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Assessment of Left Ventricular Function by 2D Speckle Tracing Imaging in Patients with Subclinical Hypothyroidism

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Abstract

Objective: To evaluate cardiac functions in patients with Subclinical Hypothyroidism by 2D Echocardiography and Speckle Tracking Imaging.

Background: Heart is a major target organ for thyroid hormone action. Subclinical thyroid disease has been associated with systolic and diastolic cardiac dysfunction and previous studies have shown that thyroxin replacement improved cardiac function in subjects with SH.

Patients and methods: we prospectively included 50 patients with subclinical hypothyroidism (SH) (Group I; 16 male, 34 female, Mean ± SD age: 34.08 ± 9.66 years) and the control group included 75 healthy volunteers (30 male, 45 female, Mean ± SD age: 31.47 ± 7.99 years). Left ventricular (LV) functions were assessed with speckle tracking imaging.

Results: Age and sex distributions were similar among the two groups. Mean serum TSH was13.01 ± 6.91 μIU/mL for group I and 1.64 ± 0.58 μIU/mL for group II and free T4 levels were 1.138 ± 0.186 ng/dL for group I and 1.172 ± 0.172 ng/dL for group II; (p=0.001, p=0.303). The SH patients had significantly lower LV strain values compared to controls, there was a highly significant statistical difference between the two groups with group I (patients) showing significant reduction in values (p-value=0.001).

Conclusion: The Global LV Peak Longitudinal Strain is significantly reduced in patient with Subclinical Hypothyroidism comparing with the healthy control group.

Keywords

Left ventricular function; Subclinical hypothyroidism; LV longitudinal Strain; Speckle tracking echocardiograph

Introduction

Thyroid hormones act an important role on the cardiovascular system and thyroid diseases have a prominent adverse effect on myocardial and vascular functions [1].

Frequency of thyroid dysfunction increases with aging. Subclinical hypothyroidism (SH) is an asymptomatic condition defined by increased serum thyroid-stimulating hormone (TSH) with normal free thyroid hormone levels [2]. Heart is a major target organ for thyroid hormone action. However, two-dimensional (2D) speckle tracking echocardiography (STE) provides more accurate estimates of LV function when compared to cardiac MRI reference, a finding that encouraged us to use this technique in our study. Speckle tracking allows the assessment of myocardial strain, myocardial strain is a dimensionless index of tissue deformation expressed as a fraction or per cent change. Myocardial lengthening gives a positive and shortening gives a negative strain value. Strain can be further subdivided into longitudinal, radial and circumferential strain. Longitudinal strain represents myocardial deformation directed from the base to the apex. Two-dimensional (2D) strain and analyses are novel Doppler-independent techniques to obtain measurements of myocardial movement and deformation.

The aim of this study was to evaluate cardiac functions in patients with Subclinical Hypothyroidism by 2D Echocardiography and Speckle Tracking Imaging.

Patients and Methods

This study included subjects with subclinical hypothyroidism referred from the outpatient clinic of endocrinology Department of Menoufia University Hospital to our echocardiographic laboratory, Cardiology Department Menoufia University, Egypt). Between January 2018 and October 2018, it prospectively included 50 patients with subclinical hypothyroidism (SH) (Group I; 16 male, 34 female) and the control group included 75 healthy volunteers (30 male, **45** female). Excluded patients with impairment of LV systolic function (ejection fraction<55%), significant valvular heart disease, cardiomyopathy, history of coronary artery disease, malignancy, diabetes mellitus and patients with poor echogenicity. All subjects underwent a resting electrocardiography and a two dimensional (2D) transthoracic echocardiography examination. medical histories from all patients and physical examination done. The investigation complies with the principles outlined in the Declaration of Helsinki. The study was approved by the local Ethics Committee and written informed consent was obtained from all participants.

Statistical Analysis

Sample size was calculated using Epi Info program, (Atlanta, Georgia, USA) at 95% confidence interval and power 80, the sample size was calculated to be 50 case of subclinical hypothyroidism and 75 cases for control group.

Data were analysed with the Statistical Package for the Social Sciences (SPSS) v.21 for Windows (IBM Inc. Chicago, IL), and the results were considered statistically significant when $p<0.05$. For quantitative data analysis. Simple frequencies were used for data checking. Quantitative data was expressed as mean and standard deviation (X ± SD) and analysed by Student t-test for comparison of two groups of normally distributed variables. Qualitative data was expressed as number and percentage and analysed by Chi-square test. t-test: is a test of significance for comparison between two quantitative variables with different variance. Linear regression model was constructed for cases in order to estimate regression coefficients (β) along with Odds Ratios (eβ) and their 95% CI adjusted by age, BMI, systolic blood pressure, diastolic blood pressure, heart rate, ejection fraction, LVEDD, LVESD and level of TSH.

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Results

Demographic data of this study demonstrated that patient's age ranged between 18-58 years with a Mean ± SD of 34.08 ± 9.66. The control group ages ranged between 18-45 years with a Mean ± SD of 31.47 ± 7.99. This difference was not statistically significant being higher in group I (P-value=0.102).

In this study, 46 subjects were males representing 36.8% of the study population and the remainder 79 subjects were females representing 63.2 %. Group I (Patients) included 16 males (32%) and 34 females (68%). Group II (Controls) included 30 males (40%) and 45 females (60%). This study demonstrated that patient's heart rate ranged between 69-80 beats/minute with a Mean ± SD of 74.18 ± 4.35 while in the control group heart rates ranged between 69-82 beats/minute with a Mean ± SD of 75.21 ± 4.16 This difference was not statistically significant being higher in group II (P-value=0.194).

This study demonstrated that Group I patient's systolic blood pressure (SBP) ranged between 110-130 mmHg with a Mean ± SD of 120.6 ± 5.785 and diastolic blood pressure (DBP) ranged 70-90 mmHg with a Mean ± SD of 79.41±5.21, Group II subjects systolic blood pressure (SBP) ranged between 110-120 mmHg with a Mean ± SD of 114.33 ± 4.816 and diastolic blood pressure (DBP) ranged 70-90 mmHg with a Mean ± SD of 74.66 ± 5.02. There was a significant statistical difference between the two groups as regarding blood pressure being more elevated in group I for SBP and DBP (P-value<0.001).

This study demonstrated that Group I patient's Body Mass Index BMI ranged 19-32 Mean ± SD of 24.08 ± 3.65 and group II subjects BMI ranged 17-30 with a Mean ± SD of 21.33 ± 3.38 There was a significant statistical difference between the two groups as regarding BMI being more elevated in group I (P-value<0.001).

In this study, Group I TSH ranged 8-40 mIU/L with a Mean ± SD of 13.01 ± 6.91 comparing with group II ranged 0.9 – 3.2 mIU/L with a Mean ± SD of 1.64 ± 0.58. There was a significant statistical difference between the two groups as regarding TSH being more elevated in group (P-value<0.001). No significant statistical difference between the two groups as regarding FT3 and FT4 (Table 1).

Regarding ejection fraction by M mode, there was a highly significant statistical difference between the two groups with group I (patients) 63.36% ± 4.92 And group II 68.66% ± 5.39 which shows significant statistically reduction in values (P-value=0.001) (Table 2).

Regarding left ventricular end systolic dimension, there is high significant statistical difference between the two groups, group I show high reduction in values (4.48 ± 0.739) and group II (4.59 ± 0.491) which is statistically high significant (P value<0.001).

Regarding left ventricular end diastolic dimension, there is significant statistical difference between the two groups with group I (patients) showing increasing the values (4.788 ± 0.491) and group II significant reduction in values (P-value=0.02).

Regarding E\A ratio, there was a significant statistical difference between the two groups showing reduction in group I (patients) (P-value<0.05). Regarding E/e' ratio, there was a highly significant statistical difference between the two groups showing elevation in group I (patients) (P-value<0.005). Peak longitudinal systolic strain (PLSS or Esys%), The left ventricular wall segments, Basal septal, basal anterior, basal lateral and basal inferior wall segments showed high significant statistical difference between the two groups (P-value>0.001). The Mid septal, mid anterior, mid lateral and mid inferior wall segments showed significant statistical difference between the two groups (P-value ›0.05), The remaining segments of the left ventricle apical septal no significant statistical difference, apical anterior, apical lateral and apical inferior showed significant statistical difference between the two groups being significantly reduced in group I (P-value<0.005) (Table 3). For all P values give exact values and not less than 0.05. For P<0.001, do not include the exact value but present it as <0.001.

Table 1: Comparison of cases and control groups regarding their Laboratory Thyroid Functions characters.

	(No=50) Cases	(No=75) Control	t test	p value
TSH(X ± SD)	13.01 ± 6.91	1.64 ± 0.58	14.2	<0.001*
Max-Min	7.8-40	0.9 – 3.2		
Rang	32.2	2.3		
FT3(X ± SD)	2.18 ± 0.43	2.29 ± 0.44	1.46	0.146
Max-Min	1.7 - 3.2	1.7 – 3		
Rang	1.5	1.3		
FT4(X ± SD)	1.138 ± 0.186	1.172 ± 0.172	1.03	0.303
Max-Min	0.79 - 1.4	0.9 – 1.4		
Rang	0.61	0.5		

Table 2: Comparison between the study groups regarding conventional echocardiographic measurements.

	(No=50) Cases	(No=75) Control	t test	p value
EF (X ± SD)	63.36 ± 4.92	68.66 ± 5.39	5.574	<0.001*
Max-Min	56 : 75	58-77		
Rang	19	19		
LVESD(X ± SD)	4.48 ± 0.739	4.59 ± 0.491	4.607	<0.001*
Max-Min	2.2 – 4.2	2.1 – 3.5		
Rang	2	1.4		
LVEDD(X ± SD)	4.788 ± 0.491	4.588 ± 0.491	2.246	0.02
Max-Min	3.8 -6.1	3.7 - 5.5		
Rang	2.3	1.8		

*Statistically significant.

Table 3: Comparison between study groups regarding peak Longitudinal strain (PLSS/Esys %) of analyzed LV myocardial segments.

X ± SD		Cases (No=50)	Control (No=75)	t test	p value
ANT	Basal Rang	-14.81 ± .569 -5 : -25	-21.86 ± 6.656 -11: -32	6.197	<0.001*
	MID Rang	-13.56 ± 6.054 -26: -2	-17.21 ± 7.025 -27: -6	2.996	0.003*
	Apical Rang	-14.81 ± 6.801 - 25: - 2	-16.933 ± 5.569 -26:-6	2.353	0.021*
Lateral	Basal Rang	-14.88 ±5.57 - 30: -6	-23.66 ± 4.844 -31: -16	9.351	<0.001*
	MID Rang	-11.21 ± 7.01 -23:15	-19.13 ± 4.237 -25: -8	7.888	<0.001*
	Apical Rang	-14.28 ± 4.99 -22 :-6	-19.00 ±4.318 -27 : -12	5.625	0.007*
Septal	Basal Rang	-16.58 ± 8.49 -30:16	-25.01 ± 5.53 -33:-17	6.0864	<0.001*
	Mid Rang	-17.68 ± 4.68 -27: -7	-21.61 ± 3.851 -28: -10	5.108	<0.001*
	Apical Rang	-16.24 ± 5.93 -28 : -6	-17.93 ± 3.629 -23: -8	1.981	0.051
INF	Basal Rang	-17.28 ± 5.059 -29 : -7	-23.666 ± 6.815 -33:-10	5.665	<0.001*
	Mid Rang	-17.00 ± 4.435 -27:-7	-19.13 ± 4.237 -5:-28	2.613	0.006*
	Apical Rang	-14.36 ± 8.73 -24 : 12	-19.00 ±4.318 -28:-7	3.214	0.002*

* Statistically significant.

Table 4: Linear regression analysis of factors affected global strain of the studied group (No=125).

*Factor Parameters (abnormal global strain is the) (reference group)	(Beta)	P value	Odds ratio	Confidence Interval Lower bound	upper bound
Age	0.024-	0.559	0.064-	0.056	0.104-
BMI	0.134 -	0.191	0.153	0.336	0.067-
SBP	0.231-	0.008 0.001>	0.472-	0.061-	0.401-
DBP	0.002	0.983	0.003	0.189	0.185-
HR	0.059-	0.261	0.079-	0.044	161.-
EF	0.371	0.112	0.659	0.826	0.085-
LVEDD	7.551-	0.049 0.05>	1.153-	3.211-	1.217-
LVESD	9.372	`0.131	1.181	4.066	2.835-
TSH	0.223-	0.003 0.001>	0.484-	0.149-	0.279-

Discussion

Experimental and clinical findings strongly support the concept that thyroid hormone (TH) has a fundamental role in the cardiovascular homeostasis both in physiological and pathological conditions [3]. This work designed to study the effect of Subclinical Hypothyroidism on LV function and risk of CVD. Results demonstrated that patient's heart rate is less than the control group. This difference was not statistically significant between the two groups, Liu et al. showed that decreased thyroid hormone levels after thyroidectomy lead to have low heart rate and low stroke volume that results in low cardiac output decreased systolic and diastolic function, and results in cardiac atrophy and severe cardiac dysfunction [4]. Results show that there is a significant statistical difference between the two groups as regarding BMI being more elevated in group I. This results agreed with a study by Gupta et al., done in Santosh Medical College, Ghaziabad, India. Who study the relation between Subclinical hypothyroidism and BMI on 90 women newly discovered SCH were enrolled for the study and were compared with 62 normal healthy adult women with same age group. The study reported that women with SCH are characterized by higher BMI due to their increased body weight. A positive correlation was found between TSH and BMI in SCH women as well as a control group [5] on assessment of the LV function Conventional echocardiographic measurements of the LV revealed that EF by M Mode and Simpsons biplane technique were significantly reduced in the patient group comparison with the control group, there was a highly significant statistical difference between the two groups. In a study, 23 patients with untreated SH, 21 patients with treated SH and 25 healthy volunteers, All patients and controls had normal LV ejection fraction which decreased in group A but not statistically significant [6], the study show that Comparison between study groups regarding Mitral E/A ratio and E/e', there was a significant statistical difference between the two groups showing reduction in group I (patients). Regarding E/e' ratio, there was a highly significant statistical difference between the two groups showing elevation in group I (patients).

In a study by Nicolas Rodondi et al., Participants with TSH ≥ 10.0 had a higher peak E velocity, and this difference persisted after adjustment for age, gender, heart rate and systolic blood pressure. Peak E velocity was associated with incident HF in the overall study sample and in those with TSH ≥ 10. After adjustment for age, gender and systolic blood pressure. Compared to euthyroidism, subclinical hyperthyroidism was associated with larger left atrial size, higher proportions with E/A ratio [7], By Marijana Tadic et al. Subclinical Hypothyroidism and Left Ventricular Mechanics: A Three-Dimensional Speckle Tracking Study, The parameter of LV diastolic function of the trans-mitral E/A ratio was significantly decreased, whereas mitral E to e′ ratio was increased in the SHT patients at the baseline compared with the controls and the SHT patients after replacement therapy. These changes showed that LV diastolic function was impaired in the SHT patients before therapy and significantly improved after the replacement therapy [8], in the study (2-D) Peak longitudinal systolic strain (PLSS or Esys %), The left ventricular wall segments, Basal septal, basal anterior, basal lateral and basal inferior wall segments showed high significant statistical difference between the two groups. The Mid septal, mid anterior, mid lateral and mid inferior wall segments showed significant statistical difference between the two groups, The remaining segments of the left ventricle apical septal no significant statistical difference, apical anterior, apical lateral and apical inferior showed significant statistical difference between the two groups being significantly reduced in group I. In a study, 23 patients with untreated SH (Group A; 7 male, mean age: 40.9 ± 1.6 years), 21 patients with treated SH and 25 healthy volunteers, the mean peak systolic strain, the mean peak systolic strain rate, the mean peak early diastolic strain rate and the mean peak late diastolic strain rate were lower in overt subclinical hypothyroidism compared to controls by tissue Doppler imaging, association between SH and LV function was evaluated. SH was associated with LV diastolic dysfunction [6], In a study evaluated in 30 females with SHT and 20 matched control subjects with Evidence from a magnetic resonance imaging study Left ventricular end-diastolic volume (EDV) and end-systolic volume (ESV), stroke volume (SV), cardiac index (CI), and systemic vascular resistance (SVR) were calculated by cardiac magnetic resonance (CMR). Regional greatest systolic lengthening (E1) and greatest systolic shortening (E2) were calculated by tagging CMR. Conclusion Subclinical hypothyroidism significantly decreased cardiac preload, whereas it increased afterload with a consequent reduction in SV and cardiac output. Replacement therapy fully normalized the hemodynamic alterations [9]. As shown in previous studies, untreated SH was associated with impairment in LV longitudinal myocardial function compared to healthy. In fact, cardiac functions improve with the replacement of thyroid hormone level in hypothyroid state, they also found that there was no significant difference in myocardial strain and strain rate values. So, the study findings support this hypothesis. In the present study, by using speckle tracking echocardiography LV systolic dysfunction can be early assessed in SH patients who have normal ejection fraction values. In correlation between TSH values and Global strain of the cases our study shows statistical significant negative correlation between TSH of cases group and their global strain which is adapted to the most previous meta-analysis of studies done on the patient with subclinical hypothyroidism. From the result of Linear regression analysis of factors affected global strain of the studied group A linear regression model was constructed in order to estimate odds ratios (Confidence Interval 95%) for the presence of abnormal global strain, adjusted by Age, BMI, systolic blood pressure, diastolic blood pressure, heart rate, ejection fraction, LVEDD, LVESD and level of TSH. High level of TSH, SBP and LVEDD shows significance to abnormal global strain. Linear regression analysis identified elevated TSH, increased SBP and LVEDD, as significant correlates of abnormal global strain with elevated TSH as the most dependent factor affects global strain which reflect the importance of early detection of patient with high TSH and investigate them to detect how much the affection of LV function using now modalities of non-invasive imaging 2D Speckle Tracking echocardiography (Table 4).

Conclusion

The Global LV Peak Longitudinal Strain is significantly reduced in patient with Subclinical Hypothyroidism mainly due to reduction of average septal PLSS. Other parameters of the LV as EF, E/A and E/ē, are also appear to be significantly affected in these patients.

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