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Accuracy of ECG-inclusive preparticipation screening in athletes: more work to be done

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"The controversial role of ECG during preparticipation screening remains one of the most widely and passionately debated areas in cardiovascular and sports medicine."

The sudden death of a young person during athletic participation is a rare but devastating tragedy. These events affect numerous segments of the community, including the victim's peers, family members, educators and medical professionals. Previous work has demonstrated that the majority of sport-related sudden deaths are attributable to a finite list of underlying cardiovascular diseases. This finding has lead to enthusiasm for preparticipation screening (PPS). PPS can be defined as any interaction between an athlete and a healthcare professional during which targeted steps are undertaken to assess for occult disease. The rationale for PPS relies on the notion that it can detect the cardiovascular conditions responsible for sports-related sudden death thereby facilitating appropriate, perhaps life-saving, interventions, including sport restriction. At present, PPS is recommended by most major organizations that oversee general clinical cardiovascular practice and the care of athletic patients [1–4]. Although PPS is widely endorsed, there is controversy about what constitutes the ideal strategy [5,6]. In addition, the overall efficacy of PPS for reducing sudden death remains uncertain [7]. The contemporary PPS debate most commonly focuses on the value of adding noninvasive testing, specifically 12-lead ECG, to the universally recommended medical/family history and focused physical examination. The controversial role of ECG during PPS remains one of the most widely and passionately debated areas in cardiovascular and sports medicine. Although the debate regarding the values of ECG during PPS is complex, it can be boiled down into two major categories. The first category includes issues of cost–effectiveness as it pertains to the formidable logistical challenges and financial costs associated with implementation and maintenance of an ECG-inclusive PPS [8]. The second category encompasses unresolved issues surrounding PPS testing 'accuracy' and downstream clinical implications. This editorial will address the latter issue.

The term accuracy, when used to assess the performance of a screening test, encompasses the basic metrics of sensitivity and specificity. In practice, sensitivity and specificity are often distilled into the more clinically relevant concepts of positive predictive value (PPV) and negative predictive value (NPV). PPV refers to conditional probability that an abnormal finding during screening truly reflects the presence of disease. In a similar fashion, NPV is a measure of how often a negative screening test truly reflects the absence of disease. These metrics define the reliability of a screening test thereby allowing clinicians and policy makers to make decisions about the ultimate application of a screening program. For any screening test, the derivation of PPV and NPV requires a definitive determination of disease prevalence in the specific population for which screening is intended and a careful

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EXPERT REVIEWS

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assessment, using a 'gold-standard' reference, of how a screening test performs to detect this disease.

With respect to PPS in young asymptomatic athletes, accurate determination of NPV and PPV remains unknown for the following reasons. First, there are no definitive statistics defining the prevalence of the diseases that have been associated with sudden death in an amply sized cohort of young, asymptomatic athletes. As such, disease prevalence estimates typically used in PPS modeling studies are typically extrapolated from alternative sources including general population statistics. Second, the ability of PPS to detect or exclude the relevant cardiovascular conditions, either with or without ECG, is unknown. This is largely due to the fact that the PPS has not been adequately examined in a population of athletes who have been sufficiently phenotyped with appropriate gold-standard diagnostic testing to confirm or exclude the presence of the diseases associated with sudden death. This point is of paramount importance as screening test accuracy cannot be determined in the absence of gold-standard disease determination.

> "Only with more data will we be able to responsibly determine the merits of adding ECG to the basic foundation of medical history and physical examination."

Despite these uncertainties, several publications have advanced our knowledge of this topic. Our group recently conducted a study in which US collegiate athletes were studied with echocardiography to confirm or exclude the key structural cardiac conditions associated with sudden death [9]. Next, this same population of athletes were subjected in a blinded study design to PPS limited to history and physical examination, and PPS with ECG added to history and physical examination. In this study, history and physical examination-limited PPS, as recommended by several governing organizations, performed relatively poorly particularly with respect to NPV (PPV = 15%; 95% CI: 5.1–31.9%; NPV = 98.7%; 95% CI: 97.3–99.5%). The addition of ECG to PPS improved the ability to definitively exclude underlying cardiovascular disease (NPV = 99.8%; 95% CI: 98.7–100.0%) but came with the cost of decreased PPV (10.4%; 95% CI: 5.1–18.3%) due to a marked and likely unacceptable rate of false-positive ECG findings. Two subsequent studies in similar populations, one with [10] and one without comprehensive echocardiography [11], have presented similar findings. In aggregate, the limited available data suggest that the accuracy of ECG-inclusive PPS is a 'mixed bag.' Specifically, the addition of ECG to medical history and physical examination appears to substantially improve the ability of screening to confidently exclude disease but does so at the cost of suboptimal disease detection characterized by high rates of false-positive testing. Application of recently updated criteria for ECG interpretation in athletes reduces but does not eliminate the burden of false-positive ECG testing [12].

It can be argued that detection of cardiovascular disease, the focus of the above-mentioned studies, is less important than the actual reduction of sudden death attributed to PPS. Retrospective reports examining the impact of ECG-inclusive PPS on sudden death rates in two large but very different populations present data leading to conflicting conclusions. Corrado *et al*. reported a marked reduction in the rates of sport-related sudden death over a 25-year period of ECG-inclusive PPS in the Veneto region of Italy [13]. The authors attributed this decline in deaths to improved detection of hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy largely attributable to ECG findings during PPS. In stark contrast, Steinvil and colleagues reported that the implementation of a mandatory ECG (and exercise stress test)-inclusive PPS program had no impact on the incidence of sudden death in Israel over a decade of observation [14]. Although many strengths and weaknesses of these reports have been addressed [7,15], it is safe to say that their simultaneous consideration prevents one from reaching a consensus about the impact of ECG-inclusive PPS on sudden death rates. Importantly, neither study provided data documenting the true- and false-positive detection rates of ECG-inclusive PPS for disease detection. Thus, we have no good real-world data examining the accuracy of PPS.

The only definitive way to determine the accuracy of PSS would be to perform a study with the following two-step approach. First, a large and sufficiently diverse population of young asymptomatic athletes would need to be phenotyped with the appropriate battery of tests that can definitively confirm or exclude the presence of the diseases that underlie sports-related sudden death. Second, the PPS technique in question must be examined in this precisely phenotyped population with respect to how often it finds (correct detection, PPV) and excludes (correct exclusion, NPV) these conditions. The costs and organizational challenges associated with such an effort would be substantial and thus to date, no appropriately powered study has been performed. Perhaps, the future will bring the necessary funding and organizational efforts required to perform this important work.

In the meantime, the accuracy of ECG-inclusive PPS must be considered unknown and the ultimate decision to apply this strategy will continue to be driven by speculations and personal opinions. The death of a young athlete is a catastrophe, and the clinical cardiovascular and sports medicine communities should remain committed to minimizing the incidence of this tragedy. Several steps may facilitate this important objective. First, public outreach and improved education should be emphasized as means to ensure that all athletes are provided with some form of screening. The bulk of the evidence suggests that some form of screening is better than no screening at all. Second, further study, even on a small scale is necessary. Locally manageable studies with an approach as delineated above should be undertaken to determine the accuracy of different PPS strategies. Only with more data will we be able to responsibly determine the merits of adding ECG to the basic foundation of medical history and physical examination.

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