Ventricular Functions in Patients with Graves' Ophthalmopathy

Graves Oftalmopati Hastalarında Ventrikül Fonksiyonları

Murat AKÇAY, MD,[a]
Emine AKÇAY, MD,[b]
Ekrem YETER, MD,[c]
Tahir DURMAZ, MD,[a]
Telat KELEŞ, MD,[a]
Nihal AKAR BAYRAM, MD,[a]
İsa YÜKSEL, MD,[d]
Gülhan YÜKSEL KALKAN, MD,[a]
Hüseyin SİMAVLİ, MD,[b]
Şaban ŞİMŞEK, MD,[b]
Engin BOZKURT, MD[a]

[a]2nd Cardiology Clinic,
[b]1st Ophthalmology Clinic,
[d]1st Cardiology Clinic,
Ankara Atatürk Training and Research Hospital
[c]Cardiology Clinic,
Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara

Geliş Tarihi/*Received:* 21.03.2010
Kabul Tarihi/*Accepted:* 21.05.2010

Yazışma Adresi/*Correspondence:*
Murat AKÇAY, MD
Ankara Atatürk Training and Research Hospital
2nd Cardiology Clinic, Ankara, TÜRKİYE/TURKEY
drmuratakcay@yahoo.com

ABSTRACT Objective: Graves' orbitopathy (GO) is an inflammatory syndrome that affects orbital tissues in ~50% of patients with Graves' disease. Antibodies against TSH receptors in GO patients were shown to lead to heart failure along with GO, affecting both orbital tissues and cardiac muscle. However, there are no studies which investigated cardiac functions in GO patients. In the present study we aimed to investigate the cardiac functions in GO patients with conventional and tissue Doppler imaging methods. **Material and Methods:** Fourty seven GO patients and 27 healthy individuals as a control group were included in our study. Left and right ventricular functions were assessed using echocardiography including two-dimensional, M-mode, and conventional Doppler as well as pulsed wave tissue Doppler imaging. **Results:** Left and right ventricle systolic and diastolic diameters and ejection fraction showed no difference in patients with GO and controls. Tissue Doppler analysis showed that right and left ventricle annular systolic velocities were similar between GO patients and control group. Diastolic function parameters also showed no significant difference between the patient group and controls. There were no correlation between the echocardiographically derived systolic and diastolic function parameters and TSH receptor antibody (TSHRAb) levels. **Conclusion:** Although there are some clues about the involvement of cardiac tissue in GO we showed that cardiac functions are preserved in GO and TSHRAb levels were not associated with any of the systolic and diastolic function parameters of the left and right ventricle.

Key Words: Graves' Ophthalmopathy, ventricular function, tissue Doppler echocardiography

ÖZET Amaç: Graves' orbitopathy (GO), Graves hastalarının yaklaşık olarak %50'sinde orbital dokuların inflamasyonu ile seyreden bir sendromdur. GO hastalarında TSH reseptörlerine karşı gelişen antikorların hem orbitadaki dokuları hem de kalp kasını etkileyerek GO ile beraber kalp yetersizliği kliniğine yol açtığı gösterilmiştir. Ancak GO'lu hastalarda kardiyak fonksiyonları inceleyen bir çalışma yoktur. Bu çalışmada biz GO hastalarında konvansiyonel ve doku Doppler yöntemi kardiyak fonksiyonları değerlendirmeyi amaçladık. **Gereç ve Yöntemler:** Çalışmamıza 47 GO hastası ve 27 sağlıklı birey dâhil edildi. Sol ve sağ ventrikül fonksiyonları 2-boyutlu ekokardiyografi, M-Mode ve konvansiyonel Doppler yanı sıra "pulse wave" doku Doppler görüntüleme ile değerlendirildi. **Bulgular:** Sol ventrikül ve sağ ventrikül sistolik ve diyastolik fonksiyon parametreleri açısından hasta ve kontrol grubu arasında fark izlenmedi. Doku Doppler ile sağ ve sol ventrikülün anulusundan alınan sistolik dalga hızları GO hastalarında ve kontrol grubunda benzerdi. Diyastolik fonksiyon parametreleri de hasta ve kontrol grubunda belirgin bir farklılık göstermiyordu. Ekokardiyografik olarak elde edilen sistolik ve diyastolik fonksiyon parametreleri ile TSH reseptör antikor düzeyleri (TSHRAb) arasında herhangi bir korelasyon yoktu. **Sonuç:** GO'de kalp dokusunda tutulumun olduğuna dair ipuçları olmasına rağmen biz bu çalışmada GO hastalarında kalp fonksiyonlarının korunduğunu ve TSHRAb düzeylerinin sağ ve sol ventrikülün sistolik ve diyastolik fonksiyon parametreleri ile bir ilşkisinin olmadığını gösterdik.

Anahtar Kelimeler: Graves Oftalmopatisi, ventriküler fonksiyon, doku Doppler ekokardiyografi

Turkiye Klinikleri J Cardiovasc Sci 2010;22(2):226-32

Graves' disease is an autoimmune disorder that mainly affects the thyroid gland.[1] The thyroid manifestations of the disease are caused by autoantibodies directed against the TSH receptor (TSHRAb).[2-5] These antibodies stimulate thyroid hormone synthesis from thyroid cells, resulting in hyperthyroidism and diffuse goiter. There is eye involvement called as Graves' ophthalmopathy in 25% to 50% of patients. In recent years, cases of cardiac involvement have been reported in some patients with eye involvement. This condition was considered as an autoimmune process related to TSHRAb leading to involvement of cardiac muscle together with orbital tissues.[6] Although there are several findings of cardiac involvement at molecular levels in Graves' orbitopathy (GO) patients, clinical studies on the issue are insufficient.[7]

The objective of this study was to investigate whether there was cardiac muscle involvement in euthyroid GO patients by conventional and tissue Doppler methods.

MATERIAL AND METHODS

This case-control study was conducted between February 2006 and December 2008. Forty-seven patients with GO who were clinically and biochemically euthyroid for at least 3 months were recruited in the study, and 27 age- and sex-matched healthy individuals without clinically hyperthyroidism and with normal serum free T3, free T4, and TSH levels and negative thyroid autoantibodies were included in the study as the control group. Severity of GO was rated as mild, moderate-severe, and sight-threatening according to the recommendations of European Group on Graves' orbitopathy (EUGOGO).[8] Graves' orbitopathy activity was assessed according to the recommendations of Wiersinga and colleagues.[9] Hertel exophthalmometry was used for the evaluation of proptosis. In Hertel measurements, 17 mm was considered as normal value for Turkish society.[10] Above 19 mm was defined as proptosis. Exophthalmus was classified as mild for 19-21 mm, moderate for 21-25 mm, and advanced exophthalmus for above 25 mm.[11-14] Eye lid retraction was measured by the distance of the upper eyelid margin from the center of the pupil (severe, 7 mm; moderate, >5 to <7 mm; and mild, 5 mm).

Twenty patients were on propylthiouracil and 10 patients were receiving levothyroxine (levotiron).

Blood samples were obtained in the morning after 12 h of fasting. TSH, fT3, and fT4 levels were measured. Serum hormone levels were measured by chemiluminescent immunometric assays using IMMULITE 2000 (BIO-DPC) autoanalyzer systems, according to the manufacturer's instructions. The normal values in the laboratory were as follows: TSH, 0.4-4.0 IU/mL; fT3, 1.57-4.71 pg/mL; fT4, 0.85-1.78 ng/dL.

Serum thyroglobulin, antithyroglobulin autoantibodies and antithyroid peroxidase antibody levels were assayed by immunoassay (Beckman, Coulter, Maine, USA), whereas TSHR autoantibodies were determined by radioimmunoassay method by counting the radioactivity in a gamma counter (Stratec, Birkenfeld, Germany). Detection limits were 0-40 IU/mL, 1.3 pmol/L, and 0-35 IU/mL for thyroglubulin, and antithyroglobulin antibodies, and antithyroid peroxidase antibody levels, respectively. For TSH receptor antibody, 0-9 U/ml was considered as negative, and > 9 U/mL as positive.

Blood pressure was measured using mercury sphygmomanometer after 5 minutes of resting period and in the sitting position. Two readings were taken half an hour apart and the average value was calculated.

ECHOCARDIOGRAPHY

Transthoracic echocardiographic studies were performed with the patients in the left lateral decubitus position using a Vivid 7 system (Vingmed Ultrasound, Horten, Norway). Parasternal long- and short-axis, apical two- and four-chamber, and subxiphoid long-axis views were obtained. Chamber dimensions were obtained from M-mode recordings taken in the parasternal long-axis view, guided by a two-dimensional (2-D) echocardiogram in accordance with the recommendations of

the American Society of Echocardiography.[15] Left ventricular and right ventricular ejection fractions were determined with modified Simpson method.[16] Two orthogonal echocardiographic views from the apex and subcostal windows were obtained to assess Simpson's RVEF. Tracing of the RV endocardium at end systole and end diastole were performed either by identifying opening and closing of the tricuspid valve or by visually assessing the smallest and largest RV chamber size. The Simpson's method was used to determine RV volumes and the RVEF was calculated by subtracting end-systolic volume from end-diastolic volume (EDV) divided by EDV: RVEF%=100x(EDV–end-systolic volume)/EDV.

Transmitral flow velocities were recorded from the apical window, with a 1- to 3- mm sample volume between the tips of the mitral leaflets during diastole. The peak velocity of early diastolic filling (E), late filling with atrial contraction (A), the E/A ratio, and the deceleration time (DT) were measured from the tracing of transmitral flow. The isovolumic relaxation time (IVRT) of the LV was obtained by estimating the time interval from the cessation of outflow from the LV to the onset of inflow through the mitral valve. The isovolumic contraction time (IVCT) was determined as the time interval between the cessation of mitral inflow and the onset of left ventricular outflow. To measure the velocity of tricuspid flow, the Doppler sampling volume was set in the RV near the tricuspid orifice on the apical four-chamber view. The measurements were taken at the end of expiration. From Doppler recordings of flow across the tricuspid valve, the parameters E, A, and the E/A ratio were measured.[17]

The Tissue Doppler Imaging (TDI) was performed using the apical window of the apical four-chamber view for evaluation of the septal and lateral walls. The sampling volume was set at the basal portion of the referred walls. The systolic (Sm), early (Em), and late (Am) diastolic velocities for three consecutive beats were analyzed, and the E/Em, Em/Am ratios were calculated.[18]

Tricuspid annular systolic (TSm), and early- (TEm) and late- (TAm) diastolic myocardial velocities were acquired from apical four-chamber views at the junction of the right ventricular free wall and the anterior leaflet of the tricuspid valve using TDI. The Nyquist limits were set at ±20 cm/s, using the lowest filter settings and the minimum optimum gain, as recommended by the manufacturer. The myocardial IVCT (IVCTm) and the myocardial IVRT (IVRTm) were obtained by analyzing TDI. IVCTm was defined as the time interval between the end of Am and the onset of Sm. The IVRTm was defined as the time interval between the end of Sm and the onset of Em.[19]

The following parameters were used to define ventricular systolic and diastolic functions:

1- Preserved left ventricular systolic function: LVEF ≥ 50%; and an LV end-diastolic volume index (LVEDVI), < 97 mL/m^2 ,[20]

2- E/Em>15 was used as the evidence of diastolic dysfunction. E/Em<8 was considered as normal diastolic function. If TD yields an E/Em ratio suggestive of diastolic LV dysfunction (15> E/Em> 8), other mitral inflow velocity parameters ($E/A_{<50\ years} < 1$, or $E/A_{>50\ years} < 0.5$, or $DT_{>50\ years} > 280$ ms) were obtained for diagnostic evidence of diastolic LV dysfunction according to instructions of European Society of Cardiology,[20]

3-Right ventricular diastolic dysfunction (conventional Doppler): TE/TA< 1,

4-Right ventricular diastolic dysfunction (TDI): TEm/TAm<1.

Patients with a history of cardiovascular or pulmonary disease, hypertension and diabetes mellitus were excluded from the study. Patients who are under antihypertensive therapy including beta blockers, angiotensin converting enzyme inhibitors and other antihypertensive regimes were also excluded from the study.

The protocol approved by the institutional review board of the hospital was signed by all participants.

STATISTICAL ANALYSIS

Data analysis was performed by using statistical package for Social Sciences (SPSS) version 11.5 software (SPSS Inc., Chicago, IL, United States). Data were shown as mean ± standard deviation for con-

tinuous variables. Number of patients and percentages were used for nominal variables. Continuous data were compared by Student's t-test or Mann Whitney U test, where applicable. Chi-square tests were used to assess the statistical significance of differences between groups in the frequency distribution of categorical variables, unless the expected cell size less than five, when Fisher's exact test was used. Degrees of association between continuous variables were evaluated by Spearman's correlation test. A p value less than 0.05 was considered statistically significant.

RESULTS

Clinical characteristics of the study group are presented in Table 1. There were 47 patients with GO and 27 healthy controls. Age, sex, body mass index (BMI) were similar in patients with GO and control subjects (p> 0.05). Thirty-four patients had moderate-severe GO and 13 patients had mild GO. There were no patients in clinically active period of GO. Serum Free T3, Free T4, TSH levels were similar between patients and control group (Table 1). The median thyroglobulin, antithyroglobulin, anti-thyroid peroxidase (TPO), TSHRAb, thyrotropin receptor antibody titers were 13.2 ± 9.8 IU/mL, 24.7 ± 7.2 IU/mL, 152.7 ± 81 IU/mL, 28.35 ± 3.5 IU/mL, respectively. TSHR antibody, TPO, thyroglobulin and antithyroglobulin antibody levels were detected high in 26, 30, 19, and 19 of 47 patients, respectively (Table 2).

TABLE 1: Clinical features of patients with Graves' ophtalmopathy and control group

Parameters	GO (n= 47)	Control (n= 27)	P
Age (years)	38.8	35.2	0.173
Sex (M/F)	(15/32)	(8/14)	0.340
Heart rate	78.9 ± 6.7	69.9 ± 5.6	< 0.001
BMI (kg/m^2)	25.8 ± 4.1	25.7 ± 3.3	0.920
SBP (mmHg)	119 ± 14	111 ± 11	0.023
DBP (mmHg)	70 ± 10	68 ± 12	0.444
Serum FT4 (ng/dL)	1.32 ± 0.29	1.19 ± 0.25	0.06
Serum FT3 (ng/dL)	3.47 ± 0.71	3.19 ± 0.86	0.120
Serum thyrotropin (U/mL)	1.84 ± 1.23	2.32 ± 1.0	0.051
Hertel left (cm)	19.8 ± 3.1	16.2 ± 1.6	< 0.0001
Hertel right (cm)	19.6 ± 2.8	16.4 ± 1.7	< 0.0001

BMI: Body mass index; DBP: Diastolic blood pressure; FT3: Free thyroxine; FT4: Free triiodothyronin; GO: Graves ophtalmopathy; SBP: Systolic blood pressure.

TABLE 2: Serum thyroid otoantibody levels and degree of eyelid retraction in Graves' ophtalmopathy patients.

Serum thyroglobulin (median, U/mL)	13.2 ± 9.8
Serum thyroglobulin positive (n)	19
Serum thyroglobulin antibody (median)	24.7 ± 7.2
Serum thyroglobulin antibody positive (n)	19
Serum anti-TPO (median, U/mL)	152.7 ± 81
Serum TSHRAb (median, U/mL)	28.35 ± 3.5
Serum TSHRAb positive (n)	26
Left eyelid retraction (mm)	6.1 ± 0.9
Right eyelid retraction (mm)	5.7 ± 0.9
Eyelid retraction (n)	(47)
Diplopia (n)	(2)

Anti-TPO: Anti-thyroid peroxidase; TSHRAb, Serum thyrotropin receptor antibody.

All patients had eyelid retraction. Mean values of the eye lid retraction were 6.1 ± 0.9 mm for the left eyelid, and 5.7 ± 0.9 mm for the right eyelid. Hertel exophthalmometric measures of the patients with GO were 19.8 ± 3.1 mm for the left eye and 19.6 ± 2.8 mm for the right eye.

There were no differences in systolic and diastolic blood pressures between the patients and the control group.

ECHOCARDIOGRAPHIC EXAMINATION

Left Ventricular Measurements

There were no differences between two groups for ventricular diameters and systolic function (Table 3). No statistical differences were detected between patient and control groups for diastolic function parameters measured by conventional and Doppler methods. (Table 4). Diastolic disfunction was detected in eight subjects in the patient group, while no diastolic disfunction was seen in no subjects in the control group (p= 0.06).

Right Ventricular Measurements

Ejection fraction and TSm value, indicators of right ventricular systolic function, were similar in patient and control groups (Tables 3, 4). No significant differences were seen between two groups in terms

TABLE 3: Echocardiographic variables obtained from the patients.

Variable	GO (n= 47)	Control (n= 22)	P
LA (mm)	3.25 ± 0.4	3.28 ± 2.6	0.670
LVEDD (mm)	46.4 ± 3.7	47.0 ± 4.1	0.097
LVESD (mm)	28.4 ± 3.2	28.8 ± 3.4	0.389
IVS (mm)	9.6 ± 1.1	9.3 ± +1.0	0.252
PW (mm)	9.0 ± 1.1	9.0 ± 1.0	0.991
LVEF (%)	66.5 ± 6.1	68 ± 6.1	0.336
RVEDV (mL)	31.4 ± 14	33.9 ± 13	0.589
RVESV (mL)	15.9 ± 8.6	14.3 ± 7.5	0.562
RVEF (%)	51 ± 13	55 ± 12	0.125
Mitral E velocity (cm/s)	82.8 ± 18	84.5 ± 16	0.694
Mitral A velocity (cm/s)	66.7 ± 19	58.9 ± 13	0.076
Mitral E/A	1.33 ± 0.4	1.46 ± 0.2	0.142
IVRT (ms)	97 ± 20	88 ± 20	0.093
IVCT	88 ± 16	82 ± 14	0.132
Mitral E/A < 1, n	11/35	1/26	0.054
DT (ms)	215 ± 53	197 ± +37	0.146
Tricuspid E velocity (cm/s)	57 ± 10	57 ± 8.0	0.788
Tricuspid A velocity (cm/s)	50.0 ± 11	49.0 ± 11	0.700
Tricuspid E/A	1.14 ± 0.17	1.17 ± 0.23	0.531

E/A: Ratio of E to A; DT: Deceleration time; GO: Graves ophtalmopathy IVCT: Left ventricle isovolumic contraction time; IVRT: Left ventricle isovolumic relaxation time; IVS: End-diastolic interventricular septal thickness; LA: Left atrium; LVEDD: Left ventricle end-diastolic diameter; LVEF: Left ventricle ejection fraction; LVESD: Left ventricle end-systolic diameter; PW: End-diastolic LV posterior wall thickness; RVEDV: Right ventricle end-diastolic volume; RVEF: Right ventricle ejection fraction, RVESV: Right ventricle end-systolic volume.

of parameters of right ventricular diastolic disfunction (Tables 3, 4). While there were 13 patients in the patient group meeting criteria of diastolic disfunction described for right ventricle, the number was four for the control group, and showed no statistical difference (p= 0.328).

No associations were detected between left and right ventricular ejection fractions, systolic and diastolic function parameters and amount of proptosis, right and left eye lid retractions, and TSHRAb levels in the correlation analyses. There were no differences in systolic and diastolic functions in patients with GO, regardless of whether or not they were receiving propylthiouracil and levotiron.

DISCUSSION

The present study is the first study that assessed the right and left ventricle functions with conventional and TDI methods in patients with GO. We detected that left and right ventricular systolic and diastolic functions were preserved in GO patients, and no effect was detected on cardiac functions with TSHRAb positivity which was presumed to affect cardiac muscles.

The primary pathology in Graves' patients is the involvement of retro-orbital muscles, orbital fatty layer, and fibroblasts by autoantibodies against TSH receptors. The first finding indicating the possibility of involvement of cardiac muscle was a case report published by Koshiyama and colleagues.[6] In this report, orbithopathy and cardiomyopathy progressed together in a patient with Graves' disease, and biopsy of cardiac muscle showed lymphocytic infiltration and degenerative changes. This suggested that the development of cardiac manifestations in association with GD might also have a direct autoimmune etiology and perhaps share

TABLE 4: Tissue Doppler parameters of the patients.

Variable	GO (n= 47)	Control (n= 27)	P
Septum (cm/s)			
Sm	9.1 ± 2.2	9.0 ± 1.4	0.866
Em	11.8 ± 3.3	12.5 ± 3.1	0.401
Am	9.5 ± 2.2	8.9 ± 1.7	0.263
Em/Am	1.3 ± 0.5	1.4 ± 0.5	0.307
Em/Am< 1, n	14/33	5/22	0.428
E/Em	7.3 ± 2.3	7.1 ± 2.0	0.732
Lateral (cm/s)			
Sm	10.1 ± 3.5	10.0 ± 2.9	0.241
Em	15.1 ± 4.2	14.8 ± 4.1	0.818
Am	10.1 ± 3.4	8.5 ± 1.8	0.035
Em/Am	1.7 ± 0.7	1.8 ± 0.7	0.365
MitE/Em	5.9 ± 2.1	6.2 ± 2.3	0.787
Em/Am< 1, n	8/39	0/27	0.06
Right ventricle (cm/s)			
Sm	15.75 ± 2.7	14.8 ± 1.9	0.122
Em	16.3 ± 4.1	15.2 ± 2.5	0.788
Am	16.1 ± 4.8	14.2 ± 2.5	0.085
Em/Am	1.14 ± 0.3	1.29 ± 0.3	0.567
Tricuspid E/Tricuspid Em	3.9 ± 1.4	3.9 ± 1.2	0.771
Tricuspid EM/Tricuspid AM< 1, n	13/34	4/23	0.328

Am: Late diastolic myocardial velocity; Em: Early diastolic myocardial velocity; IVCTm: Myocardial isovolumic contraction time; IVRTm: Myocardial isovolumic relaxation time; Sm: Systolic myocardial velocity.

an antigen common to heart and thyroid. Following that study, Selliti and colleagues reported that TSH receptors were most frequently seen at coronary arteries, epicardial fatty tissue, and right atrium in the heart.[5] Ventricle was reported to be the site containing the least TSHR. Later a study by Busuttil and colleagues showed that TSHR was expressed in extra-ocular tissues, but not in cardiac muscle tissues.[21] In the light of these studies, whether autoimmune process leads to cardiac muscle involvement in patients with Graves' disease is still controversial, and clinical studies on this topic are quite few. The first study examining the heart echocardiographically in patients with Graves' disease was carried by Kage and colleagues.[22] In the study by Kage and colleagues, no difference was found in the patient group in terms of left ventricular end systolic diameter, end diastolic diameter, and left ventricular EF, compared to the control group.[22] Similarly, no remarkable change was detected in left ventricular functions in the present study. Given that the ventricles contained the least TSH receptors in the study by Selliti and colleagues which investigated TSH receptors in the heart, it may be presumed that the least affected sites in the heart would be the ventricles, thus ventricular functions would be preserved.[5] No impairment in the ventricular function may also be related to the prevalence of TSHRAb positive patients in the study group. TSHRAb was 55% positive in the present study, but this was considerably low when compared with 97% TSHRAb positivity in the patients who developed severe GO in the study by Eckstein and colleagues.[23] As a result of low blood TSHRAb titers in the present study, ventricular involvement may have not become evident. High antibody titers are common particularly at the active and pre-treatment stages of the disease. Eckstein and colleagues reported that antibody titers increased 3-5 times the normal in patients with mild GO at the inactive stage, and 10-15 times the normal in severe GO patients at the active stage. In the present study, TSHRAb levels increased three times, and it can be stated that there was less ventricular involvement as all patients were at mild or moderate GO patients at the inactive stage.[24] Impairment in systolic and diastolic functions in GO patients, which is the hypothesis of the present study, may be associated with intensive antibody levels at the active stage. Future studies on this topic would clarify whether there was an association between cardiac involvement and active stage of the disease.

Another reason for no effect on ventricular functions in the present study may also be the result of the absence of TSH receptors in the heart, as claimed in the study by Busuttil and colleagues.[21]

STUDY LIMITATION

One of the limitation of this study is that some of the patients were taking medications such as propylthiouracil and levothyroxine. In our study, when we compare the patients who were taking propylthiouracil or levothyroxine and who did not, we found no differences in systolic and diastolic functions in patients with GO, regardless of whether or not they were receiving one of the aforementioned treatments. However, this study was not designed to compare the right and left ventricle systolic and diastolic functions before and after treatment with propylthiouracil and levothyroxine. Therefore, further studies are needed to more thoroughly examine this question. The other limitation of this study is that heart rate was different in the patient group in comparison to control group. It is known that conventional Doppler indexes can be significantly influenced by physiologic variables such as preload, heart rate, and respiration[25] however the studies by Sohn et al[26] and Nagueh et al[27] demonstrated that TDI parameters were not affected by rapid heart rates, atrial fibrillation, and preload.

CONCLUSION

Cardiac functions were preserved in patients with GO who were clinically inactive and euthyroid. TSHRAb levels have no affect on both left and right ventricles in patients with GO.

REFERENCES

1. Arikan S, Bahceci M. Graves' Ophtalmopathy. Turkiye Klinikleri J Endocrin 2008;3(2): 68-76.
2. Perros P, Kendall-Taylor P. Pathogenesis of thyroid-associated ophthalmopathy. Trends Endocrinol Metab 1993;4(8):270-5.
3. Burch HB, Wartofsky L Graves' ophthalmopathy: current concepts regarding pathogenesis and management. Endocr Rev 1993;14(6):747-93.
4. Bahn RS, Heufelder AE. Pathogenesis of Graves' ophthalmopathy. N Engl J Med 1993;329(20):1468-75.
5. Sellitti DF, Hill R, Doi SQ, Akamizu T, Czaja J, Tao S, et al. Differential expression of thyrotropin receptor mRNA in the porcine heart. Thyroid 1997;7(4):641-6.
6. Koshiyama H, Sellitti DF, Akamizu T, Doi SQ, Takeuchi Y, Inoue D, et al. Cardiomyopathy associated with Graves' disease. Clin Endocrinol (Oxf) 1996;45(1):111-6.
7. Drvota V, Janson A, Norman C, Sylvén C, Häggblad J, Brönnegård M, et al. Evidence for the presence of functional thyrotropin receptor in cardiac muscle. Biochem Biophys Res Commun 1995;211(2):426-31.
8. Bartalena L, Baldeschi L, Dickinson A, Eckstein A, Kendall-Taylor P, Marcocci C, et al; European Group on Graves' Orbitopathy (EUGOGO). Consensus statement of the European Group on Graves' orbitopathy (EUGOGO) on management of GO. Eur J Endocrinol 2008;158(3):273-85.
9. European Group on Graves' Orbitopathy (EUGOGO), Wiersinga WM, Perros P, Kahaly GJ, Mourits MP, Baldeschi L, Boboridis K, et al. Clinical assessment of patients with Graves' orbitopathy: the European Group on Graves' Orbitopathy recommendations to generalists, specialists and clinical researchers. Eur J Endocrinol 2006;155(3):387-9.
10. Beden U, Ozarslan Y, Oztürk HE, Sönmez B, Erkan D, Oge I. Exophthalmometry values of Turkish adult population and the effect of age, sex, refractive status, and Hertel base values on Hertel readings. Eur J Ophthalmol 2008;18(2):165-71.
11. Asman P. Ophthalmological evaluation in thyroid-associated ophthalmopathy. Acta Ophthalmol Scand 2003;81(5):437-48.
12. Boulos PR, Hardy I. Thyroid-associated orbitopathy: a clinicopathologic and therapeutic review. Curr Opin Ophthalmol 2004;15(5):389-400.
13. Terwee CB, Prummel MF, Gerding MN, Kahaly GJ, Dekker FW, Wiersinga WM. Measuring disease activity to predict therapeutic outcome in Graves' ophthalmopathy. Clin Endocrinol (Oxf) 2005;62(2):145-55.
14. Wiersinga WM, Prummel MF. Graves' ophthalmopathy: a rational approach to treatment. Trends Endocrinol Metab 2002;13(7):280-7.
15. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al; Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography.Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18(12):1440-63.
16. Miller D, Farah MG, Liner A, Fox K, Schluchter M, Hoit BD. The relation between quantitative right ventricular ejection fraction and indices of tricuspid annular motion and myocardial performance. J Am Soc Echocardiogr 2004;17(5):443-7.
17. Appleton CP, Jensen JL, Hatle LK, Oh JK. Doppler evaluation of left and right ventricular diastolic function: a technical guide for obtaining optimal flow velocity recordings. J Am Soc Echocardiogr 1997;10(3):271-92.
18. Quiñones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA; Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of J Am Soc Echocardiogr 2002;15(2):167-84.
19. Alam M, Wardell J, Andersson E, Samad BA, Nordlander R. Characteristics of mitral and tricuspid annular velocities determined by pulsed wave Doppler tissue imaging in healthy subjects. J Am Soc Echocardiogr 1999;12(8):618-28.
20. Paulus WJ, Tschöpe C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers FE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. Eur Heart J 2007;28(20):2539-50.
21. Busuttil BE, Frauman AG. Extrathyroidal manifestations of Graves' disease: the thyrotropin receptor is expressed in extraocular, but not cardiac, muscle tissues. J Clin Endocrinol Metab 2001;86(5):2315-9.
22. Kage K, Kira Y, Sekine I, Okabe F, Nakaoka T, Hashimoto E, et al. High incidence of mitral and tricuspid regurgitation in patients with Graves' disease detected by two-dimensional color Doppler echocardiography. Intern Med 1993;32(5):374-6.
23. Eckstein AK, Plicht M, Lax H, Neuhäuser M, Mann K, Lederbogen S, et al. Thyrotropin receptor autoantibodies are independent risk factors for Graves' ophthalmopathy and help to predict severity and outcome of the disease. J Clin Endocrinol Metab 2006;91(9):3464-70.
24. Gerding MN, van der Meer JW, Broenink M, Bakker O, Wiersinga WM, Prummel MF. Association of thyrotrophin receptor antibodies with the clinical features of Graves' ophthalmopathy. Clin Endocrinol (Oxf) 2000; 52(3):267-71.
25. Rakowski H, Appleton C, Chan KL, Dumesnil JG, Honos G, Jue J, et al. Canadian consensus recommendations for the measurement and reporting of diastolic dysfunction by echocardiography: from the Investigators of Consensus on Diastolic Dysfunction by Echocardiography. J Am Soc Echocardiogr 1996;9(5):736-60.
26. Sohn DW, Chai IH, Lee DJ, Kim HC, Kim HS, Oh BH, et al. Assessment of mitral annulus velocity by Doppler tissue imaging in the evaluation of left ventricular diastolic function. J Am Coll Cardiol 1997;30(2):474-80.
27. Nagueh SF, Mikati I, Kopelen HA, Middleton KJ, Quiñones MA, Zoghbi WA Doppler estimation of left ventricular filling pressure in sinus tachycardia. A new application of tissue doppler imaging. Circulation 1998;98(16): 1644-50.