Research Article

The Evaluation of Diastolic Dysfunction with Tissue Doppler Echocardiography in Women with Subclinical Hypothyroidism and the Effect of L-Thyroxine Treatment on Diastolic Dysfunction: A Pilot Study

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Background. Subclinical hypothyroidism (SH) predominantly affects women. The necessity of treatment in SH is controversial. Objective. We aimed to investigate the response of diastolic dysfunction to thyroid hormone replacement therapy (THRT) in women. Methods and Results. Twenty-two female subjects with SH and 20 euthyroid female controls were enrolled. Baseline and follow-up biochemical, hormonal, and echocardiographic evaluations were performed. Repeat echocardiograms were performed three months after the achievement of a euthyroid status with THRT. Mean baseline myocardial performance index (MPI) was 0.27 ± 0.08 in the SH group, and 0.22 ± 0.06 in the control group (P = 0.03). MPI did not change significantly after THRT. Pulsed-wave Doppler findings were not different among the groups. However, tissue Doppler-derived mitral annular E’ velocities were significantly lower in the SH group. A moderate but significant improvement was observed in E’ velocities after THRT (13.52 ± 3.87 versus 14.53 ± 2.75, P = 0.04). We also observed left ventricular concentric remodeling in SH patients which was reversible with THRT. Conclusions. Tissue Doppler echocardiography may be a useful tool for monitoring the response of diastolic dysfunction to thyroid hormone replacement therapy in patients with SH. Our findings suggest that THRT may reverse diastolic dysfunction in women with SH.

1. Introduction

Subclinical hypothyroidism (SH) is a generally asymptomatic condition defined as normal serum levels of thyroid hormones and elevated thyroid stimulating hormone (TSH) levels. SH is frequently a laboratory diagnosis, because clinical signs and symptoms are either absent or mild [1]. Framingham study reported an increase in the prevalence of SH with increasing age, with a prevalence of 16.9% in women and 8.2% in men older than 60 years [2]. In the majority of patients, chronic autoimmune thyroiditis is the etiology, demonstrated by serum anti-thyroid peroxidase antibodies [3].

Previous studies concerning the cardiovascular effects of SH have shown a decrease in pre-ejection period (PEP) and PEP/LVET (left ventricular ejection time) ratio which is reversible with T4 replacement therapy [4–6]. Left ventricular systolic function is normal at rest but impaired during exercise in patients with SH when compared to euthyroid controls [7–9]. Exercise-induced systolic dysfunction has been attributed to diastolic dysfunction at rest; the impairment of left ventricular relaxation may lead to impaired
ventricular filling and thus systolic dysfunction that becomes manifest only during exercise [10, 11].

Isovolumetric relaxation time (IVRT) is prolonged and pulsed Doppler-derived transmitral A wave velocity is increased in SH. These findings of diastolic dysfunction (DD) are normalized after T4 replacement therapy [12, 13]. Time-to-peak filling rate is prolonged and normalized after T4 replacement in a radionuclide ventriculographic study, reflecting the reversal of diastolic dysfunction in SH [14].

Myocardial performance index (MPI) is a sensitive parameter that expresses overall left ventricular function [15]. Isovolumetric contraction time (ICT) is prolonged and the ejection time (ET) is shortened in systolic dysfunction. Diastolic dysfunction causes prolongation of the IVRT. MPI, calculated by dividing the sum of ICT and IVRT by ET, is below 0.40 if the overall ventricular function is normal. An MPI greater than 0.40 reflects diastolic and/or systolic dysfunction. MPI is increased in patients with SH [16].

Tissue Doppler echocardiography (TDE) allows us to measure diastolic mitral annular velocities and thus gather information about diastolic function. Mitral annular velocity measured during diastole reflects the rate of change in LV longitudinal dimension and LV volume. In the presence of abnormal myocardial relaxation, the ratio of mitral annular motion during atrial systole to total diastolic annular motion is increased. Previous TDE studies reported diastolic dysfunction in patients with SH [17, 18]. Beneficial effects of thyroid hormone replacement on right ventricular systolic and diastolic function were reported in a TDE study [19].

To the best of our knowledge, the response of MPI to THRT has been investigated in only one study [20]. Considering the relative paucity of studies assessing the role of TDE in monitoring the response to THRT in SH, we designed this study. One distinguishing aspect of this study is that only female subjects are included, considering that SH is a condition that predominantly affects female subjects. Thus, we specifically aimed to investigate the effect of THRT on altered cardiac function in female subjects with SH, particularly using TDE.

2. Materials and Methods

2.1. Patients. Twenty-two consecutive female patients diagnosed with SH in the outpatient clinic of a tertiary care center were enrolled in the study. Criteria for inclusion were being 18 years of age or older, female sex, and a serum TSH level between 4.2 and 9.9 mU/L, and having none of the exclusion criteria listed below. Twenty age-matched, euthyroid female subjects who presented to the outpatient clinic because of symptoms unrelated to the endocrine or cardiovascular systems were included in the study as the control group.

Criteria for exclusion were as follows: age greater than 60 years, atrial fibrillation, diabetes mellitus, systemic arterial hypertension, history of coronary artery disease, moderate to severe valvular heart disease, cardiomyopathy, history of previous hyperthyroidism, previous use of antithyroid agents, and lipid lowering therapy in last 6 months. The same exclusion criteria are applied to the control subjects as well. Subjects older than 60 years of age were excluded because left ventricular diastolic relaxation abnormalities could be observed physiologically.

Also, women with a TSH level of 10 mU/L or greater were not included in the study, because cardiovascular involvement in patients with manifest hyperthyroidism (TSH level equal to or greater than 10 mU/L) including diastolic dysfunction and heart failure is well established [21].

Patients with SH were classified according to etiology as follows:

1. Hashimoto’s thyroiditis (n = 16),
2. SH due to thyroidectomy (n = 1),
3. SH with negative thyroid auto-antibodies and not due to surgery (n = 5).

Written informed consent was obtained from all participants. The study protocol was approved by the local ethics committee and conforms to the Helsinki Declaration.

2.2. Drug Regimen. L-Thyroxine treatment was administered to patients whose TSH levels were between 4,2 and 10 mIU/L (Levotiron 0,1 mg, Abdi Ibrahim, Istanbul, Turkey). Dose was titrated up every 15 days to a level that achieved and maintained a normal TSH level.

2.3. Laboratory Assessment. All of the patients and controls underwent laboratory assessment. Baseline hemoglobin, fasting blood glucose, total, LDL, and HDL, cholesterol, triglyceride levels were determined.

Serum-free T3, T4, and TSH were assessed using the microparticle enzyme immunoassay method (Axsym, Abbott, USA).

Anti-microsomal antibody (anti-M) and anti-thyroglobulin antibody were assessed using radioimmunoassay (RIA). Normal limits were assumed as 0–60 IU/L for both antibodies.

2.4. Echocardiographic Evaluation. An echocardiographic examination was performed before enrollment and three months after euthyroid state was achieved. The cardiologists (A.F.E. and M.C.) who performed and interpreted the echocardiograms were blind to the clinical and treatment status of the patients.

A Vingmed System V echocardiography unit was used (General Electric, Norway). Frequency of the probe was 1.7 MHz and it was capable of harmonic imaging. B-mode, M-mode, continuous wave Doppler, and colour Doppler examinations were performed utilising parasternal long axis, parasternal short axis, and apical two- and four-chamber views with the patient in the left lateral decubitus position. Left ventricular end-diastolic and end-systolic diameters, systolic and diastolic thicknesses of the interventricular septum, and the posterior wall were measured during M-mode examination. Left ventricular mass index (LVMI) was calculated according to Devereux’s formula [18]. Left ventricular ejection fraction was calculated according to Teichholz method.

Transmitral flow velocities were measured using pulsed-wave Doppler in the apical four-chamber view. A sample volume of 2 mm was placed between the mitral leaflet tips, E
and A velocities were measured, and E/A ratio was calculated. E wave deceleration time was measured in milliseconds.

Using continuous-wave Doppler tracings obtained at the aortic five-chamber view, isovolumetric contraction time (ICT), isovolumetric relaxation time (IVRT), and aortic ejection time (ET) were measured. Myocardial performance index (MPI) was calculated by dividing the sum of ICT and IVRT by ET.

Tissue Doppler was employed to measure systolic and diastolic mitral annular velocities. Tissue Doppler sample volume was placed on septal and lateral localizations of the mitral annulus in the apical four-chamber view and the anterior and inferior localizations in the apical two-chamber view. Systolic (S) and diastolic (E′ and A′) velocities of the annulus were measured Pulsed wave Doppler-derived E wave velocity/tissue Doppler-derived E′ velocity ratio (E/E′).

2.5. Statistical Analysis. Data was analyzed using SPSS 12 software package. Results were expressed as mean ± standard deviation. The normal distribution of variables was verified with the Shapiro-Wilk test. As the distribution was normal, Student’s t-test was employed for comparisons between the groups. Paired t-test was used for comparisons within the groups. A P value less than 0.05 was considered statistically significant. To assess the significance of change in clinical and laboratory parameters before and after treatment, we used the Student’s t-test.

3. Results

Baseline characteristics and biochemical examinations were not different between the SH group and the euthyroid control group.

| Table 1: Thyroid function tests before and after thyroid hormone replacement therapy (THRT). |
|---------------------------------|----------------|----------------|
| Before THRT | After THRT | P value |
| fT3 (pg/mL) | 2.62 ± 0.39 | 2.67 ± 0.44 | 0.07 |
| fT4 (ng/dL) | 0.89 ± 0.13 | 1.02 ± 0.12 | 0.005 |
| TSH (mIU/mL) | 7.17 ± 1.74 | 2.28 ± 0.63 | <0.001 |
| fT3: free triiodothyronine; fT4: free thyroxine; TSH: thyroid stimulating hormone. |

As expected, mean serum TSH level in the SH group (7.17 ± 1.74 µIU/mL) was significantly higher when compared to the control group (1.31 ± 0.72 µIU/mL) (P < 0.001). While free T3 levels were not significantly different, free T4 levels were significantly lower in SH patients, although they were still within the normal range. AntiMicrosomal antibody levels were overtly higher in the SH group (1430.98 ± 348.07 IU/mL), when compared to the control group (28.24 ± 9.34 IU/mL), (P < 0.001). In a similar fashion, anti-thyroglobulin levels were higher in the SH group when compared to the control group (254.66 ± 99.76 IU/mL versus 17.05 ± 6.16 IU/mL, P = 0.02).

Patients with subclinical hypothyroidism received THRT as described in the methods section and euthyroidism was achieved in all subjects. Thyroid function tests before and after treatment, are given in Table 1.

3.1. Echocardiographic Parameters. Table 2 summarizes B-mode and M-mode echocardiographic findings in SH and control groups. The intraobserver and interobserver variations for these echocardiographic measurements were 2% and 3%, respectively. While ejection fraction and left ventricular-end diastolic diameter did not differ, mean left ventricular posterior wall thickness was greater in the SH group when compared to the control group (1.0 ± 0.13 cm versus 0.92 ± 0.13 cm, P = 0.04). Mean interventricular septum thickness was 0.97 ± 0.12 cm in the SH group and 0.88 ± 0.10 in the control group (P = 0.01).

Mean left ventricular mass index calculated according to the Devereux formula was similar among the SH and control groups (77.34 ± 2.14 g/m² versus 77.39 ± 2.39 g/m²; P = 0.92).

The mean left atrial diameter corrected according to the body surface area in the subclinical hypothyroidism (SH) patients was statistically significantly higher when compared to the healthy controls (2.1 cm/m² versus 1.8 cm/m², P = 0.039). It was also noted that the mean BSA-corrected left atrial diameter approximated the upper limit of normal (2.2 cm/m²) in the SH group. There was a mild reduction in left atrial diameter after 3 months of THRT, which was not statistically significant (2.1 cm/m² before THRT versus 2.0 cm/m² after THRT, P = 0.11).

Table 3 summarizes pulsed-wave Doppler-derived parameters. Transmitral E and A velocities, E/A ratio, and E

| Table 3: Pulsed wave Doppler-derived parameters. |
|---------------------------------|----------------|----------------|
| SH | Control | P value |
| E vel (cm/sn) | 84 (0.14) | 86 (0.13) | 0.67 |
| A vel (cm/sn) | 64 (0.16) | 60 (0.11) | 0.37 |
| E/A | 1.39 (0.33) | 1.44 (0.15) | 0.58 |
| DT (msn) | 178.86 (41.98) | 169.26 (23.68) | 0.37 |
| ET (msn) | 297.68 (21.10) | 298.20 (19.83) | 0.93 |
| MPI | 0.27 (0.08) | 0.22 (0.06) | 0.03 |

E vel: E wave velocity; A vel: A wave velocity; DT: Deceleration time (of mitral E wave); ET: Ejection time; MPI: Myocardial performance index. All results are expressed as mean values and numbers in brackets denote Standard Deviation.

The mean interventricular septum thickness was 0.97 ± 0.12 cm in the SH group and 0.88 ± 0.10 in the control group (P = 0.01).

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Table 3 summarizes pulsed-wave Doppler-derived parameters. Transmitral E and A velocities, E/A ratio, and E
wave deceleration time (DT) were not different among the SH and control groups. On the other hand, mean MPI, which reflects overall ventricular function, was 0.27 ± 0.08 in the SH group and 0.22 ± 0.06 in the control group (P = 0.03).

Tissue Doppler echocardiography parameters are given in Table 4. Mitral annular systolic velocities (S) were similar across the groups. Mitral annular E’ velocities obtained from septal and anterior localizations were significantly lower in the SH group when compared to the controls.

Table 5 summarizes 2D and M-mode findings before treatment and three months after euthyroid state was achieved in the SH group. There was a mild yet significant reduction in left ventricular posterior wall thickness.

Relative wall thickness (RWT), which is the basis for diagnosis of concentric remodeling, was 0.43 at baseline in SH patients, slightly above the cut-off value of 0.42. After 3 months of THRT, RWT was normalized (0.39).

Pulsed wave Doppler-derived conventional diastolic indices did not differ before and after treatment.

As seen in Table 6, a moderate but significant improvement was observed in tissue Doppler-derived anterior E’ velocities after treatment (13.2 ± 3.87 versus 14.53 ± 2.75, P = 0.04).

4. Discussion

The necessity of thyroid hormone replacement in SH is controversial [22]. The generally accepted opinion is that treatment can be started to prevent progression to manifest hypothyroidism or to alleviate symptoms if they are present [22].

It has been established that SH also has cardiovascular manifestations. Rotterdam study reported that SH is a strong independent predictor for aortic atherosclerosis and myocardial infarction in elderly women. It was shown in this study that positive thyroid antibodies were associated with increased cardiovascular risk only when accompanied by SH [23].

In a recent reanalysis of the Whichham survey, an association was found between incident ischemic heart disease (IHD) events and IHD-related mortality with SH over the 20 years of follow-up. Treatment of SH with levothyroxine seems to attenuate IHD-related morbidity and mortality, and the authors conclude that properly designed controlled trials of treatment of SH are required to clarify this issue [21].

Vitale et al. were the first to report myocardial dysfunction in SH patients using tissue Doppler echocardiography [17]. Myocardial precontraction time (PCTm) and myocardial relaxation time (RTm) were prolonged and PCTm/myocardial contraction time ratio was increased and positively correlated to serum TSH levels.

In the present study, other potential causes of diastolic dysfunction such as hypertension, obesity, and coronary artery disease were excluded. Left ventricular ejection fraction and cavity diameters were not different among the groups.

Mean left ventricular posterior wall thickness and interventricular septum thickness were slightly yet significantly increased in SH. However, left ventricular mass index was not different between the groups. Echocardiographic follow-up three months after the achievement of euthyroid state displayed a mild yet significant decrease in left ventricular posterior wall thickness. These findings suggest that SH may cause concentric remodeling rather than hypertrophy, and concentric remodeling may be reversible with THRT. Mild left ventricular hypertrophy is an established feature of cardiovascular involvement of overt hypothyroidism [24]. In the Cardiovascular Health Study [24], over a course of five years, left ventricular mass increased among those with a TSH level of 10 mU/L or greater, but not among those with a TSH level between 4.5 and 9.9 mU/L. This is consistent with our findings since no concentric hypertrophy (i.e., increase in ventricular mass) but only concentric remodeling was

| Table 4: Tissue Doppler-derived parameters. |
|-------------------------------------------|
|               | SH       | Control  | P value |
|----------------|----------|----------|---------|
| Septal S       | 7.68 (0.97) | 8.14 (0.99) | 0.14    |
| Lateral S      | 9.52 (1.73) | 9.42 (1.50) | 0.83    |
| Anterior S     | 8.83 (1.94) | 8.32 (0.90) | 0.29    |
| Inferior S     | 8.21 (1.13) | 8.49 (0.96) | 0.40    |
| Septal E’      | 11.45 (3.24) | 13.24 (2.44) | 0.04    |
| Lateral E’     | 15.70 (3.97) | 16.89 (2.74) | 0.27    |
| Anterior E’    | 13.20 (3.87) | 15.65 (2.43) | 0.02    |
| Inferior E’    | 13.47 (3.77) | 14.94 (2.10) | 0.13    |
| Septal A’      | 9.15 (2.28) | 8.65 (1.39) | 0.40    |
| Lateral A’     | 10.14 (2.74) | 9.85 (1.61) | 0.67    |
| Anterior A’    | 9.70 (2.94) | 9.22 (1.24) | 0.49    |
| Inferior A’    | 9.92 (2.08) | 9.25 (1.45) | 0.24    |
| Mean E’        | 13.70 (3.39) | 15.12 (2.26) | 0.12    |
| Mean A’        | 9.63 (2.27) | 9.24 (0.97) | 0.47    |
| E’/A’          | 1.52 (0.58) | 1.63 (0.25) | 0.43    |
| E/E’           | 6.13 (1.12) | 5.09 (1.08) | 0.15    |

All results are expressed as mean values and numbers in brackets denote Standard Deviation.

| Table 5: Response of 2D and M-Mode echocardiographic parameters to thyroid hormone replacement therapy. |
|---------------------------------------------------------------|
| Before treatment      | After treatment | P value |
|------------------------|-----------------|---------|
| LVEF (%)               | 71.72 (4.61)    | 72.77 (4.67) | 0.50    |
| DIASTOLIC SEPTUM THICKNESS (cm) | 0.97 (0.12) | 0.93 (0.10) | 0.21    |
| DIASTOLIC POSTERIOR WALL THICKNESS (cm) | 1.0 (0.13) | 0.92 (0.11) | 0.04    |
| LV EDD (cm)            | 4.61 (0.34)     | 4.64 (0.40) | 0.71    |
| LV ESD (cm)            | 2.92 (0.26)     | 2.95 (0.34) | 0.70    |
| LVMI (gr/m²)           | 77.34 (2.14)    | 77.21 (2.27) | 0.43    |

LVEF: Left ventricular ejection fraction; LVEDD: Left ventricular end-diastolic diameter; IVESD: Left ventricular end-systolic diameter; LVMI: Left ventricular mass index. All results are expressed as mean values and numbers in brackets denote Standard Deviation.
observed in our population of SH patients. As concentric remodeling is the precursor of ventricular hypertrophy, the reversal of concentric remodeling suggests that THRT may also prevent ventricular hypertrophy in the long term. Considering that left ventricular hypertrophy is a predictor of future adverse cardiac events [25, 26], prevention of hypertrophy with THRT may be associated with better cardiovascular outcomes in patients with SH.

The mean left atrial diameter corrected according to the body surface area in the subclinical hypothyroidism (SH) patients was statistically significantly higher when compared to the healthy controls (2.1 cm/m² versus 1.8 cm/m², \( P = 0.039 \)). It was also noted that the mean BSA-corrected left atrial diameter approximated the upper limit of normal (2.2 cm/m²) in the SH group. This relative left atrial dilatation, which also tended to be near the upper limit of normal, can also be an important clue of diastolic dysfunction in the SH group. It is well documented that the increased left ventricular filling pressure and the resultant elevated left atrial pressure lead to left atrial dilatation in patients with diastolic dysfunction. Nevertheless, we did not observe a significant reduction in left atrial size after THRT. It may be speculated that the left atrial size would require a longer treatment period to decrease; however, a study with a longer follow-up period is needed to clarify this issue.

Our study did not show any difference in terms of pulsed-wave Doppler-derived diastolic indices such as E and A velocities, E/A ratio, and E wave deceleration time between the SH and control groups. This may be due to the fact that diastolic dysfunction is relatively mild in SH and conventional indices may not be sensitive enough to detect this degree of dysfunction.

Myocardial performance index (MPI), calculated by dividing the sum of isovolumetric contraction time (ICT) and isovolumetric relaxation time (IVRT) by aortic ejection time (ET), is a parameter which displays both systolic and diastolic (global) performance of the ventricle. Mean MPI was 0.27 ± 0.08 in the patient group and 0.22 ± 0.06 in the control group (\( P = 0.03 \)). An MPI below 0.40 is accepted as normal, and lower MPI values reflect better overall (systolic and diastolic) ventricular function. Modestly yet significantly increased MPI in the SH group suggests that overall ventricular function is slightly impaired in these patients, when compared to healthy controls.

We observed no change in MPI after thyroid hormone replacement therapy in subjects with SH. In a study by Yazici et al. [20], a significant reduction of MPI was observed in the L-thyroxine treated, but not in the untreated, patients with SH after one year of follow-up (0.53 ± 0.05 before treatment versus 0.42 ± 0.07 after treatment, \( P < 0.001 \)). The inconsistency of the findings of these two studies may be explained in two ways. First, the mean baseline MPI in the study by Yazici et al. is higher than that of our study population (0.53 ± 0.05 versus 0.27 ± 0.08). As the magnitude of overall ventricular dysfunction is greater in the study population of Yazici et al., one may speculate that the effect of treatment would be more pronounced. Second, the longer follow-up period may have allowed more time for the overall ventricular function to recover.

On the other hand, evaluation of regional diastolic function employing tissue Doppler echocardiography (TDE) revealed significantly decreased mitral annular E′ velocities in septal and anterior localizations in the SH group compared to euthyroid controls. Regional diastolic dysfunction in SH had been reported by Vitale et al. previously [17]. In addition to the findings of Vitale et al., we found reversal of diastolic dysfunction after thyroid hormone replacement therapy. A modest but significant increase was observed in anterior E′ velocities in the follow-up TDE study performed three months after euthyroid state was achieved. These findings are in line with those of Franzoni et al. [27]. In their study, Franzoni et al. utilised TDE and detected lower E′ velocities and consequently lower E′/A′ ratio in SH patients when compared to euthyroid controls. Then, the SH patients were randomly assigned to receive or not THRT. After 6 months, a significant increase was observed in E′ and hence E′/A′ ratio in the treated, but not in the untreated patients. These findings, taken into account together with the findings of our study, suggest that TDE may be a sensitive and useful

### Table 6: The response of tissue Doppler-derived parameters to thyroid hormone replacement therapy.

|                      | Before treatment | After treatment | \( P \) value |
|----------------------|------------------|----------------|--------------|
| SEPTAL S VELOCITY (cm/sn) | 7.68 (0.97)      | 7.63 (0.99)    | 0.85         |
| LAT S VELOCITY (cm/sn)    | 9.52 (1.73)      | 8.86 (1.19)    | 0.11         |
| ANT S VELOCITY (cm/sn)    | 8.83 (1.94)      | 8.17 (1.10)    | 0.16         |
| INF S VELOCITY (cm/sn)    | 8.21 (1.13)      | 8.22 (0.83)    | 0.97         |
| SEP E′ VELOCITY (cm/sn)   | 11.45 (3.24)     | 11.94 (2.89)   | 0.45         |
| LAT E VELOCITY (cm/sn)    | 15.70 (3.97)     | 16.43 (3.12)   | 0.19         |
| ANT E′ VELOCITY (cm/sn)   | 13.20 (3.87)     | 14.53 (2.75)   | 0.04         |
| INF E′ VELOCITY (cm/sn)   | 13.47 (3.77)     | 14.38 (2.95)   | 0.14         |
| SEP A′ VELOCITY (cm/sn)   | 9.15 (2.28)      | 8.59 (1.78)    | 0.25         |
| LAT A′ VELOCITY (cm/sn)   | 10.14 (2.74)     | 9.72 (1.66)    | 0.36         |
| ANT A′ VELOCITY (cm/sn)   | 9.70 (2.94)      | 9.17 (2.19)    | 0.40         |
| INF A′ VELOCITY (cm/sn)   | 9.92 (2.08)      | 9.40 (1.34)    | 0.14         |
| MEAN E′ VELOCITY (cm/sn)  | 13.70 (3.39)     | 14.45 (2.52)   | 0.13         |
| MEAN A′ VELOCITY (cm/sn)  | 9.63 (2.27)      | 9.19 (1.35)    | 0.22         |
| E′/A′                 | 1.52 (0.58)      | 1.60 (0.39)    | 0.31         |
| E/E                  | 6.13 (1.12)      | 6.2 (1.01)     | 0.63         |

All results are expressed as mean values and numbers in brackets denote Standard Deviation.
diagnostic tool for detecting mild and reversible alterations of diastolic function in SH and their response to THRT.

The main limitations of this study are the small sample size and relatively short follow-up period. The exclusion of patients older than 60 years may also be considered as a limitation.

We conclude that SH is associated with mild left ventricular diastolic dysfunction, which is reversible with thyroid hormone replacement therapy. While it is generally agreed upon that this therapy is indicated for patients in whom serum TSH levels are greater than 10 mIU/mL, initiating thyroid hormone replacement therapy for patients whose TSH levels are between 4.2 and 10 mIU/mL is controversial. In this study, improvement of left ventricular diastolic function in SH with thyroid hormone replacement therapy was shown using tissue Doppler. This finding may contribute to justification of treating patients whose TSH levels are between 4.2 and 10 mIU/mL, considering that diastolic dysfunction has been consistently reported in this patient group. Findings of this study also suggest that TDE may be a sensitive and useful tool to detect diastolic dysfunction and its response to thyroid hormone replacement therapy in patients (especially women) with SH.

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Authors’ Contributions

G. Erkan and S. Karahmetoglu screened and recruited the patients. G. Erkan also contributed in study design, implementation, and the preparation of the manuscript. M. Cemri and A. F. Erkan performed the echocardiographic examinations. A. F. Erkan also contributed in analysis and preparation of the manuscript. A. Cengel contributed in the study design and analysis. M. Cesur contributed in the study design and preparation of the manuscript.

Authors’ Disclosures

All authors have no conflict of interest to disclose.

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