Frequency of the early repolarization syndrome, types and associations with various cardiovascular pathologies – Systematic Review
Table of contents:

1. SUMMARY ..............................................................................................................................................3
2. ACKNOWLEDGEMENTS AND CONFLICT OF INTERESTS ......................................................4
3. ABBREVIATIONS .......................................................................................................................................5
4. TERMS .....................................................................................................................................................6
5. INTRODUCTION .......................................................................................................................................7
6. AIM AND OBJECTIVES OF THE THESIS .......................................................................................8
7. LITERATURE REVIEW ..............................................................................................................................9
    7.1 Definition ...........................................................................................................................................9
    7.2 Ionic and cellular mechanism ...........................................................................................................10
    7.3 Genetic background ..........................................................................................................................10
    7.4 Types ................................................................................................................................................11
    7.5 Diagnosis .........................................................................................................................................13
    7.6 Stratification ........................................................................................................................................13
8. RESEARCH METHODOLOGY AND METHODS ..............................................................................15
9. RESULTS ..................................................................................................................................................16
10. DISCUSSION .........................................................................................................................................21
11. CONCLUSIONS ....................................................................................................................................22
12. RECOMMENDATIONS .........................................................................................................................23
13. BIBLIOGRAPHY ....................................................................................................................................24
SUMMARY

Santiago Martín Just

Frequency of the early repolarization syndrome, types and associations with various cardiovascular pathologies – Systematic review

**Research aim:**
The aim of this study is to evaluate the frequency of the early repolarization (ER) syndrome, types and associations with various cardiovascular pathologies by the literature data.

**Objectives:**
Through a selection of articles, evaluate the early repolarization syndrome definition, its types, the diagnostic criteria, the frequency among populations worldwide and its association with cardiovascular diseases.

**Methodology:**
Through the use of major scientific databases (Ovid Medline, Embase, and Pubmed) and searching of the needed terms seeking the adequate studies, a quantity of 7 studies have been chosen and compared with each other to assess the frequency of early repolarization and 15 studies have been chosen to assess the association of early repolarization and cardiac diseases.

**Study participants:**
No study participants have been revised excluding participants of systematic reviews.

**Research results:**
The comparison of the studies proved that the frequency of early repolarization varies through different populations, being the benign type more frequent; and early repolarization can be associated to cardiac diseases in case of malignant form (according to Tikkanen classification in both cases)

**Conclusions:**
There’s higher incidence of early repolarization in groups with high physical activity, young males, Afro-American and Asian groups (mostly within the benign form of ER).

Early repolarization is associated with lone atrial fibrillation, ventricular fibrillation, sudden cardiac death (SCD) and coronary slow flow phenomenon in malignant form of ER.

**Recommendations:**
Test regularly (ECG, holter) for complications in patients with ER to prevent SCD.
CONFLICT OF INTERESTS AND ACKNOWLEDGEMENTS

Conflict of interest:
The author reports no conflicts of interest.

Acknowledgements:
Special thanks to my supervisor, Eglė Kalinauskienė, who helped me all along and Dr. Rosa López, which helped me with the search of information regarding Early Repolarization.
ABBREVIATIONS

- **AF**: atrial fibrillation
- **CAS**: coronary artery spasm
- **ECG**: electrocardiogram
- **ER**: early repolarization
- **ITO**: transient outward current
- **SCD**: sudden cardiac death
- **SHD**: structural heart disorders
- **STEMI**: ST elevation myocardial infarction
- **UCA**: unexplained cardiac arrest
- **VTA**: ventricular arrhythmias
TERMS

- **Arrhythmias:**
  Group of medical conditions in which the heart does not beat with a regular rhythm, or at the normal rate.

- **Depolarization:**
  Elimination or neutralization of polarity.

- **Hypocalcaemia:**
  An abnormally low amount of calcium in the blood and in the cells of a tissue.

- **Hypothermia:**
  A serious medical condition in which a person's body temperature falls below the usual level as a result of being in severe cold for a long time.

- **Idiopathic:**
  A disease or medical condition which has no known cause.

- **Repolarization:**
  The restoration of a polarized state across a membrane.
INTRODUCTION

Early repolarization is a cardiac syndrome which can lead, in some cases, to diagnose other cardiovascular conditions. The opinion in the health has changed since it was first described 70 years ago. From then, different definitions and opinions have been proposed surrounding this cardiac syndrome. With a consensus about its definition and diagnosis some years ago, a window has been opened to investigate and relate this syndrome with other known cardiac diseases; helping to prevent and lower mortality among patient with cardiovascular conditions.

In this systematic review, I tried to focus on get a proper definition of the syndrome, all the ionic and cellular mechanism involved, its genetic background, the types of early repolarization and the diagnosis. My intention was to synthesize all this information to create a collection of studies showing the different frequency of early repolarization in different populations and groups worldwide, showing the difference of frequency depending on lifestyle changes and the ethnicity. Also I wanted to collect different studies associating this syndrome with cardiac diseases, proving that it can be related to a numerous amount of cardiovascular diseases and it could be used as a risk marker for those diseases, preventing them, lowering their mortality and improving the patient's life.
AIM AND OBJECTIVES OF THE THESIS

The main aim of this thesis is to evaluate the frequency of the early repolarization syndrome, types and associations with various cardiovascular pathologies by the literature data.

Objectives:

1. Selection of the articles with a topic of early repolarization syndrome.
2. To assess the different types of early repolarization syndrome.
3. To evaluate the frequency of early repolarization syndrome among the different populations.
4. Assessment of the associations of early repolarization syndrome with various cardiovascular pathologies.
Definition

The term “early repolarization” has been object of discussion since its first definition as a ‘unusual RT-segment deviation’, ‘juvenile ST variant’ or ‘normal RS-T segment elevation variant’ made 70 years ago. Over the years, multiple authors such as Wasserburger and Friedman [1] have included little changes in their studies, always keeping in mind that ER was a benign condition. In 1988, Schamroth correlated the ER with the athletes hearts, to indicate a common normal pattern characterized by the presence of a thickening or slur of the terminal part of the QRS that may appear as a distinct notch or ‘hook’ on the distal limb of the QRS complex associated with concave upward elevated ST segment, tall and symmetrical T waves [1].

On the other hand, many studies over the 80’s and the 90’s start correlating ER pattern and the J-wave with cardiovascular diseases; such as idiopathic ventricular fibrillation, arrhythmias and SCD [1].

Surawicz and Macfarlane et al, [2] note that the term “early repolarization” is confusing and unnecessary, arguing that it should not be used with descriptions of ECGs. Instead, they believe that the existing ECG terminology (ex, ST-segment elevation and duration) should be used when describing ECG findings [2]. They also argue that the J wave is part of the ST segment and rarely observed in patients who do not have hypothermia [2].

However, Antzelevitch provided proofs for using the terms “early repolarization and J wave syndrome” in identifying people who are at high risk for adverse events [3].

In response to reports that challenged early repolarization as a benign normal variant and to the controversies over the criteria for defining early repolarization, a consensus paper was published that provides terminology and new definitions for early repolarization [4, 5].

In this new definition, if the ST segment slopes upward and is accompanied by an upright T wave, the pattern is described as ER with an ascending ST segment. If there is a horizontal or downward sloping ST segment, is described as ER with a horizontal or descending ST
segment. An ECG showing ER pattern in leads II, III, aVF, and V4-V6 (inferolateral leads) may have evidence of an end QRS notch in lead V4 and end QRS slur in lead III. This is also described as ER with an ascending ST segment because ST segment slopes upward and is followed by an upright T wave [4, 5].

An ECG that has ST-segment elevation without a slur or notch should not be defined as ER [4, 5].

**Ionic and Cellular Mechanism**

Being a syndrome related to the ECG and to the heart’s physiology, it’s important to mention the changes in the cellular mechanism that can produce ER.

The inward movement of Na across the cell membrane through a specific channel produces inward current and causes depolarization. Outward movement of K causes repolarization. The plateau phase of action potential AP depends on balance between inward (depolarizing) and outward (repolarizing) currents. The heart has three main layers (endocardium, myocardium and epicardium) and in normal state there is homogenous genesis of action potential across the three layers.

An abnormality of any layer would lead to aberration in action potential and development of ionic gradient between the layers with consequent development of slow conduction, forming a substrate for reentry in phase 2. The first phase of repolarization with a dome like small hump is due to K current called Ito (transient outward current). Uneven distribution with resultant gradient of Ito between the epicardium and endocardium results in J-point elevation. Hypothermia and hypocalcaemia enhance J wave development [6, 7].

**Genetic Background**

Mutations have been identified in ATP-dependent potassium current (KCNJ8 and ABCC9), in the calcium channel (CACAN1c, CACNB2b, CACNA2D1), and in the sodium channel (SCN5A, SCN10A) (see table 1). While mutations of potassium channels are associated with a gain of function effect, loss of function is observed in calcium and sodium channel mutations [8, 9, 10].
A word of caution is appropriate here. The genetic basis for early repolarization is not well defined. Genetic contributions to ER are suggested by anecdotal observations of a common familial history of SCD in subjects with ER and idiopathic VF. Familial ER has been reported to have an autosomal dominant inheritance pattern with incomplete penetrance. Studies also have suggested some degree of inheritance of the ER patterns in the general population, but the familial inheritance of malignant ER patterns has not been clearly demonstrated; those mutations are identified in a small proportion of cases (<20%) [9, 10].

In summary, it is clear that is only started to scratch the surface of the genetic background, and therefore, genetic testing has currently a marginal role in the clinical management of ER [9, 10].

**Table 1: Description of all the genes involved in the genetic background of ER.**

<table>
<thead>
<tr>
<th>Gene/Protein</th>
<th>Locus</th>
<th>Ion Channel</th>
<th>Functional Defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>KCNJ8, Kir6.1</td>
<td>12p11.23</td>
<td>↑IK-ATP</td>
<td>Incomplete closing of the ATP-sensitive potassium channels</td>
</tr>
<tr>
<td>CACNA1C, Cav1.2</td>
<td>12p13.3</td>
<td>↓ ICa</td>
<td>Loss of function, reduced Ca21 current</td>
</tr>
<tr>
<td>CACNB2b, Cavβ2b</td>
<td>10p12.33</td>
<td>↓ ICa</td>
<td>Loss of function, reduced Ca21 current</td>
</tr>
<tr>
<td>CACNA2D1, Cavα2</td>
<td>7q21.11</td>
<td>↓ ICa</td>
<td>Loss of function, reduced Ca21 current</td>
</tr>
<tr>
<td>ABCC9, SUR2A</td>
<td>12p12.1</td>
<td>↑IK-ATP</td>
<td>Gain of function, increased outward current</td>
</tr>
<tr>
<td>SCN5A, Nav1.5</td>
<td>3p21</td>
<td>↓ INa</td>
<td>Loss of function, reduced Na1 current</td>
</tr>
<tr>
<td>SCN10A, Nav1.8</td>
<td>3p22.2</td>
<td>↓ INa</td>
<td>Reduced NaV1.8 current</td>
</tr>
</tbody>
</table>

**Types**

According to definition of the ER syndrome, relating it to ST elevation or not, different subtypes are described.

- Antzelevitch et al, [9, 10, 12] described early repolarization syndrome into three subtypes:
**Type 1:** Early repolarization pattern seen in the lateral precordial leads. This form is very prevalent among healthy male athletes and is rarely related to cardiac diseases.

**Type 2:** Early repolarization pattern seen in the inferior or inferolateral (most common) leads. Numerous cases of this subtype are related to cardiac diseases (mostly idiopathic VF) but this is also prevalent in healthy young males.

**Type 3:** Early repolarization pattern globally in the inferolateral and right or anterior precordial leads and is associated with the highest level of risk for development of malignant arrhythmias and cardiac diseases.

- Tikkanen proposed another classification [7] in which ER is J-point and ST segment elevation >1 mm in 2 or more contiguous leads. Two types of J-point elevation are described:

  1. J-point with rapidly ascending ST segment, considered a Benign form.
  2. J-point with horizontal or descending ST segment, considered a Malignant form.

**Table 2: Differences between physiological and pathological J wave [7].**

<table>
<thead>
<tr>
<th>Characters</th>
<th>Physiological J Wave</th>
<th>Pathological J wave</th>
</tr>
</thead>
<tbody>
<tr>
<td>J point Elevation</td>
<td>&lt;0.1 mV</td>
<td>&gt;0.2 mV</td>
</tr>
<tr>
<td>Height of J wave</td>
<td>1-2 mm</td>
<td>&gt;2mm</td>
</tr>
<tr>
<td>Descent of J wave</td>
<td>Up-sloping</td>
<td>Horizontal or Downsloping</td>
</tr>
<tr>
<td>ECG Leads</td>
<td>Only V4-6 or II,III,aVF</td>
<td>Both, V4-6 plus II,III,aVF</td>
</tr>
</tbody>
</table>

ER in inferolateral lead is more associated with ventricular fibrillation. ER ECG pattern (>1 mm) in the inferior/lateral leads occurs in 1-13% of the general population and with 15-70% of Idiopathic VF cases. In the pediatric age group is more prevalent. Male sex is strongly associated with ER ECG pattern, since over 70% of subjects with ER are males, its prevalence declines in males from early adulthood until middle-age, showing its peak in the
third decade of life, suspecting a relation which suggests a hormonal influence of testosterone on the presence of ER. The ER pattern is more common in young physically active individuals, athletes, and African-Americans. There is an increased prevalence of ER reported in Southeast Asians. Other suggestions associate this ER pattern with high vagal tone, as well as hypothermia and hypocalcaemia [11, 13].

**Diagnosis**

Diagnosis of ER is based through ECG or Holter monitoring based on the classification previously mentioned, risk factors and possible concomitant cardiac diseases. Some of the criteria are the following [3, 7, 11, 13]:

1. Asymptomatic and incidentally detected ER is very common in young athletes. The prevalence and magnitude of ER increase as their training intensifies.

2. Malignant variety with Idiopathic VF and Sudden cardiac death (SCD).

3. ER with Coronary artery disease (CAD) with increased risk of having ischemic VF. ER pattern recorded during ischemic event is strongest predictor of VF occurrence.

4. ER has been linked to high cardiac death and arrhythmic death rates in vasospastic angina.

5. Idiopathic VF is reported with horizontal or down-sloping ST following J-point elevation.

**Stratification**

The magnitude of the J-point elevation has a high value of prognostic significance. Either slurred or notched J-point elevation of more than 0.2 mV is relatively rare in the general populations, but is associated with an increased risk and a pathologic J-wave [7]. Also, J-point elevations in idiopathic VF patients are of greater amplitude and ECG lead distribution compared to those with an established cause. Inferior leads combined with J-
wave amplitude more than 2mm can show a greater risk for ER complications and worse prognostic than inferolateral leads or amplitude of 1mm in J-wave. The data provided in studies shown later on this work also suggest that transient changes in the amplitude of J-point elevation carry a higher risk for VF. A horizontal or descending ST segment following J-point elevation is associated with a worse outcome in the general population [9, 11, 14].
RESEARCH METHODOLOGY AND METHODS

In this systematic review, a total of 7 studies which focused on the frequency of ER in different groups of population were studied and data and conclusions were taken from them. Through the use of major scientific databases (Ovid Medline, Embase, Pubmed) and searching of the needed terms seeking the adequate studies, studies have been chosen and compared with each other to obtain the frequency of ER between different populations and groups. The sample of studied people ranges from 306 (in study number 3) to 9690 (study number 7).

Regarding the other objective, which are the associations of early repolarization syndrome with various cardiovascular pathologies, in this systematic review, a total of 15 studies have been studied and data and conclusions were taken from them. Through the use of major scientific databases (Ovid Medline, Embase, and Pubmed) and searching of the needed terms seeking the adequate studies, studies have been chosen to collect process and obtain this association of ER and various cardiac diseases. The sample of studied people ranges from 34 (in case of study number 8) to 7268 (in study number 6). This wide range is due to the different cardiac diseases compared and associated below.

All the studies taken are within the range of the last 10 years (2009-2019) to get the latest results possible and get the most appropriate conclusions. This is especially important due to the changing of opinions and definitions of ER in the last few years, leading to the diagnosed cases of ER in the studies below with the latest and most accurate diagnostic criteria. The only exception is the study of Michel Haïssaguerre (2008), but as being one of the pioneer researchers in the area of ER, it had to be included within these studies.
RESULTS

The data extracted from the studies are shown in the tables which compares the frequency of ER (see table 3) and association of ER with various diseases (see table 4).

In table 3, the population and the origin of the sample chosen, the methods of diagnostics of ER and the main conclusions of each study are shown below.

In table 4, the population, the sample (specifying if the study had control group), the disease associated and the main conclusions are shown below.

In both tables, ER was diagnosed. The most used methods were ECG and Holter ECG, including in some cases echocardiography and exercise ECG test. The parameters followed to make an appropriate diagnosis include a positive J wave, which is a slurring or notch at the QRS terminal which is ≥0.1mV or more above the isoelectric line in ≥2 contiguous leads; classifying as inferior (II, III, and aVF), lateral (I, aVL, and V4 to V6), or both (inferolateral).

Regarding the origin of the studies and the samples, it’s important to highlight them due to the different frequency of ER in various ethnicities (Asian and Afro-American) [18, 19] and group populations (such as elite forces or professional athletes) [19, 20] and therefore can influence the incidence an association in cardiovascular diseases.

On both tables, samples are specified if they are general populations or specific groups or populations. Also is specified if there’s a control group and if the ratio men/women is not 50/50.
### Table 3: Frequency of ER in different populations

<table>
<thead>
<tr>
<th>Nr</th>
<th>Study</th>
<th>Population</th>
<th>Sample</th>
<th>diagnostics</th>
<th>Conclusions</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>W. Amara et al. (2017)</td>
<td>Maghreb (Argelia)</td>
<td>441</td>
<td>ECG</td>
<td>The inferolateral ER pattern was present in 55 subjects (12.4%). A malign ER (&gt; 2 mm) was present in 5 subjects (9% of ER). An ER pattern was more frequent with young age, male, bradycardia and T wave in V1 lead</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>Ahmed Tageldien Abdellah et al. (2018)</td>
<td>Egypt (General population)</td>
<td>1850</td>
<td>ECG, Holter ECG</td>
<td>ER was prevalent in 124 individuals (6.7%). The most frequent ER types were inferolateral (50%), and antero-lateral (38%). A malign ER (&gt; 2 mm) was only found in 8 patients. Egyptians with ER pattern are generally young, mostly males, lean, and physically fit</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>Gwénolé Rohel et al. (2017)</td>
<td>France (female flight crew)</td>
<td>306</td>
<td>ECG, Holter ECG</td>
<td>The prevalence of early repolarization was 9.2% (28 patients). After 4 years, prevalence drop to 7.5%. Most common type was in inferior leads with 64.3%, with a J-wave of less than 1 mm.</td>
<td>17</td>
</tr>
<tr>
<td>4</td>
<td>Jacob P. Kelly, et al. (2018)</td>
<td>USA (Afro-American population)</td>
<td>4978</td>
<td>ECG, Holter ECG</td>
<td>The frequency of ER in studied population is 1,410 (28%); being the anterior leads 97.8%, lateral leads 8.3%, and inferior leads 2.9% (subjects could have more than one kind of leads; ex, inferolateral) Population with ER were younger, more likely to be male and current smokers, and less likely to have hypertension.</td>
<td>18</td>
</tr>
<tr>
<td>5</td>
<td>Nicolas-Charles Roche et al. (2018)</td>
<td>France (Elite Special Forces)</td>
<td>2,508 Men</td>
<td>ECG, Holter ECG</td>
<td>From the population studied: 1,689 Whites (14% with ER), 388 Afro-Caribbeans (33% with ER) and 431 Asians (27% with ER) - J point ≥0.1 mV: 416 (16.6%), from which were Inferior (53%), Lateral (34%) and Inferolateral (13%) - J point &gt;0.2 mV: 73 (2.4%) from which were Inferior (49%), Lateral (14%) and Inferolateral (37%)</td>
<td>19</td>
</tr>
<tr>
<td>6</td>
<td>Wibke Reinhard et al. (2018)</td>
<td>Germany (Elite Athletes)</td>
<td>623</td>
<td>ECG, Echocardiography, Exercise ECG</td>
<td>The frequency of ER was 17% (108). ER-positive athletes were predominantly male (71%) and showed a lower heart rate and a higher body mass compared to ER-negative. Regarding amplitude of J-wave, 88% were less than 2 mm and malignant form represented 12% Regarding region affected, most common was inferolateral (54%), followed by inferior (28%) and anterior leads(18%)</td>
<td>20</td>
</tr>
<tr>
<td>7</td>
<td>Peter Noseworthy et al. (2011)</td>
<td>Finland (General population)</td>
<td>9690</td>
<td>ECG,</td>
<td>The frequency of ER was 4,4% (423), increasing in male sex and with young age. Also was found that the frequency in patients with siblings with ER increased till 11,6%</td>
<td>21</td>
</tr>
</tbody>
</table>
**Table 4: association of ER and various cardiovascular diseases.**

<table>
<thead>
<tr>
<th>Nr.</th>
<th>Study</th>
<th>Population</th>
<th>Sample</th>
<th>Disease associated</th>
<th>Conclusions</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yuki Hasegawa et al. (2019)</td>
<td>Japan</td>
<td>79 with AF,</td>
<td>Lone atrial fibrillation</td>
<td>Early repolarization in the inferior and/or lateral leads were more common in patients with atrial fibrillation (25%) than controls (10%). The location and magnitude ER were similar between the two groups . Early repolarization may indicate increased frequency to atrial fibrillation.</td>
<td>22</td>
</tr>
<tr>
<td>2</td>
<td>Patrick W. McNair, et al. (2017)</td>
<td>USA</td>
<td>182 with AF,</td>
<td>Lone atrial fibrillation</td>
<td>Patients with lone AF and controls had similar frequencies of ER pattern (15% and. 19%).</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>Alan Sugrue, et al. (2018)</td>
<td>USA</td>
<td>528</td>
<td>Long QT syndrome</td>
<td>Patients (57% female, 43% males) with genotype-confirmed LQTS (283 with LQT1, 193 with LQT2, and 52 with LQT3) were reviewed. ER was shown in 82 patients (15.5%); male/female 50% each. Although ERP is common in LQTS, is that study was concluded that ER was not correlated with diagnosis of long QT syndrome.</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>Navraj Malhi, et al. (2018)</td>
<td>Canada</td>
<td>289</td>
<td>Unexplained cardiac arrest</td>
<td>ER was found in 75 patients. There was a high prevalence of the ER pattern in UCA survivors who had first-degree relatives with the ER pattern (29%). This high prevalence and the similar changes on ECG, suggests that genetically complex factors can contribute to electrocardiographic patterns that predispose to cardiac arrest.</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>Lauri T.A. Holmström et al. (2017)</td>
<td>Finland</td>
<td>275</td>
<td>Non-ischaemic SCD</td>
<td>Hypertensive cardiomyopathy (25%), alcohol related dilated cardiomyopathy (24%), obesity associated cardiomyopathy (23%), and idiopathic myocardial fibrosis (15%) were the most common causes of non-ischaemic SCD. The prevalence of inferolateral ER among non-ischaemic SCD victims is high (20.7% compared to general population 5.3%). Almost all ER patterns are accompanied with the malignant horizontal/descending ST segment morphology (95%) suggesting that inferolateral ER is not only associated with an ischaemic SCD but also a non-ischaemic SCD.</td>
<td>26</td>
</tr>
<tr>
<td>6</td>
<td>Tikkanen et al. (2009)</td>
<td>Finland</td>
<td>10,864</td>
<td>Sudden Cardiac Death</td>
<td>ER in inferior leads was associated with increased risk of death from cardiac causes.</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Author(s)</td>
<td>Country</td>
<td>Participants</td>
<td>Event</td>
<td>Findings</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>------------------------------------</td>
<td>-----------</td>
<td>--------------</td>
<td>-------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Sinner et al. (2010)</td>
<td>Germany</td>
<td>6,213</td>
<td>Sudden Cardiac Death</td>
<td>ER with J point $&gt;$0.2 mV had markedly increased risk of death from cardiac causes. J point $&gt;$0.1 mV: 1,429 (23.9%), 57% male, - Inferior: 30%, - Lateral: 40%, - Both: 30% ERP was associated with a two- to fourfold increased risk of cardiac mortality in individuals between 35 and 54 years. An inferior localization of ER was associated with a particularly increased risk</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Haruta et al. (2011)</td>
<td>Japan</td>
<td>5,976</td>
<td>Sudden Cardiac Death</td>
<td>J point $&gt;$0.1 mV: 1,429 (23.9%), 57% male, - Inferior: 30%, - Lateral: 40%, - Both: 30% ERP was associated with an elevated risk of unexpected death and a decreased risk of cardiac and all-cause death</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Serra-Grima et al. (2015)</td>
<td>Spain</td>
<td>299</td>
<td>Sudden Cardiac Death</td>
<td>Patients with ER: 94 (31.4%) - Inferior: 6.4% - Lateral: 57.4% - Both: 37.2%. After a long follow-up period (24 years), no difference in outcome of sudden cardiac death was seen</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Yun-Jiu Cheng et al. (2017)</td>
<td>China</td>
<td>7268</td>
<td>Sudden Cardiac Death, Ventricular arrhythmias with Structural Heart Diseases</td>
<td>The results suggest that ER may independently increase the risk of VTAs or SCD, including VF, SCA, and SCD, in patients with SHD. It specially increases in ER in inferior leads, high amplitude of J wave (more than 2 mm), a notching morphology, and ER with horizontal or descending ST segment</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Murat Sucu et al. (2018)</td>
<td>Turkey</td>
<td>115 cases</td>
<td>Coronary slow flow phenomenon</td>
<td>ER was more common among cases than among controls (65% vs. 28%). Compared with the controls, cases were more likely to have J-point elevation in the inferior leads (25% vs. 13%), anterior leads (22% vs. 15%) and lateral leads 17.3% vs. 0%.</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Tsukasa Kamakura, et al. (2018)</td>
<td>Japan</td>
<td>34</td>
<td>Coronary artery spasm (CAS) and VF</td>
<td>Out of all the cases, 40% of patients with CAS with documented VF and inferolateral J wave did not experience chest symptoms at the first VF, and could have been misdiagnosed as having ER.</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Michel Haïssaguerre, et al. (2008)</td>
<td>USA</td>
<td>206 cases</td>
<td>Idiopathic ventricular fibrillation</td>
<td>Early repolarization was more frequent in patients with idiopathic ventricular fibrillation than in control populations (31% vs. 5%). Among case patients, those with ER were more likely to be males and with a history of syncope or sudden cardiac arrest during sleep than those without ER. Concluding, patients with a history of IVF, have an increased prevalence of ER.</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Qi Chen et al. (2017)</td>
<td>China</td>
<td>1460</td>
<td>Anterior STEMI, Ventricular arrhythmias</td>
<td>The presence of ER had a multivariable-adjusted association with increased risk of sustained VT/VF in patients with anterior STEMI in the early 30 days</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Tetsuji Shinohara</td>
<td>Japan</td>
<td>50</td>
<td>Variant Angina,</td>
<td>This study suggest that an ER pattern in</td>
<td></td>
</tr>
<tr>
<td>et al. (2018)</td>
<td>Ventricular Fibrillation</td>
<td>VA patients is a risk factor for VF. The presence of ER pattern may be one of the useful factors for indication of treatment in VA.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION OF RESULTS

The variety of studies analyzed provide a sight about how interest about ER has increased in research area worldwide. Also shows the range of incidence of ER in different populations and its related cardiovascular diseases.

In the case of frequency of ER (table 3) is seen how frequency increases in groups with high physical exercise groups, such as professional athletes and military forces, proving also the higher frequency of “benign” ER in those groups. The higher incidence of young males is also a risk marker for developing ER. This frequency is also increased in Afro-American and Asian samples, leading to think that it could be marked as a risk for ER.

On the table 4, a wide range of variety of studies about cardiovascular diseases are shown. Not all of them have been proven to be associated with ER, but the increasing amount of these studies show the increasing interest in proper diagnose of ER and using ER as a possible tool of an early diagnosis and risk marker of multiple cardiac diseases in the future. This interest is especially remarkable in those regarding sudden cardiac deaths and ventricular fibrillations, where in both cases this association has been proven positive.

It’s also remarkable the association of lone atrial fibrillation with ER (table 4) which was proved negative on one study (nr.2; Patrick W. McNair et al.) of 2017 and proved positive in a newer study of researcher Yuki Hasegawa et al. in 2019 from a different country (Japan).
CONCLUSIONS

ER is a relatively new syndrome, which underwent through many different definitions and criteria of diagnostics. These changes and new definitions have created an increased interest in investigators, which have carried multiple studies, proving hypothesis suspected for many years and leading to; in an early future, an appropriate diagnosis of ER and preventing possible diseases associated with it.

Regarding our objective of evaluating the frequency of ER among different populations we can conclude that this range varies depending on ethnicities (Africans and Afro-American have the higher rates), sex (more predominant in males), age (more predominant in young age), work and lifestyle choices (groups with high exercise routines, or high demanding physical work like being an elite athlete or a military have shown higher incidence of ER). Even in high predominance populations of ER, most of cases can be reported as “non-malignant” type due to the amplitude of J-wave (less than 2mm). We can also conclude that the most common affected leads are the inferolateral leads.

Regarding the association of ER with cardiovascular diseases, it can be conclude that many cardiac diseases have a link with ER. The most remarkable one seen from the studies above are sudden cardiac death (SCD) and ventricular fibrillation (VF). Those association could help preventing SCD and VF, using ECG and the early diagnosis of ER as a useful tool and a risk marker. Other risk markers are seen through the results, such as male predominance, high physical activity and ethnicity.
RECOMMENDATIONS

ER is a syndrome which can develop in some cases, not many fortunately, to some cardiac diseases (such as ventricular fibrillation and sudden cardiac death). It’s important for doctors, especially family practitioners to inform their patients and assist those with risk factors according to the criteria mentioned previously to get an early an appropriate diagnosis of ER and prevent possible cardiovascular diseases. Some simple tests can be done regularly in order to prevent and diagnose ER, such as ECG and holter ECG.

Genetic tests looking for specific genes causing ER can be expensive and may not provide as much information to prevent possible consequences as it seems, due to its limitations.

Finally, with an early diagnosis of ER can be prevented or treated more efficiently those cardiovascular diseases, leading to a lower economic costs of the health system.


