McClean, G, Riding, NR, Pieles, G, Sharma, S, Watt, V, Adamuz, C, Johnson, A, Tramullas, A, George, KP, Oxborough, D and Wilson, MG

Prevalence and significance of T-wave inversion in Arab and Black paediatric athletes: Should anterior T-wave inversion interpretation be governed by biological or chronological age?

Prevalence and significance of T-wave inversion in Arab and Black paediatric athletes; should Anterior T-wave Inversion interpretation be governed by biological or chronological age?

Gavin McClean[1,2], Nathan R Riding[1], Guido Pieles[3], Sanjay Sharma[4], Victoria Watt[5], Carmen Adamuz[5], Amanda Johnson[6], Antonio Tramullas[6], Keith P. George[2], David Oxborough[2] and Mathew G Wilson[1,2]

[1.] Athlete Health and Performance Research Centre, Aspetar Orthopaedic and Sports Medicine Hospital, Qatar.
[2.] Research Institute for Sport and Exercise Science, Liverpool John Moores University, UK.
[3.] National Institute for Health Research (NIHR) Cardiovascular Biomedical Research Centre, Congenital Heart Unit, Bristol Royal Hospital for Children and Bristol Heart Institute, UK.
[4.] Department of Cardiovascular Sciences, St Georges University of London, UK
[5.] Department of Sports Medicine, Aspetar Orthopaedic and Sports Medicine Hospital, Qatar.
[6.] Aspire Academy Sports Medicine Centre, Aspire Academy, Qatar

Correspondence to:

Professor Mathew G. Wilson
Athlete Health and Performance Research Centre
Aspetar Orthopaedic and Sports Medicine Hospital
PO BOX 29222, Doha, Qatar;
mathew.wilson@aspetar.com
Twitter: @gavin_mcclean @Prof_MatWilson

Abstract: 282

Word Count: 3231

Figures 5, **Tables** 3, **References** 37

ABSTRACT

Background: International electrocardiographic (ECG) recommendations regard anterior T-wave-inversion (ATWI) in athletes <16 years to be normal.

Design: Identify the prevalence, distribution, and determinants of TWI by ethnicity, chronological and biological age within paediatric athletes. Secondly, establish diagnostic accuracy of international ECG recommendations against refinement within athletes who present ECG variants isolated to ATWI (V_1-V_4) using receiver operator curve (ROC) analysis. Clinical context was calculated using Bayesian analysis.

Methods: 418 Arab and 314 black male athletes (11-18 years) were evaluated by ECG, echocardiogram and biological age (via radiological x-ray) assessment.

Results: 116 (15.8%) athletes presented ATWI (V_1-V_4), of which 96 (82.8%) were ECG variants isolated to ATWI. 91 (12.4%) athletes presented ATWI confined to V_1-V_3, with prevalence predicted by black ethnicity (odds ratio (OR) 2.2; 95% CI 1.3-3.5) and biological age <16 years (OR 2.0; 95% CI 1.2-3.3). Of the 96 with ATWI (V_1-V_4) observed in the absence of other ECG findings considered to be abnormal as per international recommendations for ECG interpretation in athletes, diagnostic accuracy was 'fail' (0.47 95% CI 0.00-1.00) for international recommendations and 'excellent' (0.97 95% CI 0.92-1.00), when governed by biological age <16 years, providing a positive (+LR) and negative (-LR) likelihood ratio of 15.8 (95% CI 1.8-28.1) and 0.0 (95% CI 0.0-0.8), respectively.

Conclusion: Interpretation of ECG variants isolated to ATWI (V_1-V_4) using international recommendations (chronological age <16 years), warrants caution, but governance by biological age yielded an 'excellent' diagnostic accuracy. In clinical context, the 'chance' of detecting

cardiac pathology within a paediatric male athlete presenting ATWI in the absence of other ECG findings considered to be abnormal as per international recommendations for ECG interpretation in athletes (+LR=15.8), was 14.4%, whereas a negative ECG (-LR=0.0) was 0%.

Key words: Athlete's Heart, Paediatric, Maturation, Electrocardiogram, T-Wave-Inversion, Sudden Cardiac Death.

INTRODUCTION

T wave inversion (TWI) may represent the only sign of cardiac pathology predisposing to sudden cardiac death/arrest (SCD/A) without phenotypic manifestation on secondary investigation[1]. Whilst lateral, inferolateral and inferior TWI are universally recognised as abnormal, international recommendations for electrocardiographic (ECG) interpretation in athletes regard anterior TWI (ATWI) in V_1–V_4 when preceded by J termination (Jt) and/or ST-segment elevation in black athletes, in V_1–V_3 when chronological aged <16 years, and biphasic in V_3 only, to be normal and does not require further evaluation in the absence of other clinical or ECG features suggestive of cardiomyopathy[2].

Prior work within white athletes recognizes ATWI extending beyond V_2 to be rare in those aged ≥16 years (0.1%)[3] and beyond V_3 with complete pubertal development (1.6%)[4]. Subsequently, 16 years marks the cut off (TWI in V_1–V_3) for international ECG interpretation recommendations. Additional work within white and black adult athletes demonstrates that detailed assessment of Jt and/or ST-segment amplitude preceding ATWI can accurately discriminate physiological adaptation from cardiomyopathy, independent of ethnicity[5]. Yet, the appropriateness of such assessments in Arab and black paediatric athletes is unknown. Unlike chronological age, maturation status is not linear; varying in extreme cases by six years between two 9-year-old males[6]. Previous investigators have considered maturational status when interpreting an ECG[4] but used Tanner staging assessment[7], now regarded as inappropriate due to child protection concerns. Furthermore, self-assessment yields poor validity (27%)[8]. Alternatively, skeletal age (biological age) assessment via radiological hand-wrist X-ray examination is recognised by the International Olympic Committee as the ‘gold standard’ estimate of maturity status[9]. To interpret presentation

of ATWI in clinical context, especially when there is no 'gold standard' test to identify cardiac pathology, Bayesian analysis allows for the quantification of 'chance' of pathology as per examination methodology (in this case, ECG interpretation), based upon pre- and post-test odds[10].

Accordingly, our primary aim was to identify the prevalence, distribution, and determinants of TWI by ethnicity, chronological and biological age within a large cohort of Arab and black paediatric athletes. Secondarily, we aimed to establish diagnostic accuracy of international ECG recommendations against refinement in paediatric athletes who present ECG variants isolated to ATWI (V_1-V_4,) by receiver operator curve (ROC) analysis. Clinical context was calculated using Bayesian analysis.

METHODS

Ethical Approval

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

Participants

Between 2009-2017, 418 Arab and 314 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. Ethnicity was self-determined by the athlete (or guardian) in accordance to definitions offset by the UK government's statistical service[11]. Based on 2-year chronological age categories participants' demographic distribution is described in Table 1. Whilst we acknowledge

ECG interpretation criteria were developed for athletes aged 12-35 years[2], 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 (with primary guardians) regarding family history of cardiovascular disease and personal symptoms, together with anthropometric (height and body mass; body surface area [BSA][12]) and left brachial artery blood pressure assessment in collaboration with an Arabic, French, and/or English-speaking nurse. Precordial auscultation in supine and standing positions and assessment for underlying congenital or syndromal disorders 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). All 732 ECGs were retrospectively interpreted by GMC applying international recommendations[2], whilst blinded to pathology. ECG variants isolated to ATWI (V_1-V_4), were secondarily interpreted by: Jt and/or ST-segment elevation irrespective of ethnicity and biological age <16 years when confined to V_1-V_3.

The amplitude of the J termination (Jt)[13] was measured at the end of the QRS complex (the onset of the ST-segment) with reference to the onset of the QRS complex and was considered elevated if Jt ≥0.1mV or depressed if Jt ≤-0.1 mV (Figure 1). The ST-segment was considered elevated if

the amplitude of the ST-segment 100ms after Jt (interval M) were greater than the amplitude at Jt, depressed if below and isoelectric if in line with the Jt.

Echocardiography

2D transthoracic echocardiographic examination was performed using IE33 (Philips, USA) and Artida (Toshiba Medical Systems, Japan) ultrasound systems. Standard views were obtained and analysed for left and right ventricular wall thickness and cavity dimensions as well as the identification of the origins of the left and right coronary arteries in accordance with current guidelines[14].

Chronological and Biological Age Assessment

Chronological age was calculated as the difference between date of birth as per passport and date of examination. Radiological hand-wrist imaging using a Digital Diagnost (Philips, USA) of the left hand-wrist allowed biological age estimation by the Fels method[15], by a single examiner with previously demonstrated intra-class correlation coefficient of 0.998[6]. Radiation exposure is considered almost negligible (0.00017 millisievert); corresponding to 1 hour of background radiation from major cities in the UK[16,17].

Further Investigations

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 may have included 24h-ECG or ambulatory blood

pressure monitoring, maximal cardiopulmonary exercise testing, electrophysiology study, computerized tomography and cardiac magnetic resonance imaging. Diagnosis of disease was established and managed in accordance to guidelines[18–24].

Statistical Analysis

Data were expressed as mean (±SD) or percentages as appropriate and analysed 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 χ^2 test or Fisher's exact tests for categorical variables by ethnicity (Arab vs. black), and biological age (<16 vs. ≥16 years). Z tests, adjusted for Bonferroni ($P \leq 0.05$), allowed for multiple comparisons to explain the effect of biological age (10-12 years. vs. 13-14 years. vs. 15-16 years. vs. 17-18 years.), within ethnicity, upon the prevalence of TWI by territory. Univariate and multivariate binomial logistic regression was used to determine which factors (black ethnicity, chronological, or biological age <16 years) were significantly associated with the presence of TWI by territory; calculated from those with no identified cardiac pathology. International recommendations[2] guided selection of chronological and biological age of <16 years.

ROC curve analysis was used to describe the sensitivity and specificity of ECG interpretation criteria to identify cardiac pathology that may predispose to SCA/D[25]. Area under the curve represented 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]. Positive

(+LR) and negative likelihood ratios (-LR) were calculated from the specificity and sensitivity values of ECG interpretation criteria, to allow estimation of 'chance' of cardiac pathology, after application of ECG interpretation criteria. Specifically, base prevalence rate was determined from the pre-test odds, and the +LR and –LR was used to compute the post-test odds[10].

RESULTS

Demographics

Arab athletes descended from West-Asia (85.8%), Africa (14.0%), and North America (0.2%). Black athletes descended from Africa (66.2%), West-Asia (30.6%), and Central America (3.2%). Athletes participated in 26 different sports, with football (60.5%) dominating. Whilst chronological age (14.6 ± 2.0 vs. 14.2 ± 1.5, years, $p<0.01$), and BSA (1.63 ± 0.22 vs. 1.59 ± 0.29, m^2, $p<0.05$) were significantly greater in Arab than black athletes, biological age (16.6 ± 1.7 vs. 15.7 ± 2.1, years, $p<0.001$) was significantly greater in black than Arab athletes (Table 1).

Abnormal ECG findings

Abnormal ECGs that required further evaluation were more frequent in black than Arab athletes (12.1% vs. 4.3%, $P<0.001$) (Figure 2). Specifically, 5.1% and 2.2% of black and Arab athletes, presented an abnormal TWI according to international recommendations, with a diagnostic yield for cardiac pathology of 3.0% and 3.4%, respectively.

Prevalence of ATWI (V_1-V_4)

Overall, 116 (15.8%) paediatric athletes presented ATWI (V_1-V_4), of which 96 (82.8%) were observed in the absence of other ECG findings considered to be abnormal as per international recommendations for ECG interpretation in athletes. Prevalence was more common in athletes biologically aged <16 than ≥16 years (18.8% vs. 13.6%, $p<0.05$), and in black than Arab athletes (23.2% vs. 10.3%, $p<0.0001$).

Distribution of ATWI

Ninety-one (12.4%) athletes presented with ATWI confined to V_1-V_3, constituting 79.3% of all ATWI cases (Figure 3). A further 25 (3.4%) athletes exhibited ATWI beyond V_3, with prevalence similar in athletes biologically aged ≥16 and <16 years, but more common in black than Arab athletes (7.0% vs. 0.7%, $p<0.001$). Prevalence was similar across biological age groups for black athletes (10-12 years. [7.1%], 13-14 years. [4.0%], 15-16 years. [5.6%] and 17-18 years. [8.4%]) compared to zero cases in Arab athletes biologically aged >14 years (Table 2).

JT elevation and ST-segment morphology preceding ATWI confined to V_1-V_3

ATWI confined to V_1-V_3 was preceded by Jt elevation in 37.4%. Jt elevation was more common in athletes biologically aged ≥16 than <16 years (52.5% vs. 25.5%, $p<0.01$) and in black than Arab athletes (56.9% vs. 12.5%, $p<0.001$).

ATWI in V_1-V_3 was preceded by ST morphology that was isoelectric in 62.6%, and ascending convex in 37.4% (Figure 4). Isoelectric ST-segment morphology was more frequent in athletes biologically aged <16 than ≥16 years (74.5% vs. 47.5%, p<0.01).

JT elevation and ST-segment morphology preceding ATWI extending beyond V_3

ATWI extending beyond V_3 was preceded by Jt elevation in 52.0%. Whilst prevalence did not differ by biological age, this observation was confined to black athletes (59.1%). ATWI extending beyond V_3 was frequently preceded by ST morphology that was isoelectric in 48.0%, and ascending convex in 52.0% (Figure 4). No healthy athlete with ATWI demonstrated a depressed Jt/ST-segment.

Lateral, Inferolateral and Inferior TWI

Fifteen (2.0%) athletes presented lateral TWI with prevalence unaffected by biological age, but more common in black than Arab athletes (3.5% vs. 1.0%, p<0.02); prevalence was sustained across all biological age groups in black athletes. Four (0.5%) and eight (1.1%) athletes presented with inferior and inferolateral TWI, respectively, whilst neither form of repolarization demonstrated an association with ethnicity, chronological or biological age.

Determinants of TWI

Of the 726 athletes with no detected cardiac pathology, univariate predictors of ATWI confined to V_1-V_3 were black ethnicity (odds ratio (OR) 1.9; 95% CI 1.2-3.0), chronological age <16 (OR 2.6; 95% CI 1.3-5.4), and biological age <16 years (OR 1.9; 95% CI 1.2-3.0). On multivariable analysis

only black ethnicity (OR 2.2; 95% CI 1.3-3.5) and biological age <16 years (OR 2.0; 95% CI 1.2-3.3) remained. Black ethnicity was the only univariate predictor of ATWI extending beyond V_3 (OR 8.9; 95% CI 2.6-30.4), and lateral TWI (OR 4.0; 95% CI 1.1-15.2).

Diagnostic yield and accuracy of TWI interpretation

Anterior TWI

Four of 116 (3.4%) with ATWI (V_1-V_4) and 1 of 96 (1.0%) with ATWI (V_1-V_4) observed in the absence of other ECG findings considered to be abnormal as per international recommendations for ECG interpretation in athletes, were diagnosed with pathology (Table 3). Of these 96, diagnostic accuracy was 'fail' [0.47 95% CI 0.00-1.00] for international recommendations, 'fail' [0.48 95% CI 0.00-1.00] for international recommendations when governed by Jt and/or ST-segment elevation irrespective of ethnicity, and 'excellent' [0.97 95% CI 0.92-1.00] for international recommendations when governed by biological not chronological age <16 years (Figure 5)

Lateral, Inferolateral and Inferior TWI

Three of 15 (20.0%) athletes with lateral TWI were diagnosed with pathology. Of these fifteen, 8 presented ECG abnormalities confined to lateral TWI, with pathology diagnosed in the only Arab athlete. 1 of 4 (20%) and 1 of 8 (12.5%) athletes with inferior and inferolateral TWI, respectively, were diagnosed with pathology. No pathology was diagnosed in athletes with ECG abnormalities confined to inferior (n=3) or inferolateral (n=2) TWI.

Diagnostic accuracy of international recommendations in all athletes

Diagnostic accuracy of cardiac pathology was 'fair' (0.79 95% CI 0.57-1.00) for international recommendations (specifically, a 'poor' [0.65 95% CI 0.28-1.00] diagnostic accuracy for Arab and an 'excellent' [0.94 95% CI 0.90-99] diagnostic accuracy for Black athletes), and 'good' (0.88 95% CI 0.71-1.00) when governed by biological age <16 years (specifically, a 'good' [0.81 95% CI 0.49-1.00] diagnostic accuracy for Arab and an 'excellent' [0.94 95% CI 0.90-99] diagnostic accuracy for Black athletes) (Figure 5).

Clinical implications when governing international recommendations by biological age

Overall, international recommendations provided a +ve and -ve LR of 9.3 (95% CI 4.0-14.5) and 0.4 (95% CI 0.1-0.8), respectively. When governed by biological age, +ve and -ve LR were 11.4 (95% CI 5.7-16.0) and 0.2 (95% CI 0.03-0.6), respectively. When split by ethnicity, +ve and -ve LR were 15.4 (95% CI 4.5-29.3) and 0.3 (95% CI 0.06-0.8) in Arab and 8.9 (95% CI 3.0-11.2) and 0.0 (95% CI 0.0-0.6) in Black athletes, respectively.

Of the 96 with ECG variants isolated to ATWI (V_1-V_4), international recommendations provided a +ve and -ve LR of 0.0 (95% CI 0.0-22.8) and 1.1 (95% CI 0.1-1.0), respectively. If governing by biological age in this cohort, +ve and -ve LR were 15.8 (95% CI 1.8-28.1) and 0.0 (95% CI 0.0-0.8), respectively.

DISCUSSION

Differentiating benign from pathological T-wave inversion represents one of sports cardiology greatest conundrums. This study of 418 Arab and 314 black male paediatric athletes demonstrated that: ATWI confined to V_1-V_3 was prevalent among 12.1% of athletes, with prevalence predicted by black ethnicity and biological age, but not chronological age <16 years; whilst ATWI extending beyond V_3 was rare (3.4%), its prevalence was predicted by black ethnicity, and sustained across all biological age groups for this ethnicity; and finally diagnostic accuracy of international recommendations for cardiac pathology in athletes presenting ECG variants isolated to ATWI (V_1-V_4), improved from 'fail' to 'excellent' with biological not chronological age governance. In clinical context, the 'chance' of detecting cardiac pathology within a paediatric male athlete presenting ECG variants confined to ATWI (V_1-V_4) is approximately 1%. A positive ECG (+LR=15.8) using biological age governance to international recommendations means the same athlete now has a 14.4% 'chance' of pathology, whereas a negative ECG (-LR=0.0) has a 0% 'chance'.

Prevalence and Distribution of ATWI

In a recent systematic review with meta-analysis of over 6000 white and 500 black male paediatric athletes[27], a relatively high prevalence of ATWI was observed (4.2% vs 12.2%, respectively). We observed AWTI confined to V_1-V_3 in 16.2% and 9.6% of black and Arab paediatric athletes, respectively. Although this may represent a 'juvenile' ECG when aged <16 years[2]; of the 11 articles[3,4,28–36] whom previously detailed its prevalence and significance, only 4[3,4,32,35] documented maturity status, of which 3[4,32,35] relied on Tanner Staging. For the first time we considered biological age, recognised by the International Olympic Committee as the 'gold standard' estimate

of maturity[9]. Biological age <16 years and black ethnicity, not chronological age <16 years predicted ATWI confined to V_1-V_3. In extension to Sheikh et al.[36] who observed ATWI extending beyond V_2 in black athletes (14-18 years) in 74% of cases, we demonstrated ATWI extending beyond V_3 within black athletes (11-18 years) in 30.0%. Furthermore, prevalence was sustained irrespective of biological age group for this ethnicity, suggesting that this may represent a benign, ethnic manifestation of the athlete's heart, irrespective of biological age.

Potential markers of pathology in paediatric athletes with ATWI

The prevalence of ATWI confined to V_1-V_3 is increased in male paediatric athletes of younger biological age, with presentation in 15.2% Arab and 27.1% black athletes biologically aged <16 years. Thus creating considerable overlap in the differential diagnosis of myocarditis, arrhythmogenic right ventricular cardiomyopathy and hypertrophic cardiomyopathy. Accordingly, international recommendations for ECG interpretation in athletes[2] recognize the 'juvenile ECG pattern' (TWI in V_1-V_3, chronological aged <16 years) to be normal. This assumes, however, an immature heart unlikely to have undergone complete formation of adult ventricular mass, with TWI in V_1–V_3, attributable to right ventricular dominance. In reality, whilst chronological age is a linear factor, growth and maturation are not[6]. Subsequently, international recommendations failed to detect one case of myocarditis, with TWI in V_1-V_3 in an Arab athlete (chronological age 14 years), yielding a 'failed' diagnostic accuracy for ECG variants isolated to ATWI (V_1-V_4). In contrast to observations of adult athletes by Calore et al.[5], assessment of the preceding Jt and/or ST-segment amplitude irrespective of ethnicity, yielded a 'failed' diagnostic accuracy. Further, ATWI confined to V_1-V_3, where preceded by a Jt in line with the onset of the QRS and/or ST-segment that were isoelectric in 62.6%, of which 66.7% were biologically aged <16 years. Finally,

international recommendations governed by biological not chronological age <16 years, yielded an 'excellent' diagnostic accuracy. We believe that when presented with an asymptomatic paediatric athlete with ECG variants isolated to TWI in V_1-V_3, biological age assessment presents an opportunity to reassure the concerned parent/guardian and athlete. TWI in V_1-V_3 in athletes biologically aged <16 years is likely a 'juvenile ECG pattern' not warranting further investigation, but when biologically aged >16 years, further investigation may be warranted.

Lateral, Inferolateral and Inferior TWI

In this study of 732 athletes, TWI was detected in lateral leads in 2.0%, inferior leads in 1.1% and, inferolateral leads in 0.5%, with presentation of lateral TWI predicted by black ethnicity. These repolarization patterns are considered abnormal, as confirmed by a recent study[37] which observed that in black athletes with cardiomyopathy or a genetic mutation of cardiomyopathy, all presented lateral TWI. Whilst ECG abnormalities confined to lateral TWI yielded cardiac pathology in the only Arab athlete, pathology was not detected in any black athlete. Whether this represents the first sign of cardiac pathology, with phenotypic manifestations appearing on secondary investigation in later life or an ethnic manifestation of the athlete's heart remains to be determined. It is universally recognized, however, that these ECG patterns require serial long-term follow-up.

Clinical implications when governing international recommendations by biological age

If presented with a paediatric athlete for ECG screening, diagnostic accuracy of international recommendations improved from 'fair' to 'good', when governed by biological age <16 years. With consideration to Bayesian analysis[10], our overall baseline 'chance' of detecting cardiac

pathology was 0.8%. A positive ECG (+LR=11.4), means that the same athlete now has an 8.6% 'chance' of cardiac pathology, whereas an athlete with a negative ECG (-LR=0.2), would have a 0.2% 'chance'. We therefore provide further evidence that ECG screening is an effective strategy for detecting cardiac pathology that may predispose to SCD/A in the paediatric athlete[38,39]. Whilst international recommendations represent the current 'gold-standard' for ECG interpretation in the paediatric athlete[40], their governance by biological age, irrespective of cardiac pathology prevalence, increases the likelihood of correctly triggering further evaluation to identify cardiac pathology, whilst reducing the likelihood of incorrectly clearing an athlete to play with potential sinister consequences.

Limitations

Although no cardiac pathology was detected in paediatric athletes presenting ECG variants isolated to ATWI in V_1-V_3 with a biological age <16 years, we cannot exclude the development of cardiac pathology in later years due to the cross-sectional design. Accordingly, we consider observation to provide only reassurance that this likely represents a 'juvenile ECG pattern', requiring annual follow-up until resolution. Tanner staging assessment was not conducted in conjunction to biological age assessment due to numerous child protection concerns in addition to a lack of validity for this estimation of maturity when conducted by self-assessment. Finally, our population were exclusively Arab and black male athletes, limiting application of our data to other ethnicities and the female paediatric athlete.

Conclusion

Interpretation of ECG variants isolated to ATWI in V_1-V_4 using international recommendations based on chronological age <16 years, warrants caution, but when governed by biological age <16 years yielded an ‘excellent’ diagnostic accuracy. Interpretation of the paediatric athletes ECG using biological age governance to international recommendations provides the best likelihood of triggering further evaluation in the attempt to detect cardiac pathology.

Acknowledgments

The authors acknowledge the sterling efforts of the Aspire Academy Sports Medicine Centre and Aspetar's athlete screening team in the data collection: Roula Mattar, Christelle Mourad, Eleni Makri, Nelly Khalil, Pascal Tahtouh, Farah Demachkieh, Nisrine Sawaya, Ahmad Al Qasim, Mohammad Mustafa and Nancy Abdel Karim.

Sources of Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest:

None declared.

Author Contributions:

GMC and MGW contributed to the conception and design of this manuscript. GMC undertook ECG and statistical analysis. AJ undertook skeletal age (biological age) analysis. All authors contributed to data interpretation. GMC and MGW wrote the manuscript. NRR, GP, VW, CA, SS, AJ, AT, KPG and DO critically revised the manuscript for important intellectual content. MGW is the author of correspondence.

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Figure Legends

Figure 1. Measurement of J termination (Jt) elevation and classification of ST-segment morphology, preceding anterior T wave-inversion. (A) The horizontal dashed line through the onset of the QRS complex, acted as a reference for the measurement of J termination (Jt). The vertical dashed line defines the M interval (100ms). ST-segment morphologies are shown as the following: (B) ascending convex, and (C) isoelectric.

Figure 2. International recommendations for ECG interpretation in Arab and Black paediatric athletes.

Key: data are presented as n (%). AV, atrioventricular; CRBBB, complete right bundle branch block; CLBBB, Complete left bundle branch block; IRBBB, Incomplete right bundle branch block; IVCD, intraventricular conduction delay; LAD, left axis deviation; LAE, left atrial enlargement; RAD, right axis deviation; RAE, right atrial enlargement; PVCs, premature ventricular contractions.

*$p \leq 0.05$, significantly more prevalent in black than Arab athletes' ** $p \leq 0.001$, significantly more prevalent in black than Arab athletes; † $p \leq 0.001$, significantly more prevalent in Arab than black athletes.

Figure 3. Prevalence and distribution of T-wave inversion in both Arab and black. Numbers in brackets express percentages (%) of each cohort.

Figure 4. Bar graph shows ST-Segment morphology type preceding anterior T-wave inversion confined to V_1-V_3 by (A) ethnicity, and (B) biological age (BA) and anterior T-wave inversion extending beyond V_3 by (C) ethnicity, and (D) biological age. *$P < 0.05$, significant effect of group.

Figure 5. Receiver-operating curves according to ECG interpretation criteria to detect cardiac pathology predisposing to sudden cardiac death/arrest only. Area under curve (AUC) represents test accuracy in differentiating athletes with cardiac pathology predisposing to an increased risk of sudden cardiac death/arrest. (A) Athletes presenting with ECG variants isolated to T-wave inversion V_1-V_4 by (1) international recommendations, (2) when governed by Jt and/or ST-segment elevation irrespective of ethnicity and, (3) when governed by biological age (BA) < 16 years with T-wave inversion confined to V_1-V_3. (B) All athletes by (1) international recommendations and (2) when governed by biological age < 16 years with anterior T-wave inversion confined to V_1-V_3

TABLES

Table 1. Anthropometric data of paediatric athletes

Chronological age group (years)	Group	N	%	Biological age	Height (cm)	Body mass (kg)	BSA (m^2)
11-12	Total	147	20.1	13.4 ± 1.4	151.6 ± 8.8	44.3 ± 10.7	1.36 ± 0.19
	Arab	111		13.2 ± 1.3	150.1 ± 7.8	43.2 ± 9.0	1.34 ± 0.16
	Black	36		13.8 ± 1.6*	156.1 ± 10.1**	47.4 ± 14.4	1.42 ± 0.25*
13-14	Total	355	48.5	16.2 ± 1.6	166.3 ± 9.5	128.8 ± 56.1	1.60 ± 0.21
	Arab	148		15.5 ± 1.5	163.3 ± 10.2	54.6 ± 14.5	1.56 ± 0.24
	Black	207		16.8 ± 1.4***	168.7 ± 8.3***	57.4 ± 10.4	1.63 ± 0.18**
15-16	Total	135	18.4	17.3 ± 1.1	172.3 ± 8.6	64.8 ± 18.6	1.75 ± 0.28
	Arab	92		17.4 ± 0.9	173.2 ± 8.6	66.9 ± 20.0	1.78 ± 0.29
	Black	43		17.2 ± 1.3	170.1 ± 8.1	60.0 ± 13.7	1.67 ± 0.22
17-18	Total	95	13.0	17.8 ± 0.5	174.3 ± 6.8	70.0 ± 10.4	1.8 ± 0.2
	Arab	67		17.9 ± 0.5	174.5 ± 7.1	66.7 ± 9.5	1.79 ± 0.15

Black	28	17.8 ± 0.5	173.9 ± 6.2	67.7 ± 12.3	1.80 ± 0.18

Values are mean ± standard deviation; BSA, Body surface area.

*p≤0.05, significantly more prevalent or greater in black than Arab athletes

** 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

Table 2. Athletes with TWI by biological age group within ethnicity and by territory

	Arab	Black	Arab	Black	Arab	Black	Arab	Black
	10-12 years		13-14 years		15-16 years		17-18 years	
	n=52	n=14	n=122	n=50	n=66	n=72	n=178	n=178
Anterior								
V_1-V_3	7 (13.5)	2 (14.3)	20 (16.4)†	13 (26.0)	3 (4.5)	10 (13.9)	10 (5.6)	26 (14.6)*
Beyond V_3	2 (3.8)	1 (7.1)	1 (0.8)	2 (4.0)	0 (0)	4 (5.6)	0 (0)	15 (8.4)*
Lateral	2 (3.8)	0 (0)	0 (0)	1 (2.0)	2 (3.0)	4 (5.6)	0 (0)	6 (3.4)*
Inferolateral	1 (1.9)	0 (0)	0 (0)	0 (0)	1 (1.5)	2 (2.8)	0 (0)	1 (0.6)
Inferior	1 (1.9)	0 (0)	0 (0)	0 (0)	3 (4.5)	1 (1.4)	1 (0.6)	1 (0.6)

Data are presented as number (%) for each column.

Lateral, leads I and AVL, V5 and/or V6 (only one lead of TWI required in V5 or V6); Inferolateral, leads II and aVF, V5-V6, I and AVL; Inferior, leads II and aVF.

*p≤0.05, significantly more prevalent in black than Arab athletes of the same biological age group

†p≤0.05, significantly more prevalent than in Arab athletes biologically aged 17-18 years.

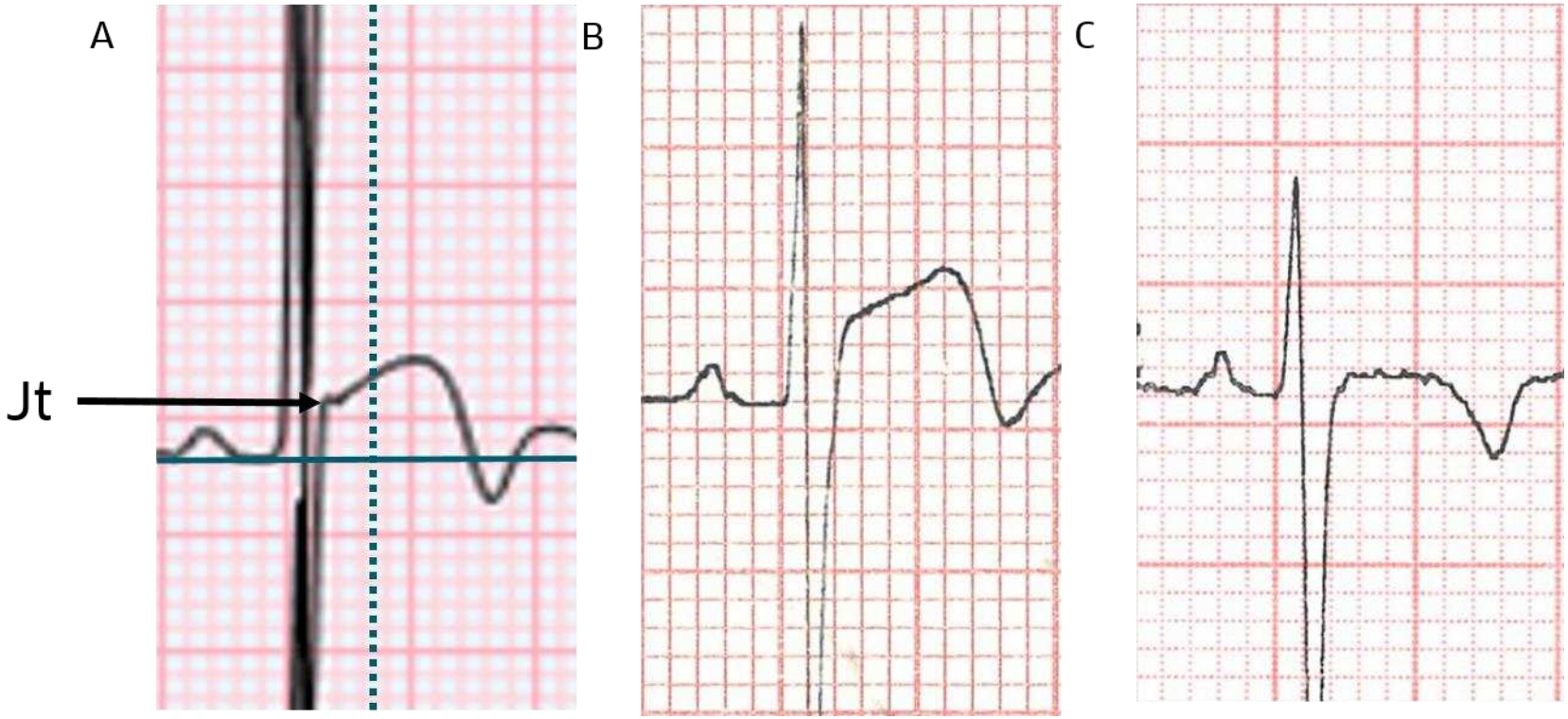
Table 3. Clinical characteristics of athletes diagnosed with cardiac pathology that may predispose to SCD/A.

Condition	Chronological Age	Biological Age	Ethnicity	International	International governed by Biological Age	TWI	Other
Aneurysm with dilated ascending aorta	12	11.6	Arab	-	-	-	-
HCM	13	18	Black	+	+	AVL, V_2-V_5	Q waves II, III, AVF, V_5, V_6
LVNC	13	17	Black	+	+	II, III, AVF, V_1-V_6	Q waves II, III, AVF, V_4 -V_6

Myocarditis, with anterolateral, lateral and inferolateral mid-wall fibrosis at basal level.	14	17.7	Arab	-	+	V_1-V_3	-
Myocarditis, with anterolateral, lateral and inferolateral mid-wall fibrosis at basal and mid ventricular level	13	15.4	Arab	+	+	AVL, V_1, V_4-V_5	-
WPW ECG pattern	13	18	Black	+	+	AVL,V_1-V_4	Short PR interval Delta Wave Wide QRS

Hypertrophic cardiomyopathy; LVNC, left ventricular non-compaction; MVP; Mitral Valve Prolapse; MR; mitral regurgitation; SCA/D, sudden cardiac arrest/death; TWI, T-wave inversion; WPW; Wolf-Parkinson-White syndrome.

FIGURES



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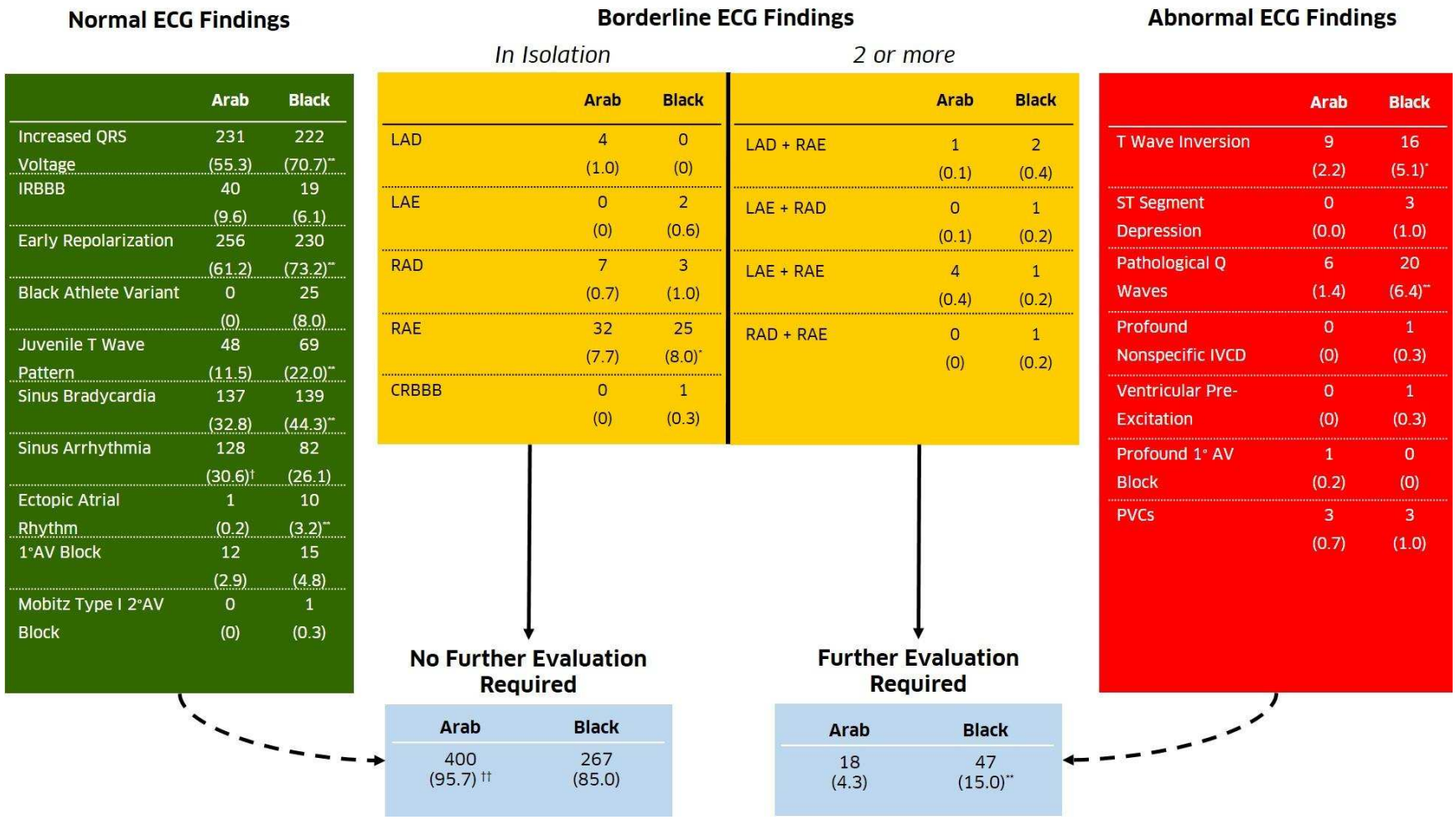

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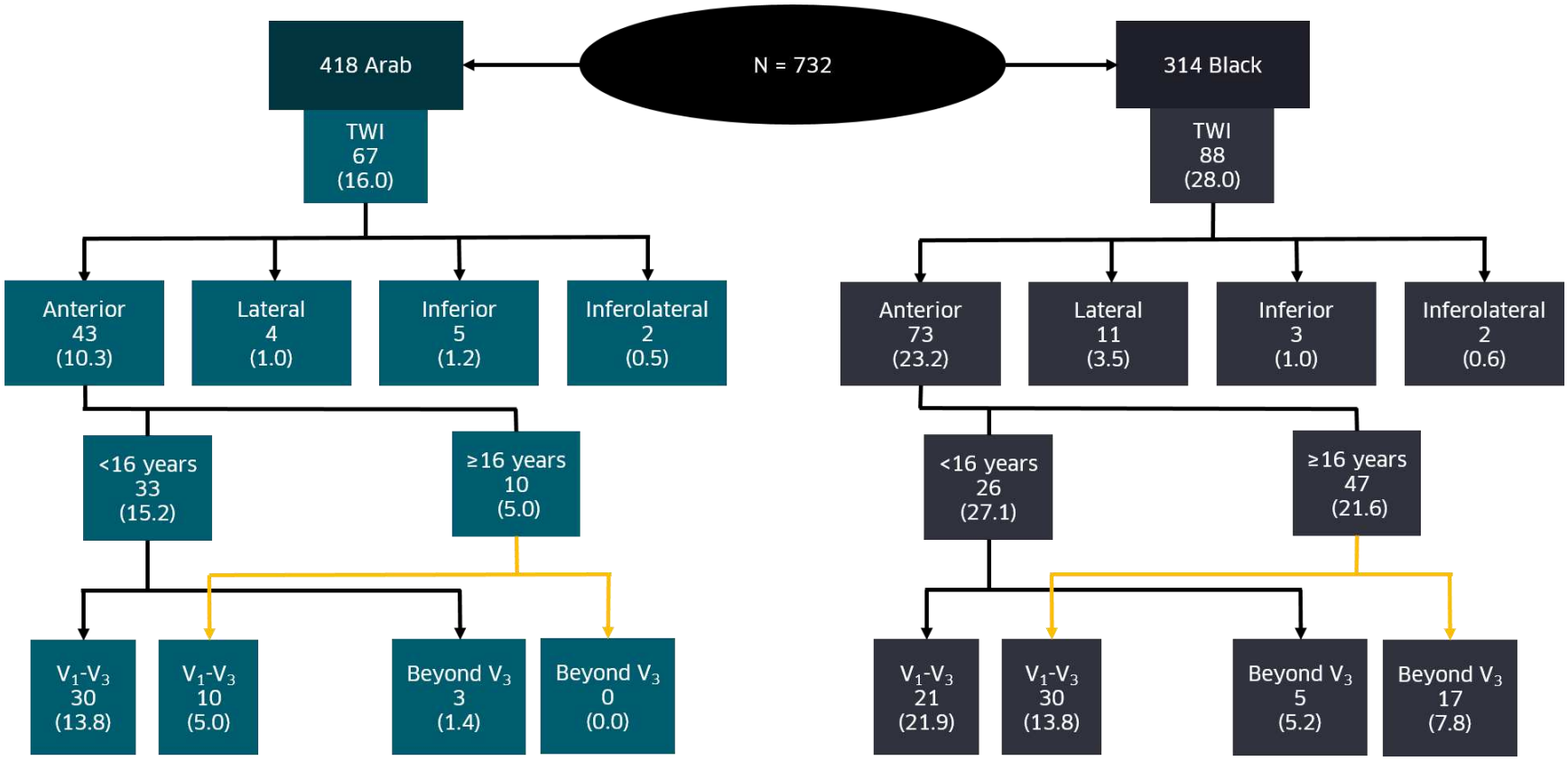

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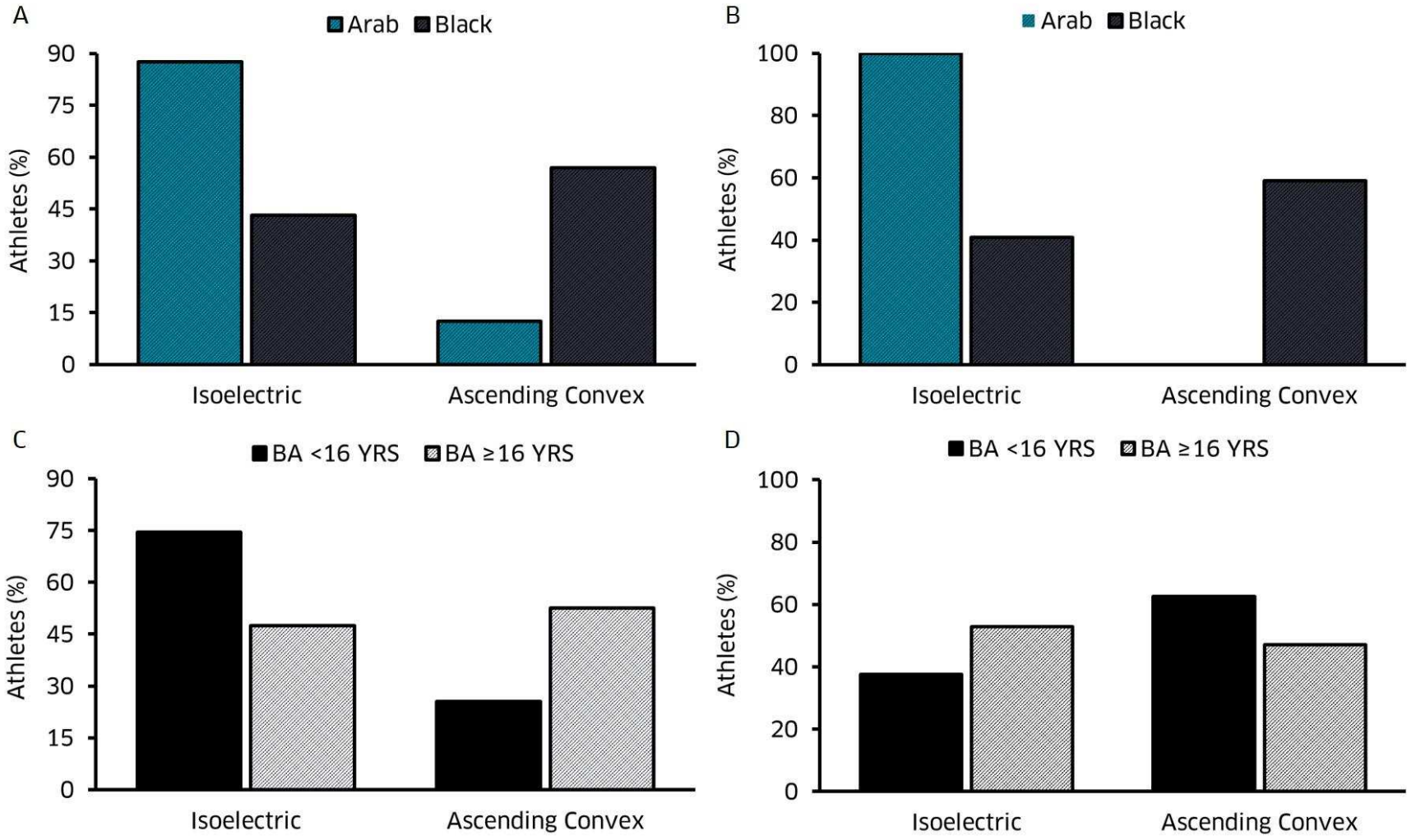

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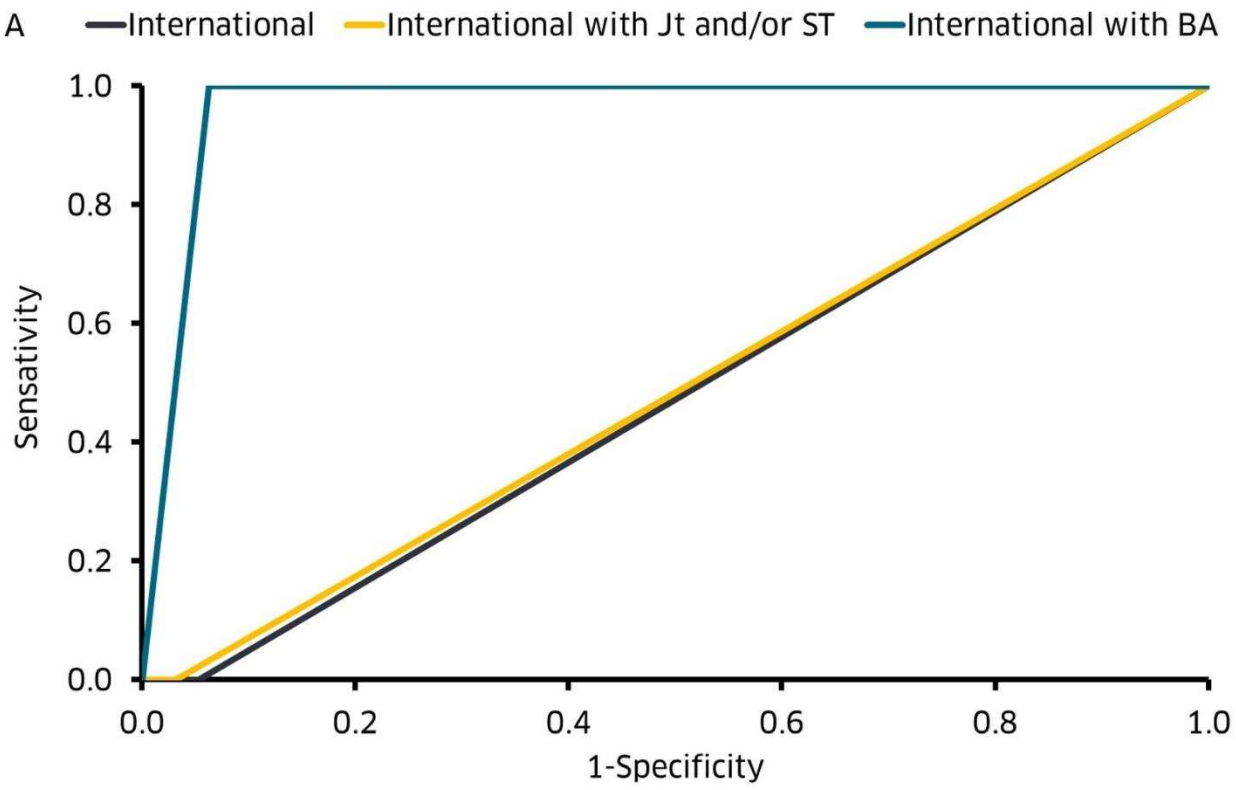
A
International
International with Jt and/or ST
International with BA
1.0
0.8
0.6
0.4
0.2
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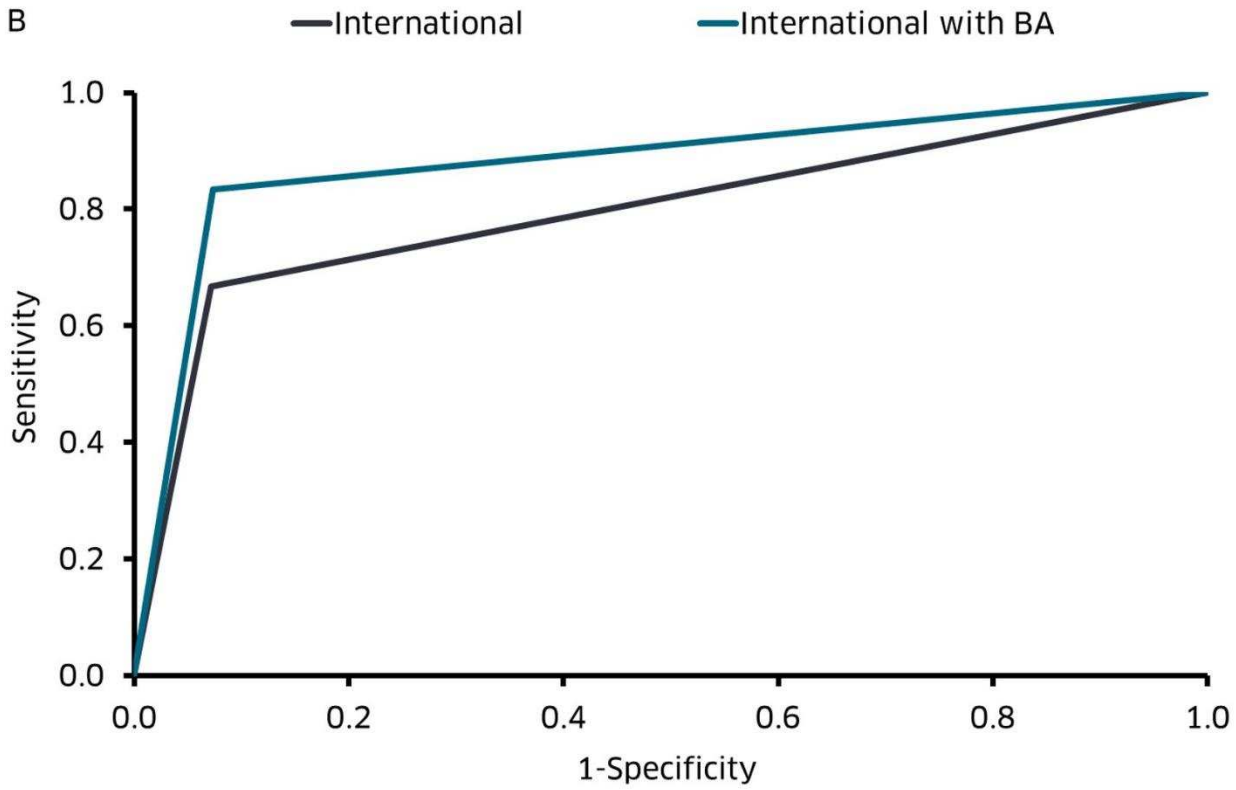
Sensativity
0.0
0.2
0.4
0.6
0.8
1.0
1-Specificity


B
International
International with BA
1.0
0.8
0.6
0.4
0.2
0.0
Sensitivity
0.0
0.2
0.4
0.6
0.8
1.0
1-Specificity

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