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FULL PAPER

CT pulmonary densitovolumetry in patients with acromegaly: a comparison between active disease and controlled disease

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Objective: Our purpose was to compare the findings of CT pulmonary densitovolumetry and pulmonary function in patients with active acromegaly and controlled acromegaly and, secondarily, to correlate these findings.

Methods: 11 patients with active acromegaly, 18 patients with controlled acromegaly and 17 control subjects, all non-smokers, underwent quantification of lung volume using multidetector CT (Q-MDCT) and pulmonary function tests.

Results: Patients with active acromegaly had larger total lung mass (TLM) values than the controls and larger amounts of non-aerated compartments than the other two groups. Patients with active acromegaly also had larger amounts of poorly aerated compartments than the other two groups, a difference that was observed in both

total lung volume (TLV) and TLM. TLV as measured by inspiratory Q-MDCT correlated significantly with total lung capacity, whereas TLV measured using expiratory Q-MDCT correlated significantly with functional residual capacity.

Conclusion: Patients with active acromegaly have more lung mass and larger amounts of non-aerated and poorly aerated compartments. There is a relationship between the findings of CT pulmonary densitovolumetry and pulmonary function test parameters.

Advances in knowledge: Although the nature of our results demands further investigation, our data suggest that both CT pulmonary densitovolumetry and pulmonary function tests can be used as useful tools for patients with acromegaly by assisting in the prediction of disease activity.

INTRODUCTION

Acromegaly is an endocrine disease of insidious onset, most common in patients between 30 and 50 years old, without gender predilection. It is caused by the lasting exposure to high levels of growth hormone (GH) and insulin-like growth factor I (IGF-I), determining cardiovascular, respiratory and neoplastic changes.¹ Both GH and IGF-I are the classic and the most important hormonal parameters for the diagnosis of acromegaly. They are currently the most widely accepted measures for monitoring the response to treatment and disease activity. Several

studies have linked hormonal control in patients with acromegaly to a lower mortality rate and comorbidity reduction.^{2,3}

Mortality from respiratory disease is approximately three times higher in patients with acromegaly than that observed in healthy subjects. It is estimated that respiratory involvement accounts for 25% of all deaths that occur in this patient group.^{1,2,4,5} Interestingly, acromegaly duration does not appear to have any significant influence on the overall mortality of these patients and, in particular,

on pulmonary disease; however, some studies have correlated respiratory system involvement with disease activity.^{2,6} There are several studies that discuss the changes in lung volume in patients with acromegaly and the relationship between the increases in GH and alveolar growth in these patients, which reinforces the importance of new studies on disease activity.^{5,7}

Although there have been few studies evaluating pulmonary function in patients with acromegaly, subclinical hypoxaemia, increased lung volume, reduced respiratory muscle strength and lower airway involvement have all been observed in the lungs of these individuals.^{1,5,8,9} In regards to imaging, new studies and methods have been proposed. It is known that CT is a good tool for the early diagnosis of pulmonary involvement in various systemic diseases.^{10,11} Quantification of volume is particularly effective using multidetector CT (Q-MDCT), which is more accurate in predicting lung function and estimating regional volumes in different compartments, thus providing more information than classical methods.^{10,12,13}

Experimentally, the expression and activity levels of GH and IGF-I have been investigated in various types of human and rodent respiratory cells, and there is evidence that these two hormones exert proliferative effects on both smooth muscle and lung cells.^{5,14–17} Studies using muscle biopsy have demonstrated segmental fibre degeneration, small-cell infiltration foci, membrane thickening and variable degrees of hypertrophy involving Type I and II fibres.⁵

In view of the importance of pulmonary involvement in acromegaly, several morphological and functional parameters relating to lung disease require further study to be incorporated as additional markers of disease activity. We hypothesized that the histopathological changes that occur in the acromegalic lung as a result of the actions of GH and IGF-I may lead to an increase in the average density of lung parenchyma and may thus have an impact on lung function. Thus, this study aimed to compare the findings of pulmonary densitovolumetry and pulmonary function in patients with active and controlled acromegaly and, secondarily, to correlate these findings.

METHODS AND MATERIALS

Patients

Between June 2012 and July 2014, a cross-sectional study of 37 patients with acromegaly was performed. Subjects were over 18 years of age and were regularly seen at Clementino Fraga Filho University Hospital of the Federal University of Rio de Janeiro, Rio de Janeiro, Brazil. All patients had a diagnosis of suspected disease owing to clinical characteristics. The diagnosis was confirmed based on high levels of non-suppressed GH falling to levels $<0.4 \text{ ng ml}^{-1}$ after an oral glucose tolerance test or IGF-I levels above the upper limit of the normal range.^{18,19} Later, the patients were subdivided into “active disease” and “controlled disease” groups according to serum IGF-I levels. Patients were considered to have controlled acromegaly when IGF-I levels were within the reference values adjusted for age and when their basal GH level was $<1 \text{ ng ml}^{-1}$; otherwise, they were considered to have active acromegaly.¹⁹ Smoking and comorbidities not related to acromegaly that could interfere with

the results of the Q-MDCT and pulmonary function tests were considered exclusion criteria. There was also a control group of individuals who were invited to undergo pulmonary function tests after having already had chest CT in our service for other reasons. This group consisted of 17 subjects (11 females) who also met the inclusion and exclusion criteria. All participants signed the consent form, and the protocol was approved by the Research Ethics Committee of the State University of Rio de Janeiro under number 234362.

Pulmonary function testing

The pulmonary function tests consisted of spirometry, body plethysmography, diffusing capacity for carbon monoxide and respiratory muscle strength. Measurements were conducted using an high definition classic pulmonary function laboratory (nSpire Health, Inc., Longmont, CO) following the standards for the procedure and interpretation.²⁰ The pulmonary function testing results were expressed as the percent of the predicted values for the Brazilian population.^{21–24}

Densitovolumetry

The CT images were acquired using a 64-channel helical CT scanner (Brilliance 40; Philips Medical Systems, Cleveland, OH) at full inspiration and end expiration without the use of contrast medium and using the following parameters: reading time set to 0.4 s; X-ray tube current between 130 and 190 mA; and voltage of 120 kVp. Each image acquisition consisted of a block with 2-mm-thick cross-sections separated by 1 mm, and the images were represented by a square matrix of 768 rows and 768 columns. All images were reconstructed using a standard reconstruction algorithm (Convolution Kernel D-Philips Medical, Best, Netherlands).

Lung parenchyma segmentation was performed, and the images were exported to software (CT Processing) written in MATLAB® (MathWorks®, Natick, MA) developed at the Laboratory of Respiration Physiology of the Carlos Chagas Filho Institute of Biophysics of the Federal University of Rio de Janeiro, Rio de Janeiro, Brazil. After this entire process, it was possible to perform lung densitometry using Q-MDCT.

Total lung volume (TLV), total air volume and total lung mass (TLM) were calculated considering only the image contained within the region of interest (pulmonary parenchyma).

TLV (*i.e.* the sum of air plus tissue volume) was calculated as follows:^{25,26} $[(\text{size of the pixel})^2 \times \text{slice thickness} \times \text{total number of pixels of the region of interest for the whole lung}]$.

Mass of the lungs was calculated as follows:^{25,26} $[(1 - \text{voxel density}/-1000) \times (\text{size of the pixel})^2 \times \text{slice thickness} \times \text{total number of pixels of the region of interest for the whole lung}]$.

A frequency distribution histogram was then created of the voxels as a function of density in Hounsfield units (HU). The histogram was then divided into compartments ranging between -1000 and $+100$ HU. The images were analysed for the calculation of percentages of hyperaerated (-1000 to -900 HU), normally aerated (-900 to -500 HU), poorly aerated (-500 to

2100 HU) and non-aerated (-100 to $+100$ HU) compartments in TLV (Figure 1).^{25,26}

Data analysis

Descriptive results are reported as median and interquartile range values or frequencies (percentage). The data distribution was assessed by using the Shapiro–Wilk test. Numerical variables and categorical variables were compared using the Mann–Whitney test and Fisher’s exact test, respectively. Spearman’s rank correlation coefficient was calculated to investigate associations. Data analysis was performed using SAS® v. 6.11 software (SAS Institute, Inc., Cary, NC). The level of statistical significance was set at $p < 0.05$.

RESULTS

8 of the 37 initially recruited patients with acromegaly were excluded for the following reasons: refusal to participate in the

study (6) and inability to reach the acceptability criteria in pulmonary function tests (2). Of the 29 study participants, 11 had active acromegaly and 18 had controlled acromegaly. At the time of observation, the controlled acromegaly group had been receiving treatment for 29 months (11.5–42 months). When compared with control subjects, patients with acromegaly did not differ regarding age, gender or height ($p < 0.05$ for all). The general characteristics of patients with acromegaly with active disease and controlled disease and the control group are outlined in Table 1.

In inspiratory Q-MDCT, patients with active acromegaly exhibited larger lung mass values than the control subjects [885 g (723–994 g) vs 696 g (599–769 g), $p = 0.017$]. We observed that patients with active acromegaly had greater amounts of non-aerated compartments than the patients with controlled acromegaly and control subjects [0.37 (0.31–0.51) vs 0.29

Figure 1. A 53-year-old female with active acromegaly. (a) End-expiratory transversal chest CT scan slice presenting ground-glass opacity in dorsal regions. (b) Three-dimensional representation of the lungs reconstructed from the binary matrix region of interest shows poorly aerated areas (dark grey). (c) Histogram of the frequency of occurrence of voxels: the poorly aerated areas are located between -500 and -100 HU.

Table 1. General characteristics of patients with acromegaly and healthy individuals

Variable	Active acromegaly (<i>n</i> = 11)	Controlled acromegaly (<i>n</i> = 18)	Control group (<i>n</i> = 17)	<i>p</i> -value
Demographic data				
Age (years)	45 (32–57)	51.5 (45.5–59.3)	41 (29–52)	0.062
Female sex (%)	7 (63.6)	13 (72.2)	11 (64.7)	0.85
Body mass (kg)	102.7 (77–105)	80 (71.3–90.3)	76 (63.5–87)	0.042^a
Height (cm)	168 (161–180)	163.3 (155.4–168.5)	167 (160.5–170)	0.37
Body mass index (kg m ⁻²)	32.6 (27.5–37.9)	32.5 (27.2–33.4)	27.2 (23.4–31.3)	0.033^b
Clinical data				
Time since diagnosis of disease (months)	72 (15–108)	109.5 (63–152.3)	–	0.087
Growth hormone (µg L ⁻¹)	3 (2–4.3)	0.60 (0.37–1.05)	–	0.0002^c
IGF-I (µg L ⁻¹)	741 (367–859)	186.5 (160.5–222.5)	–	0.0001^c
IGF-I (% upper limit normal value)	241 (141–353)	83 (68–94)	–	0.0001^c

IGF-I, insulin-like growth factor I.

Values are presented as median (interquartile range) or number (%). Bold values indicate significant differences.

^aA ≠ C.

^bA, B ≠ C.

^cA ≠ B.

(0.08–0.34) vs 0.25 (0.20–0.32) %TLV, *p* = 0.039]. Patients with active acromegaly also had higher amounts of poorly aerated compartments than the other two groups, a difference that was observed when calculated in millilitres [130 (118–161) vs 102 (78–125) vs 83 (65–91), *p* = 0.0001], %TLV [3.25 (2.55–3.46) vs 2.24 (1.70–2.56) vs 1.70 (1.45–2.15), *p* = 0.001] and grams [82.6 (75.4–100.2) vs 63.9 (49.1–80.3) vs 54.2 (42.2–59.2), *p* = 0.0001]. Patients with active acromegaly also had higher amounts of poorly aerated compartments than the controls when calculated in %TLM [10.5 (8.97–13.4) vs 7.25 (6.35–8.40), *p* = 0.004].

In expiratory Q-MDCT, patients with active acromegaly had larger lung mass values than patients with controlled disease and control subjects [899 g (718–988 g) vs 793 g (741–903 g) vs 637 g (536–736 g), *p* = 0.007]. Patients with active acromegaly had higher amounts of non-aerated compartments than the other two groups, a difference that was observed when calculated in millilitres [47.3 (37.4–66.1) vs 32.7 (15–59.4) vs 10.2 (8.39–11.7), *p* = 0.0006], %TLV [2.13 (1.62–2.42) vs 1.33 (0.58–2.60) vs 0.52 (0.31–0.63), *p* = 0.007], grams [46.6 (37–65.4) vs 32.3 (14.6–58.7) vs 9.92 (8.15–11.4), *p* = 0.0006] and %TLM [5.70 (4.92–6.08) vs 4.26 (1.91–6.33) vs 1.51 (1.13–1.78), *p* = 0.002]. Table 2 shows a comparison of the inspiratory and expiratory CT findings between patients with active acromegaly, controlled acromegaly and control subjects.

In regards to the control group, we observed that patients with controlled disease had higher forced vital capacity values (%predicted) [114 (109.8–122.5) vs 102 (96.5–106.5), *p* = 0.001], forced expiratory volume in 1 second (%predicted) [110 (103–120.3) vs 103 (94.5–106), *p* = 0.037] and functional residual capacity

(FRC, %predicted) [88 (83.8–99.5) vs 74 (70–85), *p* = 0.024]. When compared with controls, patients with acromegaly (active disease and controlled disease) showed higher total lung capacity (TLC) values (%predicted) [109 (94–115) vs 109 (103–119.5) vs 93 (87–101.5), *p* = 0.0007] and residual volume (RV)/TLC [32.8 (28.4–40.4) vs 33.4 (30.6–38.9) vs 25.4 (17.9–33.2), *p* = 0.011]. We also observed that patients with active acromegaly exhibited larger RV values (%predicted) relative both to patients with controlled acromegaly and the control group [116 (97.8–135) vs 109.5 (82–121) vs 74 (56–94), *p* = 0.0002]. Table 3 shows a comparison between patients with active acromegaly, patients with controlled acromegaly and the control group according to the pulmonary function tests.

We also evaluated the correlations between the serum levels of GH and IGF-I, pulmonary densitovolumetry findings and the pulmonary function test parameters of the patients with acromegaly. The poorly aerated compartment measured in inspiratory CT was significantly correlated with GH and IGF-I levels (*r*_s = 0.407, *p* = 0.029; *r*_s = 0.467, *p* = 0.011, respectively). TLV as measured by inspiratory Q-MDCT was significantly correlated with TLC (*r*_s = 0.742, *p* = 0.0001), whereas TLV measured using expiratory Q-MDCT was significantly correlated with FRC (*r*_s = 0.606, *p* = 0.0005).

DISCUSSION

The main findings of this study were as follows: (1) patients with active acromegaly have larger lung mass values than control subjects; (2) patients with active acromegaly have greater amounts of non-aerated and poorly aerated compartments than patients with controlled acromegaly and control subjects; (3) patients with acromegaly have higher lung

Table 2. Variables of inspiratory and expiratory CT according to the group

Variable	Inspiratory CT				Expiratory CT			
	Active acromegaly (n = 11)	Controlled acromegaly (n = 18)	Control group (n = 17)	p-value	Active acromegaly (n = 11)	Controlled acromegaly (n = 18)	Control group (n = 17)	p-value
TLV (ml)	4616 (3760–5005)	4645 (4102–5712)	4264 (3721–5287)	0.60	2388 (1981–3083)	2450 (2277–2904)	1963 (1372–3225)	0.31
Total air volume (ml)	3760 (3067–4109)	3951 (3368–4869)	3653 (3170–4606)	0.60	1673 (1134–1973)	1687 (1461–1988)	1345 (836–2527)	0.46
TLM (g)	885 (723–994)	779 (639–858)	696 (599–769)	0.017^a	899 (718–988)	793 (741–903)	637 (536–736)	0.007^b
Non (ml)	15.3 (9.82–24.1)	13.1 (3.68–19.1)	12.2 (7.61–15.5)	0.34	47.3 (37.4–66.1)	32.7 (15–59.4)	10.2 (8.39–11.7)	0.0006^b
Poor (ml)	130 (118–161)	102 (78–125)	83 (65–91)	0.0001^c	352 (212–516)	301 (209–433)	243 (100–291)	0.081
Norm (ml)	3741 (2984–4021)	3288 (2868–3649)	2861 (2605–3375)	0.071	1788 (1411–2445)	2072 (1796–2390)	1706 (1084–2752)	0.51
Hyper (ml)	769 (544–863)	1124 (759–2178)	1152 (947–1930)	0.11	74.9 (29.1–285.3)	90.6 (39.4–129.4)	34.4 (16.3–363.3)	0.63
Non (%TLV)	0.37 (0.31–0.51)	0.29 (0.08–0.34)	0.25 (0.20–0.32)	0.039^b	2.13 (1.62–2.42)	1.33 (0.58–2.60)	0.52 (0.31–0.63)	0.007^b
Poor (%TLV)	3.25 (2.55–3.46)	2.24 (1.70–2.56)	1.70 (1.45–2.15)	0.001^b	16.1 (6.82–25.4)	12.6 (8.60–17.2)	12.8 (3.16–18.1)	0.72
Norm (%TLV)	80.3 (74.7–82.8)	73.3 (59.7–79.2)	68.5 (57.1–77.7)	0.079	78.4 (69.8–80.4)	82.2 (77.6–86)	83.9 (80.4–85.3)	0.077
Hyper (%TLV)	17.0 (13.7–21)	24.1 (18.3–38.7)	29.7 (19.7–40.4)	0.047^d	2.43 (1.54–6.86)	3.73 (1.75–4.62)	1.58 (1.03–11.2)	0.78
Non (g)	15.0 (9.57–23.6)	12.8 (3.48–18.8)	11.9 (7.40–15.2)	0.33	46.6 (37–65.4)	32.3 (14.6–58.7)	9.92 (8.15–11.4)	0.0006^b
Poor (g)	82.6 (75.4–100.2)	63.9 (49.1–80.3)	54.2 (42.2–59.2)	0.0001^c	222 (132–321)	184 (135–273)	144 (63–174)	0.073
Norm (g)	726 (590–760)	613 (529–665)	512 (448–655)	0.010^b	562 (432–733)	586 (492–625)	489 (365–600)	0.43
Hyper (g)	51.1 (38.4–62.9)	80.2 (52.6–145.3)	80.7 (64.4–130.3)	0.15	4.82 (1.53–19.9)	6.15 (2.57–8.78)	2.06 (0.91–24.7)	0.66
Non (%TLM)	1.89 (1.57–2.38)	1.69 (0.45–2.42)	1.57 (1.26–2.14)	0.53	5.70 (4.92–6.08)	4.26 (1.91–6.33)	1.51 (1.13–1.78)	0.002^b
Poor (%TLM)	10.5 (8.97–13.4)	8.41 (7.58–9.93)	7.25 (6.35–8.40)	0.004^d	27.6 (16.1–37.7)	23 (17.8–29)	22.8 (9.16–28.8)	0.72
Norm (%TLM)	81.5 (76.8–82.3)	79.1 (69.5–84.1)	77.8 (69.4–82.3)	0.73	65.1 (56.3–76)	72.7 (61–77.6)	75.4 (69.3–85.9)	0.080
Hyper (%TLM)	6.51 (4.74–7.86)	10.4 (7.68–18.9)	13.8 (7.96–18.9)	0.033^d	0.43 (0.21–1.81)	0.80 (0.33–1.13)	0.28 (0.16–3.55)	0.83

Hyper, hyperaerated compartment; Non, non-aerated compartment; Norm, normally aerated compartment; Poor, poorly aerated compartment; TLM, total lung mass; TLV, total lung volume. Values are presented as median (interquartile range) or number (%). Bold values indicate significant differences.

^aA ≠ C.

^bA ≠ B, C.

^cA ≠ B ≠ C.

^dA ≠ B.

Table 3. Variables of pulmonary function tests according to the group

Variable	Active acromegaly (<i>n</i> = 11)	Controlled acromegaly (<i>n</i> = 18)	Control group (<i>n</i> = 17)	<i>p</i> -value
Spirometry				
FVC (%predicted)	112 (89–115)	114 (109.8–122.5)	102 (96.5–106.5)	0.001^a
FEV ₁ (%predicted)	102 (86–115)	110 (103–120.3)	103 (94.5–106)	0.037^a
FEV ₁ /FVC	82.4 (74.2–85)	78.8 (76.3–81.9)	82.3 (79–87.3)	0.102
Maximum forced expiratory flow (%predicted)	98 (81–104)	104.5 (90–127)	93 (84–127.5)	0.573
Body plethysmograph				
TLC (%predicted)	109 (94–115)	109 (103–119.5)	93 (87–101.5)	0.0007^b
Functional residual capacity (%predicted)	97 (71–114)	88 (83.8–99.5)	84 (74–85)	0.024^a
RV (%predicted)	116 (97.8–135)	109.5 (82–121)	84 (76–94)	0.0002^c
RV/TLC	32.8 (28.4–40.4)	33.4 (30.6–38.9)	25.4 (17.9–33.2)	0.011^b
Airway resistance (cmH ₂ O L ⁻¹ s ⁻¹)	2.64 (2.02–3.42)	2.45 (1.44–3.76)	1.64 (1.39–2.13)	0.063
Diffusing capacity				
DLco (%predicted)	99 (91–120)	107 (95.2–113.5)	107 (94.5–114)	0.900
DLco/alveolar volume (%predicted)	113 (90–126)	106 (88.5–122)	111 (104–128.5)	0.285
Respiratory muscle strength				
Maximal inspiratory pressure (%predicted)	57 (38–67)	57.5 (45–93)	76 (55.5–87.5)	0.178
Maximal expiratory pressure (%predicted)	53 (41–64)	52 (35–65.7)	62 (52.5–67.5)	0.333

DLco, diffusing capacity for carbon monoxide; FEV₁, forced expiratory volume in 1s; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity.

Values are presented as median (interquartile range) or number (%). Bold values indicate significant differences.

^aB ≠ C.

^bA, B ≠ C.

^cA ≠ B ≠ C.

volumes, as measured by pulmonary function tests; and (4) there are significant correlations between the inspiratory and expiratory Q-MDCT findings and pulmonary function test parameters.

Both pulmonary function tests and Q-MDCT may more accurately describe the effects of acromegaly on the respiratory system. However, as with any other method of investigation, it is necessary to eliminate confounding factors that may compromise the interpretation of the study results. Thus, we included only non-smokers to eliminate the effects that smoking can have on the respiratory systems of these individuals from the points of view of pulmonary function tests (obstructive disorder) and Q-MDCT (emphysema). As expected, we observed that patients with acromegaly had higher body mass indices than control subjects. This difference is explained by the fact that GH counteracts the effects of insulin on both glucose and lipid metabolism and causes anabolic interactions in protein metabolism.^{5,27}

Q-MDCT is accurate in estimating regional volumes in different compartments and can even determine lung air and non-air contents, thus providing quite accurate information on both the mass of the organ and its compartments.^{13,28} This study showed that patients with acromegaly have more lung mass than control subjects. Even more important, we observed that patients with active acromegaly have more lung mass in inspiratory CT than those with controlled acromegaly. Also in line with these findings, we observed that there was a significant correlation between GH and IGF-I levels and poorly aerated compartments evaluated in inspiratory CT. Based on these findings, we believe that the proliferative effects of GH and IGF-I on pulmonary cytoarchitecture can explain, at least in part, the mass increase of lung tissue in patients with acromegaly.²⁹ It is noteworthy that left ventricular hypertrophy, diastolic dysfunction and systolic dysfunction are common findings in patients with acromegaly.^{30,31} Thus, echocardiograms could help assess the potential impact of acromegalic cardiomyopathy contributing to increased pulmonary mass in these patients.

This study showed an increase in the average density of lung parenchyma in individuals with acromegaly, particularly in the group with active acromegaly, which was expressed by increased non-aerated and poorly aerated compartments. These findings are in line with other studies showing histopathological changes compatible with cell proliferation in acromegaly. Interestingly, in rodent studies,^{15,29} Lobie et al¹⁵ have shown that GH and IGF-I have direct effects on both smooth muscle cells and the lungs through interactions with cognate receptors. Fryburg et al²⁹ noted that both GH and IGF-I have the capacity to increase the synthesis of Type I and II collagen fibres and mucopolysaccharides. Radiologically, the increase in the average density of lung parenchyma may represent areas of pulmonary consolidation or ground-glass opacities, which are determined by substantial increases in cells at both the alveolar and the pulmonary interstitium levels.^{25,26}

We observed an increase in both TLC and RV in patients with acromegaly compared with control subjects. Similar to these findings, Evans et al³² and Melmed et al³ reported increases in lung volume using pulmonary function tests. The cause of increased static lung volumes in patients with acromegaly has been discussed in the literature, and while some studies point to alveolar hyperplasia, others point to a growth in the number of alveoli.^{7,8,33,34} More recently, García-Río et al⁸ observed a reduction in lung compliance and increased lung recoil pressure after hormonal control of the disease. According to these authors, the observed pathophysiological findings suggest that alveolar hyperplasia in patients with acromegaly is the main mechanism for the increase in lung volume.

We observed that there were correlations between the pulmonary densitovolumetry findings and the pulmonary function test parameters. TLV obtained using inspiratory densitovolumetry showed a significant correlation with TLC, whereas TLV obtained using expiratory densitovolumetry showed a significant correlation with FRC. TLC measured by body plethysmography represents the entire volume of gas within the thorax, and TLV obtained using inspiratory CT represents the TLV measured by densitovolumetry, which ultimately represents the total amount of air in the lung after a maximal inspiration. FRC measured by

body plethysmography represents the volume of gas at the end of a maximal expiration, and TLV obtained using expiratory CT represents the total amount of air in the lungs after a maximal expiration. Although these measures are obtained using different diagnostic methods, the physiological and conceptual similarity between them means that both Q-MDCT and body plethysmography can be used as important tools for monitoring these patients.

The strength of this study is that it is the first to evaluate the effects of GH in patients with active acromegaly and controlled acromegaly on both the structure and function of the lungs. Moreover, it is the first study to use CT pulmonary densitovolumetry and to correlate the results with pulmonary function in patients with acromegaly. The small number of patients in the subgroups should be considered a limitation of the study, but we were careful to eliminate confounding factors such as smoking. We also believe that histopathology could reinforce the findings of this study by providing a more detailed analysis of lung microarchitecture. Despite these limitations, we believe that our results justify the conduction of further studies using CT pulmonary densitovolumetry and pulmonary function tests for patients with acromegaly, which could increase our understanding of the pathophysiological mechanisms related to lung involvement in acromegaly.

CONCLUSION

This study shows that patients with active acromegaly have more lung mass and greater amounts of non-aerated and poorly aerated compartments. Furthermore, there is a relationship between the CT pulmonary densitovolumetry findings and pulmonary function test parameters in acromegaly. Although the nature of our results demands further investigation, our data suggest that both CT pulmonary densitovolumetry and pulmonary function tests can be used as useful tools for patients with acromegaly by assisting in the prediction of disease activity.

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