



Pre-participation screening for risk of sports-related sudden death: can rest electrocardiogram be useful?

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Defining the most effective strategy for pre-participation cardiovascular screening of athletes to prevent sudden death remains controversial. The inclusion of the 12-lead electrocardiogram is debated.

On one hand, rest ECG seems to do much better than history interview and physical examination. The well-known Italian experience had spectacular results, with a 90% decrease in the incidence of cardiac sudden deaths among athletes between 1979 and 2004.

On the other hand, the incidence of cardiac sudden deaths among young athletes remains very low, from 0.5 to 1 event per 100,000 person-years, less than 50 events each year in France. The systematic use of an electrocardiogram, even if interpreted by a trained professional, leads to a high rate of false positives. This lack of specificity is detrimental for patients' health. What is more, the use of a systematic ECG would involve major costs, including purchasing of device, training and medical fees.

In conclusion, existing data do not seem to justify the implementation of a systematic ECG in pre-participation cardiovascular screening of athletes to prevent sudden death.

Introduction

Regular practice of sports has beneficial effects on health. However, serious accidents can occur during intense practice. Cases of sudden death are often publicized, and their emotional impact on the general population is considerable. Sudden death is considered as secondary to the practice of sport when it occurs during moderately to intensely strenuous sports-related effort, or during the hour following its cessation¹.

Sports-related sudden death is a rare pathology, of which the incidence varies according to studies and countries from 0.5 to 4 out of 100,000 sportspersons a year²⁻⁴. In 80 to 90% of the reported cases non-traumatic sudden deaths are of cardiovascular origin^{5,6}. In sportspersons aged over 35 years, coronary disease is predominant; when they are younger, the deaths are generally secondary to cardiac arrhythmia, cardiomyopathy or congenital anomaly^{7,10}. The main etiologies involve hypertrophic cardiomyopathy (25 to 50% of sudden deaths according to Anglo-Saxon data)¹¹, arrhythmogenic right ventricle dysplasia (the first cause in Italy of sports-related sudden death)¹² and a congenital anomaly of the coronary arteries, which accounts for 15 to 20% of sudden deaths of American athletes^{11,13}.

Other, considerably more infrequent etiologies have been described; they include myocarditis,

Wolff-Parkinson-White syndrome, long QT syndrome and Brugada syndrome⁷. On the average, 9 out of every 10 cases of sudden death involve men rather than women^{3,11}. Afro-Caribbean subjects are the most vulnerable, and football and basketball are the most commonly implicated sports.

Since 1999, an article in the French sports code¹⁴ has provided a framework for the sports certificates produced during dedicated consultations ("non-contraindication for sports"). The theoretical objective of these medical checks is to screen for the cardiovascular anomalies causing sudden death. The non-contraindication for sports certificate is mandatory with regard to sports competitions and to sports licenses for competitive purposes, whatever the sport practiced and the age of the patient. It has got to be issued annually. And even though recreational activities and leisure sports are not subject to any official regulatory text, a certificate can be requested by the person supervising the physical activity. Finally, in the framework of school-based sports practice, a non-contraindication for sports certificate is not required. However, in a French school setting a certificate of total or partial incapacity can be delivered at the request of a third party (<http://vosdroits.service-public.fr/particuliers/F1030.xhtml>).

Key words

Mass screening

Death sudden cardiac

Electrocardiography



In France, for sportspersons other than professional athletes, the contents of the non-contraindication for sports consultation (the VNCI) are not standardized. A VNCI can be carried out by any physician, unless otherwise decided by a given sports federation. The medical visit is not reimbursed by French social security. That said, the French sports medicine society (SFMS) suggests organization of a complete physical examination including a detailed questionnaire¹⁵. And in 2009, the French cardiology society (SFC) issued its proposals on VNCI contents regarding practice of competitive sports by subjects aged from 12 to 35 years⁶. Based on the guidelines of the European Society of Cardiology (ESC), they recommend, in addition to the questionnaire and the clinical examination, performance of a rest electrocardiogram (ECG) in view of detecting the underlying cardiovascular diseases responsible for sudden deaths¹⁶. The ECG would be carried out every three years from the ages of 12 through 20, and once every five years from the age of 20. Systematic addition of an ECG to the VNCI is a subject that has been hotly debated in the scientific community. A few months ago, an official statement from the national college of general practitioner teachers (CNGE) contested the recommendation, claiming that it was supported by low-level evidence¹⁷. The position of the CNGE is in agreement with the stand taken by the American Heart Association¹³.

Every year, the overwhelming majority of the more than 15 million sports licenses issued in France are delivered by general practitioners¹⁸. The contents of the non-contraindication for sports consultation, and particularly the interest of including a rest ECG, are consequently of paramount importance. In this respect, several questions call for an answer. What is the actual incidence of sudden deaths in sportspersons? What are the conclusions of foreign-based experiments on the inclusion of an ECG in the sports-related VNCI? What would be the consequences, particularly with regard to false positives and attendant costs, of adding an ECG to the clinical examination?

Sudden sports-related deaths: Their incidence and the difficulties of data gathering

34 million sportspersons

In France, 34 million persons ranging in age from 15 to 75 years practice a sports activity at least once a week throughout the year 18. One third

of them are from 15 to 30 years old¹⁹. Among these 34 million sportspersons, 9 million participate in competitions, 8% of which require high-level training. Among the 9 million competitors, half are less than 35 years of age, and they are the 4.5 million sportspersons relevant to the recommendations of the SFC on use of an electrocardiogram in the sports-related VNCI. Finally, professional sportspersons or athletes in France number approximately 15000¹⁸. It is worth noting that definitions of the latter, that is to say of the population to which the recommendations could apply, differ significantly from one country to the next. For example, the American Heart Association defines an elite athlete or competitive athlete as a person participating in an individual or team sport necessitating systematic training and involving regular competitions with a high level of excellence; the athletes may be either professionals or high school or college and university students. On the other hand, the European Society of Cardiology does not include school-based athletes in its definition of sportspersons at risk¹⁶.

Low and difficultly measurable incidence of sudden deaths

It is difficult to accurately gauge the actual incidence of sports-related sudden deaths; the available data in the literature are highly disparate.

In the United States, incidence of sudden death in young sportspersons varies according to the different studies from 0.5 to 4 cases for 100,000 sportspersons per year^{2,11,21-23}. In Italy during the 1980s, incidence of sudden death in sportspersons aged from 12 to 35 years came to 3.76 cases for 100,000 per year. At present, the measured incidence in Italy is lower than 1 case for 100,000 sportspersons per year^{12,24}.

In France, a prospective multicenter study took place between 2005 and 2010. All cases of sports-related sudden death were reported by means of a centralized database including information from all the emergency medical services (SAMU) in France. Over the five-year period, some 820 cases of sports-related sudden death were reported, which meant a yearly incidence of 0.46 cases for 100,000 sportspersons with ages ranging from 15 to 75. Only 6% of the cases of sudden death involved competitive athletes of 10 to 35 years of age^{3,25}.

The results of these different studies should be considered with caution. For one thing, the populations analyzed are not systematically



comparable. Most of the American data involve sudden deaths of sportspersons having practiced in a school or university environment conducive to a professional athlete rather than a typical license-holder; as a result, generalization is far from easy. For another, the working methods applied were highly diversified. While the French and Italian studies were prospective, the other studies implemented retrospective data collection methods, using information originating in the media, the insurance industry or retrospective electronic records. The variations in incidence can be partially explained by the variations in methodology^{2,22}.

Screening programs including an ECG: contradictory results

Several systematic screening programs for risk of sports-related sudden death have been set up in various countries. While some of them involve performance of an electrocardiogram, others do not. Among the former, the Italian and Israeli programs have been the subjects of several publications. The Italian program is by far the most famed, and also the oldest^a. Its foundations were laid down in the aftermath of the 1960 Rome Summer Olympics. In 1971, a medical protection law for sports activities was paved the way to introduction of preventive interventions aimed at identifying diseases potentially fatal to sportspersons. A 1982 decree specified the constitutive elements of this early detection program²⁶. It was relevant to persons aged from 12 to 35 who were participating in an organized sports program involving regular training and competition. The minimal protocol provides for collection of information on personal and family medical history, a clinical examination and a 12-lead ECG. Supplementary tests are carried out when the initial evaluation yields positive results¹². The tests are administered by sports physicians in dedicated public centers. The effectiveness of this screening method was evaluated in 2004 in a study conducted in the Veneto region based on data that had been gathered since 1979. The results showed that yearly incidence of sudden cardiovascular deaths in the screened athletes had fallen by 89% (from 3.6 deaths for 100,000 persons per year in 1979-1980 to 0.4 deaths for 100,000 persons per year in 2003-2004; $p < 0.001$). Over the same period of time, the mortality rate for non-screened individuals essentially remained the same, suggesting that the

a) The first initiative involving systematic use of ECG as a screening test was actually Japanese, and dates back to the 1970s. As it only considered children, it will not be a topic in this article.

significantly lowered mortality in the screened group was not due to modifications of the mortality rate in the population taken as a whole¹².

In 1997, Israel introduced a mandatory screening applicable to all sportspersons²⁷. It involved all individuals practicing a sport, whatever their age. It comprised a medical questionnaire, a clinical examination and a rest electrocardiogram. In addition, a stress test was supposed to take place once every four years for sportspersons aged 17 to 34, and then every year once they were 35. As was the case in Italy, the tests were administered by sports physicians. A study was conducted in 2009 to assess the effectiveness of this screening program. Incidence of sports-related sudden deaths was measured through systematic analysis of the two main Israeli information newspapers. Mean yearly incidence of sports-related sudden deaths was 2.54 for 100,000 inhabitants per year prior to 1997, and 2.66 for 100,000 inhabitants per year subsequent to 1997 ($p = 0.88$)²⁷.

Whatever the procedure, validity remain questionable

Screening for cardiovascular anomalies prior to participation in sports activity is aimed at suspecting or identifying possible preexisting cardiovascular anomalies likely to place would-be sportspersons at risk¹³. Given the circumstances, the proposed procedures require assessment in terms of sensitivity (proportion of false negatives) and specificity (proportion of false positives). The notions of cost and feasibility, which shall be discussed later on, have also got to be taken into account. At present, scholarly associations agree on the existence of a "ground zero" set of data to collect during a VNCI: individual and family history of cardiovascular disease, the end results of a targeted medical examination. A complete list of the 14 items of interest during a VNCI compiled by the American Heart Association was recently updated (see box 1). However, all concerned parties are in agreement on the exceedingly low sensitivity of the procedure. A retrospective study on sports-related sudden deaths of individuals previously screened by questionnaire and clinical examination found that cardiovascular disease had been diagnosed in less than 5% of the cases²⁸. Except for hypertrophic cardiomyopathy, in which systolic murmurs can be found in approximately one quarter of the patients, most of the heart diseases responsible for sudden death present little if any clinical expression^{13,20}.

In terms of sensitivity, on the other hand, additional use of an electrocardiogram yields an



appreciable advantage.

In the study by Corrado et al., in which 34,000 Italian athletes were screened using an ECG, 3016 underwent cardiac ultrasound. Among the 22 athletes in whom hypertrophic cardiomyopathy was discovered, 5 (23%) presented with family history or a suspicious clinical sign, and 18 of them (82%) presented with electrocardiographic abnormalities²⁹. However, addition of an ECG to the screening procedure has an impact on specificity, and consequently on the proportion of false positives.

The heightened false positive rate is mainly related to the presence of electrical modifications in the athlete's heart; it is likewise frequently associated with non-pathological cardiac hypertrophy³⁰.

These considerations prompted the publication by the European Society of Cardiology in 2010 of the electrocardiographic criteria through which these electrical anomalies can be distinguished and classified as physiological or pathological (see box 2)³¹. Notwithstanding application of these criteria, however, the proportions of false positives have remained elevated. The data the most favorable to screening by ECG report false positive rates of 9%, but they were collected in Italy, where the ECGs of sportspersons are interpreted by specially trained sports physicians¹². In a British study published in 2014, 4081 competitive athletes and 7764 individuals not practicing a sport received ECG screening. Without taking into account the ECG abnormalities specific to the athlete's heart and associated with training, 33% of the sportspersons and 22% of the non-sportspersons presented with pathological ECGs³². And while new electrocardiographic criteria (the Seattle criteria) were recently defined, their validation currently remains incomplete.

The false positive rates have several repercussions. First of all, they can be a source of considerable anxiety for the person involved. They can also prompt the healthcare professional to ask him or her to undergo additional tests so as to confirm (or not) the existence of cardiovascular disease. While some of these complementary examination are non-invasive (cardiac ultrasound, Holter monitor, stress test, magnetic resonance imagery), others are invasive: ventriculography, coronarography, clinical cardiac electrophysiology and myocardial biopsy. Not only may these tests be potentially iatrogenic, but they also have considerable economic impact.

Hard-to-manage organizational and financial consequences

It is difficult to estimate the cost-effectiveness of the establishment of ECG screening during non-

contraindication for sports consultations. Once again, the available data are both limited and contradictory. Wheeler et al. have estimated at \$42000 that cost per saved year of life of an ECG added to the screening procedure. However, this result should be taken with caution; for one thing, risk of sudden death has been evaluated using the Italian rather than the American data; for another, screening was restricted to a group of competitive athletes ranging in age from 14 to 22 years. In this study, neither screening by questionnaire and physical examination alone nor screening by ECG applied to large patient cohorts were considered as cost-effective³³.

Box 1- List of the 14 items in the VNCI sports consultation recommended by the American Heart Association in screening for cardiovascular anomalies of the competitive athlete

Medical history

Individual medical history

1. Chest pain/discomfort upon exertion
2. Unexplained fainting or near-fainting
3. Dyspnea, excessive and unexplained fatigue associated with exercise
4. Known heart murmur
5. High blood pressure
6. Prohibited or restricted practice of a sport
7. Cardiac exploration prescribed by a physician

Family medical history

8. One or more relatives who died of heart disease, before age 50
9. Close relative under 50 with disability from heart disease
10. Certain cardiac conditions in family members: hypertrophic or dilated cardiomyopathy, long QT syndrome, channelopathy, Marfan syndrome, cardiac arrhythmia or other genetic cardiovascular disease in a close relative

Physical examination

11. Physical appearance of heart murmur
12. Femoral pulses to exclude narrowing of the aorta
13. Physical appearance of Marfan syndrome
14. Brachial artery blood pressure (in a sitting position)

Box 2 - Electrocardiographic criteria necessitating specialized consultation (according to the European Society of Cardiology)

- Left atrial enlargement: negative portion of the P wave in lead V1 $\geq 0.1\text{mV}$ in dept and $\geq 0.04\text{s}$ in duration
- Right atrial enlargement: peaked P wave in leads II or III or V1 $\geq 0.25\text{mV}$ in amplitude
- Frontal-plane QRS axis deviation right $\geq +120^\circ$ or left -30° to -90°
- Increased voltage: amplitude of an R or S wave in a standard lead $\geq 2\text{mV}$, or $\geq 3\text{mV}$ in V1, V2, V5 or V6
- Abnormal Q waves $\geq 0.04\text{s}$ in duration or $\geq 25\%$ of the ensuing R wave or QS pattern in ≥ 2 leads
- Right or left bundle-branch block with QRS duration $\geq 0.12\text{s}$
- R or R' wave in lead I $\geq 0.5\text{mV}$ in amplitude an R/S ratio ≥ 1
- ST-segment depression or T-wave flattening or inversion in more than 2 leads
- Corrected QT interval $> 0.44\text{ s}$ in men, and $> 0.46\text{ s}$ in women
- Premature ventricular beats or more severe ventricular arrhythmia
- Supraventricular tachycardia, atrial flutter or atrial fibrillation
- Ventricular preexcitation : short PR interval ($< 0.12\text{ s}$) with or without delta wave
- PR interval ($< 0.12\text{ s}$) with or without delta wave
- AVB 1, AVB 2 or AVB 3
- Sinus bradycardia lower than 40 beats/min at rest with increase lower than 100 beats/min during moderate exercise

However, the 2007 report of the American Heart Association draws different conclusions. Implementation of a systematic program of ECS screening of American high school and university athletes would cost around 2 billion dollars a year. The "bill" for prevention of each theoretical case of sudden death would be as high as 3.4 million dollars¹³.

In France, possible future establishment of a systematic ECG screening program in primary care medicine would encounter several organizational limits. First of all, 50% of French GPs are not equipped with an ECG apparatus³⁴. Moreover, they would require training in ECG interpretation, particularly with regard to the criteria of the aforementioned SFC. And from a financial standpoint, there exist few French data on the consequences of implementation of this type of screening.

Taking into account the 4.5 million sportspersons aged from 12 to 35 years and the frequency of ECG use recommended by the SFC, the yearly cost of a rest electrocardiogram would come to 1.3 million euros¹⁸. According to the most recent version of the French *Classification commune des actes médicaux*, today's prices for 12-lead ECG and cardiac ultrasound are 14.02 and 96.49 euros respectively (<http://www.ameli.fr/accueil-de-la-ccam/index.php>). The cost of consultations including ECG for VNCIs would consequently amount to around 122 million euros. And considering that a mere 10% of ECGs are likely to detect pathological signs, an estimate decidedly on the low side, the supplementary cost of ultrasound alone for but 130,000 athletes would approach 13 million euros. Even if these summarily processed figures can in no way replace an actual cost-effectiveness study, the estimated sum total of 135 million euros should be put in relation with the sports-related sudden deaths in subjects aged from 12 to 35 years, that is to say with regard to a number of cases ranging from 20 to 50³. It should be noted, to conclude, that this estimate does not take into account either equipment costs or those entailed by the initial and ongoing training of general practitioners.

Synthesis

According to the World Health Organization, one of the required criteria for establishment of systematic screening is the relative frequency of a given disease. Even though it is tragically severe, the sudden death of a young athlete is a rare pathology, involving at most 50 cases per year in France.

That much said, the addition of an electrocardiogram to the traditional screening procedure is not without interest. When interpreted by a trained healthcare professional able to distinguish anomalies secondary to training from potentially pathological abnormalities, an ECG yields conclusions of pronouncedly greater validity than those drawn from a patient's medical history and physical examination alone. However, the conclusions come at the price of unusually elevated number of false positives. The low degree of specificity engenders multiple difficulties, first from the patient's standpoint in terms of anxiety and potential iatrogenesis, and second from a social angle in terms of cost.

Current recommendations by the French and European societies of cardiology are largely based on Italian data¹². Even though it has been subjected to numerous critical appraisals, in terms of implementation of an intervention and as regards long-term large-scale collection of epidemiological data the Italian experience constitutes an exemplary success. That much said, for several reasons its generalizability is limited. For one thing, the professionals involved in screening are not general practitioners; they are sports physicians who have been specially trained in the interpretation of electrocardiograms; their training is likely to partially explain the low percentage of false positives. For another, while the Italian intervention undoubtedly helped to reduce the rate of sudden sports-related deaths among the young, initial incidence of the latter was 10 times greater than their incidence in France according to the statistics compiled by Marijon³. At a time when the effectiveness of a number of screening procedures is being contested, and when over diagnosis has come into prominence as a possible danger, there is a lack of data sufficing to justify systematic use of an electrocardiogram when screening for the sudden death risk incurred by a young athlete³⁵. This does not mean that the issue of sudden sports-related death should be neglected. Alternatives exist, consisting particularly in improved pre-hospital treatment of cardiorespiratory arrest. It also involves enhanced sensitization and training of the general public in measures of first aid resuscitation, including the use of public-access implantable automatic defibrillators³⁶.



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