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Research Article

Right Ventricular Strain Assessment by Speckle Tracking Echocardiography before and after treatment of clinical and subclinical hypothyroidism

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Abstract

Background: Hypothyroidism is prevalent endocrinological disease that raises cardiovascular disorders. Due to the complexity of right ventricular (RV) geometry and its challenging non-invasive testing, speckle tracking echocardiography (STE) emerges as contemporary tool for identifying early changes in RV function. **Aim:** RV function evaluation in clinical and subclinical hypothyroidism patients before and after treatment using STE. **Methods:** Total 74 individuals underwent for STE. 24 clinical hypothyroidism subjects (group I), 24 subclinical hypothyroidism subjects (group II), and 26 normal individuals as a control group. RV function evaluated prior to the treatment regimen and three months after reaching euthyroid stage. **Results:** Prior to therapy, global longitudinal strain (GLS) was significantly lower in patients groups compared with controls. (GLS in group I= -25.2 ± 0.3 Vs. -27.8 ± 0.5 in control group (P value <0.01) and GLS in group II= -25.3 ± 0.2 Vs. -27.8 ± 0.5 in control group (P value <0.01), but no statistically significant difference was found regarding ejection fraction (EF %). After three months at euthyroid stage, the values were not totally reversed but there was significant improvement of GLS, (GLS in group I after treatment= -27.2 ± 0.4 Vs. -25.2 ± 0.3 before treatment (P value <0.05) and GLS in group II after treatment= -27.4 ± 0.2 Vs. -25.3 ± 0.2 before treatment (P value <0.05). **Conclusion:** Early detection and treatment of both clinical and subclinical hypothyroidism patients partially reverse RV functional abnormality. STE may efficiently detect early contractile changes, before changes in EF occurs.

Key words: Clinical hypothyroidism, subclinical hypothyroidism, right ventricular ejection fraction and right ventricular global longitudinal strain.

Introduction

Thyroid hormones have a substantial impact on the cardiovascular system [(1)]. The intracellular impacts of thyroid hormones in cardiomyocytes are mediated through two distinct mechanisms: genomic and non-genomic, with the genomic pathway prevailing [(2).] RV dysfunction is also a crucial factor in the development of multi-systemic organ failure and death associated with heart failure [(3)]. Nevertheless, due to its intricate geometry, evaluating the RV with echocardiography could prove to be exceedingly challenging. The assessment of right ventricular function and mechanics has become feasible and reliable after introduction of advanced echocardiographic techniques, including tissue Doppler and speckle tracking imaging modalities.

Aim of The Work:
To evaluate the impact of treatment on right ventricular function in both clinical and subclinical hypothyroidism patients using two-dimensional speckle tracking echocardiography.

Patients and Methods

A prospective study was undertaken at the cardiology department of Minia University from March 2022 to April 2023. This study was authorized by the hospital's ethics committee, and signed agreement was obtained from each participant (Approval No. 317:1/2022, Date: 24 January 2022).

The Study included 48 patients who were recently diagnosed with clinical and subclinical hypothyroidism, together with 26 euthyroid individuals who were included as a control group. The patients were recruited from the outpatient clinics of the internal medicine department following the treatment plan provided by the endocrinology unit of Minia university hospital. For an average adult, the initial levothyroxine sodium dose is approximately 1.7 mcg/kg/day and dose was adjusted at intervals of 4–6 weeks based on thyroid stimulating hormone levels (4).

A) Patients:

Inclusion criteria:
The study included newly diagnosed clinical and subclinical hypothyroidism patients.

Exclusion criteria:
- Prior medical history of thyroid disease or already on treatment for thyroid dysfunction.
- History of cardiovascular disorders including hypertension, ischemic heart disease, cardiomyopathies, atrial fibrillation, or significant valvular heart disease. Additionally, exclusion criteria were patients with Diabetes, Chronic pancreatitis, Hepatic or renal disorders, and Pregnancy.

Methods:

All included individuals were subjected to:
A detailed clinical assessment was conducted, which included a detailed history, general and local examination, including a thorough cardiac examination and measurement of both systolic and diastolic blood pressure.

2- Twelve- lead resting ECG.

3- Blood samples for:
A): Routine Samples including:
- Complete blood count.
-HbA1C, fasting and random blood sugar.
-Renal function (Urea and Creatinine)
-liver function (ALT and AST)
-lipid profile

B): Thyroid function tests including:
-TSH, Free T3 and Free T4 samples were drawn at first visit for diagnosis of hypothyroidism and repeated every 4-6 weeks for follow up and to adjust levothyroxine dose when needed.

According to the American Thyroid Association, the acceptable range for TSH levels is around 0.4 mIU/L to 4.0 mIU/L, however the exact numbers at the lower and upper ends of the range may vary slightly. Clinical hypothyroidism is diagnosed in individuals when their thyrotropin (TSH) levels rise above 10 mIU/L, along with a proportional decrease in free thyroxin (T4) (4). Subclinical hypothyroidism is defined as having a thyroid-stimulating hormone (TSH) level that is higher than the top limit of the normal reference range, while the levels of thyroid hormones remain within the normal range.

4- Echocardiographic assessment of the right ventricular function:

Transthoracic Echocardiography was conducted prior to initiating the treatment regimen and repeated three months after reaching a state of normal thyroid function using the SIEMENS ACUSON SC 2000 ultrasound machine (manufactured in Germany by Siemens) with its specialized 4V1 probe, which was used for all participants. The Echocardiographic measurements were conducted in accordance with the guidelines provided by the American Society of Echocardiography/European Association of Cardiovascular Imaging (5). Two blinded examiners performed the measurements and the results were averaged. The calculation of two-dimensional RV volumes and ejection fraction was performed using the modified Simpson's rule (6).

Two Dimensional speckle tracking:

Speckle Two-dimensional images were obtained from the four-chamber view for offline analysis. The software utilizes real-time tracking of natural acoustic markers to derive two-dimensional strain and strain rate. This is accomplished by analyzing the movement of speckles relative to each other over the cardiac

cycle. The software manually tracked and monitored the endocardial border of the right ventricle to calculate the longitudinal strain and strain rate. In order to assess regional systolic strain, the RV free wall and inter-ventricular septum were divided into three segments (basal, mid, and apical). The global longitudinal systolic strain (GLS) was quantified by assessing the entire traced contour of the right ventricle [7].

Statistical analysis:

The data analysis was conducted with the IBM SPSS 20.0 statistical package software. The data were presented as the mean value plus or minus the standard deviation (SD), together with the lowest and maximum values for quantitative parametric measurements. The Student t-test was employed to compare parametric data between two independent groups. ANOVA was employed to compare parametric data among multiple independent groups. The outcomes before and after therapy were compared using a paired t-test. The chi-square test was employed to compare categorical variables. P value 0.05 or lower was considered a significant value. The graphs were generated using Microsoft Office 365's Excel. (All tests included within our study).

Results:

Based on their thyroid stimulating hormone and free T4 levels, the individuals were categorized into three groups, First one comprised 24 individuals diagnosed with clinical hypothyroidism, second one comprised 24 individuals diagnosed with subclinical hypothyroidism. Additionally, a control group of 26 euthyroid people was included.

Regarding demographic data, there was no statistically significant difference found among the three groups. (Table 1)

Regarding echo parameters, no statistically significant difference was present between the first two groups regarding RV EF% and RV GLS. In comparison with control group, RV GLS was significantly lower in Group I and Group II, while no statistically significant difference was found regarding RV EF%. (Table 2)

After treatment, there was a statistically significant increase in RV GLS values in clinical and subclinical hypothyroidism groups compared to baseline values (Table 3) (figure 1 & 2).

Comparison between treated groups and control group:

Although there was a significant improvement in RV GLS values in both group I and group II after receiving therapy, still there was a statistically significant difference when compared to the control group. (Table 4)

Table (1): Demographic measures of the studied groups :

	Clinical hypothyroidism	Subclinical hypothyroidism	Control	p value
Age	36.2 ± 9.2	37.3 ± 9.1	34.6 ± 9.5	0.584
Sex:				
Females	20 (83.3%)	19 (79.2%)	15 (57.7%)	0.088
Males	4 (16.7%)	5 (20.8%)	11 (42.3%)	

-Data were expressed as mean ± standard deviation (SD), minimum and maximum of range for quantitative parametric measures**.**

-P-value considered significant at <0.05

Table (2): Echocardiographic data of group I, II at baseline and control group:

	Clinical hypothyroidism (group I)	Subclinical hypothyroidism (group II)	p value
RV EF%	60.5 ± 3.0	60.7 ± 2.2	0.847
RV GLS	-25.2 ± 0.3	-25.3 ± 0.2	0.824
	Clinical hypothyroidism	**Control**	**p value**
RV EF%	60.5 ± 3.0	62.5 ± 2.4	0.113
RV GLS	-25.2 ± 0.3	-27.8 ± 0.5	**<0.01***
	Subclinical hypothyroidism	**Control**	**p value**
RV EF%	60.7 ± 2.2	62.5 ± 2.4	0.084
RV GLS	-25.3 ± 0.2	-27.8 ± 0.5	**<0.01***

RV EF =right ventricular ejection fraction, RV GLS =right ventricular global longitudinal strain

Table (3): RV GLS of group I & II before and after treatment:

	Group I (before treatment)	Group I (after treatment)	p value
RV GLS	-25.2 ± 0.3	-27.2 ± 0.4	**<0.05***
	Group II (before treatment)	**Group II (after treatment)**	**p value**
RV GLS	-25.3 ± 0.2	-27.4 ± 0.2	**<0.05***

Table (4): RV GLS of treated groups and control group:

	Group I (after treatment)	Control	p value
RV GLS	-27.2 ± 0.4	-27.8 ± 0.5	**<0.05***
	Group II (after treatment)	**Control**	**p value**
RV GLS	-27.4 ± 0.2	-27.8 ± 0.5	**<0.05***

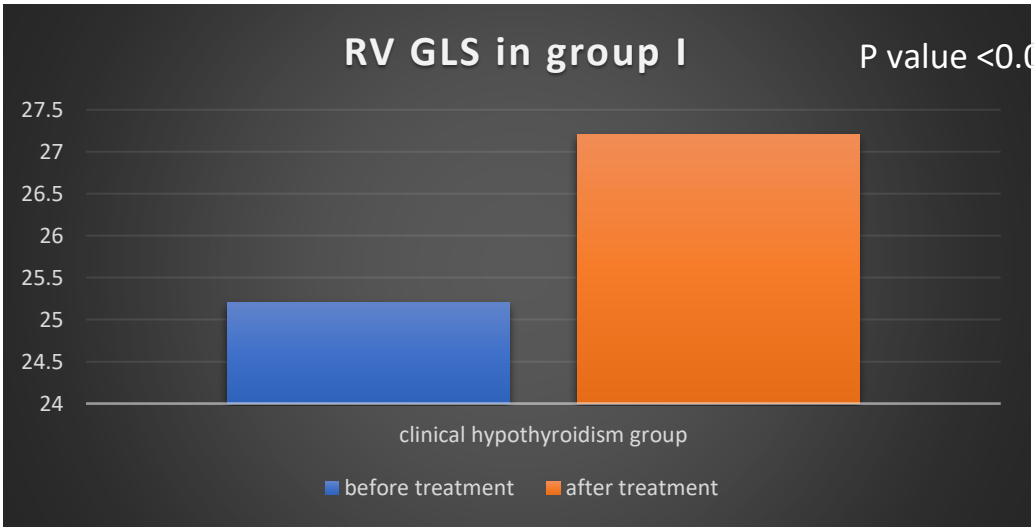

Figure 1: RV GLS in Group I before and after treatment

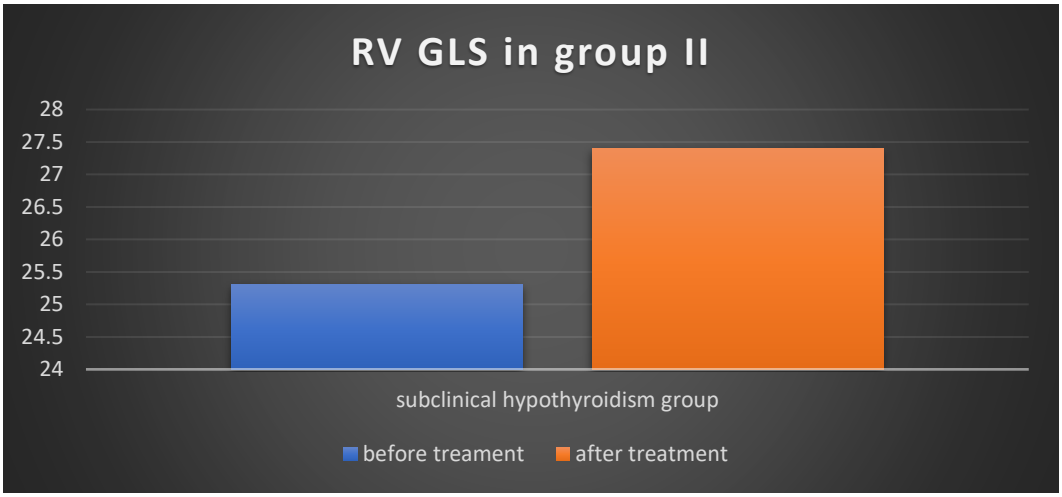

Figure 2: RV GLS in Group II before and after treatment

Discussion

The clinical manifestations of hypothyroidism predominantly result from thyroid hormone deficiency and its effects on the structure and function of the cardiovascular system. The enlarged cardiac borders, pericardial effusion, reduced electrocardiographic voltage, and slow indolent heart action are frequently seen in cases of overt hypothyroidism [(8)]. The clinical presentation of subclinical hypothyroidism may not be well defined and its symptoms are generally less apparent in comparison to overt hypothyroidism. It had been shown that it can have a significant impact on many metabolic and organ function indicators, which gradually become clinically significant over time. The introduction of more advanced echocardiographic techniques has allowed a clear understanding of the changes in myocardial contractile function that occur in both clinical and subclinical thyroid dysfunction [(9)].

The results of our study showed that there was no statistically significant difference found between group I and group II in terms of RV GLS and RV EF, while in comparison to controls, RV GLS was significantly lower in hypothyroidism patients. Regarding RV EF, no statistically significant difference was found between the hypothyroidism patients and the controls. After three months at euthyroid stage, there was significant improvement of RV GLS values compared to its baseline values.

The RV has limited research attention due to its complex geometry and the absence of a dependable and easily accessible imaging modality. There is a limited number of research that have investigated the structure and function of the right ventricle in people with hypothyroidism. Turhan et al., demonstrated a correlation between subclinical hypothyroidism and impaired right ventricular systolic performance [(10)]. Ripoli et al., demonstrated, through the use of cardiac MRI, that people with subclinical hypothyroidism had a significant reduction in cardiac preload and an increase in afterload, resulting in a decrease in stroke volume and cardiac output [(11)]. The study conducted by Ilic et al., examined a group of 45 untreated women with subclinical hypothyroidism and compared them to a group of 35 healthy women. The results of the study indicated that patients with subclinical hypothyroidism had a significant decline in right ventricular (RV) function and mechanics [(12)]. Our findings also indicated a same pattern in patients with clinical hypothyroidism, consistent with the study conducted by Kosar et al., that also revealed a correlation between clinical hypothyroidism and right ventricle dysfunction [(13).]

Our study revealed that RV GLS was significantly improved in both hypothyroidism patients groups after treatment which is similar to the results found in Turhan et al and ilic et al., studies [(10, 12)]

We can explain the disturbance of right ventricular mechanics in patients with hypothyroidism and subclinical hypothyroidism through various pathways. As an illustration, free T3 and free T4 hormones are able to enter the cell by a unique transport mechanism then attach to the triiodothyronine receptor located in the nucleus. This intricate structure subsequently attaches to the thyroid hormone response element found in various genes responsible for cellular components then regulates the activity of Calcium-ATPase, myosin, β-adrenergic receptors, adenylyl cyclase, guanine nucleotide binding proteins, Na+/Ca2+ modifier, Na+/K+-ATPase, and the transcription of genes that encode voltage-gated potassium channels in the sarcoplasmic reticulum. Thus, it improves the strength of the heart's contractions by causing an increase in calcium levels inside the cells [(14)]. The cardiac dysfunction found in individuals with hypothyroidism can be linked to the breakdown of these numerous physiological processes. Subclinical hypothyroidism is linked to many tissue modifications, such as abnormalities in the compatibility of cardiac fibers, capillary redistribution, changes in collagen structure, and dehydration [(15, 16)]. The interaction between the ventricles is also a significant factor in the remodeling of the right ventricle (RV) in patients with hypothyroidism. This interaction takes place in two manners: via the interventricular septum, which transfers excessive pressure and volume from the left ventricle to the right ventricle; and via conveying increased pressure in the filling of the left ventricle through the pulmonary vascular bed to the right ventricle [(17)].

Conclusion and recommendations: The RV global longitudinal strain, as evaluated by speckle tracking echocardiography, is markedly impaired in individuals with hypothyroidism. Levothyroxine therapy improved RV myocardial function and deformation. This implies that longer substitution therapy is necessary for complete recovery of the right ventricle in patients with hypothyroidism. We recommend conducting further research that includes longer study periods and a larger number of participants to confirm our findings, establish the optimal duration of treatment required for complete restoration of cardiac function, evaluate the long-term effectiveness of Levothyroxine replacement therapy, and assess the potential need for supplementary treatments to improve cardiac function in individuals with hypothyroidism.

Limitations of the study: The study had a relatively small sample size. This restriction could be partially explained by the deliberate selection of patients with newly diagnosed hypothyroidism and subclinical hypothyroidism, without any other accompanying medical conditions.

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