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# Subclinical Hypothyroidism Effects on Cardiac Function

[1]M. Niafar, [2]M. Toufan, [3]S. Ghafoori and [1]N. Aghamohammadzadeh
[1]Endocrinology and Metabolism Section, Department of Medicine, Imam Reza Hospital,
Tabriz University of Medical Sciences, Tabriz, Iran
[2]Cardiology Section, Department of Medicine, Madani Hospital,
Tabriz University of Medical Sciences, Tabriz, Iran
[3]Resident of Internal Medicine, Department of Internal Medicine, Imam Reza Hospital,
Tabriz University of Medical Sciences, Tabriz, Iran

**Abstract:** To evaluate heart function in subclinical hypothyroid women in comparison with healthy subjects, a prospective study was performed on newly detected subclinical hypothyroid women presenting to endocrinology clinic of Tabriz Sina Hospital from October 2007 to February 2008. Thirty five women with Subclinical Hypothyroidism (SH) in case group were matched with 35 healthy euthyroid women in control group. All patients in both groups were studied by two dimensional echocardiography and Tissue Doppler Imaging (TDI) in Tabriz Shahid Madani Hospital. The FT4 and TSH levels were measured. Comparison of TDI results in Right Ventricle (RV) showed the significantly lower mean $T_v$ excursion in case group with no significant difference in other parameters. In Left Ventricle (LV), the mean $A_m$, $A_v$ and $E_v/E_m$ were significantly higher and E/A was lower in the case group, but there was no significant difference in other parameters. No RV diastolic dysfunction was documented in both groups. There was no case with LV systolic dysfunction in both groups. There were 21 (60%) patients with LV diastolic dysfunction in the case group comparing with 11 (31.4%) cases in the control group ($p = 0.016$, OR = 0.306). Frequency of LV diastolic dysfunction was significantly higher in the case group in patients aged ≥40 years (94.1% vs. 53.3%; $p = 0.013$). There was no case of pericardial effusion in the studied population. According to our results, SH may cause LV diastolic dysfunction. Likewise, minor RV systolic dysfunction might be seen in these patients.

**Key words:** Subclinical hypothyroidism, tissue doppler imaging, diastolic dysfunction

## INTRODUCTION

There is biological plausibility to the premise that subclinical thyroid dysfunction may cause adverse cardiac consequences (Cappola, 2007). Multiple studies have examined the relationships between endogenous SH (Dorr *et al*., 2005; Owen *et al*., 2006; Franzoni *et al*., 2006; Aghini-Lombardi *et al*., 2006; Kosar *et al*., 2005; Turhan *et al*., 2006) and echocardiographic measures of systolic and diastolic function (Cappola, 2007). SH can have repercussions on the cardiovascular system, as well as on other organs and systems (Biondi and Cooper, 2008).

Subclinical Hypothyroidism (SH) is an apparently asymptomatic condition defined by slightly increased serum Thyroid-Stimulating Hormone (TSH) concentrations and normal free thyroid hormone levels. As reported, in iodine sufficient areas, SH occurs in 4-9.5% of the general population, being more frequent in women and in the elderly (Aghini-Lombardi *et al*., 2006; Duarte *et al*., 2009; Ochs *et al*., 2008; Papi *et al*., 2007; Surks *et al*., 2004). In view of the minimal hormonal impairment and the apparent failure of symptoms, the need of a life-long treatment with levothyroxine ($L\text{-}T_4$) is a matter of controversy. Nevertheless, this condition may be clinically relevant at level of target organs over a period of several years. Cardiovascular system is very sensitive to minimal defects of circulating thyroid hormones and cardiovascular disorders are usually associated with overt hypothyroidism (Kahaly and Dillmann, 2005). Furthermore, the abnormalities in myocardial contractility and the changes of the lipoprotein profile that are frequently documented in hypothyroid patients have been reported by Kahaly and Dillmann (2005) and Sahin *et al*. (2005). Therefore, SH may be considered a true risk factor for the development of coronary heart disease (Kahaly and Dillmann, 2005; Fazio *et al*., 2004). Indeed, a progression of coronary angiographic lesions in untreated SH patients in

**Corresponding Author:** Mitra Niafar, Endocrinology and Metabolism Section, Department of Medicine, Imam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran

comparison with L-$T_4$-treated SH patients has been reported (Kahaly and Dillmann, 2005; Sahin *et al*., 2005; Fazio *et al*., 2004). Recently, it has been reported by an ultrasonic tissue characterization technique (videodensitometry) that SH is associated with early abnormalities in both myocardial function and structure, which are reversible with replacement therapy (Aghini-Lombardi *et al*., 2006). However, there has been heterogeneity in studies of SH. Two studies have shown no difference in left ventricular mass or function between individuals with and without SH (Dorr *et al*., 2005; Owen *et al*., 2006) and of the remaining studies that have detected systolic and/or diastolic abnormalities using echocardiography, no pair of these studies report the same pattern of abnormal parameters (Franzoni *et al*., 2006; Aghini-Lombardi *et al*., 2006; Kosar *et al*., 2005; Turhan *et al*., 2006; Vitale *et al*., 2002).

The aim of the present study was to evaluate heart function in subclinical hypothyroid women, in comparison with healthy subjects by conventional echocardiography and Tissue Doppler Imaging (TDI).

## MATERIALS AND METHODS

The study was prospective performed on newly detected subclinical hypothyroid women presenting to endocrinology clinic of Tabriz Sina Hospital from October 2007 to February 2008. According to the earlier studies and using $N = Z^2pq/d^2$ formulation ($Z^2 = 3.84$, $p = 0.1$, $q = 0.9$), the required sample size was calculated as 35 (Ariola *et al*., 2006; Wayne and Terrell, 1986). Thirty five women with Subclinical Hypothyroidism (SH) in case group were matched with 35 healthy euthyroid women in control group. Exclusion criteria were use of thyroid or other hormonal drugs, antihypertensive agents, congenital or acquired heart disease and pregnancy. Patients and normal control subjects were enrolled consecutively to make number, BMI and age become the same in both groups. Written informed consent was obtained from each patient. All patients in case and control groups were studied by two dimensional echocardiography and tissue Doppler imaging in Tabriz Shahid Madani Hospital.

The patients parameters were recorded including age, BMI, systolic and diastolic blood pressure, heart rate, free thyroxine (FT4) and thyrotropin and pleural effusion (if any). The right ventricle parameters measured by TDI and 2D echocardiography were as following: Ev/Em, Ev, E/A, Em, Av, EDECT, Am, Sm, TvE, TPC, RVDD, RVSP, TRg, TRv and RV systolic and diastolic function. The left ventricle parameters measured by TDI and two dimensional echocardiography were as following: Ev/Em, Ev, E/A, Em, Av, EDECT, Am, Sm, EF, LVMI, LVDD, LVSD, LAD, TPC and LV systolic and diastolic function. The echocardiographic parameters in tow groups of <40 years and ≥40 years were compared with each other. Immediately after rapid centrifugation of a blood sample collected at 7 AM from an antecubital vein, FT4 and TSH levels were measured (Singh *et al*., 2008; Rodondi *et al*., 2008; Zoncu *et al*., 2005).

Echocardiography was performed for all cases and control subjects by one subspecialist. The echochardiologist was unaware about the thyroid function status of studied person. Transthoracic echocardiography (TTE), was performed by Vivid7®USA echocardiography machine, using 3.5MHz prob. The achieved graphs were recorded in standard parasternal long axis and apical views, by following methods: M-mode, 2D echo, color Doppler and Tissue Doppler Imaging (TDI). Ejection Fraction (EF) was calculated by both M-mode and eyeball methods. The LV mass index was calculated by both M-mode using following formulation:

$$\text{LV mass} = 0.8[(\text{IVSD}+\text{LVDD}+\text{PWT})^3-(\text{LVDD})^3]+0.6(g)$$

(Singh *et al*., 2008; Rodondi *et al*., 2008; Zoncu *et al*., 2005).

The LV diastolic function was assessed by tissue Doppler method in base lateral wall of LV. The RV assessments were performed in four chamber view as measurement of RV size and evaluation of TV excursion for determination of RV longuitional contraction during systole. The TDI method was used for evaluation of motion speed of myocardial muscle of RV free wall during systole and diastole. The collected data were analyzed by SPSS-15 statistical software using the following methods: student t-test (independent samples) for comparison of quantitative variables, Chi-square test or Fishers Exact test for comparison of qualitative (categorical) variables. The $p = 0.05$ were considered significant (Singh *et al*., 2008; Rodondi *et al*., 2008; Zoncu *et al*., 2005).

## RESULTS

Thirty five subclinical hypothyroid women (case group) with average age of 38.89±11.32 year were compared with 35 normal healthy women (control group) with average age of 40.43±10.75 year ($p = 0.838$). The women with age <40 year was 18 (51.4%) in case and 20 (57.1%) in control group. The women with age ≥40 year was 17 (48.6%) in case and 15 (42.9%) in control group.

Average BMI was 26.32±4.78 kg $m^{-2}$ in case and 26.84±4.73 kg $m^{-2}$ in control group ($p = 0.648$). Average Systolic Blood Pressure (SBP) was 115.40±11.99 mmHg in

Table 1: Echocardiographic parameters of right and left ventricles in case and control groups

| Right ventricle | | | | Left ventricle | | | |
|---|---|---|---|---|---|---|---|
| Variables | Group | Average | p-value | Variables | Group | Average | p-value |
| $E_v/E_m$ | Case | 4.36±1.89 | 0.184 | $E_v/E_m$ | Case | 6.60±2.43 | 0.049 |
| | Control | 3.87±1.02 | | | Control | 5.63±1.53 | |
| $E_v$ (m sec$^{-1}$) | Case | 0.58±0.10 | 0.706 | $E_v$ (m sec$^{-1}$) | Case | 0.85±0.14 | 0.884 |
| | Control | 0.57±0.10 | | | Control | 0.85±0.13 | |
| E/A | Case | 1.21±0.24 | 0.162 | E/A | Case | 1.23±0.34 | 0.168 |
| | Control | 1.31±0.32 | | | Control | 1.35±0.38 | |
| $E_m$ (cm sec$^{-1}$) | Case | 14.77±4.77 | 0.561 | $E_m$ (cm sec$^{-1}$) | Case | 14.37±5.24 | 0.286 |
| | Control | 15.37±3.77 | | | Control | 15.57±4.02 | |
| $A_v$ (m sec$^{-1}$) | Case | 0.49±0.10 | 0.198 | $A_v$ (m sec$^{-1}$) | Case | 0.72±0.16 | 0.136 |
| | Control | 0.46±0.11 | | | Control | 0.67±0.14 | |
| $E_{DECT}$ (m sec) | Case | 240.39±83.12 | 0.287 | $E_{DECT}$ (m sec) | Case | 213.86±44.59 | 0.751 |
| | Control | 260.69±75.08 | | | Control | 217.24±44.08 | |
| $A_m$ (cm sec$^{-1}$) | Case | 14.23±4.50 | 0.122 | $A_m$ (cm sec$^{-1}$) | Case | 11.00±3.63 | 0.114 |
| | Control | 16.06±5.24 | | | Control | 9.77±2.72 | |
| $S_m$ (cm sec$^{-1}$) | Case | 15.20±3.29 | 0.314 | $S_m$ (cm sec$^{-1}$) | Case | 11.31±2.97 | 0.928 |
| | Control | 14.51±2.28 | | | Control | 11.26±2.27 | |
| $T_vE$ (cm) | Case | 2.10±0.23 | 0.047 | MAE (cm) | Case | 1.49±0.27 | 0.273 |
| | Control | 2.24±0.33 | | | Control | 1.56±0.23 | |
| TPC (m sec) | Case | 148.89±28.38 | 0.569 | TPC (m sec) | Case | 115.22±30.00 | 0.792 |
| | Control | 152.91±30.17 | | | Control | 113.16±35.05 | |
| RVDD (cm) | Case | 2.84±0.36 | 0.480 | EF (%) | Case | 58.43±2.36 | 0.803 |
| | Control | 2.90±0.29 | | | Control | 58.29±2.41 | |
| RVSP (mmHg) | Case | 26.83±5.00 | 0.704 | LVMI (g m$^{-2}$) | Case | 82.25±19.63 | 0.144 |
| | Control | 27.26±4.19 | | | Control | 75.95±15.81 | |
| $TR_g$ (mmHg) | Case | 17.14±4.65 | 0.781 | LVDD (cm) | Case | 4.33±0.34 | 0.336 |
| | Control | 17.44±4.23 | | | Control | 4.25±0.39 | |
| $TR_v$ (m sec$^{-1}$) | Case | 2.09±0.26 | 0.991 | LVSD (cm) | Case | 2.93±0.32 | 0.084 |
| | Control | 2.08±0.26 | | | Control | 2.79±0.34 | |
| | | | | LAD (cm) | Case | 3.27±0.47 | 0.552 |
| | | | | | Control | 3.21±0.42 | |

case and 113/37±9.43 mmHg in control group (p = 0.434). Average Diastolic Blood Pressure (DBP) was 75.34±10.47 mmHg in case and 70.34±8.38 (mmHg) in control group. Average DBP was significantly higher in case group (p = 0.031).

Average Heart Rate (HR) was 81.89±10.04 bpm in case and 76.54±11.47 bpm in control group. Average HR was significantly higher in case group (p = 0.042). In case group, the average serum TSH was 11.68±4.37 mg L$^{-1}$ and the average serum FT4 was 1.09±0.21 μg dL$^{-1}$. Table 1 shows the average echocardiographic parameters of right and left ventricles in case and control groups. As showed in Table 1, $T_v$ excursion in right ventricle was significantly less in case group. Also, $E_v/E_m$ in left ventricle was significantly more in case group. Other echocardiographic parameters of right and left ventricles were not significantly different in case and control groups. There was not pericardial effusion in case or control groups.

There was not any case of RV diastolic dysfunction and LV systolic dysfunction in case or control groups. However, there were 21 women with LV diastolic dysfunction in case group and 11 women with LV diastolic dysfunction grade I in control group. The LV diastolic dysfunction was significantly more in case group (p = 0.016, 95% CI :0.11-0.82, OR = 0.306).

Table 2 shows the average echocardiographic parameters of right and left ventricles in women aged <40 years in case and control groups. As showed in Table 2, echocardiographic parameters of right and left ventricles in this age range were not significantly different between two groups. There were 5 women with LV diastolic dysfunction in case group and 3 women with LV diastolic dysfunction in control group. LV diastolic dysfunction in women aged <40 years was not significantly different (p = 0.438, 95% CI: 0.09-2.28, OR = 0.459).

Table 3 shows the average echocardiographic parameters of right and left ventricles in women aged ≥40 years in case and control groups. As showed in Table 3, echocardiographic parameters of right ventricle in this age range were not significantly different between two groups. In left ventricle of women aged ≥40, the average $A_m$, $A_v$ and $E_v/E_m$ were significantly higher and the average E/A was significantly less in case group. There were 16 women with LV diastolic dysfunction grade I in case group and 8 women with same LV diastolic dysfunction in control group. The LV diastolic dysfunction in women aged ≥40 years was significantly more in case group (p = 0.013, 95% CI: 0.01-0.69, OR = 0.071).

Table 2: Echocardiographic parameters of right and left ventricles in women aged <40 years in case and control groups

| Right ventricle | | | | Left ventricle | | | |
|---|---|---|---|---|---|---|---|
| Variables | Group | Average | p-value | Variables | Group | Average | p-value |
| $E_v/E_m$ | Case | 3.74±1.23 | 0.604 | $E_v/E_m$ | Case | 5.05±0.84 | 0.955 |
| | Control | 3.94±1.05 | | | Control | 5.07±1.33 | |
| $E_v$ (m $sec^{-1}$) | Case | 0.58±0.10 | 0.887 | $E_v$ (m $sec^{-1}$) | Case | 0.88±0.13 | 0.771 |
| | Control | 0.59±0.11 | | | Control | 0.89±0.09 | |
| E/A | Case | 1.28±0.25 | 0.359 | E/A | Case | 1.46±0.27 | 0.732 |
| | Control | 1.36±0.30 | | | Control | 1.42±0.35 | |
| $E_m$ (cm $sec^{-1}$) | Case | 16.33±3.43 | 0.616 | $E_m$ (cm $sec^{-1}$) | Case | 17.83±4.08 | 0.787 |
| | Control | 15.70±4.19 | | | Control | 17.50±3.47 | |
| $A_v$ (m $sec^{-1}$) | Case | 0.47±0.09 | 0.422 | $A_v$ (m $sec^{-1}$) | Case | 0.61±0.09 | 0.266 |
| | Control | 0.44±0.10 | | | Control | 0.65±0.13 | |
| $E_{DECT}$ (m sec) | Case | 219.70±91.19 | 0.117 | $E_{DECT}$ (m sec) | Case | 204.54±36.15 | 0.462 |
| | Control | 264.17±79.54 | | | Control | 214.20±43.17 | |
| $A_m$ (cm $sec^{-1}$) | Case | 12.17±3.55 | 0.114 | $A_m$ (cm $sec^{-1}$) | Case | 8.72±2.35 | 0.359 |
| | Control | 14.50±5.09 | | | Control | 9.55±3.05 | |
| $S_m$ (cm $sec^{-1}$) | Case | 15.22±2.69 | 0.539 | $S_m$ (cm $sec^{-1}$) | Case | 12.39±2.97 | 0.640 |
| | Control | 14.70±2.49 | | | Control | 12.00±2.08 | |
| $T_vE$ (cm) | Case | 2.10±0.26 | 0.137 | MAE (cm) | Case | 1.46±0.23 | 0.058 |
| | Control | 2.25±0.34 | | | Control | 1.61±0.24 | |
| TPC (m sec) | Case | 157.50±26.72 | 0.754 | TPC (m sec) | Case | 109.24±24.48 | 0.847 |
| | Control | 160.28±27.43 | | | Control | 107.41±32.69 | |
| RVDD (cm) | Case | 2.90±0.33 | 0.609 | EF (%) | Case | 59.17±1.92 | 0.892 |
| | Control | 2.95±0.24 | | | Control | 59.25±1.83 | |
| RVSP (mmHg) | Case | 25.31±4.46 | 0.448 | LVMI (g $m^{-2}$) | Case | 77.25±12.59 | 0.564 |
| | Control | 26.44±4.39 | | | Control | 74.42±16.79 | |
| $TR_g$ (mmHg) | Case | 15.34±4.64 | 0.324 | LVDD (cm) | Case | 4.37±0.29 | 0.619 |
| | Control | 16.81±4.44 | | | Control | 4.32±0.37 | |
| $TR_v$ (m $sec^{-1}$) | Case | 2.04±0.22 | 0.945 | LVSD (cm) | Case | 2.97±0.26 | 0.121 |
| | Control | 2.05±0.28 | | | Control | 2.83±0.30 | |
| | | | | LAD (cm) | Case | 3.16±0.50 | 0.930 |
| | | | | | Control | 3.14±0.48 | |

Table 3: Echocardiographic parameters of right and left ventricles in women aged ≥40 years in case and control groups

| Right ventricle | | | | Left ventricle | | | |
|---|---|---|---|---|---|---|---|
| Variables | Group | Average | p-value | Variables | Group | Average | p-value |
| $E_v/E_m$ | Case | 5.01±2.26 | 0.063 | $E_v/E_m$ | Case | 8.25±2.50 | 0.017 |
| | Control | 3.78±1.02 | | | Control | 6.38±1.50 | |
| $E_v$ (m $sec^{-1}$) | Case | 0.57±0.11 | 0.402 | $E_v$ (m $sec^{-1}$) | Case | 0.82±0.16 | 0.857 |
| | Control | 0.54±0.08 | | | Control | 0.81±0.17 | |
| E/A | Case | 1.14±0.20 | 0.379 | E/A | Case | 0.99±0.21 | 0.025 |
| | Control | 1.23±0.33 | | | Control | 1.25±0.40 | |
| $E_m$ (cm $sec^{-1}$) | Case | 13.12±5.49 | 0.271 | $E_m$ (cm $sec^{-1}$) | Case | 10.71±3.58 | 0.069 |
| | Control | 14.93±3.22 | | | Control | 13.00±3.25 | |
| $A_v$ (m $sec^{-1}$) | Case | 0.51±0.11 | 0.368 | $A_v$ (m $sec^{-1}$) | Case | 0.84±0.14 | 0.006 |
| | Control | 0.47±0.11 | | | Control | 0.69±0.15 | |
| $E_{DECT}$ (m sec) | Case | 262.31±69.67 | 0.804 | $E_{DECT}$ (m sec) | Case | 223.73±51.33 | 0.889 |
| | Control | 256.05±71.15 | | | Control | 221.29±46.46 | |
| $A_m$ (cm $sec^{-1}$) | Case | 16.41±4.44 | 0.303 | $A_m$ (cm $sec^{-1}$) | Case | 13.41±3.18 | 0.002 |
| | Control | 18.13±4.84 | | | Control | 10.07±2.28 | |
| $S_m$ (cm $sec^{-1}$) | Case | 15.18±3.91 | 0.424 | $S_m$ (cm $sec^{-1}$) | Case | 10.18±2.58 | 0.916 |
| | Control | 14.27±2.02 | | | Control | 10.27±2.19 | |
| $T_vE$ (cm) | Case | 2.11±0.21 | 0.214 | MAE (cm) | Case | 1.53±0.32 | 0.703 |
| | Control | 2.23±0.32 | | | Control | 1.49±0.20 | |
| TPC (m sec) | Case | 139.78±27.96 | 0.757 | TPC (m sec) | Case | 121.55±34.53 | 0.955 |
| | Control | 143.07±31.74 | | | Control | 120.83±37.72 | |
| RVDD (cm) | Case | 2.78±0.40 | 0.708 | EF (%) | Case | 57.65±2.57 | 0.480 |
| | Control | 2.83±0.34 | | | Control | 57.00±2.54 | |
| RVSP (mmHg) | Case | 28.44±5.16 | 0.903 | LVMI (g $m^{-2}$) | Case | 87.54±24.34 | 0.196 |
| | Control | 28.24±3.85 | | | Control | 77.98±14.71 | |
| $TR_g$ (mmHg) | Case | 19.05±3.93 | 0.580 | LVDD (cm) | Case | 4.29±0.39 | 0.342 |
| | Control | 18.27±3.93 | | | Control | 4.15±0.41 | |
| $TR_v$ (m $sec^{-1}$) | Case | 2.13±0.30 | 0.955 | LVSD (cm) | Case | 2.89±0.39 | 0.309 |
| | Control | 2.14±0.23 | | | Control | 2.75±0.39 | |
| | | | | LAD (cm) | Case | 3.39±0.41 | 0.457 |
| | | | | | Control | 3.29±0.31 | |

## DISCUSSION

Subclinical Hypothyroidism (SH), defined by elevated serum levels of Thyroid Stimulating Hormone (TSH) with normal levels of free thyroid hormones, belongs to the most common disorders encountered in an endocrine office practice. It is assumed that elevated TSH levels in patients with SH do not reflect pituitary compensation to maintain euthyroidism but probably represents SH (Krysiak *et al*., 2008; Rodondi *et al*., 2008). The cardiovascular signs and symptoms of thyroid disease are some of the most profound and clinically relevant findings that accompany hypothyroidism. On the basis of the understanding of the cellular mechanisms of thyroid hormone action on the heart and cardiovascular system, it is possible to explain the changes in cardiac output, cardiac contractility, blood pressure, vascular resistance and rhythm disturbances that result from thyroid dysfunction (Klein and Danzi, 2007).

Iqbal *et al*. (2007) in a case-control study on 66 hypothyroid patients suggest that there are no adverse effects of persistent SH on cardiac function (Cappola, 2007). The mean TSH level of study participants with SH was 5.4 mU $L^{-1}$) and their mean age was 61 year. In other studies that included participants with higher mean serum TSH levels and younger age, there were measurable differences in echocardiographic parameters between subclinically hypothyroid and euthyroid subjects (Franzoni *et al*., 2006; Aghini-Lombardi *et al*., 2006; Kosar *et al*., 2005; Turhan *et al*., 2006). This discrepancy highlights the importance of refining the at risk population and the need to link abnormalities in these surrogate echocardiographic markers with adverse clinical cardiac events, such as congestive heart failure (Cappola, 2007; Rodondi *et al*., 2005). It is estimated that as many as 7-10% of older women have SH. Although, SH is frequently asymptomatic, many patients have symptoms of thyroid hormone deficiency. Lipid and lipoprotein metabolism is abnormal in SH (Klein and Danzi, 2007; Rodondi *et al*., 2005; Duntas, 2002; Razvi *et al*., 2007). C-reactive protein, a risk factor for heart disease, is increased in SH (Christ-Crain *et al*., 2003). In addition, atherosclerosis (Ochs *et al*., 2008; Kanaya *et al*., 2002), coronary heart disease and myocardial infarction risk are increased in women with SH (Klein and Danzi, 2007; Rodondi *et al*., 2006). The SH should be screened more carefully in the community. There are evidences that treatment of SH is beneficial (Papi *et al*., 2007; Krysiak *et al*., 2008; Rodondi *et al*., 2008). Treatment of SH in pregnant women is mandatory to decrease risks for pregnancy complications and impaired cognitive development in offspring. Children with SH should be treated to prevent growth retardation. Whether non-pregnant adult patients with SH should be treated (Papi *et al*., 2007).

In the present study, LV diastolic dysfunction was significantly higher in subclinical hypothyroid women than controls. Yazici *et al*. (2004) study confirms the above-cited findings. Aghini-Lombardi *et al*. (2006) studied 24 subclinical hypothyroid patients in comparison with 24 sex- and age-matched healthy volunteers and found a significant impairment of left ventricular diastolic function in subclinically hypothyroid patients. A study by Vitale *et al*. (2002) on 20 subclinically hypothyroid and 20 healthy women showed cardiac functional abnormalities due to stable SH, mainly by changes in myocardial time intervals in several LV segments. They also found more LV diastolic dysfunction in subclinical hypothyroid patients. Septal myocardium is the most affected region of left ventricle in SH. The relaxation time is the best criteria of cardiac involvement and monitoring the effect of TRT (Arinc *et al*., 2006). Zoncu *et al*. (2005) showed a delay in diastolic relaxation and a decrease in the compliance to the ventricular filling in subclinically hypothyroid patients. In series of SH patients, the results confirmed the impairment of both systolic and diastolic myocardial function (Di Bello *et al*., 2000; Monzani *et al*., 2001), a decreased myocardial intrinsic contractility and a high ultrasonic myocardial reflectivity suggesting an altered myocardial texture. These subtle myocardial alterations were reversible after replacement L-T4 therapy (Aghini-Lombardi *et al*., 2006; Di Bello *et al*., 2000). Vitale *et al*. (2002) reported both an impairment of global longitudinal ventricular diastolic function and an alteration of myocardial time intervals, in patients with SH. Zoncu *et al*. (2005) demonstrated systolic and diastolic changes in patients with borderline hypothyroidism. Several studies suggested that SH was associated with a small increased risk for CHD and cardiovascular mortality (Ochs *et al*., 2008; Rodondi *et al*., 2008; Iacoviello *et al*., 2008; Biondi, 2007; Bakiner *et al*., 2008; Iervasi *et al*., 2007; Singh *et al*., 2008). In the present study, LV diastolic dysfunction in women aged ≥40 years was significantly higher in case group than controls, indicating the importance of early screening of cardiac complications in older ages. An advantage of this study is the use of TDI in evaluation of right ventricle. To date, we did not find such study in this field. The average $T_v$ Excursion in case group was lower significantly, indicating impaired longitudinal systolic contractility of right ventricle due to SH and presence of mild systolic dysfunction in these patients. Considering the advantage of TDI and its relative independence of load condition and for strain also a relative independence from heart rotational and

translational motions, this technique allows a very early diagnosis of systolic and diastolic dysfunction, when conventional echo-Doppler parameters of left ventricular function are still within normal range (Aghini-Lombardi *et al*., 2006; Zoncu *et al*., 2005). It is also an accurate modality to investigate the cardiac effects of SH (Vitale *et al*., 2002; Arinc *et al*., 2006).

## CONCLUSION

In summary, our data suggest that subclinical thyroid dysfunction might represent a potentially modifiable risk factor for cardiac dysfunction. Assuming that treatment is effective, given the high prevalence of thyroid disease even a small increase in cardiac morbidity or mortality rates among persons with subclinical dysfunction would have public health implications. From a health policy perspective, it would be premature to recommend screening for thyroid dysfunction in the general population. Given the pattern of modestly increased risk for cardiac morbidity and mortality associated with subclinical thyroid dysfunction, lower risk estimates in higher-quality studies and the remaining uncertainty, treatment of subclinical thyroid dysfunction with cardiac disease as an end point should be studied in randomized, placebo-controlled trials to assess the efficacy of $T_4$ replacement or anti-thyroid medications before current recommendations are updated. This supports the need for prospective studies aimed at clarifying the most appropriate therapeutic approach to sub-clinical hypothyroidism in such patients.

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