The Role of Right Ventricular Contractility in Patients Who Experienced Neurogenic Syncope

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ABSTRACT

Introduction: Left ventricular hyper contractility has been thought to have a major role at early phases of vasovagal syncope. However the right ventricular function during syncope has not been delineated clearly. The present study evaluated the right myocardial contractility in patients who experienced vasovagal syncope during head-up tilt test (HUTT).

Patients and Methods: A total of 89 Patients, who experienced syncope between January 2012 and March 2014, were included in the study. All the patients underwent HUTT and were followed by transthoracic echocardiography.

Results: Fifty patients experienced syncope during HUTT. There was no significant difference between the patients, who experienced syncope versus who did not, in terms of gender, age, ejection fraction (p> 0.05). Mitral lateral annular systolic (s') velocity (14 ± 3.8 vs. 13.3 ± 3.6; p= 0.625), septal annular s' velocity (11 ± 3.7 vs. 10.3 ± 2; p= 0.951) were similar following HUTT in patients with and without syncope respectively. However, tricuspid valve lateral annular s' velocity after tilt testing was higher in patients, who experienced syncope (17 ± 2.7 vs. 15.1 ± 3.0; p= 0.003).

Conclusion: While left ventricular functions are not affected, right ventricular contraction is more powerful in patients who experience syncope during HUTT.

Key Words: Echocardiography; head-up tilt testing; neurogenic syncope

Nörojenik Senkop Geçiren Hastalarda Sağ Ventrikül Kontraksiyonunun Rolü

ÖZET

Giriş: Nörojenik senkopun erken safhasında sol ventrikül kontraktilite artışının önemli rolü olduğu düşünülmektedir. Fakat senkop esnasında sağ ventrikül fonksiyonu net olarak ortaya konmamıştır. Bu çalışmada eğik masa testinde (EMT) nörojenik senkop geçiren hastalarda sağ ventrikül fonksiyonu değerlendirilmiştir.

Hastalar ve Yöntem: Ocak 2016 ve Mart 2017 tarihleri arasında senkop geçiren 89 hasta çalışmaya dahil edilmiştir. Tüm hastalara EMT ve ardından transtorasik ekokardiyografi uygulanmıştır.

Bulgular: Eğik masa testinde 50 hastada senkop gelişmiştir. Senkop gelişen ve gelişmeyen hastalarda cinsiyet, yaş ve ejeksiyon fraksiyonu açısından fark gözlenmemiştir (p> 0.05). Mitral lateral anüler sistolik (s') velositesi (14 ± 3.8'e karşı 13.3 ± 3.6 p= 0.625), septal anuler s' velositesi (11 ± 3.7'ye karşı 10.3 ± 2 p= 0.951) senkop gelişen ve gelişmeyen hastalarda benzer izlenmiştir. Fakat senkop geçiren hastalarda triküspit lateral anüler s' velositesi daha yüksek saptanmıştır (17 ± 2.7'e karşı 15.1 ± 3.0, p= 0.003).

Sonuç: Eğik masa testinde senkop gelişen hastalarda sol ventrikül fonksiyonları değişmezken sağ ventrikül kontraksiyonunda artış gözlenmiştir.

Anahtar Kelimeler: Ekokardiyografi; eğik masa testi; nörojenik senkop

INTRODUCTION

Syncope is characterized by sudden and temporary loss of postural tone followed by spontaneous recovery as a result of a reduction in cerebral perfusion[(1)]. Syncope accounts for 1% of emergency admissions, and it is an important cause of morbidity and loss of work force[(2-4)].

Neurogenic syncope is the most common cause of syncope, and it accounts for 60% of the patients presenting to the emergency rooms with fainting[(5)]. The uncontrolled response of autonomic nervous system has been implicated in neurogenic syncope, although its physiopathol-

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ogy remains unknown[6].Uncontrolled and excessive response of the autonomic nervous system is the mostly accepted theory. Excessive activation of the parasympathetic system, which occurs depending on the increased activation of the sympathetic nervous system response, leads to bradycardia and hypotension, and thus, leads to neurogenic syncope[7,8]. Consequently, increase in cardiac contractility as a result of increased sympathetic activity causes increased parasympathetic response and this imbalance in the autonomic nervous system plays role in the pathophysiology of neurogenic syncope.

Some of the echocardiographic studies confirmed that left ventricular contraction increased dramatically during syncope. However, the role of right ventricular function during neurogenic syncope is not clearly known. This study evaluated right ventricular contraction using tissue Doppler systolic velocity in patients who experienced syncope during Head-up tilt testing (HUTT).

PATIENTS and METHODS

The present study included patients, who experienced syncope without any apparent reason but suspected neurally mediated syncope between January 2012 and March 2014. After a careful history and physical examination, 12-lead electrocardiogram, orthostatic blood pressure readings, serum glucose and electrolytes were obtained and neurology and psychiatric consultation was requested in selected cases prior to HUTT to rule out malignant dysrhythmic, metabolic, cardiac mechanical or psychological/neurological etiologies of syncope.

The patients with coronary artery disease, heart failure, atrial fibrillation, cerebrovascular disease, hypertension, diabetes mellitus, smokers, and patients with permanent pacemaker, chronic renal failure, and those with a history of rheumatic disorders were excluded. Age and gender were recorded before the procedure. All the patients underwent HUTT. Before and after the HUTT, ejection fraction and tissue Doppler parameters were calculated with transthoracic echocardiography (TTE). All the patients provided verbal and written informed consent before the test. The local ethics committee approved this study.

"Head-up" Tilt Table Test Method

The HUTT was performed in accordance with the protocol recommended by Benditt[9]. The patients were divided into groups according to revised VASIS classification based on their hemodynamic responses during the test[10].

Transthoracic Echocardiography

All the patients underwent TTE before and immediately after HUTT. The ejection fraction and tissue Doppler parameters of the patients were evaluated. i.E33, Philips medical systems, Andover, mass S5 probe (2 and 4 MHz) was used to perform the echocardiography. The standard 2-dimensional and tissue Doppler views were acquired in accordance with the recommendations of the European echocardiography association[11].

Two experienced operators, who were kept blind against the clinical data of the patients, independently evaluated echocardiographic views. The ejection fraction (EF) was calculated based on the Simpson's method[11]. The data for tissue Doppler was obtained by placing the pulse wave Doppler probe on the lateral and septal portion of the mitral annulus and on the lateral portion of the tricuspid annulus for the right ventricle.

Statistical Analysis

SPSS 18.0 for Windows (SPSS Inc., Chicago, Illinois, USA) software package was used to perform the statistical analysis. Visual (histogram and probability graphs) and analytic (Kolmogrow-Smirnow) methods were used to check if the variables were normally distributed. After determining normal distribution, the data of the patients, who experienced syncope, were compared to those who did not experience syncope during tilt test using the independent sample t-test. Paired samples t-test was used to compare the values before and after HUTT. Overall, 5% type-1 error level was used to infer statistical significance.

RESULTS

A total of 89 patients underwent HUTT. Fifty patients developed neurogenic syncope during HUTT. The mixed type and cardioinhibitory syncope were the most common types of syncope followed by vasodepressor syncope (Table 1).

There were no significant difference between the patients who experienced syncope versus the patients who did not; in terms of gender, age, mitral lateral annular systolic velocity, and septal annular systolic velocity ($p > 0.05$). However, tricuspid lateral annular systolic velocity was higher in patients, who experienced syncope compared to those who did not experience syncope ($p = 0.003$) (Table 2). Mitral lateral annular systolic velocity and septal annular systolic velocity were similar before and after tilt testing in patients with and without syncope ($p > 0.05$). In addition, tricuspid lateral annular systolic velocity was similar in patient without syncope ($p > 0.05$). However, right ventricular s' velocity after tilt testing was higher in the patients with syncope in comparison to those without syncope ($p = 0.003$).

Table 1. Number and percentage of patients with syncope

Syncope type	N, (%)
Mixed syncope	20, (40%)
Cardioinhibitor syncope	20, (40%)
Vasodepressor syncope	10, (20%)

n, (%): Number, percentage.

Table 2. The differences between patients who experienced syncope and those who did not in terms of gender, age, tissue doppler parameters

	Syncope negative n= 39	Syncope positive n= 50	p
Women n, (%)	17 (44%)	22 (44%)	0.969
Age years (n ± SD)	26 ± 9.9	26 ± 12.3	0.402
Ejection fraction (%)	64 ± 3.9	62,6 ± 4,0	0.105
Left ventricular lateral s'* (n ± SD)	13.4 ± 3.5	13.7 ± 3.9	0.714
Left ventricular lateral s'** (n ± SD)	13.3 ± 3.6	14 ± 3.8	0.625
Septal s' * (n ± SD)	10.2 ± 1.8	10.1 ± 1.8	0.884
Septal s'** (n ± SD)	10.3 ± 2	11 ± 3.7	0.951
Right ventricular lateral s' * (n ± SD)	15.1 ± 3.1	15.3 ± 3.2	0.828
Right ventricular lateral s' ** (n ± SD)	15.1 ± 3.0	17 ± 2.7	0.003

* Values before tilt testing.
* * Values after tilt testing.
n, (%): Number, percentage, (n ± SD): Number ± standard deviation.

DISCUSSION

To our knowledge, this is the first study that evaluates right ventricular function in neurogenic syncope. According to the results of this study, ventricular contractility using tissue Doppler s' velocity was higher in patients with neurogenic syncope than those without syncope.

HUTT is a laboratory procedure that has been used over the past 60 years to investigate the neurogenic reactions, including syncope, and it can be helpful in confirmation of neurally mediated hypotension and bradycardia in subjects believed to be susceptible to neurogenic syncope[12].

The exact pathophysiological mechanisms responsible for neurogenic syncope have not been elucidated totally. After the initiating events of neurogenic syncope, complex hemodynamic changes occur, resulting in marked hypotension, bradycardia, and loss of consciousness. Several theories have been recommended to account for these hemodynamic changes, including the ventricular theory, the baroreflex dysfunction theory, the reduced blood volume theory, the neurohumoral theories (epinephrin, serotonin, Renin, Vasopressin, b-Endorphin, Endothelin, and Nitric Oxide) and the active vasodilation theory which could not clearly delineate the mechanism for neurogenic syncope[13-16].

Echocardiographic examination has a major role for the explanation of the "ventricular theorem" which is the most widely accepted pathophysiological reason of neurogenic syncope. Shaley et al. showed that patients, who experienced syncope passively or with isoproterenol provocation in the HUTT, had a significant decrease in the left ventricular systolic diameters and a severe increase in myocardial contractility compared to the patients, who did not experience syncope or those in the control group[17]. In the study by Moon et al., echocardiography was performed during the HUTT and left ventricular hyper contractility was observed in patients with HUTT induced neurogenic syncope occurring immediately after passive tilting[18]. In another study, patients were evaluated with strain echocardiography after 6 months of HUTT. They found a decrease in myocardial strain to be predictive of a positive tilt test[19]. It is possible that individuals prone to neurogenic syncope may demonstrate a decreased myocardial strain at rest, but increased strain and contractility with provoking stimuli.

The studies mentioned above yielded information about the physiology of the left ventricular functions. However, the timing of echocardiography was not uniform. In addition, the methods of the studies were quite different. Therefore, the results may have been different in those studies ultimately making clear statement of left ventricular functions in syncope is not possible.

The tissue Doppler imaging is the most commonly used echocardiographic method in daily practice, and it is employed to evaluate myocardial systolic and diastolic functions. The systolic (s) velocity detected by tissue Doppler has been found to be directly related to the EF[20]. Unlike two-dimensional measurement of the EF, tissue Doppler method provides clear information regarding myocardial contractility independent of the findings of cardiac loading, atrial functions, and heart rate [21,22]. In the study by Folino et al., no remarkable difference was observed between patients who experienced syncope versus who did not experience syncope during HUTT in terms of atrial and ventricular dimensions; however, a modest increase has been observed in tissue Doppler systolic velocity as the measure of myocardial contractility, although this increase was statistically insignificant[23]. There are no data regarding right ventricle functions during syncope. The present study did not show a significant difference between patients who experienced syncope versus who did not experience syncope immediately after HUTT in terms of left ventricular lateral

and septal tissue Doppler systolic velocity. However, right ventricular tissue Doppler systolic velocity was significantly higher in patients who experienced syncope. In the study by Mangin et al., peak endocardial acceleration was evaluated as the measure of myocardial contractility by inserting a sensor to the right ventricular lead of the patients in whom a permanent dual pacemaker has been implanted previously. The contractility was higher in patients, who experienced syncope during HUTT [24]. Based on the current data, right ventricle contractility was found to be higher in patients who experienced neurogenic syncope compared to patients in the control group. Decreased volume load in the right ventricule associated with prolonged standing increases the sympathetic response, and this may have caused a further increase in right ventricular contractility. Higher cardiac contractility in patients with neurogenic syncope can be more easily detected in the thin-walled right ventricle than the thick walled left ventricle. Right ventricle is more vulnerable to volume changes, and higher contractility of the right ventricle in these patients compared to the control group seems to be resulting in syncope by causing bradycardia and hypotension in addition to the imbalance in parasympathetic response. This may be the reason why left ventricle contractions are found similar in both syncope and non-syncope group in our study. Echocardiographic right ventricular systolic s' velocity is the marker that demonstrates more powerful contraction of right ventricle which can be detected more easily than left ventricle and can contribute pathophysiological explanation of the tilt test neurogenic syncope. Although left ventricular contractility are similar in the syncope and control groups, right ventricular contractility are significantly higher in the syncope group. The increased cardiac contractility may be associated with syncope mechanism in neurogenic syncope patients.

Study Limitations

Although the findings of the present study seem to support the findings of the previous studies, there are methodological differences. Echocardiographic examination was performed immediately after syncope and not during tilt test. In addition, we used s' velocities for myocardial contractility measurements but not strain because we did not have that software package available while we were conducting our study.

CONCLUSION

The patients, who experienced syncope during HUTT, had higher right ventricular contractility, which is reflected by an increase in echocardiographic tissue Doppler systolic velocity. This increase can contribute to the pathophysiologic explanation of neurogenic syncope.

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CONFLICT of INTEREST

The authors reported no coflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: UK
Analysis/Interpretation: CN
Data Acquisition: FL, EÖ
Writting: VE
Critical Revision: MT
Final Approval: All of authors

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