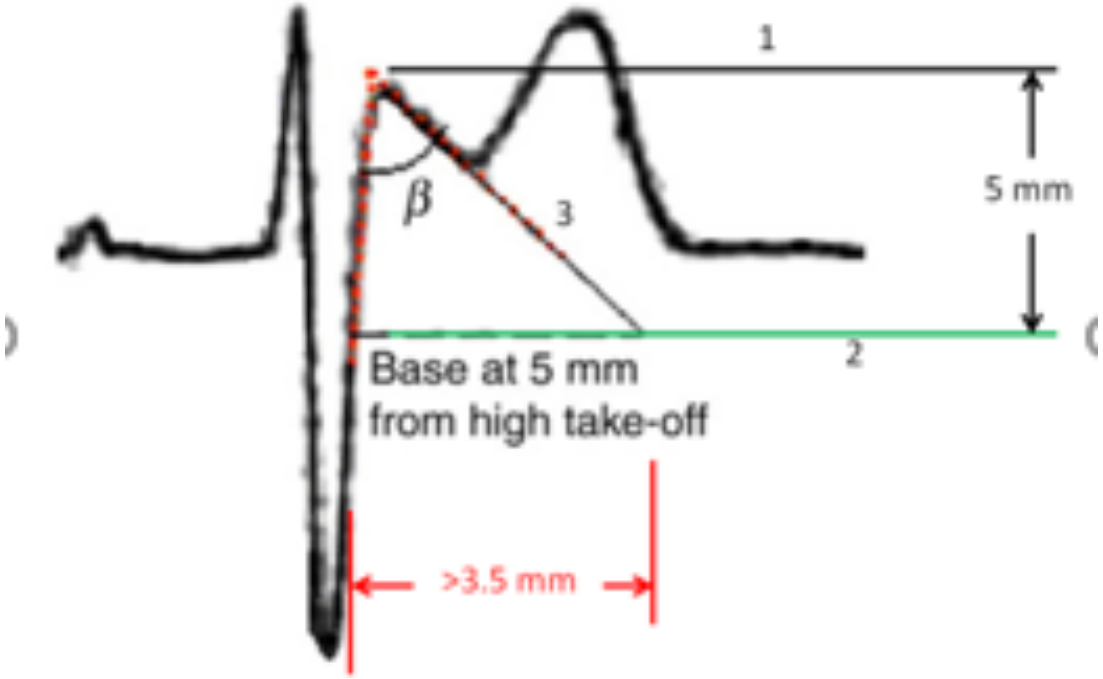
ECG criteria to differentiate the Type-2 BrP from ECG of healthy athletes with r′-wave in leads

Serra et al compared 50 BrS patients with type-2 BrP and positive ajmaline challenge with 58 healthy athletes with an *r′*-wave in leads V1–V2. The triangle formed by the ascendant and descendant arms of the *r′*-wave in leads V1–V2 of two were compared. The duration of the base of the triangle at 0.5 mV (5 mm) from top of r' wave (high take-off) ≥160 ms (4 mm) has a specificity (SP) of 95.6%, sensitivity (SE) 85%, positive predictive value (PPV) 94.4%, and negative predictive value (NPV) 87.9%. The duration of the base of the triangle at the isoelectric line ≥60 ms (1.5 mm) in leads V1–V2 has an SP of 78%, SE 94.8%, PPV 79.3%, and NPV 93.5%. The ratio of the base at isoelectric line/height from the baseline to peak of *r′*-wave in leads V1–V2 has an SP of 92.1%, SE 82%, PPV 90.1%, and NPV 83.3%.(**Serra 2014**). The measurement of the base of the triangle of *r′* in V1 V2 taken at 5 mm from the top of *r′* is much easier to perform than the Chevalier β angle (**Chevalier 2011**) and has even greater accuracy.



1. Draw a horizontal line from top of r' wave (black line 1)
2. Draw a horizontal line 5 mm below this (green line 2)
3. Extend the downsloping r'-ST segment (black line 3) until it intersects the green line Measure the base. If greater than 3.5 mm, then meets criteria (this is equivalent to a 35 degree β angle)

Summary of differential diagnosis of rSr', benign verus malign pattern

A. Benign Patterns: -r' is of fast inscription, unlike in RBBB or Brugada, both of which have a wider R'. Caused by:

1. Higher placement of leads V1, V2
2. Normal variant, with late activation of the inferobasal LV : IRBBB, with delayed conduction through right bundle. No associated adverse outcomes. However, there is a higher incidence of subsequent development of complete RBBB.
3. Athletes: 35-50% due to physiologic RV enlargement: Early repolarization is typically observed in highly trained athletes as a physiologic consequence of increased vagal tone. The variant of anterior (V1 to V3) ER characterized by "domed" ST-segment elevation and negative T wave raises problems of differential diagnosis with the type 1 BrP of BrS. The study compared the electrocardiographic tracings of 61 healthy athletes (80% men, median age 23 ± 8 years), showing "domed" ST-segment elevation and negative T wave in leads V1 to V3, with those of 92 consecutive age- and sex-matched BS patients with a "coved-type" electrocardiographic pattern. Zorzi et al (**Zorzi 2015**) analyzed ECGs of athletes focused on the ST-segment elevation at J point (STJ) and at 80 milliseconds after J point (ST_{80}). The authors verified that Athletes had a lower maximum amplitude of STJ and lower STJ/ST_{80}. All patients (100%) with BrS showed a downsloping ST-segment configuration (STJ/ST_{80} >1) versus only 2 (3%) athletes. An upsloping ST-segment configuration (STJ/ST_{80} <1) showed a sensitivity of 97%, a specificity of 100%, and a diagnostic accuracy of 98.7% for the diagnosis of ER. At multivariate analysis, STJ/ST_{80} ratio remained the only independent predictor for ER (odds ratio 87, 95% confidence interval 19 to 357, p <0.001). In conclusion, the STJ/ST_{80} ratio is a highly accurate ECG parameter for differential diagnosis between anterior ER of the athlete and BrS. These results may help in reducing the number of athletes who undergo expensive diagnostic workup or are unnecessarily disqualified from competition for changes that fall within the normal range of athlete's heart. The takeoff/downstroke of the ST segment in V1 and V2 is not flat enough β-angle not wide enough) for it to be type 2 BrP. A pronounced r'-wave is common in athletes
4. Pectus Excavatum, due to change of heart location in chest.

B. Pathological Patterns: **-r'** often taller then **-r**, with slower ascent/descent

1. Type 2 Brugada pattern
2. RV enlargement, hypertrophy from a variety of pathologies
3. Arrhythmogenic RV dysplasia (ARVC/D)
4. WPW
5. Hyperkalemia
6. Na^+ channel blockers (anti-dysrhythmics, TCAs)

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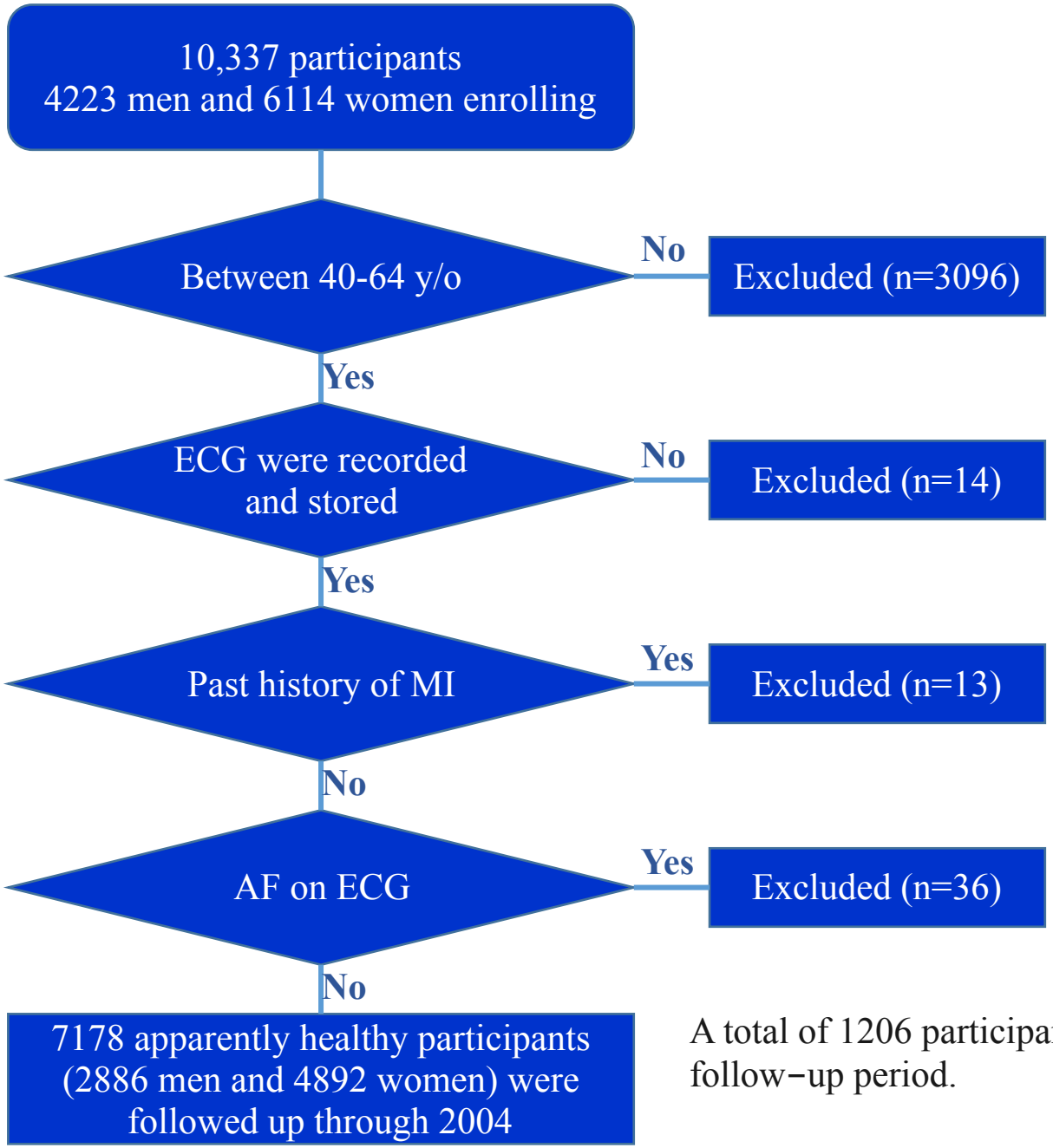
The accuracy of the PPV and NPV will vary according to the prevalence of the disease in the population and therefore are rarely generalizable outside the reported study population. When the prevalence of the disease in low, the PPV decreases and can result in a greater proportion of false positive results (or diagnostic misclassification). This has significant implications for the patient not only in terms of further testing and intervention but as mentioned by the authors this could impact on their ability to perform competitive sports.
For the reason, we ask that the authors consider reporting the likelihood ratios (LRs) for the new ECG criteria. The accuracy of LRs is not affected by the prevalence of the disease in the population(**Grimes 2005**), and therefore constitutes one of the best ways to measure and express diagnostic accuracy (**McGee 2002**). Likelihood ratios enable the clinician to calculate the post-test probability of the disease based on an estimate of the pre-test probability. In essence, LR encapsulate how many times more (or less) likely a patient with the disease has that particular result than patients without the disease. They provide us with how a particular test result predicts the risk of abnormality. Unfortunately, sensitivities and specificities do not provide the clinician with this information; they describe how abnormality or normality predicts a particular test results() **Deeks 2004**).
Reporting of the LRs on the new ECG criteria described by the authors would enable the clinician to refine their clinical judgement without concerns about the disease prevalence (**Sugrue 2015**).

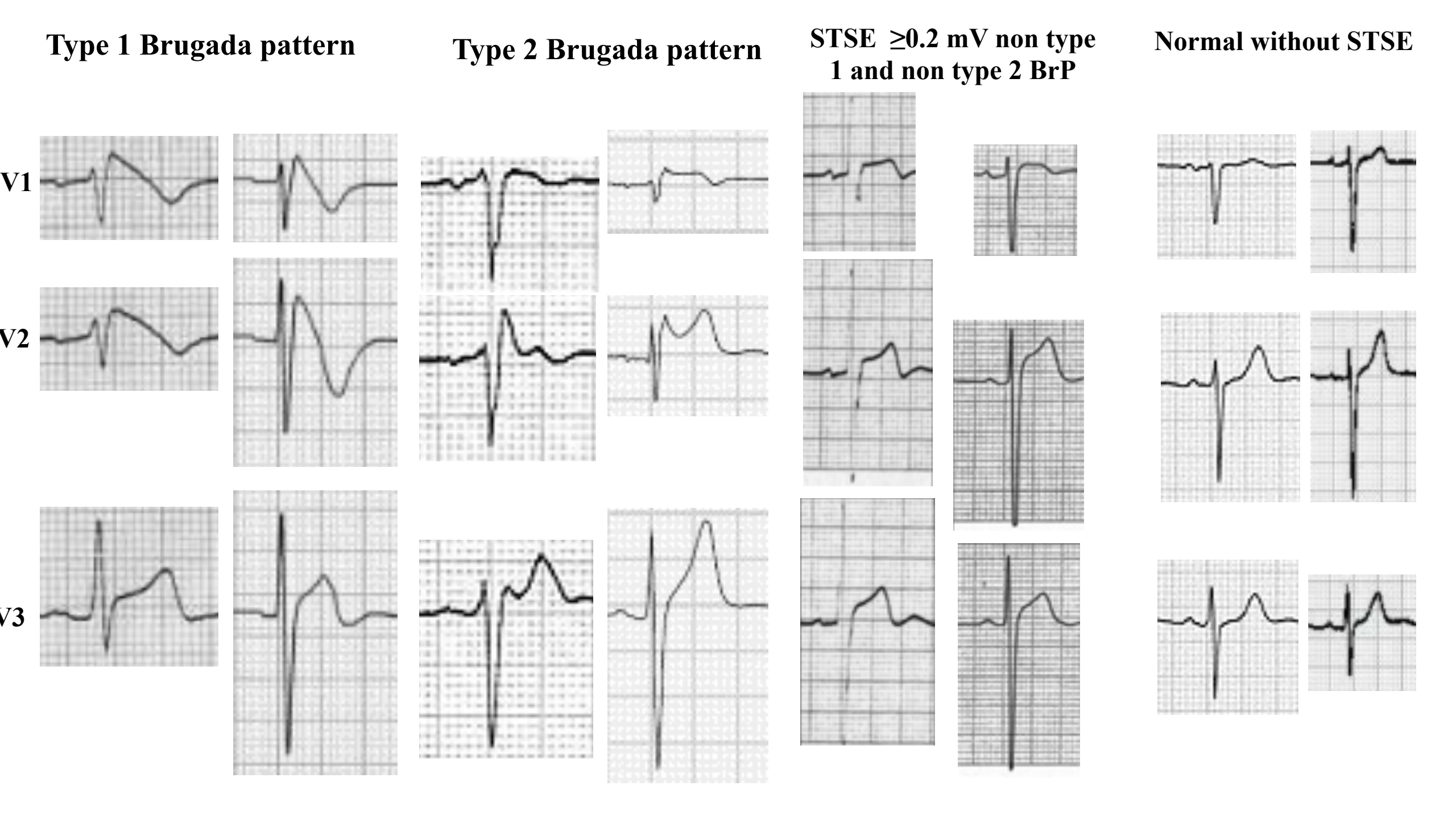
Another STSE pattern on right precordial leads with J point elevation ≥0.2 mV in the right precordial leads non type 1 and non type 2 BrP

Tsuneoka e al (**Tsuneoka 2016**) studied a coorte of 7178 people (2886 men, 4292 women) who constituted the participants of this study
The study included community residents aged 40 to 64 years who enrolled in a community-based cohort of the Circulatory Risk in Community Study (CIRCS). CIRCS is a prospective community-based study that was launched to examine risk factors of cardiovascular disease from 1963 The authors recruited 10 337 participants (4223 men, 6114 women) who underwent a health checkup from 1982 to 1986.
Non coved and non saddle back ST-T morphology with J point elevation ≥0.2 mV in the right precordial leads. The authors observed an interesting finding in this large-scale and long-term observational study: Participants with**: noncoved (type 1 BrP) and nonsaddleback ST-T morphology (type 2 BrP) with J point elevation ≥0.2 mV in the right precordial leads (**STERP) had an excess risk of SCD compared with those in the non-ST group. This study is the first to find that STERP is a distinct clinical entity with a high risk of SCD in the middle-aged Japanese general population. The arrhythmogenic potential of ER in the inferior leads was highlighted by Haïssaguerre et al (**Haïssaguerre 2009**). Nevertheless, in the cohort studies examining ERS, the right precordial leads were not included in the analysis to avoid including BrS or ARVC. Kamakura et al extended the definition of non–type 1 BrS and concluded that the long-term prognosis of probands with non–type 1 BrS was similar to that of probands with type 1 BrS in a hospital-based multicenter study (**Tikkanen 2009**). Moreover, Kamakura et al investigated the significance of non–type 1 anterior ER in patients with idiopathic VF and inferolateral ER in their hospital-based study (**Kamakura 2009**). They concluded that the coexistence of non–type 1 anterior ER was a predictor of poor outcome in patients with inferolateral ER and VF; however, these studies included patients with non–type 1 BrS. Little is known about what ST-T morphology, except for BrS in the right precordial leads, is associated with malignant arrhythmia. Consequently, the authors investigated ECGs with STERP without BrS and analyzed the clinical characteristics and long-term prognosis of participants with STERP. These participants had a markedly elevated risk of SCD compared with those with non-STSE. This report is the first to show a significantly higher risk of SCD in participants with STERP. Additionally, participants with STERP were predominantly male (94.7%) and were significantly younger than participants in the non-STSE group, which is the same as that with BrS and ERS (**Ohira 2012; Tikkanen 2009; Nam 2010**). This suggests a particular young and male background that relates to heredity, hormonal factors, or autonomic nervous function. Haruta et al proposed a hypothesis that testosterone may modulate cardiac mortality in ERS (**Haruta2011**).
Exclusion criteria: 1) Age <40 or >64 years; 2) No previous ECGs on record; Past history of MI; 4) AF. SCD was defined as a sudden unexpected death either within 1 hour of symptom onset (for witnessed events) or within 24 hours of having been observed alive and symptom free.

Flowchart of the entry process for the 7178 participants



A total of 1206 participants (16.8%) died during the follow−up period.


Type 1 Brugada pattern
Type 2 Brugada pattern
STSE ≥0.2 mV non type 1 and non type 2 BrP
Normal without STSE
V1
V2
V3

The plasma concentration of testosterone is higher in men with BrS than in other age−matched men (**Kamakura 2013**) and was reported to increase net Ito of the epicardium, to aggravate the transmural voltage gradient between the epicardium and endocardium, and to lead to the J point seen in ERS and BrS (**Sekiguchi 2013**). In this study, there was no significant difference in body mass index that would indicate an influence by testosterone between the STERP and non−ST groups, indicating that testosterone may not play a leading role in the prognosis of participants with STERP even if it could influence the J point amplitude. Junttila et al (**Junttila 2013**) reported that testosterone levels were closely associated with not only lateral J point elevation but also with a rapidly ascending ST−segment after J point elevation, which Tikkanen et al (**Tikkanen 2011**) reported as being benign in 3 types of ST−segments (ascending, horizontal, or descending.) The mechanism of the J point in the right precordial leads associated with testosterone would be the same as that in the inferior leads.

In the large number of participants without BrS, the higher amplitude of the J point in the right precordial leads was significantly associated with SCD incidence. A hospital−based study with a small number of participants (n=85) reported that the incidence of SCD of probands with non–type 1 BrP including ECGs with a J point amplitude ≥0.1 to <0.2 mV was similarly as high as those with type 1 BrP (**Kamakura 2013**). In terms of J point amplitude, our result is identical to that of a previous large−scale community−based study that investigated the inferior leads and showed that J point elevation of at least 0.1 mV in the inferior leads was associated with a high risk of cardiac death, and J point elevation of >0.2 mV in the inferior leads had a higher risk of arrhythmia events and cardiac death (**Nam 2010**). Similarly, the authors focused on the right precordial leads in this middle−aged Japanese general population without BrS and revealed that the amplitude of the J point elevation in the right precordial leads had some prognostic value, and there was a higher risk of SCD among participants with a markedly elevated J point (>0.2 mV) than among those with more moderate elevation (≥0.1 mV).

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