

Letter to the Editor (Chang)

RE: Vetter et al. Cardiovascular monitoring of children and adolescents with heart disease receiving stimulant drugs: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young Congenital Cardiac Defects Committee and the Council on Cardiovascular Nursing. *Circulation*. 2008 May 6;117(18):2407-23.

To the Editor:

In a recent Scientific Statement, the AHA recommends the assessment and monitoring of children and adolescents on stimulant drugs for treatment of attention deficit hyperactive disorder (ADHD).¹ The statement writing group reviewed the relevant literature and used the evidence-based methodologies developed by the American College of Cardiology/AHA Task Force on Practice Guidelines. The recommendations for initial screening include patient and family history, physical examination and a 12-lead electrocardiogram (ECG). A thorough history and physical examination has always been the cornerstone for any initial clinical evaluation. However, recommending the use of 12-lead ECG in initial cardiovascular screening carries important implications for clinical practice, insurance reimbursement, healthcare manpower and cardiovascular prevention in other populations.

There are little epidemiology and clinical data available on sudden cardiac death (SCD) related to use of stimulant drugs. The concerns of stimulant drugs for ADHD leading to adverse cardiac events were raised because of the cases submitted to the Adverse Event Reporting System (ARES) database at the Food and Drug Administration. Because of limited information

on prevention of SCD related to use of stimulant drugs, the statement writing group drew experiences from preparticipation screening of athletes, and reviewed the literature on SCD in athletes and use of ECG for screening.² Although the writing group did make direct comparison in the statement between SCD in athletes and SCD in ADHD patients on stimulant drugs, I think a side-by-side comparison of these two groups is helpful (Table).

Table. Comparisons of SCD in athletes and SCD in ADHD patients on stimulant drugs.

	Athletes	Patients with ADHD on Stimulant Drugs
Presumed physiologic basis for SCD	Increase adrenaline and cardiac output with exercise	Sympathomimetic amines increase heart rate and blood pressure
Population at risk (in the US)	10 million ²	2.5 million ¹
Incidence of SCD (in the US)	100 per year (1 per 100,000 per year) ³	Unclear (25 deaths reported to AERS in 1999-2003) ⁴
Sex (M:F)*	9 to 1	2.4 to 1
Major causes of SCD*	<ol style="list-style-type: none"> 1. Hypertrophic cardiomyopathy 2. Unexplained cardiac hypertrophy 3. Anomalous coronary arteries 4. Myocarditis 	<ol style="list-style-type: none"> 1. Unexplained cardiac hypertrophy 2. History of heart murmur or syncope 3. Unexplained increase or toxic medication level 4. Hypertension
AHA recommendations for initial screening ^{1,2}	Patient history Family history Physical examination	Patient history Family history Physical examination 12-lead ECG
AHA recommendations for continuing assessment	Repeat screening in 2 years	Blood pressure and pulse within 1-3 months, and follow-up every 6-12 months Repeat ECG if any symptoms, change of history, or after 12 years

Evidence for ECG use	Class IIa, Level B**	old if initial ECG done at <12 years of age Class IIa, Level C
Concerns with ECG use	Low specificity for athletes Cost consideration	No specificity or cost information available

* data on SCD in ADHD patients taking stimulant drugs were from the Adverse Event Reporting System (ARES) database.⁴

** Level B evidence assigned because of data available from nonrandomized studies.

As listed in the Table, the epidemiology of SCD in athletes is better defined, and the incidence of SCD in athletes is probably higher than SCD in ADHD patients on stimulant drugs. The major causes of SCD are also better documented in athletes. The causes of SCD in ADHD patients remain to be further defined. There are more evidences for ECG use in athlete screening because of the European experiences and data from some nonrandomized studies. There are no data on the use of ECG in patients on stimulant drugs. The 2007AHA recommendations for preparticipation screening of athletes indicate the concerns with ECG use for its low specificity in athletes and cost consideration.² In contrast, the specificity of ECG and cost for screening patients on stimulant drugs are not mentioned in the recent statement.¹

In an online survey on cardiovascular screening in children conducted in April 2007, I sent email invitations to 1045 pediatric cardiologists in North America and received 363 (35%) responses. When asked whether stimulant drugs increase the risk for SCD, 51% respondents agreed, 24% disagree and 25% had no opinion. 34% respondents agreed and 48% disagreed that a “*Black Box Warning*” of increased risk for SCD be placed on stimulant drugs. In this survey, 57% respondents agreed that all children on stimulant drugs should have a 12-lead ECG for

cardiovascular screening. A similar proportion (51%) of respondents agreed that all high school and college athletes should have a 12-lead ECG included as part of preparticipation cardiovascular screening.

Recommending changes of clinical practice based on limited information is a difficult task. If one uses the evidence and rationale for recommending ECG in children and adolescents on stimulant drugs, ECG screening of young athletes is also a “reasonable” practice. In fact, ECG screening of athletes has been recommended by the European Society of Cardiology and International Olympic Committee.^{5,6}

The call for a registry of SCD in the young in the statement¹ is both timely and important. Data from a SCD registry will have important implications for many aspects of cardiovascular screening in children, including screening of newborns for critical congenital heart disease, infants for long QT syndrome, and young athletes for risk of SCD.

References

1. Vetter VL, Elia J, Erickson C, Berger S, Blum N, Uzark K, Webb CL. Cardiovascular monitoring of children and adolescents with heart disease receiving stimulant drugs: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young Congenital Cardiac Defects Committee and the Council on Cardiovascular Nursing. *Circulation*. 2008;117:2407-23.
2. Maron BJ, Thompson PD, Ackerman MJ, Balady G, Berger S, Cohen D, Dimeff R, Douglas PS, Glover DW, Hutter AM, Jr., Krauss MD, Maron MS, Mitten MJ, Roberts WO, Puffer JC. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a

scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation.

Circulation. 2007;115:1643-455.

3. Faber L, van Buuren F. Athlete screening for occult cardiac disease: no risk, no fun? *J Am Coll Cardiol*. 2008;51:1040-1.
4. US Food and Drug Administration, Drug Safety and Risk Management Advisory Committee Meeting. February 9–10, 2006. Available at: http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4202_00_TOC.htm. Accessed May 14, 2008.
5. Corrado D, Pelliccia A, Bjornstad HH, Vanhees L, Biffi A, Borjesson M, Panhuyzen-Goedkoop N, Deligiannis A, Solberg E, Dugmore D, Mellwig KP, Assanelli D, Delise P, van-Buuren F, Anastasakis A, Heidbuchel H, Hoffmann E, Fagard R, Priori SG, Basso C, Arbustini E, Blomstrom-Lundqvist C, McKenna WJ, Thiene G. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. *Eur Heart J*. 2005;26:516-24.
6. IOC Medical Commission, International Olympic Committee. Sudden Cardiovascular Death in Sport: Lausanne Recommendations: Preparticipation Cardiovascular Screening. December 10, 2004. Available at: http://multimedia.olympic.org/pdf/en_report_886.pdf. Accessed May 16, 2008.

Response:

Thank you for your response and especially for recognizing the lack of specific data available to the Writing Group. We found your Table interesting, but would like to point out a few issues for clarification.

The Table presented is interesting, but a few points need clarification. First, the true "Incidence of SCD" is not known in either the athlete or ADHD population and Unknown or Unclear would be the best designation for both groups. Secondly, the list of Major Causes of SCD should include Arrhythmia (channelopathies, WPW, etc) for both categories. Other causes noted in the FDA database for the AERS reported deaths include coronary artery anomalies, family history of arrhythmia, and history of palpitations. Bicuspid aortic valve and mitral valve prolapse as well as enlarged heart were noted. The data available on this group of individuals reported through AERS is very minimal and summarized, not the actual data.

The recommendation the author is referring to regarding the Class IIa, Level of Evidence B note under Athletes and Evidence for ECG use is not clear. Similarly, the note of low specificity for athletes under Athletes column may refer to another study, but the published data suggests a 98.8% specificity in the Pellecia study.¹

The manuscript on *Cardiovascular Monitoring Of Children And Adolescents With Heart Disease Receiving Medications For ADHD: A Scientific Statement From The American Heart Association Council On Cardiovascular Disease In The Young Congenital Cardiac Defects Committee And The Council On Cardiovascular Nursing* was not intended to be an efficacy or cost effectiveness report since such data are not available.

The survey presented, although interesting, cannot be considered scientifically valid or a representative sample of practice among pediatric cardiologists. This is highlighted by the

differences in your findings and that of the PACES Survey and points out the weaknesses of using survey data to determine practice. The fact that 51% of your respondents agreed that all high school athletes should have a 12-lead ECG included as part of the preparticipation exam and that 57% also felt that all children on stimulant drugs should have an ECG indicates that the pediatric cardiology community is considering this issue.

Your rationale that obtaining an ECG is a reasonable practice in athletes as being consistent with the recommendations of the Writing Group for ADHD patients is understandable, but we emphasize that we were not addressing the athlete group in this statement. Thus, we cannot comment on the athlete group. We agree that Registry data will be helpful in answering these questions and could be applied to all children who experience sudden cardiac death.

Reference List

- (1) Pelliccia A, Di Paolo FM, Corrado D et al. Evidence for efficacy of the Italian national preparticipation screening programme for identification of hypertrophic cardiomyopathy in competitive athletes. *Eur Heart J* 2006 September;27(18):2196-200.