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ORIGINAL ARTICLE

Neurocardiogenic syncope in children: head-up Tilt Test response evaluation

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Tilt-Table Test,
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Abstract

Introduction: Syncope is a sudden and transient loss of consciousness associated with the loss of postural tone followed by spontaneous recovery. Vasovagal (neurocardiogenic) syncope is the most common one in children. The head-up Tilt Test is used as one of the diagnostic criteria and can have three different types of response: a vasovagal one (either vasodepressor, cardioinhibitory or mixed types), a dysautonomic one, and orthostatic postural tachycardia syndrome. **Methods:** Cross-sectional, observational clinical study with data collection from the electronic medical records of children and adolescents diagnosed with syncope submitted to the head-up tilt test in a tertiary hospital. The significance level was 5%. **Results:** Syncope was clinically diagnosed in 378 patients, and 209 (55.3%) of them were submitted to the head-up tilt test. A total of 212 tests were performed, with a statistically significant predominance of negative results (58.8%). The neurocardiogenic response (89.5%) prevailed over dysautonomia and orthostatic postural tachycardia syndrome. The vasodepressor type response was more frequent than the mixed response, which was more frequent than the cardioinhibitory response. The median age was higher in patients undergoing the head-up tilt test (152.5 months x 115.4 months; $p<0.05$), as well as in those who had a positive result (170.7 months x 138.8 months; $p<0.05$). **Conclusion:** Most patients had a negative result, revealing that the exam was performed without proper indication for more than half of them. The indication for the head-up tilt test needs to be based on more objective criteria, otherwise it is an unnecessary and costly practice.

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INTRODUCTION

Syncope is a sudden and transient loss of consciousness associated with loss of postural tone, followed by spontaneous recovery, and approximately 15% of individuals experience an episode before the end of adolescence. Although the etiology of syncopal events in children is more often benign, syncope may also occur as a result of more serious conditions (usually cardiac) with potential for sudden death. The vast majority of cases of syncope in the pediatric age group represent benign alterations in vasomotor tone[1]. Syncopes may be autonomic non-cardiac, cardiac, neuropsychiatric, or metabolic. Autonomic non-cardiac syncopes may result from orthostatic intolerance (vasovagal/neurocardiogenic syncope, orthostatic hypotension, and postural orthostatic tachycardia syndrome), exercise-related syncope, situational syncopes (apnea, cough, micturition, defecation, post-exercise, weight lifting, postprandial, carotid sinus hypersensitivity), and excessive vagal tone. Vasovagal syncopes are mediated by orthostatic stress or emotional stress, pain, or fear[2] (Figure 1).

Among the cardiac causes of syncope, which although rare may be associated with a risk of sudden death, are arrhythmias such as long QT syndrome and Wolff–Parkinson–White syndrome, side effects of cardiotoxic agents, structural heart diseases, and congenital heart diseases[1]. Some aspects of the clinical history may suggest cardiac causes, such as syncope during exercise and syncope without prodromes[8]. Hydroelectrolytic disturbances may be the underlying cause of arrhythmias, with potassium abnormalities being the most frequent[1]. Long QT syndrome is a disorder of myocardial repolarization that can potentially degenerate into polymorphic ventricular tachycardia; acquired causes of the syndrome are generally related to hydroelectrolytic disturbances or medications[1]. Pre-excitation syndromes, such as Wolff–Parkinson–White, are described in prospective studies of patients who experienced sudden death; in these patients, accessory conduction pathways promote ventricular pre-excitation, which can lead to tachycardia and arrhythmias[1]. Medications and drugs may have cardiotoxic effects and trigger arrhythmias. Structural heart diseases and congenital heart diseases may also be causes of sudden death[1]. Hypoglycemia is a metabolic cause of syncope[1]. In these cases, the patient may present prodromal symptoms such as tremors, sweating, lethargy, and mental confusion, and may develop seizures and even coma when not identified early. Vasovagal syncope is the most common cause of syncope in children, with an incidence of 64–73% of cases. A thorough history is a useful tool to identify the etiology and guide further evaluation of a syncopal event. In this regard, the context preceding the episode must be identified, such as the child's position and the activity in which they were involved. Children who present vasovagal syncope usually remained upright for a long period or changed position rapidly shortly before the event, and may also have been exposed to a trigger such as pain or emotional stress. In addition, individuals with vasovagal syncope frequently report prodromal symptoms such as dizziness, sweating, nausea, weakness, and visual disturbances, and may experience fatigue for hours after the event. Other factors to be analyzed include the patient's medical history and that of their family members. The most frequent mechanism for vasovagal syncope is a mixed hemodynamic response that combines cardioinhibitory characteristics (cardiac slowing, usually to up to 30 beats per minute and/or pauses > 5 seconds) and vasodepressor characteristics (a drop in systemic blood pressure independent of changes in heart rate). It is uncommon for a patient to present syncope characterized entirely by vasodepressor or cardioinhibitory responses. These

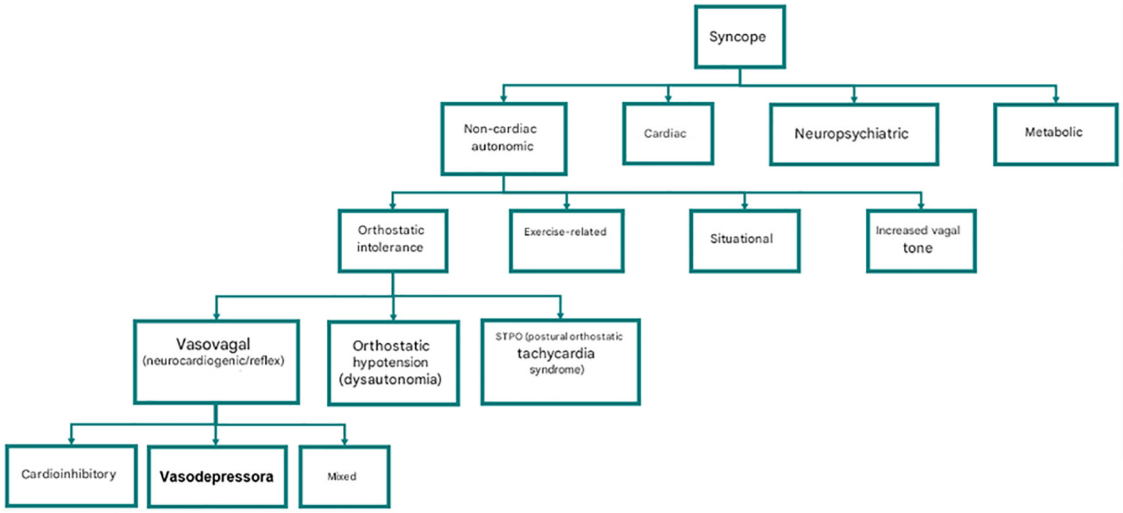


Figure 1. Classification of syncopes. Source: Image by the author.

responses arise from changes in autonomic activation, either an increase in parasympathetic activation in the cardioinhibitory response or inhibition of peripheral sympathetic activity in the vasodepressor response[5]. In most cases, the evaluation of syncope is performed through history taking, physical examination, and blood pressure measurements in orthostatic and supine positions. Complementary tests may be necessary, such as electrocardiography (ECG) and the tilt test[6]. The tilt test (head-up tilt test) is a valuable tool and, when correctly indicated, can avoid other unnecessary tests in the investigation of syncope[6]. In the pediatric population, its sensitivity and specificity may be as high as 76.6% and 86.7%, respectively[6]. The test should be indicated for patients with recurrent episodes of syncope or a single episode of syncope with a high risk of physical injury or occupational risk, and it may also be useful in the differential diagnosis with neurological causes of loss of consciousness[7]. In addition, it is used for diagnostic confirmation in cases of vasovagal syncope when the initial clinical evaluation is uncertain, and for defining the type of vasovagal syncope response, which will influence patient counseling and treatment[7]. However, the test is contraindicated in patients with severe coronary artery disease and/or cerebrovascular disease, in whom hypotension may cause myocardial and cerebral ischemia, and it should also not be performed in pregnant women[7]. Typically, the tilt test is performed in a specialized laboratory with the presence of a motorized tilt table that elevates the patient to 60–70 degrees above the supine position rapidly, in less than 10 seconds (figure 2). The patient should fast for 3–4 hours before the examination, and venous access should be established[7]. Continuous cardiac monitoring by electrocardiogram and blood pressure measurement are employed throughout the test[7].

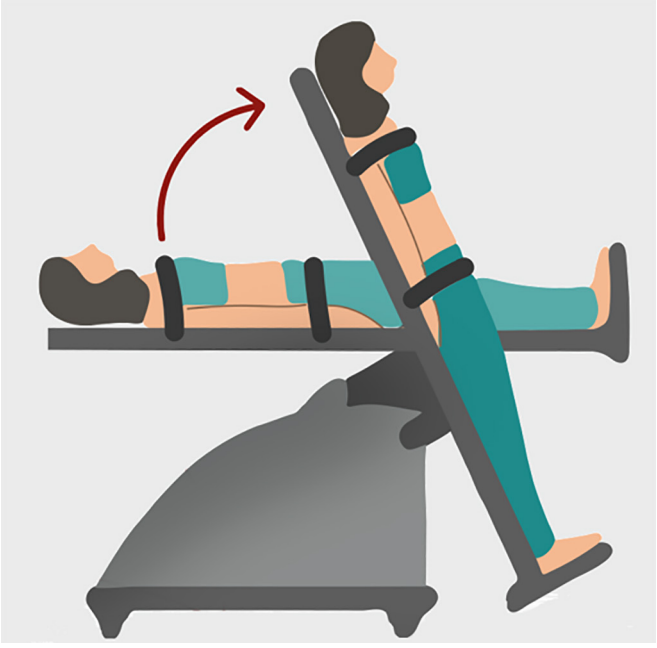


Figure 2. Illustration of the performance of the tilt test. Source: Hospital SOS Cárdio Facebook page[1]

[1]Available at: https://www.facebook.com/hospitalsoscardiosc/fotos/a.1495828237401817/2749406752043953/. Accessed on Jan 10, 2024.

To initiate the test, the patient should remain in the supine position for 10–20 minutes, and monitoring is started. After that, the table is tilted to 60–70 degrees, a position in which the patient may remain for 20–45 minutes, while symptoms and electrocardiographic and blood pressure changes are observed[7]. Subsequently, if the initial test response is negative, some medications, such as isoproterenol or nitroglycerin, may be administered as a way to provoke a reflex response. In these cases, the test is usually performed for an additional 10 or 20 minutes, and medication doses vary according to the protocol used[7].

The test is indicated for patients with suspected vasovagal syncope, orthostatic hypotension, postural orthostatic tachycardia syndrome, or psychogenic pseudosyncope. These etiologies should be considered if the tilt test reproduces symptoms consistent with the characteristic circulatory pattern of these conditions. It also serves to educate the patient to recognize symptoms and learn physical maneuvers to prevent syncope[8].

A positive test for vasovagal syncope is characterized by the development of syncope associated with a cardioinhibitory and/or vasodepressor response, triggering symptomatic hypotension. The vasovagal reflex observed during a tilt test may reflect a given patient's predisposition to vasovagal syncope; however, the physiological response during the test may differ from clinically experienced episodes. Therefore, tilt test findings should always be interpreted in the context of the patient's history and spontaneous symptoms[7]. During the examination, four possible responses may occur: in patients with reflex syncope, there is a significant drop in blood pressure or heart rate accompanied by loss of consciousness or inability to maintain posture[5,7]. In cases of orthostatic hypotension, a progressive and slow decrease in systolic blood pressure is observed, with or without symptoms[7,9], without bradycardia; whereas in postural orthostatic tachycardia syndrome, there is a sustained increase in heart rate greater than 30 beats per minute or an increase to 120 beats per minute or higher within the first 10 minutes of the passive phase[7,10]. In psychogenic pseudosyncope, there may be an inability to maintain body position without a significant drop in blood pressure or heart rate[7,11].

However, the tilt test may present false-positive and false-negative results and must be interpreted in light of the patients' clinical presentation. In a study of 70 normal adolescents who had never experienced syncope or presyncope, tilting to 70° or 80° with the head up for up to 30 minutes resulted in significant symptoms, with a significant number of syncopal episodes, in addition to two episodes of asystole[12,13], showing that the specificity of the examination in a random population was low; however, in a selected population, at

least 85% become symptomatic with the tilt test, indicating excellent sensitivity.

There are few data available in the literature evaluating the response of pediatric patients with syncope to the tilt test.

METHODOLOGY

This is an observational cross-sectional clinical study, with data collection from children and adolescents diagnosed with syncope who were seen at the cardiology outpatient clinic of a tertiary hospital in the interior of the state of São Paulo and who underwent the tilt test between January 1, 1996, and December 31, 2021. The study was approved by the ethics committee (CAAE: 58943022.0.0000.5411). The selection of patients diagnosed with syncope was carried out through consultation of the service's database. After patient selection, children and adolescents who were followed at the pediatric cardiology outpatient clinic of the service during the period described above, with a clinical diagnosis of syncope and who underwent the tilt test, were included. Data were entered into an electronic spreadsheet and submitted to appropriate statistical analysis, considering a significance level of 5%. Nonparametric tests were used, considering that the Kolmogorov test showed that the distribution of numerical variables did not follow a normal distribution. The study of the association between sex and tilt test results in patients with syncope was performed using the Goodman test involving contrasts between multinomial proportions. The nonparametric analysis of variance technique for a two-factor model was also applied, complemented by Dunn's multiple comparison test.

RESULTS

During the study period, 378 patients were clinically diagnosed with syncope, of whom 209 (55.3%) underwent the tilt test, with 55.5% female and 44.4% male. The results are shown in the tables below. Analyzing the distribution of tilt test performance according to sex, 55.4% of male patients and 55.2% of female patients underwent the test. A total of 209 tests were performed, and among them there was a predominance of negative results (58.8%; $p < 0.05$). Among male patients, 41.9% had a positive test, while 58.1% had a negative test. Regarding female patients, 40.5% of tests were positive and 59.5% were negative. There was no statistical association between tilt test results and patient sex. Considering all tests with positive results (41.2%), there was a significant difference according to the type of response, with predominance of the vasovagal response (89.5%), with the vasodepressor-type response (40.7%) being more frequent than the mixed response (31.4%), which in turn was more frequent than the cardioinhibitory-type response (17.4%) (Table 1). The frequency of results was configured as follows: (Vasodepressor = Mixed) > (Cardioinhibitory = POTS) > Dysautonomia. Thus, vasodepressor and mixed responses were significantly more predominant than the others.

Table 1. Distribution of positive results according to type of response to the tilt test.

Type of response	N (%)
Dysautonomia	1 (1.2)
POTS	8 (9.3)
Vasodepressor	35 (40.7)*
Cardioinhibitory	15 (17.4)
Mixed	27 (31.4)*
Total	**86 (100)**

*$p < 0.05$ (vasodepressor and mixed responses *vs.* other responses - Goodman test); N = number; % = percentage.
POTS = postural orthostatic tachycardia syndrome.

There was a significant difference between the median age (in months of life) of patients who underwent the tilt test and those who did not (median age in males: 153.4 months in patients who underwent the test and 115.4 months in patients who did not; median age in females: 151.8 months in patients who underwent the test and 115.3 months in those who did not), with higher medians among patients who underwent complementary testing; however, there was no significant difference when comparing patients who did or did not undergo the tilt test according to sex. Regarding age (in months of life) and sex of patients with negative and positive tilt test results, in males the mean age was 140.7 months in patients with a negative result and 169.6 months in those with a positive result, while in females the mean age was 130.9 months in patients with a negative result and 171.5 months in those with a positive result. There was no significant difference between sexes; however, there was a significant difference in age, with higher ages in patients with positive tests. Analyzing the distribution of median and interquartile range of age (in months) according to the type of response in the tilt test and according to sex, there was a significant difference in the cardioinhibitory-type response, with a lower value in males (168.5 months, whereas in females a median of 180.8 months was found), showing that the cardioinhibitory response predominated in younger male patients. There was no statistically significant difference among vasodepressor, mixed, and POTS responses when correlated with age and sex of the patients (Table 2).

DISCUSSION

Syncope is a complaint that frequently leads children to seek medical care, especially in urgent and emergency

Table 2. Descriptive measures of age according to type of response on the tilt test and sex.

Sex	POTS – Md (Q1–Q3)	Vasodepressor – Md (Q1–Q3)	Cardioinhibitory – Md (Q1–Q3)	Mixed – Md (Q1–Q3)
Male	172.7 (147.2–192.3)	177.1 (103.4–231.8)	168.5* (87.7–184.4)	158.2 (100.8–184.1)
Female	165.7 (137.6–184.5)	171.2 (121.5–204.6)	180.8* (174.3–193.9)	169.2 (118.9–221.4)

*$p < 0.05$ (male vs. female age – Dunn test) Md = median age in months; Q1 = first quartile; Q3 = third quartile.

settings. Approximately 15% of patients will experience at least one episode of syncope before the age of 18[16]. In this context, the tilt test is important to assist in the etiological diagnosis of syncope and also in the differential diagnosis with other conditions, such as epilepsy[16]. This study aimed to evaluate the types of responses to the tilt test performed in pediatric patients followed at a Pediatric Cardiology outpatient clinic of a tertiary hospital. Based on the data found in the study, most tilt tests (58.8%) were negative, demonstrating that many patients underwent the test without presenting vasovagal syncope, dysautonomia, or POTS. In these cases, the tilt test was indicated without real necessity. Moreover, in children, the requirements for performing the test, such as fasting, are not always feasible. Among the positive test responses, there was a predominance of vasodepressor (40.7%) and mixed (31.4%) responses, showing that vasovagal syncope was more prevalent among patients. In the literature, a higher prevalence of vasovagal etiology is described, with the mixed response being most commonly found[5]. OLIVEIRA et al. published a study in 2023 evaluating 73 patients aged between 6 and 18 years in Minas Gerais and found vasodepressor response rates of 77.4%[6], corroborating our study. In addition, no association was found between female and male sex and the presence or absence of the tilt test. In the study by OLIVEIRA et al., there was also no statistically significant difference between sexes regarding performance of the test[6]. However, in both sexes, the age of patients who did not undergo the test was lower than that of those who did, showing that the tilt test is more frequently applied in older patients. Analyzing age and test positivity, the study showed that, in both sexes, the age of patients with negative results was lower than that of those with positive results; that is, negative tests predominated in younger children, indicating that the etiology of syncope in these patients is not related to vasovagal, dysautonomic, or POTS causes. In this context, it can be stated that performing the tilt test in younger children is, in most cases, unnecessary. A review article by the Brazilian Society of Cardiology, published in 2010[17], which describes the recommended methodology for performing the tilt test, reinforces the need for fasting for at least 4 hours before the examination, rest for 10–20 minutes before starting the test, venipuncture, and continuous ECG monitoring and blood pressure measurements during the examination[17]. Given the requirements for proper test performance, it is possible to question the feasibility of performing the test in very young children; however, no formal contraindication based solely on patient age was found in the literature. Given the difficulty in classifying and evaluating the complementary tests required for patients with syncope, PARIS et al. published a study in 2016 in the *Journal of the American Heart Association* analyzing a tool for standardizing clinical evaluation and management to guide decision-making in these patients (SCAMPS)[18]. The study evaluated patients aged 7 to 21 years over a 2.5-year period with a clinical diagnosis of syncope. The tool used data such as clinical history, family history of heart disease, orthostatic vital signs, physical examination, and electrocardiogram, in addition to subjective scales to assess severity and stratify patients who would require additional investigation. Among the results, 85% of patients presented neurocardiogenic syncope, in agreement with our study, and most were female, unlike our findings, in which no sex difference was observed. Furthermore, the electrocardiogram was considered an examination with high negative predictive value, used to exclude serious heart diseases such as Wolff–Parkinson–White syndrome and long QT syndrome. The authors concluded that the methodology used (SCAMP) was effective in distinguishing patients with greater severity and, therefore, with a need for complementary tests, and also concluded that most patients can be evaluated in an outpatient setting using minimal healthcare resources. This study aimed to evaluate the characteristics of patients who underwent the tilt test. Most patients had negative test results, showing that the test was performed without appropriate indication in more than half of the patients. In addition, younger patients predominantly presented negative tilt tests, indicating that the origin of syncope is not vasovagal, postural orthostatic tachycardia syndrome, or dysautonomia. Therefore, the indication for performing the tilt test must be based on more objective criteria; otherwise, it becomes an unnecessary and costly practice. Further studies are needed to develop and implement flowcharts for the management of patients with syncope and to define precise indications for complementary tests.

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