34 - CARDIO RESPIRATORY DISFUNCTIONS IN PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM

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Introduction

Subclinical hypothyroidism is characterized by increased serum value of thyrotropin (TSH) and normal concentrations of free triiodothyronine (FT3) and free thyroxine (FT4), without relevant clinic symptoms.

Romaldini *et al* (2004) reported that this pathology has greater prevalence in women over 60 years of age and is frequently caused by auto immune diseases. Within all the observed clinic abnormalities, those related to blood, neuropsychiatry, cardiovascular and lipids metabolism can be highlighted.

The present study aimed to observe possible cardio pulmonary and antropometric alterations. In order to achieve this aim, a direct measurement of gas exchange was used by spiroergometry technique.

Spiroergometry exams are easily applied and calculate heat production through the verification of pulmonary gas exchange, especially measurements of oxygen uptake (VO2) and carbon dioxide output (VCO2). This technique permits to monitor and register pulmonary ventilation and gas exchanges (Silva *et al*, 1998).

Due to the lack of publications that relates cardiopulmonary variables and this kind of pathology, this research compared patients and control women physical capacity level. Body composition; cardiopulmonary variables behavior; arterial pressure (AP) curve; and perceived exertion rate were evaluated - in effort and recovery period.

It is import to emphasize that data showed in this paper are a part of a wider study in development.

Materials and Methods

Seven patients and seven control women (aging 30 to 60 years old) were submitted to the experiment. The patients should not have another clinic abnormality that could compromise results analysis. Patient was judged by elevated serum TSH and normal FT4 levels (mean TSH: 7.41 ± 2.44 mU/L; mean FT4: 1.07 ± 0.33 mU/L). Groups were not different in mass (Patients: 71.81 ± 18.32 kg x Control: 64.13 ± 10.82 kg, p=0.80), stature (1.57 ± 0.09 m x 1.60 ± 0.08 m, p=0.53) and age (45.14 ± 6.04 years old x 44.57 ± 6.05 years old, p=0.71).

All patients gave their informed written consent to the study in the first medical consult at Clementino Fraga Filho University Hospital (HUCFF UFRJ). After this fist contact with the endocrinology service, they were routed to Exercise Physiology Laboratory at Physical Education and Sports School Federal University of Rio de Janeiro (EEFD-UFRJ).

Women that presents infectious disease, heart attack and/or angina pectoris in the last three months, potentially serious arrhythmia, diabetes mellitus, pain or other physical problems that hinder the patient to walk or were in use of heart rate and arterial pressure control drugs were exclude of this study.

Anthropometric measurements were done in accord to the proceedings described by International Society for Advancement in Kinanthropometry - ISAK (Norton *et al*, 2000).

Sproergometric test was performed in a treadmill (ECAFIX EG 700.2), using a modified Balke protocol that consisted of a gradual gradient of slope increase of 3% in every 2 minutes, with constant velocity of 4.8 km/h.

Participants were argued about their perceived exertion level during the test by means of a reproduction of *Borg* scale (ranging from 6 no tiredness to 20 maximal tiredness), placed on the wall just ahead the treadmill, facilitating its visualization.

The interruption of the test occurred when symptoms that could represent risk to the tested woman appeared or when she request. In order to control limit symptoms, American College of Sports Medicine Guidelines (ACSM, 2003) were observed, such as: angina initiation; significantly decrease (20 mmHg) or absence of increase in systolic arterial pressure (SAP) after an augment of exercise intensity; SAP > 220 mmHg or diastolic arterial pressure (DAP) > 115 mmHg; dizziness; confusion; pallor; absence of heart rate increase after an augment of exercise intensity; altered electrocardiogram (ECG); and physical or verbal manifestations of extreme fatigue.

Gas exchange relationship was measured by means of a pneumotachograph (Pt) (MEDGRAF medium size) that was attached to a differential pressure transductor and had a gas analyzer capillary connected to it.

The examined person, wearing a nose clip, was connected to the ventilation data acquisition system by means of a mouthpiece. The sample rates of the flux sign and the gas concentrations were 1000 Hz.

Respiratory output (sampled breath by breath by VO2000 MEDGRAF) and ECG signs (Medical Diagnostic Workstation (MDW) Cardio Control 2000/2001) were processed at real time.

Arterial pressure (AP) was measured at rest, after every three minutes of exercise period and in the first and third minute of recovery, utilizing the auscultatory technique with a mercury column sphygmomanometer (Narcosul, 1400-/C).

Patients were requested not to: do any tiring physical activity, drink alcoholic drinks or caffeine since the anterior night and smoke in the four hours that preceded the exam.

The analyzed variables are described in Table 1.

Table 1 Analyzed Variables

Table 1 – Analyzed Variables	
	Variable
BF	Body Fat
REST SAP	Rest Systolic Arterial Pressure
PEAK SAP	Peak Systolic Arterial Pressure
REC 1 SAP	Systolic Arterial Pressure at the 1 st minute of recovery
REC 3 SAP	Systolic Arterial Pressure at the 3 st minute of recovery
DIF 1 SAP	PEAK SAP - REC 1 SAP
DIF 3 SAP	PEAK SAP - REC 3 SAP
DIF 1-3 SAP	REC 1 SAP - REC 3 SAP
MAX-REST SAP	PEAK SAP - REST SAP
REST DAP	Rest Diastolic Arterial Pressure
PEAK DAP	Peak Diastolic Arterial Pressure
REC 1 DAP	Diastolic Arterial Pres sure at the 1st minute of recovery
REC 3 DAP	Diastolic Arterial Pressure at the 3 st minute of recovery
DIF 1 DAP	PEAK DAP - REC 1 DAP
DIF 3 DAP	PEAK DAP - REC 3 DAP
DIF 1-3 DAP	REC 1 DAP - REC 3 DAP
MAX-REST DAP	PEAK DAP - REST DAP
REST HR	Rest Heart Rate
PEAK HR	Peak Heart Rate
TEST DUR	Test duration
PEAK LOAD	Peak (maximal) load
PEAK BORG	Peak Perceived Exertion Value
PEAK VE	Peak Pulmonary Ventilation
PEAK VO2 ($ml.kg^{-1}.min^{-1}$)	Peak Relative Oxygen Uptake
PEAK VCO2 ($ml.kg^{-1}.min^{-1}$)	Peak Relative Carbon Dioxide Uptake
PEAK O2 EQUIV	Peak Ventilatory Equivalent for Oxygen
PEAK CO2 EQUIV	Peak Ventilatory Equivalent for Carbon Dioxide
PEAK RQ	Respiratory Exchange Ratio

Results

Body Fat

There was no difference between the two groups for body fat, with p value=0.62.

Systolic Arterial Pressure (SAP)

At rest, there was no significant difference for SAP (p=0.13). However, at peak time, control group presented statistically higher SAP (167.86 ± 19.97 mmHg x 141.43 ± 21.16 mmHg; p=0.04) comparing to patient group. At the first minute of recovery, SAP shows a trend to be more elevated in control group (157.14 ± 20.79 mmHg x 136.43 ± 11.07 mmHg; p=0.05), just to the third minute of recovery (145 ± 23.45 mmHg x 125.83 ± 8.01 mmHg; p=0.13).

In order to verify in a better way the SAP control capacity after a maximal effort, differences between Peak SAP and SAP at the periods of recovery (DIF 1 SAP and DIF 3 SAP) and between these periods (DIF 1-3 SAP). There were no statistically proved differences, neither any important graphic trends for these variations of SAP.

MAX-REST SAP was also higher for control group (p=0.01), but this result was certainly influenced by Peak SAP.

Figure 1 shows a resume for the most important results of SAP.

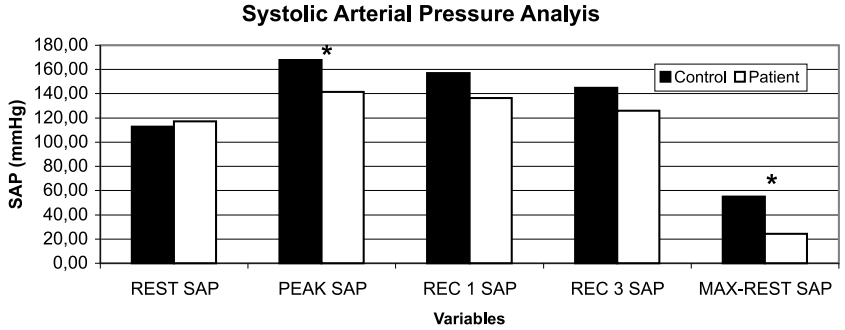

Figure 1 SAP behavior at rest (REST SAP), at peak exercise (PEAK SAP), at the first and third minutes of recovery (REC1 SAP and REC3 SAP) and the difference between PEAK SAP and REST SAP (MAX-REST SAP). The (*) symbol indicates statistically different groups (p < 0.05).

Distolic Arterial Pressure (DAP)

Patients presented a greater REST DAP mean (81.43 ± 4.76 mmHg x 75 ± 5 mmHg), but this result did not achieved significance (p=0.05) (Figure 2). Peak DAP, REC1 DAP and REC3 DAP values were not different neither.

Comparison about the capacity of recovery DAP basal values after a high intensity effort was also done through DIF1 DAP, DIF3 DAP and DIF 1-3 DAP. DIF 1 DAP was not different between groups, however DIF 3 DAP and DIF 1-3 DAP showed other behavior. PAD DIF 3 was greater in control group (10 ± 5.48 mmHg x 4.17 ± 4.92 mmHg), but without statistical prove (p=0.09). PAD DIF 1-3 was significantly higher for control group (7.5 ± 4.18 mmHg x 1.67 ± 2.58 mmHg; p=0.04). The same occurred to MAX-REST DAP (PEAK DAP REST DAP): 15.71 ± 4.5 mmHg x 2.86 ± 11.85 mmHg; p=0.01 (Figure 2).

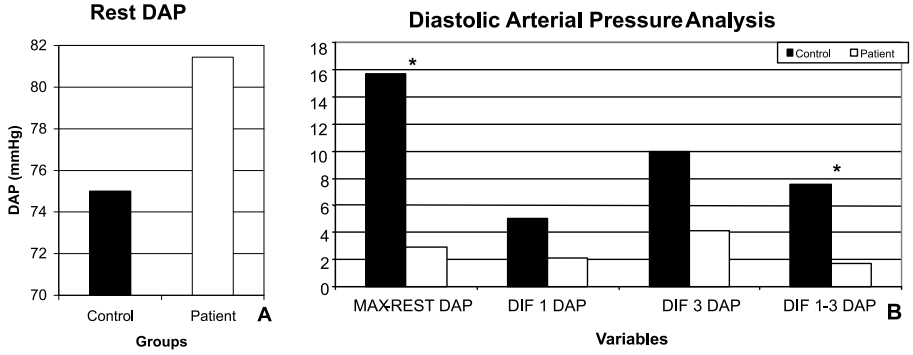

Figure 2 A) Mean Rest Diastolic Arterial Pressure Patient and Control Group. B) Difference between: Peak DAP and Rest DAP (MAX-REST DAP), Peak DAP and REC1 DAP (DIF 1 DAP), Peak DAP and REC 3 DAP (DIF 3 PAD), and REC 1 PAD and REC 3 PAC (DIF 1-3 DAP). *The (*) symbol indicates statistically different groups (p < 0.05).*

Heart Rate (HR)

Rest and Peak heart rate values were not different between groups (p=0.45 e p=0.80, respectively).

Perceived Exertion Values (Borg), Peak Load and Test Duration

The two groups perceived the final of the test the same way, with mean values of 18 (control) and 17 (patient) of *Borg* scale.

To Peak Load e Test Duration, control group presented higher values than patient group. Mean peak load, express in % grade of slope, was 17.71 ± 2.43 x 15.43 ± 2.23 and mean test duration was 13.15 ± 2.49 min x 9.28 ± 4 min. The discovered differences were not significant, however, the p value suggest a tendency in data (p = 0.10 e p = 0.05, respectively).

Figure 3 displays test duration for each patient and control. One can observe that there are two different baselines: one higher (control) and other lower (patients).

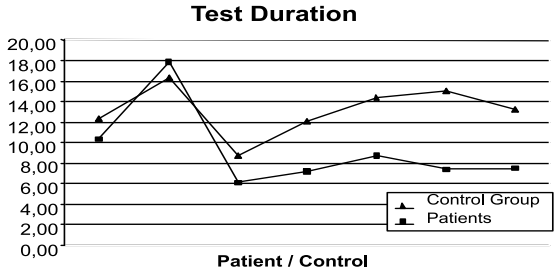

Figure 3 Test duration for each patient / control measured in minutes. Observe two different levels (control group, with higher values). The patient presenting the highest test duration value practices systematic aerobic physical activity on a treadmill, justifying her performance in this evaluation.

Spirometric Variables

Among all the ventilatory analyzed variables, the only one that showed difference between groups was peak relative oxygen uptake, higher in control group (28.34 $\pm$ 5.1 ml.kg^{-1}.min^{-1}x 23.36 $\pm$ 8.17 ml.kg^{-1}.min^{-1}; p=0.05 not statistically difference).

A very interesting behavior in these data is that while 57.14 % of control group achieved the anaerobic threshold, only in one patient's data (14.19 %) was possible do characterize it. Because of this, the spirometric variables were compared only at peak and not at threshold period (quantity of values very different between groups).

Discussion

Body fat percent indicates that subclinical hypothyroidism do not promote alterations in corporal composition of patients, possibly because the serum modifications in this case are more related to TSH than thyroid hormones, and these, for Weineck (1991) and Bianco and Dimura (1999), influence lipolytic activity.

It is found in the review of Romaldini *et al* (2004) that there is a reduction in myocardial contractility in subclinical hypothyroidism patients. The diminished peak SAP in patients, found in the present experiment, comparing to the control group, corroborates with this indication, demonstrating less efficient myocardial contraction at peak exercise. This result could also had been influenced by another fact: the patients could have not been submitted to a real maximal effort to cardio respiratory system, interrupting the test because of a high global fatigue or apprehension to continue the exam.

It is already known the presence of a diastolic dysfunction in overt or subclinical hypothyroidism (Biondi e Klein, 2004; Biondi *et al*, 1999). The difference found in rest DAP between groups occurred probably due to an increased peripheral vascular resistance inherent of hypothyroidism patients (Hamano and Inoue, 2005; Dagre *et al*, 2005; Biondi and Klein, 2004). Further the alterations in REST DAP, another results that shows the problems in diastolic function for this pathology is the worse DAP recovery kinetics in this patients, presented by smaller values of DIF 1 DAP, DIF 3 DAP and DIF 1-3 DAP. DIF 1-3 DAP was significantly higher in control group. Controls' values of DIF 1 DAP and DIF 3 DAP were also higher (even without statistically difference) than the patients' ones, informing that control women have a better capacity of DAP recovery in the firsts minutes after a high intensity effort. The wide discussion about the latest results presented can be related to the fact that the diastolic usually precedes systolic dysfunction (Biondi *et al*, 2002).

Modifications in arterial pressure were not accompanied by alterations in heart rate at rest or at peak effort. This confirms the findings of Monzani *et al* (2001) and Biondi *et al* (1999): all their patients had normal heart rate. In other hand, hyperthyroidism patients demonstrate higher rest HR than euthyroid people (Kahaly *et al*, 1998).

Data from the present study suggest diminished test duration and peak load, a not well explored information in literature. The difference could not have achieved significance because there was a patient who trained on a treadmill, what increased patients' mean test duration and peak load. This study will continue detaching physical activity factor to better analyze the variables.

The difference found in peak relative oxygen uptake indicates a cardiopulmonary dysfunction in patients at maximal effort. Even not being a statistical difference, this results corrobrates with Caraccio *et al* (2005), whose findings showed reduced maximal VO2 in hypothyroidism patient group.

Cardiorespiratory evaluation revealed another interesting behavior: only one of the seven patients presented anaerobic threshold, while in data of four control women (in a total of seven) was possible to characterize this threshold. “It is known that an exercise realized in a intensity higher than anaerobic threshold will lead to an abrupt augment in catecholamine and renin levels, and this can expose the patient with high risk cardiac conditions to arrhythmias, hypertension, ischemia and cardiac insufficiency” (Silva *et al*, 1998), and, possibly, the patients protected themselves of such intensity.

Conclusion

Subclinical Hypothyroidism seems to influence some cardiorespiratory variables at rest and exercise. The most sensible variables to this pathology that came from a spiroergometry test were arterial pressure, peak oxygen uptake, test duration, peak load and characterization of anaerobic threshold. In the other hand, data from this present study do not indicate modifications in corporal composition for this kind of patient. In order to improve the scientific expression of the presented results, the number of patients evaluated will be enhanced, with separate investigation of active and sedentary women. Patient's and controls' accompaniment will happen in six months and one year after the achievement of euthyroidism state through pharmacologic treatment.

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CARDIORESPIRATORY DISFUNCTIONS IN PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM

The subclinical hypothyroidism is characterized by the increased serum value of thyrotropin (TSH), normal concentrations of triiodothyronine free (FT3) and serum free thyroxine (FT4). The aim of the present study was to compare the level of physical condition of seven patients with seven healthy women, by the ergoespirometry. The data had been compared through the test of Mann-Whitney U ($p<0.05$). The body fat was not different between the groups ($p=0.62$). The maximal systolic arterial pressure (SAP) was higher in the control group (167.86 ±19.97 mmHg; 141.43 ± 21.16 mmHg; $p=0.04$) just to the third minute of recovery. The patients' diastolic arterial pressure (DAP) in rest condition presented a trend of being higher and the difference between the DAP in the third and in the first minute of recovery was higher for the control group (7.5 ±4.18mmHg; 1.67 ±2.58 mmHg; $p=0.04$). The diastolic dysfunction that comet this patients already is known by literature. The heart hate in the rest and exercise peak was not modified in the patients, results that corroborate with Monzani *et al* (2001). The load, the total duration of the test and the relative oxygen uptake in the exercise peak ($ml.kg^{-1}.min^{-1}$) had tended to be bigger in the control group, but only 14.19% of the patients reached the anaerobic threshold, while 57.14% of the control group reached it. The subclinical hypothyroidism seems to influence some cardio respiratory variable in rest and during the exercise. The most sensible variables were the arterial pressure, the peak oxygen uptake, the duration of the test, the maximal load and the characterization of the anaerobic threshold.

Key words: Subclinical Hypotyreoidism, Ergoespirometry, Cardio respiratory capacity.

DYSFONCTIONNEMENTS CARDIORESPIRATOIRES DE PATIENTS PRESENTANT HIPOTIREOIDISM SUBCLINIQUE

Le hipotiroidism subclinique est caractérisé par la plus haut sérum valeur du thyrotropin (TSH), des sérum concentrations normales du triiodothyronine (FT3) et de la thyroxine libres (FT4). Le but de la présente étude était de comparer le niveau de l'état physique de sept patients avec sept femmes normal, par l'ergoespirometry. Les données avaient été comparées par l'essai de Mann-Whitney U ($p<0,05$). La graisse corporal n'était pas différente entre les groupes ($p=0,62$). La pression artérielle sistolic maximale (PAS) était plus haute dans le groupe normal (167.86 ±19,97 mmHg;141.43 ±21.16 mmHg; $p=0,04$) juste à la troisième minute du rétablissement apés le exercice. La pression artérielle diastolique de patients (PAD) en état de repos a présenté une tendance d'être plus haute et la différence entre le PAD dans le tiers et dans la première minute du rétablissement était plus haute pour le groupe normal (7,5 ±4,18mmHg; 1,67 +2,58 mmHg; $p=0,04$). Le dysfonctionnement diastolique que comète des patients déjà est connue par la littérature. La fréquence du pouls dans le repos et d'exercice n'a pas été modifiée dans les patients, ce résultats corroborent avec Monzani et autres (2001). La charge final, la durée de l'exercice et la consommation d'oxygène relative a la fin d'exercice (ml.kg-1.min-1) avaient tendu à être plus elevé dans le groupe normal. Seulement 14,19% des patients ont atteint le seuil anaérobie, alors que 57.14% du groupe normal l'atteignaient. Le hipotireoidism subclinique semble influencer une certaine variable cardiorespiratoire dans le repos et pendant l'exercice. Les variables les plus sensibles étaient la pression artérielle, la consommation d'oxygène maximale, la durée de l'exercice, la charge maximale et la caractérisation du seuil anaérobie.

Mots clés: Hipotireoidism Subclinique, Ergoespirometry, Capacité cardiorespiratoire.

DISFUNCIONES CARDIORESPIRATORIAS EN PACIENTES CON HIPOTIROIDISMO SUBCLINICAL

El hipotiroidismo subclinical es caracterizado por el valor creciente del suero del thyrotropin (TSH), e de las concentraciones normales del suero del triiodothyronine (FT3) y del thyroxine libres (FT4). El objetivo del actual estudio era comparar el nivel de la condición física de siete pacientes con siete mujeres normais, por el ergoespirometry. Los datos

habían sido comparados por de la prueba de Mann-Whitney U (p<0,05). Las grasas del cuerpo no eran diferentes entre los grupos (p=0,62). La presión arterial sistólica máxima (PAS) era más alta en el grupo de control (167,86 ±19,97 mmHg; 141,43 ±21,16 mmHg; p=0,04) apenas al tercer minuto de la recuperación. La presión arterial diastólica de los pacientes (PAD) en la condición del resto presentó una tendencia de ser más alta y la diferencia entre el PAD en el tercero y en el primer minuto de la recuperación era más grande para el grupo de control (7,5 ±4,18 mmHg; 1,67 ±2,58 mmHg; p=0,04). La disfunción diastólica que el cometa los pacientes es sabido ya por la literatura. La respuesta de la frecuencia cardiaca en el reposo y en el pico del ejercicio no fue modificado en los pacientes, los resultados que corroboran con Monzani *et al* (2001). La carga máxima del ejercicio, la duración total de la prueba y el consumición de oxígeno relativo en el pico del ejercicio ($ml.kg^{-1}.min^{-1}$) habían tendido para ser más grandes en el grupo de control, pero solamente 14,19% de los pacientes alcanzaron el umbral anaerobio, mientras que el 57.14% del grupo de mujeres normais lo alcanzaron. El hipotiroidismo subclinical se parece influenciar por una cierta variable cardiorespiratoria en resto y durante el ejercicio. Las variables más sensibles eran la presión arterial, el consumición de oxígeno máximo, la duración de la prueba, la carga máxima y la caracterización del umbral anaerobio.

Palabras claves: Hypotyreoidism subclinical, Ergoespirometry, Capacidad cardiorespiratoria.

DISFUNÇÕES CARDIO-RESPIRATÓRIAS EM PACIENTES COM HIPOTIREOIDISMO SUBCLÍNICO

O hipotiroidismo subclínico se caracteriza por um valor sérico aumentado do Hormônio Tirotrófico (TSH) e concentrações normais de Triiodotironina Livre (FT3) e Tiroxina Livre (FT4). O presente trabalho buscou comparar o nível de aptidão física de sete pacientes portadoras dessa disfunção ao de sete mulheres controle, através da ergoespirometria. Os dados foram comparados através do teste de *Mann-Whitney U* (p<0,05). O percentual de gordura não foi diferente entre os grupos (p=0,62). A pressão arterial sistólica (PAS) de pico foi maior nas mulheres controle (167,86 ±19,97 mmHg; 141,43 ±21,16 mmHg; p=0,03), perfil mantido até o terceiro minuto de recuperação. A pressão arterial diastólica (PAD) em repouso apresentou uma tendência de ser maior nas pacientes, e a diferença entre a PAD do terceiro e do primeiro minuto de recuperação foi estatisticamente maior para o grupo controle (7,5 ±4,18 mmHg; 1,67 ±2,58 mmHg; p=0,04). A disfunção diastólica que acomete esses pacientes já é conhecida pela literatura. A freqüência cardíaca, tanto em repouso como no pico do exercício não apresentou resultados alterados nas pacientes, resultados que corroboram com Monzani *et al* (2001). A carga máxima de exercício, a duração do teste e o consumo de oxigênio relativo de pico ($ml.kg^{-1}.min^{-1}$) apresentaram tendência a valores mais elevados no grupo controle. Apenas 14,19% das pacientes atingiu o limiar anaeróbico (ventilatório), enquanto que nos dados de 57,14% das mulheres controle foram caracterizados esse limiar. O hipotireoidismo subclínico parece influenciar algumas variáveis cardio-respiratórias em repouso e em esforço. As variáveis mais sensíveis foram a pressão arterial, o consumo de oxigênio relativo de pico, a duração do teste, a carga máxima e a caracterização do limiar ventilatório.

Palavras-Chave: Hipotireoidismo Subclínico, Ergoespirometria, Capacidade cardio-respiratória.