Cardiac Structural Alterations of Acromegalic, Without Alteration in Cardiac Function, Evaluated by Doppler Echocardiography with Speckle Tracking

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Abstract

Background: Acromegaly is most commonly caused by growth hormone secreting pituitary (GH) macroadenoma. Cardiovascular events are the leading cause of death in this population.

Objective: To analyze the cardiac structural and functional changes in patients with acromegaly and to correlate the findings with the concentrations of GH and IGF-1 post treatment and with the presumed time of disease.

Method: A quantitative study involving 19 individuals with acromegaly, 10 with inactive disease and 9 with active disease and 16 healthy individuals, matched by sex and age. Age ranged from 19 to 78 years. Two-dimensional echocardiogram and speckle tracking were performed.

Results: Mean left ventricular mass index (LVMI) were significantly higher in acromegalic patients (89.1 ± 27.9) compared to the control group (66.9 ± 15.7) ($p = 0.015$). There was a direct correlation between IGF-1 mean concentration and left ventricular systolic volume (LVSV) in acromegalic patients ($r = 0.64$; $p = 0.004$) even when the disease was inactive ($n=10$; $r = 0.9$; $p = 0.002$) and between IGF1 mean concentration and left ventricular diastolic volume (LVDV). The left ventricular ejection fraction (EF) and the global longitudinal strain (GLS) did not differ between groups ($p > 0.05$).

Conclusion: Although patients with acromegaly had higher LVMI, they did not show difference in GLS indicating a small chance of progression to systolic disfunction. Direct correlation between IGF-1 and LDVD and LVSV demonstrates the relevance of a good hormonal control to reduce cardiac changes.

Keywords: acromegaly, heart, echocardiography

1. Introduction

Acromegaly is commonly caused by growth hormone secreting pituitary macroadenoma (Melmed, 2016). Growth hormone (GH) hypersecretion leads to overproduction of insulin-like growth factor 1 (IGF-1), causing multisystemic disease characterized by somatic overgrowth, physical disfigurement, multiple comorbidities, and premature mortality (Melmed, 2016; Oliveira Jr & Barkan, 2012).

The diagnosis is confirmed by the elevation of GH and IGF-1 levels, non-suppression of GH during the oral glucose tolerance test (OGTT), and presence of tumor at the magnetic resonance imaging of the sella turcique (Melmed, 2016; Dineen, Stewart, & Sherlock, 2017; Katznelson et al., 2014; Colao, Ferone, Marzullo, & Lombardi, 2004).

The treatment involves the surgical excision of the tumor followed by administration of somatostatin analogues and, in some situations, by radiotherapy. It aims to normalize GH and IGF-1 concentrations to reduce morbimortality (Melmed, 2016; Katznelson et al., 2014).

Cardiovascular events are the leading cause of death in patients with acromegaly due to prolonged tissue exposure to excess GH and IGF-1 (Clayton, 2003). The pathogenesis of myocardial injury involves direct action of these

hormones or indirect mechanisms by which GH and IGF-I excess induce hypertension and disorders of glucose and lipid metabolism, resulting in glycotoxicity, lipotoxicity and cardiac remodeling (Isgaard, Tivesten, Friberg, & Bengtsson, 1999; Colao et al., 2001).

In a study carried out at the Clinical Hospital of the Federal University of Triângulo Mineiro, 12.4% of the patients evaluated presented arterial hypertension, indicating the need for a specific approach of the cardiovascular system in acromegalics, motivating a more in-depth observation of the cardiovascular complications in these patients in our clinic (Borges et al., 2017).

The objective of the present study is to evaluate the presence and frequency of structural and functional cardiac changes in acromegalic patients considering the activity of the disease (according to concentrations of GH and IGF-1) and its relation to the presumed time of disease.

2. Methods

2.1 Study Population

This is a cross-sectional and quantitative study with a group of healthy individuals for comparison. It was approved by the Research Ethics Committee of the Clinical Hospital of the Federal University of Triângulo Mineiro (UFTM) (protocol number 2307012). Prior to the investigation, a free and informed consent form was obtained.

The study included 19 patients with acromegaly aged over 18 years, whose diagnosis was confirmed by non-suppression of GH concentrations below 0.4 ng/mL during OGTT, and elevated IGF-1 levels for age and sex, and treatment at the Endocrinology and Metabology clinic of the UFTM. These patients will be referred to as acromegalic group (AG). The exclusion criteria were the presence of concomitant severe diseases, such as heart failure, chronic renal failure or coagulation disorders.

According to the effectiveness of the treatment related to GH and IGF-1 concentrations, AG was divided in two sub-groups: patients with inactive disease (IDG; n=10) and active disease (ADG; n=9). Inactive diseases was considered when GH was less than 1.0 ng/mL with normal IGF-1 concentrations and active disease when GH was greater than 1.0 ng/mL with increased IGF-1 levels.

A group of 16 healthy volunteers matched by sex and age participated as a comparative group referred as CG. Presence of comorbidities, such as heart failure, chronic renal failure, severe dyslipidemia and diabetes were exclusion criteria.

2.2 Demographic, Anthropometric, Clinical and Biochemical Evaluation

Demographic and anthropometric parameters were obtained and anthropometric measurements were performed in participants with light clothing and without shoes. The weight measured with digital electronic scale, brand Lider-LD 1050, the height determined in upright position by Toneli® stadiometer, model E150. Body mass index (BMI) analyzed according to the World Health Organization and the body surface calculated by the Mosteller formula (Mosteller, 1987).

Blood pressure (BP) was measured by Premium® aneroid sphygmomanometer and Littman® stethoscope, being considered hypertensive those using antihypertensive drugs or who had blood pressure levels equal to or greater than 140 mmHg systolic pressure or 90 mmHg diastolic pressure, according to the 7th Brazilian Arterial Hypertension Guideline (Sociedade Brasileira de Cardiologia, 2016).

GH and IGF-1 were measured by chemiluminescence using IMMULITE XPI equipment, SIEMENS. Fasting glycemia (FG) and glycated hemoglobin (HbA1c) were determined by the enzymatic method with hexokinase and turbidimetry, respectively; Total colesterol (TC) and fractions were also determined by the enzimatic method with hexokinase and LDL-c, calculated by the Friedewald, Levy and Fredrickson (1972) equation. All were measured after 12 hours of fasting, processed by the COBAS-6000 device - Roche-Hitachi module C501.

Following 2017-2018 guidelines of the Brazilian Society of Diabetes (Lang et al., 2015), fasting plasma glucose equal or greater than to 126 mg/dL, at random equal or greater than to 200 mg/dL with symptoms of hyperglycemia (polyuria, polydipsia and loss of weight), HbA1c equal or greater than to 6.5 and/or glycemia two hours after glucose overload 200 mg/dL were considered as diabetes mellitus (DM). Altered fasting glycemia was defined as glucose equal or greater than 100 and less than 126 mg/dL and/or HbA1c equal or greater than 5.7 and less than 6.5%.

The Global Risk Score (GRS) was calculated according to the Brazilian Dyslipidemia Guideline Update of 2017 (Sociedade Brasileira de Cardiologia, 2017); TC greater than 190 mg/dL, HDL-c lower than 40 mg/dl and triglycerides (TG) greater than 150 mg/dL were considered altered. Regarding LDL-c and non-HDL-c, participants were classified as: very high, high, intermediate and low risk according to GRS.

2.3 Transthoracic Doppler Echocardiogram

Two-dimensional and Doppler echocardiograms were performed as recommended by the American Society of Echocardiography (Lang et al., 2015), by the Philips iE33 device (Bothell, WA, USA), by a single examiner and without distinction between groups.

The left ventricular ejection fraction (EF) was performed by the biplanar disc method (modified Simpsom's rule). The speckle tracking technique was used to evaluate the cardiac deformation by Global Longitudinal Strain (GLS). The parameters obtained by the exam were: left ventricular volume index (LVVI), left ventricular diastolic volume (LVDV) and left ventricular systolic volume (LVSV), left ventricular diastolic diameter (LVDD) and left ventricular mass index (LVMI) were calculated according to the Devereux formula (Lang et al., 2005). With the exception of LVDD, the variables were corrected by the body surface.

2.4 Statistical Analysis

The variables were submitted to descriptive analysis, expressed by measures of central tendency and dispersion. To verify the behavior of the variables, the Shapiro-Wilk test followed by the Levene test was used. When the normality assumptions were not met or the homogeneity of variances was verified, the variables were transformed through $\sqrt{x}$, log x and boxcox.

Comparisons between means were done by the Student t test for two independent groups or unidirectional ANOVA followed by the Tukey multiple comparisons test to compare three or more groups. For the correlations, the Pearson or Spearman correlation coefficient was used according to the behavior of the variables. The significance level adopted was 5% ($p < 0.05$), and the data processed in the Statistical Package for Social Science (SPSS) software, version 23.

3. Results

3.1 Demographic, Anthropometric and Clinical Data

Of the 19 patients with acromegaly, 12 (63.2%) were male and 7 (36.8%) were female. In the CG, 7 (43.8%) were female and 9 (56.3%) were male. Anthropometric and clinical characteristics are shown in Table 1.

Table 1. Anthropometric and clinical characteristics of patients with acromegaly and comparative group

	AG n= 19	IDG n= 10	ADG n= 9	CG n= 16
Age (years)	58.0 (19-78)	59.2 (26 – 78)	46.1 (19 – 64)	53.0 (24 – 72)
Weight (kg)	90.1 ± 26.8	97.1 ± 31.4	86.2 ± 21.7	70.5 ± 10.4
Height (cm)	173.2 ± 15.2	173.3 ± 14.4	173.2 ± 16.8	167.3 ± 11.3
BMI (kg/m²)	29.7 ± 5.8[a]	30.8 ± 7.1[b]	28.5 ± 3.7	25.0 ± 2.9[a][b]
SBP (mmHg)	129.2 ± 12.0	130.5 ± 8.3	127.8 ± 15.6	120.9 ± 9.5
DBP (mmHg)	82.6 ± 10.8	83.0 ± 7.9	82.2 ± 14.0	74.2 ± 6.4
Assumed time of illness (years)	11.5 ± 8.1	14.1 ± 8.1	8.0 ± 7.2	-

AG: acromegalic group / IDG: inactive disease group / ADG: active disease group / CG: comparative group/ BMI: Body mass index / SBP: systolic blood pressure / DBP: diastolic blood pressure.

a: p = 0.006 // b: p <0.011 // Further comparisons: p> 0.05.

Source: The author, 2018.

Regarding the BMI of the acromegalic patients, 5 (26.3%) were overweight, 8 (42%) presented grade I obesity, 1 patient (5.3%) had grade III obesity and 5 (26.3%) had normal weight. The CG presented normal BMI in 7 patients (36.8%) and was compatible with overweight in 9 (47.3%). The BMI was significantly higher in AG compared to CG, and in IDG compared to CG, and no difference was found in ADG when compared to IDG.

Systemic arterial hypertension (SAH) was present in ten patients (52.6%) with acromegaly and all were receiving antihypertensive drugs. The CG group did not present SAH. There was no difference regarding SBP and DBP when compared to the groups studied.

3.2 Laboratory Data

The laboratory data of patients with acromegaly and the comparative group are shown in Table 2.

Table 2. Laboratory data of patients with acromegaly and comparative group

	AG	IDG	ADG	CG
	n= 19	n= 10	n= 9	n= 16
FG (mg/dL)	104.5 ± 23.3[a]	100.6 ± 16.4	108.7 ± 29.0	91.9 ± 4.4[a]
HbA1c (%)	5.6 ± 0.43[b]	5.5 ± 0.5	5.7 ± 0.4	5.3 ± 0.5[b]
TC (mg/dL)	156.7 ± 30.8[c]	168.8 ± 24.9	143.2 ± 32.3[d]	187.6 ± 38.6[c][d]
LDL-c (mg/dL)	87 ± 26.1[e]	97.4 ± 26.7	75.6 ± 21.2[f]	109.4 ± 29.2[e][f]
HDL-c (mg/dL)	46.1 ± 14.6	46.9 ± 9.7	45.2 ± 19.2	49.6 ± 13.2
TG (mg/dL)	110.7 ± 61.7	110.2 ± 63.1	111.2 ± 63.9	131.9 ± 99.2
Non-HDL-c (mg/dL)	111.9 ± 29.8[g]	124.5 ± 27.9	97.9 ± 26.7[h]	136.2 ± 36.2[g][h]

AG: acromegalic group / IDG: inactive disease group / ADG: active disease group / CG: comparative group.

GJ: fasting glycemia / HbA1c: glycated hemoglobin / CT: total cholesterol / LDL-c: LDL-cholesterol / HDL-c: HDL-cholesterol / TG: triglycerides / non-HDL-c: non-HDL-cholesterol.

a: p = 0.033 // b: p = 0.048 // c: p = 0.013 // d: p = 0.009 // e: p = 0.023 // f: p = 0.018 // g: p = 0.037 // h : p = 0.025 // Further comparisons: p> 0.05.

Source: The author, 2018.

With regard to preexisting comorbidities in acromegalics, five (26.3%) had DM and six (31.6%) pre-diabetes, all receiving medication treatment. FG was altered in 11 patients (57.8%). In the CG, FG was normal in all of them. When compared between the groups, FG was significantly higher in the AG in relation to the CG, but there was no difference between the IDG and ADG and between these groups and CG.

Regarding HbA1c in the AG, 4 patients (21%) had increased HbA1c levels while in the CG concentrations were normal. The CG showed no change in HbA1c. When comparing the groups, it was significantly higher in the AG than in the CG, but there was no difference between IDG and ADG among themselves and with the CG.

In the AG, 10 patients (52.6%) had high cardiovascular risk, 4 (21%) intermediate risk and 5 (26.3%) had low cardiovascular risk. All CG participants had low cardiovascular risk.

The comorbidity dyslipidemia was present in 8 (42.1%) of the acromegalic patients, all in drug treatment. Analyzing the lipid profile of the same group, 15 (78.9%) had increased TC, 7 (36.8%) had decreased HDL-c, 8 (42%) had increased LDL-c, 3 (15.7%) had increase in triglyceride (TG) concentrations and 8 (42%) with increase in non-HDL-c. In relation to the CG, 9 (56.3%) had increased TC, 5 (31.3%) had decreased HDL-c, 3 (18.8%) had increased LDL-c, 6 (37.5%) had increased triglycerides and non-HDL-c was increased in 3 patients (18.8%).

When compared between groups, TC was significantly higher in the AG compared to the CG, and also in the ADG compared to the CG. There was no significant difference when comparing ADG and IDG, and in this one compared to CG. LDL-c was significantly higher in the AG compared to the CG, and also significantly higher in the ADG compared to the CG. There was no significant difference between ADG and IDG, and in the IDG compared to the CG. Non-HDL-c was significantly higher in the AG and ADG compared to the CG. There was no significant difference when comparing the ADG and IDG, and between IDG and CG. There was no significant difference between the studied groups regarding HDL-c and TG.

3.3 Doppler Echocardiography Data

Data from the Doppler echocardiogram are shown in Table 3.

Table 3. Transthoracic Doppler data in acromegalic patients and in the comparative group

	AG n= 18	IDG n= 9	ADG n= 9	CG n= 15
LVDV(mL/m²)	50.3 ± 16.3[a]	49.9 ± 21.2	50.7 ± 9.6	39.5 ± 5.9[a]
LVSV(mL/m²)	22.5 ± 11.8[b]	19.7 ± 8.2	25.3 ± 14.6[c]	15.9 ± 4.6[b)(c]
LVDD(mm)	47.2 ± 3.7[d]	47.4 ± 4.4	47.0 ± 3.2	43.9 ± 3.4[d]
LVMI(gr/m²)	89.1 ± 27.9[e]	95.9 ± 33.3[f]	80.2 ± 17.7	66.9 ± 15.7[e)(f]
LAVI(mL/m²)	34.9 ± 6.8[g]	34.2 ± 8.2[h]	35.6 ± 5.5[i]	26.4 ± 8.5[g)(h)(i]
EF (%)	60.0 ± 5.9	60.9 ± 3.9	59.2 ± 7.5	61.5 ± 4.5
GLS (%)	20.8 ± 3.5	20.6 ± 1.9	21.0 ± 4.7	20.9 ± 1.7

AG: acromegalic group / IDG: inactive disease group / ADG: active disease group / CG: comparative group.

LVDV: Left ventricular diastolic volume / LVSV: Left ventricular sistolic volume / LVDD: Left ventricular diastolic diameter / LVMI: Left ventricular volume index / LVVI: left atrial volume index / EF: ejection fraction / global longitudinal strain.

a: p = 0.018 // b: p = 0.033 // c: p = 0.054 // d: p = 0.012 // e: p = 0.015 // f: p = 0.019 // g: p = 0.003 // h : p = 0.057 // i: p = 0.022 // Further comparisons: p> 0.05.

Source: The author, 2018.

Doppler echocardiography was performed in 19 acromegalic patients, but in 1 of them it was not possible to perform the echocardiographic measurements due to morbid obesity and the presence of arrhythmia (atrial fibrillation). The LVDV was altered in 1 (5.5%) patient, while the LVSV was increased in 2 (11.1%). The LVMI was increased in 2 (11.1%) of the patients, the LAVI increased in 7 (38.8%), the EF was reduced in 1 (5.5%) and GLS was decreased in 2 (11, 1%). Regarding the LVDD, no patient presented alteration.

In the CG, 15 participants were submitted to the examination, and presented normal LVDV, LVSV, LVDD, LVMI, EF and GLS. LAVI was increased in 2 (13.3%) patients (Table 3).

The variables LVDV, LVSV, LVDD, LVMI and LAVI were significantly higher in the AG compared to the CG. The LVDV and the LVDD did not present a significant difference when comparing IDG and ADG and of these with the CG. LVSV was significantly higher in the AG and ADG compared to the CG. However, there was no difference when compared ADG with IDG and between IDG and CG. The LVMI was significantly higher in the AG and IDG when compared to the CG, but there was no difference when compared the groups ADG with IDG and ADG with the CG. The LAVI was significantly higher in the AG, IDG and ADG compared to the CG. However, when comparing the ADG with the IDG, there was no significant difference. There was also no significant difference in EF and GLS when compared AG with CG, ADG with IDG and each other with CG (Table 3).

3.4 Correlations between IGF-1 and GH with the Variables of the Doppler Echocardiogram

The values of GH and IGF-1 were correlated with the variables of the Doppler echocardiogram studied, as presented in Table 4 and Figures 1, 2 and 3.

Table 4. Correlation between GH and IGF-1 levels with the Doppler echocardiogram variables in AG, ADG and IDG

	GH * (AG)		IGF-1 † (AG)		GH * (ADG)		IGF-1 † (ADG)		GH * (IDG)		IGF-1 † (IDG)	
	r	p	r	p	r	p	r	p	r	p	r	p
LVDV	0.211	0.400	0.530	0.020	0.446	0.228	0.460	0.213	0.199	0.608	0.529	0.116
LVSV	0.154	0.556	0.640	0.004	0.414	0.308	0.235	0.542	0.168	0.666	0.879	0.002
LVDD	-0.044	0.862	0.154	0.543	0.176	0.651	0.577	0.104	-0.312	0.414	-0.034	0.931
LVMI	0.077	0.792	-0.013	0.964	0.515	0.295	0.486	0.329	0.108	0.799	-0.024	0.955
LAVI	0.216	0.389	0.046	0.857	0.040	0.919	-0.218	0.572	0.606	0.084	-0.034	0.931
EF	0.081	0.749	-0.171	0.643	0.102	0.793	-0.200	0.606	0.033	0.933	0.111	0.777
GLS	0.061	0.811	0.212	0.399	0.055	0.888	0.202	0.602	0.362	0.339	0.255	0.507

AG: acromegalic group / ADG: active disease group / IDG: inactive disease group.

LVDV: left ventricular diastolic volume / LVSV: left ventricular systolic volume / LVDD: left ventricular diastolic diameter LVMI: left ventricular mass index / LAVI: left atrial volume index / FE: left ventricular ejection fraction / GLS: global longitudinal strain.

Notes: * Pearson's correlation; † Spearman correlation.
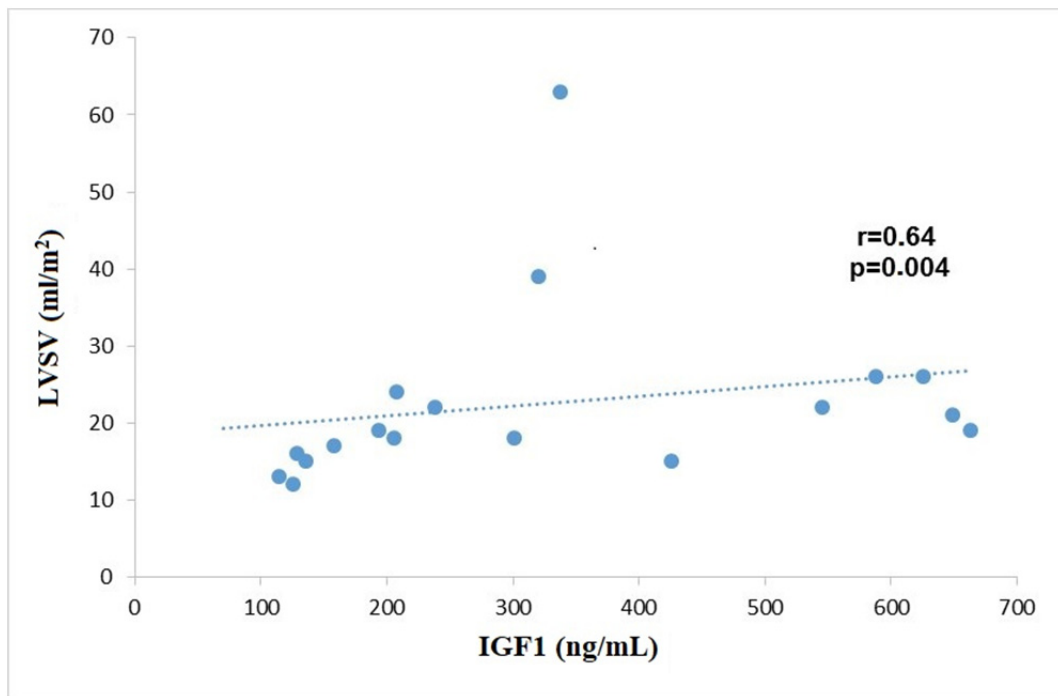
Source: The author, 2018.

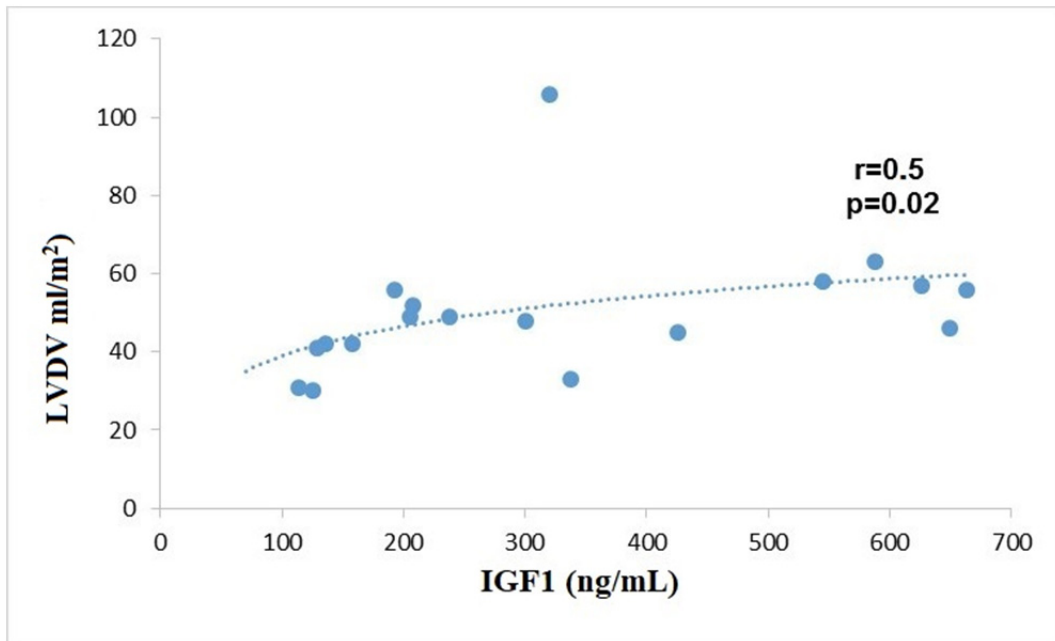Figure 1. Correlation between IGF1 and LVSV in the acromegalic group

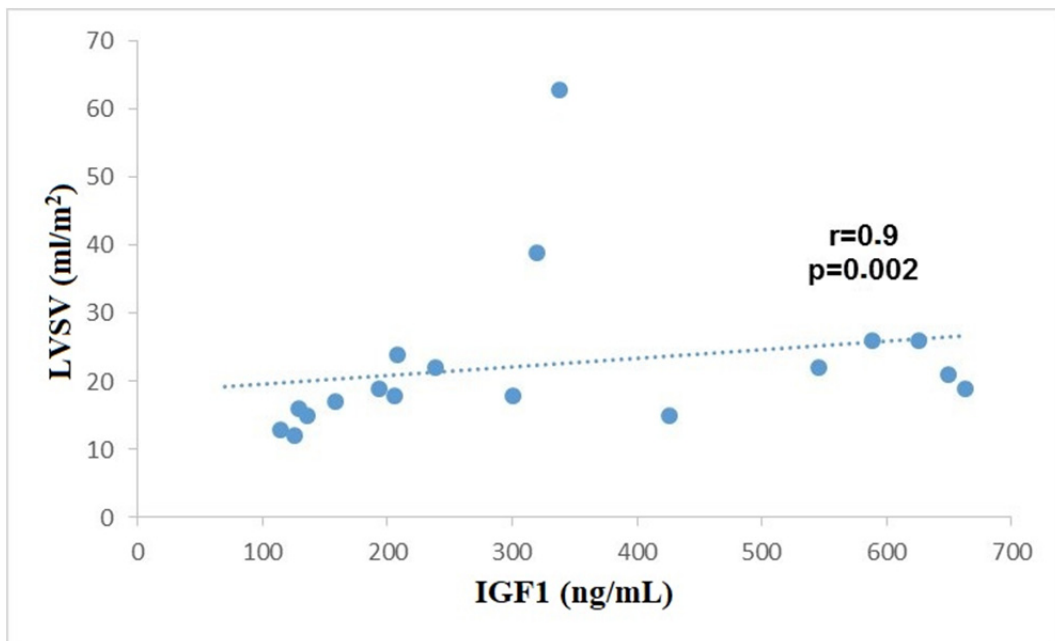Figure 2. Correlation between IGF1 and LVDV in the acromegalic group

Figure 3. Correlation between IGF1 and LVSV in the inactive disease group

A direct correlation between IGF-1 and LVSV were observed in the AG and IDG, and also between IGF-1 and LVDV in the AG. In the other variables, there was no correlation.

3.5 Correlations between Alterations Found in the Doppler Echocardiogram and Presumed Disease Time

The variables of the Doppler echocardiogram were correlated with disease time and as shown in Table 5, there was no correlation.

Table 5. Correlation between Doppler echocardiogram variables and disease time in AG, ADG and IDG

	Disease time (AG) *		Disease time (ADG) *		Disease time (IDG) *	
	r	p	r	p	r	p
LVDV	-0.050	0.843	-0.083	0.832	0.019	0.961
LVSV	-0.056	0.831	-0.020	0.963	-0.020	0.959
LVDD	-0.181	0.472	0.338	0.374	-0.603	0.086
LVMI	0.219	0.451	0.386	0.450	0.078	0.855
LAVI	-0.024	0.926	0.248	0.520	-0.148	0.703
EF	0.162	0.520	0.000	0.999	0.376	0.318
GLS	-0.102	0.688	-0.408	0.275	0.656	0.055

AG: acromegalic group / ADG: active disease group / IDG: inactive disease group.

LVDV: left ventricular diastolic volume / LVSV: left ventricular systolic volume / LVDD: left ventricular diastolic diameter LVMI: left ventricular mass index / LAVI: left atrial volume index / EF: ejection fraction/ GLS: global longitudinal strain.

* Pearson's Correlation.

Source: The author, 2018.

4. Discussion

Acromegaly is a chronic systemic disease, and mortality rates due to cardiovascular, cerebrovascular and metabolic comorbidities are about two times higher in relation to the general population (Katznelson et al., 2014). In the literature, there is a description of specific heart disease called acromegalic myocardiopathy and Doppler echocardiography is the most widely used method for the diagnosis of left ventricular hypertrophy, with the left ventricular mass as the fundamental parameter for its detection (Colao et al., 2001).

When the AG was analyzed, we observed significantly higher means of LVDV, LVSV, LVDD, LAVI and LVMI when compared to the CG. Several studies have demonstrated an increased LVMI in acromegalic patients when compared to healthy individuals without the disease (Vitale et al., 2004; Colao et al., 2003; Colao et al., 2000), indicating that the heart of patients with acromegaly due to excess GH and IGF-1 undergo remodeling. The LVMI was significantly higher in the AG than in the CG, and the IDG presented significantly higher mean LVMI when compared to the CG. As the IDG has a higher average age, it may contribute to the abnormalities found. Although Colao et al. (2002) demonstrated higher LVMI in patients with disease duration of more than five years, our study did not demonstrate a direct correlation between duration of disease and LVMI. It is possible that the time of exposure to high levels of GH and IGF-1 (active disease), would be more implicated in cardiac structural disease than the presumed time of disease.

Although the present study showed no difference when the Doppler echocardiogram variables were compared between ADG and IDG groups, there was a direct correlation between IGF-1 and LVSV in the AG and IDG, and also between IGF-1 and LVDV in the acromegalic group. Casini et al. (2006) demonstrated a direct correlation between cardiac hypertrophy and IGF-1 concentrations, corroborating the importance of IGF-1 normalization for the reduction of cardiovascular complications.

Despite a significantly higher mean of LVMI, only 11.1% of the patients had left ventricular hypertrophy (LVH). According to autopsies, Lie (1980) observed myocardial hypertrophy and interstitial fibrosis in 93 and 85% of the patients, respectively. A study by Silva et al. (2015) performed myocardial resonance in 40 patients and finding prevalence of 5% in LVH and 13.5% in myocardial fibrosis. It is known that cardiac structural changes are partially reversible with the treatment of the disease (Mosca et al., 2013; Minniti et al., 2001; Colao, 2009), which may justify a reduction in the prevalence of LVH in the studied population, considering that the study by Lie (1980) was carried out in 1980 and the treatment of acromegaly did not count on the therapeutic arsenal currently used.

We observed that there was no significant difference in GLS between groups (AG versus CG, ADG versus IDG, and ADG and IDG versus CG). Several studies report that the presence of heart failure in acromegalic patients is uncommon, with prevalence ranging from 1 to 10% (Colao et al., 2001; Mosca et al., 2013; Colao et al., 1999; Bihan et al., 2004). Although acromegalic participants present with an increased LVMI, Volschan et al. (2017) concluded that there was no harm, no strain when compared to the CG, similar to that found in the present study.

The analysis in question shows that 73.6% of patients in the AG were overweight. They had significantly higher BMI than CG. In the survey of the Brazilian Institute of Geography and Statistics (IBGE) in 2017, 54% of adults were overweight (Brasil, 2018). The higher the degree of obesity, the higher the prevalence of metabolic syndrome components, demonstrating that obesity is clearly associated with greater cardiovascular risk (Cercato, Silva, Sato, Mancini, & Halpern, 2000). The difference in the prevalence of overweight between groups could be atributed to the fact that acromegalic patients are more resistant to perform physical activity due to orthopedic problems and common arthropathies in this population.

The prevalence of hypertension was 52.6%. The prevalence of hypertension among patients with the disease varies between 20 and 60% (Colao et al., 2004; Isgaard, Arcopinto, Karason, & Cittadini, 2015), therefore similar to that found in the present study.

The AG had a significantly higher mean of FG and HbA1c compared to the CG. The prevalence of DM and glucose intolerance was 26.3% and 31.6%, respectively, in the AG. According to Dreval et al. (2014), the prevalence glucose metabolism abnormalities varies from 19 to 52%, therefore similar to that found in the present study. Excess GH and IGF-1 induce disorders of glucose metabolism, common in the population studied (Isgaard et al., 1999; Colao et al., 2001).

We observed that patients in the AG had significantly lower mean TC, LDL-c, and non-HDL-c when compared to the CG. Abnormalities of the lipid profile have also been frequently reported, although highly variable. The concentrations of TC can be increased, normal or even reduced, depending on the phase in which it is assessed in the context of acromegaly (Colao et al., 2004; Minniti et al., 2001; Colao, 2009). Patients in the AG are regularly monitored and comorbidities treated at our service, which justifies the lower concentrations found in relation to the CG, which should not take the same health care.

As the presence of comorbidities was higher in the AG than in the CG and knowing that these risk factors are classically determinant of cardiac structural alterations and increase in cardiovascular mortality (Nascimento et al., 2018), the findings may be a consequence of comorbidities presented and not only due to acromegaly. Despite this, the study reinforces the need to investigate actively and treat risk factors in patients with acromegaly.

Limitations of the study include a small sample due to the rarity of the disease and a short-term evaluation of cardiovascular complications. The heterogeneity of the studied groups regarding age, comorbidities and time of disease activity are also limiting. Despite this, the findings corroborate with the literature and can motivate further studies.

5. Conclusion

Acromegalic individuals present higher LVMI, LAVI, LVDV, LVSV and LVDD when compared to healthy individuals, but the presumed disease time did not correlate with the alterations found. No difference were found when active and inactive disease groups were compared, but the IGF-1 level had a direct correlation with the LVSV and LVDV, reinforcing the need for normalization of IGF-1 to reduce cardiac complications. There was no difference in EF and GLS, demonstrating that despite the structural findings, there was no difference in systolic function, according to recent data from the literature. It is known that risk factors may contribute considerably to the structural findings, requiring further studies to investigate acromegalic heart disease. Early investigation and treatment of the risk factors found in this population is desirable in further studies.

Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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