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Assessment of Left Ventricular Outflow Tract Velocity Time Integral in Pediatric Patients with Vasovagal Syncope

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Abstract

Background

Syncope is an important and common clinical condition, and the neurally mediated syncope is the most frequent type of syncope. Head up tilt testing is considered as a first line diagnostic test. The aim of this study was to assess the left ventricular outflow tract velocity time integral in echocardiography of pediatric patients with vasovagal syncope.

Materials and Methods: In this case-control study, between January 2019 and December 2020 92 patients who referred in in Mofid Children Hospital in Tehran, Iran, for vasovagal syncope in the case group and 92 healthy children with maximum matching of sex and age in the control group were included in the study. Demographic, clinical and para-clinical data were recorded for each patient in the respective checklists, and HUTT and echocardiography were reviewed, then the results of two groups were compared.

Results: The mean age of the patients with vasovagal syncope was 12.12 ±5.18 years. 66.3% of patients in the case group were female. There was a statistically significant relationship between LVOT-VTI and positive result of HUTT ($p<0.001$). There was no relationship between LVOT VTI in case and control groups ($p=0.14$).

Conclusion

The mean LVOT VTI index in patients with negative tilt test is higher than patients with positive tilt test. Although echocardiographic indices in children with vasovagal syncope are in normal range, accurate measurement of LVOT-VTI can be helpful in predicting a positive HUTT result.

Key Words: Children, LVOT VTI, HUTT, Vasovagal syncope.

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1- INTRODUCTION

Syncope is a decrease in the consciousness level due to a transient decrease in global blood flow of the brain, which is characterized by rapid onset, short duration, and complete spontaneous recovery (1). The peak incidence of syncope is between the ages of 15 and 19 in both genders; although syncope appears to be more common in girls (2), and it is uncommon in children under 6 years old (3). Syncope accounts for a lifetime prevalence of between 1% to 3% for emergency room visits and ≥30% for hospital admission (4). The reflex syncope is known as the neurally-mediated syncope and affects about one-third of people and it is divided into the vasovagal syncope (which is mainly stimulated by emotion, pain, and standing stimulation), the situational syncope, the orthostatic hypotension and the carotid sinus syncope (5, 6). Of all the causes, vasovagal syncope in children is the most common type of syncope (61-80%) (7).

The mechanism of vasovagal syncope is explained by the Bezold–Jarisch reflex, which is triggered due to decreased venous return resulting in inadequate ventricular filling and vigorous cardiac contraction. It occurs by the action of mechanoreceptors (C fibers) preferentially located in the inferolateral wall of the left ventricle, but also in the atria and in the pulmonary artery, and manifests with hypotension and paradoxical bradycardia due to increased activity of inhibitory receptors and consequent parasympathetic hyperactivity (8). The Head up Tilt test (HUTT) is a potential diagnostic tool used to diagnose neurocardiogenic syncope that has been used since 1986 (9), and has a central part in the diagnosis of vasovagal syncope (10). The purpose of this test is to stimulate a real event to show the pathophysiological relationship and thus prove the cause of syncope (11). The sensitivity of the HUTT for the diagnosis of vasovagal syncope is reported to be 67-85% and its specificity is about 90% (12, 13). The left ventricular outflow tract (LVOT) velocity time integral (VTI) is an echocardiographic parameter used to estimate cardiac output (CO) by multiplying it with the LVOT area and heart rate (14). Cardiac output is the most common value by which to judge cardiac function. Transthoracic echocardiography is the most common monitoring technique; moreover, the accuracy of evaluation of cardiac output by Doppler echocardiography has been proven in multiple studies (15, 16). The aim of this study was to assess of LVOT VTI as an echocardiographic parameter in patients with vasovagal syncope.

2- MATERIALS AND METHODS

2-1. Study design and population

This study was done as a case control study. Between January 2019 and December 2020, 92 patients in the age range of 6 to 18 years who referred in in Mofid Children Hospital in Tehran, Iran, for vasovagal syncope in the case group and 92 healthy children with maximum matching of sex and age in the control group were included in the study.

2-2. Methods

All patients and control subjects underwent careful history taking, a physical and neurological examination, and an echocardiographic Doppler examination. For more detailed examination and comparison of LVOT VTI with the case group, the control group was also considered. All echocardiographic investigations selected for this analysis were collected. Then in the case group HUTT was performed while in the control group there was no need to do it.

2-3. Measuring tools

Echocardiographic examinations were performed using a Samsung system

machine HS70 with adequate transducer 3-7 MHz depending on the patient's body size. LVOT VTI is calculated by placing the pulsed Doppler sample volume in the outflow tract below the aortic valve and recording the velocity (cm/s) during supine position of the patient. The VTI was plotted manually during echocardiographic examination at the outer level of the maximum flow.

2-4. Intervention

HUT testing was carried out on a mechanical tilt table with a footboard for weight-bearing and safety belts at a 60° tilt. The test was performed by a pediatric cardiologist in a quiet standard room at 21–25°C with the lights dimmed. The patients initially fasted for 6 hours. Pharmacological provocation was not used in any of the cases. During the tilt period, patient's vital signs and ECGs were taken and reported at 3-5 min intervals. A pediatric cardiologist and a technician were present during the entire procedure. All patients were closely observed for 15 min in the clinic after completion of testing. A positive test was defined as the reproduction of previously presyncopal or syncopal symptoms in addition to a vasodepressor response (≥30 % decrease in systolic BP), a cardioinhibitory response (an abrupt decrease of at least 30% in heart rate), or both, while in the tilted position (17). The case group with vasovagal syncope was sub-classified into three types of responses to orthostatic change: Vasodpressor, Cardioinhibitor, or Mix type response.

2-5. Ethical consideration

The current study made no harm or excessive charge on patients and all the patients had informed consent about participating in the study. In the control group, echocardiography was performed free of charge. Also, this study is approved by the Ethics committee of Shahid Beheshti University of Medical Sciences with ethics ID 1399.644.

2-6. Inclusion and exclusion criteria

All pediatric patients with vasovagal syncope who referred to the heart clinic were included the study. Along with it, the same number of healthy children with maximum gender and age matching were included. Patients with present or past history of arrhythmia, structural heart disease, or renal failure and other medical problems were excluded.

2-7. Data Analysis

All quantitative and qualitative patient data were registered in a computerized database. Quantitative data are expressed as mean and standard deviation (SD). Qualitative and quantitative data are fully described and summarized in the tables. A P-value less than 0.05 was considered statistically significant**.** Correlation between qualitative variables chi square test and fisher's exact test and for quantitative variables t-test were used.

3- RESULTS

Out of 92 patients entered into the study, 31 (33.7%) were male and 61(66.3%) were female. The mean age of the patients was 12.12 ±5.18 years. In control group there was also 92 healthy children that 52 (56.5%) were female. **Table.1** shows the demographic and echocardiographic findings between case and control groups. Among 92 patients with vasovagal syncope, 44 children (47.8%) had a positive HUTT, of which 22 patients had mixed type and 22 patients had vasodepressor type.

Table-1: Demographic and echocardiographic findings between case and control groups.

Variables	Case group (patients with vasovagal syncope) (n=92)	Control group (healthy children) (n=92)	P-value
Age (year)	12.12±5.18	12.07±4.19	0.94
Female (% in each group)	61(66.3%)	52(56.5%)	0.17
Ejection Fraction (%)	64.37±4.35	64.88±4.07	0.41
Left Ventricle Outflow Tract Velocity Time Integral (cm)	24.26±3.21	24.74±3.03	0.30

Table.2 shows the demographic and clinical characteristics of the study population and comparison between the two groups. The mean of LVOT-VTI in patients was 24.26±3.21cm and in control group was 24.74±3.03 (p=0.3). The results of linear regression model were performed to measure the factors related to VTI. There was a statistically significant relationship between LVOT-VTI and HUTT. The mean VTI index in patients with negative tilt test is 3.76 cm higher than patients with positive tilt test (β=3.76, 95%CI: 2.68-4.85, P<0.001). Comparison of two groups that have positive HUTT results (Mixed type and Vasodepressor type) shows in **Table.3**. LVOT-VTI index was not statistically significant in the two positive groups of HUTT (P=0.14).

Table-2: Demographic and clinical characteristics of the case group and comparison between negative and positive HUTT.

Variables	Total (n=92)	Negative HUTT (n=48)	Positive HUTT (n=44)	P-value
Age (years)	12.12±5.18	13.37±5.27	10.75±4.76	0.01
Female (% in each group)	61(66.3%)	35(72.9%)	26(59.1%)	0.16
Positive family history of convulsion, (% in each group)	10(11%)	4(8.3%)	6(13.6%)	0.41
Weight, kg	44.65±20.69	48.48±21 .07	38.79±13.86	0.053
Supine blood pressure (mmHg)	109.61±13.12	109.61±13.12	104.9±8.83	0.102
Upright blood pressure (mmHg)	104.96±11.63	106.81±12.20	102.94±12.73	0.096
Supine heart rate (beat/min)	90±16	89.37±17.24	93.26±12.08	0.553
Upright heart rate (beat/min)	94±20	92.81±17.38	97.42±12.49	0.402
Ejection Fraction (%)	64.37±4.35	65.16±3.98	63.50±4.62	0.06
Left Ventricle Outflow Tract Velocity Time Integral (cm)	24.26±3.21	26.06±2.81	22.29±2.31	0.0001

HUTT: Head up Tilt test.

Table-3: Comparison of two groups of positive HUTT (Mixed type and Vasodepressor type).

Variable	Mixed type (n=22)	Vasodepressor type (n=22)	P-value
Age (year)	10.45±4.16	11.05±5.39	0.68
Female (% in each group)	12 (54.5%)	14 (63.6%)	0.54
Ejection Fraction (%)	63.27±4.88	63.73±4.45	0.74
Left Ventricle Outflow Tract Velocity Time Integral (cm)	21.77±2.20	22.82±2.46	0.14

HUTT: Head up Tilt test.

4- DISCUSSION

The aim of this study was to assess of LVOT VTI as an echocardiographic parameter in pediatric patients with vasovagal syncope. In this study, we evaluate aortic velocity time integral (VTI) as a parameter of echocardiographic finding for children with vasovagal syncope. In contrast, the control group is also considered, although the normal range of LVOT VTI has been present in other studies (14). Aortic and LVOT VTI use for estimation of cardiac output. LVOT VTI instead of aortic VTI for measurement of cardiac output is preferable because of interpretation of the area under the Doppler waveform (VTI) is often challenging, it can be influenced by numerous factors, such as heart rate (HR), the configuration of outflow tracts, and chamber size (18).

In this study, as in other studies, the prevalence of vasovagal syncope was more common in females (19, 20). Patients with vasovagal syncope are prone to hypotension, despite have anatomically and functionally normal heart. LVOT VTI in children with vasovagal syncope is the range of normal population. This study showed that the LVOT VTI in children with positive HUTT is lower than children with negative HUTT. Decrease LVOT VTI during test due to reduce left ventricular blood flow may be cause positive HUTT. LVOT VTI can be a useful alternative measure of LV performance in children over 1 year (21). Aortic VTI ranged from mean 13.8 cm (10.0-18.4 cm 5-95th percentile) in neonates to 25.1 cm (19.6-32.8 cm 5-95th percentile) in children >17 years of age and had a positive correlation with age ($r=0.685$, $p < 0.001$), BSA ($r=0.645$, $p<0.001$), and a negative correlation with HR ($r = -0.710$, $p< 0.001$) (13). Heart failure patients with low cardiac output are known to have poor cardiovascular outcomes. Thus, extremely low LVOT VTI may predict heart failure patients at highest risk for mortality. Tan et al show that extremely low LVOT VTI strongly predicts adverse outcomes and identifies patients who may benefit most from advanced heart failure therapies (22). The LVOT VTI provides a reliable estimate of cardiac function and is commonly followed in the management of shock LVOT (23). VTI<15cm is defined as an abnormality suggesting reduced left ventricular stroke volume, however it is unknown whether it correlates with low cardiac output syndrome (LOS) or not.

Lindenberger et al. showed the women who prone to vasovagal syncope demonstrate reduced cardiac preload, lower cardiac output. The results emphasize the importance of venous return and cardiac output in the pathogenesis of vasovagal syncope (24). Echocardiography was performed in patients with syncope who underwent tilt test and in control group who did not need tilt test. If there were any abnormal findings on the echocardiogram, they were excluded. Therefore, we expected the finding to be within the normal range, but no significant relationship was found between the case and control groups, but in the case group, patients who had a positive HUTT had lower LVOT VTI than those who had negative HUTT.

4-1. Study Limitations

This study was conducted in only one center; the sample size and accessibility to patients were limited. It was difficult to find individuals in the control group and to match gender and age with the control group.

5- CONCLUSION

The mean LVOT VTI index in patients with negative tilt test is higher than patients with positive tilt test. LVOT VTI is a parameter used to estimate of cardiac output. Although echocardiographic indices in children with vasovagal syncope

are in normal range, accurate measurement of LVOT-VTI can be helpful in predicting a positive HUTT result.

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7- CONFLICT OF INTEREST: None.

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