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Acromegaly: evidence for a direct relation between disease activity and cardiac dysfunction in patients without ventricular hypertrophy

B. L. Herrmann*, C. Bruch†, B. Saller*, T. Bartel†, S. Ferdin*, R. Erbel† and K. Mann*

*Divisions of *Endocrinology and †Cardiology, University of Essen, Essen, Germany*

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Summary

BACKGROUND AND AIMS Cardiac abnormalities, such as cardiomegaly and congestive heart failure, occur frequently in advanced acromegaly. Abnormalities of systolic and diastolic function, mostly associated with left ventricular (LV) hypertrophy, have been reported. The impact of disease activity on LV performance in patients with normal or slightly elevated LV muscle mass has not been demonstrated.

PATIENTS AND METHODS Conventional two-dimensional/Doppler echocardiography and tissue Doppler imaging (TDI) of the mitral annulus were performed in 13 patients with active acromegaly (AA) and normal or slightly elevated LV muscle mass (< 140 g/m^2) and in 19 cured/well-controlled patients (CA). A group of 21 volunteers without symptoms or signs of cardiac disease served as controls (CON). The combined myocardial performance index (Tei-Index) was determined in all patients and controls.

RESULTS Muscle mass index of the left ventricle, ejection fraction, fractional shorting, E/E_T-ratio, systolic (S_T) and late diastolic (A_T) annular velocities did not differ significantly between the three groups. In the AA group, the early diastolic annular velocity E_T [7·13 ± 2·11 (AA); 9·83 ± 3·29 (CA); 10·10 ± 1·70 m/s (CON); $P < 0.05$ AA *vs.* CA, $P < 0.005$ AA *vs.* CON] and the E_T/A_T-ratio [0·71 ± 0·26 (AA); 0·95 ± 0·33 (CA); 1·00 ± 0·15 m/s (CON); $P < 0.05$ AA *vs.* CA, $P < 0.005$ AA *vs.* CON] were significantly reduced. Patients with AA had a longer deceleration time [209 ± 19 (AA); 179 ± 22 (CA); 185 ± 26 ms (CON); $P < 0.05$]. The Tei-Index was significantly higher in AA in comparison with CON [0·50 ± 0·15 (AA); 0·48 ± 0·12 (CA); 0·41 ± 0·10 (CON); $P < 0.05$ AA *vs.* CON]. Subjects with CA did not differ significantly from controls with respect to 2-D/Doppler echo- and TDI-derived parameters.

CONCLUSION The data demonstrate that diastolic dysfunction can be verified by tissue Doppler imaging in patients with active acromegaly with normal or slightly elevated muscle mass of the left ventricle and seems to be related to disease activity. The Tei-Index as a sensitive combined myocardial performance index can be used to complete the assessment of systolic and diastolic LV performance in acromegalic patients.

Patients with active acromegaly suffer from cardiovascular complications such as cardiomyopathy, coronary heart disease and arrhythmias (Kahaly *et al.*, 1992; Lombardi *et al.*, 1997; Ozbey *et al.*, 1997; Colao, 2001; Herrmann *et al.*, 2001). Beside accompanying risk factors (arterial hypertension, dyslipoproteinaemia, diabetes mellitus) of acromegaly (Saruta, 1989; Moller *et al.*, 1991; Oscarsson *et al.*, 1994), the duration and activity of the disease determine the cardiac involvement (Colao *et al.*, 1999a). Abnormalities of cardiac structure have been well demonstrated by echocardiography, so that acromegalic cardiomyopathy seems to be a specific disease that is related to GH and/or IGF-1 hypersecretion (Fazio *et al.*, 1993a,b,c; Lombardi *et al.*, 1996; Ciulla *et al.*, 1999). Diastolic dysfunction has been reported as an early sign of acromegalic cardiomyopathy whereas systolic function was found to be normal. In most studies, Doppler echocardiographic analysis of the mitral inflow profile was used to assess left ventricular (LV) diastolic function. Tissue Doppler imaging (TDI) is a new imaging modality which can provide valuable additional information to complement established parameters in evaluating systolic and diastolic performance (Rodriguez *et al.*, 1996). The peak early diastolic velocity of the mitral annulus (E_T) has been demonstrated to behave as a preload-independent index of LV relaxation (Nagueh *et al.*, 1997; Sohn *et al.*, 1997). The peak mitral E/E_T-ratio relates closely to mean pulmonary capillary wedge pressure, permitting the noninvasive estimation of LV filling pressure (Nagueh *et al.*, 1997).

The Tei-Index was described as a sensitive indicator of overall cardiac dysfunction in patients with mild to moderate congestive heart failure. This index is defined as the summation of the

Correspondence: Dr Burkhard L. Herrmann, University of Essen, Department of Internal Medicine, Division of Endocrinology, Hufelandstr. 55, D-45 122 Essen, Germany. Tel.: +49 201 723 3235; Fax: +49 201 723 5976; E-mail: burkhard.herrmann@uni-essen.de

Table 1 Clinical data for patients with acromegaly and the control subjects

	Active ($n = 13$)	Cured/well-controlled ($n = 19$)	Controls ($n = 21$)
Male/Female	8/5	10/9	12/9
Age (years)	52 ± 15	51 ± 14	58 ± 9
Hypertension	4 (31%)	7 (37%)	0
Disease duration (years)	8 ± 10	7 ± 8	
Surgery	9 (69%)	17 (89%)	
Irradiation	3 (23%)	7 (37%)	
Somatostatin analogues	5 (38%)	6 (32%)	
Gonadotrophin deficiency	9 (69%)	10 (53%)	
ACTH deficiency	4 (31%)	7 (37%)	
Thyrotrophin deficiency	4 (31%)	8 (41%)	
Diabetes insipidus	0 (0%)	2 (11%)	

isovolumetric contraction and relaxation times divided by the ejection time (Tei *et al.*, 1996; Bruch *et al.*, 2000). In patients with dilated cardiomyopathy and cardiac amyloidosis, the assessment of the Tei-Index is more effective for analysis of global cardiac dysfunction than systolic and diastolic measurements alone (Eidem *et al.*, 2000; St John Sutton & Wiegers, 2000).

The aim of this study was to determine systolic and diastolic filling dynamics by two-dimensional / Doppler echocardiography and TDI in acromegalic patients with normal or slightly increased muscle mass of the left ventricle and its relation to the activity of the disease.

Patients and methods

Patients

Thirty-two patients (18 males, 14 females; age range 30–82 years) suffering from acromegaly were included in the study (Table 1) with a muscle mass index of the left ventricle (LVMMI) < 140 g/m^2. The diagnosis of acromegaly was made on the basis of physical examination, IGF-1 and GH levels after an oral glucose load (75 g). Considering the consensus statement of criteria for cure of acromegaly, 13 patients had active disease and 19 patients were inactive (cured) or 'well controlled'. Cure was defined as IGF-1 levels within the age-adjusted normal range and nadir GH after an oral glucose load of less than 1 μg/l (1 μg/l = 2·59 mU/l) (Giustina *et al.*, 2000). Patients treated with somatostatin analogues were defined as 'well controlled' if they had an IGF-1 value within the age-adjusted normal range of the IGF-1 assay (25–39 years, 114–492 μg/l; 40–54 years, 90–360 μg/l; ≥ 55 years, 71–290 μg/l). The duration of disease was assumed to be the interval between the clinical onset determined by comparison of old photographs and the time of treatment.

Six of 19 patients in the group who were either cured or well controlled were treated with somatostatin analogues [two with lanreotide (30 mg every 2 weeks i.m.), four with octreotide acetate (30 mg Sandostatin LAR® every 4 weeks i.m.]. Five patients in the active group were treated with somatostatin analogues [one with lanreotide (30 mg every 2 weeks i.m.), four with octreotide acetate (30 mg Sandostatin LAR® every 4 weeks i.m.]. All patients underwent standard and exercise electrocardiograms. In four patients coronary heart disease was excluded by coronary angiography. Patients with known coronary heart disease were not included in the study.

For every patient, the following parameters were measured in the morning after an overnight fast: weight, height, body mass index (BMI), systolic and diastolic blood pressure, and lipid profile. Pituitary function was assessed by measuring the basal levels of free thyroxine, triiodothyronine, TSH, cortisol, testosterone or oestradiol, FSH, LH, prolactin, GH and IGF-1. All patients with hypopituitarism had been receiving adequate substitution therapy at a stable dose for at least 6 months before study entry.

Control group

A group of 21 volunteers, comparable for age (58 ± 9 years, range 42–72 years) and sex distribution (12 males, 9 females), without symptoms or signs of cardiac disease served as non-acromegalic controls for echocardiography.

Echocardiographic examination

Images were taken with patients in the left lateral decubitus position at end expiration with a 3·75-MHz sector probe using a Toshiba SA 380 A Power Vision machine. For each patient, an electrocardiogram was recorded simultaneously. The echocardiographic examination was carried out using standard views and techniques according to the guidelines of the American Society of Echocadiography (Rakowski *et al.*, 1996). For Doppler recordings of the mitral inflow, the sample volume (size 2 mm) of the pulsed Doppler was placed between the tips of the mitral leaflets in the apical four-chamber-view. The mitral inflow velocity was traced and the following variables derived: peak velocity of the early (E) and late (A) filling and deceleration time of the E wave

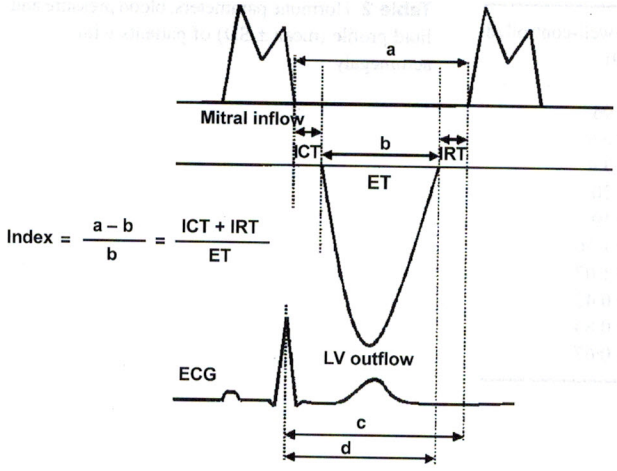

Fig. 1 Scheme for measurements of Doppler time intervals. The index [isovolumetric contraction time (ICT) + isovolumetric relaxation time (IRT)/ejection time (ET)] is derived as (a – b)/b where 'a' is the interval between cessation and onset of the mitral inflow, and 'b' is the ET of the left ventricular (LV) outflow. IRT is measured by subtracting the interval 'c' between the R wave (ECG, electrocardiogram) and the cessation of LV outflow from the interval 'd' between the R wave and the onset of mitral inflow. ICT is derived by subtracting IRT from 'a – b'.

velocity (Tenenbaum *et al.*, 1996). The ratio of early to late peak velocities (E/A) was calculated. Using continuous wave Doppler echocardiography, the cursor was positioned between the LV outflow and mitral inflow to record the isovolumetric relaxation time. The deceleration time was measured as the time from peak E velocity to the intercept of the deceleration of flow with the baseline (Rakowski *et al.*, 1996).

Doppler time intervals were measured from mitral inflow and LV outflow Doppler tracings as described by Tei *et al.* (1996). The interval 'a' from cessation to onset of mitral inflow is equal to the sum of isovolumetric contraction time (ICT), ejection time 'b' and isovolumetric relaxation time (IVRT). The ejection time 'b' is derived from the duration of the LV outflow Doppler velocity profile. The sum of ICT and IVRT was obtained by subtracting 'b' from 'a'. The Tei-Index (normal range < 48) was calculated as (a – b)/b (Fig. 1). IVRT was measured by subtracting the interval 'd' between the R wave in the ECG and cessation of LV outflow from the interval 'c' between the R wave and the onset of mitral inflow (Klein *et al.*, 1994). ICT was calculated by subtracting IVRT from (a – b).

Pulsed-wave TDI was performed by activating the TDI function on the same machine. Because of filter modification, the Nyquist limit was adjusted to a velocity range of –15 to 20 cm/s. From the apical four-chamber view, a 5-mm sample volume was located at the septal side of the mitral annulus. The resulting velocities were recorded for five cycles at a sweep speed of 50 mm/s and stored on a videotape for later playback and analysis. From TDI recordings, the following measurements were performed by an observer who had no knowledge of the clinical data (Fig. 2): peak systolic velocity (S_T), early (E_T) and late (A_T) diastolic velocities, and the E_T/A_T-ratio. The mitral E/E_T-ratio was calculated according to Nagueh *et al.* (1997). For each value the mean of three cardiac cycles was assessed.

Hormone assays

Serum GH levels were determined by a chemiluminescence immunometric assay (Nichols Institute Diagnostics GmbH, Bad Nauheim, Germany). The assay was calibrated against the WHO

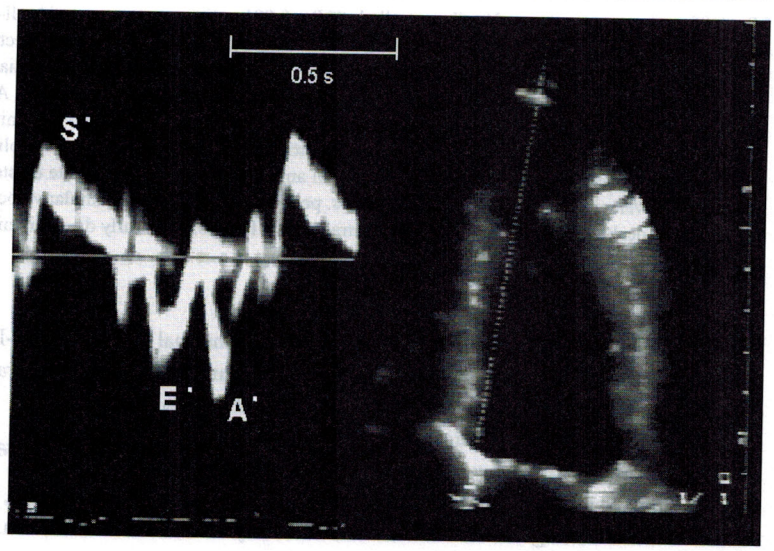

Fig. 2 Pulsed Doppler recordings of mitral inflow (*left side*) and LV outflow (*right side*) in a patient with active acromegaly. The value of the Tei-Index [(ICT + IRT)/ET = (a – b)/b] is 0·80.

Table 2 Hormone parameters, blood pressure and lipid profile (mean ± SD) of patients with acromegaly

	Active ($n = 13$)	Cured/well-controlled ($n = 19$)
IGF-1 (μg/l)	454 ± 194***	210 ± 96
Growth hormone (μg/l)	19·9 ± 53·5***	0·6 ± 0·6
Body mass index (kg/m^2)	26·4 ± 4·3*	30·4 ± 3·4
Systolic blood pressure (mmHg)	134 ± 16	134 ± 20
Diastolic blood pressure (mmHg)	84 ± 10	87 ± 10
Total cholesterol (mmol/l)	5·51 ± 1·59	5·82 ± 1·56
LDL cholesterol (mmol/l)	3·72 ± 1·51	4·26 ± 1·07
HDL cholesterol (mmol/l)	1·35 ± 0·42	1·30 ± 0·42
Triglycerides (mmol/l)	1·63 ± 0·78	1·83 ± 0·84
Blood glucose (mmol/l)	5·77 ± 1·01	5·38 ± 0·67

***$P < 0·0005$; *$P < 0·01$.

Table 3 2-D-Doppler echocardiography and Doppler-derived variables, tissue Doppler imaging in patients with acromegaly and in control subjects

	Active ($n = 13$)	Cured/well-controlled ($n = 19$)	Controls ($n = 21$)
EF (%)	61 ± 7	61 ± 7	61 ± 10
LVMMI (g/m^2)	109 ± 23	116 ± 20	105 ± 22
FS (%)	35 ± 7	35 ± 5	32 ± 5
Heart rate (beats/min)	73 ± 8	74 ± 9	73 ± 8
CI (l/min)	2·3 ± 0·2	2·5 ± 0·3	2·6 ± 0·9
SVI (ml/m^2)	37 ± 10	30 ± 11	28 ± 10
Tei-Index	0·50 ± 0·15**	0·48 ± 0·12	0·41 ± 0·10
E (m/s)	0·58 ± 0·16**	0·66 ± 0·12	0·73 ± 0·19
A (m/s)	0·71 ± 0·18	0·66 ± 0·22	0·66 ± 0·10
E/A	0·82 ± 0·23*‡	1·12 ± 0·41	1·14 ± 0·33
DT (ms)	209 ± 19**†	179 ± 22	185 ± 26
IVRT (ms)	79 ± 14	75 ± 14	77 ± 19
S_T (m/s)	7·79 ± 1·04	8·38 ± 1·41	8·39 ± 1·39
E_T (m/s)	7·13 ± 2·11*‡	9·83 ± 3·29	10·10 ± 1·70
A_T (m/s)	10·45 ± 1·84	10·56 ± 1·94	10·18 ± 1·65
E_T/A_T	0·71 ± 0·26*‡	0·95 ± 0·33	1·00 ± 0·15
E/E_T	v8·7 ± 3·0	7·1 ± 3·0	7·4 ± 2·5

*$P < 0·05$ active group *vs.* cured/well-controlled; **$P < 0·001$ active group *vs.* cured/well-controlled; †$P < 0·05$ active group *vs.* controls; ‡$P < 0·001$ active group *vs.* controls. EF, ejection fraction; LVMMI, left ventricular muscle mass index; FS, fractional shortening; CI, cardiac index; SVI, stroke volume index; E, peak velocity of the early diastolic transmitral flow; A, peak velocity of the late diastolic transmitral flow; E/A, ratio of peak early *vs.* late transmitral flow velocity; DT, deceleration time; IVRT, isovolumetric relaxation time; S_T, peak systolic mitral annular velocity; E_T, peak early diastolic mitral annular velocity; A_T, peak late diastolic mitral annular velocity; E_T/A_T, ratio of peak early *vs.* peak late diastolic mitral annular velocity; E/E_T, ratio of peak velocity of the early diastolic transmitral flow *vs.* peak early diastolic mitral annular velocity.

First International Standard (80/505) for human GH. The normal range was 5 μg/l. Intra- and interassay coefficients of variation (CVs) for a low point on the standard curve were 5·4% and 7·9%, respectively. Plasma IGF-I concentrations were measured by an immunoradiometric assay (Nichols Institute Diagnostics GmbH). The assay was calibrated against the WHO First International Reference Reagent 87/518. Intra- and interassay CVs for low IGF-I concentrations were 2·4% and 5·2%, respectively. All other parameters were determined by routine methods.

Statistical analyses

The data, if not marked otherwise, represent the mean ± standard deviation. In case of skewed distribution the median was also

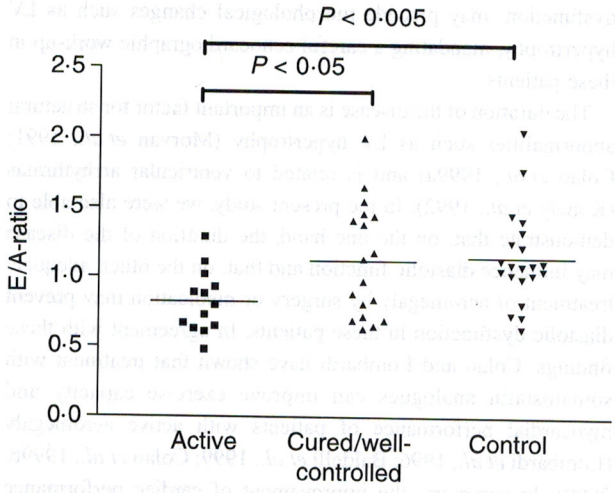

Fig. 3 Doppler-derived variables: mitral inflow velocities (ratio of peak velocity of early E and late A filling) in patients with acromegaly and in control subjects.

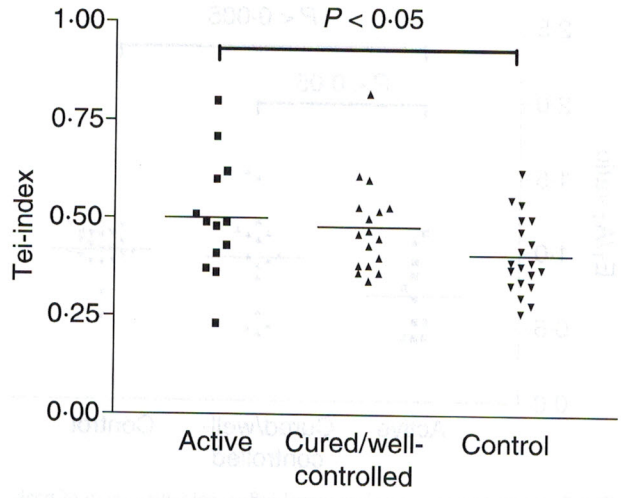

Fig. 4 Tei-Index in patients with acromegaly and in control subjects.

determined. Comparisons of dichotomous variables were performed by Fisher's exact test. Continuous data were tested statistically by the *U*-test according to Wilcoxon, Mann and Whitney on differences between the groups. All tests were two-tailed and *P*-values < 0·05 were considered statistically significant.

Results

Tables 1 and 2 summarize the clinical and hormone parameters of the patients and the control group. Age, disease duration, prevalence of arterial hypertension, lipid status and fasting plasma glucose levels did not differ significantly in patients with active and cured/well-controlled acromegaly. Patients with active acromegaly had a lower BMI than the cured/well-controlled group.

Data derived from echocardiographic analysis are summarized in Table 3. Ejection fraction (EF) and LVMMI did not differ significantly. In the active group (AA), peak mitral E velocity and the E/A-ratio were significantly reduced, and the deceleration time was significantly prolonged in comparison to the cured/well-controlled group (CA) and the control group (CON) (Table 3; Fig. 3). The Tei-Index was significantly elevated in the active group in comparison to the control group but not the cured/well-controlled groups (Fig. 4).

TDI analysis of mitral annulus motion revealed no significant difference of systolic (S_T) and late diastolic (A_T) annular velocities (Table 3) in the three study groups. The E/E_T-ratio also did not differ significantly between the three study groups. In patients with active acromegaly, the early diastolic annular velocity E_T and the E_T/A_T-ratio were significantly reduced in comparison to the CA and the CON groups (Table 3 and Fig. 5). Subjects with cured or well-controlled acromegaly did not differ significantly from controls with respect to 2-D/Doppler echo- and TDI-derived parameters. There was a distinct correlation between the disease duration and the E_T/A_T-ratio ($r = -0{\cdot}49$; $P = 0{\cdot}0099$), the E/A-ratio ($r = -0{\cdot}37$; $P = 0{\cdot}039$) and the Tei-Index ($r = 0{\cdot}37$; $P = 0{\cdot}042$) in the AA and the CA groups, whereas the IGF-1 levels did not correlate directly with the E_T/A_T-ratio, the E/A-ratio, the LVMMI or the Tei-Index. Furthermore, the LVMMI did not correlate either with the E/A-ratio or the Tei-Index.

Intra- and interobserver variability for measurements derived from TDI analysis of mitral annulus motion (S_T, E_T, A_T, E_T/A_T) and Doppler-derived parameters (E, A, E/A-ratio, deceleration time, isovolumetric relaxation time) ranged from 1·1% to 8·9%.

Discussion

The results of conventional 2-D/Doppler echocardiography and TDI of the mitral annulus demonstrate that diastolic function is impaired in patients with active acromegaly (AA), even in the absence of LV hypertrophy. Compared to cured/well-controlled patients (CA) and healthy controls (CON) (all three groups had a comparable muscle mass index of the LV), those with active acromegaly showed a reduced mitral E wave, a lower E/A-ratio and a prolonged deceleration time. In these patients, early diastolic mitral annular velocity (E_T) and E_T/A_T-ratio derived from TDI analysis were also reduced compared to CA and to CON, suggesting that TDI analyses are more sensitive than conventional echo measurements.

Previous echocardiographic studies have demonstrated morphological alterations such as LV hypertrophy and functional abnormalities (diastolic dysfunction), followed by systolic dysfunction in patients with active acromegaly (Bolanowski *et al.*, 1992; Colao *et al.*, 1999b, 2000). Doppler echo measurements

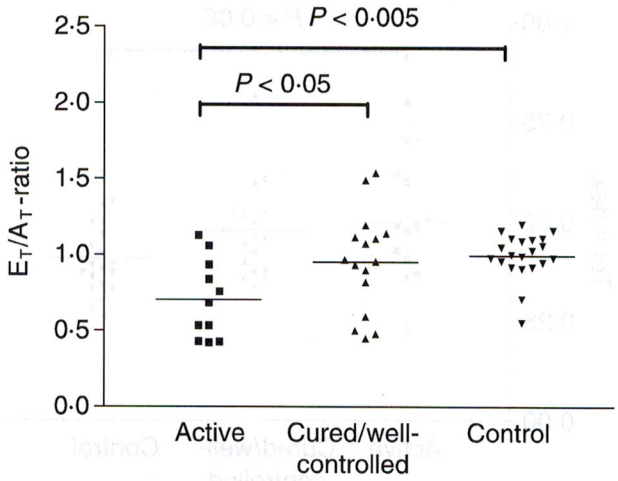

Fig. 5 Tissue Doppler imaging: mitral inflow velocities (ratio of peak velocity of early E_T and late A_T filling) in patients with acromegaly and in control subjects.

showed an abnormal LV filling, indicating impairment of diastolic function in patients with elevated muscle mass index of the left ventricle (LVMMI) in comparison with healthy controls (Minniti *et al.*, 1998). Recently, pulsed-wave TDI of the myocardium has demonstrated reduced regional systolic and diastolic peak velocities in active acromegalics with LVMMI compared with healthy controls with elevated LVMMI (Mercuro *et al.*, 2000). In contrast, in our study the findings in subjects with active acromegaly were compared to patients with cured or well-controlled disease and to a healthy control group. The additional aim of the study was to detect early myocardial dysfunction in patients with normal averaged LVMMI (maximum 139 g/m^2 of all groups).

In our study, acromegalic patients with active and cured/well-controlled disease were comparable with respect to their lipid profile, glucose levels and blood pressure, further supporting the influence of disease activity on LV performance in such patients. Furthermore, all patients with anterior pituitary insufficiency were receiving adequate substitution therapy to avoid the influence of other hormonal deficiencies on echocardiographic performance. The lower BMI in the active group may be due to the direct lipolytic effect of GH on adipose tissue, as has been shown in several studies (Bengtsson *et al.*, 1989; O'Sullivan *et al.*, 1994; Damjanovic *et al.*, 2000; Kaji *et al.*, 2001).

We demonstrated that patients with cured or well-controlled acromegaly did not differ significantly from controls with respect to echocardiographic measurements, indicating that normalization of IGF-1 levels over a longer period may directly improve diastolic function in affected patients. In comparison to previous studies demonstrating diastolic dysfunction in acromegaly with elevated LVMMI (Galanti *et al.*, 1996; Ozbey *et al.*, 1997), the findings of our study show that functional changes, i.e. diastolic dysfunction, may precede morphological changes such as LV hypertrophy, mandating a careful echocardiographic work-up in these patients.

The duration of the disease is an important factor for structural abnormalities such as LV hypertrophy (Morvan *et al.*, 1991; Colao *et al.*, 1999a) and is related to ventricular arrhythmias (Kahaly *et al.*, 1992). In the present study, we were also able to demonstrate that, on the one hand, the duration of the disease may influence diastolic function and that, on the other, adequate treatment of acromegaly by surgery or medication may prevent diastolic dysfunction in these patients. In agreement with these findings, Colao and Lombardi have shown that treatment with somatostatin analogues can improve exercise capacity and myocardial performance of patients with active acromegaly (Lombardi *et al.*, 1996; Baldelli *et al.*, 1999; Colao *et al.*, 1999b, 2000). In summary, the improvement of cardiac performance after treatment with somatostatin analogues depends on the aim of long-term normalization of IGF-1 levels.

Systolic parameters (ejection fraction, fractional shortening, peak systolic annular velocity) did not differ between the three groups, in agreement with previous observations in patients with beginning acromegalic cardiomyopathy (Musiari *et al.*, 1999). In our study, the E/A-ratio was reduced and deceleration time was prolonged in patients with active disease, but the isovolumetric relaxation time was normal. In this context, it is important to note that mitral inflow is affected not only by the rate and extent of ventricular relaxation but also by age, heart rate and loading conditions (Nishimura & Tajik, 1997). Most importantly, in our study the results of the mitral flow-derived parameters were confirmed by TDI analysis of the mitral annulus motion. Mitral annular velocities derived from TDI analysis are found to be less load-dependent than conventional mitral inflow variables (Nagueh *et al.*, 1997; Sohn *et al.*, 1997). Thus they were recommended for additional assessment of both systolic and diastolic function in various clinical settings. In conclusion, TDI analysis should complete the echocardiographic work-up in acromegalic patients to detect early diastolic dysfunction and to examine the effect of treatment.

GH stimulates the growth of various tissues (Melmed, 1990) and can induce myocardial hypertrophy with interstitial fibrosis in a progressive stage (Lie, 1980; Sacca *et al.*, 1994; Lombardi *et al.*, 1997; Sacca, 1997; Frustaci *et al.*, 1999). The fact that early diastolic dysfunction is related to disease activity and to cardiac hypertrophy might be due to abnormalities of the cell cycle and to programmed myocyte cell death (apoptosis) (Frustaci *et al.*, 1999). Frustaci *et al.* (1999) have shown that patients with active acromegaly have an increased rate of apoptosis of myocytes independent of the hormonal level of GH and IGF-1. Furthermore, it has been shown that changes in protein expression of myosin genes (Timsit *et al.*, 1990) can be seen in active acromegaly with high cardiac output and normal muscle

mass index, indicating that molecular changes may precede cardiac hypertrophy (Xu & Best, 1991; Mayoux *et al.*, 1993; Lavandero *et al.*, 1998). IGF-1 activates multiple and complex signal transduction pathways, autophosphorylation of two β-subunits of IGF-1 receptors, by increases in the phosphotyrosine content of extracellular signal-regulated kinase, insulin receptor substrate 1 and phospholipase C-γl, which may be relevant to the later hypertrophic response of the myocardium (Foncea *et al.*, 1997; Lavandero *et al.*, 1998).

The Tei-Index as a combined and sensitive parameter reflects overall cardiac dysfunction in patients with dilated cardiomyopathy and cardiac amyloidosis and provides useful information in patients with mild to moderate congestive heart failure (Tei *et al.*, 1996; Dujardin *et al.*, 1998; Katz *et al.*, 1999; Marin *et al.*, 1999; Bruch *et al.*, 2000). In the present study, the Tei-Index was assessed in subjects with active and cured/well-controlled acromegaly. The Tei-Index was elevated in the active group and significantly higher when compared to the control group, indicating an early global dysfunction. Further studies are needed to show the potential impact and prognostic value of this new index in acromegalic patients, especially regarding the influence of cure after transsphenoidal resection and the influence of treatment with somatostatin analogues in a longitudinal study.

The data demonstrate that diastolic dysfunction can be verified by tissue Doppler imaging in patients with active acromegaly with normal or slightly elevated left ventricular muscle mass and seems to be related to disease activity. Furthermore, the Tei-Index as a sensitive combined myocardial performance index is elevated in subjects with active disease.

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