

Prevalence of Electrocardiographic Anomalies in Young Individuals



Relevance to a Nationwide Cardiac Screening Program

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- Objectives** This study sought to investigate the prevalence of potentially abnormal electrocardiographic (ECG) patterns in young individuals to assess the implications for a nationwide screening program for conditions causing sudden cardiac death (SCD).
- Background** The Italian experience suggests that pre-participation screening with ECG reduces the incidence of SCD in athletes. However, the majority of SCDs occur in nonathletes. In the United Kingdom, screening for cardiac disorders is confined to symptomatic individuals or those with a family history of inherited cardiac conditions or premature cardiac death.
- Methods** Between 2008 and 2012, 7,764 nonathletes ages 14 to 35 years underwent ECG screening. Electrocardiograms were analyzed for group 1 (training-related) and group 2 (potentially pathological) patterns presented in the 2010 European Society of Cardiology position paper, which advocates further evaluation for individuals with group 2 ECG patterns. Results were compared with 4,081 athletes.
- Results** Group 1 patterns occurred in 49.1% of nonathletes and 87.4% of athletes ($p < 0.001$). Group 2 patterns occurred in 21.8% of nonathletes and 33% of athletes ($p < 0.001$). In nonathletes, QTc interval abnormalities comprised the majority (52%) of group 2 changes, whereas T-wave inversions constituted 11%. Male sex and African/Afro-Caribbean ethnicity demonstrated the strongest association with group 2 ECG patterns.
- Conclusions** The study demonstrates that 1 in 5 young people have group 2 ECG patterns. The low incidence of SCD in young people suggests that in most instances such patterns are non-specific. These findings have significant implications on the feasibility and cost-effectiveness of nationwide screening programs for cardiovascular disease in young nonathletes and athletes alike, on the basis of current guidelines. (J Am Coll Cardiol 2014;63:2028–34)
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Most cardiac diseases predisposing to sudden cardiac death (SCD) in the young (age ≤ 35 years) are identifiable during life, and the risk of fatality may be minimized through the use of a range of therapeutic strategies (1). There are supportive data that electrocardiographic (ECG) screening identifies athletes who are harboring potentially serious cardiac diseases. There is also evidence that early identification

and medical intervention reduces the incidence of SCD in competitive athletes (2). On the basis of this premise, ECG screening in athletes is endorsed by learned scientific and sporting organizations (3,4). To aid interpretation of the ECG in athletes, the European Society of Cardiology (ESC) has produced guidelines differentiating normal training-related ECG patterns (group 1) from ECG patterns suggestive of underlying heart disease (group 2), which should prompt investigation (Table 1) (3,5).

See page 2035

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Although intense exercise in individuals harboring quiescent cardiac pathology infers a 3-fold greater risk of SCD in elite athletes compared with nonathletes, the majority of SCD in the young affect the general population (6).

In most countries, young individuals are not offered cardiac screening unless they are engaged in competition at the highest level, express cardiac symptoms, and/or have a family history of premature cardiac disease (7). Moreover, attempts to institute general population screening are hampered by a paucity of data relating to the prevalence and significance of ECG changes in nonathletes.

This study aimed to establish the prevalence of group 2 ECG patterns in a large cohort of young individuals to evaluate the potential implications for a nationwide screening program in the general population.

Methods

Setting. The United Kingdom does not support a national, state-sponsored cardiac screening program. Many sporting organizations recommend pre-participation screening (PPS) and self-fund the evaluation of athletes competing at regional, national, or international levels. The charity Cardiac Risk in the Young (CRY) provides subsidized screening for conditions predisposing to SCD in individuals ages 14–35 years in the United Kingdom who wish to be tested for self-protection, irrespective of athletic status, symptoms, or family history of premature cardiac disease. Screening events are advertised in local media and on the CRY website. Individuals from the general population, including those from local high schools, self-present to screening events. Elite athletes attend specified screening events as part of PPS endorsed by their relevant sporting bodies. The senior author (S.S.) supervised the evaluations.

Subjects. Between 2008 and 2012, 11,845 consecutive individuals ages 14 to 35 years (7,764 nonathletes and 4,081

athletes) underwent evaluation comprising a health questionnaire and 12-lead ECG. A transthoracic echocardiogram was performed in individuals with group 2 ECG patterns suggestive of cardiomyopathy or structural cardiac abnormality.

Definitions. Nonathletes were defined as individuals not involved in regular, organized competitive team or individual sports, including sedentary individuals and those exercising recreationally. Athletes were defined as individuals competing in organized team or individual sports at regional, national, or international levels with a high premium on athletic excellence. Ethnicity was self-reported. Adolescents were defined as individuals <18 years of age.

Twelve-lead ECG. A resting 12-lead ECG was performed with the use of a Philips Pagewriter Trim III recorder (Philips, Bothell, Washington) with a paper speed of 25 mm/s and amplification of 0.1 mV/mm. P-, Q-, R-, S-, and T-wave voltages; ST-segments; QRS duration; PR-interval and QT-interval were measured in each lead with the use of calipers. The highest value was quoted as the absolute QT. Heart rate and QRS axis were calculated. ECG definitions were consistent with the 2010 ESC position paper (5).

Sinus bradycardia was defined as heart rate <60 beats per minute and first-degree AV block as PR-interval >200 ms. Incomplete right bundle-branch block was defined by rSR¹ morphology of the QRS complex <120 ms in lead V₁. Early repolarization was defined as an elevated J-point ≥1 mm in ≥2 contiguous leads with notching and/or slurring of the terminal QRS complex. Sokolow-Lyon voltage criteria were used for left ventricular hypertrophy (S_{V1} + R_{V5} ≥35 mm) and right ventricular hypertrophy (R_{V1} + S_{V5} ≥10.5 mm). T-wave inversion was defined as ≥2 mm in ≥2 contiguous leads excluding AVR, V₁, and III. ST-segment shift was considered significant if ≥1 mm in ≥2 contiguous leads. Pathological Q-waves were defined as ≥2 mm in depth in ≥2 contiguous leads. Left atrial enlargement was identified as a biphasic P-wave in lead V₁ in which the negative portion was ≥1 mm deep and ≥40 ms (8). Right atrial (RA) enlargement was identified by the presence of a P-wave >2.5 mm in lead II and/or >1.5 mm in lead V₁. Left-axis deviation and right-axis deviation were defined as ≤−30° and ≥+120°, respectively. Intraventricular conduction abnormalities of right bundle-branch block and left bundle-branch block morphology were identified when the QRS duration was ≥120 ms. The QT-interval was measured by means of the tangent method and corrected for heart rate with the use of Bazett's formula (9). Long-QTc interval was defined as >440 ms (men) and >460 ms (women); short-QTc interval was defined as QTc <380 ms. Brugada-like early repolarization changes were identified as J-point elevation ≥2 mm with down-sloping “coved” or “saddle-back” ST-segment elevation in leads V₁–V₃.

Abbreviations and Acronyms

- ECG = electrocardiography
- ESC = European Society of Cardiology
- PPS = pre-participation screening
- SCD = sudden cardiac death

Table 1

European Society of Cardiology Classification of Changes of the Athlete's Electrocardiogram

Group 1: Common and Training-Related ECG Changes	Group 2: Uncommon and Training-Unrelated ECG Changes
Sinus bradycardia	T-wave inversion
First-degree AV block	ST-segment depression
Incomplete RBBB	Pathological Q-waves
ER	LA enlargement
Isolated QRS voltage criteria for LVH	RA enlargement
	LAD
	RAD
	RVH
	Ventricular pre-excitation
	LBBB
	RBBB
	Long-QTc interval (>440 ms, men; >460 ms, women)
	Short-QTc interval (<380 ms)
	Brugada-like ER

Data from Corrado et al. (5).

AV = atrioventricular; ECG = 12-lead electrocardiogram; ER = early repolarization; LA = left atrial; LAD = left-axis deviation; LBBB = left bundle-branch block; LVH = left ventricular hypertrophy; RA = right atrial; RAD = right-axis deviation; RBBB = right bundle-branch block; RVH = right ventricular hypertrophy.

All ECGs were read independently by authors NC and RB, who were blinded to the health questionnaire and athletic status of study participants. There was substantial agreement between the observers (Kappa coefficient, 0.78 ± 0.04 for group 1 and 0.97 ± 0.02 for group 2 ECG patterns). In cases of disagreement, the senior author (S.S.) was consulted.

Transthoracic echocardiography. Two-dimensional transthoracic echocardiography was performed with the use of a GE Vivid I (Tirat, Israel), Philips Sonos 7500, Philips iE33, or Philips CPX50 (Bothell, Washington). Standard views were obtained and analyzed in accordance with protocols specified by the European Society of Echocardiography (10). All scans were reviewed by author SS, who was blinded to the participant's identity.

Ethical approval. Ethical approval was granted by the Essex 2 Research Ethics Committee. Written consent was obtained from individuals ≥ 16 years of age and from a parent/guardian for those < 16 years of age.

Statistical analysis. Statistical analyses were performed with the use of SPSS software, version 17 (SPSS, Inc., Chicago, Illinois). Variables were tested for normality through the use of the Kolmogorov-Smirnov test and expressed as mean (standard deviation) or percentages, as appropriate. Group differences were tested with the use of Student's *t* test or one-way analysis of variance (Sidak test for post-hoc analysis) and Mann-Whitney *U* or Kruskal Wallis (Dunn's test for post-hoc analyses) tests for normally and non-normally distributed variables. Group differences of proportions were tested with the use of chi-square or Fisher's exact tests. Bonferroni correction was performed to correct for multiple comparisons where appropriate. Binary logistic regression analysis was used to assess the independence of demographic and electrocardiographic associations with group 2 ECG patterns. The goodness of fit was evaluated through the use of the Hosmer-Lemeshow test. Cohen's Kappa coefficient was used to assess the inter-operator agreement in group 1 and group 2 ECG categorization. Significance was defined as $p < 0.05$ throughout.

Results

Subjects. Nonathletes were younger and included a lower proportion of men and a higher proportion of Caucasian (white) than African/Afro-Caribbean (black) individuals compared with the athletes. Nonathletes had a smaller body surface area and higher systolic blood pressure and resting heart rate (Table 2).

Of the nonathletes, 4,667 (60.1%) were relatively sedentary, being active for ≤ 4 h per week, and 3,097 (39.9%) exercised recreationally > 4 h per week. Athletes performed 15 ± 7 h of training per week and participated in 24 different sporting disciplines, including 17.1% in endurance sports.

ECG patterns in nonathletes versus athletes. Group 1 ECG patterns were present in half of nonathletes and the

Table 2 Comparison of Demographics and Characteristics Between Nonathletes and Athletes

	Nonathletes n = 7,764	Athletes n = 4,081	p Value
Age, yrs	19.2 ± 6.0	19.5 ± 5.2	<0.001
Sex, n (% men)	5,448 (70.2%)	3,287 (80.5%)	<0.001
Ethnicity, n (% white)	7,288 (93.8%)	2,821 (69.1%)	<0.001
Height, m	1.73 ± 0.11	1.77 ± 0.10	<0.001
Weight, kg	69.0 ± 15.4	71.7 ± 14.9	<0.001
BSA, m ²	1.82 ± 0.22	1.87 ± 0.23	<0.001
Systolic BP, mm Hg	120.6 ± 14.9	114.5 ± 13.1	<0.001
Diastolic BP, mm Hg	69.5 ± 11.2	69.3 ± 21.8	0.187
Heart rate, beats/min	68.6 ± 13.3	59.1 ± 11.2	<0.001

Values are mean ± SD or n (%).

BP = blood pressure; bpm = beats per minute; BSA = body surface area.

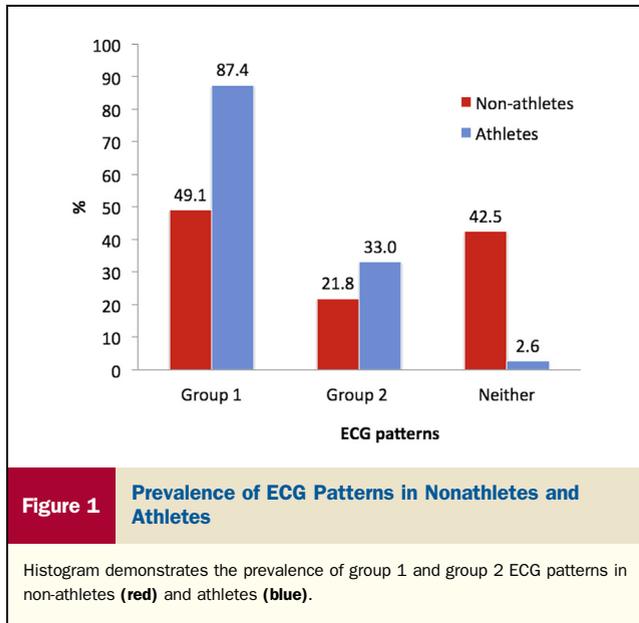
majority of athletes (49.1% vs. 87.4%; $p < 0.001$). All group 1 ECG patterns were less prevalent in nonathletes compared with athletes. Sinus bradycardia and isolated voltage criteria for left ventricular hypertrophy were common in both groups, whereas early repolarization was predominantly a feature in athletes (Table 3). The proportion of individuals with a completely normal ECG was 42.5% in nonathletes but only 2.6% of athletes ($p < 0.001$) (Fig. 1).

Table 3 Prevalence of Group 1 and Group 2 ECG Patterns in Nonathletes Compared With Athletes

	Nonathletes (n = 7,764)	Athletes (n = 4,081)	p Value
Group 1 ECG patterns			
Sinus bradycardia	26.1	57.6	<0.001
First-degree AV block	1.3	6.2	<0.001
Incomplete RBBB	7.8	13.1	<0.001
ER	2.1	31.2	<0.001
Isolated LVH	24.7	33.2	<0.001
Group 2 ECG patterns			
T-wave inversion	2.8	10.5	<0.001
Anterior	1.7	8.8	<0.001
Inferior	0.9	1.4	0.900
Lateral	0.2	0.3	0.578
ST-segment depression	0.5	0.1	0.006
Pathological Q-waves	0.2	0.5	0.005
LA enlargement	1.8	4.6	<0.001
RA enlargement	1.1	1.9	<0.001
LAD	1.5	0.9	0.004
RAD	0.8	0.9	0.866
RVH	2.8	5.2	<0.001
Ventricular pre-excitation	0.16	0.10	0.600
LBBB	0.1	0.0	0.104
RBBB	0.3	0.4	0.144
Long-QTc interval	6.5	3.3	<0.001
Short-QTc interval	6.9	13.0	<0.001
Brugada-like ER	0.06	0.0	0.172

Values are %.

AV = atrioventricular; ECG = 12-lead electrocardiogram; ER = early repolarization; LA = left atrial; LAD = left-axis deviation; LBBB = left bundle-branch block; LVH = left ventricular hypertrophy; RA = right atrial; RAD = right-axis deviation; RBBB = right bundle-branch block; RVH = right ventricular hypertrophy.



Group 2 ECG patterns were present in a significant proportion of both cohorts, though more common in athletes (21.8% vs. 33%; $p < 0.001$). The majority of nonathletes and athletes with group 2 ECG patterns exhibited only a single group 2 anomaly; a small proportion revealed multiple group 2 ECG patterns (3% of nonathletes and 8% of athletes). T-wave inversion was present in only 2.8% of nonathletes but constituted 11% of all group 2 patterns identified in this cohort (Fig. 2). Other ECG

indices suggestive of an underlying cardiomyopathy or structural cardiac abnormality including ST-segment depression, pathological Q-waves, and the presence of complete bundle-branch block were rare ($\leq 0.5\%$ each) in both groups (Table 3).

Electrocardiographic indices suggestive of ion-channelopathy, in particular abnormal QTc measurements, were common in both cohorts and accounted for 52.3% of all group 2 ECG patterns encountered in nonathletes (Fig. 2).

Impact of sex, ethnicity, and age on group 2 ECG patterns. Group 2 ECG patterns were more common in men than in women in both nonathletes (25.9% vs. 11.7%; $p < 0.001$) and athletes (35.7% vs. 22.3%; $p < 0.001$). Black ethnicity was associated with a higher prevalence of group 2 patterns, irrespective of athletic status (28.5% black nonathletes vs. 21.5% white nonathletes; $p = 0.003$; and 57.7% black athletes vs. 21.3% white athletes; $p < 0.001$). In contrast with white individuals, in whom the prevalence of group 2 ECG patterns were similar in nonathletes and athletes (21.5% vs. 21.3%; $p = 0.826$), the prevalence of group 2 ECG patterns almost doubled in black athletes compared with black nonathletes (57.7% vs. 28.5%; $p < 0.001$). Finally, the combination of adult status and athletic activity was associated with a higher prevalence of group 2 patterns, with 41% of adult athletes having at least 1 group 2 change compared with 22.8% of adolescent athletes ($p < 0.001$).

Determinants of group 2 ECG patterns. Multivariate logistic regression in the entire study population assessed the independent association of athletic status, sex, ethnicity, age, and body surface area with group 2 ECG patterns. Black

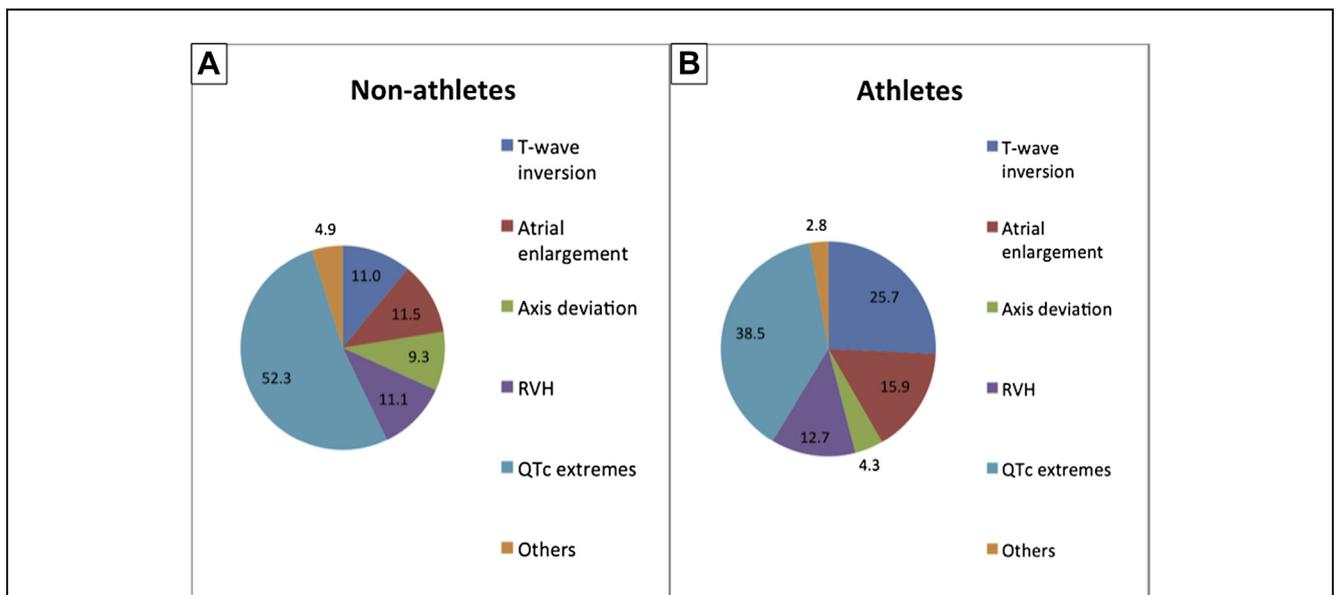


Figure 2 Prevalence of Specific Group 2 ECG Patterns in Nonathletes and Athletes

Pie charts demonstrate the prevalence of specific group 2 ECG patterns as a proportion of all group 2 patterns in (A) nonathletes and (B) athletes, respectively.

ethnicity demonstrated the strongest association (odds ratio [OR]: 3.51; 95% confidence interval [CI]: 3.09 to 4.00; $p < 0.001$) followed by male sex (OR: 2.16; 95% CI: 1.86 to 2.51; $p < 0.001$) and athletic status (OR: 1.19; 95% CI: 1.06 to 1.33; $p = 0.003$). In the non-athletic population, male sex demonstrated the strongest association with group 2 ECG patterns (OR: 2.88; 95% CI: 2.32 to 3.59; $p < 0.001$), followed by black ethnicity (OR: 2.39; 95% CI: 1.35 to 4.24; $p = 0.003$).

Clinical significance of group 2 ECG patterns. Of the 7,764 nonathletes and 4,081 athletes, 21.8% and 33%, respectively, demonstrated group 2 ECG patterns. ECG changes suggestive of cardiomyopathy or structural cardiac abnormality occurred in 10.1% of nonathletes and 20.8% of athletes ($p < 0.001$). ECG changes suggestive of ion-channelopathy or electrical heart disease occurred in 13.5% of nonathletes and 16.4% of athletes ($p < 0.001$) (Fig. 3).

Echocardiographic evaluation of all 784 nonathletes with group 2 ECG patterns suggesting cardiomyopathy or structural cardiac abnormality identified a normal heart in 84% of individuals. Ten percent ($n = 79$) of nonathletes had cardiac dimensions exceeding predicted upper limits and 4% had minor congenital anomalies. Only 2% ($n = 16$) of nonathletes with ECG patterns suggestive of structural cardiac abnormality had echocardiographic features consistent with a morphologically mild cardiomyopathy (Fig. 4). Of note, all individuals with echocardiographic features of cardiomyopathy demonstrated T-wave inversion on the ECG.

Discussion

Previous data suggest that ECG screening in athletes may minimize the risk of SCD, but there are limited data relating

to ECG patterns in young nonathletes (2). This study extrapolated current ECG criteria derived from competitive athletes to a large cohort of nonathletes of comparable age and revealed a much higher than expected prevalence of group 2 ECG patterns in both cohorts. One fifth of nonathletes and a third of athletes had at least one group 2 anomaly.

Implications of specific group 2 ECG patterns. Group 2 ECG patterns suggestive of cardiomyopathy or structural cardiac abnormality occurred in 10.1% of nonathletes; however, subsequent echocardiographic evaluation of this group revealed changes consistent with cardiomyopathy in only a small fraction (2%) of these individuals (Fig. 4). T-wave inversions were the only consistent group 2 ECG pattern in all nonathletes with suspicion of cardiomyopathy on echocardiography, which suggests that this particular repolarization anomaly should raise the possibility of underlying cardiomyopathy in most nonathletes. However, the significance of T-wave inversions should be interpreted in the context of individual demographics because it is well established that anterior T-wave inversions (V_1 - V_4) may be normal variants in adolescents (<16 years) and individuals of black ethnicity (8,11).

The most common abnormalities, accounting for 52.3% of group 2 ECG patterns in nonathletes, were a combination of long- and short-QTc intervals, which suggests that current proposed values by the ESC will generate a large number of false positive results in otherwise low-risk populations.

Impact of sex, ethnicity, and age in nonathletes. Male sex and black ethnicity doubled the likelihood of a group 2 ECG pattern. Our data imply that ECG screening of black individuals, regardless of athletic status, would have major

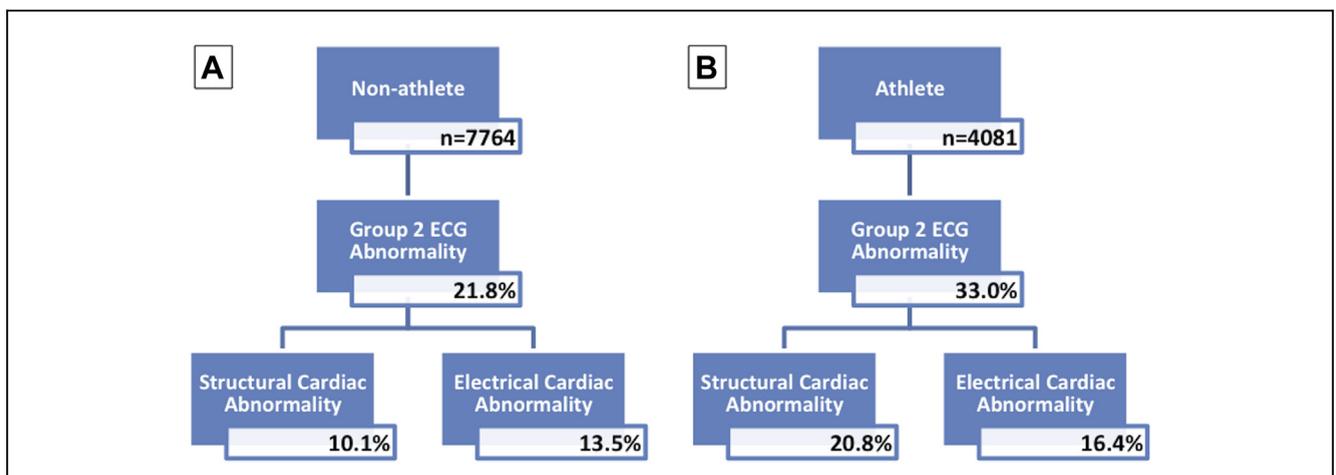
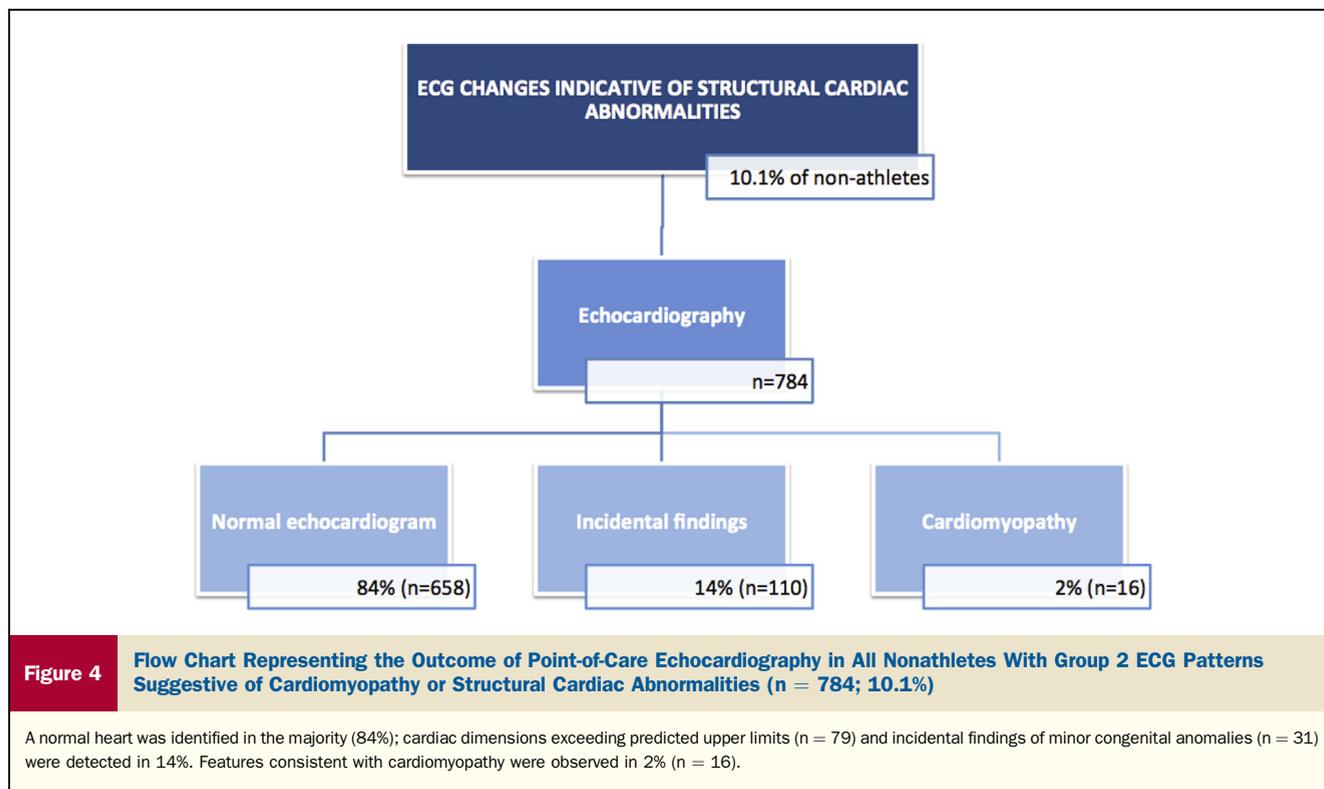


Figure 3 Flow Chart Represents the Proportion of Nonathletes and Athletes With Group 2 ECG Patterns That Would Require Further Evaluation

ECG changes suggestive of cardiomyopathy or structural cardiac abnormalities included T-wave inversion, ST-segment depression, pathological Q-waves, left atrial and right atrial enlargement, left-axis deviation and right-axis deviation, right ventricular hypertrophy, left bundle-branch block, and right bundle-branch block. ECG changes suggestive of ion channelopathy or electrical cardiac abnormalities included ventricular pre-excitation, long- and short-QTc interval, and Brugada-like early repolarization.



ramifications for countries with large populations of black individuals.

Implications for ECG-based screening. The benefits of large-scale ECG screening for conditions associated with SCD are derived from a single Italian study of competitive athletes (2). The ESC recommendations to incorporate the ECG in PPS of athletes are based on this study but have proved controversial and highly debatable (12). The American Heart Association does not support the ESC recommendations on the basis of several concerns, including a high number of false positive results.

Whereas ECG screening seems practical among elite sportsmen belonging to financially endowed sporting organizations, our study has important implications for nationwide screening of all young persons. In keeping with concerns raised by the American Heart Association, this study reveals that 20% of young individuals would fail the initial assessment after an ECG on the basis of current ESC criteria. The implications of the ensuing costs of further investigations on a financially constrained health budget in times of austerity would be insurmountable. The situation would be worse in cosmopolitan societies with large populations of black individuals. Further refinement of the criteria for group 2 ECG patterns is required to improve the specificity of the ECG before any consideration can be given to nationwide population screening.

Study limitations. Echocardiography was limited to nonathletes with group 2 ECG patterns suggestive of cardiomyopathy or structural cardiac abnormality; therefore, we

could not calculate the sensitivity or specificity of current ECG criteria for detecting structural cardiac disease. Nevertheless, we demonstrated that further investigation of most group 2 ECG patterns indicative of structural disease is associated with a low diagnostic yield. We did not report exercise tests, Holter monitors, or familial evaluation in nonathletes with long- or short-QTc intervals; therefore, we cannot comment on the true significance of these ECG anomalies. However, the prevalence of these ECG patterns in our cohort was several hundred-fold greater than the reported prevalence of the respective syndromes in the general population, which suggests that most were false positives.

Nonathletes were defined as individuals who did not participate in formal competition, but 39.9% of nonathletes exercised recreationally >4 h per week. Therefore, it is arguable that our non-athletic group includes a significant proportion of “athletes,” and their inclusion may have overestimated the prevalence of group 2 ECG patterns. However, our cohort represents a true, unselected group of young individuals that any screening program in the general population is likely to encounter.

Finally, the study was cross-sectional in design; therefore, we could not report outcomes data in individuals with group 2 ECG changes and structural features consistent with a morphologically mild cardiomyopathy. Given the low event rates in cardiomyopathy in asymptomatic individuals, a very protracted prospective study would be required to ascertain whether pre-symptomatic detection may have affected prognosis.

Conclusions

This study demonstrates a high prevalence of group 2 ECG patterns in the general population and suggests that more than one-fifth of young individuals would require further cardiac investigation if an ECG-based screening program were implemented using current recommendations. The logistical implications deem such practice impossible until serious consideration is given to refinement of current group 2 ECG patterns.

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