Impact of ethnicity on the prevalence of early repolarization pattern in children: comparison between Caucasian and non-Caucasian populations

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Abstract

Introduction

The patterns and prevalence of early repolarization pattern (ER in paediatric populations from different ethnic backgrounds other than Caucasian have not been determined.

Methods

We analyzed ECGs of black children (ages xx-yy) who were prospectively recruited in the north-west Madagascar and compared them to age & sex matched Caucasian ethnicity individuals. ERP was defined by ≥0.1 mV J-point elevation in at least two contiguous inferior and/or lateral ECG leads.

Results

A total of 616 children were included. There was a trend toward a higher frequency of ERP in the Africans compared to the Caucasians (23.3% vs 17.1% respectively, p=0.053). The subtype (slurred versus notched) and location of ERP (lateral, inferior or infero-lateral) were significantly different in the two groups (p<0.001 and p=0.020, respectively). There was no significant difference in the number of high-risk ECG features of ERP (i.e. horizontal/descendent pattern, inferior or infero-lateral location or J-waves ≥2 mm) between Malagasy and Caucasian children. On the multivariate analysis, Malagasy ethnicity and faster heart rate were independent predictive factors of ERP (OR 3.57, 95%CI 2.04-6.25, p<0.001 and 0.98, 95%CI 0.962-0.987, p<0.001, respectively).

Conclusions

African children have an increased risk of ER compared to Caucasian counterparts. Future studies should clarify the clinical and prognostic significance of ERP in the pediatric population, and whether ethnicity has an impact on the outcomes.

Introduction

The early repolarization (ER) pattern has been defined as an elevation of J-point ≥ 0.1 mV in at least two contiguous inferior and/or lateral leads of a standard 12-lead electrocardiogram (ECG) [1-2]. ERP has traditionally been considered a benign variant [3-5]. The possible correlation of ERP with polymorphic ventricular tachycardia (VT) and ventricular fibrillation (VF) was firstly described in experimental studies on coronary-perfused wedge preparations [6-8]. More recently, clinical evidence for an increased risk of sudden cardiac death (SCD) and life-threatening arrhythmias among adult Caucasian patients with ERP has been provided [9-12]; however, it is not clear whether these results apply to the black African population as well. Furthermore, the clinical significance of ERP in the young is not well understood. ERP has been found in a substantial proportion of paediatric first-degree relatives of sudden arrhythmic death probands [12]. Although ERP occurs with increased frequency in black adult cohorts [13-16], to the author's knowledge, descriptions of the patterns and prevalence of ERP in paediatric populations of ethnic backgrounds other than Caucasian are unknown. The aim of this study is to define the patterns and prevalence of ERP in children from a sub-Saharan African country, and to compare them to matched Caucasian ethnicity individuals.

Methods

African (North-Malagasy) group

Children aged 4-12 years old were prospectively recruited in October 2015 as part of a screening program for cardiovascular diseases in two schools of Ambanja, northwest Madagascar. The Malagasy population combines morphological and cultural traits of both Bantu and Austronesian ancestry [17-18]. The coastal area where we collected these data is mainly inhabited by Sakalava people, a Negroid group with predominant "African features", but mixed Bantu-Austronesian genetic background [17]. Consent to the study was given by parents or attorneys, and ethics approval was obtained. Each child underwent physical examination, ECG and transthoracic echocardiogram. Subjects with known cardiovascular disease and/or pathological echocardiographic findings (i.e. cardiomyopathy or valvular heart disease) were excluded.

Caucasian group

We analysed de-identified ECGs of consecutive Caucasian children, aged 4-12 years old, who underwent an ECG between 2016 and 2017 as part of either a pre-participation screening for non-competitive sport, routine pre-assessment before surgery or hospital admission at the University Hospital of Udine (Italy). Subjects with known cardiovascular diseases were excluded. Parents of the individuals included had previously given consent to use clinical data of their children for epidemiological research purposes.

ECG analysis

All ECGs were recorded at rest at 25 mm/s and 10 mm/mV (0.05-150 Hz). ECGs were analysed by two experienced cardiologists. A third cardiologist intervened to resolve disputes whenever the two reviewers were in disagreement regarding the interpretation. ERP was defined as a J-point elevation ≥0.1 mV in at least two contiguous inferior (II, III, aVF) and/or lateral (V5-V6, I, aVL) leads, in the presence of a QRS duration <120 ms [19-20]. ERP was classified either as slurred or notched terminal part of the QRS (Fig. 1-2) [19-20]. The ST segment elevation 100 ms after the J-point was measured and classified either as horizontal/descendent (<1 mm, continuing as a flat/descending segment until onset of the T wave) or ascendant (≥1 mm, ascending gradually until the T wave) [19-20]. The amplitude of the J-wave was also measured. The number of high-risk ERP features (e.g. horizontal/descendent pattern, inferior or infero-lateral location or J-waves ≥2 mm) [12, 19-20] was noted for each individual. Other measurements included PR interval, QT and corrected QT (Bazett formula).

Statistical analysis

Student's t-test or Mann-Withney test was employed for comparison of continuous variable. The chi-square test was utilized to compare nominal variables expressed as proportions. Multivariate binary logistic regression (forward likelihood ratio method; probability for stepwise 0.05) was performed for identifying independent predictors of ERP. All P-values were considered significant when <0.05. SPSS version 19.0 was used for all analyses.

Results

African (North-Malagasy) group

A total of 300 subjects were included (mean age±SD 7.5±2.7, 47.7% boys). ERP was observed in the 23.3% of the group and there was a trend toward a higher frequency in males compared to females (25.1% vs 21.7% respectively, p=0.47). ERP was more commonly located in the lateral leads (47.1%) or in both the inferior and lateral leads (28.6%) (Table 1). Notched QRS pattern was significantly more frequent than slurred QRS pattern (82.9% vs. 17.1%, respectively). The mean J-point elevation was 1.1 mm (range 1 to 2 mm) and 4 children (5.7%) had a J point elevation ≥2 mm. The mean QT was 363±41 ms and the mean cQT was 468±48 ms. Main results are shown in Table 1.

Caucasian group

Among the 316 children included (mean age±SD 7.6±2.7, 49% boys), ERP was observed in 17.1% (54), with a similar distribution between males and females (17% vs 18%, respectively, p=0.89). The ERP was infero-lateral in 50% of cases, lateral in 29.6% and inferior in the remaining 20.4% (Table 1). A slurred QRS pattern was more frequent than a notched QRS pattern (33.3% vs 66.7%, respectively). The mean J-point elevation was 1.1 mm (range 1 to 2 mm) and 5 children (9.3%) had an elevation ≥2 mm. The mean QT was 330±29 ms and the mean corrected QT interval; was 396±18 ms. Results are shown in Table 1.

North-Malagasy versus Caucasian children

Demographic characteristics were similar in the two groups (Table 1). The Africans, compared to the Caucasians, showed a significantly faster heart rate (103±18 vs 84±15 bpm, p<0.001) and a longer QT interval (346±39 vs 330±29, p<0.001). There was a trend toward a higher frequency of ERP in the Africans compared to the Caucasians (23.3% vs 17.1% respectively, p=0.053). The subtype of ERP (slurred versus notched) and location of ERP (lateral, inferior or infero-lateral) were significantly different in the two groups (p<0.001 and p=0.020, respectively). J waves ≥2 mm were significantly more frequent in the Caucasian subjects (p=0.033). There was no significant difference in the number of high-risk ECG features of ERP (i.e. horizontal/descendent pattern, inferior or infero-lateral location or J-waves ≥2 mm) between Malagasy and Caucasian children (Table 1).

Univariate and multivariate analysis

On both univariate and multivariate analysis, Malagasy ethnicity and faster heart rate were independent predictive factors of ERP (on the multivariate, OR 3.57, 95%CI 2.04-6.25, $p<0.001$ and 0.98, 95%CI 0.962-0.987, $p<0.001$, respectively) (Table 2).

Discussion

ERP is a relatively common ECG finding, with an estimated prevalence of 0.6%-24% [14-16]. Some reports suggest a higher prevalence of ERP in the Afro-Americans [1] [21]. ERP has been traditionally considered as a benign finding, especially in young people. The American Heart Association/American College of Cardiology Foundation/Heart Rhythm Society International in 2009 defined ER as “a normal variant commonly characterized by J-point elevation and rapidly upsloping or normal ST segment” [5]. More recent evidence has revealed an increased prevalence of ERP in subjects with idiopathic ventricular fibrillation [9-12]. The absolute risk difference for arrhythmia death has been estimated at 70 cases per 100,000 subjects with ERP per year [20]. The presence of ERP in the inferior leads, giant J-waves (i.e. ≥2 mm) and horizontal/descending ST morphology have been proposed as ECG features suggestive of an increased risk of VF [19-20]. Although ERP has been associated with higher mortality risk in Caucasians, evidence in non-white populations is limited. In a recent observational study, ERP was not associated with long-term mortality in a large prospective black adult community cohort, suggesting that ERP may be a benign finding in blacks [22]. However, no data are available regarding black paediatric population. To the best of our knowledge, this is the first study to analyse the prevalence and characteristics of ERP in black children. We found a trend toward a higher prevalence of ERP in black African children compared to white Caucasian children. Notably, the Malagasy ethnicity was associated with a significant higher risk of ERP in a multivariate analysis. These results confirm what previously documented among black adults and highlight the importance of genetic background in the cardiac repolarization. We have found no difference between the two populations on the numbers of ECG features associated with increased risk of VF (giant J-waves, inferior or infero-lateral location and horizontal/descendent pattern of ST). However, it is unclear whether these criteria can be adopted for risk stratification in children as well as in adults.

Longitudinal studies are warranted to clarify whether ERP has the same prognostic value in blacks compared to whites, particularly in the paediatric population.

An additional finding of this study was that Malagasy children showed a significant longer QT/QTc interval compared to the Caucasians. As we previously reported [23], malnutrition was common among Malagasy children included in this study. It is possible that malnutrition might cause some changes in the cardiac repolarization, leading to a prolongation of the QT interval [24].

Strengths and limitations

A strength of this study is that analyses of ECG from Caucasian and Malagasy children were performed by two independent cardiologists, with the intervention of a third one for cases with discordant interpretation. The main limitation is the lack of any prospective data regarding clinical outcomes and long-term follow-up of children with ERP.

Conclusions

Children of Bantu-Austronesian origin from north Madagascar have an increased risk of ERP compared to Caucasian counterparts living in Italy. Future studies should focus on clarify the exact prevalence of ERP in sub-Saharan Africa, the clinical and prognostic significance of ERP in the pediatric population, and whether ethnicity has an impact on the outcomes.

Disclosure

Authors have no conflicts of interest to declare.

Comments:

Nice descriptive study.

1. Given the importance of malnutrition you should control for this and consider plotting a histogram of different BMI gps or body weight e,g <10-15% ideal, <10% ideal, ideal, >10% etc or divide into quintiles to see of there is a sig diff in degree of ER. Could be a good discussion point.
2. I assume no data on FHX SCD
3. Is there any association between septal lead V1-V3 high take off ie usual African pattern and freq of ER?

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Table 1 Demographic and results.

<table>
<tr><th colspan="2">Variable</th><th>All sample (n=616)</th><th>Madagascar (n=300)</th><th>Caucasian (n=316)</th><th>p</th></tr>
<tr><td colspan="2">Age</td><td>7.5±2.7</td><td>7.5±2.7</td><td>7.6±2.7</td><td>0.819</td></tr>
<tr><td colspan="2">Male</td><td>47.4% (292)</td><td>47.7% (143)</td><td>47.2% (149)</td><td>0.898</td></tr>
<tr><td colspan="2">Heart Rate</td><td>94±18</td><td>103±18</td><td>84±15</td><td><0.001</td></tr>
<tr><td colspan="2">PR</td><td>138±21</td><td>140±23</td><td>137±18</td><td>0.067</td></tr>
<tr><td colspan="2">Short PR</td><td>1.1% (7)</td><td>2.3% (7)</td><td>0% (0)</td><td>0.006</td></tr>
<tr><td colspan="2">1st degree AV Block</td><td>9.6% (59)</td><td>14.0% (42)</td><td>5.4% (17)</td><td><0.001</td></tr>
<tr><td colspan="2">QT</td><td>346±39</td><td>363±41</td><td>330±29</td><td><0.001</td></tr>
<tr><td colspan="2">QTc</td><td>431±50</td><td>468±48</td><td>396±18</td><td><0.001</td></tr>
<tr><td colspan="2">Brugada pattern</td><td>0% (0)</td><td>0% (0)</td><td>0% (0)</td><td>N.A.</td></tr>
<tr><td colspan="2">ERP</td><td>20.1% (124)</td><td>23.3% (70)</td><td>17.1% (54)</td><td>0.053</td></tr>
<tr><td colspan="2">J-point ≥2mm</td><td>7.3% (9)</td><td>5.7% (4)</td><td>9.3% (5)</td><td>0.033</td></tr>
<tr><td rowspan="3">Location</td><td>Lateral</td><td>39.5% (49)</td><td>47.1% (33)</td><td>29.6% (16)</td><td rowspan="3">0.020</td></tr>
<tr><td>Inferior</td><td>22.6% (28)</td><td>24.3% (17)</td><td>20.4% (11)</td></tr>
<tr><td>Inferolateral</td><td>37.9% (47)</td><td>28.6% (20)</td><td>50% (27)</td></tr>
<tr><td colspan="2">Slurring</td><td>38.7% (48)</td><td>17.1% (12)</td><td>66.7% (36)</td><td><0.001</td></tr>
<tr><td colspan="2">Notching</td><td>61.3% (76)</td><td>82.9% (58)</td><td>33.3% (18)</td><td><0.001</td></tr>
<tr><td colspan="2">Ascendant ST-segment</td><td>87% (108)</td><td>85.7% (60)</td><td>89.9% (48)</td><td rowspan="2">0.838</td></tr>
<tr><td colspan="2">Horizontal ST-segment</td><td>13% (16)</td><td>14.3% (10)</td><td>11.1% (6)</td></tr>
<tr><td rowspan="4">Number of ECG high-risk features[a]</td><td>0</td><td>44</td><td>29</td><td>15</td><td rowspan="4">0.310</td></tr>
<tr><td>1</td><td>60</td><td>31</td><td>29</td></tr>
<tr><td>2</td><td>20</td><td>10</td><td>10</td></tr>
<tr><td>3</td><td>0</td><td>0</td><td>0</td></tr>
</table>

Note. [a] ECG high-risk features were defined as J wave ≥2 mm, inferior or infero-lateral location and horizontal/descendent pattern of the ST-segment.

Table 2 Predictors of early repolarization pattern.

Variable	Univariate			Multivariate		
	OR	95%CI	P	OR	95%CI	P
Age	1.04	0.996-1.103	0.071	-	-	-
Male	1.44	1.006-2.073	0.046	-	-	-
Malagasy	1.25	0.87-1.15	0.228	3.57	2.04-6.25	<0.001
Heart rate	0.98	0.970-0.990	<0.001	0.97	0.961-0.984	<0.001
PR	1.00	0.994-1.011	0.607	-	-	-
QT	1.01	1.000-1.009	0.035	-	-	-
QTc	1.00	0.993-1.001	0.107	0.992	0.986-0.998	0.012

Fig. 1 Example of early repolarization *slurred* pattern.

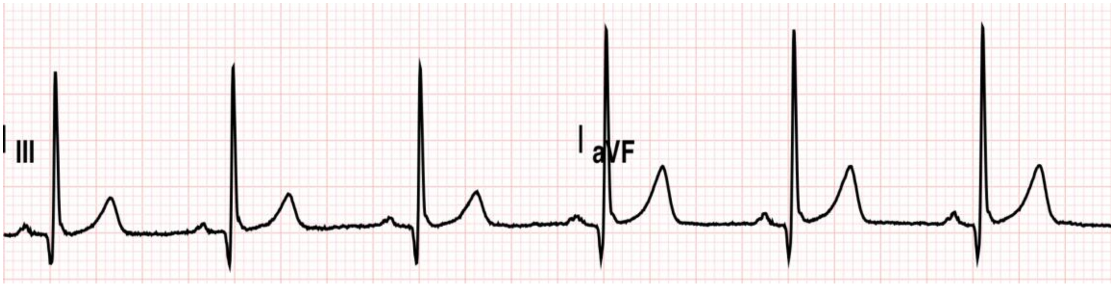

Fig 2. Example of early repolarization *notched* pattern.