Diagnostic accuracy and Bayesian analysis of new international ECG Recommendations in Paediatric athletes

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ABSTRACT

Objective: Historically, electrocardiographic (ECG) interpretation criteria for athletes were only applicable to adults. New international recommendations now account for athletes ≤16 years, but their clinical appropriateness is unknown. We sought to establish the diagnostic accuracy of new international ECG recommendations against the Seattle criteria and 2010 European Society of Cardiology (ESC) recommendations in paediatric athletes using receiver operator curve (ROC) analysis. Clinical context was calculated using Bayesian analysis.

Methods: 876 Arab and 428 black male pediatric athletes (11-18 years) were evaluated by medical questionnaire, physical examination, ECG and echocardiographic assessment. ECGs were retrospectively analyzed according to the 3 criteria.

Results: Thirteen (1.0%) athletes were diagnosed with cardiac pathology that may predispose to sudden cardiac arrest/death (SCA/D) [8 (0.9%) Arab and [5 (1.2%) black]. Diagnostic accuracy was poor [0.68, 95% CI 0.54-0.82] for 2010 ESC recommendations, fair [0.70, 95% CI 0.54-0.85] for Seattle criteria and fair [0.77, 95% CI 0.61-0.93] for international recommendations. False positive rates were 41.0% for 2010 ESC recommendations, 21.8% for Seattle criteria, and 6.8% for international recommendations. International recommendations provided a positive (+LR) and negative (-LR) post-test likelihood ratio of 9.0 (95% CI 5.1-13.1) and 0.4 (95% CI 0.2-0.7), respectively.

Conclusion: In Arab and black male paediatric athletes, new international recommendations outperform both the Seattle criteria and 2010 ESC recommendations, reducing false positive rates, whilst yielding a ‘fair’ diagnostic accuracy for cardiac pathology that may predispose to SCA/D. In clinical context, the ‘chance’ of detecting cardiac pathology within a paediatric male athlete with a positive ECG (+LR=9.0) was 8.3%, whereas a negative ECG (-LR=0.4) was 0.4%.

Key words: Paediatric, athlete’s heart, screening, electrocardiography, echocardiography.

What is already known about this subject?

- It has been proposed that electrocardiographic (ECG) screening of athletes is not effective due to outdated incidence data and flawed methodology.
- Recently, new international recommendations for ECG in athletes, have been demonstrated to reduce the number of abnormal ECGs, but in a primarily white adult athletic population.
- It has been proposed that T wave inversion V_1-V_3 in athletes ≤16 years is physiological, and should not prompt further evaluation in the absence of symptoms, signs or a family history of cardiac disease.

What does this study add?

- For the first time, new international recommendations for ECG interpretation in athletes were assessed by diagnostic accuracy and Bayesian analysis in a paediatric athletic cohort (aged 11-18 years) of 876 Arab and 428 black male athletes.
- New international recommendations for ECG interpretation in athletes significantly reduce false positive rates for pathology that may predispose to SCA/D (6.8%) irrespective of ethnicity and chronological age, compared with the 2010 ESC recommendations (41.0%) and Seattle criteria 21.8%), respectively).
- New international recommendations for ECG interpretation in athletes yield a 'fair' (0.77, 95% CI 0.61-0.93) diagnostic accuracy (area under the curve) for cardiac pathology that may predispose to SCD/A in sports.

How might this impact on clinical practice?

- The 'chance' of detecting cardiac pathology that may predispose to SCA/D in sports within a paediatric male athlete was approximately 1%.

- A positive ECG (+LR = 9.0) as per new international recommendations for ECG interpretation in athletes, means that the same athlete now has an 8.3% ‘chance’ of pathology, whereas a negative ECG (-LR = 0.4) a 0.4% ‘chance’.
- New international recommendations for ECG interpretation can be applied to paediatric (11-18 years) athletes of both Arab and black athletes for the detection of cardiac pathology that may predispose to SCD/A in sports, and outperform previous ECG recommendations.

INTRODUCTION

Studies based on high school populations in the United States reveal that paediatric athletes (14-18 years) are 3.6-times more likely to experience a sudden cardiac arrest than their non-athletic peers [1]. In the United Kingdom, 22% of all sudden cardiac deaths occur in athletes aged under 18 years [2]. The European Society of Cardiology (ESC) [3] and the Association of European Paediatric Cardiology [4], recommend initiating 12-Lead electrocardiography (ECG) screening to coincide with the onset of competitive athletic activity. Screening aims to identify underlying cardiac pathology predisposing to sudden cardiac arrest/death (SCA/D), and thereby reduce the incidence of such catastrophic events.

Until recently clinicians undertaking ECG screening in athletes applied interpretation criteria that were applicable only to adults [5,6]. In a recent systematic review with meta-analysis [7], we observed a high but similar prevalence of anterior (V_1-V_3) T-wave inversion (TWI) in ≥9000 paediatric athletes and ≥800 paediatric non-athletes (6.5% vs 5.7%), suggesting that this repolarization pattern is maturational and not abnormal within the paediatric athlete. New ECG interpretation recommendations now account for athletes aged ≤16 years, with particular focus on individuals displaying anterior (V_1-V_3) TWI (often called juvenile T-wave pattern) [8–10]. Whilst these new recommendations have been shown to significantly reduce the number of abnormal ECGs compared to previous ECG criteria [2010 ESC recommendations [5] and Seattle criteria [6]], this result was observed in a primarily white adult athletic population [11].

The past few decades have observed an exponential increase in the number of Arab and black athletes excelling in international competitive sport, with ethnicity now universally recognized as an important determinant of the electrical manifestations of an athlete's heart [12]. Sports academies throughout the USA, Europe and Asia, who undertake ECG screening in paediatric athletes of Arab and Black ethnicity require knowledge of the clinical appropriateness of these new ECG recommendations to distinguish physiological cardiac adaptations from cardiac pathology predisposing to SCA/D. A second conundrum relates to ensuring that ECG screening results are interpreted in context, especially when there is no 'gold standard' test to identify cardiac pathology. Bayesian analysis allows for the quantification of 'chance' of having a disease as per examination methodology (in this case, ECG interpretation recommendations), based upon *pre-* and *post-test odds* [13].

Accordingly, the aim of this study was to establish the diagnostic accuracy of new international ECG interpretation recommendations for athletes against the Seattle criteria and 2010 ESC recommendations in a large cohort of Arab and black male paediatric athletes using receiver operator curve (ROC) analysis. Clinical context was calculated using Bayesian analysis.

METHODS

Ethics Approval

Ethics approval was provided by Anti-Doping Laboratory Qatar (IRB #E2013000003 and #E20140000012), with all parents or guardians providing informed consent.

Participants

Between 2009 and 2017, 876 Arab and 428 black male paediatric athletes registered with the Qatar Olympic Committee [exercising ≥6 hours/week, aged 11-18 years] presented at our institution for ECG screening. No athlete had been previously screened. Based on 2-year chronological age categories, athletes were distributed as per Table 1. Whilst we acknowledge ECG interpretation criteria were developed for application in athletes aged 12-35 years [8–10], a minority of athletes <12 years presented at the request of the Qatar Olympic Committee.

Preliminary Investigations

Health questionnaire and physical examination

Athletes completed a health questionnaire regarding family history of cardiovascular disease and personal symptoms, together with anthropometric (height and body mass; body surface area (BSA) [14]) and left brachial artery blood pressure assessment in collaboration with an Arabic, French, and/or English-speaking nurse. To ensure accurate medical history was taken, primary guardians were present where appropriate. Precordial auscultation in supine and standing positions, and assessment for any physical characteristics of underlying congenital or syndromal disorder were undertaken by a sports medicine physician.

Resting 12-lead ECG

ECG was recorded with standard 12-lead positions using a GE Mac 5500 (New York, USA), as described elsewhere [15]. All 1304 ECGs were retrospectively interpreted by GMC applying the 2010 ESC recommendations [5], the Seattle Criteria [6], and the new international recommendations (Figure 1) [8–10]. At the time of ECG interpretation, GMC was blinded to all pathological conditions that were subsequently diagnosed.

Echocardiography

2D transthoracic echocardiographic examination was performed using a IE33, (Philips, USA) and Artida (Toshiba Medical Systems, Japan) ultrasound systems. Standard views were obtained and analysed for left and right ventricular wall thickness, cavity dimension measurements, as well as the identification of the origins of the left and right coronary arteries in accordance with current guidelines [16,17].

Further Evaluation

Athletes presenting with an abnormal health questionnaire, physical examination, ECG or echocardiographic examination suggestive of underlying cardiovascular pathology were invited for further evaluation. Subsequent examinations included (but were not limited to) 24h ECG or ambulatory blood pressure monitoring, maximal cardiopulmonary exercise stress testing, electrophysiology study, computerized tomography and cardiac magnetic resonance imaging including contrast studies. Diagnosis of disease was established and managed in accordance to established guidelines [18–25].

Statistical Analysis

Data were expressed as mean ± SD or percentages as appropriate and analyzed with SPSS software (Version 21.0, Chicago, IL). Continuous variables were tested for normality using the Shapiro-Wilk test. Comparisons between groups were performed using a student *t*-test for continuous variables by ethnicity (Arab vs. black), and $\chi 2$ test or Fisher's exact tests for categorical variables by ethnicity (Arab vs. black) and age, both within and between ECG interpretation criteria. A p value <0.05 was considered significant.

ROC analysis was used to describe the sensitivity and specificity of the 3 ECG interpretation criteria to identify cardiac pathology that may predispose to SCA/D in sports[2]. Area under the curve (AUC) represents diagnostic accuracy in differentiating athletes with cardiac pathology; interpreted as excellent (>0.90), good (0.80-0.90), fair (0.70-0.80), poor (0.60-0.70), or fail (<0.60) [26]. False positives were calculated from the specificity and sensitivity values of the 3 ECG interpretation criteria. Bayesian analysis was used to calculate the positive (+LR) and negative likelihood ratios (-LR) from the specificity and sensitivity values of the ECG interpretation criteria, allowing estimation of the chance of cardiac pathology after application of the 3 ECG interpretation criteria. Specifically, the base prevalence rate was determined from the *pre-test odds*, and the +LR and –LR was used to compute the *post-test odds* [13].

Inter-intra observer variability in ECG interpretation

Inter- and intra-observer reproducibility for ECG interpretation using the new international recommendations, Seattle Criteria and ESC 2010 recommendations were assessed using Cohen κ coefficient between two physiologists (GMC, NRR). Data were interpreted as poor (<0.20), fair

(0.20-0.40), moderate (0.41-0.60), good (0.61-0.80) and very good (>0.80) [27]. A power calculation using R package CIBinary determined that 361 athletes were sufficient to detect a 'good' reliability (0.75 95% CI (0.60-0.85) when prevalence of abnormalities was 5.9%. Type 1 error was 5% and power was set 0.80. Inter- and intra-observer reliability was therefore conducted on 400 consecutive independent athletes. Inter-observer reliability for categorizing an ECG as abnormal was very good for ESC 2010 recommendations (k=0.85; 95% CI 0.71-0.99), very good for Seattle criteria (k=0.90; 95% CI 0.86-0.94), and very good for new international recommendations (k=0.90; 95% CI 0.88-0.92). Intra-observer reliability was very good for ESC 2010 recommendations (k=0.95; 95% CI 0.91-0.99), very good for Seattle criteria (k=0.91; 95% CI 0.78-1.00), and very good for new international recommendations (k=0.91; 95% CI 0.78-1.00).

RESULTS

Demographics

Arab athletes descended from West-Asia [836; 80.3%], Africa [171; 19.5%], and Europe [2; 0.2%]. Black athletes descended from Africa [275; 64.2%], West-Asia [139; 32.5%], Central America [7; 1.6%], South America [5; 1.2%], and Europe [2; 0.5%]. Athletes participated in 33 different sports with football (50%) dominating. Mean chronological age (15.9 ± 2.0 vs. 15.2 ± 1.9 years, $p<0.001$) was significantly greater in Arab than black athletes, whilst BSA (1.7 ± 0.3 vs 1.7 ± 0.3 m^2, $p=0.68$) was not different (Table 1).

Health questionnaire and physical examination

Overall, 242 (18.6%; 20.2% Arab and 15.2% black) athletes revealed cardiovascular abnormalities identified by health questionnaire and/or physical examination. Specifically, 216 (16.6%; 18.3% Arab and 13.1% black) athletes self-reported cardiovascular medical issues and 31 (2.4%; 2.1% Arab and 3.0% black) athletes demonstrated an abnormal physical examination.

ECG patterns between ethnicity using new international recommendations

Normal and borderline ECG findings

Normal ECG findings were significantly more frequent in black than arab athletes (93.0% vs. 89.0%; $p \leq 0.001$) (Figure 2). TWI in V_1-V_3 was observed in 69 (16.1%) black athletes compared to 56 (6.4%) Arab athletes aged <16 years old ($p<0.0001$). Borderline ECG findings, either in isolation or in association with a recognized training-related ECG finding, were significantly more frequent in black than Arab athletes (11.0% vs. 7.4%; $p<0.05$), with an increased prevalence of isolated right atrial enlargement (8.9% vs. 5.1%; $p<0.01$).

Abnormal ECGs findings

Abnormal ECGs that required further evaluation were more frequent in black than Arab athletes (10.5% vs. 6.1%; $P<0.01$). Specifically, abnormal TWIs were significantly more frequent in black than Arab athletes (7.0% vs. 2.1%, $p<0.001$); with an increased prevalence of both anterior (2.6% vs, 1.0%; $P<0.05$), and lateral (3.3% vs. 1.4%; $p<0.05$) TWI. Black athletes demonstrated a greater prevalence of pathological Q waves than Arab athletes (4.4% vs. 1.6%; $p<0.01$). Other abnormal

ECG findings were rarely observed in paediatric athletes (≤1.3%), with no statistical difference observed between ethnicity.

Identification of cardiac pathology

Thirteen (1.0%, 95% CI 0.5-1.7) athletes were diagnosed with pathology that may predispose to SCA/D [8 (0.9%, 95% CI 0.4-1.8) Arab and 5 (1.2%, 95% CI 0.4-2.7) black] (Table 2). Of these 13, 6 (46.2%) demonstrated an abnormal health questionnaire and/or physical examination, 10 (76.9%) an abnormal ECG according to ESC 2010 recommendations, and 8 (61.5%) an abnormal ECG according to both the Seattle Criteria and the new international recommendations.

False positive rates per criteria

The false positive rate for pathology that may predispose to SCA/D was 41.0% for the 2010 ESC recommendations, 21.8% for the Seattle criteria, and 6.8% for the new international recommendations (specifically, 5.5% and 9.5% for Arab and black athletes).

Specific false positives per criteria

Ventricular pre-excitation was a false positive in 7.0% of athletes as per 2010 ESC recommendations (short PR interval with/without evidence of delta wave) compared to zero cases using the Seattle criteria and new International recommendations (PR interval <120 ms with a delta wave (slurred upstroke in the QRS complex) and wide QRS [≥120 ms]). Reclassifying axis deviation, atrial enlargement and complete right bundle branch block to be normal when observed in isolation or in association with a recognized training-related ECG finding, reduced false positive rates from 11.8% and 11.2% using the 2010 ESC recommendations and Seattle criteria, respectively, to 0.7% using the new international recommendations (Figure 3, Data Supplement 1-4). The false positive rate for anterior TWI was 12.8% for 2010 ESC recommendations, 3.0% for Seattle criteria and 1.2% for new international recommendations.

Impact of chronological age on false positive rates per criteria

New international ECG recommendations significantly ($p<0.0001$) reduced the false positive rate for pathology that may predispose to SCA/D compared to the Seattle Criteria and 2010 ESC recommendations in athletes aged ≤16 years (6.9% vs. 23.4% vs. 45.6%), ≤14 years (8.7% vs. 27.9% vs 52.7%), and ≤12 years (8.6% vs 29.3% vs 68.1%), respectively (Figure 4).

Diagnostic accuracy per criteria

For pathology that may predispose to SCA/D, diagnostic accuracy was poor [0.64, 95% CI 0.47-0.81] for health questionnaire and/or physical examination, poor [0.68, 95% CI 0.54-0.82] for the 2010 ESC recommendations, fair [0.70, 95% CI 0.54-0.85] for the Seattle criteria and fair [0.77, 95% CI 0.61-0.93] for new international recommendations (Figure 5, Table 3).

Clinical implication of using the new international recommendations

New international recommendations provided an overall +ve and -ve LR of 9.0 (95% CI 5.1-13.1) and 0.4 (95% CI 0.2-0.7), respectively. When split by ethnicity, 9.0 (95% CI 3.8-15.8) and 0.5 (95% CI 0.2-0.8) for Arab, and 8.5 (95% CI 3.8-12.5) and 0.2 (95% CI 0.04-0.7) for black athletes, respectively.

DISCUSSION

The correct differentiation of physiological cardiac adaptation owing to sustained and intensive exercise from an inherited cardiac pathology is paramount to correctly identify athletes at risk of SCA/D. In this study of 876 Arab and 428 black male paediatric athletes, it was observed that new international ECG recommendations significantly reduce false positive rates by 83.4% and 68.7% respectively when compared to the Seattle criteria and 2010 ESC recommendations, irrespective of chronological age, whilst yielding a 'fair' diagnostic accuracy for conditions that may predispose to SCA/D. To place new international recommendations into clinical context, the 'chance' of detecting cardiac pathology that predispose to SCA/D within a paediatric male athlete is approximately 1%. A positive ECG (+LR=9.0) as per new international recommendations, means that the same athlete now has an 8.3% 'chance' of pathology, whereas a negative ECG (-LR=0.4) has a 0.4% 'chance'.

Diagnostic Accuracy of new international recommendations in paediatric Arab and Black athletes

When applying the 2010 ESC recommendations to our athletes, almost 1 in 3 Arab and 1 in 2 black athletes would warrant further evaluation, demonstrating a poor (0.68) AUC (diagnostic accuracy). The Seattle criteria improved these rates to 1 in 5 Arab and 1 in 4 black athletes, with a fair (0.70) overall diagnostic accuracy. While the 2010 ESC recommendations are based upon consensus rather than scientific evidence, the Seattle Criteria modified its interpretation criteria by applying evidence that 1) accounted for black ethnicity (J-point elevation and convex ['domed'] STsegment elevation followed by TWI in leads V_1–V_4), a false positive in 6.9% of our black paediatric athletes and 2), by adjusting ventricular pre-excitation criteria to require a concomitant delta wave (slurred upstroke in the QRS complex) and wide QRS (>120ms) in addition to a short PR (<120ms), a false positive in 7.0% of our paediatric athletes.

To further reduce false positive ECG rates and improve diagnostic accuracy, new international recommendations now categorize the presence of atrial enlargement (8.9% in our athletes), axis deviation (1.9% in our athletes), and complete right bundle branch block (0.4% in our athletes), as 'borderline' findings when observed in isolation or in association with a recognized training-related ECG change, as they correlate poorly with cardiac pathology predisposing to SCA/D in sport [28,29] (Figure 1). Our data supports these recommendations, by observing 112 athletes (8.6%) with isolated borderline ECG findings, and just 9 athletes (0.7%) with ≥2 borderline ECG findings that would trigger additional investigation; with none found to have pathology predisposing to SCA/D in sports (Figure 2 and 3). False positive rates were again further reduced by deeming the juvenile T-wave pattern to be physiological, a false positive in 121 (17.3%) athletes aged <16 years compared to 36 (6.1%) athletes ≥16 years. In real terms, when new international recommendations are applied to our athletes, 1 in 17 Arab and 1 in 10 black athletes would warrant further evaluation, with a fair (0.77) overall diagnostic accuracy [specifically, a fair (0.72) diagnostic accuracy for Arab but importantly, a good (0.85) diagnostic accuracy for black athletes].

Clinical application of new international recommendations in paediatric Arab and Black athletes

Our data confirm that like their adult counterparts (4.9%) [15], a comparable proportion of paediatric athletes demonstrate a false positive ECG (6.9%) when utilizing similar ECG criteria; a result observed irrespective of chronological age (≤16 years [7.6%] vs. ≤14 years [9.6%] vs. ≤12 years [8.6%]. This finding is important as the ESC state that ECG screening should start at the beginning of competitive athletic activity, which for the majority of sporting disciplines corresponds to an age of 12–14 years [30]. Whilst this low false positive rate is reassuring, care is warranted however, if considering the sensitivity of ECG screening. Dhutia et al. [11] diagnosed 15 athletes (from 4,925 screened; 0.3%) with cardiac pathology that may predispose to SCA/D, all of whom presented with an abnormal ECG according to new international recommendations (i.e. 100% sensitivity). We diagnosed 13 athletes with cardiac pathology that may predispose to SCA/D, of which just 8 (61.5% sensitivity) had an abnormal ECG according to new international recommendations (Table 2). However, the ECG is unable to detect anomalous coronary arteries (n=1), aortopathies (n=2) and valvular disease (=1) [8–10], and thus helps explain the reduced sensitivity observed. In line with previous literature [31], we confirm that medical questionnaires and/or physical examinations were associated with poor sensitivity (46.2%) for conditions predisposing to SCA/D.

Bayesian analysis allows for the quantification of ‘chance’ that a patient with an abnormal or normal ECG will have a cardiac pathology that may predispose them to SCA/D [13]. As the first study to apply Bayesian analysis in any young athletic population, our data demonstrates that baseline ‘chance’ of having cardiac pathology predisposing to SCA/D was 1% for the entire cohort.

The findings presented here show that a positive ECG has a +LR=9.0 meaning that the same athlete with a positive test has an 8.3% 'chance' of cardiac pathology. Conversely, an athlete with a negative ECG (-LR=0.4) would have an 0.4% chance. Our analysis also demonstrate that the new international recommendations provide a greater positive likelihood (+LR=9.0) compared to the 2010 ESC recommendations (+LR=1.9) and the Seattle Criteria (+LR=2.7), respectively (Table 3).

Limitations

Our results are based on observational cross-sectional data, and thus we may have underestimated prevalence of cardiac pathology that may predispose to SCA/D in sport, since it is recognized that gene carriers of inherited cardiac pathology may not exhibit phenotype evidence until early adulthood. Secondly, our population were exclusively Arab and black male athletes, limiting application to other ethnicities and the female paediatric athlete. Finally, whilst we only recruited athletes who were registered with the Qatar Olympic Committee exercising ≥6 hours/week, we did not define fitness (such as aerobic capacity).

Conclusion

In conclusion, new international ECG interpretation recommendations for athletes outperform both the Seattle criteria and 2010 ESC recommendations by reducing false positive rates in Arab and black paediatric male athletes, whilst yielding a 'fair' diagnostic accuracy for conditions that may predispose to SCA/D in sports Interpretation of the paediatric athletes ECG by new international recommendations provides the best likelihood of triggering further evaluation in the attempt to detect cardiac pathology.

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TABLES

Table 1. Anthropometric data of pediatric athletes

Age group (years.)	Group	*n*	%	Height (cm)	Body mass (kg)	BSA (m^2)
11-12	Total	117	9.0	152.8 ± 9.4	45.2 ± 11.0	1.38 ± 0.20
	Arab	91		151.1 ± 8.5	44.3 ± 9.5	1.36 ± 0.17
	Black	26		158.5 ± 10.4**	48.5 ± 15.1	1.45 ± 0.26†
13-14	Total	5410	31.4	167.9 ± 9.5	58.3 ± 13.8	1.6 ± 0.23
	Arab	204		166.6 ± 9.7	58.1 ± 15.9	1.63 ± 0.25
	Black	206		169.2 ± 9.1*	58.6 ± 11.5	1.66 ± 0.19
15-16	Total	351	26.9	174.9 ± 9.6	67.3 ± 16.4	1.80 ± 0.25
	Arab	261		174.1 ± 8.6	66.7 ± 16.6	1.79 ± 0.25
	Black	90		177.2 ± 11.8**	69.0 ± 15.9	1.83 ± 0.25
17-18	Total	426	32.7	177.2 ± 8.6	70.5 ± 14.3	1.86 ± 0.22
	Arab	320		176.7 ± 8.0	70.4 ± 14.0	1.86 ± 0.12
	Black	106		178.6 ± 10.3	70.8 ± 15.2	1.87 ± 0.23

Values are mean ± standard deviation.
* p≤0.01, significantly more prevalent or greater in black than Arab athletes
*** p≤0.001, significantly more prevalent or greater in black than Arab athletes
† p≤0.01, significantly more prevalent or greater in Arab than black athletes
BSA, Body surface area.

Table 2. Characteristics of athletes diagnosed with cardiac pathology that may predispose to sudden cardiac death in sports.

Pathology	Age	Ethnicity	Sport	H + P Abnormality	ECG Abnormality	ESC 2010	Seattle	International	Diagnostics	Risk Stratification
Anomalous origin of left coronary artery	15	Arab	Football	Nil	Short PR interval	+	-	-	Echo, CMRI, CT	EST, Holter
ARVC	18	Black	Football	Family history of cardiomyopathy	TWI V_2-V_6	+	+	+	Echo, CMRI	EST, Holter
Aneurysm with aortic root dilatation (Z score 4)	12	Arab	Football	Nil	Nil	-	-	-	Echo, CMRI, CT	Gene Test
Aortic coarctation with aortic root dilatation (moderate [Valsalva Sinus – Z Score 3.06] to mild [ascending aorta – Z score 2.98]), BAV and moderate PR	18	Arab	Football	Murmur	Nil	-	-	-	Echo, CMRI, Angiogram	EST
HCM	13	Black	Football	Nil	TWI AVL, V_2-V_5 Q waves II, III, AVF, V_5, V_6	+	+	+	Echo, CMRI	EST, Holter, Gene Test
LVNC	13	Black	Football	Nil	TWI II, III, AVF, V_1-V_6 Q waves II, III, AVF, V_4 -V_6	+	+	+	Echo, CMRI	EST, Holter, Gene Test

MVP with severe MR, necessitating surgical repair	18	Black	800m runner	Murmur Chest Pain	Nil	-	-	-	Echo	-
Myocarditis, with anterolateral, lateral and inferolateral mid-wall fibrosis at basal level.	14	Arab	Football	Nil	TWI V_1-V_3	+	+	-	Echo, CMRI	EST, Holter
Myocarditis, with anterolateral, lateral and inferolateral mid-wall fibrosis at basal and mid ventricular level.	13	Arab	Golf	Family history of cardiomyopathy	TWI AVL, V_1 V_4-V_5	+	+	+	Echo, CMRI	EST, Holter
Myocarditis, with anterolateral and lateral mid-wall fibrosis at basal level.	16	Arab	Football	Syncope	TWI III, AVF, V_1, V_4-V_6	+	+	+	Echo, CMRI	EST, Holter
SVT with re-entry	14	Arab	Football	Nil	Short PR interval PVCs	+	+	+	Echo, CMRI	EST, Holter, EPS
WPW	13	Arab	Swimmer	Nil	Short PR interval Delta Wave Wide QRS	+	+	+	Echo	EST, Holter, EPS
WPW	13	Black	Football	Family history of SCA/D	Short PR interval Delta Wave Wide QRS TWI AVL, V_1-V_4	+	+	+	Echo, CMRI	EPS

ARVC; arrhythmogenic right ventricular cardiomyopathy; BAV; bicuspid aortic valve; CMRI; Cardiac Magnetic Resonance Imaging; ECG; 12-lead electrocardiogram; EST; Exercise Stress Testing; H + P = history and physical examination; HCM; hypertrophic cardiomyopathy; LVNC, left ventricular non-compaction; MVP; Mitral Valve Prolapse; MR; mitral regurgitation; PR; pulmonary regurgitation; SCA/D, sudden cardiac death; SVT, supraventricular tachycardia; TWI, T-wave inversion; WPW; Wolf-Parkinson-White syndrome.

Table 3: Positive and Negative likelihood ratios of three ECG interpretation criteria to detect cardiac pathology that may predispose to sudden cardiac death/arrest only

	Combined Athletes (n=1304)			Arab Athletes (n=876)			Black Athletes (n=428)		
	ESC 2010	Seattle Criteria	International Criteria	ESC 2010	Seattle Criteria	International Criteria	ESC 2010	Seattle Criteria	International Criteria
Sensitivity,%	76.9 (46.2-95.0)	61.5 (31.6-86.1)	61.5 (31.6-86.1)	75.0 (34.9-96.8)	50.0 (15.7-84.3)	50.0 (15.7-84.3)	80.0 (28.4- 99.5)	80.0 (28.4-99.5)	80.0 (28.4-99.5)
Specificity, %	59.0 (56.3-61.7)	78.2 (75.9-80.5)	93.2 (91.7-94.5)	62.4 (59.1-65.7)	79.7 (76.9-82.4)	94.5 (92.7-95.9)	52.0 (47.1-58.9)	75.2 (70.8-79.2)	90.5 (87.4-93.2)
AUC	0.68 (0.54-0.82)	0.70 (0.54-0.85)	0.77 (0.61-0.93)	0.69 (0.51-0.86)	0.65 (0.44-0.86)	0.72 (0.50-0.94)	0.66 (0.44-0.88)	0.77 (0.57-0.98)	0.85 (0.65-1.00)
+ve likelihood ratio	1.9 (1.2-2.3)	2.7 (1.6-3.9)	9.0 (5.1-13.1)	2.0 (1.1- 2.5)	2.5 (1.1-4.0)	9.0 (3.8-15.8)	1.7 (0.8-2.1)	3.2 (1.5-4.3	8.5 (3.8-12.5)
-ve likelihood ratio	0.4 (0.1-0.9)	0.5 (0.2-0.8)	0.4 (0.2-0.7)	0.4 (0.1- 0.9)	0.6 (0.3-1.0)	0.5 (0.2-0.8)	0.4 (0.07-1.2)	0.3 (0.05-0.8)	0.2 (0.04-0.7)
+ve post-test chance of pathology, %	1.9 (0.9-3.4)	2.7 (1.2-5.3)	8.3 (3.3-14.3)	1.8 (0.7- 3.9)	2.3 (0.6-5.6)	7.7 (2.1-18.2)	2.0 (0.5-4.8)	3.8 (1.0-8.8)	8.1 (2.1-18.2)
-ve post-test chance of pathology, %	0.4 (0.08-1.2)	0.5 (0.2-1.2)	0.4 (0.1-1.0)	0.4 (0.04-1.3)	0.5 (0.2-1.5)	0.5 (0.1-1.2)	0.5 (0.01-2.5)	0.4 (0.0-1.8)	0.2 (0.0-1.5)

Data are presented as % (95 % CI)

AUC, area under the curve; +ve, positive; -ve, negative.

FIGURES

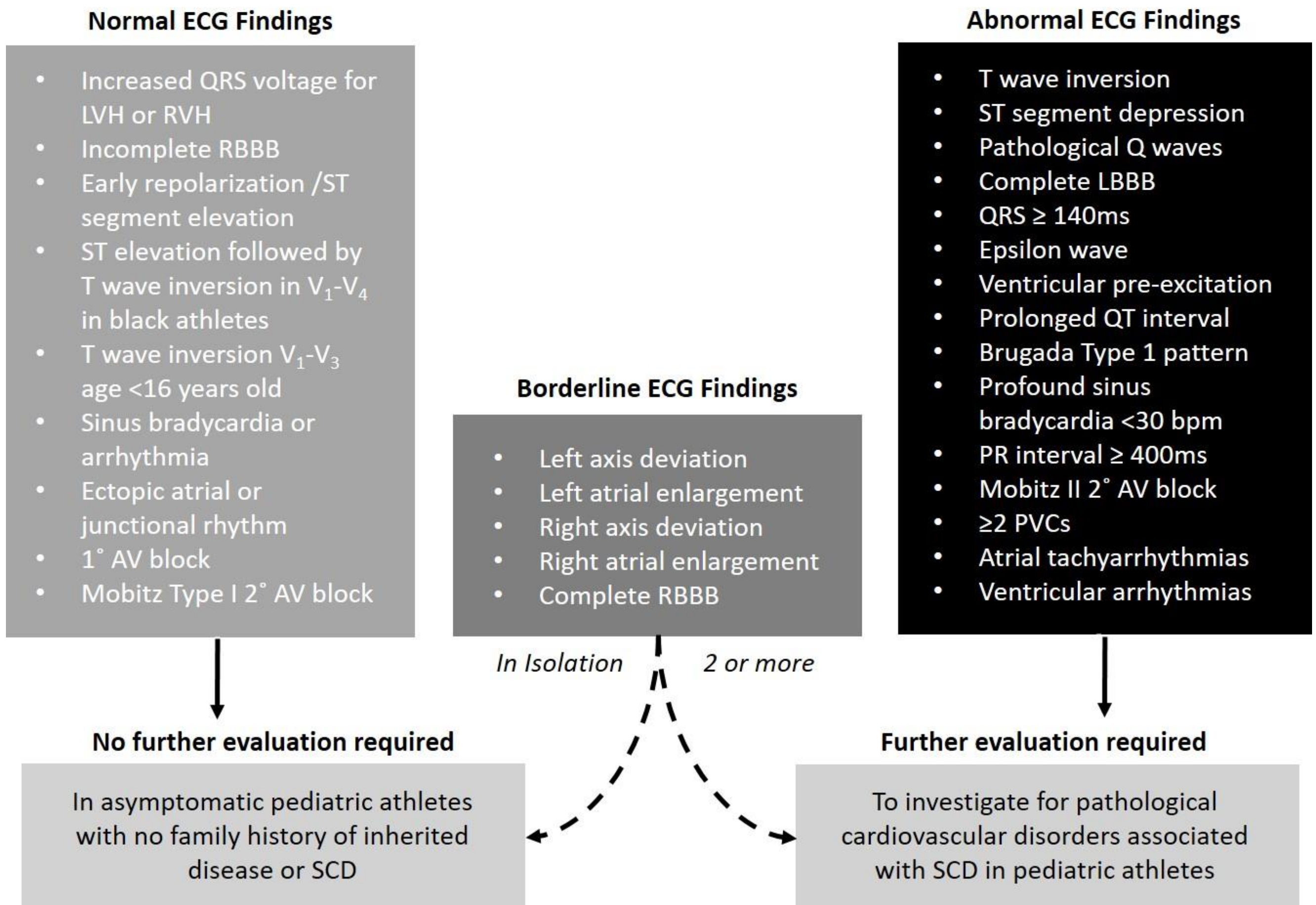

Figure 1. International recommendations for electrocardiographic interpretation in athletes

Key: AV; atrioventricular LBBB; left bundle branch block; LVH, left ventricular hypertrophy; ms; milliseconds; PVCs, premature ventricular contractions; RBBB; right bundle branch block; RVH; right ventricular hypertrophy; RBBB; right bundle branch block.

Normal ECG Findings

	Arab	Black
11-12	125 (87)	29 (88)
13-14	244 (86)	242 (93)
15-16	349 (87)	117 (98)
17-18	415 (92)	118 (90)

Borderline ECG Findings

In Isolation

	Arab	Black
11-12	12 (8)	1 (3)
13-14	25 (9)	34 (13)
15-16	29 (7)	10 (8)
17-18	28 (6)	21 (16)

2 or more

	Arab	Black
11-12	1 (0.7)	0 (0.0)
13-14	1 (0.4)	4 (2)
15-16	0 (0.0)	0 (0.0)
17-18	3 (0.7)	0 (0.0)

Abnormal ECG Findings

	Arab	Black
11-12	5 (4)	5 (15)
13-14	8 (3)	31 (12)
15-16	13 (3)	6 (5)
17-18	23 (5)	8 (6)

In Isolation

2 or more

No further evaluation required

	Arab	Black
11-12	136 (96)	28 (85)
13-14	275 (97)	227 (87)
15-16	388 (97)	114 (95)
17-18	426 (94)	123 (94)

Further evaluation required

	Arab	Black
11-12	6 (4)	5 (15)
13-14	9 (3)	34 (13)
15-16	13 (3)	6 (5)
17-18	26 (6)	8 (6)

Figure 2. Prevalence of normal, borderline and abnormal ECG findings by chronological age group for Arab and black pediatric athletes according to International recommendations.

Key: Data are presented as n (%)

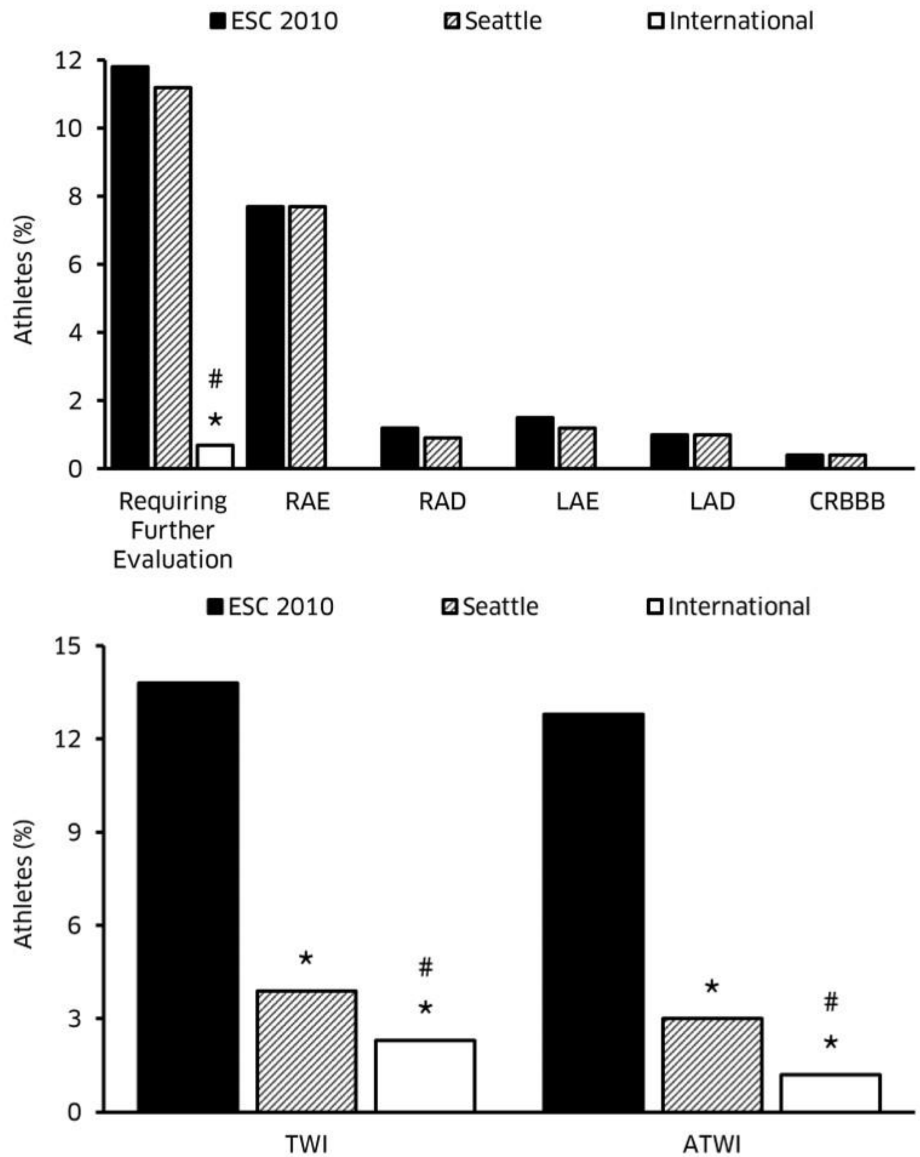

Figure 3. Bar chart shows specific ECG false positives rates with reference to to the 3 ECG interpretation criteria.

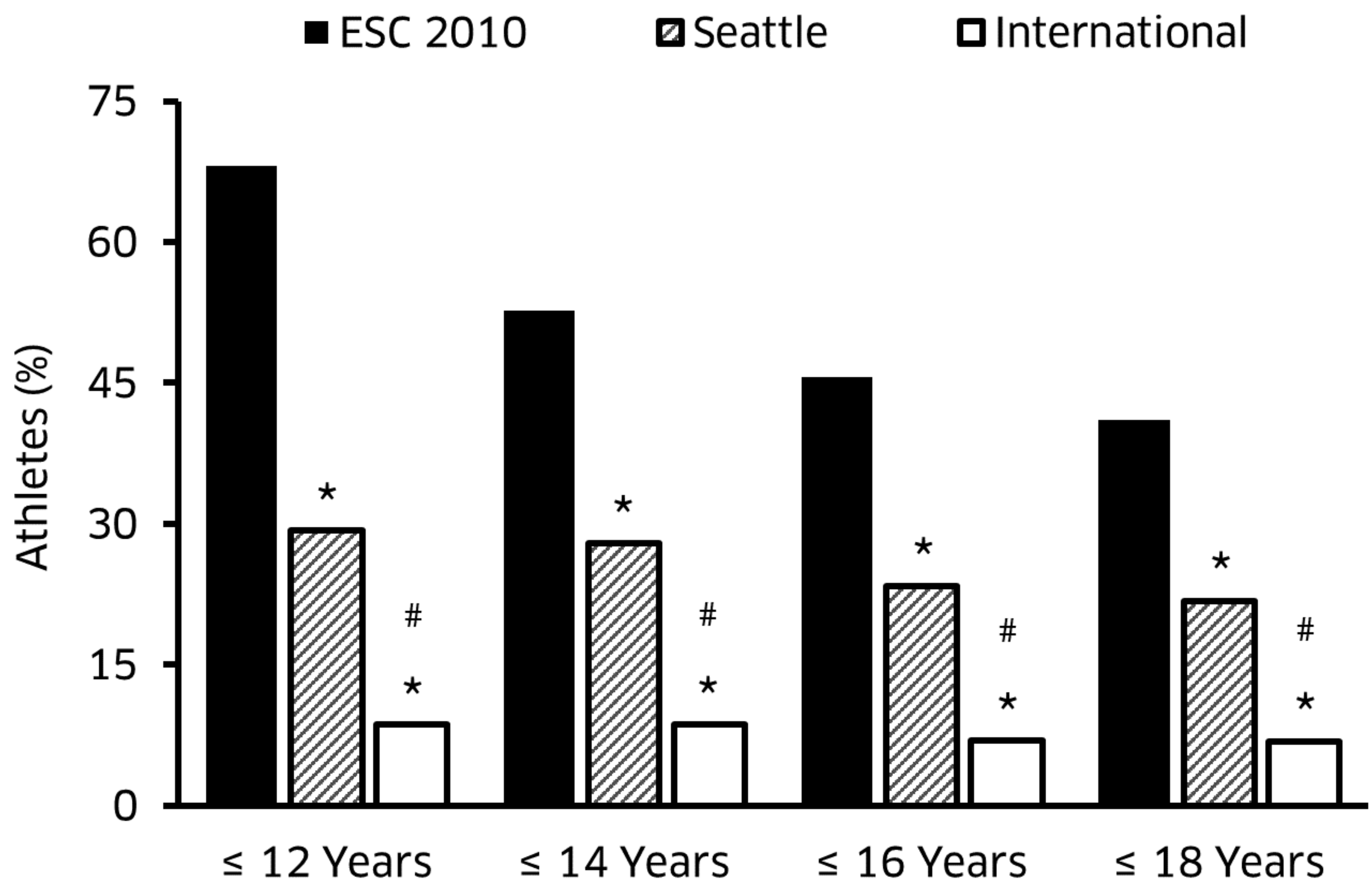

Figure 4. Bar chart shows percentage of false positive ECG findings according to the 3 ECG interpretation criteria by chronological age. *P <0.05, Significantly reduced prevalence to ESC 2010 recommendations. # P <0.05, Significantly reduced prevalence to Seattle Criteria.

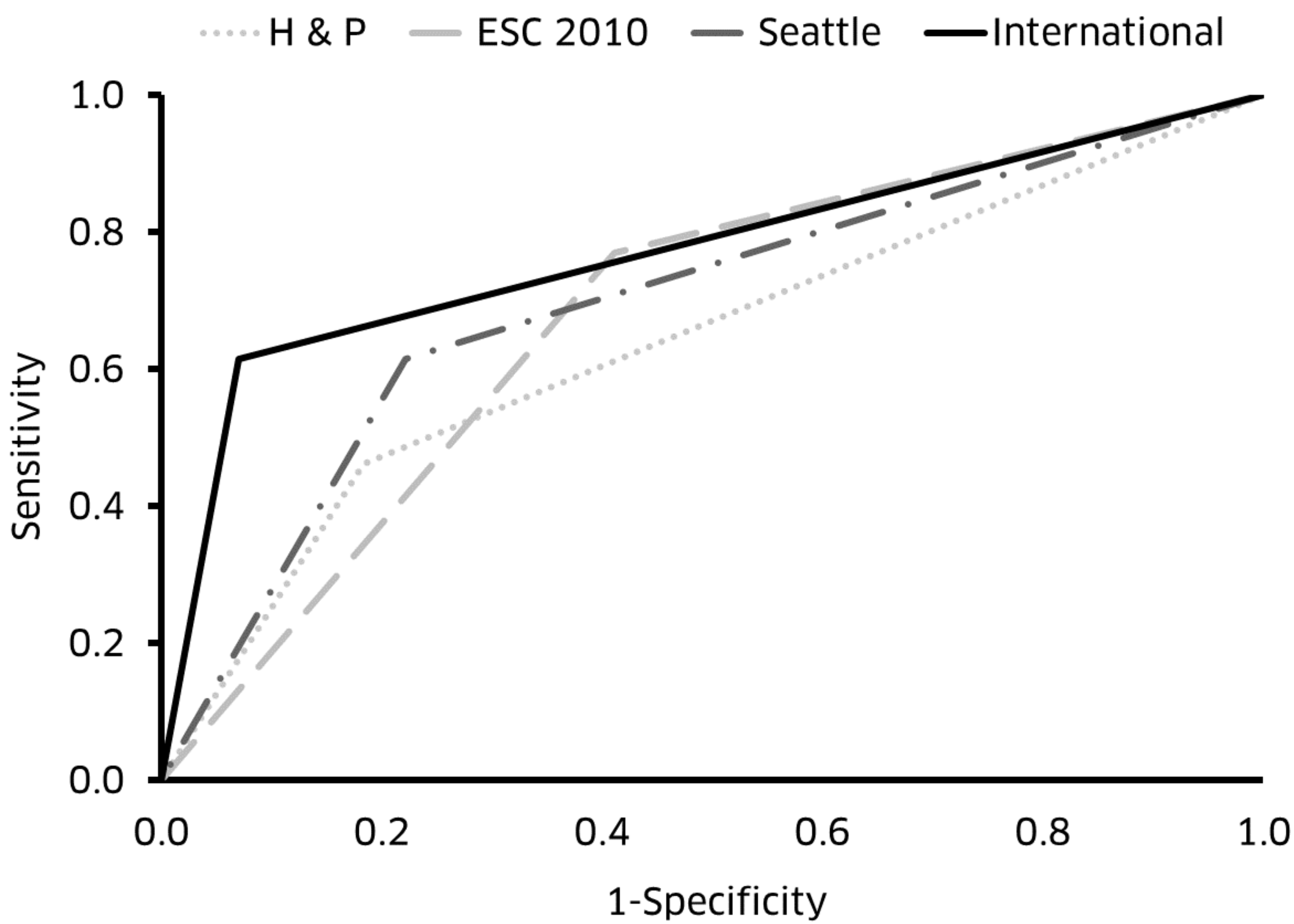

Figure 5. Receiver-operating curves according to health questionnaire and/or physical examination and the 3 ECG interpretation criteria to detect cardiac pathology that may predispose to sudden cardiac death/arrest.