Эфендиев

Аспирант

Московский областной научно-исследовательский клинический институт имени М.Ф. Владимирского
129110, ул. Щепкина, 61/2, г. Москва, Российская Федерация
<https://orcid.org/0000-0002-5276-3873>

Малкан Амхадова

Доктор медицинских наук, профессор

Московский областной научно-исследовательский клинический институт имени М.Ф. Владимирского
129110, ул. Щепкина, 61/2, г. Москва, Российская Федерация
<https://orcid.org/0000-0002-9105-0796>

Анна Сизова

Кандидат медицинских наук, ассистент

Федеральное государственное бюджетное образовательное учреждение
высшего образования «Российский университет медицины»
Министерства здравоохранения Российской Федерации
127006, ул. Долгоруковская, 4, г. Москва, Российская Федерация
<https://orcid.org/0000-0002-1592-7584>

Аннотация. Акромегалия – это хроническое нейроэндокринное заболевание, обусловленное длительной гиперсекрецией гормона роста и инсулиноподобного фактора роста-1 и приводящее к системной гипертрофии мягких тканей, при этом состояние слюнных желез изучено недостаточно. Цель исследования состояла в том, чтобы сравнить размеры поднижнечелюстных слюнных желез по данным ультразвукового исследования у пациентов с активной акромегалией и у сопоставимых по возрасту и полу здоровых лиц, а также выявить клиникобиохимические факторы, ассоциированные с объемом желез. В проспективное сравнительное исследование включены 27 пациентов с активной акромегалией и 26 здоровых добровольцев. Всем выполнено ультразвуковое исследование поднижнечелюстных желез с измерением длины, ширины и толщины каждой железы и расчетом объема. У пациентов дополнительно оценивались возраст, длительность симптомов, индекс инсулиноподобного фактора роста-1, наличие гиперпролактинемии и экзоструктуру паренхимы. У пациентов с акромегалией медианный объем правой железы был выше, чем у здоровых (10,0 против 6,3 см³), как и объем левой (8,8 против 7,0 см³; $p < 0,01$ для обеих), при достоверном увеличении длины и ширины и отсутствии различий по толщине. Объем желез отрицательно ассоциировался с возрастом и длительностью симптомов, был выше у мужчин и имел тенденцию к снижению при гиперпролактинемии; независимыми предикторами объема оказались мужской пол и длительность симптомов. Акромегалия сопровождалась выраженной гипертрофией поднижнечелюстных слюнных желез преимущественно за счет увеличения длины и ширины, что позволяет рассматривать ультразвуковую оценку этих желез как дополнительный неинвазивный маркер тканевого ответа при акромегалии

Ключевые слова: поднижнечелюстные слюнные железы; ультразвуковое исследование; объем слюнных желез; инсулиноподобный фактор роста-1; гиперпролактинемия

Введение

Акромегалия – хроническое нейроэндокринное заболевание, обусловленное длительной гиперсекрецией гормона роста (ГР) аденомой гипофиза с последующим повышением уровня инсулиноподобного фактора роста-1 (ИФР-1) и активацией

оси ГР/ИФР-1 [1-3]. Избыточная секреция ГР/ИФР-1 приводит к прогрессирующей гипертрофии мягких тканей, увеличению внутренних органов и ремоделированию костей с формированием системных осложнений [2,3]. Для заболевания