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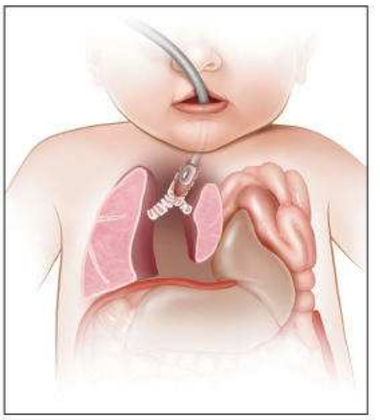

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Early Screening for Cardiovascular Abnormalities With Preparticipation Echocardiography

Utility of Focused Physician-Operated Echocardiography in Preparticipation Screening of Athletes

Eugene S. Yim, MD, MPH, Frederick Basilico, MD, Gianmichel Corrado, MD

Objectives—We have developed the Early Screening for Cardiovascular Abnormalities With Preparticipation Echocardiography protocol to improve false-positive rates, reduce referrals, and broaden the spectrum of disease that can be captured through preparticipation screening of athletes. This study documents the first application of this protocol and uses case analysis to discuss the potential utility of portable sonography in screening.

Methods—Sixty-five male collegiate athletes, aged 18 to 25 years, were prospectively enrolled. Each athlete was screened with a history and physical examination, electrocardiography (ECG), and focused echocardiography performed by a noncardiologist sports medicine physician. The history and physical examination were based on the 12-element American Heart Association recommendations; 2010 European Society of Cardiology criteria were used to screen ECGs. Focused physician-operated echocardiography was performed to assess for hypertrophic cardiomyopathy and aortic root dilatation. Athletes screening positive were referred to a cardiologist.

Results—Most of the athletes (n = 59) did not screen positive by any screening modality. Three athletes screened positive on ECG but had normal focused echocardiographic findings. Three athletes screened positive by history and physical examination but had normal ECG and focused echocardiographic findings. All athletes screening positive were referred to a cardiologist and eventually cleared for sports participation. No athlete screened positive by focused echocardiography alone. Focused echocardiography was able to reduce the referral rate for hypertrophic cardiomyopathy by 33% and obtained measurements statistically similar to those of formal echocardiography.

Conclusions—This study provides evidence that focused physician-operated echocardiography can improve false-positive rates and broaden the spectrum of disease that is detectable through preparticipation screening of athletes.

Key Words—aortic root dilatation; athletes; echocardiography; preparticipation screening; point-of-care ultrasound; sonography; sudden cardiac death

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Abbreviations

ECG, electrocardiography; ESCAPE, Early Screening for Cardiovascular Abnormalities With Preparticipation Echocardiography

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Every year, young athletes across the world are dying of preventable conditions that lead to sudden cardiac death. In the United States alone, nearly a dozen young competitive athletes die unexpectedly during sports participation every year.[1] Previous estimates of the incidence of sudden cardiac death in athletes has ranged widely, from 1 per 23,000 to 1 per 300,000 worldwide.[2,3] Most of these deaths (≈85%) are from cardiovascular conditions such as hypertrophic cardiomyopathy, an anomalous

coronary artery, an aortic aneurysm, aortic valve stenosis, myocarditis, dilated cardiomyopathy, arrhythmogenic right ventricular dysplasia, mitral valve prolapse, an atherosclerotic coronary artery, long-QT syndrome, sarcoidosis, and the sickle cell trait. Among these conditions, hypertrophic cardiomyopathy is the leading cause of sudden cardiac death in young athletes in the United States, and as a result, this condition is a particular focus of concern in the context of preparticipation screening.

Despite the consensus that routine cardiovascular screening for athletes is warranted, there is ongoing debate regarding the specific components of screening that should be incorporated. As this debate ensues, athletes with cardiovascular abnormalities continue to go undetected, leading to unnecessary and tragic loss of life. In the United States, the American Heart Association and American College of Cardiology recommend the use of a history and physical examination for screening, while citing the limitations of electrocardiography (ECG) and echocardiography.[4] The main concern with ECG is its "low specificity as a screening test in athletic populations largely because of the high frequency of ECG alterations associated with the normal physiological adaptations of the trained athlete's heart."

In response to these concerns, modified criteria for ECG interpretation have been developed to help differentiate patterns resulting from normal physiologic adaptations from those representing underlying pathologic conditions.[5–7] Among these were the 2010 criteria presented by the European Society of Cardiology, an update of prior recommendations from 2005.[6] Such modified criteria have helped decrease false-positive rates to as low as 1.9% in the hands of experienced physicians.[8] More recent evidence has also demonstrated that providing less-experienced clinicians with a simple tool that illustrates these criteria can improve the sensitivity and specificity of ECG screening.[9] The interest in developing modified criteria for ECG continues to grow, which is evidenced by the recent American Medical Society for Sports Medicine summit in 2012, which brought together global authorities to establish a consensus on these matters and to establish improved criteria for ECG interpretation.[10]

To complement these efforts, focused physician-operated echocardiography by noncardiologist sports medicine physicians may further enhance the effectiveness of cardiovascular screening by improving false-positive rates of screening for conditions such as hypertrophic cardiomyopathy and also identifying cardiovascular conditions that are not detectable by current screening modalities. The American Heart Association recognized the potential advantages of echocardiography in its very statement that disapproved of specialized testing, stating that "it is a reasonable expectation that echocardiography can also detect other relevant abnormalities responsible for sudden death in young athletes, such as aortic stenosis and mitral valve prolapse, aortic root dilatation associated with Marfan syndrome or bicuspid aortic valve, dilated cardiomyopathy, and other forms of left ventricular dysfunction."[3]

Despite such potential advantages, the American Heart Association does not recommend routine screening with echocardiography, largely because of concerns regarding cost and accessibility. However, an underlying assumption of such arguments is that echocardiography will be performed by a sonographer in a specialized laboratory, based on referral from the primary clinicians evaluating athletes. Focused physician-operated echocardiography may serve as solution, providing a more accessible approach to screening that could address these concerns.

Our research group recently demonstrated that focused echocardiography for hypertrophic cardiomyopathy can be accurate and reliable in the hands of noncardiologist sports medicine physician operators.[11] As a follow-up to that study, we have developed the Early Screening for Cardiovascular Abnormalities With Preparticipation Echocardiography (ESCAPE) protocol, which was applied in this study to an initial cohort of athletes. The overarching hypothesis behind the ESCAPE protocol is that adding focused physician-operated echocardiography to preparticipation screening based on ECG can improve the specificity of testing, improve false-positive rates, reduce rates of unnecessary referrals to specialists, and expand the spectrum of cardiovascular disease that can be captured through screening. The incorporation of portable echocardiography into screening is not meant to supplant the use of ECG in screening but rather may serve a role in helping determine which athletes with abnormal ECG findings warrant further evaluation. Such a screening protocol would still rely on expert cardiology consultation to make management decisions for athletes who screen positive.

By providing direct visualization of cardiac dimensions, focused physician-operated echocardiography could provide a more direct assessment for hypertrophic cardiomyopathy compared to current screening modalities, which may improve false-positive rates and reduce referral rates to specialists when applied to cases with a concern for hypertrophic cardiomyopathy based on ECG screening. Focused echocardiography by noncardiologist sports medicine physicians could also evaluate for conditions that are prevalent among athletes but difficult to detect on the basis of current screening strategies. For example, focused

protocols for echocardiography could be developed to detect an anomalous coronary artery, aortic stenosis, mitral valve prolapse, aortic root dilatation, a bicuspid aortic valve, dilated cardiomyopathy, and other forms of left ventricular dysfunction.

Although some of these entities may be difficult to detect with portable echocardiography, conditions such as aortic root dilatation may be feasible in this context. The aortic root diameter is a fairly straightforward measurement to obtain with portable echocardiography and is also diagnostic for aortic root dilatation. Including such a measurement in screening would be beneficial considering the substantial prevalence of aortic root dilatation (≈1%) among athletes and the potential for this condition to lead to major health sequelae if left undetected.[12–14]

As physicians become more experienced with sonography, focused echocardiography by noncardiologist sports medicine physicians may become standard practice in larger screening practices. Similar precedents have also been set in other fields, in which physician-operated sonography has become the standard of care.[15,16] As sonography becomes more avidly incorporated into clinical practice, the potential use of portable sonography in this manner should be considered. This study explores the possibility by reporting the application of the ESCAPE protocol to an initial cohort of young athletes. The primary goal of the study was therefore to implement the ESCAPE protocol in a cohort of athletes and to discuss the potential utility of adding portable sonography to current screening protocols based on ECG. The study was not designed or powered to evaluate the effects of the ESCAPE protocol on false-positive screening rates or to delineate test characteristics of the screening modality, but the potential utility of sonography in screening is discussed by analyzing specific cases in the cohort that screened positive with other screening modalities.

The plan is to expand these efforts into a multicenter trial to better delineate the utility of portable sonography in screening. The development of such a screening strategy holds promise in enhancing the efficacy of current screening modalities and also expanding the spectrum of disease that can be detected by preparticipation screening. The ultimate goal of such efforts is to prevent unnecessary and tragic loss of life in young athletes.

Materials and Methods

Participant Recruitment and Selection

Sixty-five National Collegiate Athletic Association Division I male athletes, aged 18 to 25 years, were recruited. No specific demographic groups were targeted (sex, ethnicity/race, socioeconomic level, or literacy level). Athletes were recruited during preparticipation screening examinations that occurred at the beginning of the school year. Before beginning preparticipation screening, athletes received a copy of the informed consent documents pertaining to the study. Only athletes consenting to involvement were included.

Research Design and Methods

The study was a prospective cohort study. Institutional Review Board approval was obtained through Northeastern University. Study participants were Division I National Collegiate Athletic Association athletes at Northeastern University. These athletes were scheduled for preparticipation screening sessions in coordination with the athletic training staff. Athletes were screened in groups, according to their different teams. Screening occurred during preseason preparticipation screening at the beginning of the 2012–2013 academic year.

On the day of screening, each participant first received a focused history and physical examination based on the 12-element American Heart Association recommendations for preparticipation cardiovascular screening. The history and examination were performed by either a sports medicine fellow or an attending sports medicine physician on staff. Each athlete then received an ECG, obtained by a technologist. This procedure was followed by physician-operated echocardiography by a noncardiologist sports medicine physician, who was board certified in sports medicine with greater than 5 years of clinical experience in sonography. The physician received residency training in sonography and also completed a weekend course in advanced echocardiography before the onset of the study.

Physicians performing echocardiography were blinded to the history and physical examination as well as ECG results. The total screening time for each athlete was 7 minutes. Portable echocardiography was performed using a left parasternal long-axis view to acquire the following measurements during end diastole: (1) interventricular septal wall thickness; (2) left ventricular internal diameter; (3) left ventricular posterior wall thickness; and (4) aortic root diameter at the sinuses of Valsalva. Athletes screening positive by any of the screening modalities were referred for specialty evaluation by a cardiologist.

Main Outcome Measures

The main outcome measures of the study were the number of athletes screening positive by each screening modality and the number of these cases screening positive by

ECG or the history and physical examination that could have been negated by normal echocardiographic findings. Results were categorized for each screening modality. For history taking, categories were based on the 12-element American Heart Association recommendations for preparticipation screening: exertional chest pain/discomfort; unexplained syncope/near syncope; excessive exertional or unexplained dyspnea/fatigue with exercise; prior recognition of a heart murmur; elevated systemic blood pressure; family history of premature death; family history of disability from heart disease in a close relative; and specific knowledge of certain cardiac conditions in family members (hypertrophic cardiomyopathy, long-QT syndrome, Marfan syndrome, and arrhythmias). For physical examination, categories relevant to the American Heart Association guidelines included the following: heart murmur; unequal femoral pulses; physical stigmata of Marfan syndrome; and brachial artery blood pressure. The 2010 European Society of Cardiology criteria were used to categorize abnormal ECGs: T-wave inversion; ST-segment depression; pathologic Q waves; left atrial enlargement; left-axis deviation/left anterior hemiblock; right-axis deviation/left posterior hemiblock; right ventricular hypertrophy; ventricular preexcitation; complete right or left bundle branch block; long or short QT interval; and Brugada-like early polarization. For echocardiography, the following categories relevant to the diagnosis of hypertrophic cardiomyopathy were used: interventricular septal wall thickness greater than 15 mm; and interventricular septal wall thickness-to-left ventricular posterior wall thickness ratio greater than 1.3 in normotensive athletes and greater than 1.5 in hypertensive athletes.[17] For the aortic root diameter, a cut off of 39.1 mm in male athletes was used, according to recent guidelines established by a consortium of governing authorities (such as the American College of Cardiology, American Heart Association, American Association for Thoracic Surgery, and American College of Radiology).[18] For athletes referred for specialty evaluation, intraclass correlation coefficients were calculated to assess concordance of echocardiographic measurements obtained by focused physician-operated echocardiography in comparison to formal echocardiography.

Results

Most of the athletes (n = 59) did not screen positive based on any screening modality. These athletes met none of the criteria for positive screening based on the 12-element American Heart Association recommendations for the history and physical examination. They also had normal ECG findings based on the 2010 European Society of Cardiology criteria. Focused echocardiography showed normal cardiac parameters (Table 1).

Three athletes screened positive for abnormal ECG findings. Of these, 2 had QRS durations greater than 120 milliseconds, and 1 had an ECG indicating a left atrial abnormality. Focused physician-operated echocardiography on these athletes showed normal cardiac parameters, without evidence of hypertrophic cardiomyopathy or aortic root dilatation (Table 2). After referral to a cardiologist, all of these athletes were cleared for sports participation.

Three athletes screened positive by history and physical examination. Two reported near syncope with exercise, and 1 described palpitations. All of these athletes had normal findings on both ECG and focused echocardiography performed by the noncardiologist sports medicine physician (Table 3). These athletes were referred to a cardiologist and were all ultimately cleared for sports participation.

For the 6 athletes who were referred to a cardiologist, the measurements obtained by focused physician-operated echocardiography were statistically similar to those obtained by formal echocardiography by a cardiac sonog-

Table 1. Cardiac Parameters in Athletes Screening Negative (n = 59)

Value	LVD, mm	IVS, mm	PW, mm	AR, mm
Minimum	4.49	0.79	0.81	2.24
Maximum	5.95	1.29	1.28	3.76
Average	5.16	1.04	1.02	2.80

AR indicates aortic root diameter; IVS, interventricular septal wall thickness; LVD, left ventricular internal diameter; and PW, left ventricular posterior wall thickness.

Table 2. Cardiac Parameters in Athletes Screening Positive by ECG (n = 3)

Value	LVD, mm	IVS, mm	PW, mm	AR, mm
Minimum	4.93	0.94	0.88	2.70
Maximum	5.72	1.38	1.12	3.47
Average	5.33	1.17	1.05	2.94

Abbreviations are as in Table 1.

Table 3. Cardiac Parameters in Athletes Screening Positive by History and Physical Examination (n = 3)

Value	LVD, mm	IVS, mm	PW, mm	AR, mm
Minimum	5.00	0.85	0.89	3.33
Maximum	6.40	1.16	1.39	3.33
Average	5.60	0.98	1.16	3.16

Abbreviations are as in Table 1.

rapher at follow-up. Intraclass correlation coefficient calculations between measurements were as follows: 0.84 for left ventricular internal diameter; 0.76 for interventricular septal wall thickness; 0.81 for left ventricular posterior wall thickness; and 0.76 for the aortic root. These findings indicated strong interoperator reliability and concordance of measurements of focused echocardiography compared to formal echocardiography.

None of the athletes screened positive on focused echocardiography performed by the noncardiologist sports medicine physicians. More specifically, none of the athletes met criteria for diagnosis of hypertrophic cardiomyopathy or aortic root dilatation. Also importantly, none of the athletes in the study were ultimately disqualified from participation in sports on the basis of screening.

Discussion

This study demonstrates the potential utility of focused echocardiography by noncardiologist sports medicine physicians in preparticipation screening for athletes. Portable echocardiography can be particularly helpful in augmenting screening that relies on ECG for referral to specialists. This procedure will help address concerns by the American Heart Association and American College of Cardiology regarding the high false-positive rates of ECG as a screening modality.

One approach to improving false-positive rates has been to revise the ECG criteria. The 2010 European Society of Cardiology criteria have been particularly useful in this manner, over prior recommendations from 2005.[7] If the 2005 recommendations had been used in our study, 2 athletes would have screened positive based on their QRS voltage. On the basis of the 2010 European Society of Cardiology criteria, however, these athletes did not screen positive in the absence of other findings of concern. The use of the modified ECG criteria alone therefore would have decreased the referral rate by 25% compared to the original ECG criteria. Further developments and refinement of ECG criteria will help continue improvements in the specificity and false-positive rate of preparticipation screening based on ECG.

Focused physician-operated echocardiography by noncardiologist sports medicine physicians may prove to be an effective adjunct to modified ECG criteria. Echocardiography was incorporated into the preparticipation screening program of our study to evaluate its potential utility in this setting. In our study, portable echocardiography did not show any abnormalities indicating hypertrophic cardiomyopathy or aortic root dilatation. Since every athlete did not receive formal echocardiography, the sensitivity and specificity of the screening tool could not be fully evaluated. However, the strong intraclass correlation coefficients for those who did receive follow-up indicate that the physician-operated measurements were accurate. Future studies with follow-up confirmatory echocardiography for all participants will be required to validate its use in this setting and to assess sensitivity and specificity.

The potential utility of focused echocardiography by noncardiologist sports medicine physicians in screening can be assessed, however, by evaluating the cases that were referred to a cardiologist on the basis of existing screening modalities. Of the athletes referred on the basis of ECG or the history and physical examination, none of the athletes had portable echocardiographic measurements suggestive of hypertrophic cardiomyopathy or aortic root dilatation. Of the many ECG abnormalities that have been associated with hypertrophic cardiomyopathy, a prolonged QRS duration is among the specific criteria that have been associated with phenotypic expression of hypertrophic cardiomyopathy based on magnetic resonance imaging.[19] Of the athletes in our study, 2 screened positive on the basis of a prolonged QRS duration. If used as a secondary screening modality in these athletes, focused echocardiography would have obviated their referral to a specialist for concern about hypertrophic cardiomyopathy and would have reduced the referral rate by 33% overall and by 100% for hypertrophic cardiomyopathy specifically. Focused physician-operated echocardiography may therefore prove useful if used in a selective manner to assess athletes screening positive by ECG.

In addition to its potential in improving false-positive screening rates for hypertrophic cardiomyopathy, echocardiography also had the added advantage of evaluating for cardiovascular conditions that are not detectable by existing screening modalities. Although aortic root dilatation was not detected in any of the athletes screened in our study, focused echocardiography by noncardiologist sports medicine physicians holds the potential to detect this condition in athletes. Further studies with larger population sizes will be required to validate its use in this setting and to justify incorporating focused physician-operated echocardiography into preparticipation screening.

Furthermore, additional protocols in focused echocardiography could potentially be developed to screen for other prevalent cardiovascular conditions, such as a bicuspid aortic valve and an anomalous coronary artery. A bicuspid aortic valve is the most common congenital cardiac disorder in the general population, with a prevalence

of 0.5% to 2.0% and a 3:1 male predominance.[20,21] It is usually asymptomatic but is associated with other threatening cardiovascular abnormalities, such as aortic root dilatation, coarctation of the aorta, and acute dissection.[22–24] However, the diagnosis of a bicuspid aortic valve requires additional views and imaging techniques by the operator, and further training and experience by noncardiologist sports medicine physicians will be required before this application becomes a possibility.

As noncardiologist sports medicine physicians become more adept at echocardiography, they may also be able to diagnose conditions that require even more skill and precision. For example, an anomalous coronary artery is another threatening cardiovascular abnormality in athletes, with an estimated prevalence of 1% in the general population.[25] More importantly, it is a leading cause of sudden death among athletes and is second to only hypertrophic cardiomyopathy in this regard.[1] Diagnosis of both of these conditions relies on echocardiography if used as a secondary screening modality in these athletes; therefore, current screening programs are not equipped to detect these threatening but often silent conditions in athletes. Incorporating portable echocardiography into preparticipation screening would open up the potential to detect these entities through routine screening.

Expanding the spectrum of cardiovascular disease that could be captured through preparticipation screening may help justify the incorporation of focused echocardiography into larger screening practices. Current cost-effectiveness arguments against the incorporation of routine echocardiography into preparticipation screening suggest that the cost of providing routine echocardiography to all athletes is not justifiable given the low prevalence of detectable conditions. Such arguments are often focused on the use of screening to diagnose hypertrophic cardiomyopathy, which is a relatively rare condition with a prevalence of around 0.1% to 0.2%.[26] Given that aortic root dilatation has nearly a 10-fold higher prevalence than hypertrophic cardiomyopathy, the cost-effectiveness discussion may need to be readdressed with conditions such as aortic root dilatation in mind. In addition, the implementation of focused physician-operated echocardiography rather than comprehensive echocardiography may further improve the cost-effectiveness profile of a screening program that uses echocardiography for preparticipation evaluation. Furthermore, if focused echocardiography could be targeted to higher-risk athletes rather than routinely to all athletes, the cost-effectiveness would be further improved.

The determination of cost-effectiveness is complex, however, and the final determination of the cost-effectiveness of a screening protocol such as ESCAPE will ultimately require further investigation. If portable echocardiography by noncardiologist sports medicine physicians is incorporated into practices, and these practitioners end up billing for these diagnostic tests, then cost may not be reduced on a larger systems level. Should a screening protocol such as ESCAPE be adopted on a larger scale, data regarding billing, referral rates, and test characteristics (such as specificity, sensitivity, and negative and positive predictive values) will be critical for establishing cost-effectiveness.

In conclusion, our study provides preliminary evidence for the utility of focused physician-operated echocardiography in preparticipation screening for athletes. Previous screening programs have proven to be overly sensitive, leading to unnecessary referrals to cardiology and delays in sports participation. Modifications to existing ECG criteria have helped address this factor, but focused echocardiography by noncardiologist sports medicine physicians may provide an adjunctive screening technique that can work synergistically with ECG-based screening programs, whether it is applied systematically for all athletes or as a selective second level of screening. In addition, focused echocardiography by noncardiologist sports medicine physicians holds the potential to screen for conditions that are not detectable by current screening modalities. By improving false-positive rates and broadening the types of disease that are detectable in athletes, focused echocardiography by noncardiologist sports medicine physicians will hopefully improve the detection of threatening cardiovascular conditions in athletes and allow for a safer environment for sports participation.

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