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Causes of sudden cardiac arrest and death and the diagnostic yield of sport preparticipation screening in children

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ABSTRACT

Objective Evidence on the increased risk of sports-related sudden cardiac arrest and death (SCA/D) and the potential benefit of cardiovascular preparticipation screening (PPS) in children is limited. We assessed the burden and circumstances of SCA/D and the diagnostic yield of cardiovascular PPS in children aged 8–15 years.

Methods Data on the incidence and causes of SCA/D from 2011 to 2020 were obtained from the Veneto region (Italy) sudden death registry, hospital records and local press. During the same period, we assessed the results of annual PPS in 25 251 young competitive athletes aged 8–15 years who underwent 58 185 evaluations (mean 2.3/athlete) in Padua, Italy.

Results Over 10 years, 26 SCA/D occurred in children aged 8–15 years in the Veneto region: 6 in athletes (incidence 0.7/100 000/year, all ≥12 years) versus 20 in non-athletes (0.7/100 000/year, 17/20 ≥12 years). In total, 4/6 athletes versus 1/20 non-athletes survived. The cause of SCA/D remained unexplained in four athletes and in nine non-athletes. No athlete suffered SCA/D from structural diseases potentially identifiable by PPS. The incidence of SCA/D in athletes and non-athletes was 0.2/100 000/year in the 8–11 years group versus 1.3/100 000/year in the 12–15 years group. PPS identified 26 new diagnoses of cardiovascular diseases (CVDs) at risk of SCA/D, more often in children ≥12 years old (0.06%/evaluation) than <12 years old (0.02%/evaluation, p=0.02). Among athletes with a negative PPS, two suffered unexplained SCA/D during follow-up, one during exercise.

Conclusions In children aged 8–15 years, the incidence of SCA/D and the yield of PPS for identifying at-risk CVD were both substantially higher in those ≥12 years, suggesting that systematic PPS may be more useful beyond this age.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

⇒ Competitive sports may increase the risk of sudden cardiac arrest/death (SCA/D) in athletes with underlying cardiovascular diseases (CVDs). Preparticipation screening (PPS) offers the potential to identify CVD earlier and may reduce risk through disease-specific management. However, evidence about the efficacy of PPS in children is limited.

WHAT DOES THIS STUDY ADD?

⇒ The incidence of SCA/D and the yield of PPS for identifying CVD at risk of SCA/D were substantially higher in children aged 12–15 years compared with children aged <12 years. Although SCA/D was rare among young athletes who underwent PPS, the majority of cases had a structurally normal heart, suggesting that screening does not identify all at-risk individuals.

HOW MIGHT IT IMPACT ON CLINICAL PRACTICE IN THE FUTURE ?

⇒ Systematic PPS may be more useful beyond the age of 12 years. As SCA/D can occur from conditions not identifiable by PPS, strategies to prevent SCA/D in young athletes should also include emergency preparedness for rapid on-field resuscitation.

INTRODUCTION

Competitive sports participation may increase the risk of life-threatening ventricular arrhythmias and sudden cardiac arrest and death (SCA/D) in athletes with underlying cardiovascular diseases (CVDs).[1 2] Preparticipation screening (PPS) offers the potential to identify CVD early, which allows disease-specific management and possibly the modulation of the exercise intensity to mitigate risk.[3 4] Many scientific societies such as the American Heart Association (AHA) and the European Society of Cardiology (ESC), as well as most sports organisations recommend PPS, although the optimal screening strategy (eg, with or without inclusion of an ECG) remains debated.[3 5–8]

Another important question is determining the age at which the PPS should start.[9] According to current guidelines, PPS should be performed when athletes begin their competitive activity.[5–8] In Italy, PPS is mandatory and the starting age ranges from 8 to 15 years old, depending on the sport discipline. The start of PPS at a young age may be justified because children may unknowingly harbour CVD at risk for SCA/D, and the intensity of training and the level of competition quickly become high. On the contrary, there are arguments against early screening. First, the boundary and distinction between an athletic and a non-athletic child is blurred; second, the incidence of SCA/D in younger athletes is low[10 11]; third, some important substrates of SCA/D such as cardiomyopathies usually become

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overt only after pubertal development[12–17]; and fourth, current criteria for interpretation of athlete ECGs apply to individuals older than 12 years and differentiation between physiology and pathology in ECGs of younger athletes in the context of cardiovascular screening may be difficult.[18]

We designed this study to investigate SCA/D and the role of PPS in children aged 8–15 years divided into two groups: 8 to <12 years and ≥12 to 15 years. The threshold of 12 years corresponds to the minimum age of enrolment of a previous large Italian study[19] and to the age from which the International Criteria for ECG interpretation in athletes are considered valid.[18] The objectives of this study were to: (1) compare the burden of SCA/D, either resuscitated SCA with survival or sudden cardiac death (SCD), between children engaged in competitive sports (defined as 'athletes') and non-athletes, and (2) evaluate the diagnostic yield of PPS for CVD at risk of SCA/D in children aged 8–15 years from the Veneto region of Italy.

METHODS

Incidence and causes of SCA/D in the Veneto region

Since 1982, all the hearts of SCD victims 1–35 years of age in the Veneto region (northeast Italy) were collected, pathologically investigated and preserved at the University Hospital of Padova. Only Veneto region residents were included in this study. SCD is defined as a witnessed sudden and unexpected death occurring within 1 hour of the onset of symptoms or death of an individual who had been seen in stable conditions <24 hours before being found dead.[20] Demographic, clinical and pathological data were recorded in the electronic database of the regional Registry of Cardio-Cerebro-Vascular Pathology, which acts as referral centre for SCD of northeast Italy. We reviewed the registry for the incidence and causes of death during the study period 1 January 2011 through 29 February 2020. Additionally, local press archives and hospital records were searched for cases of SCA. We focused on individuals who were 8–15 years of age at the time of the event and who suffered SCA due to cardiovascular causes eliminating non-cardiac aetiologies. Mean incidence rates were calculated based on the number of Veneto residents in the different age groups according to the Italian Census Bureau 2011. The proportion of athletes (17% in the age group 8–11 years and 27% in the age group 12–15 years) among Veneto region residents aged 8–15 years was calculated based on the number of sports eligibility certificates issued during the study period. This information was obtained from a regional database where all issued certificates are recorded.

Athlete PPS

We retrospectively included all individuals 8–15 years of age of both sexes who underwent annual PPS from 2011 to 2020 at the Center for Sports Medicine, Padua (a city of the Veneto region), National Health System, Italy. We assessed the diagnostic yield of PPS for any CVD and for CVD at risk of SCD. Conditions that were already known at the time of the evaluation were excluded. The data supporting this study are available from the corresponding author on reasonable request.

Protocol for PPS

In Italy, it is required by law that people who wish to practice competitive sport must undergo PPS carried out by a physician with a postgraduate degree in sports medicine. The age at which PPS should start depends on the sporting discipline and is established by the individual federations according to when competitive activity is deemed to begin (ranging from 8 to 15 years). The screening protocol is established by the Italian law and regional regulations. It includes personal and family history, physical examination with blood pressure measurement, spirometry, urine dipstick, visual acuity test, resting 12-lead ECG and limited stress ECG. The latter test, performed on a bicycle, aims particularly at evaluating ventricular arrhythmia inducibility and consists of a brief warm-up, 3 min of constant-load exercise (starting with 2–3 W/kg with load adjustment aimed at reaching at least 85% of the maximal theoretical heart rate) and 3 min recovery/post-exercise ECG. Family history was focused on hereditary CVD at risk of SCD in first-degree or second-degree family members. Personal history was considered positive if the athlete referred chest pain, palpitations, near-syncope or syncope and shortness of breath disproportionate to the physical effort. Resting 12-lead ECG was interpreted according to the 2010 European Society of Cardiology recommendations (before 2017)[21] and to the 2017 International Criteria for ECG interpretation in athletes (after 2017).[18] The athletes with abnormal findings at first evaluation underwent further diagnostic cardiovascular testing. In case of CVD diagnosis, the athlete's management followed the Italian guidelines.[22] According to these recommendations, those who received a diagnosis of a CVD at risk of SCD were disqualified temporarily if a curative treatment was available, otherwise disqualified permanently as shared decision-making is not permitted by the law. If CVD is diagnosed, the University Hospital of Padua also offers follow-up evaluation including molecular genetic testing and cascade family screening when appropriate. Cascade family screening is also offered to relatives of SCD victims.

Costs

During the study period, the cost for each PPS evaluation in medical centres of the Italian National Health System was predetermined (62€). The cost for further investigations was variable and depended on the number and type of additional tests that were required. A detailed analysis of costs for second-line investigations was performed for the subgroup of athletes who underwent PPS in 2019 and was then extrapolated to the entire study cohort. The cost for each cardiovascular test within the National Health System was derived from the 'rate tables of the Veneto region for medical investigations and procedures within the National Health System'.

Follow-up

We assessed the incidence of SCA/D occurring in the screened athletic population within 1 year after the last PPS (ie, the duration of the eligibility certificate). Outcome data were obtained from office visits, interrogation of the Registry of Cardio-Cerebro-Vascular Pathology of the Veneto region of Italy and review of hospital records of young athletes admitted after SCA.

Equity, diversity and inclusion statement

We included all athletes aged 8–15 years undergoing PPS in the Padua sports centre during the study period, and all identified cases of SCA/D in the same age range who were Veneto region residents at the time of the event. The study population was inclusive of all sexes, race/ethnicities, socio-economic backgrounds and marginalised communities. The author group is gender balanced and consists of junior, mid-career and senior researchers from different disciplines; however, all members of the author group are from one country (Italy).

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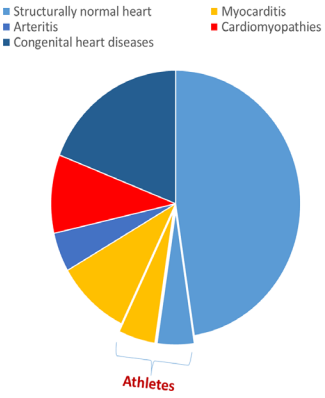

	Total	Athletes
Congenital coronary abn.	2	
Congenital aortic stenosis	2	
Hypertrophic cardiomyopathy	1	
Arrhythmogenic cardiomyopathy	1	
Arteritis	1	
Acute myocarditis	3	1
CPVT	1	
Unexplained SCD	10	1

Figure 1 Causes of sudden cardiac death in the Veneto region of Italy in children aged 8–15 years. CPVT, catecholaminergic polymorphic ventricular tachycardia; SCD, sudden cardiac death.

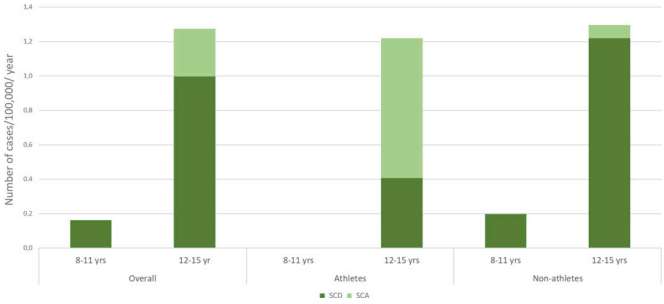

Figure 2 Incidence of sudden cardiac death (SCD) and sudden cardiac arrest (SCA) with survival for 100 000 persons in the overall population, athletes and non-athletes, according to age group.

Statistical analysis

Data are expressed as n (%) or mean (±SD). Differences between the two age groups (8–11 years and 12–15 years) were evaluated with the χ^2 test or the Fisher exact test as appropriate. A p value <0.05 was considered significant.[23] Data were analysed with SPSS V.29 (IBM).

RESULTS

SCA/D in the Veneto region

Between 2011 and 2020, 26 cases of SCA/D (21 SCD and 5 SCA) occurred in the age group 8–15 years, resulting in a mean incidence of 0.7/100 000/year.

SCA/D in athletes

Six (2 SCD and 4 SCA with survival, 4/6 males) of the 26 cases of SCA/D involved athletes who had undergone PPS within 1 year before the event, resulting in a mean incidence of 0.7/100 000/year. Four (66.7%) SCA/D cases occurred during exercise, and 3 out of 4 of these exercise-related events survived.

Of the two SCD cases, one was diagnosed with a structurally normal heart at autopsy and one with myocarditis (figure 1). Among the four SCA cases, all had a structurally normal heart, including one who was diagnosed with catecholaminergic polymorphic ventricular tachycardia, which later was also diagnosed in another family member. Even after family screening, the cause of SCA/D remained unexplained in four (66.7%) cases (one SCD and three SCA) with a structurally normal heart.

SCA/D in non-athletes

Twenty (19 SCD and 1 SCA with survival, 13/20 males) cases of SCA/D involved non-athletes, resulting in a mean incidence of 0.7/100 000/year. The circumstances of SCA/D were known in 15 cases: 4 (26.7%) occurred during exercise.

On autopsy, the most common diagnosis was a structurally normal heart accounting for ten cases (figure 1). In only one of these cases, postmortem genetic diagnosis revealed a pathogenic mutation in the ryanodine receptor 2 gene that causes catecholaminergic polymorphic ventricular tachycardia, while the cause of death remained unexplained in the remaining nine (47.3%) cases even after family screening. Other causes of SCD included congenital coronary abnormalities (N=2), congenital aortic stenosis (N=2), acute myocarditis (N=2), arteritis (N=1), hypertrophic cardiomyopathy (N=1) and arrhythmogenic cardiomyopathy (N=1). The only non-athlete who survived was diagnosed with hypertrophic cardiomyopathy and experienced the event at rest.

SCA/D according to sex and age group

The incidence of SCA/D in the overall study population was higher in males (0.9/100 000/year) than in females (0.5/100 000/year). It was not possible to compare the incidence of SCA/D between athletes and non-athletes according to sex.

In the subgroup aged 8–11 years, there were three SCD and no SCA with survival, all non-athletes, one male and two females, accounting for an incidence of 0.2/100 000/year in the overall population (0 among athletes vs 0.2/100 000/year among non-athletes).

In the subgroup aged 12–15 years, there were 23 SCA/D cases (18 SCD and 5 SCA with survival, 7/23 females) resulting in an SCA/D incidence of 1.3/100 000/year in the overall population. Six cases occurred among athletes (incidence 1.2/100 000/year) and 17 among non-athletes (1.3/100 000/year) (figure 2).

PPS results

During the study period, a total of 58 185 PPS evaluations for 25 251 paediatric athletes (mean age at time of first evaluation 12±1.5 years, male 62.7%, 87% Caucasian) were performed (average 2.3/athlete) in the Center for Sports Medicine Centre, Padua. Specifically, 23 274 evaluations were performed in athletes aged 8–11 years and 34 911 in athletes aged 12–15 years.

Twenty-six athletes (0.1%) received a new diagnosis of a disease at risk of SCD including hypertrophic cardiomyopathy (N=11), long QT syndrome (N=3), bicuspid aortic valve with aortic dilatation (N=3), dilated cardiomyopathy (N=2), at-risk ventricular pre-excitation (N=2), anomalous origin of coronary artery with interarterial course (N=2) and other (N=3), corresponding to a diagnostic yield of 0.04%/PPS (table 1).

The diagnosis of at-risk CVD was prompted by abnormalities at history (N=5, 19%), physical examination (N=3, 12%), ECG (N=11, 42%) and/or exercise testing (N=13, 50%) (table 1).

In addition to these 26 athletes, another 40 (0.16%) received a new diagnosis of a CVD not at risk of SCD but considered clinically relevant for the athlete's health and requiring follow-up or therapy such as frequent/complex ventricular arrhythmias unrelated to an underlying heart disease, simple congenital heart diseases or valvular diseases.

The rate of diagnosis of CVD at risk of SCD according to the age of the athlete at the time of the PPS is shown in figure 3. Five of the 26 athletes who received a diagnosis of a CVD at risk of SCD were younger than 12 years (diagnostic yield 0.02%/evaluation) while the remaining 21 were older (diagnostic yield 0.06%/evaluation, p=0.02).

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Table 1 Details of the 26 athletes who received a diagnosis of cardiovascular diseases at risk of sudden cardiac death diagnosed in the period 2011–2020 by preparticipation screening

N	Sport	Age	H	P/E	ECG	ET	Diagnosis
1	Volleyball	≥12	–	–	+	–	Hypertrophic cardiomyopathy
2	Soccer	<12	–	–	+	+	Long QT syndrome
3	Soccer	≥12	–	–	–	+	Hypertrophic cardiomyopathy
4	Soccer	≥12	–	+	–	–	Bicuspid aortic valve+aortic dilation
5	Basket	≥12	+	–	–	–	Hypertrophic cardiomyopathy
6	Athletics	<12	–	–	+	+	At-risk ventricular pre-excitation*
7	Basket	<12	+	–	–	–	Left ventricular non-compaction
8	Volleyball	≥12	–	–	+	–	Hypertrophic cardiomyopathy
9	Athletics	<12	–	–	+	+	At-risk ventricular pre-excitation*
10	Soccer	≥12	+	–	–	–	Anomalous origin of coronary artery with interarterial course
11	Volleyball	<12	–	–	+	+	Long QT syndrome
12	Basket	≥12	–	–	–	+	Hypertrophic cardiomyopathy
13	Soccer	≥12	–	–	–	+	Dilated cardiomyopathy
14	Water polo	≥12	–	–	+	–	Hypertrophic cardiomyopathy
15	Soccer	≥12	+	–	–	–	Anomalous origin of coronary artery with interarterial course
16	Water polo	≥12	–	–	–	+	Hypertrophic cardiomyopathy
17	Soccer	≥12	–	–	–	+	Hypertrophic cardiomyopathy
18	Soccer	≥12	–	+	–	–	Bicuspid aortic valve+aortic dilation
19	Baseball	≥12	–	–	+	–	Long QT syndrome
20	Basket	≥12	–	–	–	+	Hypertrophic cardiomyopathy
21	Basket	≥12	–	–	+	–	Hypertrophic cardiomyopathy
22	Rugby	≥12	–	–	–	+	Hypertrophic cardiomyopathy
23	Swimming	≥12	–	–	–	+	Arrhythmogenic cardiomyopathy
24	Soccer	≥12	–	+	–	–	Bicuspid aortic valve+aortic dilation
25	Soccer	≥12	–	–	+	+	Dilated cardiomyopathy
26	Soccer	≥12	+	–	+	–	Cardiac rhabdomyoma

*Based on the refractory period of the accessory pathway evaluated by electrophysiological study <240 ms at baseline and/or <200 ms during isoproterenol infusion.
ET, exercise testing; F, female; H, family and personal history; M, male; P/E, physical examination.

Costs

A detailed analysis of costs for second-line investigation was performed in a cohort of 1307 athletes (mean age 11.3±1.5 years, 57% male) screened in 2019. Additional tests were prescribed after 72 PPS sessions (5.5%) for a total cost of 11 461€ (average 8.77€ per screened athlete). Adding to this, average cost for second-line investigations was the fixed cost of 62€ per athlete for first-line screening, giving a total of 70.77€ per athlete. Based on this figure, we estimated the total cost of the PPS programme over the 10-year study period to be 4 117 752€ or 62 390€ for each clinically relevant CVD and 158 375€ for each CVD at risk of SCD diagnosed. Considering the differences in the diagnostic yield between the two age groups, costs per diagnosis of at-risk CVD were higher in athletes aged 8–11 years (329 420€/diagnosis) than in those aged ≥12 years (117 650€/diagnosis).

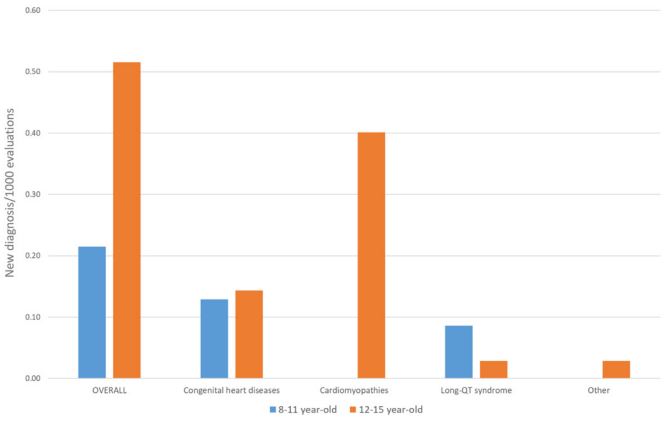

Figure 3 Diagnostic rate of preparticipation screening for detection of cardiovascular diseases at risk of sudden cardiac death according to the age of the athlete at the time of evaluation.

Follow-up

During a mean follow-up of 6.2±4.1 years for the athletes screened at the Center for Sports Medicine, Padua, two athletes suffered SCA/D despite a normal PPS. The first was a ≥12-year-old track and field athlete who suffered SCD unrelated to exercise. The previous three PPS were unremarkable, as was the last performed 8 months before the SCD. The second was a ≥12-year-old soccer player who suffered ventricular fibrillation during a training session. An automated external defibrillator (AED) was promptly used and the athlete was successfully resuscitated without brain damage. The last PPS 9 months before the event was also unremarkable, as were the previous two PPS. In both cases, the cause of SCA remained unexplained after a thorough investigation including genetic testing.

Follow-up data were available for 21 of 26 athletes who received a diagnosis of CVD at risk of SCD and were disqualified from sport participation; they had no adverse events.

DISCUSSION

We designed this study to assess and compare the incidence of SCA/D in athletes and non-athletes and the diagnostic yield of

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sport PPS in two groups of children: 8–11 years and 12–15 years. The main findings were: (1) the incidence of SCA/D during the study period was 0.7/100 000/year, with higher incidence in those aged 12–15 years versus 8–11 years and in males compared with females; (2) the diagnostic yield of PPS was significantly higher (and cost per diagnosis lower) among children aged 12–15 years compared with the younger age group; (3) 4/6 athletes versus 1/20 non-athletes who suffered SCA/D were successfully resuscitated; and (4) the most common substrate found after SCA/D in this young population, both in athletes and in non-athletes, was a structurally normal heart.

SCA/D in children

A previous study from the Veneto region enrolling people aged 12–35 years observed a significant decrease in the incidence of SCD among athletes from 3.6 to 0.4/100 000/year 22 years after PPS became mandatory in 1982, while the incidence of SCD among non-athletes remained unchanged (≈0.8/100 000/year).[19] Similar to this previous study in an older population, we also observed that the incidence of SCD was lower among screened athletes (0.2/100 000/year) versus unscreened non-athletes (0.7/100 000/year) aged 8–15 years.

The overall incidence of SCA/D among children aged 8–15 years in the Veneto region of Italy was the same in athletes and non-athletes: 0.7/100 000/year. These data are in line with previous reports, suggesting that SCA/D is infrequent in this early period of life probably because important arrhythmic substrates such as cardiomyopathies and coronary artery disease become overt at a later age.[1] However, important differences were observed by dividing the study cohort using 12 years as an age cut-off. In younger children (8–11 years), SCA/D was rare and occurred only in three non-athletes, accounting for an incidence of 0.2/100 000/year. Conversely, the incidence of SCA/D in the group aged 12–15 years was 1.3/100 000/year (1.2/100 000/year in athletes vs 1.3/100 000/year in non-athletes). Moreover, similar to previous studies, the risk of SCA/D was lower in females compared with males.[24]

PPS in children

In parallel to SCA/D incidence, the diagnostic yield and costs of PPS differed between the two age groups. Overall, the rate of diagnosis of at-risk CVD per PPS was 0.04% per evaluation. Significant differences were noted between the two age groups, with higher diagnostic rates in the older age group. Therefore, the cost per each diagnosis of CVD at risk of SCD was substantially higher among the younger age group of athletes. These data are similar to those of another sports medicine centre of the Veneto region, reporting a 0.05% diagnostic yield of PPS in children aged 7–11 years and 0.12% in those aged 12–18 years.[25] The underlying conditions diagnosed also differed between groups: while in younger children long QT syndrome and congenital heart diseases were the only identified conditions, cardiomyopathies accounted for the majority of diagnoses in the older age group, consistent with the age-related penetrance of such diseases.[25 26]

The rate of diagnosis by PPS in our study was substantially lower than the 0.3–0.5% diagnostic yield reported in previous studies.[16 16 19 26–31] This difference may be due to the fact that in most previous studies the enrolled population was older than in our study. Moreover, the screening was often done once, whereas in Italy children practising competitive sport undergo PPS every year. Finally, our PPS protocol did not include echocardiography as a first-line diagnostic tool.

A peculiar aspect of the Italian PPS model is that the sports medicine doctor is responsible for the decision to issue an eligibility certificate or not and that shared decision-making in case of CVD at risk of SCD is not permitted. To mitigate the psychological and social consequences of sports disqualification in young individuals, specialised centres of the public health system can offer an individualised exercise prescription programme with the aim to adapt physical activity in relation to the specific cardiovascular risk.[32]

Substrates of SCA/D and role of PPS

In the present investigation, we found that the majority of cases of SCA/D in children remained unexplained (structurally normal heart). These data are in line with some studies reporting that autopsy-negative SCD accounted for nearly half of cases in young individuals,[10 11 33 34] while in other series the majority of SCD cases were explained by an identified cardiovascular disorder.[35–37] In particular, a recent autopsy study on adolescents who died suddenly in the UK reported that the heart was structurally normal in 63% of cases.[38] Many factors may account for this heterogeneity, including case selection, age range, ethnicity and the experience of pathologists performing the autopsy. In the Veneto region of Italy, all juvenile SCD cases are systematically investigated by experienced cardiac pathologists who guarantee a homogeneous study protocol including postmortem genetic testing.[39] In previous autopsy studies of young (aged <40 years) SCD victims, we reported that cardiomyopathies and coronary atherosclerosis were the most common causes while the prevalence of unexplained SCD was only 17%.[40 41] The much higher rate of idiopathic SCD in children aged 8–15 years suggests that the SCA/D substrates vary across different age groups. A probable explanation lies in the lower prevalence and milder phenotypic expression of structural CVD (particularly coronary atherosclerosis and cardiomyopathies) compared with older individuals, thus making primary arrhythmia syndromes a more likely cause in younger children.

It may be also hypothesised that the high number of SCA/D victims with structurally normal hearts and myocarditis reflects the selection bias of routine medical checks including PPS that are most likely to identify structural CVD. We must acknowledge that our observational data do not allow drawing definite conclusions on the role of PPS in mitigating the risk of SCA/D in young athletes, and whether in the absence of systematic screening the incidence and distribution of causes would have been different. However, it is noteworthy that no adolescent athlete suffered SCA/D due to conditions potentially identifiable by screening such as congenital heart diseases and cardiomyopathies, which were the most common causes found during PPS leading to sport disqualification. Thus, it is reasonable to consider that the diagnoses from the PPS contributed to the finding that the predominant SCA/D cases in this cohort had a structurally normal heart. In particular, athletes who suffered SCA/D within 1 year from their last PPS had a structurally normal heart and the cause of the event remained unexplained despite thorough clinical investigations.

Role of cardiopulmonary resuscitation

Half of children who died suddenly showed a structurally normal heart on autopsy. Myocarditis was another important substrate of SCD that is usually missed by PPS because of its acquired nature. These data highlight that PPS cannot identify all causes of SCA/D and that prevention of SCD in athletes should be considered a two-tier system consisting of primary prevention

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by PPS and secondary prevention by widespread availability of AEDs and trained personnel.[42] The importance of secondary prevention has been previously demonstrated by analysis of the FIFA sudden death registry, which showed that cardiopulmonary resuscitation resulted in a survival rate of 85% with the use of an AED compared with 35% without.[34] Other studies have also demonstrated a survival rate of >80% for exercise-related SCA in young athletes who receive prompt resuscitation and use of an on-site AED.[43–45]

In Italy, the presence of an AED during sports competitions has been compulsory since 2012 and since 2021 it has been compulsory also during training. Our data suggest that this has had a positive effect as 4 of 6 (66.7%) athletes who suffered SCA/D were successfully resuscitated compared with only 1 of 20 (5%) non-athletes. In particular, 3 of 4 athletes who suffered an exercise-related SCA/D survived because of prompt resuscitation. As shown by Torell *et al*,[46] a possible explanation is that exercise-related out-of-hospital cardiac arrests are more often witnessed, have higher rates of bystander cardiopulmonary resuscitation and have more frequent AED utilisation.

Study limitations

The main limitation of this study is that identification of SCA cases with survival relied on a retrospective review of the local press (three cases) and hospital records (two cases) rather than on a prospective registry with mandatory reporting (such as the Veneto SCD registry, where all cases of SCD were included). For this reason, we cannot exclude underestimation of the incidence of SCA particularly in the non-athlete subgroup, as cases occurring in public places such as sports arenas are more likely to be reported. The mean incidence rates were calculated based on the number of Veneto residents in the different age groups according to the Italian Census Bureau 2011 report, which counted the population in that particular year. More recent reports by the Italian Census Bureau were not conducted. Thus, a variation in the actual number of the population during the study period is possible and could have impacted the incidence results. The definition of 'athlete' was based on participation in competitive sport requiring PPS rather than on the true exercise load: this is relevant because many children are extremely active even if they do not formally compete in sport. Finally, because of the particular study setting which was characterised by a relatively low ethnic diversity and mandatory annual PPS, results may not be equally applicable to other countries.

CONCLUSIONS

Our study showed that the incidence of SCA/D was low in children aged 8–11 years and increased in those aged 12–15 years. In parallel, the yield of PPS was higher and the costs per diagnosis lower in those ≥12 years. These findings may have practical implications for designing PPS programmes for children engaged in sports activities. Our data supports that after the age of 12 years, PPS should be performed on all athletes and repeated periodically (perhaps annually) for identification of newly developed cardiomyopathies which have an age-related phenotypic penetrance.[25] Defining the optimal PPS programme in athletes <12 years requires additional research. Finally, we found that a sizeable proportion of paediatric victims of SCA/D showed a structurally normal heart and in most cases the event remained unexplained and could not have been identified by PPS. Given a law mandating the presence of an AED at all sporting venues, two-thirds of athletes suffering SCA/D were successfully resuscitated. These observations serve as a reminder that early access to defibrillation should always complement PPS as a comprehensive strategy against SCD in athletes.

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REFERENCES

1 Corrado D, Zorzi A. Sudden death in athletes. *Int J Cardiol* 2017;237:67–70.
2 Basso C, Rizzo S, Carturan E, *et al*. Cardiac arrest at rest and during sport activity: causes and prevention. *Eur Heart J Suppl* 2020;22:E20–4.
3 Pelliccia A, Sharma S, Gati S, *et al*. ESC guidelines on sports cardiology and exercise in patients with cardiovascular disease. *Russ J Cardiol* 2020;26:4488.
4 Corrado D, Basso C, Thiene G. Sudden cardiac death in athletes: what is the role of screening *Curr Opin Cardiol* 2012;27:41–8.
5 Mont L, Pelliccia A, Sharma S, *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.
6 Mitten MJ, Zipes DP, Maron BJ, *et al*. 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:e346–9.
7 Fritsch P, Pozza RD, Ehringer-Schetitska D, *et al*. Cardiovascular pre-participation screening in young athletes: recommendations of the Association of European Paediatric Cardiology. *Cardiol Young* 2017;27:1655–60.
8 Ljungqvist A, Jenoure PJ, Engebretsen L, *et al*. The International Olympic Committee (IOC) consensus statement on periodic health evaluation of elite athletes. *Clin J Sport Med* 2009;19:347–65.
9 Zorzi A, Graziano F, Corrado D. Arrhythmogenic cardiomyopathy in children: identification at preparticipation screening and diagnosis by the "Padua criteria". *Int J Cardiol* 2022;354:38–40.
10 Winkel BG, Holst AG, Theilade J, *et al*. Nationwide study of sudden cardiac death in persons aged 1-35 years. *Eur Heart J* 2011;32:983–90.
11 Bagnall RD, Weintraub RG, Ingles J, *et al*. A prospective study of sudden cardiac death among children and young adults. *N Engl J Med* 2016;374:2441–52.

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12 Maron BJ, Olivotto I, Spirito P, *et al*. Epidemiology of hypertrophic cardiomyopathy-related death: revisited in a large non-referral-based patient population. *Circulation* 2000;102:858–64.
13 Maron BJ. Hypertrophic cardiomyopathy: a systematic review. *JAMA* 2002;287:1308–20.
14 Niimura H, Bachinski LL, Sangwatanaroj S, *et al*. Mutations in the gene for cardiac myosin-binding protein C and late-onset familial hypertrophic cardiomyopathy. *N Engl J Med* 1998;338:1248–57.
15 Maron BJ, Niimura H, Casey SA, *et al*. Development of left ventricular hypertrophy in adults in hypertrophic cardiomyopathy caused by cardiac myosin-binding protein C gene mutations. *J Am Coll Cardiol* 2001;38:315–21.
16 Maron BJ, Spirito P, Wesley Y, *et al*. Development and progression of left ventricular hypertrophy in children with hypertrophic cardiomyopathy. *N Engl J Med* 1986;315:610–4.
17 Maron BJ, Haas TS, Ahluwalia A, *et al*. Incidence of cardiovascular sudden deaths in Minnesota high school athletes. *Heart Rhythm* 2013;10:374–7.
18 Drezner JA, Sharma S, Baggish A, *et al*. International criteria for electrocardiographic interpretation in athletes: consensus statement. *Br J Sports Med* 2017;51:704–31.
19 Corrado D, Basso C, Pavei A, *et al*. Trends in sudden cardiovascular death in young competitive athletes after implementation of a Preparticipation screening program. *JAMA* 2006;296:1593–601.
20 Zeppenfeld K, Tfelt-Hansen J, de Riva M, *et al*. 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J* 2022;43:3997–4126.
21 Corrado D, Pelliccia A, Heidbuchel H, *et al*. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. *Eur Heart J* 2010;31:243–59.
22 Delise P, Mos L, Sciarra L, *et al*. Italian cardiological guidelines (COCIS) for competitive sport eligibility in athletes with heart disease: update. *J Cardiovasc Med (Hagerstown)* 2021;22:874–91.
23 Mansournia MA, Collins GS, Nielsen RO, *et al*. A checklist for statistical assessment of medical papers (the CHAMP statement): explanation and elaboration. *Br J Sports Med* 2021;55:1009–17.
24 Finocchiaro G, Westaby J, Bhatia R, *et al*. Sudden death in female athletes: insights from a large regional registry in the United Kingdom. *Circulation* 2021;144:1827–9.
25 Sarto P, Zorzi A, Merlo L, *et al*. Value of screening for the risk of sudden cardiac death in young competitive athletes. *Eur Heart J* 2023;44:1084–92.
26 Malhotra A, Sharma S. Outcomes of cardiac screening in adolescent soccer players. *N Engl J Med* 2018;379:524–34.
27 McKinney J, Lithwick DJ, Morrison BN, *et al*. Detecting underlying cardiovascular disease in young competitive athletes. *Can J Cardiol* 2017;33:155–61.
28 Dhutia H, Malhotra A, Gabus V, *et al*. Cost implications of using different ECG criteria for screening young athletes in the United Kingdom. *J Am Coll Cardiol* 2016;68:702–11.
29 Drezner JA, Owens DS, Prutkin JM, *et al*. Electrocardiographic screening in national collegiate athletic association athletes. *Am J Cardiol* 2016;118:754–9.
30 Riding NR, Sheikh N, Adamuz C, *et al*. Comparison of three current sets of electrocardiographic interpretation criteria for use in screening athletes. *Heart* 2015;101:384–90.
31 Williams EA, Pelto HF, Toresdahl BG, *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.
32 Corrado D, Zorzi A, Sarto P. Pre-participation screening for safe sports activity. *Eur Heart J* 2023;44:2258–9.
33 Finocchiaro G, Papadakis M, Robertus J-L, *et al*. Etiology of sudden death in sports: insights from a United Kingdom regional registry. *J Am Coll Cardiol* 2016;67:2108–15.
34 Egger F, Scharhag J, Kästner A, *et al*. FIFA sudden death Registry (FIFA-SDR): a prospective, observational study of sudden death in worldwide football from 2014 to 2018. *Br J Sports Med* 2022;56:80–7.
35 Peterson DF, Kucera K, Thomas LC, *et al*. Aetiology and incidence of sudden cardiac arrest and death in young competitive athletes in the USA: a 4-year prospective study. *Br J Sports Med* 2021;55:1196–203.
36 Harris KM, Mackey-Bojack S, Bennett M, *et al*. Sudden unexpected death due to myocarditis in young people, including athletes. *Am J Cardiol* 2021;143:131–4.
37 D'Ascenzi F, Valentini F, Pistoresi S, *et al*. Causes of sudden cardiac death in young athletes and non-athletes: systematic review and meta-analysis: sudden cardiac death in the young. *Trends Cardiovasc Med* 2022;32:299–308.
38 Finocchiaro G, Radaelli D, D'Errico S, *et al*. Sudden cardiac death among adolescents in the United Kingdom. *J Am Coll Cardiol* 2023;81:1007–17.
39 Basso C, Aguilera B, Banner J, *et al*. Guidelines for autopsy investigation of sudden cardiac death: 2017 update from the Association for European Cardiovascular Pathology. *Virchows Arch* 2017;471:691–705.
40 Thiene G, Rizzo S, Schiavon M, *et al*. Structurally normal hearts are uncommonly associated with sudden deaths in athletes and young people. *J Am Coll Cardiol* 2019;73:3031–2.
41 Thiene G. Sudden cardiac death in the young: a genetic destiny? *Clin Med (Lond)* 2018;18:s17–23.
42 Pelto HF, Drezner JA. Design and implementation of an emergency action plan for sudden cardiac arrest in sport. *J Cardiovasc Transl Res* 2020;13:331–8.
43 Schattenkerk J, Kucera K, Peterson DF, *et al*. Socioeconomic factors and outcomes from exercise-related sudden cardiac arrest in high school student-athletes in the USA. *Br J Sports Med* 2022;56:138–43.
44 Drezner JA, Toresdahl BG, Rao AL, *et al*. Outcomes from sudden cardiac arrest in US high schools: a 2-year prospective study from the National Registry for AED use in sports. *Br J Sports Med* 2013;47:1179–83.
45 Drezner JA, Peterson DF, Siebert DM, *et al*. Survival after exercise-related sudden cardiac arrest in young athletes: can we do better *Sports Health* 2019;11:91–8.
46 Torell MF, Strömsöe A, Zagerholm E, *et al*. Higher survival rates in exercise-related out-of-hospital cardiac arrests, compared to non-exercise-related - a study from the Swedish register of cardiopulmonary resuscitation. *Eur J Prev Cardiol* 2017;24:1673–9.

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