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Assessment of right ventricular functions in acromegaly: comparison of active disease with remission

Aim	Cardiac involvement in acromegaly is defined as acromegalic cardiomyopathy, an insidious and chronic disease. Previous research on acromegalic cardiomyopathy was largely focused on morphological and functional assessment of the left heart. Since the literature data regarding right heart function in acromegalic patients are limited, we aimed to evaluate the structure and function of the right heart in such patients.
Material and Methods	We included 43 adult participants as the acromegaly group and 42 individuals as the control group. All patients underwent echocardiographic evaluation. The results were compared between acromegaly and control groups and between active and controlled acromegaly groups.
Results	The acromegaly group had increased interventricular septum thickness, right ventricular (RV) free wall thickness, right atrium (RA) minor diameter, RV basal and longitudinal diameters, RV end-diastolic and end-systolic areas, E/E' ratio, isovolumetric relaxation time, and RV ejection time. The E/A ratio and E' velocity were reduced. GH and IGF-1 were positively correlated with RV longitudinal diameter, indexed RA minor-axis dimension, and indexed RV end-diastolic area. Patients with active acromegaly had increased RV index of myocardial performance (RVIMP) and isovolumetric contraction time and shortened RV ejection time compared to patients in remission. A RVIMP value of 0.435 predicted active acromegaly with a sensitivity and specificity of 0.83 and 0.64, respectively (p=0.002).
Conclusions	Increases in the size and diameters of the right heart chambers along with RV free wall thickness may be attributed to acromegalic cardiomyopathy. RVIMP, isovolumetric contraction time, and ejection time are parameters that can be used in the evaluation of active acromegaly disease.

Keywords	Acromegaly; right heart, function
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Introduction

Acromegaly is a chronic, multisystemic disease characterized by subtle and slow progression. The prevalence and incidence of acromegaly, a relatively rare disease, varies from 28 to 137 cases per million population in different races and from 2 to 11 cases per million population in different populations [1]. The fundamental disorder in patients with acromegaly is an abnormal increase in serum concentrations of growth hormone (GH), mostly secreted from the adenoma of the pituitary gland, and insulin-like growth factor (IGF-1). Long-term exposure to high GH/IGF-1 concentrations leads to impairment of the cardiovascular system. This condition is defined as acromegalic cardiomyopathy, and it is an important cause of mortality and morbidity in acromegalic patients [2]. Moreover, if cardiovascular disease is present at the time of diagnosis, the mortality rate can reach up to 100% within the following 15 yrs [2]. Morbidity and mortality rates are higher in patients with active acromegaly, in which high serum hormone concentrations have not been controlled by surgery or medical treatment, than in the general population [3]. Although the incidence of hypertension, valvular heart disease, and arrhythmia increases in patients with acromegaly, acromegalic cardiomyopathy is typically manifested as biventricular hypertrophy, myocardial fibrosis, and diastolic dysfunction [4].

In the early stages of the cardiac involvement associated with acromegaly, a hyperdynamic circulatory condition is evident with increased cardiac contractility and output. Biventricular concentric hypertrophy and diastolic dysfunction develop over time in untreated cases. In the last stage of acromegalic cardiomyopathy, systolic function

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becomes impaired, and patients in the terminal stage of acromegalic cardiomyopathy experience congestive heart failure and its complications [5]. Abnormalities, such as left ventricular (LV) hypertrophy and diastolic dysfunction that occur at an early stage of acromegalic cardiomyopathy can be restored by inhibition of the GH/IGF-1 axis [6] Therefore, early recognition of acromegalic cardiomyopathy and initiation of treatment are paramount in preventing complications and reducing mortality [2].

The right ventricle (RV), which develops embryologically from the bulbus cordis, differs from the left ventricle owing to its thinner wall thickness and crescent-shaped structure [7]. Moreover, the cardiomyocytes of the RV are approximately 15% smaller than those of the left ventricle. The RV contains 30% more collagen, but its compliance is greater than that of the left ventricle [8] In addition, the RV differs from the left ventricle by its greater longitudinal systolic contraction in its response to increased preload/afterload [9].

Although many studies have described derangements of the left heart structure and function in acromegalic cardiomyopathy, the effect of the disease on the right heart has not been adequately elucidated. Thus, we investigated the effect of acromegaly on the structure and functions of the right heart.

Material and Methods

Study Population

This cross-sectional, case-control study involved 85 participants that were divided into an acromegaly group of 43 acromegalic patients and a control group of 42 subjects with normal serum IGF-1 and GH. Patients with atrial fibrillation, arrhythmias, moderate/severe valvular disease, heart failure, ischemic heart disease, thyroid dysfunction, and renal and/or hepatic insufficiency were excluded from the study. Acromegaly was diagnosed according to published guidelines [10], presence of the typical clinical and radiological characteristics, and nonsuppressed serum GH and high serum IGF-1 among patients treated in the department of endocrinology in our institution. The control group was consisted of healthy participants who were matched to acromegalic patients in terms of age, sex, and comorbidities.

Body mass index (BMI) was calculated as body weight (kg) divided by height (m) 2. Body surface area (BSA) was estimated with Mosteller's formula [11]. At the final visit, acromegaly disease activity was assessed in accordance with the Acromegaly Consensus Group guidelines [12]. Blood pressure of all patients was measured at least 15 min before echocardiographic examination. Glomerular filtration rate (GFR) and hemoglobin values obtained at the patients' last hospital visits were extracted from the hospital's registration system. If the patients had random age adjusted GH value higher than 1 ng/ml or higher than 0.4 ng/ml after an oral glucose tolerance test (OGTT), they were identified as having active acromegaly disease. Likewise, if they had age adjusted GH value less than 1 ng/ml or less than 0.4 ng/ml after OGTT, they were considered in remission.

IGF-1 concentrations were assessed using a solid-phase, enzyme-labeled chemiluminescense immunoassay that had intra- and inter-coefficients of variation (CV) of 3.1% and 6.6%, respectively (Immulite 2000, Siemens Healthcare Diagnostics). GH concentrations were measured by using a two-step chemiluminescense immunoassay that had intra- and inter-assay CV of 3.7% and 6.2%, respectively (Immulite 2000, Siemens Healthcare Diagnostics). The system had sensitivity of 0.01 g/l. IGF-1 concentrations were adjusted according to the upper limit of the reference interval (ULR). If the patient had a IGF-1 to ULR ratio less than one, the patient was considered as having a normal IGF-1 value.

Echocardiographic Examination

All echocardiographic examinations were carried out by two cardiologists who were blinded to the patients' clinical status. All patients underwent echocardiographic examinations with a Vivid 9 device using a sector transducer of 3.2 MHz (GE Medical systems, Horten, Norway). Echocardiographic assessments were in compliance with current guidelines [13].

The modified Simpson's method was used to assess LV ejection fraction. LV volumes were quantified from apical four- and two-chamber views. Left atrial and LV linear internal measurements and septal, posterior wall measurements were performed in the parasternal long-axis view using M-mode echocardiography. Right atrium (RA) internal sizes were delineated from the apical four-chamber view. Longitudinal and transverse dimensions of the RV and right ventricular end-diastolic and end-systolic areas were measured from a RV-focused 4 chamber apical view. The RV fractional area change (FAC) was estimated from the formula: 100 × end systolic area (ESA)/end diastolic area (EDA). The right ventricular free wall (RVFW) thickness was measured just below the tricuspid annulus at end-diastole. Tricuspid annular plane systolic excursion (TAPSE) was assessed by M-mode echocardiography, which measures the longitudinal excursion of the tricuspid annulus between end-diastole and peak-systole. Tricuspid annular tissue and lateral wall velocities were obtained from RV-focused apical view by using pulsed-wave Doppler. Isovolumetric contraction time (IVCT), ejection time (ET), and isovolumetric relaxation time (IVRT) intervals were measured. The RV index of myocardial performance (RIMP) was estimated from IVCT + IVRT/ET. Peak velocity of the tricuspid regurgitant jet was used to estimate

Table 1. Comparisons of demographic and clinical data between the two groups

Variable	Acromegaly Group	Control Group	p
Age (yrs)	46.5±13.1	49.8±12.9	0.244
Sex Female Male	 31 (72.1%) 12 (27.9%)	 28 (66.7%) 14 (33.3%)	0.587
CAD	2 (4.7%)	2 (4.8%)	1.000
Hypertension	13 (30.2%)	6 (14.3%)	0.078
Diabetes mellitus	9 (20.9%)	11 (26.2%)	0.568
BMI (kg/m²)	29.1±4.3	29.0±9.5	0.318
BSA (m²)	1.91±0.23	1.83±0.20	0.106
SBP (mmHg)	122.2±18.8	122.3±16.8	0.948
DBP (mmHg)	83.3±11.2	80.3±10.6	0.599
GFR (ml/min),	107.2±21.9	93.1±20.6	0.802
Hemoglobin (g/dl)	12.8±1.5	13.7±1.1	0.137
Growth Hormone (ng/ml)	2.69±3.82	1.33±2.50	<0.001
IGF-1 (ULN)	1.02±0.58	0.53±0.13	<0.001

Data are number (percentage) or mean±standard deviation.
BMI, body mass index; BSA, body surface area; CAD, coronary artery disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; GFR, glomerular filtration rate; IGF-1, insulin-like growth factor-1; ULN, upper limit of normal.

peak pulmonary artery pressure (PAP), taking into account the RA pressure. The diastolic functions of RV were evaluated on the basis of the following parameters: 1) tricuspid lateral annulus tissue Doppler early diastolic velocity' (E', cm/s); 2) ratio of tricuspid E-wave velocity to tricuspid E' velocity (E/E'); 3) ratio of tricuspid E-wave velocity to tricuspid A-wave velocity (E/A). At the beginning of the study, the inter- (4%) and intra-observer variabilities (2%) were tested in a sample group of 8 patients in the acromegaly and in 8 patients in the control group).

The local ethics committee approved the study (protocol number 2020/106, dated 16/03/2020), and the study was performed in compliance with the principles of the Declaration of Helsinki. All subjects gave written informed consent to participate.

Statistical Analysis

The data were analyzed with the IBM Statistical Package for the Social Sciences (SPSS, version 23). Categorical variables were expressed as number and percentage, and numerical variables were expressed as mean ± standard deviation. The normality of the distribution of quantitative variables was evaluated with the Kolmogorov–Smirnov test. Two independent groups were compared with the Student t test for parametric variables or with the Mann–Whitney U test for nonparametric variables. Categorical variables were compared using the Pearson chi-square test. Receiver operating characteristic curve (ROC) analysis was used to evaluate RIMP values for predicting active acromegaly. Correlations of echocardiographic parameters with hormone levels were examined with Spearman correlation analysis. Variables with two-tail p-values <0.05 were considered statistically significant.

Results

Forty-three patients (50.6%) diagnosed with acromegaly constituted the "Acromegaly group" and 42 patients (49.4%) with normal serum GH and IGF-1 levels constituted the "control group". Clinical variables of the groups are depicted in Table 1. Average age of all the participants included in the study was 48.1±13 yrs (range, 23–76 yrs). Of the subjects, 59 (69.4%) were women, 4 (4.7%) had coronary artery disease, 19 (22.4%) had hypertension, and 20 (23.5%) had diabetes mellitus. The two groups did not differ with respect to the demographic and clinical variables. Mean GH value was 2.02±3.29 ng/ml (range, 0.05–22.00 ng/ml), and mean IGF-1 was 0.78±0.49 ULN (range, 0.28–2.67 ULN) for all the study participants. Both the GH

Table 2. Comparison of acromegaly and control groups

Variable	Acromegaly Group	Control Group	p
LVEF (%)	60.3±2.5	61.0±4.3	0.081
LVEDD (mm)	47.7±4.5	46.5±4.1	0.419
IVS (mm)	12.0±1.2	9.5±1.2	<0.001
PW (mm)	11.2±1.0	9.1±1.0	<0.001
LA AP (mm)	39.1±3.5	33.5±4.3	<0.001
RVFW (mm)	8.1±2.1	4.3±1.2	<0.001
RA minor-axis dimension (mm/m²)	20.6±2.7	17.5±3.7	<0.001
RV BD (mm)	38.2±5.3	34.5±5.8	0.003
RV LD (mm)	6.2±0.9	5.3±0.7	<0.001
RV EDA indexed to BSA (cm²/m²)	9.8±1.9	8.1±1.5	<0.001
RV ESA indexed to BSA (cm²/m²)	5.3±1.2	4.6±0.8	<0.014
RV FAC (%)	45.4±6.5	44.1±4.5	0.824
TAPSE (mm)	22.3±2.1	22.7±2.9	0.836
Peak PAP (mmHg)	28.8±6.4	27.0±4.6	0.549
E/A	0.68±0.12	1.36±0.47	<0.001
E'Lat (cm/s)	5.6±1.4	8.1±1.6	<0.001
E/E'	10.7±3.3	4.4±0.9	<0.001
RV ET (msec)	308.8±29.2	278.2±34.7	<0.001
RV IVCT (msec)	63.4±20.5	62.3±12.2	0.857
RV IVRT (msec)	83.3±19.0	62.0±12.2	<0.001
RIMP	0.47±0.10	0.45±0.09	0.276

Data are mean±standard deviation LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LA AP, left atrial anteroposterior diameter; IVS, interventricular septum; LA, left atrium; RVFW, right ventricle free wall; RA, right atrium; BSA, body surface area; RV, right ventricle; BD, basal diameter; LD, longitudinal diameter; FAC, fractional area change; EDA, end-diastolic area; ESA, end-systolic area; TAPSE, tricuspid annular plane systolic excursion; PAP, pulmonary artery pressure; RV ET, right ventricular ejection time; RV IVCT, right ventricular isovolumetric contraction time; RV IVRT, right ventricular isovolumetric relaxation time; RIMP, right ventricular index of myocardial performance.

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and IGF-1 concentrations were higher in the acromegalic patients compared to the control subjects (2.69±3.82 ng/ml vs. 1.33±2.50 ng/ml, p<0.001 and 1.02±0.58 ULN vs. 0.53±0.13 ULN, p<0.001, respectively).

A comparison of the groups' echocardiography variables is shown in Table 2. Interventricular septum (IVS) thickness, posterior wall (PW) thickness, LA anteroposterior diameter, RA minor-axis dimension indexed to BSA, RV basal diameter, RV longitudinal diameter, RVFW thickness, RV EDA indexed to BSA, RV ESA indexed to BSA, E/E' ratio, RV ET, and RV IVRT were significantly higher, E/A ratio, E velocity were significantly lower in the patients of the acromegaly group. No significant differences in the other variables were found.

GH was correlated positively with RV IVCT, RV IVRT, RV longitudinal diameter, peak PAP, RIMP, RV fractional area change, indexed RA minor-axis dimension, and indexed RV EDA. GH correlated negatively with the E/A ratio. IGF-1 was correlated positively with IVS, PW, LA, RA diameter, indexed RV minor-axis dimension, RV basal diameter, RV free wall thickness, RV ET, RV IVRT, RV longitudinal diameter, E/E' ratio, indexed RA minor axis dimension, indexed RV EDA, indexed RV ESA indexed to BSA. IGF-1 was correlated negatively with RV ejection fraction and E/A ratio. Tables 4 and 5 show correlations of echocardiographic variables with GH and IGF-1, respectively.

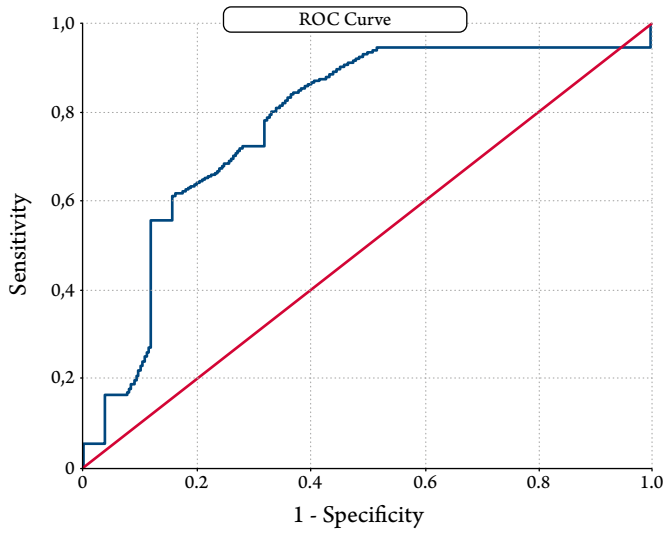
Among the patients with acromegaly group, 18 (41.8%) had active acromegaly, and 25 (58.2%) had controlled acromegaly. Comparisons between the active and controlled acromegaly groups are shown in Table 3. In the active acromegaly group, the mean GH was 4.78±5.14 ng/ml, whereas in the controlled acromegaly group, this value was 1.18±1.11 ng/ml (p<0.001). The IGF-1 concentrations in the active acromegaly group were significantly higher than those in the controlled acromegaly group (1.54±0.56 ULN vs. 0.67±0.24 ULN, p<0.001). RV IVCT and RIMP values were significantly higher in the active acromegaly group, whereas RV ET was significantly higher in the controlled acromegaly group. ROC curve analysis showed that a RIMP value of 0.435 predicted active disease with a sensitivity and specificity of 0.83 and 0.64, respectively (AUC: 0.776, p=0.002, 95% CI: 0.628–0.924; Figure 1).

Table 3. Comparison of active and controlled acromegaly groups

Variable	Active acromegaly	Controlled acromegaly	p
Heart Rate (bpm)	79.20±15.97	75.5±15.37	0.355
GH (ng/ml)	4.78±5.14	1.18±1.11	<0.001
IGF-1 (ULN)	1.54±0.56	0.67±0.24	<0.001
LVEF (%)	60.2±3.1	60.4±2.0	0.923
LVEDD (mm)	47.3±4.9	48.0±4.2	0.474
IVS (mm)	12.3±1.3	11.7±1.1	0.113
PW (mm)	11.4±1.0	11.0±1.0	0.319
LA AP (mm)	39.9±3.9	38.5±3.2	0.428
RA minor-axis dimension (mm/m^2)	21.2±3.0	20.3±2.6	0.423
RV BD (mm)	38.7±5.2	37.8±5.5	0.523
RV LD (mm)	6.3±0.7	6.1±0.9	0.498
RVFW (mm)	9.4±1.6	7.1±1.2	0.693
RV EDA (cm^2/m^2)	19.5±5.4	17.8±3.8	0.596
RV ESA (cm^2/m^2)	5.5±1.3	5.1±1.2	0.560
RV FAC (%)	24.7±5.1	23.9±4.6	0.785
TAPSE	22.4±2.3	22.2±1.9	0.835
Peak PAP (mmHg)	31.8±5.3	26.1±6.3	0.114
E/A	0.64±0.13	0.70±0.11	0.102
E'med. (cm/s)	5.3±1.3	5.8±1.3	0.247
E/E'	10.6±3.6	10.8±3.1	0.825
RV ET (msec)	295.6±29.3	318.4±25.6	0.02
RV IVCT (msec)	70.8±17.8	58.0±21.0	0.02
RV IVRT (msec)	87.1±24.0	80.6±14.3	0.554
RIMP	0.53±0.10	0.43±0.09	0.002

Data are mean±standard deviation LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LA AP, left atrial anteroposterior diameter; IVS, interventricular septum; LA, left atrium; RVFW, right ventricle free wall; RA, right atrium; BSA, body surface area; RV, right ventricle; BD, basal diameter; LD, longitudinal diameter; FAC, fractional area change; EDA, end-diastolic area; ESA, end-systolic area; TAPSE, tricuspid annular plane systolic excursion; PAP, pulmonary artery pressure; RV ET, right ventricular ejection time; RV IVCT, right ventricular isovolumetric contraction time; RV IVRT, right ventricular isovolumetric relaxation time; RIMP, right ventricular index of myocardial performance.

Figure 1. ROC curve analysis of RIMP for prediction of active disease



Diagonal segments are produced by ties.

Discussion

In this study, patients with acromegaly had increased right heart chambers without obvious signs of clinical heart failure, whereas patients with active disease had considerable deterioration of parameters reflecting right ventricular function, including RIMP, ET and IVCT.

Bones, cartilages, and soft tissues in the entire body that are exposed to excessively high GH/IGF-1 concentrations over a long period respond by proliferating. Biventricular

Table 4. Correlations of GH with echocardiographic variables

Variables	r	p
RV IVCT	0.298**	0.006
RV IVRT	0.284**	0.009
RV LD	0.215*	0.048
Peak PAB	0.542**	0.005
RIMP	0.392**	<0.001
E/A	-0.349**	0.001
RV FAC	0.226*	0.041
RA minor-axis dimension	0.249*	0.033
RV EDA	0.419**	<0.001

Data are mean±standard deviation LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LA AP, left atrial anteroposterior diameter; IVS, interventricular septum; LA, left atrium; RVFW, right ventricle free wall; RA, right atrium; BSA, body surface area; RV, right ventricle; BD, basal diameter; LD, longitudinal diameter; FAC, fractional area change; EDA, end-diastolic area; ESA, end-systolic area; TAPSE, tricuspid annular plane systolic excursion; PAP, pulmonary artery pressure; RV ET, right ventricular ejection time; RV IVCT, right ventricular isovolumetric contraction time; RV IVRT, right ventricular isovolumetric relaxation time; RIMP, right ventricular index of myocardial performance.

Table 5. Correlatiaon of IGF-1 with echocardiographic variables

Variable	r	p
IVS	0.348**	0.001
PW	0.345**	0.001
LA	0.332**	0.002
RVEF	-0.338**	0.002
RA minor-axis dimension	0.450**	0.000
RV BD	0.232*	0.044
RVFW	0.452**	<0.001
RVET	0.228*	0.037
RV IVRT	0.230*	0.035
RVLD	0.528**	<0.001
E/E' ratio	0.465**	<0.001
E/A ratio	-0.450**	<0.001
RA minor axis dimension	0.312**	0.007
RV EDA	0.440**	<0.001
RV ESA	0.385**	<0.001

Data are mean±standard deviation LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LA AP, left atrial anteroposterior diameter; IVS, interventricular septum; LA, left atrium; RVFW, right ventricle free wall; RA, right atrium; BSA, body surface area; RV, right ventricle; BD, basal diameter; LD, longitudinal diameter; FAC, fractional area change; EDA, end-diastolic area; ESA, end-systolic area; TAPSE, tricuspid annular plane systolic excursion; PAP, pulmonary artery pressure; RV ET, right ventricular ejection time; RV IVCT, right ventricular isovolumetric contraction time; RV IVRT, right ventricular isovolumetric relaxation time; RIMP, right ventricular index of myocardial performance.

concentric hypertrophy is characteristic of acromegalic cardiomyopathy and occurs in the early stage of the disease. In the Italian population, Colao et al. found that the most frequent cardiac involvement in patients with acromegaly was biventricular concentric hypertrophy [2]. In the recent, systematic review of Yang et al., the incidence of LV hypertrophy in patients with acromegaly ranged from 10.8% to 78.9% (mean, 41.9%) [14]. In a small-sample study, Fazio et al. reported increased RVFW thickness in patients with acromegaly [15]. Moreover, Guo et al. showed that male acromegalic patients had a significant increase in RVFW thickness as compared to their female counterparts [16]. In the current study, we found a significant increase in IVS thickness, LV PW, and RVFW in patients with acromegaly, agreeing with the results of prior studies. Furthermore, we found positive, although weak, correlations between IGF-1 concentrations and both PW and IVS thickness.

In the present study, LA anteroposterior diameter, RA minor-axis dimension, and RV basal and longitudinal diameters, EDA, and ESA were increased in acromegalic patients in contrast to control subjects, without impaired FAC and TAPSE. Increased RV longitudinal diameter, RA minor-axis dimension indexed to BSA, and RV EDA indexed to BSA were associated with increase in GH and IGF-1 concentrations. Similar to our results, Guo et al. reported that the RV longitudinal dimension increased in patients with acromegaly as compared to controls [17]. Another recently published study showed a statistically insignificant increase in RVED in patients with acromegaly [18]. Kormányos et al. performed a RA-focused study in acromegaly patients and demonstrated significant increases in RA volume in acromegaly patients as compared with healthy counterparts [19]. Especially in the early stages of acromegaly, peripheral resistance and afterload decrease, whereas cardiac output increases, leading to a hyperkinetic circulation [20]. The RV becomes dilated and hypertrophied in response to the hyperkinetic state, but usually tolerates this condition better than the pressure load [21]. In a echocardiographic study of right heart function in athletes, Pagourelias et al. found significant increases in RV EDA and diameter as compared to the control group, especially in endurance athletes with volume overload [22].

Previous studies reported impaired LV and RV diastolic filling in acromegaly patients without systolic dysfunction [23, 24]. Similarly, in the current study, we found significantly lower E/A ratio, E′ velocity, and increased E/E′ ratio in acromegaly patients as compared to controls. As a consequence of increased wall thickness, decreased ventricular wall elasticity, and interstitial remodeling, patients with acromegaly usually develop moderate diastolic dysfunction. Diastolic dysfunction observed at an early stage

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of acromegaly cardiomyopathy can be improved with treatment, but whether the disease is active or under control does not affect the response to treatment [24].

RIMP is a useful, noninvasive, and reproducible parameter for evaluating systolic and diastolic RV function. Previous studies showed the prognostic importance of RIMP in various diseases [25]. In the present study, RIMP was slightly higher in acromegalic patients than in healthy controls, but this difference did not reach statistical significance. However, we also determined that the patients with active acromegaly had significantly higher RIMP compared to those with controlled acromegaly. Bruch et al. evaluated LV performance in patients with acromegaly and found that the LV myocardial performance index was significantly higher in that group of patients compared to patients with controlled acromegaly [26]. In addition, we found that the RV IVRT and RV ET values were prolonged in the acromegaly group as compared with the non-acromegaly group. Baykan et al. also reported a significant increase in the LV IVRT value using tissue Doppler imaging in patients with acromegaly [27]. Hemodynamically, the presence of a significant prolongation of IVRT indicates RV diastolic dysfunction, while prolonged ET reflects increased RV afterload. Moreover, we found a significant prolongation in IVCT of the patients with active acromegaly compared to that of patients with controlled acromegaly. A prolonged IVCT may be an indicator of impaired contractile function in patients with active acromegaly. In a study in which LV functions were evaluated with tissue Doppler echocardiography, Galderisi et al. found a significant increase in the LV IVCT value of patients with active acromegaly [28].

Our study has some limitations. First, although it is the most widely used tool for evaluating the structure and function of the right heart, echocardiography is not the gold standard for such evaluations. Studies using cardiac magnetic resonance imaging and hemodynamic catheterization are needed to support our findings. Second, echocardiographic evaluation is more difficult in patients with acromegaly because they have:

1) a narrow intercostal space because of bone remodeling and rib thickening;
2) higher BMIs;
3) thicker skin, which reduces echocardiographic image clarity.

Finally, we did not know the exact duration of acromegaly in our patients, so we could not distinguish between early-, mid-, and late-stage acromegalic cardiomyopathy.

Conclusions

Increases in the size and diameters of the right heart chambers along with RV free wall thickness may be attributed to acromegalic cardiomyopathy. In addition, a deterioration in RV diastolic function was noted. RVIMP, isovolumetric contraction time, and ejection time were parameters that can be used in the evaluation of active acromegaly disease. RIMP value was higher in the patients with active acromegaly than in the patients with controlled acromegaly. To the best our knowledge, our study is the first to evaluate right heart function by using advanced echocardiographic methods in patients with acromegaly. However, our findings must be supported by studies with a larger number of patients evaluated using cardiac magnetic resonance imaging and hemodynamic catheters in addition to echocardiography.

No conflict of interest is reported.

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