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Screening Electrocardiogram in Young Athletes and Military Members: A Systematic Review and Meta-Analysis

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Objective: To determine the effect of electrocardiogram (ECG) screening on the prevention of sudden cardiac arrest and death in young athletes and military members.

Data Sources: MEDLINE, Embase, CENTRAL, Web of Science, BIOSIS, Scopus, SPORTDiscus, PEDro, and ClinicalTrials.gov were searched from inception to dates between February 21 and July 29, 2019.

Study Selection: Randomized and nonrandomized controlled trials in which preparticipation examination including ECG was the primary intervention used to screen athletes or military members aged ≤40 years. Acceptable control groups were those receiving no screening, usual care, or preparticipation examination without ECG. Three published studies and 1 conference abstract were identified for inclusion.

Data Extraction: In all 4 studies, risk of bias was assessed using the Cochrane risk-of-bias tool and was found to be generally high. Two studies had data extracted for random effects meta-analysis, and the remaining study and conference abstract were included in the narrative review. The overall quality of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation approach.

Data Synthesis: We included 4 nonrandomized studies (11 689 172 participants), of which all had a high risk of bias. Pooled data from 2 studies (n = 3 869 274; very low-quality evidence) showed an inconclusive 42% relative decrease in risk of sudden cardiac death (relative risk = 0.58; 95% CI = 0.23, 1.45), equating to an absolute risk reduction of 0.0016%. The findings were consistent with a potential 77% relative decreased risk to a 45% relative increased risk in participants screened using ECG. Heterogeneity was found to be high, as measured using I^2 statistic (71%). Data from the remaining study and abstract were similarly inconclusive.

Conclusions: Existing evidence for the effect of ECG screening is inconclusive and of very low quality. In our meta-analysis, we observed that screening ECG may result in a considerable benefit or harm to participants. Higher-quality studies are needed to reduce this uncertainty.

Key Words: sudden cardiac arrest, sudden cardiac death

Key Points

- Although electrocardiogram (ECG) screening of athletes has been shown to be more effective than history and physical examination alone for diagnosing conditions that put the athlete at risk for sudden cardiac arrest (SCA) or death (SCD), few data are available to answer the question of the effectiveness of ECG screening in preventing SCA and SCD in young athletes.
- We identified only 4 published accounts (3 full papers and 1 conference abstract) of nonrandomized studies reporting on the effectiveness of ECG screening to prevent SCD in young athletes and military members.
- No difference was identified between screened and nonscreened athletes in data synthesis of 2 of the published articles eligible for meta-analysis.

In 2005, the European Society of Cardiology[1] recommended using electrocardiogram (ECG) screening as part of a preparticipation examination (PPE) of young competitive athletes to reduce the risk of sudden cardiac arrest (SCA) and death (SCD). Updated guidelines have maintained this recommendation.[2] Professional bodies around the world have followed these guidelines with recommendations of their own and various degrees of agreement. The International Olympic Committee[3] recommended ECG screening for elite athletes, and the Australasian College of Sports and Exercise Physicians[4] recommended screening with some limitations; however, organizations in the United States have continued to resist calls for ECG screening of all athletes as part of a PPE.[5,6] The evidence base to support the inclusion of ECG screening for reducing the incidence of SCA and SCD in young athletes has not undergone systematic review. In a previous systematic review, Harmon et al[7] assessed the effectiveness of ECG screening to detect potentially lethal cardiac disorders but did not address the effect on SCA and SCD and the potential negative effects of ECG screening.

A systematic summary of existing data on the outcomes of ECG screening will provide the public, health care providers, and policy makers with vital information about the health effects of ECG screening in these populations compared with history and physical examination alone. The aim of this study was to review all available evidence assessing the effect of adding ECG screening to PPEs in young athletes and military populations on the incidence of SCA and SCD and to synthesize the available research to evaluate the effect of the addition of ECG on the occurrence of SCA and SCD.

METHODS

This review was part of a project with the following 2 objectives: identifying the global incidence of SCA and SCD in athletes and military members[8] and evaluating the effect of screening ECG on SCA and SCD in the same population. In this review, we focused on the effect of ECG screening, and the incidence portion was published elsewhere.[8] It was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[9] and was registered at PROSPERO March 18, 2019, under CRD42019125560. Ethical approval was not necessary, as only publicly available data were included in this review.

Data Sources and Searches

The search strategy was designed in conjunction with a medical librarian experienced in systematic reviews (M.S.), and the dual objectives were combined into a single search. The search strategy is included in the Supplementary Material 1. We searched MEDLINE, Embase, CENTRAL, Web of Science, BIOSIS, Scopus, SPORTDiscus, and the Physiotherapy Evidence Database between February 22 and March 1, 2019, and ClinicalTrials.gov on July 29, 2019. Review articles and position statements were reviewed for eligible articles.[10–12] No limitations existed for language or date of publication.

Study Selection

Studies eligible for inclusion were randomized and nonrandomized controlled trials in which PPE including ECG was the primary intervention used to screen athletes or military members aged ≤40 years. Acceptable control groups were those receiving no screening, usual care, or PPE without ECG. Age 40 years was selected because of the increased incidence of coronary artery disease as a cause of SCA and SCD with increasing age and the desire to focus on causes other than coronary artery disease.[11,13]

The prespecified primary outcome was the difference in SCA and SCD in athletes and military populations screened using ECG compared with control groups not screened using ECG. Secondary outcomes of the athlete's removal from sport, follow-up treatment, and potential return to sport and subgroup analysis were planned but not carried out because of the lack of existing data. Details on these outcomes are listed in the Supplementary Material 2 and 3.

Data Extraction and Quality-of-Evidence Assessment

Independent dual-investigator article screening, selection, risk-of-bias (ROB) assessments, and extraction were performed using Covidence systematic review software (Veritas Health Innovation; https://www.covidence.org). The primary author (A.L.) screened all titles, and the second reviewer was from a team of 3 (C.M., N.P., and V.L.).

The Cochrane ROB tool,[14] native to Covidence, was used for ROB assessment. Disagreements were resolved via discussion between the primary author (A.L.) and the second reviewer. We used the Grading of Recommendations, Assessment, Development and Evaluation approach (Table 1) to assess the overall quality of evidence for the primary outcome and reported these assessments in Table 2.[15]

Table 1. Grading of Recommendations, Assessment, Development and Evaluation

Does screening ECG in athletes/military members prevent sudden cardiac arrest and death?
Population: Competitive athletes participating in an organized sport and active-duty military members aged ≤40 y.
Intervention: Performance of PPE with screening ECG with or without echocardiogram to find conditions that are known to lead to sudden cardiac arrest associated with sports/athletic activity.
Comparison: No PPE or PPE without screening ECG.
Outcome: (1) Sudden cardiac arrest or death in screened vs those not screened with ECG. (2) Rate of athletes/military members removed from sport/activity. (3) Rate of athletes/military members with abnormal findings who underwent treatment as a result of screening. (4) The number of treated athletes/military members who returned to sport/activity.

Abbreviations: PPE, preparticipation examination; ECG, electrocardiogram.

Data Synthesis and Analysis

A meta-analysis was performed using the statistical package native to RevMan (version 5.3.5; The Cochrane Collaboration) via the random-effects Mantel-Haenszel method based on the clinical heterogeneity within the included studies. Data are presented as relative risk (RR) with 95% CI in participants screened using ECG compared with those of participants not screened using ECG when possible. Heterogeneity was reported using summary statistics I^2 and χ^2, with prespecified values of <30% considered *low*; 30%–70%, *moderate*; and >70%, *high*. A P value of ≤.10 for the χ^2 statistic indicated statistical heterogeneity. Sensitivity analysis and publication bias assessment (eg, funnel plot asymmetry) were planned but not performed because of the small number of included studies.

RESULTS

After removing 10 780 duplicates and adding 11 titles after a hand search, we screened 20 059 titles and abstracts. A full-text screening was carried out on 322 articles. Four of these articles, consisting of 3 published articles and 1 conference abstract, met the criteria for inclusion (Figure 1).

Included Studies

The 3 studies and 1 conference abstract were nonrandomized controlled trials. The 3 articles included a total of 6 431 380 athletes,[16–18] and the conference abstract included 5 257 792 male military conscripts.[19] Two studies and the conference abstract were historical controlled

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Table 2. Grading of Recommendations, Assessment, Development and Evaluation Summary of Findings

Outcome	Intervention	No. of Studies	Absolute Risk, No ECG or Examination With No ECG	Absolute Risk, ECG Screened	Relative Effect (95% CI)	No. of Participants	Quality of the Evidence[a]
Sudden cardiac death in athletes	ECG, 1 study; ECG + exercise stress test, 1 study	2 Studies evaluating prevention of sudden cardiac death	0.00328%	0.00171%	0.58 (0.23, 1.45)	3 869 274 (2 Historical controlled trials[b])	Very low

Abbreviation: ECG, electrocardiogram.

[a] Summary of decisions on quality of the evidence
Study design: Nonrandomized historically controlled trials at high risk of bias.
Risk of bias: Very serious concern. Downgraded for significant risk of bias in these historically controlled trials, including in categories of randomization, allocation, blinding and sequence generation, as well as risk of significant confounding due to historical nature of the studies.
Inconsistency: Serious concern based on differences in the estimate of effect and high heterogeneity with I^2 of 71% and significant X^2 P value of .06.
Indirectness: No concern. The studies included evaluate the event of interest, in the population of interest.
Imprecision: Serious concern. Downgraded for wide CIs despite meeting the optimal information size. With the calculated event rates in these combined studies, a power analysis with $P = .05$, and $\beta = 0.80$, a total of 3177808 (1548556 per group) is suggested for a randomized trial.
Publication bias: Not evaluated due to small number of studies.
Other factors: Significant confounding has likely occurred in these trials and increased the effect estimate.

[b] A *historical controlled trial* was one in which a cohort that did not receive ECG screening (historical control group) was compared with a cohort of participants receiving ECG screening after the initiation of this practice in their country or organization (intervention group).

trials.[16,18,19] These studies included a cohort that did not receive ECG screening (historical control group) compared with a cohort of participants receiving ECG screening after the initiation of this practice in their country or organization (intervention group). In the third article, researchers compared the following 2 cohorts of athletes from studies published previously: 1 cohort had not been screened using ECG as part of the PPE and 1 had been screened using ECG.[17] No studies in which authors reported an outcome of SCA were identified.

Only 2 studies, both on athletes, were included in the meta-analysis.[16,17] In both studies, it was unclear if the historical control group received a screening PPE or no examination.[16,17] The intervention group of Corrado et al[18] received ECG screening as part of their PPEs. The intervention group of Steinvil et al[16] received PPE with ECG. Initially, participants aged 17 to 34 years also received an exercise stress test every 4 years, with those aged ≥35 years receiving an annual exercise stress test. After the initial 2 years of screening, the exercise stress test transitioned from the Bruce protocol to a symptom-limited stress test.

Two studies were not included in the meta-analysis for different reasons. The conference abstract[19] was not included because it did not provide extractable data for the meta-analysis. Maron et al[17] included participants from the research of Corrado et al[18] who were already included in the meta-analysis; therefore, we did not include that article to avoid double counting participants. In the conference abstract, Abächerli et al[19] compared SCD rates before and after the initiation of ECG screening before Swiss Army service only for conscripted males. Maron et al[17] compared the rate of SCD in an Italian cohort that had been screened using PPE including ECG with the rate in a US cohort that received PPE without ECG. Full descriptions and characteristics of these 4 studies are presented in the Supplementary Material 4.

The ROB Assessment

All included studies had either unknown or high ROB in most categories evaluated (Table 3). No included studies reported funding that increased their ROB. Details on the ROB determination are available in the Supplementary Materials 4 and 5.

Effectiveness of ECG Screening

Corrado et al[18] reported a comparison of SCD in athletes before and after the initiation of a mandated ECG screening program in the Veneto region of Italy. The primary conclusion of the authors was based on a comparison of a 2-year period before the initiation of screening (1979–1980) with the final 2 years of the screening period (2003–2004), in which they reported an 89% decrease in the incidence of SCD during the 2003–2004 period. For our meta-analysis, we used all extractable data comparing the initial 3 years of athlete SCD before screening (1979–1981) with the 23 years of SCD after the initiation of ECG screening (1982–2004). Our results showed a 63% decreased risk of SCD in the ECG-screened group (RR = 0.37; 95% CI = 0.20, 0.69).

Steinvil et al[16] compared SCD events in athletes reported in 2 newspapers in Israel that cover 90% of the country's population. The authors compared reports of SCD for 12 years before and after the initiation of a mandated cardiac screening program in 1997. They showed a 5% decrease in the risk of SCD, which was not different, in those athletes undergoing preparticipation electrocardiology screening, with substantial uncertainty in the CI (RR = 0.95; 95% CI = 0.43, 2.13).

In a conference abstract, Abächerli et al[19] compared SCD in male Swiss Army conscripts separated into age groups (16–19, 20–24, and 25–29 years). The authors compared episodes of SCD between cohorts with data collected before (historical control group) and after (intervention group) the initiation of ECG screening. In the group aged

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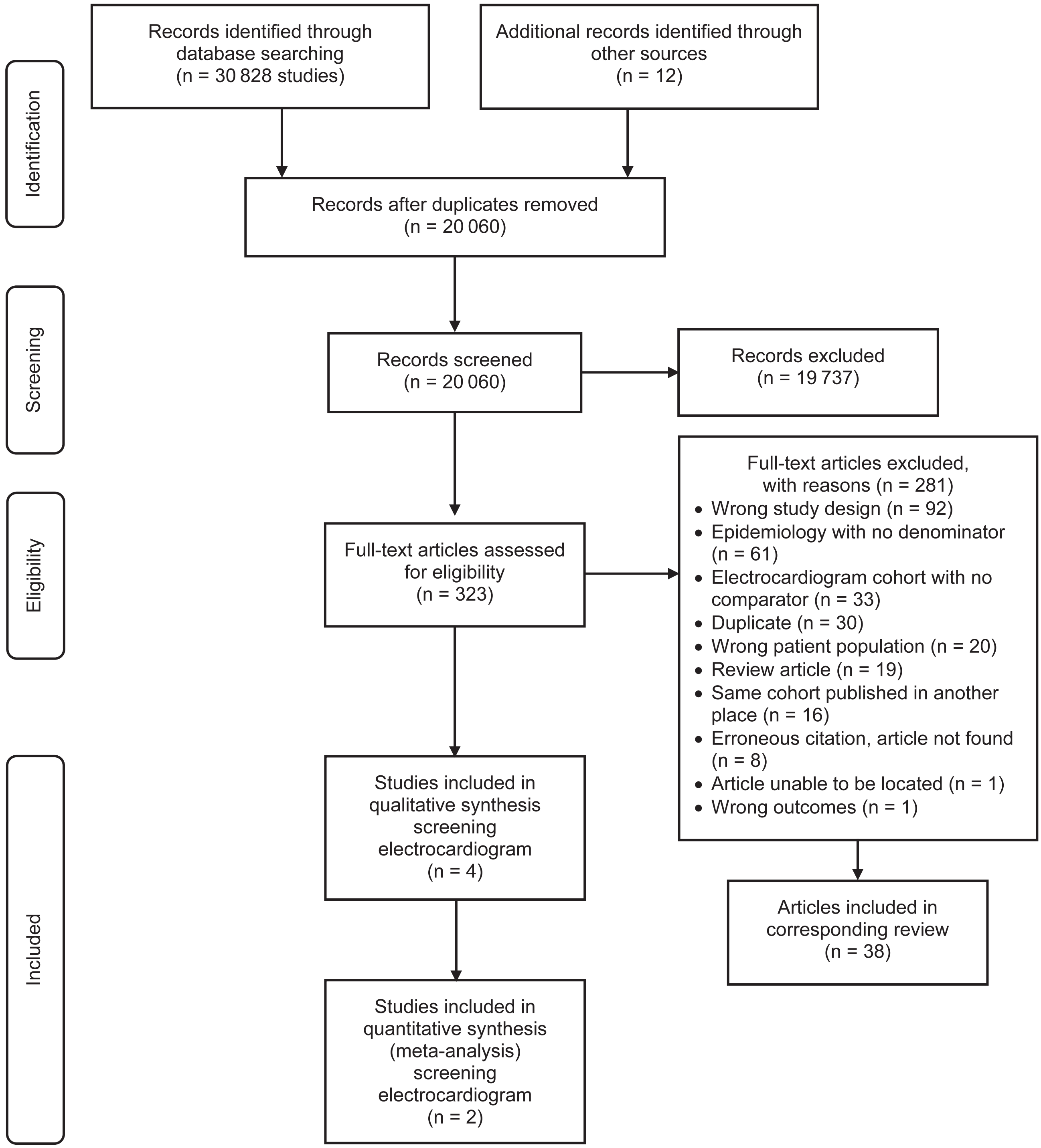

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flowchart.

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Table 3. Risk of Bias in Included Nonrandomized Trials in Objective 2, Based on Cochrane Risk-of-Bias Tool

Study	Sequence Generation	Allocation Concealment	Participant Blinding	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Risk of Bias
Corrado et al[18]	High	Unclear	Unclear	High	Low	High	High
Maron et al[17]	High	Unclear	Unclear	High	Low	High	High
Steinvil et al[16]	High	Unclear	Unclear	High	High	Low	High
Abächerli et al[19]	High	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear

Study	Electrocardiogram Screen Events, No.	Electrocardiogram Screen Total, No.	No Electrocardiogram Screen Events, No.	No Electrocardiogram Screen Total, No.	Weight, %	Risk Ratio, Mantel-Haenszel, Random (95% CI)
Corrado et al[20] (2006)	41	2 613 353	14	334 129	54.0	0.37 (0.20, 0.69)
Steinvil et al[18] (2011)	11	433 071	13	488 721	45.6	0.95 (0.43, 2.13)
Total (95% CI)	52	3 046 424	27	822 850	100.0	0.58 (0.23, 1.45)

Heterogeneity: $\tau^2 = 0.32$, $\chi^2_1 = 3.41$, $P = .06$, $I^2 = 71\%$

Test for overall effect: $Z = 1.17$, $P = .24$

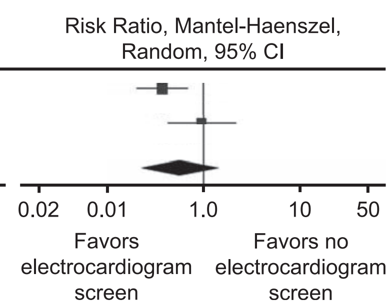

Figure 2. Meta-analysis of studies reporting data on outcomes of sudden cardiac death in athletes screened using electrocardiogram (experimental group) compared with athletes not screened using electrocardiogram (control group).

20 to 24 years, they reported a reduction in SCD in the ECG-screened cohort, with a point estimate of 0.56 (95% CI = 0.35, 0.91). The same comparison in men aged 16 to 19 years was 0.89 and aged 25 to 29 years was 1.04. These values were described as nonsignificant, with only the point estimates and no CIs reported. The abstract was unclear as to whether the statistical method used was RR or odds ratio, making interpretation of the findings difficult. No extractable data were present. Contact with the author revealed that no full-text article was produced from these data, and the authors were unable to share the data at the time of contact.

Maron et al[17] compared a cohort of US athletes in Minnesota who had undergone PPE without ECG screening with ECG-screened athletes from the Corrado et al[18] Italian cohort over a similar period. The authors reported a 6% decrease, which was not different, in the risk of SCD in the ECG-screened cohort, with significant uncertainty in the 95% CI (RR = 0.94, 95% CI = 0.41, 2.12).

Two studies[16,18] involving athletes were included in the meta-analysis (Figure 2). The results showed a relative decreased risk of 42% for SCD in athletes screened using ECG, which was not different, but uncertainty was high, with a potential 77% relative decrease in risk to a 45% relative increase in risk in those screened using ECG (RR = 0.58; 95% CI = 0.23, 1.45; $I^2 = 71\%$, $\chi^2 = 3.41$, $P = .06$). The heterogeneity present in the analysis was shown to be high when we used both I^2 and χ^2 methods.

Corrado et al[18] did report outcome data beyond SCD but only in a portion of the intervention group, which did not allow any comparison to the control group. The authors reported that 9% (3914/42 386) of athletes screened with ECG underwent further cardiac testing based on their original results, and a further 2% (879/42 386) were ultimately removed from sport. The authors did not describe the treatment rendered to athletes with positive screening ECG beyond the further diagnostic studies used and did not report on athletes returning to sport after treatment.

Quality of Evidence

For the primary outcome of SCD, we judged the evidence to be of very low certainty because of high ROB, serious inconsistency, and serious imprecision (Table 3).

DISCUSSION

We found very low-quality, inconclusive evidence that ECG screening decreases the risk of SCD in young athletes and military members. Caution is needed when considering this finding. Authors of only 1[18] of the 4 included studies observed a statistically significant risk when evaluating the effect of ECG screening on SCD, and in the remaining studies,[16,17,19] authors reported CIs that included both considerable decreased and increased risk with ECG screening. The findings of the included conference abstract were based on data[19] that were not published in a full paper. We were able to perform a meta-analysis with only 2 studies.[16,18] The absolute risk reduction from pooling these studies was 0.00157% by using a single-year assessment,[20] resulting in the need to screen 63 694 people to prevent 1 death in 1 year. Given the high ROB, high heterogeneity, and poor precision of effect estimates, the overall certainty of the existing evidence on the effectiveness of ECG screening to prevent SCA and SCD was judged to be very low. Taken together, we believe that these findings could change with further high-quality research.

The existing evidence base to support the use of ECG screening to prevent SCD in athletes is largely confined to the data presented by Corrado et al,[18] which are included in this review. Substantial methodologic concerns exist about this article, including the inherent bias and likely confounders introduced by comparing a small historical control group to a much larger intervention group some 20 years later. Concerns have also been raised about the transparency of the data reported and further follow-up data on the Italian screening program.[21] Although no recent controlled studies have been published, 2 recently published cohort studies may call into question the ability of screening athletes to prevent SCA and SCD. Both studies reported on cohorts consisting of mostly male, professional soccer players who underwent ECG screening as part of PPEs.[22,23] Both reported results with relatively high rates of SCA and SCD at 6.8[22] and 63[23] per 100 000 athlete-years compared with other published incidence rates of SCA or SCD in populations that have not been screened, with estimates around 1 to 2 per 100 000 athlete-years.[24,25]

In a recent report, the UK National Screening Committee[26] reviewed available data on ECG screening in athletes and recommended against its use based on the overall low incidence of SCA and SCD, which is consistent with our

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recent systematic review,[8] as well as the lack of an effective screening test to identify those at risk of SCA and SCD. In addition, published data on events of SCA and SCD have suggested that approximately 60% of cardiac conditions that cause SCA and SCD in athletes may be identifiable using ECG screening.[27,28] When the relative rarity of events of SCA and SCD is combined with the questionable ability of ECG to identify a large proportion of those at risk for SCA and SCD, real doubt exists about whether using ECG screening to prevent SCA and SCD is congruent with recommendations of the World Health Organization for an effective screening program.[29]

Although there remains disagreement and a general lack of empirical data to support the use of screening ECG to prevent SCA and SCD, some have advocated its addition to the PPE to better identify conditions putting athletes at risk for SCA and SCD.[30] In a systematic review in 2015, Harmon et al[7] provided evidence to support this position. They included studies in which researchers compared the likelihood that history, physical examination, and ECG identified potentially lethal cardiac disorders. The authors reported the superiority of ECG in sensitivity (ECG = 94%, history = 20%, physical examination = 9%), positive likelihood ratio (ECG = 14.8, history = 3.22, physical examination = 2.93), and false-positive rate (ECG = 6%, history = 8%, physical examination = 10%). In a recent cohort study focusing on collegiate athletes in the United States, Drezner et al[31] compared the ability of history and physical examination alone with history and physical examination with the ECG screening to identify potentially lethal cardiac disorders in the same cohort of patients. They found false-positive rates of 33.3% for history alone, 2% for physical examination alone, and 3.4% for ECG alone. Sensitivity with ECG was reported as 100% compared with 15.4% for history and 7.7% for physical examination.

As demonstrated in this review, no controlled trial data exist to answer the questions of how ECG screening affects the athlete's removal from sport, follow-up treatment, and potential return to sport. However, cohort data exist on some of these outcomes, including data from Corrado et al.[18] Reporting on a small portion of the total number screened using ECG, the authors indicated that 9% had abnormal findings and received further testing, ultimately resulting in 2% being excluded from sport. A 2014 scientific statement from the American Heart Association (AHA)[32] detailed results from multiple cohort studies on ECG screening in athletes aged 12 to 25 years. The AHA statement reported abnormal ECG rates from 2.5% to 25%, further testing rates from 2.5% to 24%, and disqualification from sport rates of 0.2% to 2% of those screened. When attempting to answer the question of whether history including the AHA[33] questionnaire and physical examination alone compared with history and physical examination with the addition of screening ECG result in more abnormal screening findings, authors of 2 recent cohort studies[31,34] provided useful information. In both cases, the authors compared screening results in the same patients before and after adding ECG screening to the history with AHA questionnaire and physical examination alone. They found that with the addition of ECG, the number of participants with abnormal screens decreased. It is difficult to determine how these findings affected further testing and treatment, as all participants received history, physical examination, and ECG screening interventions. Drezner et al[31] reported that 0.25% of US collegiate athletes included in their study who received a full evaluation were found to have a serious cardiac condition. They also reported that athletes spent an average of 2.6 days out of sport for evaluation of ECG abnormalities discovered during the screening.

In ECG screening studies, authors reported the cardiac abnormalities they identified, and Wolff-Parkinson-White syndrome was the most common finding, often making up most of the identifiable cardiac conditions considered serious by the authors.[31,34,35] Although true risk exists for SCA and SCD in asymptomatic individuals with Wolff-Parkinson-White syndrome, it is thought to be low.[36] This has been identified as a limitation to the screening strategy as a mechanism to reduce SCA and SCD.[37]

Over the past decade, refinement of the ECG criteria for diagnosing potentially lethal cardiac conditions has continued to both increase the sensitivity and decrease the false-positive rate.[38] Although these advancements in the diagnostic capability of ECG screening have been well documented, no controlled trials comparing the ability of PPE with history and physical examination alone and the ability of PPE with ECG to prevent SCA and SCD have been published. The need for a prospective study in which researchers test the utility of screening ECG to prevent SCA and SCD in athletes is great; however, with the rarity of SCA and SCD events, carrying out a prospective study may not be possible. To undertake such a project, one could consider randomizing clusters of high school and collegiate athletes to receive ECG screening with PPE compared with PPE alone. A prospective study may be more feasible in the military, for which randomization of the many entering recruits each year could be possible and there may be sufficient power to identify an effect of screening using ECG if one exists. Another possibility of comparing nonrandomized cohorts of similar athletes exists in the United States where many universities have transitioned to including ECG screening as part of PPEs for their varsity athletes. A comparison of the rates of SCA and SCD in athletes in these universities with those of universities that do not screen using ECG should also be technically feasible.

We believe the strength of this review lies in the breadth of the search for controlled trials in which the ability of screening ECG in athletes or military members to prevent SCA and SCD has been reported. The primary limitation of our review was the low quality of evidence provided by the included studies, as well as the high clinical and statistical heterogeneity present in the meta-analysis, which leads to uncertainty for decision making. The limitations lie in both the paucity and poor quality of the identified research in which outcomes on SCA and SCD in our population have been reported. The use of historical control groups in the meta-analyzed results introduces potential confounders into the results of these trials, which have not been accounted for by the authors. This could take the form of substantially different patient populations participating in sport, such as the ever-increasing female participation; improved medical care, such as emergency medical response systems or presence of automated external defibrillators at sites where practice and games occur; or a change in athlete health behavior, such as nutrition and alcohol, drug, and tobacco use over time.

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CONCLUSIONS

In this review, we found inconclusive and very low-quality evidence of a decreased risk of SCD in participants undergoing additional ECG screening based on the pooled effect estimate. Imprecision around the estimate suggests the possibility of both considerable benefit and harm. We have very low confidence that these findings would not change substantially with data from higher-quality research.

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