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CLINICAL RESEARCH
Epidemiology, prevention, and health care policies

Value of screening for the risk of sudden cardiac death in young competitive athletes

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Abstract

Aims This study aimed to report the long-term findings of the Italian programme of cardiovascular preparticipation screening (PPS) in young, competitive athletes.

Methods and results The study assessed the diagnostic yield for diseases at risk of sudden cardiac death (SCD), the costs of serial evaluations, and the long-term outcomes of PPS in a large population of Italian children (age range, 7–18 years). The PPS was repeated annually and included medical history, physical examination, resting electrocardiogram, and stress testing; additional tests were reserved for athletes with abnormal findings. Over an 11-year study period, 22 324 consecutive children [62% males; mean age, 12 (interquartile range, 10–14) years at first screening] underwent a total of 65 397 annual evaluations (median 2.9/child). Cardiovascular diseases at risk of SCD were identified in 69 children (0.3%) and included congenital heart diseases ($n = 17$), channelopathies ($n = 14$), cardiomyopathies ($n = 15$), non-ischaemic left ventricular scar with ventricular arrhythmias ($n = 18$), and others ($n = 5$). At-risk cardiovascular diseases were identified over the entire age range and more frequently in children ≥12 years old ($n = 63$, 91%) and on repeat evaluation ($n = 44$, 64%). The estimated cost per diagnosis was 73 312€. During a follow-up of 7.5 ± 3.7 years, one child with normal PPS findings experienced an episode of resuscitated cardiac arrest during sports activity (event rate of 0.6/100.000 athletes/year).

Conclusion The PPS programme led to the identification of cardiovascular diseases at risk of SCD over the whole study age range of children and more often on repeat evaluations. Among screened children, the incidence of sport-related cardiac arrest during long-term follow-up was low.

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Structured Graphical Abstract

Key Question

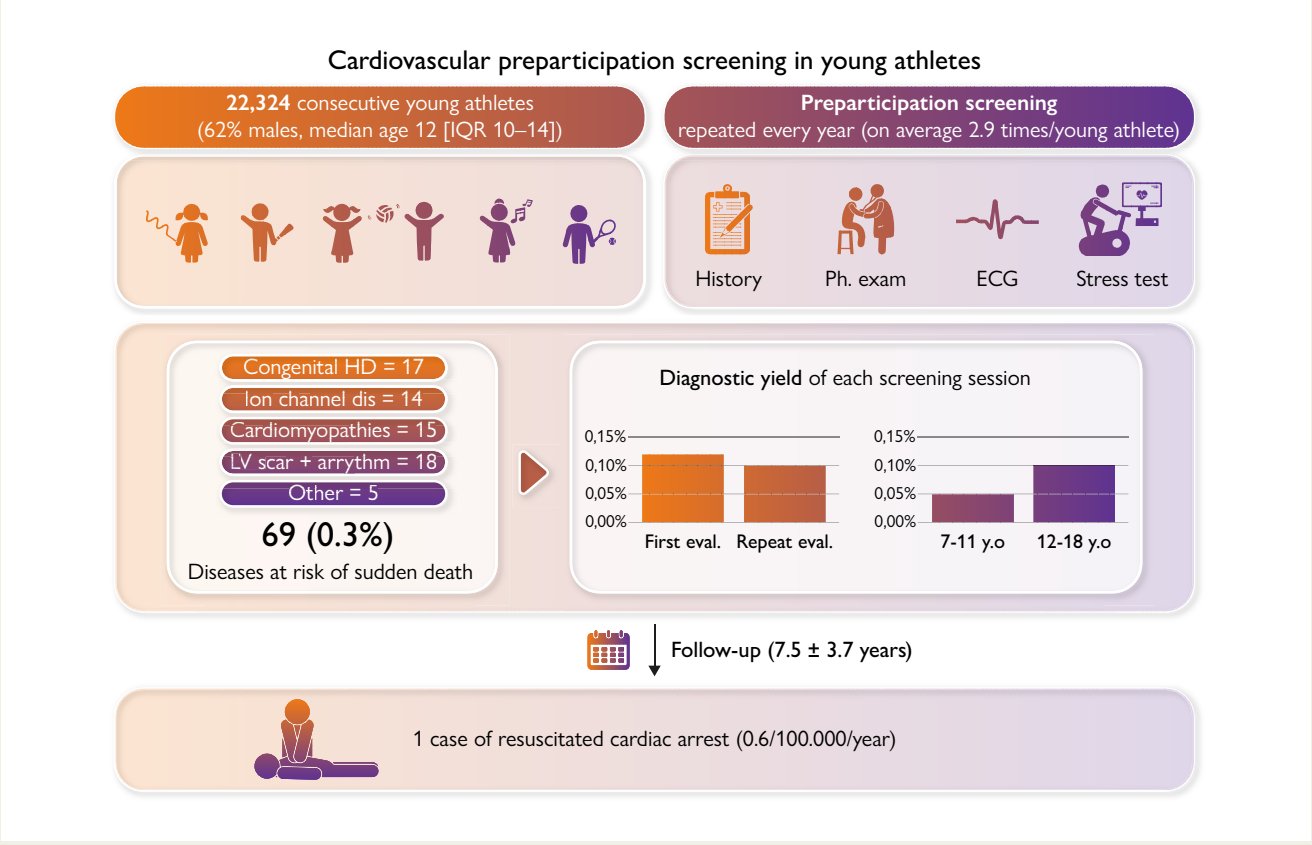
• What are the diagnostic yield and costs of a preparticipation screening program based on early start (<14 years old) and annual evaluations of young athletes?
• What is the outcome of screened young athletes?

Key Finding

• Diseases at risk of sudden death were identified both at first and repeat evaluations and over the whole study age range.
• The incidence of cardiac arrest during a long-term follow-up was low.

Take Home Message

The diagnostic yield and favorable long-term outcome provide support for preparticipation screening of young athletes based on annual evaluations.



The study enrolled a cohort of 22 324 children who underwent a mean of 2.9 annual preparticipation screening that included history, physical examination, resting ECG, and exercise testing. Cardiovascular diseases at risk of sudden cardiac death were identified in 69 children (0.3%). The diagnostic yield of each screening session was 0.12% at the first evaluation and 0.1% at repeat evaluation. Moreover, it was 0.05% in children 7- to 11-year-old vs. 0.12% in those 12- to 18-year-old. During a follow-up of 7.5 ± 3.7 years, one child with normal preparticipation screening findings experienced an episode of resuscitated cardiac arrest during sports activity. HD, heart disease; LV, left ventricular; IQR, interquartile range.

Keywords Athlete • Cardiac arrest • Cardiomyopathy • Screening • Sports cardiology

Introduction

Sudden cardiac death (SCD) in young competitive athletes is caused by a wide spectrum of cardiovascular conditions, including congenital heart diseases, genetic cardiomyopathies and channelopathies, and acquired conditions.[1] Cardiovascular evaluation of athletes before participation in competitive sports offers the possibility to identify athletes with cardiovascular disease at risk of SCD and to prevent sport-related fatalities.[2] Preparticipation screening (PPS) is recommended by the American Heart Association (AHA), the European Society of Cardiology (ESC), the International Olympic Committee, and most medical associations and sports federations worldwide.[2–5] However, the optimal PPS protocol

is still debated,[1] with particular reference to the inclusion of a screening electrocardiogram (ECG), the appropriate starting age and frequency of repeat cardiovascular evaluations, and eligibility of athletes diagnosed with cardiovascular diseases at risk of SCD.

An outcome study on English football players undergoing a single PPS session including once-only evaluation at the age of 16 years reported an incidence of SCD over a long-term follow-up much greater than historical estimates.[6] At variance with this screening modality, the Italian programme, that has been in practice since 1982, mandates that the preparticipation cardiovascular evaluation including ECG starts at the beginning of athletic activity (even in early childhood) is repeated every year and entails the non-eligibility to competitive sports activity of athletes diagnosed with cardiovascular disease at risk of SCD.[7]

The present study was designed to evaluate the results of the Italian PPS programme in a large population of children (age, 7–18 years), by assessing the diagnostic yield of heart diseases at risk of SCD, the costs of serial cardiovascular evaluations, and the long-term outcome.

Methods

Study population

The study population included children aged 7–18 years with no history of cardiovascular disease who underwent serial cardiovascular screening before participation in competitive sports activity during the time interval from 2009 to 2019 at the Center for Sports Medicine of Treviso, Veneto Region of northeastern Italy. This centre serves the entire population of children of the Treviso country area undergoing PPS, which is provided for free by the National Health System (funded with taxes) under the age of 18 years. The Center for Sports Medicine of Treviso is a leading centre for sports medicine in the Veneto region of Italy and is a representative regional observatory for monitoring the outcome of the Italian PPS programme.

The results of PPS were evaluated from the first screening session to the last repeat evaluation or until their 18th birthday. Preliminary and limited data on PPS of the subgroup of adolescents have been previously published in the form of a Research Letter.[8]

The study was approved by the Ethical Committee of the Treviso province, and because the study reports observational and fully anonymized data, consent was waived. Study data are available from the corresponding author upon reasonable request.

Screening protocol

According to Italian law,[9] all individuals who participate in an organized sports programme requiring regular training and competition must undergo an annual medical evaluation by a physician with a specialty degree in sports medicine. The age when competitive sports activity starts is established by the Italian Sport Federations and varies for different sport disciplines (see Supplementary material online, *Table S1*). Accordingly, the minimal age of the first PPS session in the present study varied for the specific sports activity practiced by the child-athlete. Screening is repeated on a regular basis every year.

The Italian protocol of cardiovascular evaluation before participation in competitive sports activity has been previously reported in detail.[7] In brief, it includes a personal and family history questionnaire, physical examination, resting 12-lead ECG, and stress testing. A family history of SCD, cardiomyopathy, Marfan's syndrome, long-QT syndrome, Brugada syndrome, or other hereditary cardiovascular diseases in the first- or second-degree family members is considered significant and warrants more evaluation. The personal history is considered positive if the subject reported experiencing chest pain or discomfort during exertion, syncope or near-syncope, irregular heartbeats or palpitations, or shortness of breath or fatigue disproportionate to the degree of physical effort. Electrocardiograms were interpreted according to the international recommendations for interpretation of the athlete's ECG or previous iterations depending on the year of the evaluation.[10,11] Limited bicycle ECG stress testing, which was originally required by the Law for the calculation of the heart rate recovery as an index of athlete's physical fitness, is now used to evaluate the occurrence of effort-dependent ventricular arrhythmias.[12] This test lasts ~3 min and is performed on a cycle ergometer starting abruptly with a workload of 2 W/kg in females or 3 W/kg in males with load adjustments, if necessary, until reaching at least 85% of maximal heart rate. The test ends abruptly and is followed by 3 min of post-exercise monitoring.

Further testing

Athletes with a positive medical or family history, abnormal physical examination, ECG, or stress test underwent further investigations such as 12-lead 24-h ambulatory ECG monitoring (including a training session), maximal exercise testing (until muscle exhaustion), and echocardiography including the evaluation of the origin of coronary arteries. Cardiac magnetic resonance was prescribed for athletes with clinical, ECG, echocardiographic abnormalities or exercised-induced ventricular arrhythmias raising the suspicion of genetic cardiomyopathies, acute myocarditis, or post-inflammatory myocardial scar. Athletes with ventricular preexcitation on resting ECG were risk-stratified on the basis of the anterograde refractory period of the accessory pathway which was first evaluated non-invasively by the abrupt termination or persistence of preexcitation during maximal stress testing. Invasive electrophysiologic test was reserved to athletes with persistent preexcitation during exercise.

Management of athletes with cardiovascular diseases

According to the Italian Law, athletes with a diagnosis of a cardiac disease at risk of SCD were considered ineligible for competitive sports either temporarily (if a curative treatment was available) or permanently. All athletes not eligible for competitive sports were enrolled in a specific tailored leisure time exercise prescription programme in order to mitigate the consequences to their physical and mental health. The programme, called 'The second half of Julian Ross', also offers psychological support and follow-up medical management.

Costs analysis

A costs analysis of the cardiovascular PPS programme at the Sports Medical Center of Treviso was reported in detail in a previous study.[7] The cost analysis of PPS in the present study was performed according to this previous analysis, in which the total age-adjusted cost of a screening session, including both the fixed cost for first-line evaluation (62€) and the variable cost for additional investigations in the subset of athletes with suspicion of cardiovascular abnormalities, was estimated at 67€ in the age group 7–11 years and 79€ in the age group 12–18 years (Supplementary material online, *Table S2*). The cost per diagnosis was calculated as the number of diagnoses divided by the number of evaluations multiplied by the cost for each screening session. The incremental cost-effective ratio (ICER) for screening older vs. younger children was calculated as the ratio between the different costs and the different diagnostic yields of each screening session.

Outcome

The primary surveillance outcome was SCD or resuscitated cardiac arrest occurring in the screened athletic population, including both sport-eligible and non-eligible athletes. The surveillance period lasted from the first evaluation to the end of 2021. Outcome data were obtained from office visits, interrogation of the Registry of Juvenile SCD of the Veneto region of Italy in which reporting of all deaths is mandated by law, and review of all records of young patients admitted for resuscitated cardiac arrest in all hospitals of the Treviso province and the Padua University Hospital (regional hub for paediatric cardiac emergences). Moreover, systematic research in the local and national press was conducted for daily monitoring of reports

of cardiac arrests or SCD occurring during the study period either in those individuals permanently resident in the Treviso area or in those who moved to other regions or countries. Annual follow-up data were also available for all former athletes considered non-eligible for competitive sports who underwent annual cardiovascular evaluation in the sports cardiology outpatient clinic of the Center for Sports Medicine of Treviso.

Statistical analysis

Categorical data are expressed as counts (%) while continuous data are expressed as mean with standard deviation or median with interquartile range (IQR) according to distribution.

Results

The study population included 22 324 consecutive athletes (62% male, 89% Caucasian) who underwent a total of 65 397 annual preparticipation cardiovascular evaluations (mean 2.9 per athlete) over the 11-year study period. The median age at the first screening was 12 (IQR, 10–14) years. Additional investigations were prescribed after 5828 (8.9%) first-line evaluations and included echocardiography ($n = 5,493$, 8.4%), 24-h ambulatory ECG monitoring ($n = 5,297$, 8.1%), maximal exercise testing ($n = 2616$, 4.0%), and cardiac magnetic resonance imaging ($n = 131$, 0.2%). Invasive electrophysiologic study or coronary angiography was performed on 14 athletes (0.02%). Reasons for additional investigations included a positive family history (2.6%), an abnormal physical examination (1.0%), or alterations of resting 12-lead ECG (3.0%), or exercise testing (5.1%).

Diagnostic yield

With multiple evaluations, a diagnosis of cardiovascular disease was made in 403 athletes, and included conditions unassociated (334; 1.5%) with or associated with SCD (69; 0.3%; *Table 1*).

At-risk cardiovascular conditions included congenital heart diseases in 17 athletes (including abnormal origin of coronary arteries in 11), channelopathies in 14, cardiomyopathies in 15, post-inflammatory or idiopathic non-ischemic left ventricular scar (NILVS) with ventricular arrhythmias in 18, and other conditions in 5. Fifty-one of 69 athletes (74%) with a diagnosis of a disease associated with SCD participated in team sports (soccer $n = 18$, volleyball $n = 15$, basketball $n = 10$, rugby $n = 6$, and other $n = 2$) while 18 practiced a variety of individual sports disciplines. Of the 69 athletes (70% males), 20 (29%) had a positive family history, symptoms, and/or abnormal physical examination, 41 (59%) had abnormalities on resting 12-lead ECG, and 36 (52%) demonstrated abnormalities on exercise testing (*Table 2*).

Of 69 diagnoses of cardiovascular diseases at risk of SCD, 25 (36%) were made at the initial screening evaluation and 44 (64%) on repeat cardiovascular evaluation (*Figure 1*). Cardiovascular diseases more frequently identified on repeat evaluation included inherited cardiomyopathies (11/15; 73%), NILVS with ventricular arrhythmias (15/18; 83%), and long-QT syndrome (8/13; 61%). The diagnostic yield of each screening session was 0.12% at the first evaluation (25 diagnoses of 22 324 first evaluations) and 0.1% at repeat evaluation (44 diagnoses of 43 073 repeat evaluations).

A sub-analysis of diagnoses by age showed that 6 of 69 (9%) diagnoses of cardiovascular diseases at risk of SCD were made in children who were 11 years old or younger at the time of the evaluation and 63 of 69 (91%) when children were 12 years old or older (*Figure 2*). This latter age subgroup included 13 of 15 children who were diagnosed with cardiomyopathies and all 18 children with NILVS. Fifty-one (74%) diagnoses were made in children younger than 16 years. The diagnostic yield of each screening session according to the age at the time of the evaluation was 0.05% (6 of 12 001 evaluations) in children 7–11 years old and 0.12% (63 of 53 396) in those 12–18 years old.

Cardiac conditions unassociated with SCD included idiopathic ventricular arrhythmias in 122 children, complex supraventricular arrhythmias in 54, valvular abnormalities in 45, low-risk ventricular preexcitation in 35, minor congenital coronary anomalies in 30 such as anomalous origin of the circumflex artery from the right coronary sinus with retroaortic course, simple congenital heart diseases in 26 arterial hypertension in 18, and other conditions in 4. Two athletes with partial anomalous venous returns and five with atrial septal defects underwent surgical correction.

Costs analysis

The cost of the entire screening process over the 11-year study period was 5 058 531€, with an estimated cost per diagnosis of heart disease associated with SCD of 73 312€. The cost per diagnosis, including both the cost of first-line examination and the cost of further investigations, of the serial screening process (initial *plus* repeat evaluations) was 7% higher than that of a single (initial) evaluation (73 312€ vs. 68 793€). The cost per diagnosis in the age group 7–11 years old was 140 041€ vs. 66 957€ in the age group 12–18 years old (ICER = 17 143€ per diagnosis).

Long-term outcome

During a mean (±SD) follow-up of 7.5 ± 3.7 years, one athlete from the entire cohort including both eligible and disqualified athletes experienced an episode of resuscitated cardiac arrest accounting for an event rate of 0.6/100.000 athletes/year. The athlete was a 15-year-old runner considered eligible for and participating in competitive sports activity after a normal cardiovascular evaluation 11 months before the event. The athlete collapsed during a training session due to ventricular fibrillation and was successfully resuscitated using an onsite automated external defibrillator. Despite thorough clinical investigations, including contrast-enhanced cardiac magnetic resonance, coronary computed tomography, electrophysiological study, ECG monitoring, exercise stress test, toxicological screening, sodium-channel-blocker test for Brugada syndrome and a comprehensive genetic screening panel for mutations associated with SCD, the cause of ventricular fibrillation remained unexplained. No athlete restricted from competitive sport experienced an adverse event.

Four athletes with ventricular preexcitation were allowed to resume competitive sports activity after successful catheter ablation of the accessory pathway. None of the remaining 65 children considered definitively non-eligible for competitive sports because of the diagnosis of cardiovascular diseases at risk of SCD, who entered a programme of management and annual follow-up in the outpatient sports cardiology clinic of the Center for Sports Medicine of Treviso, suffered a cardiac event.

Discussion

The present study was designed to assess the results of annual cardiovascular PPS in a large cohort of Italian children (age range, 7–18 years). The main study results were that (i) the overall yield of diagnoses of cardiovascular diseases, either associated or unassociated with SCD, among asymptomatic children was 1.8% over a mean of three PPS evaluations; (ii) the identification of cardiovascular diseases associated with SCD encompassed the entire study age range of the children with a trend toward an increasing diagnostic yield with increasing age; (iii) the diagnostic yield of repeat (annually) screening evaluations was

Table 1 Diagnoses of cardiovascular diseases at risk of sudden cardiac death over serial screening

	All evaluations $n = 65\,397$	First evaluation $n = 22\,324$	Second evaluation $n = 14\,155$	Third evaluation $n = 10\,102$	Fourth evaluation $n = 7819$	Fifth evaluation $n = 5548$	Sixth evaluation $n = 3633$	Seventh evaluation $n = 1816$
Anomalous origin of the coronary artery	11	7	—	2	1	1	—	—
Aortic coarctation	1	1	—	—	—	—	—	—
Arrhythmogenic cardiomyopathy	4	1	3	—	—	—	—	—
Brugada syndrome	1	—	—	—	—	—	—	1
NILVS scar with arrhythmias	18	3	3	7	—	1	2	2
Complicated bicuspid aortic valve	1	—	—	1	—	—	—	—
High-risk ventricular preexcitation	4	2	—	1	1	—	—	—
Hypertrophic cardiomyopathy	8	3	2	2	—	—	1	—
Long-QT syndrome[a]	13	5	4	2	2	—	—	—
Marfan syndrome	1	—	1	—	—	—	—	—
Mitral valve prolapse with arrhythmias	3	2	—	1	—	—	—	—
Other[b]	4	1	2	1	—	—	—	—
Total	69	25	15	17	4	2	3	3

NILVS, non-ischaemic left ventricular scar.
[a]Confirmed by genetic analysis.
[b]Dilated cardiomyopathy in 1, aortic dilation secondary to familial connective tissue disorder in 1, Fabry disease in 1, myocardial non-compaction in 1.

Table 2 Abnormal findings at preparticipation evaluation for cardiovascular diseases at risk of sudden cardiac death

	Family history	Symptoms	Physical examination	Resting ECG	Stress testing
Anomalous origin of the coronary artery	1 (9%)	2 (18%)	—	8 (73%)	1 (9%)
Aortic coarctation	—	1 (100%)	1 (100%)	1 (100%)	—
Arrhythmogenic cardiomyopathy	2 (50%)	—	—	4 (100%)	2 (50%)
Brugada syndrome	1 (100%)	—	—	1 (100%)	—
NILVS with arrhythmias	—	1 (6%)	—	5 (28%)	15 (83%)
Complicated bicuspid aortic valve	—	—	1 (100%)	1 (100%)	—
High-risk ventricular preexcitation	—	—	—	4 (100%)	—
Hypertrophic cardiomyopathy	3 (38%)	—	2 (25%)	6 (75%)	3 (38%)
Long-QT syndrome	2 (15%)	—	—	9 (69%)	10 (77%)
Marfan syndrome	—	—	1 (100%)	—	—
Mitral valve prolapse with arrhythmias	1 (33%)	—	2 (66%)	—	3 (100%)
Other[a]	2 (50%)	1 (25%)	—	3 (75%)	2 (50%)
Total	12 (17%)	5 (7%)	7 (10%)	41 (59%)	36 (52%)

NILVS, non-ischaemic left ventricular scar.
[a]Dilated cardiomyopathy in 1, aortic dilation secondary to familial connective tissue disorder in 1, Fabry disease in 1, and myocardial non-compaction in 1.

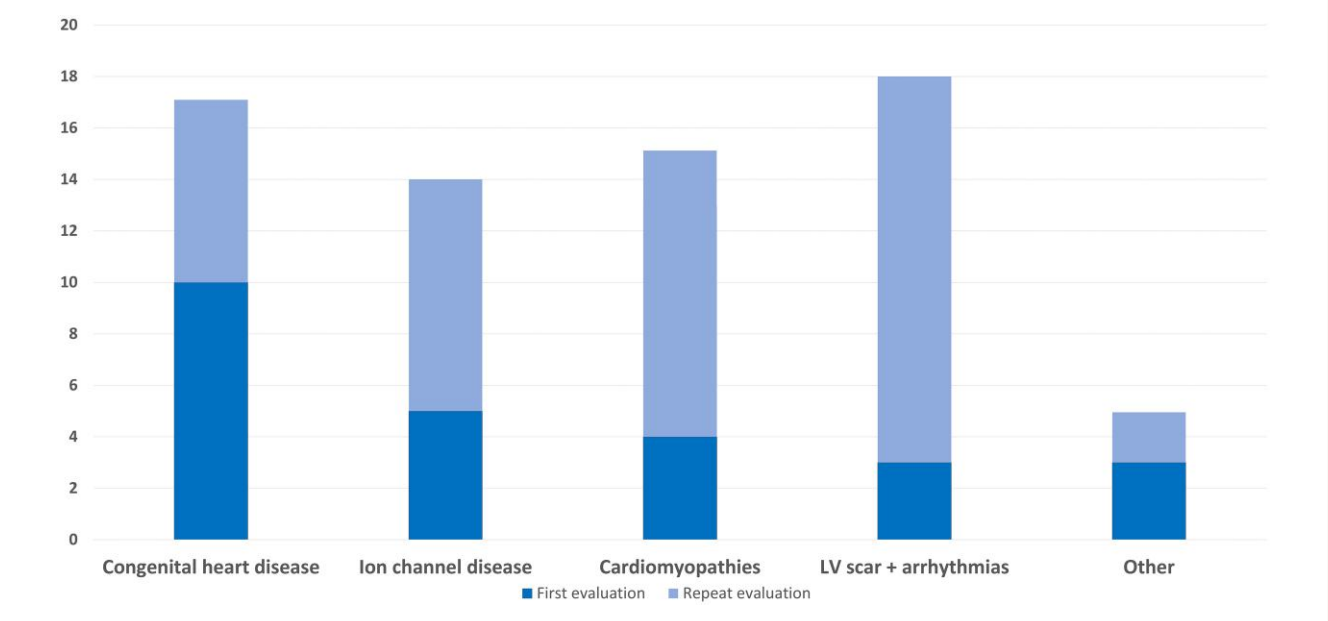


Figure 1 Distribution of diagnoses of cardiovascular diseases at risk of sudden cardiac death according to the preparticipation cardiovascular evaluations.

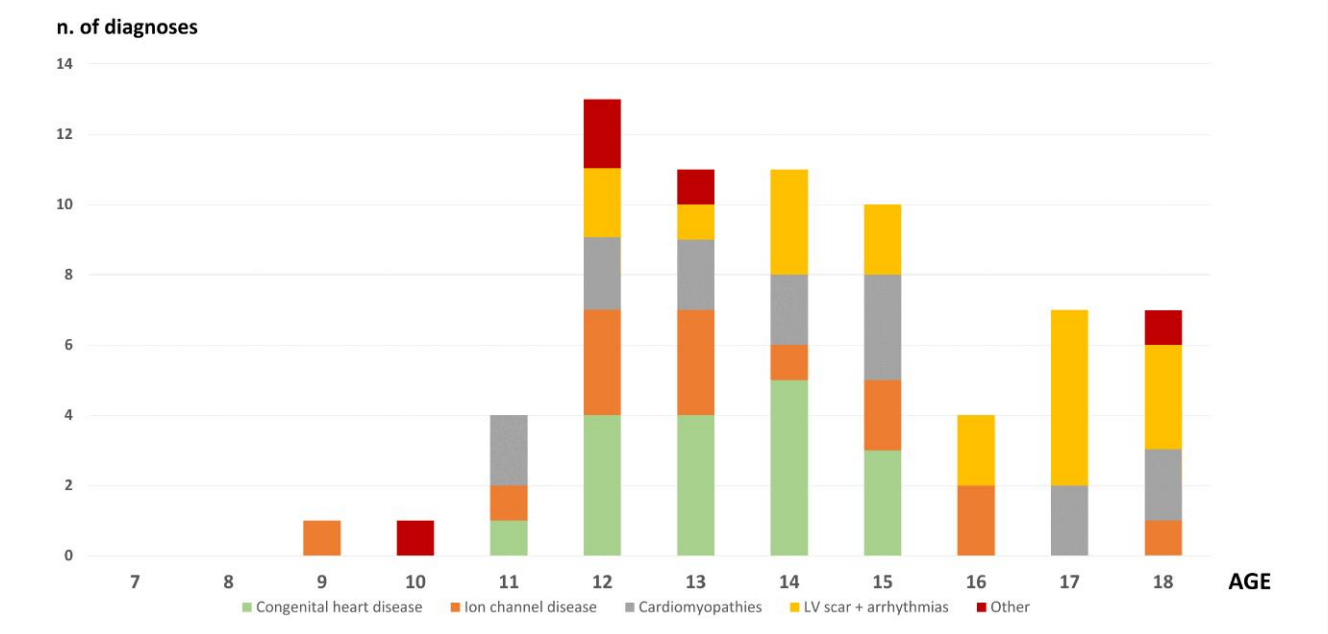


Figure 2 Distribution of cardiovascular diseases at risk of sudden cardiac death according to the age at the time of diagnosis.

similar to that of the first evaluation, accounting for an increase of the overall diagnostic yield by nearly two-thirds in comparison with once-only screening; (iv) the rate of SCD or resuscitated cardiac arrest during follow-up was 0.6/100.000/year (*Structured Graphical Abstract*).

Diagnostic yield

In the present study, preparticipation cardiovascular screening led to the identification of cardiovascular diseases at risk of SCD in 69 asymptomatic children (0.3%). This prevalence of at-risk cardiovascular diseases among screened children is consistent with that reported in previous studies of young competitive athletes (0.25%–0.5%).[13–18] In addition, other cardiovascular diseases not associated with SCD were diagnosed in 1.5% of the study population, accounting for an overall diagnostic yield of 1.8%. Less than one-third of athletes were diagnosed because of a positive family history, symptoms, or abnormal physical examination, while the remaining diagnoses were prompted by abnormalities on resting ECG or exercise testing.

According to the Italian law, all individuals who participate in an organized sports programme requiring regular training and competition must undergo a serial (annual) medical evaluation, starting at an age that is established by the various sports Federations. This screening modality differs from that of other countries: for instance, in a study reporting the UK screening programme, children underwent a single cardiovascular evaluation at the age of 16 years.[6]

Our study results suggest that the Italian PPS programme starting at a variable age of 7–14 years may allow earlier identification of cardiovascular diseases at risk of SCD during sports. Indeed, 51 (74%) diagnoses of cardiovascular diseases at risk of SCD were detected in children younger than 16 years. The spectrum of cardiovascular diseases identified in the age group <16 years included congenital heart diseases, genetic channelopathies, and either genetic or acquired heart muscle diseases. This indicates that a delay of the first preparticipation evaluation to the age of 16 years may expose a sizeable population of still unscreened younger children to the risk of sport-related SCD due to unknown heart diseases.

In our study, we found that PPS allows the identification of cardiovascular diseases at risk of SCD over the whole study age range of children (7–18 years), although a higher diagnostic yield and lower costs per diagnosis were observed in children aged ≥12 years than in younger ones. This latter finding may be plausibly explained by the age-dependency of phenotypic expression of substrates of SCD such as inherited cardiomyopathies, which rarely occurs before pubertal development.[19–21] However, it must be highlighted that 9% of diagnoses of diseases at risk of SCD were made in children who were 11 years old or younger at the time of their first evaluation. In these younger children, the earlier identification of conditions associated with the risk of SCD such as long-QT syndrome and other congenital heart diseases may lead to early preventive treatment.

Our study results showed that repeat cardiovascular evaluations increased the diagnostic yield of cardiovascular disease at risk of SCD compared with once-only PPS. The diagnostic yield of each repeat evaluation was similar to that of the first evaluation. As a consequence, after a mean of three annual screening sessions, the number of athletes who received a diagnosis of an at-risk condition increased nearly by two-thirds (from 25 to 69) in comparison with the initial evaluation. Inherited cardiomyopathies and NILVS with ventricular arrhythmias were the heart diseases more frequently identified on repeat evaluation. Indeed, serial cardiovascular evaluations expectedly increased the detection rate of both genetic cardiomyopathies with a late onset phenotype during adolescence and newly acquired heart muscle diseases. These findings are in keeping with the previous observation by serial echocardiographic studies of children and adolescents with familial hypertrophic cardiomyopathy, showing that left ventricular hypertrophy develops or progresses during childhood and adolescence when body growth is considerable.[19] Likewise, arrhythmogenic right ventricular cardiomyopathy most often becomes clinically manifest between the second and fourth decades of life.[20,21] The NILVS is a condition that may cause life-threatening ventricular arrhythmias and SCD in the athlete. The main clinical manifestation of the left ventricular scar consists of exercise-induced, often complex, ventricular arrhythmias.[22–24] In the present study, this condition was most frequently suspected based on exercise-induced ventricular arrhythmias, triggering a contrast-enhanced cardiac magnetic resonance study with demonstration of the underlying myocardial fibrosis. Of interest, in our study, QTc prolongation leading to a diagnosis of genetically proven long-QT syndrome was more frequently identified on ECG at repeat evaluation, a finding which may be explained by the inherent variability of the QT interval over time.[25]

A previous study on the outcomes of PPS of 11 168 English football players based on a single cardiovascular evaluation at the age of 16 years reported an incidence of SCD during long-term follow-up of 6.8/100.000 athletes per year.[6] Five of eight victims of SCD died because of cardiomyopathies that were undetected at the time of the single evaluation and performed a mean of 6.8 years before their death. These data raised the concern that a single cardiovascular evaluation may potentially miss genetic diseases with late phenotypic onset or newly acquired conditions. The results of our study support the concept of the limited efficacy of once-only screening by showing that 9 of 13 athletes diagnosed with cardiomyopathies were diagnosed on repeat evaluation.

Costs

In our study, the cost to identify a cardiovascular disease associated with SCD (69 athletes) was €73 312 per athlete, which was similar to that of £77 280 (€88 250 at the November 2022 exchange rate) reported by Malhotra *et al.*[6] for screening UK football players. Our study results demonstrated that serial cardiovascular screening, leading to a substantial increase of the diagnostic yield of at risk diseases, accounted for a cost per each diagnosis which slightly exceeded that of once-only screening. Of note, the cost per diagnosis doubled in children younger than 12 years compared with older children.

Outcome

Previous data from the Veneto region of Italy showed that over two decades of screening implementation, the incidence of SCD among competitive athletes 12–35 years old declined from 3.6 to 0.4 per 100.000 athletes per year.[17] In the present study focusing on younger athletes, no SCD was observed during follow-up and only one athlete experienced a resuscitated cardiac arrest of undetermined origin, accounting for an annual event rate of 0.6 per 100 000 competitive athletes per year.

The case of the child with normal PPS findings who experienced an episode of resuscitated cardiac arrest during sports activity serves as a critical reminder that PPS is not able to identify all athletes at risk of cardiac arrest/sudden death and eliminate all risk of sudden cardiac arrest. Acute myocarditis may occur unpredictably and some cardiac conditions such as atherosclerotic coronary artery disease and congenital anomalies of coronary arteries usually are asymptomatic and non-associated with abnormalities on the ECG. On the other hand, a proportion of arrhythmic cardiac arrest/SCD has no evidence of a recognized structural heart disease or inherited cardiac ion-channel defect, and the cause of death is idiopathic ventricular fibrillation.[2] Such screening limitations justify the efforts to implement all trainings and competitions a proper emergency response planning with immediate access to automated external defibrillators.[26,27]

Among the international Sports Medicine and Cardiology community, it is debated whether athletes diagnosed with a cardiovascular condition at risk of SCD should be mandated as ineligible for competitive sports.[28–30] In Italy, the non-eligibility decision of the sports medicine physician following the diagnosis of a condition at risk of SCD is legally binding. Whether this prevention strategy may be more effective in reducing the risk of catastrophic events during sports in comparison with a more liberal policy implying shared decision-making for return to play between athletes and physicians, remains to be proven. It is worth noting that in the study by Malhotra et al., amongst the five adolescent English football players diagnosed with hypertrophic cardiomyopathy at initial screening, three athletes complied with medical advice to

stop competitive sport and survived, while two athletes declined recommendations to cease competitive sport and died during exercise.[6] In our study, none of the 65 children definitively non-eligible because of conditions at risk of SCD and subsequently undergoing management (including individualized non-competitive exercise prescription) suffered a cardiac event. This finding suggests that screening children for cardiovascular diseases at risk of SCD may not merely change the mode of death of affected individuals from exercise-related to exercise-unrelated, but actually may reduce mortality during long-term follow-up thanks to subsequent risk stratification and appropriate clinical treatment aimed to prevent SCD.

Study limitations

Our study is limited by the relatively homogeneous ethnical demographic features in the Veneto region of Italy; thus, our findings may not apply to more ethnically diverse athlete populations. Sports medicine training within Italy also facilitates an experienced infrastructure of physicians to conduct the cardiovascular evaluation of athletes. Countries with less experienced clinicians or limited cardiology resources may not be able to replicate the same sensitivity or cost per diagnosis.

Although a small number of people likely moved to different regions of the country or to other countries during the study period, such mobility did not impact the death records of screened children based on the results of our systematic press search for cardiac arrest or SCD occurring at the regional and national level. All cases of cardiac arrest/SCD might not be reported by regional and national newspapers, but fatal events involving young athletes are expected to always attract press coverage because of the emotional impact on the mass media.

The cost of a diagnosis of a disease at risk of SCD and consequent non-eligibility to competitive sports activity goes beyond a crude economical estimation and should be evaluated also in terms of health, psychological well-being, and even future opportunities, including professional athletic activity. In order to mitigate such effects on the physical and mental health of non-eligibility to competitive sports, the Center of Sports Medicine of Treviso offered a tailored programme of leisure exercise activity with enrollment in a follow-up programme to all not eligible athletes.

Conclusions

The PPS programme led to a diagnosis of cardiovascular diseases at risk of SCD over the whole study age range of children and was associated with a low incidence of life-threatening cardiovascular events. The probability of identifying an at-risk condition was similar between repeat evaluation and first screening session, thus accounting for an increase of the overall diagnostic yield by nearly two-thirds in comparison with once-only screening. The favourable long-term outcome and survival provide additional support to the value of early detection through PPS and appropriate management of cardiovascular diseases at risk of SCD in the children population.

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Supplementary data

Supplementary data are available *European Heart Journal* online.

Pre-registered clinical trial number

None supplied.

Ethical approval statement

The study was approved by the Ethical Committee of the Treviso province, and because the study reports observational and fully anonymized data, consent was waived.

Data availability statement

Study data are available from the corresponding author upon reasonable request.

Conflict of interest: All authors declare no conflict of interest for this contribution.

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References

1. Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, *et al.* 2020 ESC guidelines on sports cardiology and exercise in patients with cardiovascular disease. *Eur Heart J* 2021;**42**:17–96. https://doi.org/10.1093/eurheartj/ehaa605
2. Mont L, Pelliccia A, Sharma S, Biffi A, Borjesson M, Brugada Terradellas J, *et al.* Pre-participation cardiovascular evaluation for athletic participants to prevent sudden death: position paper from the EHRA and the EACPR, branches of the ESC. Endorsed by APHRS, HRS, and SOLAECE. *Eur J Prev Cardiol* 2017;**24**:41–69. https://doi.org/10.1177/2047487316676042
3. Ljungqvist A, Jenoure P, Engebretsen L, Alonso JM, Bahr R, Clough A, *et al.* The International Olympic Committee (IOC) consensus statement on periodic health evaluation of elite athletes March 2009. *Br J Sports Med* 2009;**43**:631–643. https://doi.org/10.1136/bjsm.2009.064394
4. Maron BJ, Levine BD, Washington RL, Baggish AL, Kovacs RJ, Maron MS. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 2: preparticipation screening for cardiovascular disease in competitive athletes: a scientific statement from the American Heart Association and American College of Cardiology. *Circulation* 2015;**132**:e267–e272. https://doi.org/10.1161/CIR.0000000000000238
5. Drezner JA, O'Connor FG, Harmon KG, Fields KB, Asplund CA, Asif IM, *et al.* AMSSM Position statement on cardiovascular preparticipation screening in athletes: current evidence, knowledge gaps, recommendations and future directions. *Br J Sports Med* 2017;**51**:153–167. https://doi.org/10.1136/bjsports-2016-096781
6. Malhotra A, Dhutia H, Finocchiaro G, Gati S, Beasley I, Clift P, *et al.* Outcomes of cardiac screening in adolescent soccer players. *N Engl J Med* 2018;**379**:524–534. https://doi.org/10.1056/NEJMoa1714719
7. Vessella T, Zorzi A, Merlo L, Pegoraro C, Giorgiano F, Trevisanato M, *et al.* The Italian preparticipation evaluation programme: diagnostic yield, rate of disqualification and cost analysis. *Br J Sports Med* 2020;**54**:231–237. https://doi.org/10.1136/bjsports-2018-100293
8. Sarto P, Zorzi A, Merlo L, Vessella T, Pegoraro C, Giorgiano F, *et al.* Serial versus single cardiovascular screening of adolescent athletes. *Circulation* 2021;**143**:1729–1731. https://doi.org/10.1161/CIRCULATIONAHA.120.053168
9. Decree of the Italian Ministry of Health 18/02/1982 "Rules for the health care of competitive sport activities.
10. Corrado D, Pelliccia A, Heidbuchel H, Sharma S, Link M, Basso C, *et al.* Recommendations for interpretation of 12-lead electrocardiogram in the athlete. *Eur Heart J* 2010;**31**:243–259. https://doi.org/10.1093/eurheartj/ehp473
11. Drezner JA, Sharma S, Baggish A, Papadakis M, Wilson MG, Prutkin JM, *et al.* International criteria for electrocardiographic interpretation in athletes: consensus statement. *Br J Sports Med* 2017;**51**:704–731. https://doi.org/10.1136/bjsports-2016-097331
12. Zorzi A, Vessella T, De Lazzari M, Cipriani A, Meneghon V, Sarto G, *et al.* Screening young athletes for diseases at risk of sudden cardiac death: role of stress testing for ventricular arrhythmias. *Eur J Prev Cardiol* 2020;**27**:311–320. https://doi.org/10.1177/2047487319890973

13. McKinney J, Lithwick DJ, Morrison BN, Nazzari H, Luong M, Fordyce CB, *et al.* Detecting underlying cardiovascular disease in young competitive athletes. *Can J Cardiol* 2017;**33**: 155–161. https://doi.org/10.1016/j.cjca.2016.06.007
14. Dhutia H, Malhotra A, Gabus V, Merghani A, Finocchiaro G, Millar L, *et al.* Cost implications of using different ECG criteria for screening young athletes in the United Kingdom. *J Am Coll Cardiol* 2016;**68**:702–711. https://doi.org/10.1016/j.jacc.2016.05.076
15. Drezner JA, Owens DS, Prutkin JM, Salerno JC, Harmon KG, Prosise S, *et al.* Electrocardiographic screening in national collegiate athletic association athletes. *Am J Cardiol* 2016;**118**:754–759. https://doi.org/10.1016/j.amjcard.2016.06.004
16. Riding NR, Sheikh N, Adamuz C, Watt V, Farooq A, Whyte GP, *et al.* Comparison of three current sets of electrocardiographic interpretation criteria for use in screening athletes. *Heart* 2015;**101**:384–390. https://doi.org/10.1136/heartjnl-2014-306437
17. Corrado D, Basso C, Pavei A, Michieli P, Schiavon M, Thiene G. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. *JAMA* 2006;**296**:1593–1601. https://doi.org/10.1001/jama.296.13.1593
18. Williams EA, Pelto HF, Toresdahl BG, Prutkin JM, Owens DS, Salerno JC, *et al.* Performance of the American Heart Association (AHA) 14-point evaluation versus electrocardiography for the cardiovascular screening of high school athletes: a prospective study. *J Am Heart Assoc* 2019;**8**:e012235. https://doi.org/10.1161/JAHA.119.012235
19. Maron BJ, Spirito P, Wesley Y, Arce J. Development and progression of left ventricular hypertrophy in children with hypertrophic cardiomyopathy. *N Engl J Med* 1986;**315**: 610–614. https://doi.org/10.1056/NEJM198609043151003
20. Nava A, Bauce B, Basso C, Muriago M, Rampazzo A, Villanova C, *et al.* Clinical profile and long-term follow-up of 37 families with arrhythmogenic right ventricular cardiomyopathy. *J Am Coll Cardiol* 2000;**36**:2226–2233. https://doi.org/10.1016/S0735-1097(00)00997-9
21. Rigato I, Bauce B, Rampazzo A, Zorzi A, Pilichou K, Mazzotti E, *et al.* Compound and digenic heterozygosity predicts lifetime arrhythmic outcome and sudden cardiac death in desmosomal gene-related arrhythmogenic right ventricular cardiomyopathy. *Circ Cardiovasc Genet* 2013;**6**:533–542. https://doi.org/10.1161/CIRCGENETICS.113.000288
22. Zorzi A, Perazzolo Marra M, Rigato I, De Lazzari M, Susana A, Niero A, *et al.* Nonischemic left ventricular scar as a substrate of life-threatening ventricular arrhythmias and sudden cardiac death in competitive athletes. *Circ Arrhythm Electrophysiol* 2016;**9**:e004229. https://doi.org/10.1161/CIRCEP.116.004229
23. Schnell F, Claessen G, La Gerche A, Biogaert J, Lentz PA, Claus P, *et al.* Subepicardial delayed gadolinium enhancement in asymptomatic athletes: let sleeping dogs lie? *Br J Sports Med* 2016;**50**:111–117. https://doi.org/10.1136/bjsports-2014-094546
24. di Gioia CR, Giordano C, Cerbelli B, Pisano A, Perli E, De Dominicis E, *et al.* Nonischemic left ventricular scar and cardiac sudden death in the young. *Hum Pathol* 2016;**58**:78–89. https://doi.org/10.1016/j.humpath.2016.08.004
25. Goldenberg I, Mathew J, Moss AJ, McNitt S, Peterson DR, Zareba W, *et al.* Corrected QT variability in serial electrocardiograms in long QT syndrome: the importance of the maximum corrected QT for risk stratification. *J Am Coll Cardiol* 2006;**48**:1047–1052. https://doi.org/10.1016/j.jacc.2006.06.033
26. Pelto HF, Drezner JA. Design and implementation of an emergency action plan for sudden cardiac arrest in sport. *J Cardiovasc Transl Res* 2020;**13**:331–338. https://doi.org/10.1007/s12265-020-09988-1
27. Drezner JA, Peterson DF, Siebert DM, Thomas LC, Lopez-Anderson M, Suchsland MZ, *et al.* Survival after exercise-related sudden cardiac arrest in young athletes: can we do better? *Sports Health* 2018;**11**:91–98. https://doi.org/10.1177/1941738118799084
28. Oliva A, Grassi VM, Campuzano O, Brion M, Arena V, Partemi S, *et al.* Medico-legal perspectives on sudden cardiac death in young athletes. *Int J Legal Med* 2017;**131**:393–409. https://doi.org/10.1007/s00414-016-1452-y
29. Magavern EF, Finocchiaro G, Sharma S, Papadakis M, Borry P. Time out: ethical reflections on medical disqualification of athletes in the context of mandated preparticipation cardiac screening. *Br J Sports Med* 2018;**52**:1207–1210. https://doi.org/10.1136/bjsports-2017-097524
30. Corrado D, Schmied C, Basso C, Borjesson M, Schiavon M, Pelliccia A, *et al.* Risk of sports: do we need a pre-participation screening for competitive and leisure athletes? *Eur Heart J* 2011;**32**:934–944. https://doi.org/10.1093/eurheartj/ehq482