Cardiology in the Young (2013), **23**, 400–404
doi:10.1017/S1047951112001266

Original Article

Modified Calgary score in differential diagnosis between cardiac syncope and postural orthostatic tachycardia syndrome-associated syncope in children

Jinyan Yang,[1] Lulu Zhu,[1] Stella Chen,[2] Xueying Li,[3] Qingyou Zhang,[1] Fengwen Zhang,[1] Li Chen,[1] Chaoshu Tang,[4,5] Junbao Du,[1] Hongfang Jin[1]

[1]Department of Pediatrics, Peking University First Hospital, Beijing, China; [2]Department of Biological Sciences, University of California, San Diego, La Jolla, CA, United States; [3]Department of Medical Statistics, Peking University First Hospital, Beijing; [4]Department of Physiology and Pathophysiology, Peking University Health Science Centre, Beijing; [5]Key Laboratory of Molecular Cardiology, Ministry of Education, Beijing, China

Abstract The present study was designed to analyse the usefulness of a modified Calgary score system during differential diagnosis between cardiac syncope and postural orthostatic tachycardia syndrome-associated syncope through a large sample sized clinical investigation. The study included 213 children, including 101 boys and 112 girls, with cardiac syncope or postural orthostatic tachycardia syndrome-associated syncope in the age group of 2–19 years (mean 11.8 ± 2.9 years). A modified Calgary score was created, which was analysed to predict differential diagnoses between cardiac syncope and postural orthostatic tachycardia syndrome-associated syncope using a receiver operating characteristic curve. The median of modified Calgary scores for cardiac syncope was −5.0, which significantly differed from that of postural orthostatic tachycardia syndrome (0.0; $p < 0.01$). The sensitivity and specificity of a differentiation score of less than −2.5 was 96.3% and 72.7%, respectively. Owing to the fact that the modified Calgary score was an integer, when less than −3.0 the diagnosis could be considered as cardiac syncope. The modified Calgary score could be used to make an initial differential diagnosis between cardiac syncope and postural orthostatic tachycardia syndrome-associated syncope in the clinic.

Keywords: Calgary score; postural orthostatic tachycardia syndrome; cardiac syncope; child

Received: 29 April 2012; Accepted: 6 July 2012; First published online: 9 October 2012

SYNCOPE IS A COMMON ACUTE SYMPTOM IN CHILDREN, and the causes are not completely clear. They generally include neurally mediated syncope, cardiac syncope, and unexplained syncope. Neurally mediated syncope includes vasovagal syncope, postural orthostatic tachycardia syndrome, orthostatic hypotension, and situational syncope, and is common in children.[1–4] Vasovagal syncope and postural orthostatic tachycardia syndrome are the major reasons for syncope in children, whereas cardiac syncope accounts for 5–6%.

Correspondence to: Prof. H. Jin, Department of Pediatrics, Peking University First Hospital, Beijing 100034, P. R. China. Tel: +8610 83573209; Fax: +8610 66530532; E-mail: jinhongfang51@126.com

Postural orthostatic tachycardia syndrome is defined as, during a head-up or head-up tilt test, an increase in heart rate over 30 beats per minute or maximum heart rate over 120 beats per minute, often accompanied by symptoms of dizziness, shortness of breath, headaches, palpitations, paleness, blurred vision, fatigue, morning discomfort, and even orthostatic intolerance.[5,6] According to Stewart, postural orthostatic tachycardia syndrome is one of the signs of chronic orthostatic intolerance,[7] and could accompany syncope.

Cardiac syncope is a kind of syncope triggered by brain ischaemia caused by a sudden decrease of cardiac output, and can cause death under serious situations. Most instances of cardiac syncope have

no relation to posture, seldom have pre-symptoms, but are sometimes accompanied by cyanosis, dyspnoea, arrhythmia, weak heart sound, and abnormal electrocardiogram. The cardiac diseases that can lead to cardiac syncope are classified into three types: arrhythmia, cardiac output construction, and cardiomyopathy. Although cardiac syncope occurs only in a small proportion of child population, it is quite dangerous. Therefore, it is crucial to differentiate cardiac syncope from postural orthostatic tachycardia syndrome-associated syncope in a timely and accurate manner in the clinic. A thorough history and appropriate investigations remain essential in the assessment of syncope.[8]

By enquiring about the detailed medical history and conducting physical examinations and head-up tests and/or head-up tilt tests, we could clarify postural orthostatic tachycardia syndrome with syncopal symptoms. For the diagnosis of cardiac syncope, we selected the following examinations depending on the real situation: electrocardiogram, echocardiography, Holter electrocardiogram, serum biochemical analysis, exercise test, or intra-cardiac electrophysiologic examinations.[9] However, under emergency situations, the above-mentioned methods are sometimes not available. Thus, it is necessary to propose a useful method to differentiate cardiac syncope from postural orthostatic tachycardia syndrome-related syncopal symptoms quickly and efficiently.

The Calgary score was originally used to make differential diagnoses between adult vasovagal syncope and other types of syncope,[10,11] and included seven diagnostic questions, each producing a corresponding score. The Calgary score is then calculated. Reliable data from the history taking are crucial to an accurate Calgary score.[12] If it surpassed a threshold value, the initial diagnosis as vasovagal syncope or other types of syncope would be classified. For the purpose of an initial differential diagnosis between cardiac syncope and postural orthostatic tachycardia syndrome in children, we explored the value of a child's characteristics-based modified Calgary score in differential diagnoses of cardiac syncope and postural orthostatic tachycardia syndrome-associated syncope.

Subjects and methods

Subjects

From August, 2002 to April, 2011, a total of 213 children were diagnosed with cardiac syncope or postural orthostatic tachycardia syndrome-associated syncope in the Department of Pediatrics, Peking University First Hospital. Of these children, 22 cases, including 9 boys and 13 girls, in the age group of 2–18 years (mean of 10.5 plus or minus 4.6 years) suffered from cardiac syncope. In addition, 191 cases, including 92 boys and 99 girls, in the age group of 5–19 years (mean of 11.9 plus or minus 2.7 years) suffered from postural orthostatic tachycardia syndrome-associated syncope.

Methods

Clinical diagnostic criteria of postural orthostatic tachycardia syndrome. The diagnosis was made with reference to the criteria proposed by Stewart.[7] A positive response for the head-up test or head-up tilt test was as follows: postural orthostatic tachycardia syndrome should be considered if the heart rate increased over 30 beats per minute in a head-up tilt test during the first 10 minutes or reached a maximum heart rate of over 120 beats per minute, accompanied by symptoms such as head-up dizziness, syncope, shortness of breath, headache, palpitations, paleness, blurred vision, fatigue, and discomfort in the morning.[13] The cardiac syncope diagnostic standard referred to the Electrophysiological Disorders of the Heart edited by Saksena et al.[14]

Head-up test and head-up tilt test. The child was asked to lie down quietly for 10 minutes and baseline heart rate, blood pressure, and electrocardiogram were subsequently recorded. The child then stood upright, maintaining that position for 10 minutes, and changes in the above parameters were recorded. During the test, intolerance symptoms were closely observed.[9]

Head-up tilt test included the basic head-up tilt test and the sublingual nitroglycerin-provocated head-up tilt test. For the basic head-up tilt test, all possible drugs that could affect the autonomic nervous system were discontinued for 3 days before the test. Fasting was needed and the environment was quiet and dark with suitable light. The Dash 2000 Multileads Physiological Monitor (GE Company, Toronto, Canada) was used to test the changes in electrocardiogram and blood pressure, which were continually recorded during the test. In the beginning, the child lay in the supine position for 10 minutes, and baseline blood pressure, heart rate, and electrocardiogram were recorded. The child was then asked to stand against the 60° tilt table, and blood pressure, heart rate, electrocardiogram changes, and clinical manifestations were dynamically recorded for 45 minutes or until a positive response occurred. For sublingual nitroglycerin-provocated head-up tilt test, if the child's basic head-up tilt test was negative, he or she was asked to stand in the tilt table and orally take a nitroglycerin tablet at 4–6 micrograms per kilogram (maximum 300 micrograms) for 20 minutes or until a positive response was observed, during which blood pressure, heart rate, electrocardiogram

https://doi.org/10.1017/S1047951112001266 Published online by Cambridge University Press

Table 1. Individual items of the modified Calgary score.[12]

Question	Point (if 'yes')
1. Is there a history of bifascicular block, asystole, or supraventricular tachycardia?	−5
2. At times have bystanders noted that you turn blue during your faint?	−4
3. Did your syncope start when you were 5 years of age or younger?	−3
4. Do you remember anything about being unconscious?	−2
5. Do you feel faint with prolonged sitting or standing?	1
6. Do you sweat before a faint?	2
7. Do you feel faint with pain or in medical settings?	3

changes, and clinical manifestations were dynamically recorded.

Modified Calgary score. The modified Calgary score consisted of seven diagnostic questions relating to medical history, triggers, circumstances, as well as signs and symptoms of transient loss of consciousness (Table 1).[15] All questions were answered with "yes" or "no". The answers' corresponding scores were then summarised to obtain a total score, ranging from −14 to +6 points. In the modified Calgary score, we considered the peak age of the incidence of postural orthostatic tachycardia syndrome in children and equivalently changed the original third question "age over 35 years old" to "age less than 5 years old".

Statistical analysis

The semi-quantitative data were expressed as median, whereas the enumeration data were expressed as cases (percentage). The mean values of both groups were compared using the Wilcoxon Rank-Sum Test. The receiver operating characteristic curve was used to analyse the prediction value of the Calgary score in differentiating cardiac syncope from postural orthostatic tachycardia syndrome-associated syncope. The area under the curve represented the predictive value. Scores between 0.5 and 0.7 had low diagnostic values, between 0.7 and 0.9 had middle diagnostic values, and over 0.9 had high diagnostic values. The 95% confidence interval not including 0.5 or p-value less than 0.05 showed predictive value.[16]

Results

Comparison of the modified Calgary score

The comparison of the modified Calgary score between cardiac syncope and postural orthostatic tachycardia syndrome cases: The median score (−5.0) in cardiac syncope cases significantly differed from that of postural orthostatic tachycardia syndrome-associated syncope (0.0; $p < 0.01$).

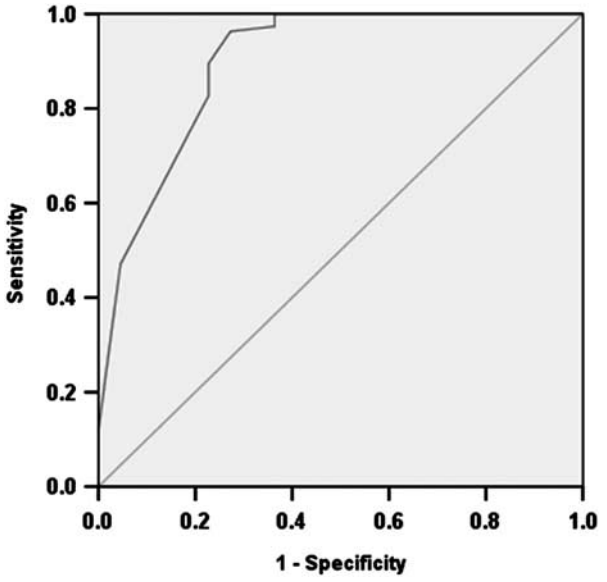

Figure 1.
The receiver operating characteristic of different Calgary scores. The longitudinal axe represents sensitivities of different Calgary scores. The transversal axe represents the false positive rate (1 − specificity). The 45° dotted line is the standard reference line, representing sensitivity being equal to false positive rates, which had no predictive value. The farther the curve from the reference line, the higher the predictive value it had. The area under the curve represents the predictive value of index on results, which was low when between 0.5 and 0.7, middle when between 0.7 and 0.9, and high when over 0.9.

Predictive value of the modified Calgary score

The prediction value of the modified Calgary score for determining cardiac syncope or postural orthostatic tachycardia syndrome-associated syncope: receiver operating characteristic (Fig 1) was used to analyse the sensitivity and specificity of the modified Calgary score for predicting cardiac syncope. The area under receiver operating characteristic was 0.898 and standard deviation was 0.042 with 95% confidence interval (0.816, 0.980), which did not include 0.5. Different modified Calgary scores were selected to analyse their sensitivity and specificity (Table 2). The results suggested that a score of −2.5 yielded a sensitivity of 96.3% and a specificity of 72.7% for differentiating cardiac syncope from postural orthostatic tachycardia syndrome-associated syncope. Owing to the fact that the scores were always integer numbers, a modified Calgary score less than −3.0 could be used to differentiate cardiac syncope from postural orthostatic tachycardia syndrome-associated syncope.

https://doi.org/10.1017/S1047951112001266 Published online by Cambridge University Press

Table 2. The different points of the modified Calgary score prediction for the differential diagnosis between CS and POTS-associated syncope.

Positive if greater than or equal to	Sensitivity	Specificity
−13.00	1.000	0.000
−9.50	1.000	0.005
−6.50	1.000	0.136
−5.50	1.000	0.182
−4.50	1.000	0.636
−3.50	0.974	0.636
−2.50	0.963	0.727
−1.50	0.895	0.773
−0.50	0.827	0.773
0.50	0.471	0.955
1.50	0.120	1.000
2.50	0.094	1.000
3.50	0.021	1.000
5.00	0.016	1.000
7.00	0.000	1.000

CS = cardiac syncope; POTS = postural orthostatic tachycardia syndrome

Discussion

Clinical issues of postural orthostatic tachycardia syndrome

The concept of postural orthostatic tachycardia syndrome in children was first proposed by Stewart et al in 1999 as one kind of orthostatic intolerance.[17] The major manifestations of postural orthostatic tachycardia syndrome are chronic orthostatic intolerance symptoms accompanied by obvious orthostatic tachycardia. Chronic symptoms include dizziness, shortness of breath, headaches, palpitations, paleness, blurred vision, fatigue, morning discomfort, and even syncope under serious conditions. At present, a large sample-based epidemiologic study on postural orthostatic tachycardia syndrome is lacking, but according to Grubb[18] at least 50,000 Americans have manifestations of postural orthostatic tachycardia syndrome. The main pathogenesis of postural orthostatic tachycardia syndrome is orthostatic low blood volume.[19] Currently, the clinical diagnosis of postural orthostatic tachycardia syndrome mainly relies on the head-up test and/or head-up tilt test, but such tests are far from efficient under emergency situations.

Cardiac syncope

Cardiac syncope is triggered by multiple pathological mechanisms during acute and chronic fatal arrhythmia and cardiac mechanic acute dysfunction. Cardiac syncope in children is most common in those with serious arrhythmia, cardiac output dysfunction, and cardiac ischaemia, such as paroxysmal tachycardia, paroxysmal atrial fibrillation, sick sinus syndrome, atrioventricular blockages, congenital heart disease, idiopathic pulmonary artery hypertension, hypertrophic cardiomyopathy, and Adams–Stokes syndrome under the most serious conditions. Under rare conditions, it can cause sudden death.[20–22] Therefore, it remains crucial to find a way to rapidly and accurately differentiate cardiac syncope from neurally mediated syncope based on a patient's medical history in emergency.

Usefulness of the modified Calgary score in the differential diagnosis of syncope in children

In 2002, Sheldon from Calgary University[23] first applied Calgary syncope symptom scores in adult syncopal diagnosis. In 2006, they applied the Calgary score in adult vasovagal syncope diagnosis. In 2009, Romme et al[12] indicated that Calgary score had high sensitivity (87%) in distinguishing vasovagal syncope from transient loss of consciousness, but with only 32% specificity. Studies revealed that most children with postural orthostatic tachycardia syndrome were older than 5 years.[24] Consequently, we modified the Calgary score according to the clinical characteristics of children, changed the third question in the original score items from "age over 35 years" to "less than 5 years", and performed receiver operating characteristic for evaluating the diagnostic value of the scores in cases of cardiac syncope or postural orthostatic tachycardia syndrome-associated syncope. The results suggested that this score yielded a sensitivity of 96.3% and a specificity of 72.7% for differentiating cardiac syncope from postural orthostatic tachycardia syndrome-associated syncope in children, and thus was of significance for clinical practice in emergency.

Limitations

There are also some limitations in this study, however, especially in subject selection. We had less cases of cardiac syncope. We need multi-centre studies in the future to improve the value of research. In addition, a small part of children are too young to understand the questions and express their feelings, and we had to obtain some useful information from their parents, which might limit the accuracy of information.

Acknowledgements

This work was supported by Capital Medical Science Development Projects of China (2009-1008), and Beijing Science and Technology Project (D10100050010059).

References

1. Chen L, Zhang QY, Ingrid S, Chen JJ, Qin J, Du JB. Aetiologic and clinical characteristics of syncope in Chinese children. Acta Paediatr 2007; 96: 1505–1510.
2. Kapoor WN, Smith MA, Miller NL. Upright tilt testing in evaluating syncope: a comprehensive literature review. Am J Med 1994; 97: 78–88.
3. Benditt DG, Remole S, Bailin S, Dunnigan A, Asso A, Milstein S. Tilt table testing for evaluation of neurally-mediated (cardioneurogenic) syncope: rationale and proposed protocols. Pacing Clin Electrophysiol 1991; 14: 1528–1537.
4. Abboud FM. Neurocardiogenic syncope. N Engl J Med 1993; 328: 1117–1120.
5. Chen L, Du JB. Children orthostatic intolerance. Chin J Med 2006; 41: 21–23.
6. Ojha A, Chelimsky TC, Chelimsky G. Comorbidities in pediatric patients with postural orthostatic tachycardia syndrome. J Pediatr 2011; 158: 20–23.
7. Stewart JM. Postural tachycardia syndrome and reflex syncope: similarities and differences. J Pediatr 2009; 154: 481–485.
8. MacCormick JM, Crawford JR, Chung SK, et al. Symptoms and signs associated with syncope in young people with primary cardiac arrhythmias. Heart Lung Circ 2011; 20: 593–598.
9. The Subspecialty Group of Cardiology, The Society of Pediatrics, Chinese Medical Association and The Editorial Board, Chinese Journal of Pediatrics. Guidelines for diagnosis of syncope in children. Chin J Pediatr, 2009; 47: 99–101.
10. Serletis A, Sheldon RS. Neurally-mediated reflex syncope: recognition by history and clinical testing. In: Benditt DG, Brignole M, Raviele A, Wieling W (eds.). Syncope and Transient Loss of Consciousness: Multidisciplinary Management. Blackwell Publishing, San Francisco, 2007, pp 44–50.
11. Sheldon R, Rose S, Connolly S, Ritchie D, Koshman ML, Frenneaux M. Diagnostic criteria for vasovagal syncope based on a quantitative history. Eur Heart J 2006; 3: 344–350.
12. Romme JJ, van Dijk N, Boer KR, Bossuyt PM, Wieling W, Reitsma JB. Diagnosing vasovagal syncope based on quantitative history-taking: validation of the Calgary Syncope Symptom Score. Eur Heart J 2009; 30: 2888–2896.
13. Low PA, Sandroni P, Joyner M, Shen WK. Postural tachycardia syndrome. J Cardiovasc Electrophysiol 2009; 20: 352–358.
14. Saksena S, Camm AJ, Boyden PA, et al. Electrophysiological Disorders of the Heart. Elsevier Limited, Amsterdam, 2005, pp 511–523.
15. Sheldon R, Rose S, Connolly S, Ritchie D, Koshman ML, Frenneaux M. Diagnostic criteria for vasovagal syncope based on a quantitative history. Eur Heart J 2006; 3: 344–350.
16. Swets JA. Measuring the accuracy of diagnostic systems. Science 1988; 240: 1285–1293.
17. Stewart JM, Gewitz MH, Weldon A, et al. Patterns of orthostatic intolerance: the orthostatic tachycardia syndrome and adolescent chronic fatigue. J Pediatr 1999; 135: 218–225.
18. Grubb BP. Postural tachycardia syndrome. Circulation 2008; 117: 2814–2817.
19. Medow MS, Stewart JM. The postural tachycardia syndrome. Cardiol Rev 2007; 15: 67–75.
20. Massin MM, Bourguignont A, Coremans C, et al. Syncope in pediatric patients presenting to an emergency department. J Pediatr 2004; 145: 223–228.
21. Zhang QZ. Diagnosis and management of cardiac syncope in infants. Chin J Pract Pediatr 2004; 19: 644–646.
22. Chen YH, Du JB. Diagnosis and treatment of cardiogenic syncope in children. J Appl Pediatr 2006; 21: 7–8.
23. Sheldon R, Rose S, Ritchie D, et al. Historical criteria that distinguish syncope from seizures. J Am Coll Cardiol 2002; 40: 142–148.
24. Chen L, Wang L, Sun J, et al. Midodrine hydrochloride is effective in the treatment of children with postural orthostatic tachycardia syndrome. Circ J 2011; 75: 927–931.