# Evaluation of Cardiovascular Parameters in Acromegalic Patients

## *Akromegalik Hastalarda Kardiyovasküler Parametrelerin Değerlendirilmesi*

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**Abstract**

Both direct action of GH/IGF-1 and secondary cardiovascular risk factors contribute to the development of alterations in cardiac anatomy and function. In the present study we investigated the cardiac involvement in 11 acromegalic patients echocardiographically and compared these measurements with 10 control patients. We also aimed to evaluate the parameters of cardiac structure and function alterations with the duration of disease, blood pressue, plasma GH and IGF-1 levels and HOMA index at the time of diagnosis. Eleven acromegalic patiens with high plasma level of IGF-1 and not suppressible GH level after 75 gr OGTT and 10 healthy controls were enrolled in this study. Insulin sensitivity (IS) was estimated by HOMA index. Cardiovascular parameters were studied with echocardiography using a 2,5-MHZ transducer. Except for aorta root all the structural dimensions of the heart were significantly higher in acromegalic patients than in controls. Left ventricule mass (LVM) index was found significantly higher in acromegalic patients than in controls (z: -1.960 p: 0.050). As a diastolic filling alteration, the rate of mitral early flow velocity (E) to mitral late flow velocity (A) (E/A) was significantly higher in acromegalic patients than in controls (z:-2.446 p: 0.014). No significant correlation was found between LVM index and duration of disease (p: 0.306), blood pressure (p: 0.966 for diastolic blood pressure and p: 0.897 for systolic blood pressure), plasma GH( p: 0.460) and IGF-1 (p: 0.613) levels and HOMA index (p: 0.071). A significant correlation between E/A and systolic blood pressure was observed (r: -0.802 p: 0.017). But no significant correlation was investigated between E/A and the other parameters (for duration of disease p: 0.196, for plasma GH level p: 0.183, for plasma IGF-1 level p: 0.585, for HOMA index p: 0.111). In order to decrease the mortality rate related to cardivascular events, secondary risk factors should be treated beside to normalization of plasma GH/IGF-1 levels. *Turk Jem 2007; 11: 1-6*

**Key words:** Acromegaly, cardiovascular risk factors

**Özet**

GH/IGF1' in direk etkisi ve sekonder kardiyovasküler risk faktörleri, kardiyak anatomi ve fonksiyon bozuklukların gelişmesine sebep olur.

Bu çalışmada akromegali tanısı almış 11 hastanın kardiyak tutulumları ekokardiyografi ile değerlendirildi ve bu ölçümler 10 kişilik kontrol grubu ile karşılaştırıldı.Ayrıca kardiyak yapı ve fonksiyon bozukluklarındaki parametreler ile hastalık süresi, kan basıncı, plazma GH ve IGF-1 düzeyleri ve HOMA indeksi arasındaki ilişki de değerlendirildi.

Yüksek plazma IGF-1 seviyesi ve 75 gr. OGTT ile baskılanamamış GH seviyesi olan 11 akromegali hastası ve 10 sağlıklı kontrol bu çalışmaya alındı. İnsülin duyarlılığı (IS), HOMA indeksi ile belirlendi. Kardiyovasküler parametreler 2,5 MHZ transduserli ekokardiyografi kullanılarak çalışıldı.

Akromegalik hastalarda kontrol grubuna oranla aort kökü haricindeki kalbin tüm yapısal boyutlarında istatistiksel olarak anlamlı bir artış saptandı.Akromegalik hastaların kontrol grubuna göre sol ventrikül kitle (LVM) indeksi anlamlı olarak yüksekti (z:-1.960 p:0.050).

Diyastolik dolum defektinin bir göstergesi olarak, mitral erken akım hızı (E)'nın mitral geç akım hızı(A)' na oranı (E/A); akromegalik hastalarda kontrol grubuna göre anlamlı ölçüde yüksek olarak bulundu (z:-2.446 p:0.014). LVM indeksi ile hastalığın süresi (p:0.306), kan basınsı (diyastolik kan basıncı için p:0.966, sistolik kan basıncı için p:0.897), plazma GH seviyesi (p:0.460), plazma IGF-1 seviyesi (p:0.613) ve HOMA indeksi (p:0.071) arasında anlamlı bir korelasyon bulunamadı. E/A ve sistolik kan basıncı arasında anlamlı bir korelasyon saptandı (r:-0.802 p:0.017) ancak E/A ile diğer parametreler arasında (hastalığın süresi p:0.196, plazma GH seviyesi p:0.183, plazma IGF-1 seviyesi p:0.585, HOMA indeksi p:0.111) anlamlı bir korelasyon gözlenmedi.

Kardiyovasküler olaylara bağlı mortalite oranını azaltmak için sekonder risk faktörleri ile beraber plazma GH/IGF-1 oranlarının normalizasyonu da tedavide yerini almalıdır. *Turk Jem 2007; 11: 1-6*

**Anahtar kelimeler:** Akromegali ve kardiyovasküler risk faktörleri

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## Introduction

The prevalence of acromegaly has been estimated as 40 cases per million patients (1). Acromegaly is associated with increased morbidity and mortality, due to cardiovascular and respiratory complications and malignancy (1-3). Approximately 60% of acromegalic patients die from cardiovascular disease, 25% from respiratory disease, and 15% from malignancies (1). Patients with acromegaly suffer from cardiovascular complications such as biventricular hypertrophy, eccentric hypertrophy and diastolic dysfunction at rest, systolic dysfunction on effort, diastolic heart failure, arrhythmias, hypertension, cardiomyopathy, coronary heart disease, endothelial dysfunction and increased carotid intima media thickness (1, 4). The most common feature is biventricular concentric hypertrophy (5). Overproduction of GH and IGF-1 might contribute to abnormal extra cellular matrix regulation in addition to proinflamatory cytokines like IL-1-b and TNF-a which increase gene expression of matrix metalloproteinases (MMP) (6).

Hyperkinetic left ventricle characterized by increased in contractility and cardiac output is the first stage in the natural history of acromegalic cardiomyopathy. Left ventricular hypertrophy, diastolic filling abnormalities at rest and impaired cardiac performance during physical exercise are diagnosed in the second stage. Valvular heart disease, impaired systolic and diastolic performances with low cardiac output even at rest are seen in the third stage (7).

Age and duration of symptoms are the major determinants of acromegalic cardiopathy (8). However short-term acromegaly can affect the heart. Cardiovascular abnormalities have even observed in a group of acromegalic patients who have short duration of disease (9-11). Acromegaly is associated with other secondary risk factors that increase the risk of cardiovascular diseases such as hypertension, impaired glucose metabolism and reduced insulin sensitivity (1, 3, 12). However some cardiovascular alterations were also revealed in uncomplicated acromegalic patients (10, 11, 13). Therefore the evaluation of cardiac involvement and risk factors are the main points in the follow-up of acromegaly (7).

Cardiac involvement in acromegaly can be assessed by standard X-rays, echocardiography, radionuclide techniques, coronary angiography, twenty-four hours electrocardiogram, Doppler ultrasound of carotid arteries and endothelial function studies. Echocardiography remains the most useful method to detect cardiac disease, especially left ventricular hypertrophy (5). Therefore we evaluated cardiac involvements in acromegalic patients by echocardiography. Moreover the correlations of the cardiovascular parameters with the secondary risk factors were investigated in this study.

## Material and Methods

### Patients and Controls

The protocol of this study was approved by the ethical committee of Dr.Lutfi Kirdar Kartal Training and Research Hospital. Eleven acromegalic patients (3 females and 8 males; mean age: 46.72±12.28 years) admitted to the Endocrine Section of Dr.Lutfi Kirdar Kartal Training and Research Hospital were included in this study. Ten healthy subjects were selected comparable for age, sex and BMI with acromegalic patients. Healthy subjects had no history of any cardiac or endocrine disease.

### Study Design

It is a cross-sectional study of echocardiographic results of acromegalic patients. The diagnosis of acromegaly was made on the basis of plasma GH concentrations (nadir GH) that were not suppressible below 2 ng/ml after 75-g oral glucose tolerance test (15.79±10.97 ng/ml; range: 2.40-35) and high plasma IGF-1 concentrations adjusted for age (1335.85±700.2713 ng/ml; range: 438-3029.50). Basal plasma GH and IGF-1 levels were also measured in the control groups. Neuroradiologic diagnosis with magnetic resonance imaging (MRI) was used to define tumor diameter and invasion.

Blood pressure was measured in the right arm with a mercury sphygmomanometer three times with 15 minutes intervals in a relaxed sitting position of the patients and controls. The average of these three measurements was undertaken. Hypertension was diagnosed in the presence of diastolic blood pressure (DBP) was equal or more than 90 mmHg and/or systolic blood pressure (SBP) was equal or more than 140 mmHg (14) .

OGTT was not performed in the patients with known history of diabetes mellitus. In these patients basal GH level was considered as nadir GH. When fasting plasma glucose was above 126 mg/dl in two measurements or when 2h-after OGTT glucose was 200 mg/dl or more, diabetes mellitus was diagnosed. When 2h-after OGTT glucose was between 126-200 mg/dl, impaired glucose tolerance was diagnosed (15). Insulin sensitivity (IS) was calculated by homeostasis model assessment (HOMA) scores which assess only hepatic insulin sensitivity: fasting serum insulin (microunit/ml) x fasting plasma glucose (milimoles/liter) /22.5 (16). Basal serum cholesterol, triglyceride (TAG) and LDL levels were also evaluated in acromegalic patients and controls.

### Echocardiography

M-mode, two-dimensional, pulsed Doppler echocardiography and segmental motion of the left ventricules were performed with ultrasound system (GEVinomed, Hertan, Norvay) using a 2.5-MHZ transducer. All patients were studied in the left lateral recumbent position after 10-min resting period.

Left atrium (LA) (cm), aorta root (AR) (cm), end diastolic diameter of the left ventricule (EDD) (cm), end systolic diameter of the left ventricule (ESD) (cm), end diastolic volume (EDV), end systolic volume (ESV), interventricular septum (IST) (cm) and posterior wall thickness (LVPWT) (cm) were evaluated on M-mode measurements. Ejection fraction (EF) (EF: EDV-ESV/EDV %) was calculated according to Ouinones method (17). The left ventricule mass (LVM) was calculated using Devereux's Formula (18) according top Penn's convention with the following regression corrected cube formula: LVM: 1.04 [(ISV+EDD+PWT)$^3$-(EDD)$^3$]-14g. LV hypertrophy was diagnosed when LVM values corrected for body surface area (LVMi) were 135g/m$^2$ or more in males and 110 g/m$^2$ or more in females. Fractional shortening (FS %) was obtained by EDD-ESD/EDD X 100 (19).

Pulsed Doppler Echocardiographic measurements provided indexes of ventricular filling derived from mitral flow velocities curves (maximal early diastolic flow velocity; E in m/s and

maximal late diastolic flow velocity; A in m/s), the ratio between E/A curves (normal value >1), aorta flow velocities curve (m/sn), tricuspid flow velocities curve (m/sn) and pulmonary flow velocities curve (m/sn).

Two dimensional echocardiography evaluated abnormalities in the mitral, aorta, tricuspid and pulmonary valves.

**Assays**

Plasma GH concentrations were measured by enzyme linked immunoassay (ELISA) (DRG International, Inc, USA). Plasma IGF-1 level was measured by IRMA (CIS Biointernational, France). Serum insulin concentrations were determined by electrochemi-luminescent immunometric assay (ECLIA) (Roche Diagnostic GmbH, 63298. Mamlein for USA).

**Statistical Analysis**

Computer-assisted data analysis was performed using SPSS for Windows 10.0 program. In addition descriptive statistical methods (mean and standard deviation), Fisher's Chi-square test was used in the comparison of qualitative measurements. Mann Whitney-U test was used to compare two groups. The relationships between the parameters were evaluated by Spearman's correlation analysis. The results were evaluated in 95% confidence interval and $P<0.05$ was considered as significant.

## Results

The mean age was 46.72±12.28 (29-71) in patients and 45.20±9.43 (26-58) in controls. Distribution of the patients' [eight (72.7%) males, three (27.3%) females] were adjustable with controls [eight (80%) males, two (20%) females]. Both acromegalic patients (4; 36.37%) and controls (5; 50%) were characterized by habitual smoking. Mean BMI was 28.01±4.37 (23.70-40.20) kg/m$^2$ in patients and 26.56±2.78 (23.60-32.80) kg/m$^2$ in controls. The duration of acromegaly defined as the interval between the clinical onset and time of the treatment was 10.18 (1-30) years. Four of the acromegalic patients were affected by hypertension in contrast to two of the controls. Mean systolic blood pressure was measured as 148.18±33.11 (90-190) mmHg in acromegalic patients and 113.00±9.48(100-130) mmHg in controls. Mean diastolic blood pressure was measured as 89.54±26.87(50-130) mmHg in acromegalic patients and 76.00±9.66 (60-90) mmHg in controls. No significant difference was found between the groups of acromegalic patients and controls for age, gender, smoking, BMI, diastolic blood pressure and plasma glucose levels. Mean systolic blood pressure was significantly higher in acromegalic patients than in controls (z:-2.814 p: 0.005) (Table 1). Three patients were diagnosed before a long time (10, 20 and 30 years, respectively) prior admission to us. Surgery was undertaken to these patients, but they did not take any medication or radiotherapy after surgery. Disease was persistent in these patients since their nadir GH (13.1, 18, 31.50 ng/ml) and IGF-1 levels were high on the time of admission to us. One patient was also diagnosed before 10 years prior to admission. Octreotide had been given to this patient after surgery and g-knife radiotherapy. Although this patient was under treatment, disease was persistent since their nadir GH was 7.5ng/ml. The other seven patients were diagnosed newly.

Nadir GH level was 15.79±10.97 ng/ml in acromegalic patients whereas mean serum GH level was measured as 0.03 ng/ml in controls. Mean basal serum IGF-1 level was significantly higher in acromegalic patients (1335.85±700.27 ng/ml) than in controls (206.70±65.14 ng/ml) (z:-3.677 p: 0.0001). 75 g OGTT could not be performed in one patients with known history of diabetes mellitus. Diabetes mellitus was diagnosed in three patients from the results of OGTT according the criteria of ADA. Basal IS calculated from HOMA formula was significantly higher in acromegalic patients (3.05±0.84) than in controls (1.95±0.79)

**Table 1. Demographic and clinic characteristics of the acromegalic patients and controls**

| | Patients (11) | Controls(10) | Test value; p |
|---|---|---|---|
| | Mean (Lower-Upper) | Mean (Lower-Upper) | |
| Age(years) | 46.72±12. 28 (29-71) | 45.20±9.43 (26-58) | z: -0.106 p: 0.916 |
| BMI(kg/m$^2$) | 28.01±4.37 (23.70-40.20) | 26.56±2.78 (23.60-32.80) | z: -0.986 p: 0.324 |
| Systolic blood pressure (mmHg) | 148.18±33.11 (90-190) | 113.00±9.48(100-130) | z:-2.814 p: 0.005 |
| Diastolic blood pressure (mmHg) | 89.54±26.87(50-130) | 76.00±9.66(60-90) | z: -1.084 p: 0.278 |
| Basal IGF-1 level (ng/mL) | 1335.85±700.27(438-3029.50) | 206.70±65.14(120-317) | z: -3.677 p: 0. 0001 |
| Basal glucose level (mg/dl) | 109.90±32.21(76-188) | 90.40±9.51(77-106) | z: -1.550 p: 0.121 |
| HOMA index | 3.05±0.84 (1.60-4.30) | 1.95±0.79 (0.96-3.40) | z: -2.613 p: 0.009 |
| Cholesterol (mg/dl) | 175.12±29.05(139-212) | 175.50±40.41(127-260) | z: -0.223 p: 0.824 |
| LDL (mg/dl) | 77.50±29.41(20-113) | 120.38±80.60 (57-332) | z: -1.022 p: 0.307 |
| TAG (mg/dl) | 140.12±86.17 (40-320) | 103.20± 46.88 (50-202) | z: -0.800 p: 0.424 |
| | n (%) | n (%) | |
| Hypertension (+) | 4(36.37%) | 2(20%) | p: 0.635 |
| Gender Females | 3(27,3%) | 2(20%) | p: 1 |
| Males | 8(72,7%) | 8 (80%) | |
| Smoking (+) | 4(36,37%) | 5(50%) | p: 1 |

(z: -2.613 p: 0.009). No significant difference in the serum levels of cholesterol, TAG and LDL between patients and controls (z: -0.223 p: 0.824 for cholesterol, z: -1.022 p: 0.307 for LDL and z: -0.800 p: 0.424 for TAG). Neuroradiologic diagnosis with magnetic resonance imaging (MRI) showed microadenoma in four and macroadenoma in seven of the patients. Evaluation of the visual field was normal in five patients, incomplete bitemporal hemianopia in one patient, peripheric vision loss in the right and the complete loss in the left eye of one patient. Evaluation could not be done in the other four patients because of poor cooperation.

Surgery was not performed in a patient. A secondary surgery was performed in three patients. Octreotide treatment was established in all except two patients who were intolerant to this medication. Radiotherapy was performed in three patients.

Table 2 gives the information about M-mode measurements of morphological changes in the acromegalic patients and controls. Left ventricule hypertrophy was diagnosed in the acromegalic patients, because LVM index ($g/m^2$) was significantly higher in the acromegalic patients (156.67± 62.73$g/m^2$) than in controls (105.55±27.15$g/m^2$) (z: -1.960 p: 0.050). Indexes of ventricular filling derived from mitral flow velocities curves (maximal early diastolic flow velocity; E in m/s and maximal late diastolic flow velocity; A in m/s), the ratio between E/A curves (normal value >1), aorta, tricuspid and pulmonary velocities curves (m/s) evaluated by pulsed Doppler echocardiography were shown in Table 3. The ratio of E/A was also found significantly lower in acromegalic patients than in the controls (z: -2.446 p: 0.014). Systolic cardiac functions in acromegalic patients and controls were presented in Table 4. Although ejection fraction was detected in the normal range, it was significantly lower in acromegalic patients than in controls (z:-2.007 p: 0.045). No significant correlation was found between LVM index and duration of disease (r: 0.385 p: 0.306), blood pressure (r: -0.017 p: 0.966 for diastolic blood pressure and r: 0.050 p: 0.897 for systolic blood pressure), plasma GH (r: 0.283 p: 0.460) and IGF-1 (r: -0.234 p: 0.613) levels and HOMA index (r: 0,714 p: 0,071). A significant correlation was observed between E/A and systolic blood pressure (r: -0.802 p: 0.017). But no significant correlation was investigated between E/A and the other parameters (for duration of disease r: -0.510 p: 0.196, for plasma GH level r: -0.524 p: 0.183, for plasma IGF-1 level r: -0.252 p: 0.585, for HOMA index r: -0.714 p: 0.111).

Two dimensional echocardiography evaluated abnormalities in the mitral, aorta, tricuspid and pulmonary valves. Mitral valve regurgitation was recorded in 5 patients (Trace in 1, mild in 3 and moderate in 1 case). Aorta valve regurgitation was described in only one case in the mild form. Tricuspid valve regurgitation was found in 5 cases in trace form whereas pulmonary valve was normal in all acromegalic patients. In controls only tricuspid valve was involved in three cases, in trace form. Wall movements were involved in only two acromegalic patients whereas they were normal in all of the controls.

## Discussion

Acromegaly is a clinical disorder characterized by GH excess (20). Excess of GH stimulates the growth of various tissues resulting visceromegaly (20, 21). Acromegaly is associated with increased cardiac morbidity and mortality (6). GH/IGF-1 contributes to a specific cardiomyopathy due to its direct effect on cardiomyocytes (12). Beside to its direct action on heart, other factors such as hypertension and insulin resistance could contribute to the increased cardiovascular events in acromegalic patients (1).

**Table 2. Comparison of morphological changes of cardiac involment in acromegalic patients and controls**

| | LVM/gr | | LAD(cm) | | EDD(cm) | | ESD(cm) | | IST(cm) | | PWT(cm) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | Median | Mean | Median | Mean | Median | Mean | Median | Mean | Median | Mean | Median |
| Patients | 156.67± 62.73 | 150.44 | 3.82±0,62 | 3.70 | 5.62±0.95 | 5.6 | 3.70±1.17 | 3.2 | 1.31±0.20 | 1.20 | 1.22±1.16 | 1.20 |
| Controls | 105. 55±27.15 | 108.08 | 2.96±0,45 | 3.05 | 4.85±0.38 | 4.9 | 2.76±0.27 | 2.65 | 0.99±0.13 | 1.00 | 0.98±0.13 | 1.00 |
| Test values | z: -1.960 | p: 0.050 | z: -2.78 | p: 0.005 | z: -2.52 | p: 0.024 | z: -2.33 | p: 0.019 | z: -3.35 | p: 0.001 | Z: -2.97 p: 0.003 | |

**Table 3. Comparison of diastolic cardiac functions in acromegalic patients and controls**

| | Mitral early flow velocities curve E (m/s) | | Mitral late flow velocities curve A (m/s) | | E/A ratio | | Aorta flow velocities curve (m/sn) | | Tricuspid flow velocities curve (m/sn) | | Pulmonary flow velocities curve (m/sn) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | Median | Mean | Median | Mean | Median | Mean | Median | Mean | Median | Mean | Median |
| Patients | 0.53±0.16 | 0.5 | 0.67±0.14 | 0.61 | 0.83±0.28 | 0.82 | 1.25±0.45 | 1.10 | 0.64±0.07 | 0.60 | 0.93±0.11 | 0.90 |
| Controls | 0.81±0.11 | 0.85 | 0.68±1.18 | 0.60 | 1.24±0.27 | 1.18 | 1.23±0.12 | 1.20 | 0.65±0.12 | 0.60 | 0.95± | 0,90 |
| Test values | z: -3.02 | p: 0.002 | z: -0.182 | p: 0.855 | z: -2.446 | p: 0.014 | z: -0.997 | p: 0.319 | z: -0.528 | p: 0.597 | z: -0.593 | p: 0.553 |

**Table 4. Comparison of systolic cardiac functions in acromegalic patients and controls**

| | FS | | EF (%) | |
|---|---|---|---|---|
| | Mean | Median | Mean | Median |
| Patients | 35.42±9.86 | 39.21 | 60.88±14.39 | 65 |
| Controls | 42.91± 5.29 | 43.80 | 72.80±6.25 | 72.5 |
| Test values | z: -1.63 p: 0.102 | z: -2.007 p: 0.045 | | |

At the early stage of disease, functional and morphologic changes related with diastolic dysfunction are observed. Systolic dysfunction occurs at later stage with a long history of disease (22). This study was designed to evaluate cardiac anatomy and function in acromegalic patients echocardiographically as well as insulin resistance as a specific risk factor for cardiovascular disease.

Structural abnormalities induce functional disturbances in acromegaly (22). They involve the alterations in the LVM index, ESD, EDD, LAD, IST and PWT. In this study compared to controls those with acromegaly were found to be affected by cardiac hypertrophy. LVM index, IST and PWT were significantly higher in acromegalic patients than in controls (Table 2). They were also above of normal range (normal ranges: 6-11 mm for IST and 7-11 mm for PWT). Increment in LVM index is an early event which progress with duration of disease in all acromegalic patients (1). Enlargement of IST and PWT have also been reported in acromegalic patients with LVH (3, 6, 21).

In the present study LAD, ESD and EDD were in the upper limit of normal ranges (normal ranges: 1.9-4 cm for LAD, 2.6-4.2 cm for the ESD and 4-5.9 cm for EDD) in consistent with literature (2, 6, 23). Compared to controls these parameters were significantly higher in acromegalic patients (Table 2). However enlargement of LAD and EDD were also described in literature (21, 24, 25). Structural abnormalities which include increment in LAD, ESD and EDD demonstrate dilatation of the heart. In acromegaly cardiac walls are thickened but cardiac chambers are rarely enlarged. They are observed at the terminal stage of acromegalic cardiomyopathy which ends with cardiac failure (7, 22, 24, 25). Thus although these parameters were found in normal range, they might be altered in the advanced stages of disease.

Structural abnormalities induce functional disturbances in acromegaly. The most important functional disturbance of early acromegalic cardiomyopathy is represented by the inadequate filling capacity shown by decreased diastoling filling wave, early to late mitral (E/A) and tricuspid velocity ratio and elongation of isovolumic relaxation time (5, 22). In this study although no significant difference was found in the peak late diastolic mitral velocity (A) between the acromegalic patients and controls, peak early diastolic mitral velocity (E) (m/sn) was significantly lower in the acromegalic patients than in the controls (z: -3.02 p: 0.002). Normally the ratio of E/A should be higher than 1. It was also found significantly lower in acromegalic patients than in controls, consistent with the literature (z: -2.446 p: 0.014) (Table 3). Uncomplicated acromegaly is accompanied by normal systolic function (5, 7, 22). In this study although diastolic function was altered, left ventricular systolic function (ejection fraction and fractional shortening) were normal in acromegalic patients, consistent with literature (Table 4) (2, 20).

Hypertension and diabetes mellitus increase the impact of cardiac alterations (1). Acromegalic patients with hypertension but without abnormalities of glucose tolerance had an increase prevalence of alterations in cardiac morphology and function, whereas patients with glucose tolerance abnormalities but without hypertension had only an increased prevalence of impaired systolic and diastolic function. Acromegalic patients suffering from hypertension and diabetes mellitus had the highest prevalence of LV hypertrophy, diastolic filling abnormalities, and impaired systolic function at rest (3). In this study although no significant correlation was found between LVM index and blood pressure, a significant negative correlation was noticed between the ratio of E/A and systolic blood pressure. A positive correlation was established between LVM index and HOMA index. But it was not found significant (r: 0.71 p: 0.07). The relatively small sample size might be the reason of this discrepancy in the study.

Cardiac valve disease is another component of ventricular dysfunction (7). It is associated with long duration of exposure to increased GH secretion (6). Mild mitral regurgitation was found in 26% of active disease, while mild-moderate regurgitation was found in 31% of active disease (26). In another study significant valve disease was more prevalent in acromegalic patients. Aortic valve regurgitation (≥trace) was present in 30% of patients and mitral regurgitation (≥moderate) was present in 5% of patients (6). In this study significant mitral (moderate, in one case) and aorta valve (mild, in one case) regurgitations were recorded whereas significant pulmonary and tricuspid valves were not described in acromegalic patients. Pathological valvular regurgitation was absent in patients with an estimated disease duration of less than 6 yr, the prevalence of aortic valve regurgitation (mild severity) increased from 12.5% for patients with a disease duration of 6–10 yr to 40% in patients with a disease duration of more than 16 yr. Prevalence of mitral valve regurgitation ( moderate severity) present in 20% of acromegalic patients with a disease duration of more than 16 yr (6). In this study pathological mitral valve regurgitation (moderate severity) was recorded in only one patient with a disease duration of about 30 years and pathological aort valve regurgitation (mild severity) was recorded in the patient with a disease duration of 16 years.

Acromegalic cardiomyopathy is a frequent complication of the disease and indicates a specific need for follow-up. It develops insidiously. Left ventricular diastolic function begins to impair during this subclinical period. So despite normal echocardiographic findings at the early stages, these values should be evaluated in the future visits. Moreover secondary risk factors should be diagnosed and treated in the early or late stages of the disease.

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## "A Note from the Editor-in-Chief"

"High Prevalence of Thyroid Dysfunction and Autoimmune Thyroiditis in Adolescents after Elimination of Iodine Deficiency in Eastern Black Sea Region of Turkey" by Emral R, Bastemir M, Erdoğan G, Gullu S, published in the January 2006 issue of The Turkish Journal of Endocrinology and Metabolism is withdrawn from the journal because of duplicate publication. Therefore this manuscript should not be not be included in the publications lists of the authors and should not be used for citation purposes.