Analysis of Right Ventricular Function in Patients with Hypothyroidism

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Summary

Background: After many studies about the left ventricle (LV), little is known about the effect of thyroid hormones deprivation at the right ventricle (RV).

Objective: This study was aimed to evaluate the right ventricular function in patients who had hypothyroidism in different degrees of disease severity.

Methods: Eighteen patients with primary hypothyroidism were submitted to two-dimensional echocardiography evaluation, of which 10 (55,6%) had TSH < 12 mIU/L (less high TSH group) and 8 (44,4%) had TSH > 12 mIU/L (highest TSH group).

Results: By comparing the two groups, there were no differences in respect of LV global systolic function or diastolic function. There was neither difference related to right atrium or RV dimensions. About the right ventricular function, it was shown a difference in the myocardial performance index (Tei index), which was higher in patients who had TSH > 12 compared with patients who had TSH < 12 (0.52 ± 0.13 vs. 0.39 ± 0.08; $p < 0.05$), indicating worse right ventricular global function in those patients with the highest TSH levels. No differences were observed between these groups related to other variables, which are: percentage of systolic change in the VD area, TAPSE and peak systolic velocity. Variables of RV diastolic function (E/A tricuspid ratio and E/E' tricuspid ratio), as well as pulmonary vascular resistance and pulmonary artery systolic pressure were not different between groups.

Conclusion: Patients with hypothyroidism who had the highest TSH levels, as compared to those with less high TSH, presented with a reduction at the overall right ventricular function, evaluated by myocardial performance index, not observed in other parameters of RV function evaluation. (Arq Bras Cardiol: Imagem cardiovasc. 2017;30(4):126-131)

Keywords: Ventricular Function, Right/physiology; Thyroid Hormones; Echocardiography.

Introduction

The cardiovascular system is greatly affected by the thyroid hormones, as it is seen in both hyperthyroidism and hypothyroidism.[1,2] Thyroid hormones have direct and indirect actions on the cardiovascular system, causing the clinical manifestations that are typical of thyroid diseases.[3]

Deficiency of thyroid hormone affects the cardiac muscle contraction,[4] slowing down myocardial relaxation, causing damages to left ventricular filling.[5] In patients with clinical hypothyroidism of short duration there is a decrease in cardiac output, associated with decreased ejection volume and heart rate.[6]

There are few prospective studies on right ventricular (RV) function in patients with hypothyroidism, and generally only in patients with subclinical hypothyroidism or short-term hypothyroidism.[1,7,10] Patients with subclinical hypothyroidism (when the TSH concentration is high but the thyroid hormones are at normal concentrations) present changes in the cardiac structure.[11]

This study aims at finding out at what level thyroid hormone deficiency damages the right heart, and whether right ventricular dysfunction may contribute to cardiorespiratory symptoms and prognosis of patients with hypothyroidism.

Method

This is a cross-sectional, prospective study. Eighteen (18) patients with primary hypothyroidism assisted at the State Health Department (SUSAM), in Manaus, Amazonas between August 2015 and June 2016 were included. Clinical care of the patients followed the normal routine adopted at the health unit.

The following patients were excluded: patients younger than 18 or older than 70 at the time of diagnosis of hypothyroidism; patients diagnosed with pre-existing cardiovascular disease: significant valve disease; coronary artery disease; dilated or hypertrophic cardiomyopathy; congestive heart failure; pulmonary thromboembolism; atrial fibrillation; significant pulmonary disease; obesity – BMI ≥ 30 kg/m^2; patients taking

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Manuscript received May 29, 2017; revised June 12, 2017; accepted July 12, 2017

DOI: 10.5935/2318-8219.20170033

anorexigenic drugs; patients taking beta-blockers; pregnant women; patients with secondary hypothyroidism.

Echocardiography

Two-dimensional and M-mode echocardiographic studies with Doppler flow and tissue Doppler were performed while TSH was high, namely:

Initially, it was assessed whether there was tricuspid regurgitation through an apical-4-chamber window. Maximum velocity of tricuspid regurgitation obtained by continuous Doppler allowed, through the Bernoulli equation, to acquire the pressure gradient between the right ventricle (RV) and the right atrium (RA) (AV gradient = 4.V2). Pulmonary artery systolic pressure (PASP) was estimated, adding to this gradient an indirect estimate of right atrial pressure, assessed by the inferior vena cava (IVC) dimension and inspiratory variation. Pulmonary arterial hypertension was defined as PASP ≥ 36 mmHg. All data were obtained as an average of 3 (three) heart beats.

The following echocardiographic variables were also evaluated:

- Calculation of cardiac output using standard Doppler echocardiography;
- RV myocardial performance index (Tei index) (13) – to evaluate ventricular function and evolution of patients. It was also obtained through tissue Doppler in the lateral annulus of the tricuspid valve;
- Systolic velocity of the tricuspid valve annulus through tissue Doppler;
- Pulmonary vascular resistance (PVR) – estimate obtained through the regression equation: PVR = 10 x (TRV/RVOFTTVI) + 0.16, where TRV is the tricuspid regurgitation velocity and RVOFTTVI is the right ventricular outflow tract time-velocity integral.
- M-mode tricuspid annular plane systolic excursion (TAPSE) – to evaluate the regional RV function, mainly the systolic wall movement in the longitudinal axis.

Echocardiography scan was taken at Hospital Universitário Francisca Mendes. All tests were performed by a single examiner experienced in RV evaluation.

Statistical Analysis

Statistical analysis of continuous variables was done through non-parametric tests – Mann-Whitney – when the data distribution was not normal, or parametric tests – Student's t test – when the distribution was normal. To compare the categorical variables, Fisher's exact test was used. Right ventricular echocardiographic variables were compared between the groups with lower TSH – less than 12 mcUI/mL – or higher TSH – greater than or equal to 12 mcUI/mL. An α significance level of 0.05 was adopted.

Results

From August 2015 to June 2016, 28 patients diagnosed with primary hypothyroidism were studied. Of these, 18 were submitted to Doppler echocardiography (Table 1). Ten patients did not show up for this test.

Analysis according to TSH level

Of the 18 patients who underwent echocardiography, 10 (55.6%) had TSH < 12 mcUI/mL and 8 (44.4%) had TSH > 12 mcUI/mL. The clinical and laboratory variables of the patients according to the initial TSH level are shown in Table 2. Only 2 (11.1%) patients had none of the cardiovascular symptoms. Patients with TSH > 12 had significantly lower BMI than patients who had TSH < 12 (p = 0.044) (Table 2).

Global systolic function and left ventricular (LV) regional systolic function, as well as LV diastolic function variables did not differ between the two groups (Table 2).

No differences were observed in the variables related to the right heart chamber dimensions, such as right atrial area and volume, right ventricular (RV) diastolic and systolic area, and RV diameter (Table 2).

Regarding right ventricular function variables, there was only a difference in the RV myocardial performance index (RVMPI), which was higher in patients with TSH > 12 than in patients with TSH < 12, indicating a worse global RV function in that group. There was no difference between groups in the RV area variation percentage, which is the other global RV systolic function. There was no difference in the RV regional systolic function variables: Tricuspid St and tricuspid annular plane systolic excursion (TAPSE) (Table 2).

RV diastolic function variables (tricuspid E/A and tricuspid E/Et ratio), PVR and PASP did not differ between the two groups (Table 2).

Discussion

There was a predominance of females in the sample, which was expected, since hypothyroidism is more prevalent in women.[1,6,11] However, the lower body mass index (BMI) of patients with hypothyroidism was more severe. It could be expected that those patients had greater weight, considering that thyroid hormone deficiency causes fluid accumulation and decreased basal metabolic rate, despite the reduced appetite usually associated with hypothyroidism.

Patients with subclinical hypothyroidism have smaller right ventricular (RV) isovolumetric acceleration (IVA) and smaller early diastolic wave (Em), which increase with levothyroxine replacement.[10]

Oner et al.[9] observed impairment of systolic velocity and left ventricular diastolic index. Regarding the right ventricle, although the systolic velocity was preserved, the diastolic functions were compromised, with abnormal Tei index[12] that went back to normal with levothyroxine therapy.

Ilic et al.[8] and Tadic et al.[1] have found, in patients with subclinical hypothyroidism, deterioration of right ventricular function, with abnormal right cardiac mechanics in strain evaluation. However, they did not find significant systolic dysfunction on TAPSE, although they have found a slight significant difference – within normality – in the RV ejection fraction using three-dimensional mode between untreated patients and controls.

One of the techniques used to evaluate global RV function in this study was the percentage of RV area variation (%ΔRVA), which includes evaluations of the cross-sectional

Table 1 – Initial characteristics of patients with hypothyroidism who underwent Doppler echocardiography (n = 18)

Variable	Results	Reference value
Age (years)	49.2 ± 13.2	
Sex (M/F)	0/18	
Enlarged thyroid gland (%)	23.5	
Smoking (%)	5.6	
Sleep disturbance (%)	44.4	
Dyspnea (%)	50.0	
Chest pain (%)	44.4	
Palpitations (%)	55.6	
BMI (kg/m^2)	26.2 ± 4.0	18.5 – 24.9
Systolic blood pressure (mmHg)	125.0 (112.5 – 140.0)	Up to 129
Diastolic blood pressure (mmHg)	80.0 (80.0 – 85.0)	Up to 84
Free T4 (ng/dl)	0.77 ± 0.23	0.7 – 1.7
Initial TSH (mcUI/mL)	11.3 (6.9 – 23.0)	0.5 – 4.5
Initial dose of levothyroxine (mcg)	50.0 (25.0 – 81.5)	
LVEF* (%)	69.4 ± 6.8	≥ 55
CO (L/min)	4.5 ± 1.1	
CI (L/min/m^2)	2.74 ± 0.63	2.8 – 4.2
Mitral st (cm/s)***	0.09 ± 0.02	≥ 0.05
Mitral (E/A)***	1.02 (0.95 – 1.49)	1.0 – 2.0
Et mitral (cm/s)***	0.13 ± 0.03	≥ 0.08
Mitral (E/Et)***	7.3 (6.0 – 8.1)	< 8.0
PCP (mmHg)	11.0 (9.4 – 12.0)	< 15.0
RV diameter (PEL**) (mm)	23.1 ± 2.7	≤ 33
RVDA (cm^2)***	15.7 ± 9.1	10 – 25
RVSA (cm^2)***	4.2 (3.8 – 6.5)	4 – 14
RA-area (cm^2)***	9.4 ± 2.4	<18
RA-volume (mL)***	18.0 ± 6.1	≤ 32
%ΔRVA	65.6 (41.2 – 77.9)	>35
TAPSE (mm)***	18.0 (17.0 – 20.8)	>16
Tricuspid St (cm/s)***	0.12 ± 0.02	>10
RVMPI***	0.45 ± 0.12	≤ 0.55
Tricuspid (E/A)***	1.39 ± 0.31	0.8 – 2.1
Tricuspid (E/Et)***	4.6 (3.2 – 5.8)	< 6
PASP (mmHg)	22.6 (19.8 – 22.6)	< 36
PVR (TRV/TVI)	0.11 (0.09 – 0.12)	< 0.20

*Values expressed as mean ± standard deviation or median and 25% and 75% percentiles. *: Teichholz method; **: longitudinal parasternal view; ***: apical 4-chamber view; LVEF: LV ejection fraction; CO: cardiac output; CI: cardiac index; St: systolic displacement velocity on tissue Doppler; E/A: E/A wave ratio; Et: initial diastolic displacement velocity on tissue Doppler; PCP: pulmonary capillary pressure; RV: right ventricle; RVDA: RV diastolic area; RVSA: RV systolic area; RA: right atrium; % ΔRVA: % of RV area variation; TAPSE: tricuspid annular plane systolic excursion; RVMPI: RV myocardial performance index; PASP: pulmonary artery systolic pressure; PVR: pulmonary vascular resistance; VRT: tricuspid regurgitation velocity; TVI: time-velocity integral.*

and longitudinal components of right ventricular contraction. Some studies[13,14] have shown that %ΔRVA has a good correlation with right ventricular function measured by magnetic resonance imaging. In this study, %ΔRVA did not differ significantly between the groups with lower or higher TSH levels. Ventricular dysfunction was not detected when the cross-sectional and longitudinal components of RV contraction were evaluated.

Table 2 – Echocardiographic characteristics of patients with hyperthyroidism according to initial TSH levels

Variable	TSH < 12 (n = 10)	TSH > 12 (n = 8)	p
Age (years)	50.8 ± 10.7	47.1 ± 16.3	NS
Female sex (%)	100.0	100.0	NS
Enlarged thyroid gland (%)	20.0	25.0	NS
Smoking (%)	10.0	0.0	NS
Sleep disturbance (%)	60.0	25.0	NS
Dyspnea (%)	50.0	50.0	NS
Chest pain (%)	40.0	50.0	NS
Palpitations (%)	50.0	63.0	NS
BMI (kg/m^2)	27.8 ± 3.7	23.9 ± 3.5	< 0.05
Systolic blood pressure (mmHg)	120.0 (120.0 – 137.5)	130.0 (107.5 – 140.0)	NS
Diastolic blood pressure (mmHg)	80.0 (80.0 – 83.8)	80.0 (77.5 – 88.8)	NS
LVEF* (%)	71.6 ± 4.9	66.6 ± 8.2	NS
CO (L/min)	4.36 ± 1.04	4.61 ± 1.15	NS
CI (L/min/m^2)	2.63 ± 0.63	2.89 ± 0.64	NS
Mitral St (cm/s)***	0.08 ± 0.01	0.09 ± 0.03	NS
Mitral E/A ***	1.10 (0.79 – 1.31)	1.46 (1 – 1.66)	NS
Mitral Et (cm/s) ***	0.12 ± 0.03	0.14 ± 0.03	NS
Mitral E/Et***	7.60 (6.8 – 8.13)	6.94 (5.72 – 8.14)	NS
PCP (mmHg)	11.33 (10.33 – 1.98)	10.5 (8.99 – 12.0)	NS
RV diameter (PEL**) (mm)	22.70 ± 2.83	23.63 ± 2.50	NS
RVDA (cm^2)***:	15.86 ± 11.11	15.55 ± 6.41	NS
RVSA (cm^2)***	5.20 (3.83 – 6.59)	5.32 (3.86-6.23)	NS
RA-area (cm^2)***	9.32 ± 2.85	9.54 ± 1.99	NS
RA-volume (mL)***	19.34 ± 6.51	16.38 ± 5.37	NS
%∆RVA***	0.58 (0.41 – 075)	0.53 (0.51 – 079)	NS
TAPSE (mm)***	19.1 (18 – 20.5)	18.63 (16 – 20.5)	NS
Tricuspid St (cm/s)***	0.11 ± 0.01	0.13 ± 0.02	NS
RVMPI***	0.39 ± 0.08	0.52 ± 0.13	< 0.05
Tricuspid E/A ***	1.38 ± 0.29	1.39 ± 0.36	NS
Tricuspid E/Et***	5.33 (3.45 – 6.21)	4.34 (2.83 – 5.53)	NS
PASP (mmHg)	21.18 (17.28 – 23.93)	23.22 (21 – 22.64)	NS
PVR (TRV/TVI)	0.1 (0.09 – 0.12)	0.11 (0.10 – 0.11)	NS

*Values expressed as mean±standard deviation or median and 25% and 75% percentiles. *: Teichholz method; **: longitudinal parasternal view; ***: apical 4-chamber view; LVDD: left ventricle (LV) diastolic diameter; LVSD: LV systolic diameter; LA: left atrial diameter; LVEF: LV ejection fraction; CO: cardiac output; CI: cardiac index; St: systolic displacement velocity on tissue Doppler; E/A: E/A waves ratio; Et: initial diastolic displacement velocity on tissue Doppler; PCP: pulmonary capillary pressure; RV: right ventricle; RVDA: RV diastolic area; RVSA: RV systolic area; RA: right atrium; % ∆RVA: % of RV area variation; TAPSE: tricuspid annular plane systolic excursion; RVMPI: RV myocardial performance index on tissue Doppler; PASP: pulmonary artery systolic pressure; PVR: pulmonary vascular resistance; TRV: tricuspid regurgitation velocity; TVI: time-velocity integral. NS: non-significant.*

Also, in this study, the predominantly longitudinal contraction pattern explored by TAPSE to express ventricular function was normal. This variable reflects the longitudinal contractile movement of the myocardial fibers, that is, from the base towards the cardiac apex.

However, patients with higher TSH had a higher RV myocardial performance index (RVMPI) than patients with lower TSH. Firstly described by Tei et al.,[12] RVMPI is widely used to evaluate RV global ventricular function (systolic and diastolic functions, together), using only isovolumetric contraction times, isovolumetric relaxation and ventricular ejection, with the advantage of not being dependent on right ventricular complex geometry. The smaller RVMPI found in this study represents a reduction in RV myocardial performance in patients with more severe hypothyroidism, characterized by higher TSH. As demonstrated by Hsiao et al.,[15] RVMPI is increased in both acute and chronic RV overload, even in the presence of preserved ejection fraction, going back to normal after treatment. Further studies would be required to re-evaluate the PVR of patients after the reestablishment of euthyroidism, that is, after normalization of TSH.

Another variable used in this study to express right ventricular function, which evaluates RV longitudinal shortening, was the tricuspid annular plane systolic excursion (tricuspid St) measured by tissue Doppler. Duan et al.,[16] evaluated the effect of preload (inferior vena cava occlusion) on the tricuspid St, in children with pulmonary arterial hypertension, and concluded that the magnitude of velocities during systole (St) and diastole (Et and At) are dependent on the preload. As in this study there was no difference in cardiac output (CO), indicating no preload difference, this could explain why there was no difference in the tricuspid St in patients with different levels of high TSH.

The limitations of this study were the small number of the sample, which could be insufficient to demonstrate differences in other variables related to right ventricular function, and the lack of a control group, without hypothyroidism, that would allow to evaluate the adequacy of the reference values of the variables analyzed in the local population.

Conclusions

Cardiovascular symptoms were frequent in patients with hypothyroidism, as well as in sleep disorders. However, no significant differences were observed in left ventricular function parameters between the groups with higher or lower TSH.

The study did not show consistent abnormalities in most right ventricular function parameters, although right ventricular myocardial performance index was found to be abnormal in patients with more severe hypothyroidism (higher TSH) compared to those with lower TSH.

This study suggests that the use of right ventricular function as an additional criterion in assessing the severity and efficacy of treatment of primary hypothyroidism should be better investigated, as well as in central hypothyroidism, by comparing right ventricular function in patients before and after euthyroidism.

Authors' contributions

Research creation and design: Souza JJS, Gazzana ML; Data acquisition: Macedo GDQ, Macedo MJQ; Data analysis and interpretation: Macedo GDQ, Macedo MJQ, Souza JJS, Gazzana ML; Statistical analysis: Macedo GDQ, Souza JJS; Funding: Souza JJS; Manuscript drafting: Macedo GDQ, Macedo MJQ, Souza JJS, Gazzana ML; Critical revision of the manuscript as for important intellectual content: Souza JJS, Gazzana ML.

Potential Conflicts of Interest

There are no relevant conflicts of interest.

Sources of Funding

This study was partially funded by Fundação de Amparo à Pesquisa do Estado do Amazonas – FAPEAM through a research grant.

Academic Association

This study is not associated with any graduate program.

References

1. Tadic M, Ilic S, Celic V. Right ventricular and right atrial function and deformation in patients with subclinical hypothyroidism: a two- and three-dimensional echocardiographic study. Eur J Endocrinol. 2013; 170(1):77-85. Doi:10.1530/EJE-13-0676

2. Klein I. Thyroid hormone and the cardiovascular system. Am J Med. 1990; 88(6):631-7. PMID:2189307

3. Woeber KA. Thyrotoxicosis and the heart. N Engl J Med. 1992; 327(2):94-8. doi:10.1056NEJM199207093270206

4. Cohen MV, Schulman IC, Spenillo A, Surks MI. Effects of thyroid hormone on left ventricular function in patients treated for thyrotoxicosis. Am J Cardiol. 1981;48(1):33-8. PMID: 7246445

5. Crowley WF JR, Ridgway EC, Bough EW, Francis GS, Daniels GH, et al. Noninvasive evaluation of cardiac function in hypothyroidism. Response to gradual thyroxine replacement. N Engl J Med. 1977; 296(1):1-6. Doi: 10.1056/NEJM197701062960101

6. Wieshammer S, Keck FS, Waitzinger J, Kohler J, Adam W, Stauch M, et al. Left ventricular function at rest and during exercise in acute hypothyroidism. Br Heart J. 1988; 60(3):204-11. PMID:3179136

7. Arinc H, Gunduz H, Tamer A, Seyfeli E, Kanat M, Ozhan H, et al. Evaluation of right ventricular function in patients with thyroid dysfunction. Cardiology. 2006 Nov 10;105(2):89-94. doi:10-1159/000089855

8. Ilic S, Tadic M, Ivanovic B, Caparevic Z, Trbojevic B,Celic V. Left and right ventricular structure and function in subclinical hypothyroidism: the effects of one-year levothyroxine treatment. Med Sci Monit. 2013 Nov 10;19:960-8.

9. Oner FA, Ner FA, Yurdakul S, Uzum AK, Erguney M. ONER E. Evaluation of the effect of L-thyroxin therapy on cardiac functions by using novel tissue Doppler-derived indices in patients with subclinical hypothyroidism. Acta Cardiol. 2011; 66(1):47-55. Doi: 10.2143/AC.66.1.2064966

10. Turhan S, Tulunay C, Cin M, Gursoy A, Kilickap M. Effects of thyroxine therapy on right ventricular systolic and diastolic function in patients with subclinical hypothyroidism: a study by Pulsed Wave Tissue Doppler Imaging. J Clin Endocrinol Metabol.. 2006; 91(9):3490-3. Doi 10.1210/20064966

11. Zoncu S, Pigliaru F, Putzu C, Pisano L, Vargiu S, Deidda M, et al. Cardiac function in borderline hypothyroidism: a study by pulsed wave tissue Doppler imaging. Eur J Endocrinol. 2005; 152(4):527-33. Doi:10.1530/eys.1.101903

12. Tei C, Dujardin KS, Hodge DI, Kyle RA, Tajik AJ, Seward JB. Doppler index combining systolic and diastolic myocardial performance: clinical value in cardiac amyloidosis. J Am Coll Cardiol. 1996; 28(3):658-64. PMID: 8772753navekar

13. Anavekar NS, SKali H, Bourgoun M,Ghali JK, Kober L, Maggioni AP, et al. Usefulness of right ventricular fractional area change to predict death, heart failure, and stroke following myocardial infarction (from the VALIANT ECHO Study). Am J Cardiol. 2008;101(5):607-12. Doi: 10.1016/j.amjcard.2007.09.115

14. Kind T, Mauritz GJ, Marcus JT, van de Veerdonk M, Westerhof N, Vonk-Noordegraaf A, et al. Right ventricular ejection fraction is better reflected by transverse rather than longitudinal wall motion in pulmonary hypertension. J Cardiovasc Magn Reson. 2010 Jun 4;12:35. Doi: 10.1186/1532-429X-12-35

15. Hsiao SH, Lee CY, Chang SM,Hang SM, Yang SH, Lin SK, et al. Pulmonary embolism and right heart function: insights from myocardial Doppler tissue imaging. J Am Soc Echocardiogr. 2006;19(6):822-8. Doi: 10.1016/j.echo.2006.01.011

16. Duan YY, Harada K, Toyono M, Ishii H, Tamura M, Takada G. Effects of acute preload reduction on myocardial velocity during isovolumic contraction and myocardial acceleration in pediatric patients. Pediatr Cardiol. 2006;27(1):32-6. Doi:10.1007/s007/s00246-005-0877-8