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# The impact of school periods and long holiday periods on the occurrence of neurally mediated syncope in children

Shuo Wang<sup>1,2</sup>, Ping Liu<sup>1</sup>, Xiaohui Gong<sup>3</sup>, Jizhi Xu<sup>3</sup>, Tuoyu Gan<sup>3</sup>, Yuwen Wang<sup>1</sup>, Hong Cai<sup>1</sup>, Runmei Zou<sup>1</sup> and Cheng Wang<sup>2\*</sup> 

## Abstract

**Objective** To explore the impact of school periods and long holiday periods on the occurrence of neurally mediated syncope (NMS) in children.

**Methods** A retrospective analysis was conducted on 262 children with NMS. The children were aged 4–17 years, 119 males. 244 cases were diagnosed as vasovagal syncope, and 18 cases as postural orthostatic tachycardia syndrome. The data on the age, sex, syncope triggers, hemodynamic types, family history of syncope of children with syncope during long holiday periods group ( $n=68$ ) and school periods group ( $n=194$ ) were compared.

**Results** (1) Incidence of syncope: The incidence of syncope during school periods (74.05%) was higher than that during long holiday periods (25.95%). (2) Comparison of sex and triggers: The constituent ratio of females with syncope during school periods was higher than that of males ( $P<0.05$ ). Among the triggers, the proportion of sudden postural change during long holiday periods was higher than that during school periods (26.47% vs. 21.13%,  $P<0.05$ ). (3) Univariate analysis: Situational syncope was a potential protective factor when syncope occurred during school periods (OR 0.23, 95%CI 0.07–0.76,  $P<0.05$ ), and being female was a potential risk factor (OR 1.92, 95%CI 1.10–3.35,  $P<0.05$ ). (4) Comparison of multiple models: In the risk of syncope occurring during school periods, situational syncope reduced the risk by 79% compared with no trigger, and being female increased the risk by 78% compared with being male.

**Conclusions** The occurrence of NMS-related syncope events in children is associated with school periods and long holiday periods. During school periods, being female is a risk factor for syncope, while situational syncope is a protective factor.

**Keywords** Neurally mediated syncope, Hemodynamic type, Head-up Tilt test, Children, School and holidays

\*Correspondence:

Cheng Wang  
wangcheng2nd@csu.edu.cn

<sup>1</sup>Department of Pediatric Cardiovasculology, Children's Medical Center, The Second Xiangya Hospital, Central South University, Changsha 410011, Hunan, China

<sup>2</sup>Department of Pediatrics, Xiangya Hospital, Central South University, Changsha 410008, Hunan, China

<sup>3</sup>Department of Pediatrics, Changsha Hospital for Maternal & Child Health Care Affiliated to Hunan Normal University, Changsha 410007, China



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## Introduction

Biological rhythms refer to the periodic changes that occur inside an organism, which can be divided into circadian rhythms, lunar rhythms, and annual rhythms. The normal physiological functions of the human body are closely related to biological rhythms. The onset time of many diseases and the time of drug application also show obvious circadian rhythm phenomena [1–3]. Neurally mediated syncope (NMS) is a common type of syncope in children and adolescents [4–6], which also exhibits circadian rhythm changes and shows different rhythms in different ages, sex, and regions [7]. In children with NMS, heart rate (HR) and blood pressure (BP) are lower at night and increase after waking up, reaching a peak around 10:00 [8]. The corrected QT interval dispersion is higher in the early morning and late at night than in other time periods [9]. In children with a positive head-up tilt test (HUTT), syncope attacks are concentrated in the morning, especially from 10:00 to 12:00, while in children with a negative HUTT, syncope attacks are concentrated in the late afternoon and evening, especially from 14:00 to 18:00 [10]. Liao et al. [11] reported that the peak of syncope attacks in 411 syncope patients aged 3–68 years old (including children and adults) occurred between 6:00 and 12:00. During this time period, the frequency of attacks was higher in males than in females, while at night, the frequency was higher in females than in males. The younger the patients were, the higher the probability of syncope attacks in the morning, and the older the patients were, the more frequently syncope attacks occurred at night. Mineda et al. [12] also reported that the peak of syncope attacks in 67.5% of adult NMS patients occurred between 6:00 and 12:00, and among the patients who had their first syncope attack during this time period, 78% of them had their subsequent syncope attacks also during this time period.

Ultradian rhythms refer to a series of biological events that occur periodically according to fixed dates and times. They can adapt to environmental changes and use external triggers to have an impact on the rhythms and behaviors of organisms. NMS also has ultradian rhythms. The frequency of syncope attacks in young and middle-aged patients with vasovagal syncope (VVS) is higher on weekdays than on weekends, with Thursday being the most obvious [13]. Syncope attacks occurred in 79.2% of syncope patients over 40 years old between 4:00 and 16:00. Among them, orthostatic syncope mainly occurred in the early morning, more frequently on weekdays and less frequently on weekends. Syncope attacks were more common in winter and less common in summer [14]. The seasonal rhythm phenomenon of syncope reflects to some extent the correlation between syncope and climate and temperature, as well as the variability of temperature during a day, such as the increase in the temperature

difference between day and night, moving from outdoors to indoors, or from a room to a bathroom. In terms of months and seasons, Anderson et al. [15] believed that the incidence of syncope was higher among syncope patients over 16 years old from December to May. Galli et al. [16] reported that among 770 syncope patients over 18 years old who visited the emergency department, the monthly incidence did not change due to seasonal changes from January to May, but decreased significantly from June to July.

The above research results show that the clinical syncope symptoms of NMS present biological rhythm phenomena. Children are in the learning stage (school periods) and have summer and winter vacations (long holiday periods) every year. Whether children's school periods or long holiday periods have an impact on the occurrence of NMS syncope has not been reported yet.

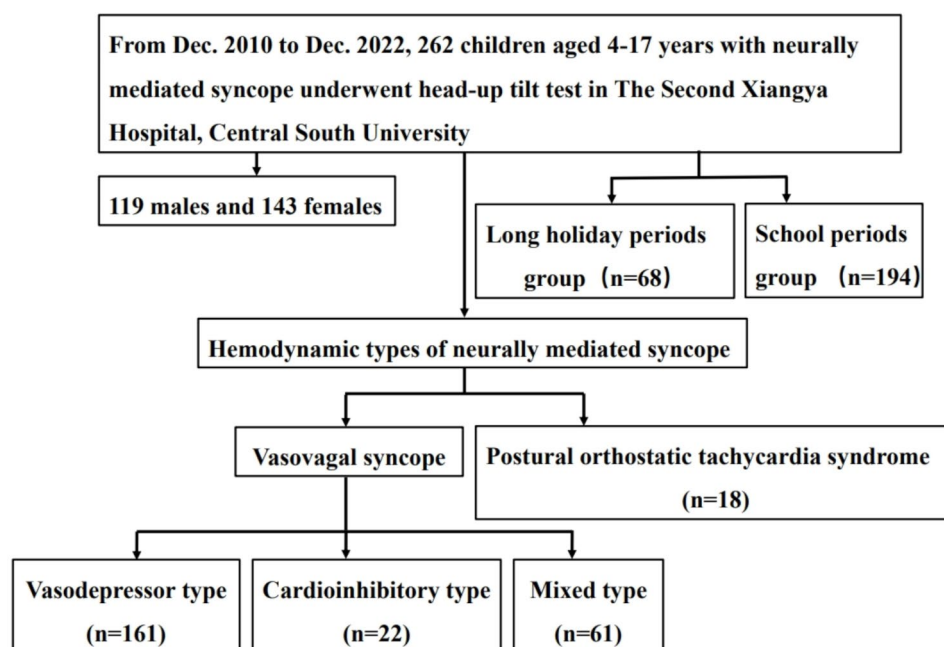
## Materials and methods

### Research population

A retrospective analysis was conducted on 262 children with NMS who visited the outpatient department or were hospitalized in The Second Xiangya Hospital, Central South University from December 2010 to December 2022 and had syncope as the first clinical manifestation. The children were aged 4–17 years, with an average age of  $11.26 \pm 2.41$  years (Fig. 1). All cases had undergone detailed medical history inquiries, physical examinations, 12-lead electrocardiograms, chest X-ray films, echocardiograms, electroencephalograms, cranial magnetic resonance imaging, blood biochemical tests (myocardial enzymes, fasting blood glucose) and other examinations to exclude organic diseases of the chest wall, heart, lungs, brain and other organs, as well as immune and metabolic diseases. The HUTT was completed after obtaining the written informed consent of the examinees or their guardians. The HUTT is a non-invasive examination and has been approved by the Hospital's Medical Ethics Committee of The Second Xiangya Hospital, Central South University [Ethical Audit No. Study 249(2022)].

### Head-up tilt test and different hemodynamic criteria

All subjects underwent HUTT. The HUTT is divided into basic HUTT (BHUT) and sublingual nitroglycerin-provoked HUTT (SNHUT), and the operation is carried out according to the method specified in the guide [4, 5]. VVS: During the HUTT, if syncope or presyncope symptoms (such as dizziness, headache, chest tightness, palpitation, nausea, vomiting, pallor, cold sweats, blurred vision, hearing impairment or abdominal pain) occur accompanied by one of the following conditions, it is considered positive reaction: (1) A decrease in BP (systolic BP  $\leq 80$  mmHg or diastolic BP  $\leq 50$  mmHg or a mean BP drop  $\geq 25\%$ ); (2) A decrease in HR (for children aged



**Fig. 1** Flow chart

4–6 years < 75 bpm, for those aged 6–8 years < 65 bpm, and for those over 8 years old < 60 bpm); (3) The appearance of sinus arrest or junctional escape rhythm; (4) Atrioventricular block and cardiac arrest lasting for as long as 3 s. VVS classification: (1) VVS-VI: mainly characterized by a decrease in BP with no significant change in HR; (2) VVS-CI: mainly characterized by a decrease in HR with no significant change in BP; (3) VVS-M: both HR and BP decrease. Postural orthostatic tachycardia syndrome (POTS): During the first 10 min of the BHUT, if the HR increases by  $\geq 40$  bpm compared to the supine position and/or the maximum HR reaches the standard (for children aged 4–12 years  $\geq 130$  bpm, for those aged 12–18 years  $\geq 125$  bpm), while the decrease in systolic BP is < 20 mmHg and the decrease in diastolic BP is < 10 mmHg [4, 5].

#### Time definition

Holiday periods (n=68): February, July, and August; School periods (n=194): January, March, April, May, June, September, October, November, and December.

#### Observation indicators

Age, sex, triggers for syncope (standing position, sitting position, sudden postural change (body position quickly changing to an upright position from supine or sitting or squatting), exercise, situational or without triggers), hemodynamic types (VVS-VI, VVS-CI, VVS-M and POTS), family history of syncope (yes or no).

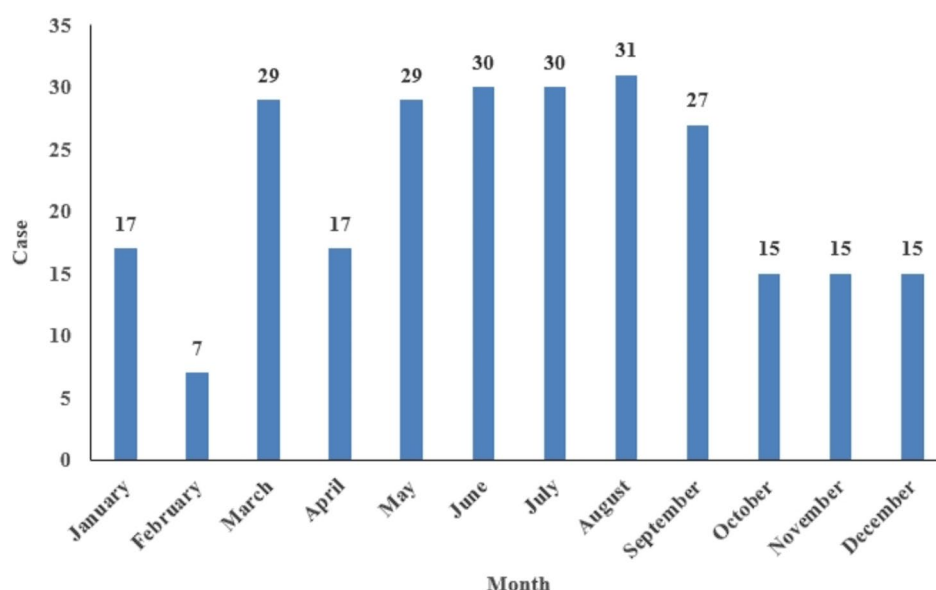
#### Statistical methods

The statistical software packages used were R (Version 3.6.1) (<http://www.R-project.org>, the R Foundation) and EmpowerStats (<http://www.empowerstats.com>, X & Y Solutions, Inc, Boston, MA). If continuous variables were normally distributed, they were expressed as mean  $\pm$  SD; categorical variables were expressed as frequencies or percentages. *T*-tests (for normally distributed variables) or  $\chi^2$ -tests (for categorical variables) were conducted as needed. Univariate analysis and multivariate Logistic regression analysis were used to analyze the possible associations between syncope and multiple factors. A *P*-value < 0.05 (two-tailed) was considered statistically significant.

#### Results

##### Comparison of syncope occurrence periods

The incidence of syncope during school periods (74.05%) was higher than that during long holiday periods (25.95%). The frequency of syncope is classified by season each year. In spring (from January to March), it accounts for 20.23% (53 out of 262 cases), in summer (from April to June), it is 29.01% (76 out of 262 cases), in autumn (from July to September), it is 33.59% (88 out of 262 cases), and in winter (from October to December), it is 17.18% (45 out of 262 cases). Evidently, summer and autumn are the seasons with a high incidence of syncope (Fig. 2).



**Fig. 2** Histogram of monthly syncope in children with NMS

**Table 1** Comparison of general data of syncope occurrence periods [Mean  $\pm$  SD, n (%)]

	Holiday periods group (n=68)	School periods group (n=194)	Standardize diff.	P-value
Age (years)	11.41 $\pm$ 2.20	11.21 $\pm$ 2.48	0.09 (-0.19,0.36)	0.556
Sex			0.33 (0.05,0.60)	0.022
Male	39 (57.35)	80 (41.24)		
Female	29 (42.65)	114 (58.76)		
Triggers for syncope			0.46 (0.18,0.74)	0.027
No	9 (13.24)	28 (14.43)		
Standing	21 (30.88)	78 (40.21)		
Sitting	3 (4.41)	16 (8.25)		
Sudden postural change	18 (26.47)	41 (21.13)		
Exercise	7 (10.29)	24 (12.37)		
Situational	10 (14.71)	7 (3.61)		
Hemodynamic type			0.27 (-0.01,0.54)	0.331
VVS-VI	44 (64.71)	117 (60.31)		
VVS-CI	8 (11.76)	14 (7.22)		
VVS-M	11 (16.18)	50 (25.77)		
POTS	5 (7.35)	13 (6.70)		
Family history of syncope			0.28 (0.01,0.56)	0.062
No	63 (92.65)	162 (83.51)		
Yes	5 (7.35)	32 (16.49)		

VVS-VI: vasodepressor type vasovagal syncope, VVS-CI: cardioinhibitory type vasovagal syncope, VVS-M: mixed type vasovagal syncope, POTS: postural orthostatic tachycardia syndrome

### Comparison of sex and triggers

There were differences in sex and different triggers between school periods and holiday periods ( $P < 0.05$ ). The constituent ratio of females with syncope during school periods was higher than that of males ( $P < 0.05$ ). Among the triggers, the proportion of sudden postural change during long holiday periods was higher than that during school periods ( $P < 0.05$ ). There was no statistically significant difference in age, hemodynamic types,

family history of syncope between the two groups of school periods and holiday periods ( $P > 0.05$ ) (Table 1).

### Univariate analysis

Situational syncope was a potential protective factor for syncope occurring during school periods, while being female was a potential risk factor for syncope occurring during school periods (Table 2).

**Table 2** Univariate analysis of incidence of syncope [Mean  $\pm$  SD, n (%)]

	Statistics	OR (95%CI)	P-value
Age (years)	11.26 ± 2.41	0.97 (0.86,1.09)	0.554
Sex			
Male	119 (45.42)	1.0	
Female	143 (54.58)	1.92 (1.10,3.35)	0.023
Triggers for syncope			
No	37 (14.12)	1.0	
Standing	99 (37.79)	1.19 (0.49,2.91)	0.697
Sitting	19 (7.25)	1.71 (0.40,7.26)	0.464
Sudden postural change	59 (22.52)	0.73 (0.29,1.86)	0.513
Exercise	31 (11.83)	1.10 (0.36,3.41)	0.866
Situational	17 (6.49)	0.23 (0.07,0.76)	0.017
Hemodynamic type			
VVS-VI	161 (61.45)	1.0	
VVS-CI	22 (8.40)	0.66 (0.26,1.68)	0.381
VVS-M	61 (23.28)	1.71 (0.82,3.58)	0.155
POTS	18 (6.87)	0.98 (0.33,2.90)	0.968
Family history of syncope			
No	225 (85.88)	1.0	
Yes	37 (14.12)	2.49 (0.93,6.67)	0.070

Result Variable: Duration of syncope occurrence (0, long holiday periods group; 1, school periods group)

Exposure variables: age, sex, height, triggers for syncope, hemodynamic type, family history of syncope

Adjust variables: none

## Comparison of multiple models

Since situational syncope and being female showed protective and risk effects respectively in the univariate analysis, we constructed two models to further demonstrate the stability of their relationships. After adjusting for age and sex factors, compared with the univariate results, both showed stable efficacy and unchanged efficacy direction (OR fluctuation < 10%). Subsequently, after we further adjusted for hemodynamic types, family history of syncope, their efficacy again demonstrated the same stability as Model 1 (OR fluctuation < 10%). Compared with no trigger, situational syncope reduced the risk of syncope occurring during school periods by 79%; compared with males, females increased the risk of syncope occurring during school periods by 78% (Table 3).

## Discussion

There are significant differences in learning environment, learning pressure, living rhythm, and activity content between students' school periods and long holiday periods. During school periods, school class hours are systematic and standardized, the time arrangement is relatively tight, the learning tasks are heavy, the social contacts are relatively limited, and the time for entertainment and leisure is short. During long holiday periods, however, the time arrangement is relatively free, without strict curriculum and work-rest restrictions. The social

**Table 3** Comparison of multiple models of the relationship between triggers, sex and duration of syncope occurrence

Triggers for syncope						Sex			
Model 1			Model 2			Model 1		Model 2	
	OR (95%CI)	P-value		OR (95%CI)	P-value		OR (95%CI)	P-value	P-value
No	1.0			1.0		男	1.0		1.0
Standing	1.04 (0.42, 2.58)	0.931		0.97 (0.39, 2.43)	0.943	女	1.97 (1.12, 3.45)	0.019	1.78 (0.98, 3.23)
Sitting	1.70 (0.40, 7.29)	0.477		1.93 (0.44, 8.42)	0.380				
Sudden postural change	0.67 (0.26, 1.73)	0.413		0.60 (0.23, 1.58)	0.304				
Exercise	0.97 (0.31, 3.05)	0.958		0.94 (0.30, 2.99)	0.920				
Situational	0.21 (0.06, 0.73)	0.014		0.21 (0.06, 0.74)	0.016				
Result Variable: Duration of syncope occurrence (0, long holiday periods group; 1, school periods group)									
Exposure variables: Triggers for syncope									
Model 1 in triggers for syncope adjusted for: age, sex									
Model 2 in triggers for syncope adjusted for: age, sex, hemodynamic type, family history of syncope									
Model 1 in sex adjusted for: age									
Model 2 in sex adjusted for: age, hemodynamic type, family history of syncope									



scope is relatively wider, the interaction time with family members increases significantly, and there is more time for entertainment and leisure. The research data of this paper show that the frequency of syncope in children with NMS is higher during school periods than during long holiday periods, and it is relatively higher in summer and autumn. The higher incidence of syncope during school periods may be related to factors such as students' intense study, high pressure, limited activity range, and hot environmental temperature and climate. Research has found that temperature, climate, or season all have an impact on NMS. High temperatures can promote the occurrence of syncope while standing. Galli et al. [17] evaluated the impact of changes in the maximum body temperature on the emergency room visits of syncope patients. In June-July, although the maximum body temperature itself is relatively high, the variability of the maximum body temperature decreases, and the number of emergency room visits for syncope decreases. Emergency room visits for syncope are related to the increase in temperature variability, not the daily maximum temperature, indicating that climate change may have a significant impact on the occurrence pattern of syncope. Alexander et al. [18] studied the relationship between the monthly average of meteorological variables in public ambulance emergency service calls and the monthly frequency of various diseases. Except for cardiac arrest and angina pectoris, other diseases showed seasonal characteristics. Except for mental illnesses, the diseases that have a certain correlation with meteorological variables have the highest occurrence frequency in winter. Temperature-related variables are the meteorological indicators that have the greatest correlation with diseases. The treatment of antihypertensive drugs is also related to the season. Huang et al. [19, 20] reported that in the dry summer, patients living in desert areas have an increased chance of syncope attacks when taking the same dose of antihypertensive drugs. Among patients taking antihypertensive drugs, the incidence of syncope secondary to dehydration or orthostatic hypotension in summer (45%) is significantly higher than that in winter (26%). In summer, the incidence of syncope in elderly patients (63%) is significantly higher than that in young patients (37%). It is believed that in the arid desert climate and among people taking antihypertensive drugs, the incidence of syncope increases in summer.

Research shows that the proportion of syncope cases among females is higher than that among males during school periods. Univariate and multi-model studies suggest that being female is a potential risk factor for syncope during school periods. Compared with males, the risk of syncope during school periods increases by 78%.

The higher incidence of syncope in females may be related to sex differences in children's muscle mass,

muscle enzymes, and venous compliance. Thijs et al. [21] believe that males have more muscle mass and stronger muscle pump contractions than females, which provides a larger blood pool and more venous return, reducing the likelihood of syncope caused by the Bezold-Jarisch reflex. Zhang et al. [22] also found that the serum creatine kinase (CK) level in female VVS children is lower than that in male VVS children. Wang et al. [23, 24] reported that the risk of syncope in female VVS children is 36% higher than that in male VVS children. Female children are an independent risk factor for syncope. Skoog et al. [25] reported that the venous compliance of female VVS patients decreases significantly under low venous pressure, and the decrease in venous compliance under low venous pressure may have an adverse effect on the mobilization of peripheral venous blood to the central circulation in female VVS patients under hypovolemic circulatory stress.

Among the factors inducing syncope, the chance of sudden postural changes is significantly higher during long holiday periods than during school periods. This may be related to factors such as an increase in students' outdoor activities (such as climbing, swimming, etc.) and more frequent sudden postural changes (such as riding roller coaster and other exciting amusement facilities) during long holiday periods.

Situational syncope refers to a sudden transient loss of consciousness that occurs in specific situations or under specific stimuli. The causes include urination (50.85%), defecation (15.82%), bathing (10.45%), swallowing (6.50%), coughing (4.80%), post-meal (3.95%), singing (3.11%), tooth-brushing (2.26%) and hair-combing (2.26%). 34.75% of situational syncope cases occur in the age group of 10–19 years old, and 74.01% of situational syncope events occur in an upright position [26]. Its mechanism is mainly related to factors such as abnormal vasomotor function, autonomic reflex disorders, and reduced cardiac output. This study showed that situational syncope was a potential protective factor for students to have syncope during school periods, with a 79% lower risk of syncope during school periods compared to no trigger. This may be because during school periods, students' study and life are relatively regular, teachers' health education makes students pay more attention to the prevention of syncope psychologically. Also, students have fewer opportunities to contact the outside world during school periods. For example, it is less likely to see blood or needles in medical settings during school periods, or the break time between classes is short, so the time for urination or defecation is relatively short, resulting in a reduced chance of situational syncope. During long holiday periods, however, students are more relaxed psychologically, free from study pressure, have more opportunities to go out and contact society, have

a relatively longer time for urination or defecation, and also have an increased chance of seeing blood or needles in medical settings, thus increasing the chances of situational syncope.

## Limitations

This study is a retrospective analysis of clinical data from a single center. The sample size was somewhat limited, and there were inevitable biases in the subjects' recall of medical histories. These factors might have influenced the research findings to some extent. In the future, it is necessary to conduct multi-center, large-sample, and prospective controlled studies.

## Conclusions

The occurrence of NMS-related syncope events in children is associated with school periods and long holiday periods. During school periods, being female is a risk factor for syncope, while situational syncope is a protective factor. The research results have certain reference value for educational administrative departments to develop personalized health education strategies for school-age children during school periods and long holiday periods.

## Abbreviations

NMS	Neurally mediated syncope
BP	Blood pressure
HR	Heart rate
HUTT	Head-up tilt test
BHUT	Basic HUTT
SNHUT	Sublingual nitroglycerin-provoked HUTT
VVS	Vasovagal syncope
VVS-VI	Vasodepressor type vasovagal syncope
VVS-CI	Cardioinhibitory type vasovagal syncope
VVS-M	Mixed type vasovagal syncope
POTS	Postural orthostatic tachycardia syndrome

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## Author contributions

SW and CW conceived the research. PL, XG, JX, TG, YW, HC and RZ collected and reviewed subjects' data. SW performed statistical analysis and drafted the manuscript. All authors contributed to its revision.

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## Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

The research was conducted according to the guidelines of the Declaration of Helsinki, and approved by The Second Xiangya Hospital, Central South University [Ethical Audit No. Study 249(2022)]. All participants or their responsible guardians were asked for and gave their written consent after being informed about the nature of the study.

## Consent for publication

All authors agreed to publish this research.

## Competing interests

The authors declare no competing interests.

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