Speckle tracking echocardiographic assessment of left ventricular longitudinal strain in female patients with subclinical hyperthyroidism

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Background   Patients with subclinical hypothyroidism (SCH) are subjected to many cardiac changes. However, these changes are of gradual onset and cannot be usually detected using conventional diagnostic methods. Speckle tracking echocardiography (STE) is capable to detect cardiac function alterations usually unidentified by conventional echocardiography. The present study aimed to evaluate the role of STE in the detection of early cardiac changes in female patients with SCH.

Methods   The study included 33 female patients with SCH and 30 matched healthy volunteer women with normal thyroid functions who served as controls. Upon recruitment, all participants were subjected to careful history taking, thorough clinical examination and routine laboratory investigations, including thyroid-stimulating hormone and Free T4. The echocardiographic examination included conventional, color Doppler and two-dimensional STE.

Results   Analysis of conventional echocardiographic data revealed that patients had significantly higher end-systolic volume when compared with controls. In addition, it was noted that SCH patients had significantly lower mitral E/A ratio, isovolumetric relaxation time and significantly higher left atrium volume index in comparison to controls. In respect to STE data, we noted that patients had significantly lower values of mid-anteroseptal, apical lateral, apical septal, apical apex, AP4L strain and global strain % when compared with controls.

Conclusions   Patients with SCH have deteriorated global strain in comparison to healthy controls. *Cardiovasc Endocrinol Metab* 10: 182–185 Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved.

Introduction

Subclinical hyperthyroidism (SCH) is a frequently reported condition characterized by low or undetectable thyroid-stimulating hormone (TSH) levels with a normal level of free thyroid hormones [1]. Its prevalence in several large studies is estimated to range from 0.6 to 16% of the general population [2–4]. In spite of the fact that the diagnosis of SCH is often underestimated, it has been demonstrated that SCH exerts a negative impact on the quality of life and increases the risk of cardiovascular morbidity [5,6].

Speckle tracking echocardiography (STE) is a new technique for assessment of left ventricular (LV) strain which is more sensitive and specific for assessment of regional myocardial function compared to conventional tissue Doppler echocardiography [7]. The clinical significance and the need for treatment of SCH are still a matter of debate as recent guidelines provide conflicting recommendations. Early detection of the cardiac consequences of SCH can guide diagnostic and therapeutic recommendations [8].

The present study aimed to evaluate the effect of SCH on LV longitudinal strain measured by speckle tracking obtained by two-dimensional echocardiography.

Materials and methods

This observational case-control study was conducted at Mansoura University Hospitals, Mansoura, Egypt. The study protocol was approved by the Institutional Review Board and all participants gave informed consent before enrollment.

The study included 33 female patients with subclinical hypothyroidism (serum TSH level <0.4 mIU/ml with normal levels of free thyroid hormones). Exclusion criteria were diabetes mellitus, congenital heart disease, systemic hypertension, valvular heart diseases, myocardial infarction, atrial fibrillation, heart failure, bronchial asthma, chronic obstructive lung disease, chronic kidney disease and abnormal liver functions. In addition to the included patients, there were 30 healthy volunteer women with normal thyroid functions who served as controls.

Upon recruitment, all participants were subjected to careful history taking, thorough clinical examination and routine laboratory investigations, including TSH and Free T4. The echocardiographic examination included conventional, color Doppler and two-dimensional STE.

Data obtained from the present study were presented as mean and SD. Comparison between the studied variables was achieved using the *t* test. *P* value less than 0.05 was considered statistically significant. All statistical calculations were achieved using SPSS, 22 (IBM, Illinois, USA).

Results

The present study was conducted on 33 SCH patients and 30 healthy controls. Before the statistical analysis of data, the reproducibility of the obtained images was confirmed. Using random numbers generating software, we randomly selected 10 cases from each group and asked two experienced echocardiographers to interpret the retrieved images in two separate occasions with at least 1-week interval. The echocardiographers were blinded to the selected cases and worked independently from each other. The intra- and interobserver variabilities were acceptable with the intraclass correlation of >0.9 for all measured parameters.

Comparison between the studied groups regarding the basic data is shown in Table 1. Patients in the SCH group had significantly lower TSH (0.048 ± 0.078 mIU/ml versus 1.43 ± 0.65; $P < 0.001$) and higher free T4 (1.55 ± 0.34 mU/l versus 1.36 ± 0.2 mU/l; $P = 0.008$) levels when compared to controls.

Analysis of conventional echocardiographic data revealed that patients had significantly higher end-systolic volume (ESV) (28.2 ± 9.14 ml versus 21.76 ± 9.33 ml; $P = 0.039$) when compared with controls. In addition, it was noted that SCH patients had a significantly lower mitral E/A ratio (1.22 ± 0.19 versus 1.46 ± 0.16; $P = 0.011$), isovolumetric relaxation time (92.4 ± 12.5 versus 97.3 ± 21.9 ms; $P = 0.023$) and significantly higher left atrium volume index (27.6 ± 4.3 versus 24.9 ± 5.5 ml/m^2; $P = 0.027$) in comparison to controls (Table 2).

In respect to STE data, we noted that patients had significantly lower values of mid-anteroseptal % (-19.38 ± 4.73 versus -23.69 ± 3.30; $P = 0.005$), apical lateral % (-21.84 ± 4.03 versus -26.38 ± 7.68; $P = 0.013$), apical septal

% (-25.13 ± 5.90 versus -29.62 ± 4.33; $P = 0.017$), apical apex % (-23.41 ± 3.81 versus -26.38 ± 3.77; $P = 0.022$), AP4L strain % (-21.04 ± 3.36 versus -23.007 ± 2.184; $P = 0.027$) and global strain % (-20.90 ± 2.75 versus -23.55 ± 2.28; $P = 0.004$) when compared with controls (Table 3).

Discussion

The impact of SCH on cardiovascular morbidity and mortality remains a highly debated issue [9,10]. STE is a noninvasive imaging modality that aids objective and quantitative evaluation of global and regional myocardial function. Global longitudinal strain (GLS) is the most clinically utilized parameter of STE [7]. The clinical advantage of GLS obtained by STE is that it can detect early myocardial dysfunction before any obvious cardiac dysfunction occurs, whereas traditional echocardiographic parameters such as left ventricular ejection fraction are normal [11]. Also, STE is better in the assessment of regional and global myocardial function than tissue Doppler imaging [12].

In the present study, women with SCH have higher end-diastolic diameters and ESV ($P = 0.039$) than the control group. They also expressed notable LV diastolic impairment in comparison with controls. These results go hand in hand with Biondi *et al.* [4] who compared the results of echocardiographic assessment performed in 23 patients with SCH and the same number of healthy controls. Moreover, Tadic *et al.* [13] reported that the LV end-diastolic volume (EDV) was significantly higher in the SCH than controls. The LV end-systolic and stroke volumes were also higher in the SCH group but with no statistically significant importance. These findings may

Table 1 Basic data of the studied groups

	Patients $n=33$	Controls $n=30$	*P* value
Age (years)	32.48 ± 9.98	31.33 ± 6.79	0.22
BMI (kg/m^2)	23.9 ± 3.7	23.6 ± 3.8	0.95
SBP (mmHg)	103.6 ± 11.4	107.7 ± 10.4	0.15
DBP (mmHg)	64.9 ± 7.1	68.7 ± 9.0	0.065
TSH (mIU/ml)	0.048 ± 0.078	1.43 ± 0.65	<0.001
Free T4 (mU/l)	1.55 ± 0.34	1.36 ± 0.2	0.008

Data presented as mean ± SD
TSH, thyroid-stimulating hormone.

Table 2 Echocardiographic findings in the studied groups

	Patients $n=33$	Controls $n=30$	*P* value
LV ESD cm	3.91 ± 0.35	3.15 ± 0.24	0.12
LV EDD cm	6.07 ± 0.23	5.14 ± 0.46	0.022
IVSd cm	0.88 ± 0.12	0.86 ± 0.21	0.666
LVPWTd cm	0.8 ± 0.12	0.74 ± 0.07	0.167
IVSs cm	1.33 ± 0.27	1.29 ± 0.22	0.621
LVPWTs cm	1.42 ± 0.21	1.57 ± 0.36	0.085
EDV ml	96.49 ± 20.12	82.76 ± 25.98	0.064
ESV ml	28.2 ± 9.14	21.76 ± 9.33	0.039
Fractional shortening%	40.38 ± 7.62	42.35 ± 6.17	0.413
Ejection fraction%	71.44 ± 7.46	73.37 ± 6.86	0.427
Mitral E (cm/s)	0.78 ± 0.14	0.86 ± 0.11	0.017
Mitral A (cm /s)	0.63 ± 0.18	0.59 ± 0.08	0.032
Mitral E/A	1.22 ± 0.19	1.46 ± 0.16	0.011
Mitral E′ (cm/s)	0.12 ± 0.03	0.15 ± 0.02	0.02
Mitral A′ (cm /s)	0.11 ± 0.02	0.1 ± 0.01	0.84
Mitral E′/A′	1.13 ± 0.17	1.52 ± 0.21	0.19
IVRT (ms)	92.4 ± 12.5	97.3 ± 21.9	0.023
LA Volume index (ml/m^2)	27.6 ± 4.3	24.9 ± 5.5	0.027
Tricuspid S′	10.91 ± 1.47	11.07 ± 1.55	0.56
Tricuspid E′	11.23 ± 1.64	12.49 ± 1.35	0.73
Tricuspid A′	17.6 ± 2.01	18.2 ± 1.91	0.68

Data presented as mean ± SD
EDV, end-diastolic volume; ESV, end-systolic volume; IVRT, isovolumetric relaxation time; IVSd, interventricular septal thickness at end-diastole; IVSs, interventricular septal thickness in systole; LA, left atrium; LV EDD, left ventricular end-diastolic dimension; LV ESD, left ventricular end-systolic dimension; LVPWTd, LV posterior wall thickness in diastole; LVPWTs, LV posterior wall thickness in systole;

Table 3   Speckle tracking echocardiographic findings in the studied groups

	Patients $n=33$	Controls $n=30$	P value
Basal anteroseptal %	−18.22±4.20	−19.77±5.55	0.313
Basal anterior %	−20.06±3.34	−21.38±3.33	0.235
Basal anterolateral %	−18.91±5.07	−21.08±2.46	0.150
Basal inferolateral %	−19.13±4.64	−18.54±3.99	0.692
Basal inferior %	−20.34±5.11	−17.31±4.30	0.06
Basal inferoseptal %	−17.56±3.66	−19.15±3.07	0.175
Mid-anteroseptal %	−19.38±4.73	−23.69±3.30	0.005
Mid-anteroseptal %	−20.75±4.37	−22.54±3.20	0.189
Mid-anterolateral %	−20.81±3.78	−22.23±1.69	0.202
Mid-inferolateral %	−21.63±5.05	−21.15±3.93	0.765
Mid-inferior %	−19.31±6.04	−20.00±2.04	0.692
Mid-inferoseptal %	−18.72±4.81	−20.00±3.76	0.396
Apical anterior %	−23.44±4.97	−23.69±3.14	0.865
Apical lateral %	−21.84±4.03	−26.38±7.68	0.013
Apical inferior %	−24.69±5.006	−27.85±4.67	0.05
Apical septal %	−25.13±5.90	−29.62±4.33	0.017
Apical apex %	−23.41±3.81	−26.38±3.77	0.022
AP2LStrain %	−21.88±3.74	−22.6±1.96	0.517
AP4LStrain %	−21.04±3.36	−23.007±2.184	0.027
AP3LStrain %	−20.75±3.41	−22.67±4.21	0.118
Global strain %	−20.90±2.75	−23.55±2.28	0.004

Data presented as mean±SD

be explained by the increase in blood volume related to thyroid hormone excess [5].

&&Moreover, we found that LV posterior wall diameter (LVPW), interventricular septum thickness (IVST) and the EDV were higher in SCH but did not reach statistical significance. These results are in parallel with Di Bello *et al*. [14] who found that no difference between both groups of SCH and control as regard the left ventricular mass index by body surface (LVMbs). This finding could be explained by the young age of the study group and the short duration of disease. Furthermore, two prospective studies performed in elderly subjects did not find an association between SCH and the increased ventricular mass [15,16]. In contrary to our results, Biondi *et al*. [4], Sgarbi *et al*. [17] and Kaminski *et al*. [18] reported a significant increase in the left ventricle mass, fractional shortening, left ventricle posterior wall and IVST in endogenous SCH. Also, Tadic *et al*. [13] revealed statistically significance higher (LVPW) and (IVST) in SCH than the control group.

By STE, the current study found that the SCH group has lower peak systolic strain than the control group in the apical lateral ($P=0.013$), apical inferior ($P=0.05$), apical septal ($P=0.017$), apical apex ($P=0.022$) and mid-anteroseptal ($P=0.005$) regions. We detected that apical segments mainly affected in SCH. This may be explained by increase in the sensitivity of the apical segments to thyroid hormone action. Furthermore, our results showed that the SCH group has lower AP4L strain ($P=0.027$) and GLS ($P=0.004$) than the control group. This result matched with Tadic *et al*. [13] who demonstrated that two dimensional (2D) LV strain was impaired in the longitudinal and circumferential direction in SCH, but there was no difference in radial strain and strain rates between the two studied groups. In addition, LV diastolic mechanical function, estimated by early and late diastolic strain rate,

was impaired in SCH suggesting that SCH associated with subclinical cardiomyopathy.

In agreement with these conclusions, Abdulrahman *et al*. [19] and Abdulrahman *et al*. [20] reported the results of LV assessment obtained by 2D strain analysis in persons with exogenous SCH due to differentiated thyroid carcinoma and on long-term TSH-suppressive levothyroxine and demonstrated that prolonged SCH can lead to impairment of the systolic and diastolic function which is reversible after reaching euthyroid state suggesting that 2D-STE is more sensitive to evaluate minimal changes in LV function in these patients.

Conclusion
The results of the present study show that STE may serve as a sensitive tool for detection of subclinical cardiac changes in women with SCH.

Conflicts of interest
There are no conflicts of interest.

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