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Cardiac Findings on Non-Contrast Thoracic Tomography in Patients with Acromegaly

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Abstract

Aim: Acromegaly occurs as a result of excessive and permanent secretion of growth hormone from the pituitary. Mortality is mostly related to cardiovascular system involvement. In our study, we aimed to evaluate the correlation between epicardial fat volume (EFV) and growth hormone level in thorax computed tomography in patients with acromegaly and coronary artery calcification, pulmonary artery diameter, ascending aorta diameter, cardiothoracic ratio (CTO) measurements with the control group patients.

Method: Our study was retrospective and included 16 patients with acromegaly who were previously diagnosed and treated by the endocrinology clinic and a control group consisting of 32 patients matched for gender and age.In thorax CT, EFV measurement of the patients was performed and main pulmonary artery diameters, ascending aorta diameters, cardio thoracic ratios, presence of coronary artery calcification were evaluated.

Results: The number of patients with large ascending aorta was higher in patients with acromegaly and it was statistically significant (p=0.041). Although the rate of patients with large main pulmonary artery diameter was higher in patients with acromegaly, no significant difference was found between the groups (p=0.355). There was no significant difference between the groups in terms of increased CTO (p=0.818) and coronary artery calcification (p=0.157).

Conclusion: In our study, a difference was found between the acromegaly and control group patients only in terms of ascending aorta diameters, but no significant difference was found in terms of other parameters. We think that regular follow-up and treatment of patients is effective in this result. Cardiovascular risks can be reduced in patients with acromegaly with early diagnosis, regular follow-up and treatment.

Keywords: Acromegaly, growth hormone, tomography, heart

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Akromegali Hastalarında Kontrastsız Toraks Tomografisinde Kardiyak Bulgular

Öz

Amaç: Akromegali hipofizdenbüyüme hormonunun aşırı ve kalıcı olarak salgılanması sonucu oluşur. Mortalite en çok kardiyovasküler sistem tutulumuna bağlıdır. Çalışmamızda akromegali hastalarında Toraks Bilgisayarlı Tomografi(BT) 'de epikardiyal yağ volümü (EYV) ile büyüme hormonu düzeyi arasındaki korelasyonu değerlendirmeyi vekoroner arter kalsifikasyonu, pulmoner arter çapı, çıkan aorta çapı, kardiotorasik oran (KTO) ölçümlerini kontrol grubu hastaları ile karşılaştırmayı amaçladık.

Yöntemler: Araştırmamız retrospektif olup daha önce endokrinoloji kliniği tarafından tanı alan ve tedavisi devam eden 16 akromegali hastası ilecinsiyet, yaş olarak eşleştirilmiş, 32 hastadan oluşan kontrol grubu dahil edildi. Toraks BT de hastaların EYV ölçümü yapıldı ve ana pulmoner arter çapları, çıkan aorta çapları, kardiotorasik oranları, koroner arter kalsifikasyon varlığı değerlendirildi.

Bulgular: Akromegali hastalarında çıkan aortası geniş olanların sayısı daha fazlaydı ve istatistiksel olarak anlamlıydı (p=0,041). Akromegali hastalarında ana pulmoner arter çapı geniş olanların oranı daha fazla olmakla birlikte gruplar arasında anlamlı farklılık saptanmadı (p=0,355). KTO artışı(p=0,818) ve koroner arter kalsifikasyonu görülmesi açısından gruplar arasında anlamlı farklılık saptanmadı (p=0,157) .

Sonuç: Çalışmamızda akromegali ve kontrol grubu hastaları arasında sadece çıkan aort çapları açısından farklılık saptanmış olup diğer parametreler açısından anlamlı farklılık saptanmadı. Hastaların düzenli takip ve tedavilerinin yapılmasının bu sonuçta etkili olduğunu düşünüyoruz. Erken aşamada tanı konulması, düzenli takip ve tedavi ile akromegali hastalarında kardiovasküler riskler azaltılabilir.

Anahtar kelimeler: Akromegali, büyüme hormonu, tomografi, kalp.

INTRODUCTION

Acromegaly is a rare and underdiagnosed disease that develops due to adenoma caused by pituitary gland cells that secrete growth hormone (GH).Insulin-likegrowth factor1(IGF-1) is overproduced as a result of GH hypersecretion, which causes multi system disease distinguished by somatic enlargement, numerous comorbidities, physical deformity, and higher mortality[1]. The occurrence of acromegaly is mostly associated with systemic comorbidities or local tumor effects. Rheumatological, metabolic, neurological, neoplastic, respiratory, and cardiovascular effects that negatively affect the quality of life determine the prognosis of the disease[2]. Cardiovascular complications of acromegaly; hypertension, cardiac arrhythmia, coronary artery disease, cardiomyopathy characterized by decreased diastolic function and cardiac output with exercise in early and advanced stages, and advanced congestive heart failure with dilated cardiomyopathy in more advanced stages[3,4].

Imaging methods such as echocardiography, angiography, and scintigraphy can be used to determine cardiovascular risk. Some cardiovascular risk findings can also be identified with thorax computed tomography (CT). The aim of this research was to make a comparison between the coronary artery calcification, pulmonary artery diameter, ascending aorta diameter, cardiothoracic ratio (CTO) measurements on thorax CT in acromegalic patients with the control group. In addition, it was also aimed to evaluate relationship between growth hormone levels and epicardial fat volume (EFV) in patients with acromegaly.

METHODS

Our study is retrospective and the results of thorax computed tomography (CT)scan for any reason in patients with acromegaly >18 years of

age, who were previously diagnosed and treated by the endocrinology clinic in Malatya TurgutOzal University Training and Research Hospital between January 2020 and December 2021, were listed on the data processing system. There were 16 patients with acromegaly who had a thorax CT scan, and all of these patients were included in the research. All examinations were obtained without contrast. A control group consisting of 32 patients who were randomly matched for acromegaly and gender and age, was formed from patients over 18 years of age who had no contrast-free thorax CT for any reason, and who did not have lung, cardiovascular or vascular disease.

Images of the patients were obtained with 128-slice multidetector CT. (Philips Medical System 128- Slice Multidetector. Koninklijke Philips N.V. Eindhoven, the Netherlands and GE Healthcare 128-Slice Multidetector Chicago, Illinois).The tube voltage was 110 kV and the section thickness was 5 mm. CT images were evaluated retrospectively by the radiologist from the hospital imaging archive system, without knowing whether the patient had acromegaly or not. In thorax CT, the main pulmonary artery diameters, ascending aorta diameters, cardio thoracic ratios, presence of coronary artery calcification were evaluated. In addition, EFV of patients with acromegaly was measured. The diameter of the main pulmonary artery ≥29 mm and the diameter of the ascending aorta >40 mm were considered as enlargement[5-6]. Epicardial fat volume was calculated with the 3D volume method in the CT viewer software on the workstation. Its value is given in cc. The clinical and laboratory results of the patients were obtained from the hospital data processing system. This retrospective research was carried out in compliance with the Declaration of Helsinki's guiding principles and authorized by the Malatya TurgutÖzal University Clinic Ethics Committee (approval no: 2022/24).

Statistical Analysis

SPSS 22.0 (Statistical Package for the Social Sciences) was employed for statistical analysis (IBMCorp. Armonk, NY, USA). All data were expressed as mean ± standard deviation or number (percent). The means of the groups were compared with the t-test. Thorax CT findings were categorized and chi-square test was used to compare groups. Spearman correlation test was used to evaluate the correlation. A p value less than 0.05 was assumed statistically significant.

RESULTS

The age of participants ranged from 28 to 79 years, with an average age of 52.9±11.9. Thirty (62.5%) of the participants were women. The disease duration of the participants with acromegaly was between 1 and 25 years and the mean was 10.0±8.3. Growth hormone levels varied from 0.1 to 35.0 ng/mL with an average of 4.1±8.7. Table 1 lists some of the medical and demographic traits of the patients.

If patients with acromegaly and control groups were compared in terms of whether there was an ascending aorta or not, the number of patients with large ascending aorta was higher in acromegaly patients and it was statistically significant (p=0.041).

Table I: Percentages of some demographic and clinical characteristics of the patients and averages.

Feature	Acromegaly patients n(%)	Control group n(%)
Age ± SD	52.8±12.2	52.9±12.0
Woman	10(62.5)	20(62.5)
Male	6(37.5)	12(37.5)
BMI mean ± SD(kg/m^2)	30.2±5.7	28.4±4.8
No additional disease	13(81.3)	20(62.5)
Additional disease(present)	3(18.7)	12(37.5)
Never smoker	12(75.0)	20(62.5)
Exsmoker	1(6.2)	3(9.4)
Current smoker	3(18.8)	9(28.1)

Additional disease: Diabetes mellitus, Hypertension, Hypercholesterolemia;

BMI: Body mass index; n : Number of patients; SD: standard deviation

Although the rate of patients with large main pulmonary artery diameter was higher in patients with acromegaly, no significant difference was found between the samples (p=0.355). There was no significant difference among the samples with respect to CTO increase (p=0.818). Coronary artery calcification was seen in 6(37.5%) of the acromegaly patients and 6 (18.8%) of the control group patients. No significant difference was found between the samples due to the coronary artery calcification (p=0.157) (Table2).

Table II: Comparison of thorax CT findings of individuals with tacromegaly and control group

Feature	Acromegalypatients n(%)	Control group n(%)	Pvalue
Normal Ascending aorta diameter	14(87.5)	32(100)	0.041
Large ascending aorta	2(12,5)	0(0)	
Normal Main PA diameter	13(81.3)	29(90.6)	0.355
IncreasedMain PA diameter	3(18.7)	3(9.4)	
CTO normal	12(75.0)	23(71.9)	0.818
CTO increased	4(25.0)	9(28.1)	
no CAC	10(62.5)	26(81.3)	0.157
CAC present	6(37.5)	6(18.7)	

CTO: cardiothoracic ratio; CAC: Coronary artery calcification;n : Number of patients; ; PA: pulmonary artery ; SD: standard deviation

Epicardial fat volume of patients with acromegaly was 80.8±17.1 cc, and a strong and significant positive correlation was observed between EFV and body mass index in patients with acromegaly (r=0.676 p=0.004). A strong negative correlation was observed between EFV and growth hormone (r=-0.637 p=0.008) (Table3).

Table III: Correlation of epicardial fat volume with body mass index and growth hormone in patients with acromegaly

	r	p
EFV-BMI	0.676	0.004
EFV-growth hormone	-0.637	0.008

BMI: body mass index; EFV: epicardial fat volume; The r and p values were calculated using the Spearman correlation test.

DISCUSSION

Cardiovascular diseases are one of the most common causes of death in individuals diagnosed with acromegaly. Duration of disease, age of patients, abnormal glucose tolerance, arterial hypertension, and elevated serum growth hormone levels are independent causes of cardiovascular mortality in these individuals. End-stage acromegalic cardiomyopathy, also known as congestive heart failure, is typically seen in elderly people with chronic, uncontrolled illness as well as associated metabolic and cardiovascular problems[7]. The relationship between coronaryartery disease and acromegaly appears to be a controversial issue as it appears to be linked to classicalcardiovascularrisk factors rather than GH and IGF-1 overexpression.

There is conflicting evidence as to whether individuals with acromegaly have increased risk of atherosclerosis. According to Cannavo et al.[8], 41% of people with acromegaly were at danger for coronary atherosclerosis, and the risk of coronary heart disease in acromegaly patients was 1.5 times higher than in age/sex matched controls. In addition, Özkan et al.[9] emphasized that procalcitonin can be used as a marker of early atherosclerosis[8]. Colao et al.[10] noted that individuals with acromegaly had significantly more atherogenic alterations according to carotid intima-media thickness. Acromegalic Patients with myocardial infarction had significantly higher total IGF-1 exposure[11]. On the other hand, Boğazzi et al.[12]

showed that the risk of coronary heart disease in acromegaly is lower than in those without. Schöfl et al.[13] from 57 endocrine centers showed that the prevalence of myocardial infarction in patients with acromegaly did not increase compared to the general population. They observed that the incidence of hypertension in individuals with cardiovascular events was higher than those without, and that classical risk factors were among the causes of cardiovascular death, but GH/IGF-1 excessive secretion was not. In our study, we evaluated coronary artery calcification, which is one of the indicators of coronary atherosclerosis. The amount of calcification reflects the extent and chronicity of the disease in the vessel wall[14]. It is known that coronary artery calcification is correlated with coronary atherosclerosis burden[15]. In our study, although patients with acromegaly had a higher rate of coronary artery calcification than the control sample did, there was no statistically significant difference.

The pathophysiology of acromegalic cardiomyopathy is not fully understood, but cardiac myocyte of growth hormone (GH) and insulin-like growth factor-I (IGF-I) appears to be associated with direct effects on. The most typical sign of cardiac involvement in acromegaly is concentric hypertrophy of the left ventricle; other signs are arrhythmias in addition to left ventricular systolic and diastolic dysfunction. Another significant risk factor for the development of cardiac dysfunction in those individuals is heart valve disease, including anomalies in the aortic and mitral valves.

Savage et al.found an increase in the diameter of the aortic root in 1 of 25 acromegaly patients[16]. According to Van der Klaauwu et al.[17], patients with acromegaly have larger sinotubular junction and ascending aortas than healthy controls. In our research, a significant difference was seen between the acromegaly patients and the control group in terms of ascending aorta diameter (p=0.041). The rate of ascending aorta enlargement was higher in patients with acromegaly.

Cardiac space enlargement, diastolic dysfunction, myocardial hypertrophy and enlargement of large vessel diameters are common comorbidities in patients with acromegaly. Increasing BMI with aging correlates significantly with diastolic dysfunction and myocardial hypertrophy. However, a long duration of disease is positively correlated with enlarged large vessel diameters. In the early course of acromegaly, the left ventricular diastolic performance is thought to deteriorated. In addition, systolic malfunction precedes the progressive deterioration of systolic performance and appears to be the cause of secondary heart failure[18-20]. In our research, no significant difference was observed between the acromegaly and control groups with regard to main pulmonary artery diameter and CTO values.

Epicardial fat thickness is clinically associated with abdominal adiposity, coronary artery disease, subclinical associated with atherosclerosis and cardiac morphology. There are limited data on the relationship between epicardial fat and the development of coronary atherosclerosis. In a study conducted in patients with acromegaly, increased epicardial adipose tissue, increased aortic stiffness, decreased aortic width and tension was found[21]. In our study, a positive and significant correlation was observed between epicardial fat volume and body mass index. There is a negative correlation between epicardial fat volume and growth hormone.

There are some limitations in our study. Our first limitation is that our study is retrospective. However, we think that the retrospective nature of our study did not affect the result, since patients with complete clinical data and regular follow-ups were included in our study. To avoid bias in our study, the radiologist who performed the radiological measurements was evaluated

without telling whether the patients had acromegaly or not. Our other limitations are being a single-centered study and relatively low number of enrollees due to the rarity of the disease.

CONCLUSION

In our study, only the diameters of the ascending aorta were found to differ between acromegaly and control group patients, but no significant difference was found in terms of other parameters. In the light of these data, we think that close follow-up is necessary for the development of complications (such as rupture and valve insufficiency) since aortic dilatation is observed more frequently in acromegalic patients. Cardiovascular risks can be reduced in patients with acromegaly with early diagnosis, regular follow-up and treatment.

Note: This study was presented as an oral presentation at the 7th Drug and Treatment Congress/2022.

Ethics Approval: This retrospective study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Malatya TurgutÖzal University Clinic Ethics Committee (approval no: 2022/24).

Conflict of Interest: The authors have no conflict of interest regarding this study.

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