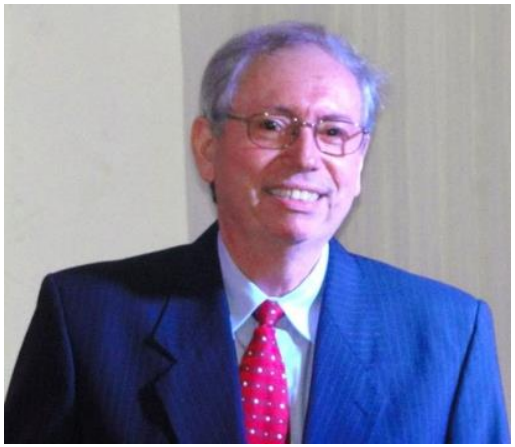
“Electrocardiographic pattern resembling Brugada pattern by compressive tumor: Brugada phenocopy?”



https://ekgvcg.wordpress.com/

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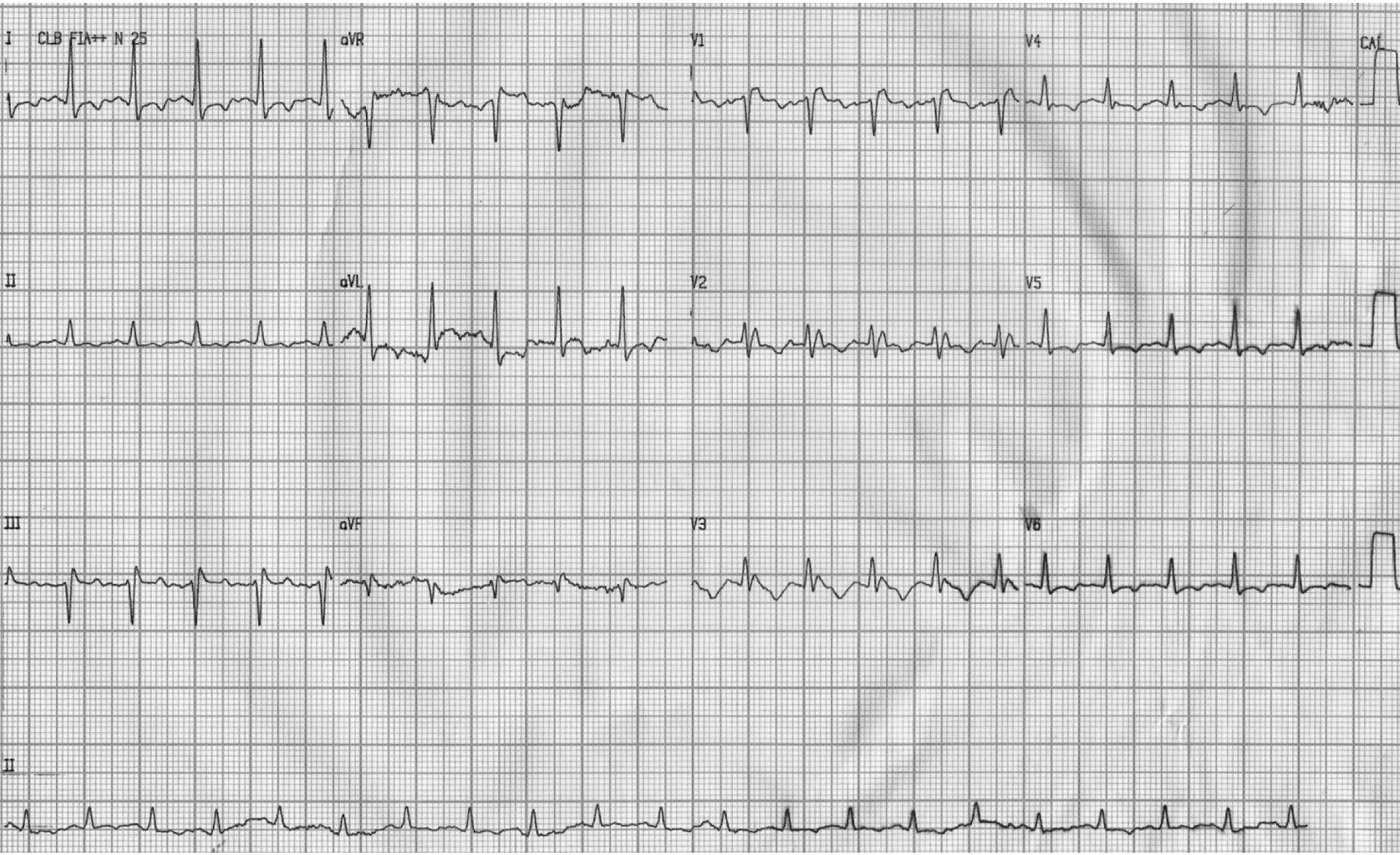
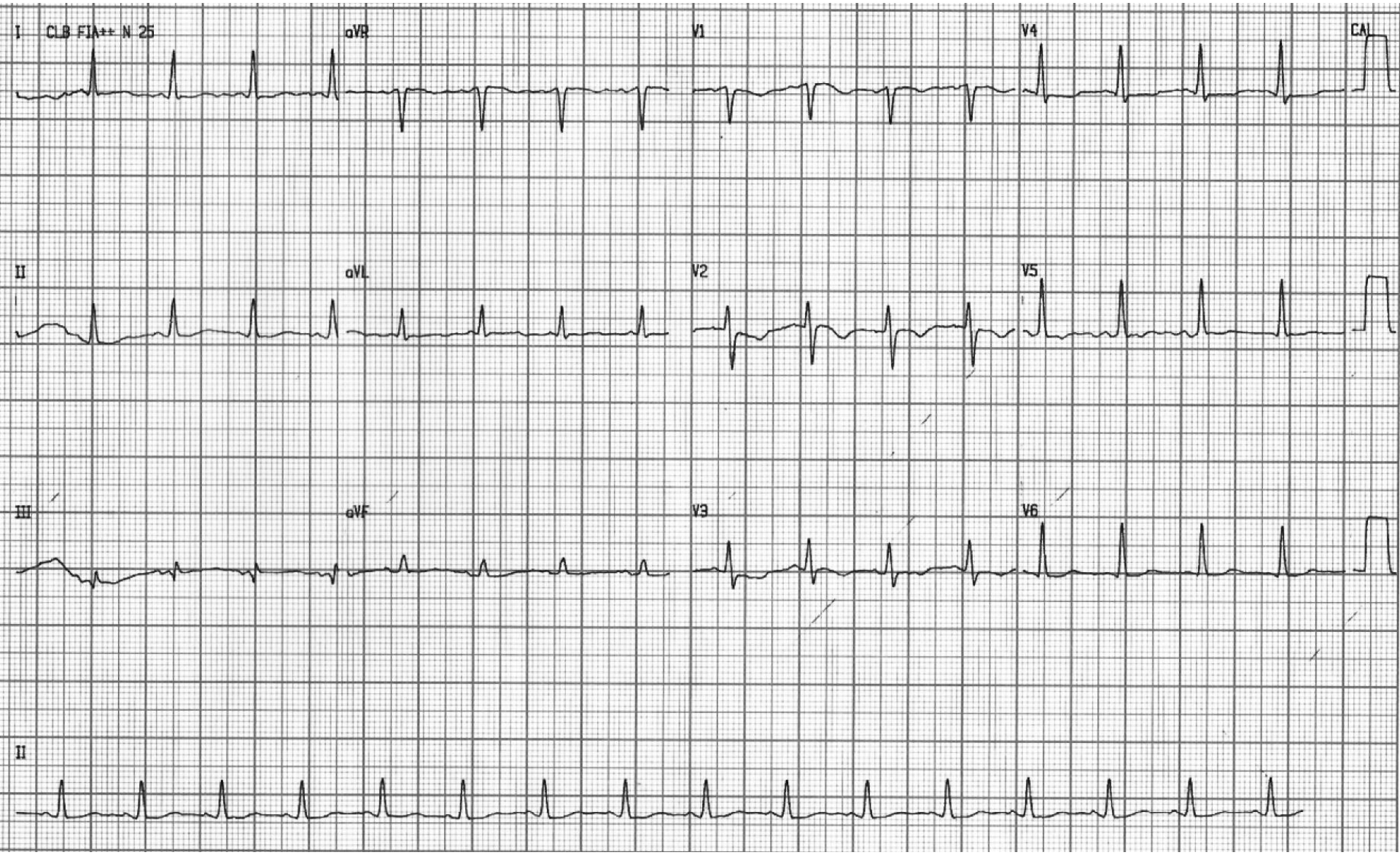
Spanish: Hombre, 50 años, Caucasiano, portador de linfoma de predominio mediastinal con derrame pericárdico voluminoso e importante compresión del tracto de salida de ventrículo derecho.
Antecedentes familiares negativos.
Ecocardiograma: escamen realizado en condiciones técnicas adecuadas. Cámaras cardiacas de diametros e espesor de las paredes normales, ventrículo izquierdo con hipocinesia difusa y función sistólica global reducida (fracción de eyección del ventrículo izquierdo de 45%), análisis de la función diastólica del ventrículo izquierdo perjudicada por la restricción al flujo mitral aproximadamente 62% con la inspiración), válvulas mitral y aórtica con discreto reflujo, ventrículo derecho con restricción diastólica importante, válvula tricúspide con análisis dificultada por el colapso de las cámaras derechas, derrame pericárdico importante con señales de inminentes taponamiento, vena cava inferior dilatada (2,1 cm) sin colapso inspiratorio. La tomografía computadorizada torácica muestra conglomerado ganglionar del mediastino y gran derrame pleural.
¿Cuál es el mas probable diagnóstico clínico-electrocardiográfico?
¿ Cuales son los pasos a seguir para el diagnóstico de certeza?

English: Man, 50 years old, Caucasian, carrying large mediastinal lymphoma with significant compression of the right ventricular outflow tract with large pericardial effusion. Negative familial background for genetic disease.
Transthoracic echocardiogram (TTE) performed in good technical condition. cardiac chambers diameters and thickness of normal Left ventricle with diffuse hyperkinesia and overall reduced systolic function (LVEF= 45%). Analysis of diastolic LV function impaired by the restriction of the mitral flow approximately 62% with inspiration). Mitral and aortic valves with discrete reflux, RV with significant diastolic restriction, tricuspid valve with analysis hampered by the collapse of the right chambers, significant pericardial effusion with signs of impending blockage, inferior vena cava dilated (2,1 cm) without inspiratory collapse.
Thoracic computed tomography shows mediastinal nodal conglomerate and large pleural effusion.
What is the most likely clinical and electrocardiographic diagnosis?
What are the steps for definitive diagnosis?

ECG1 Before pericardial drainage

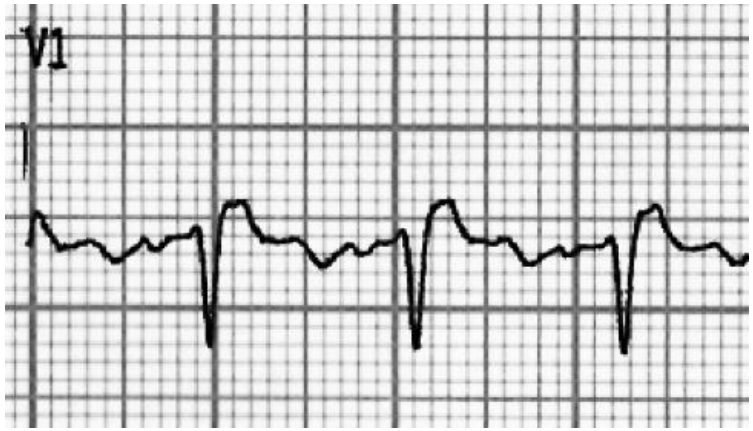


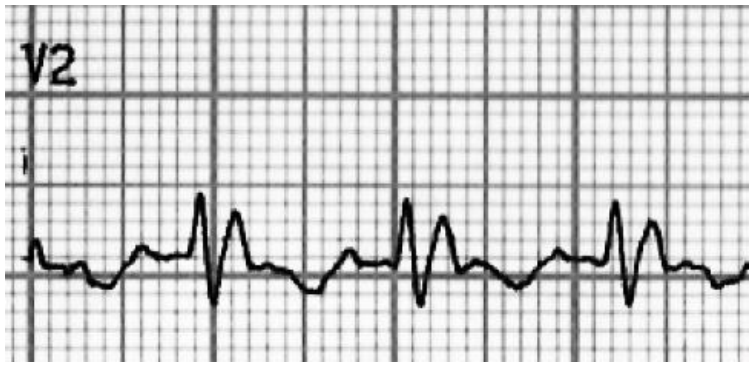
ECG2 After pericardial drainage

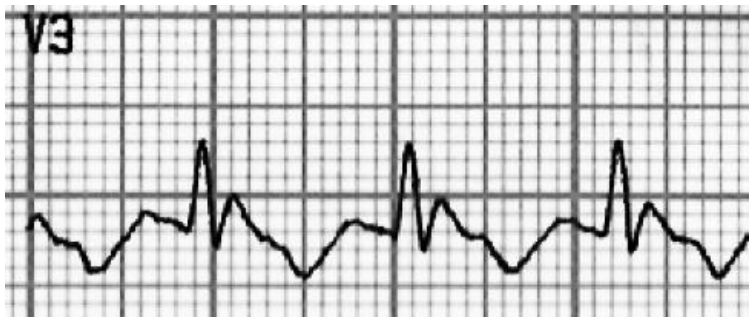


Right precordial leads

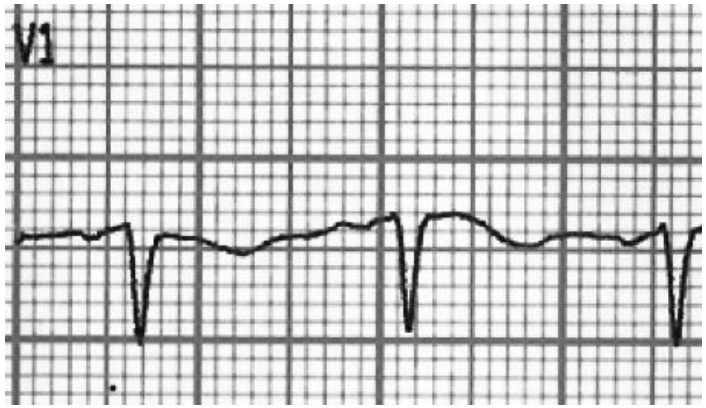
Before pericardial drainage

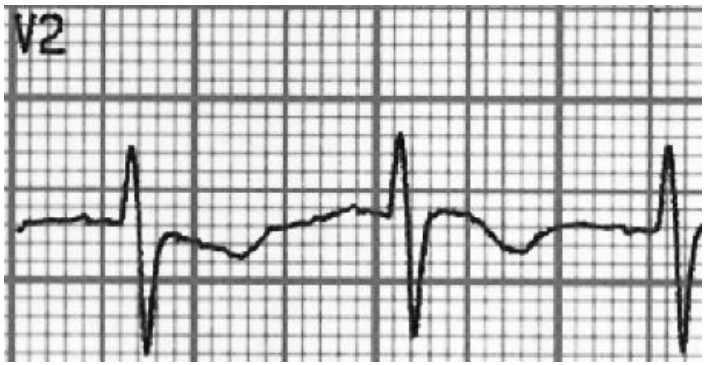


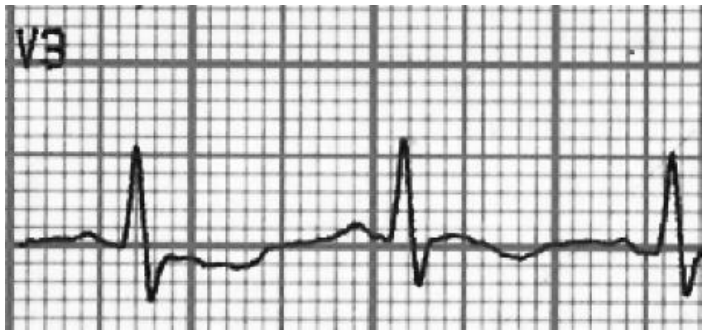


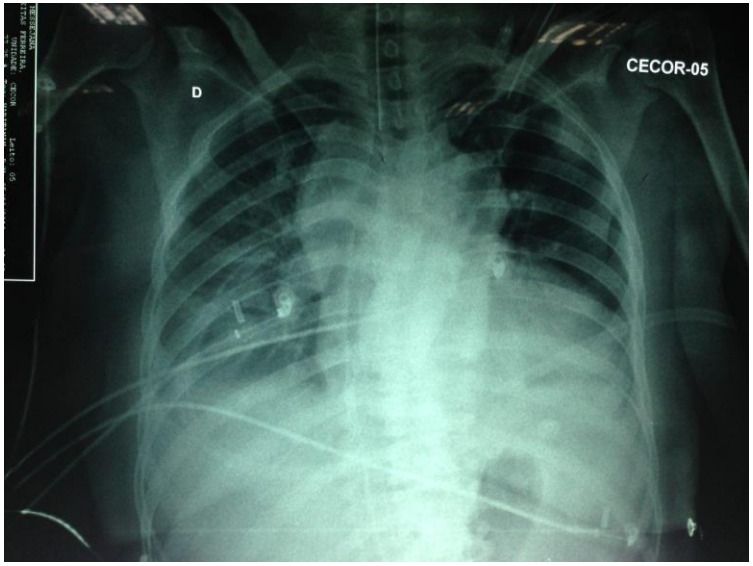


After pericardial drainage





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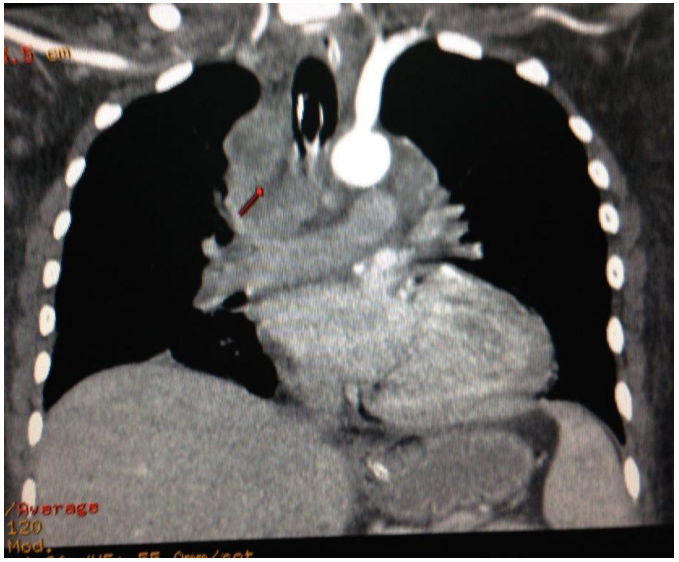
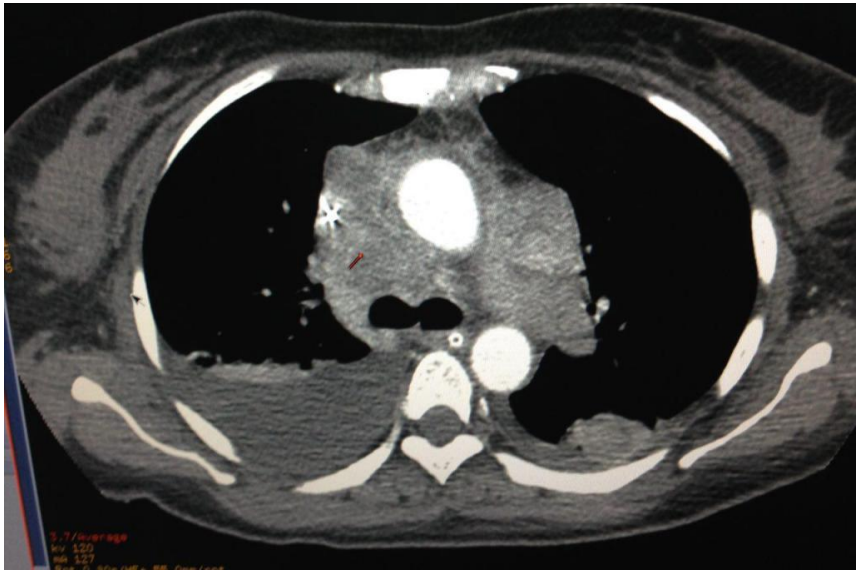
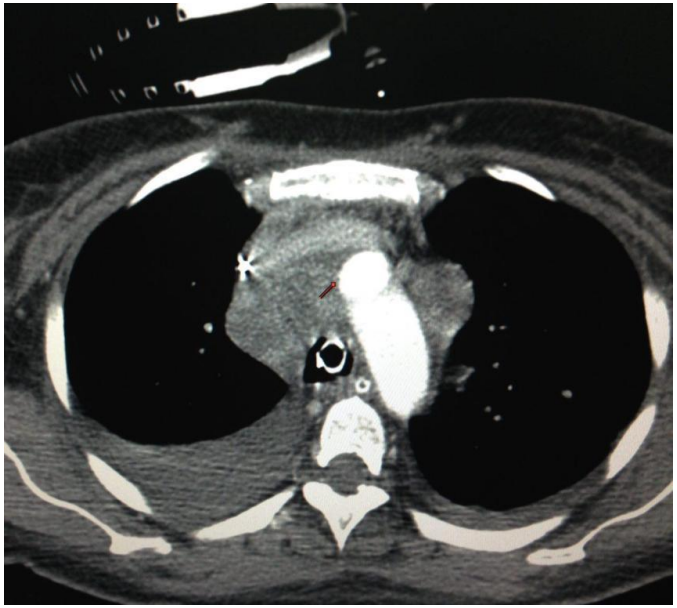






Colleagues opinions

Spanish Estimados Andrés y Raimundo: Ustedes han enviado el caso como siendo patrón Brugada. Al revisarlo encuentro discordancia en esto. Analizare lo que observo en el ECG.

1. **Taquicardia sinusal que mejora luego del drenaje pericárdico.**
2. **El intervalo PR disminuye su duración luego del mismo.**
3. **El eje eléctrico se encuentra más a la izquierda en el 1er ECG y se normaliza luego del drenaje, lo que interpreto posicional.**
4. **Incremento de la duración del QRS principalmente afectando las precordiales derechas de V1 a V3. Con patrón rSR y trastornos de la repolarización y prolongación del QTc.**
5. **El patrón resuelve luego del drenaje pero los trastornos de la repolarización continúan en precordiales derechas. Ustedes refieren patrón Brugada más yo encuentro una apenas un retraso de las fuerzas finales del QRS que llegan a afectar a V3. Al intentar medir el ángulo en V1 y V2, No encuentro que sea positivo para un patrón de Brugada, En V3 si pero no puedo considerar a esta para el diagnostico del mismo. Obviamente presenta una pericarditis por los criterios ECG. Más el patrón electrocardiográfico simula una ARVD, Más me encantara poder observar su análisis y evaluar como ha realizado la medición del ángulo, así aprende a poder medirlo en presencia de retraso de las fuerzas finales del QRS en V1 y V2.**

Un gran abrazo y muy felices pascuas para todos!

Martín Ibarrola

English

Dear Andrés and Raimundo,
You sent the case as if it was Brugada pattern. I checked it and I disagree. I will analyze what I see in the ECGs.

1. Sinus tachycardia that reverts after pericardial drainage.
2. The PR interval decreases its duration after ii
3. The electrical axis is shifted to the left in the 1st ECG that normalizes after drainage, which I interpret is positional.
4. Increase in QRS duration mainly affecting the right precordial leads from V1 to V3. rSR pattern and repolarization patterns and QTc prolongation.
5. The pattern is solved after drainage, but not so repolarization disorders that continue in the right precordial leads. You mention the existence of Brugada pattern, but I find only a delay of the final forces of QRS, that affect V3, because I do not find the beta angle to be positive for Brugada pattern. Yes in V3, but I cannot consider it for the diagnosis. Obviously, there is pericarditis considering the ECG criteria.
6. The electrocardiographic pattern resembles ARVD.

I will enjoy your analysis and analyzing how was the angle measurement made; thus I will learn to measure it in the presence of delay of QRS final forces in V1 and V2.

Warm regards and Happy Easter everyone!

Martín IbarrolaM.D. Buenos Aires Argentina

English

Answer from Andrés to Martin

Dear Martín,

Your analysis was brilliant, reflective and thorough.

You should just specify which angle do you mean, because not everyone knows what angle you are talking about. This forum is not constituted just by experts. Of course we know you mean the β angle; i.e. the angle made up by the ascending and descending ramp of r' in V1-V2. You are so right. In true Brugada pattern, according to the last consensus, this angle should be ≥58° (**Bayes de Luna 2012**). Dr. Chevalier, the pioneer of its name (**Chevalier 2011**), attributes a discretely greater mean value to it: 62±20°, so according to Chevalier, the Brugada pattern should be a β angle of at least 42°, and in this case it is just 30°. Thus, your criticism is relevant. We inappropriately titled the case, "**Brugada electrocardiographic pattern in a patient with compressive mediastinal tumor: Brugada phenocopy?**", when it should be "**Electrocardiographic pattern resembling Brugada pattern by compressive tumor: Brugada phenocopy?**"

We'll change the name.

About your statement that it seems ARVD/C, it is really an observation by someone who is very knowledgeable on ECGs. I had commented this with Adrián and Raimundo previously. In the slides 20 and 23 this is clarified.

I am extremely happy to see that you analyze the tracings wonderfully, showing your critical mind and your spectacular advancement in this field.

Andrés.

Spanish Respuesta de Andrés para Martín

Estimado Martin tu análisis fue brillante, sesuda y completa.

Apenas deberías especificar a qué ángulo te refieres porque no todos saben de qué ángulo estás hablando. Este foro no está formado apenas por expertos. Es claro que sabemos que te refieres al ángulo β es decir al ángulo formado por la rampa ascendente y descendente de la r' en V2. Estas cubierto de razón. En el verdadero patrón Brugada según el último consenso este ángulo debe ser ≥ 58° grados (Bayes de Luna 2012). Ya el pionero de la denominación, la doctora Chevalier (Chevalier 2011) le atribuye valor medio discretamente mayor: 62 ± 20° por lo tanto según Chevalier el patrón Brugada tiene que tener un ángulo β como mínimo de 42, este caso es de apenas 30°. Consecuentemente tu critica es procedente. Nosotros intitulamos impropiamente al caso "Brugada electrocardiographic pattern in a patient with a compressive mediastinal tumor: Brugada phenocopy?" Cuando debería ser: Patrón electrocardiográfico semejante al patrón Brugada por tumor compresivo: ¿Fenocopia Brugada?

Vamos a cambiar el nombre.

En relación a tu aseveración que parece una ARVD es realmente una observación de alguien que entiende mucho de ECG. Yo había comentado esto con Adrian y Raimundo previamente. En las diapositivas 20 y 23 queda esclarecido.

Me deja extremamente feliz de observar que analizas maravillosamente los trazados denotando tu agudo espíritu crítico y tu espectacular progreso en este campo.

Andrés.

Spanish: Buenas tardes y felices Pascuas a todos los integrantes del foro.

.Este caso se trata de un paciente de 50 años, con un linfoma mediastinal complicado con derrame pleural y pericárdico severo (lo cual hace suponer invasión del mismo a este nivel). Los cambios observados en el ECG en un proceso pericárdico son debidos al compromiso de las fibras musculares epicárdicas, ya que el pericardio no es excitable. Estos cambios son originados por múltiples causas: proceso inflamatorio, compresión e isquemia de la fibras miocárdicas por aumento de presión y compresión intrapericárdica, hiperemia reactiva, aumento de las concentraciones de K^+ en el líquido pericárdico que puede originar cambios del punto J, onda J y alteraciones del ST/T. En el caso presentado, como bien menciona Martín hay un cambio de eje entre ambos ECG que pueden ser posicional y a mi tampoco me impresiona un patrón típico de Brugada. El primer ECG muestra un RS más taquicárdico, las alteraciones de aVR, aVL y aVF me impresiona como artefactos y no como la alternancia eléctrica que se observa en los derrames severos. El primer vector esta orientado hacia la izquierda, abajo y adelante, el complejo QRS presenta primero una rotación anti horaria para luego ser horaria, con un eje de R desviado hacia la izquierda (-10º). De V1 a V4 mide 120 mseg y presenta no se si una onda r´ o una onda J, hecho que no voy a poder diferenciar en el ECG de superficie; el segmento ST esta rectificado en forma difusa, con ondas T negativas cuyo eje se oponen al eje del complejo QRS.

Después de la pericardiocentesis el primer vector del complejo QRS se sitúa hacia abajo a la derecha y adelante, con un complejo QRS con rotación horaria, con un eje de R en 30º, con desaparición del trastorno final del complejo QRS de V1 a V4 y las ondas T tienden a normalizarse

.Estos derrames pericárdicos son rápidamente reproducibles. Lo más importante en este caso es el tratamiento de la patología de base y evitar la nueva formación del derrame. No se a que se debe la hipocinesia generalizada por lo cual debería realizar otro ecocardiograma posterior para ver si el derrame la favorecía o era independiente de él.

Afectuosamente

Isabel Victoria Konopka MD Hospital Argerich Buenos Aires.

English: Good afternoon and Happy Easter for the members of the Forum. This case is a 50-year-old patient with mediastinal lymphoma complicated by pleural effusion and severe pericardial effusion (which leads to the assumption of invasion of it at this level). The changes observed in the ECG in a pericardial process are due to the involvement of epicardial muscular fibers, since the pericardium is not excitable. These changes originate by multiple causes: inflammatory process, compression and ischemia of myocardial fibers by increase in pressure and intrapericardial compression, reactive hyperemia, increase in K+ concentrations in the pericardial fluid that may originate changes of the J point, J wave and ST/T alterations. In this case, as Martín mentioned, there is an axis shift between both ECGs that could be positional, and for me it is not a typical Brugada pattern either. The first ECG shows a more tachycardic SR; the aVR, aVL and aVF alterations seem artifacts, unlike the electric alternation observed in severe effusions. The first vector is heading to the left, below and forward; the QRS complex presents first counterclockwise rotation, to become clockwise later, with axis of R shifted to the left (-10°). V1 to V4 measures 120 ms and it presents either r' wave or J wave, I'm not sure, a fact that I will not be able to differentiate in surface ECG; the ST segment is rectified in a diffuse way, with negative T waves, the axis of which oppose the QRS complex axis. After pericardiocentesis, the first vector of the QRS complex is located below and to the right and forward, with QRS complex with clockwise ration, with an axis of R in 30°, with disappearance of the final QRS complex disorder from V1 through V4, and T waves tend to normalize. These pericardial effusions can reproduce quickly. The most important issue in this case, is the treatment of the base pathology and preventing new effusion formation. I don't know the reason for the widespread hypokinesis, so another subsequent echocardiogram should be made, to verify if the effusion fostered it or was independent from it. Warm regards,

Isabel Victoria Konopka M.D. Hospital Argerich Buenos Aires.

Final comments

Conclusion

In the present case the pattern does not have the typical criteria for Brugada ECG pattern. Consequently, it is not a Brugada phenocopy. Why? Because:

1. The β angle is very acute. It has only 30° (see slide 21). It is necessary at least 36.8° to fulfill the criteria (**Serra 2015**), 42° (**Chevalier 2011**) or ≥ 58° (**Bayés de Luna 2012**).
2. The base of the triangle < 160 ms (see slide 23).
3. The tangent line is near the vertical line (see slide 20).
4. Located QRSd prolongation from V1 to V3. This feature is characteristic of ARVC/D and is related with the amount of fibrotic tissue in patients with VT that originate in the RV (see slide 24).

   QRSd V1 + V2 + V3 / QRS dV4 + V5 + V6 >1.2.

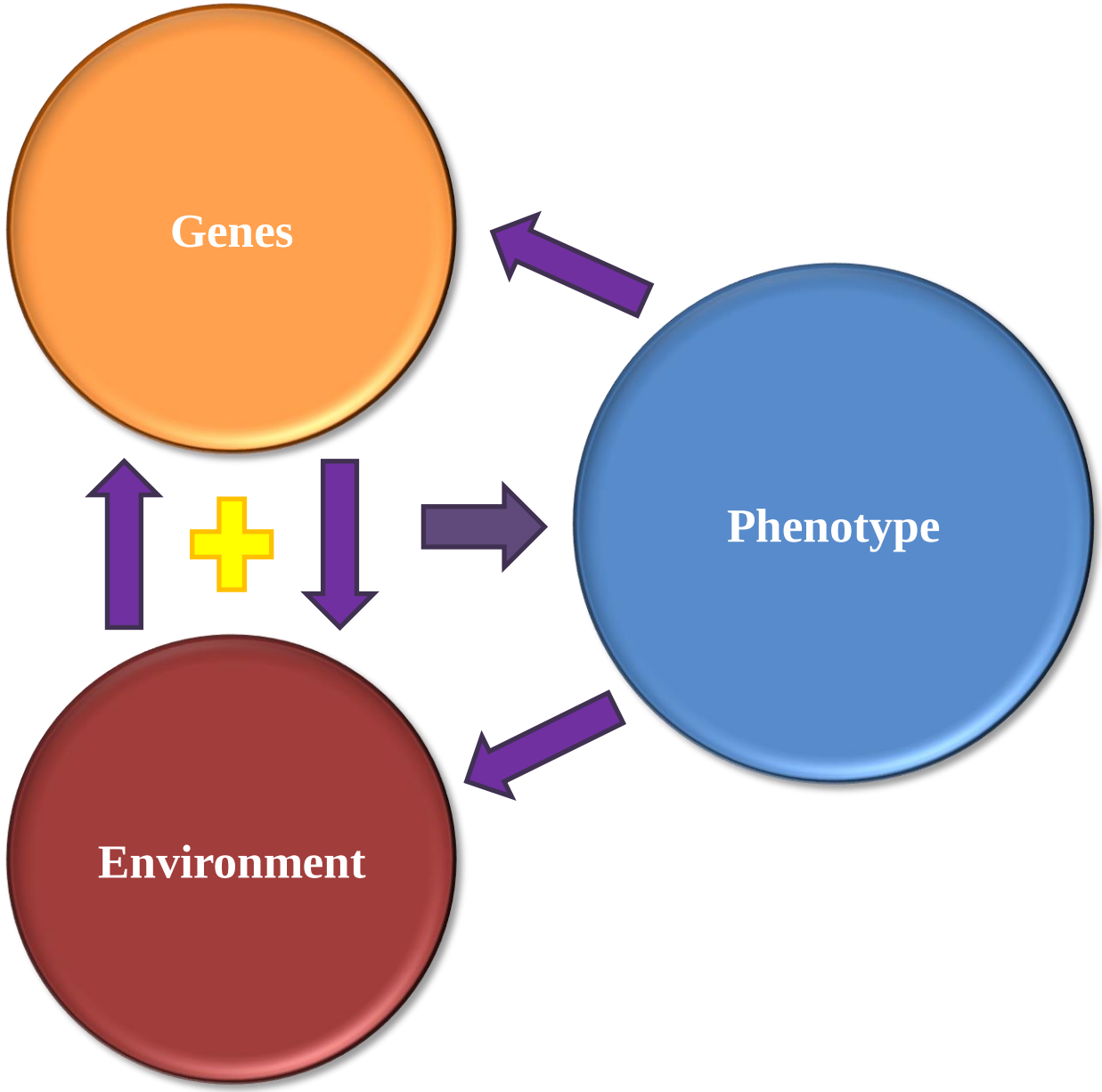
   QRSd of $^{V1+V2+V3}$ / $_{V4, V5 \text{ and } V6}$ $\geq$ 1.2

Theoretical considerations about Brugada phenocopies

What is the definition of a phenocopy? A phenocopy is an environmental condition that imitates (copies) the phenotype produced by a gene. The term phenocopy was coined by Richard Benedict Goldschmidt at the beginning of the past century (**Goldschmidt 1935**). He was a visionary Jewish-German-born American unorthodox geneticist. He did not believe that Charles Darwin's idea of slow and gradual changes could account for the origin of species. Brugada phenocopy describes conditions that present with a Brugada ECG pattern (BrP) but without true congenital channelopathy Brugada syndrome (BrS) considered a primary electrical heart disease with apparent structurally normal heart (**Dendramis 2016**) often involving the inward sodium current. Brugada phenocopies are clinical entities that present with an ECG pattern phenotypically identical to either the type 1 or type 2 Brugada patterns yet differ etiologically from true BrS (**Awad 2013**). New methodologies for measuring Brugada ECG patterns of type 1 Brugada ECG patterns such us the β-angle (cut-off values of ≥ 58° for the β-angle) and the base of the triangle (≥4mm for the base of the triangle), cannot differentiate the ECG pattern of BrS from Brugada phenocopy (**Gottschalk 2016**).

The pattern presents in association with an identifiable condition and, upon resolution of that condition, the ECG pattern normalizes. Brugada phenocopy is not due to a congenital sodium channel abnormality. Indeed, the defining feature of Brugada phenocopy is the absence of true congenital BrS. Therefore a provocative test with a sodium channel blocking agent such as ajmaline, flecainide, or procainamide will not reproduce the ECG pattern (**Baranchuk 2012**).

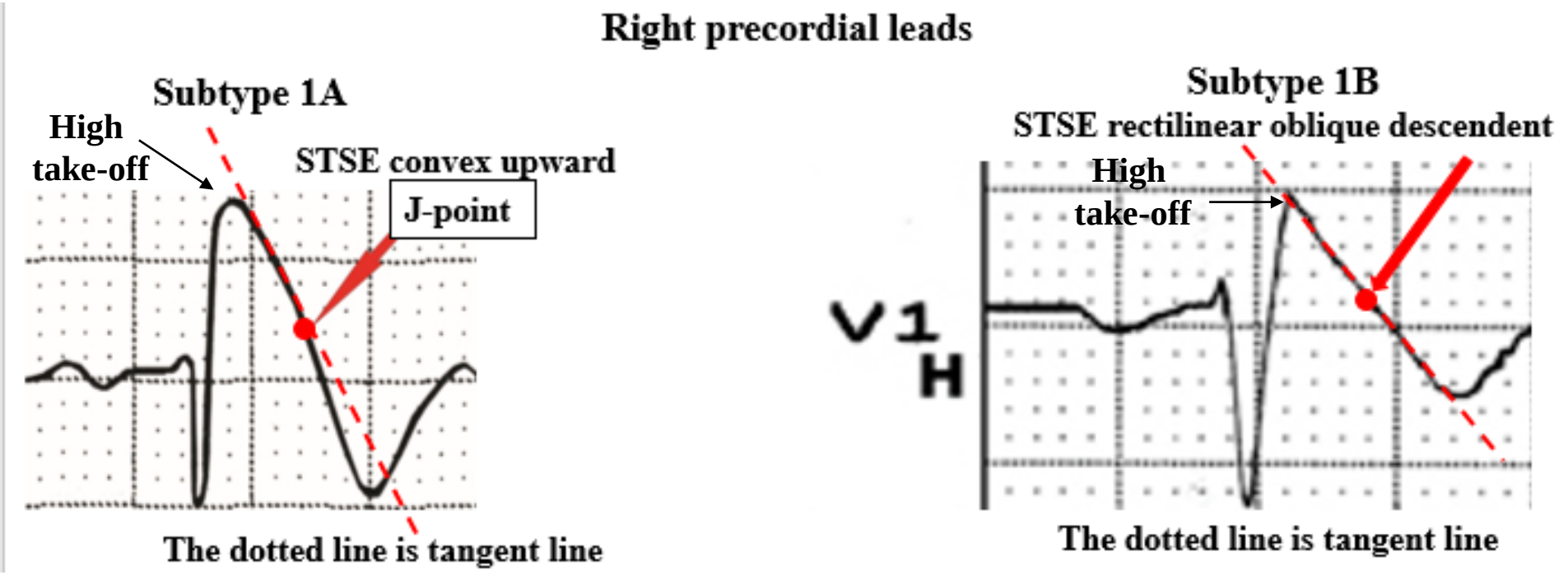
Brugada syndrome and Brugada ECG Pattern: BrS is a heterogeneous genetic cardiac channelopathy, considered a primary electrical heart disease with autosomal dominant transmission and variable penetrance, conferring a predisposition to sudden cardiac death due to polymorphic ventricular tachycardia/ventricular fibrillation (PVT/VF) in the absence of over structural heart disease. The pathogenesis of the entity is most likely a combination of both genetically determined repolarization abnormalities and conduction delay in the right ventricular outflow tract (RVOT) epicardium (depolarization abnormality). Additionally, phenotype is the appearance of an organism or part of them (i.e. electrocardiogram pattern) resulting from the interaction of the genotype and the environment (Figure next slide).



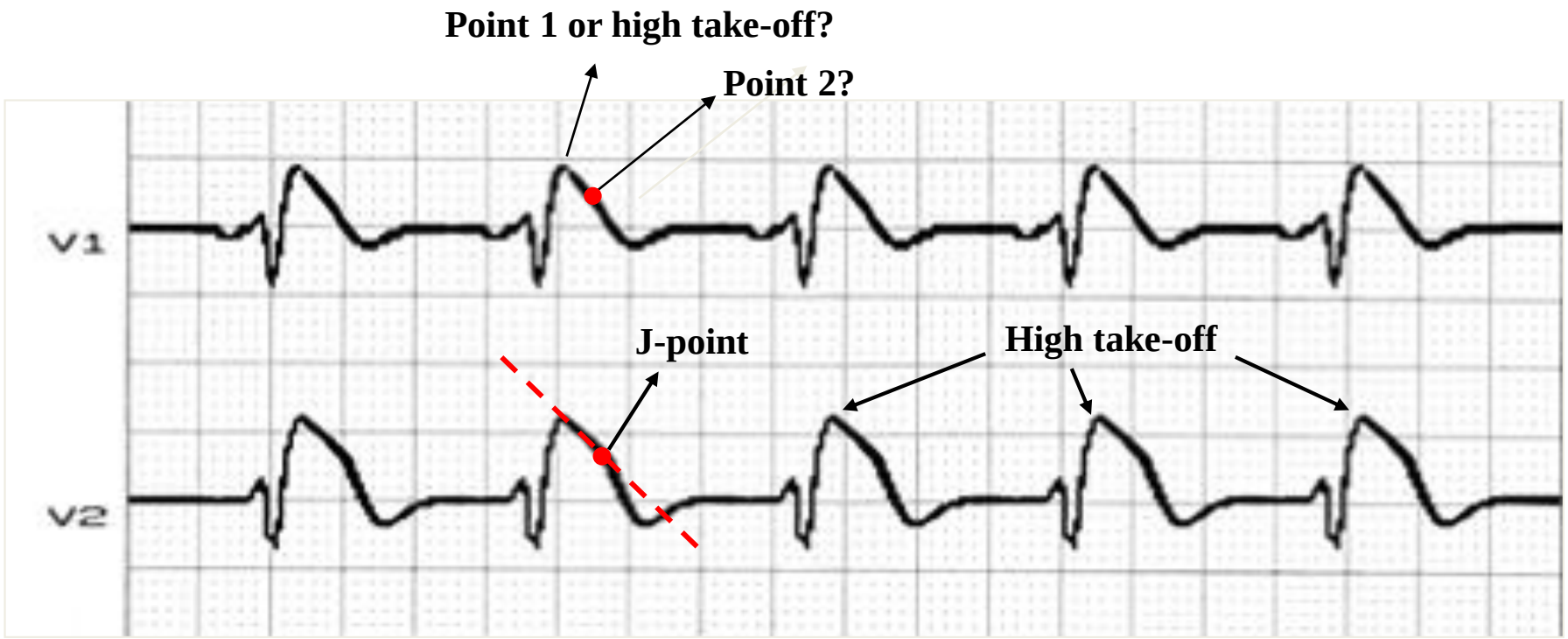
The interaction of genes and environment in the determination of phenotype.

ECG abnormalities constitute the hallmark of BrS. Unfortunately, ECG patterns are often concealed, exhibiting profound day-to-day and beat-to-beat variation in amplitude and morphology. Electrocardiographically, true congenital BrS is characterized by two ECG patterns in the right precordial leads (V1-V3). These patterns involve J point and ST elevations that produce either the type 1 "*coved*" or type 2 "*saddleback*" patterns (**Bayés de Luna 2012**).

The Type-1 electrocardiographic (ECG) Brugada pattern has a high take-off J point and ST segment elevation ≥2 mm, with upper convexity(subtype 1A) or descending oblique rectilinear(subtype 1B) followed by negative T wave on right precordial leads (V_1-V_2 or from V_1 through V_3) and/or high right precordial leads V_{1H}, V_{2H} and V_{3H}. New methodologies for measuring Brugada ECG patterns of type 1 Brugada ECG patterns such us the β-angle (cut-off values of ≥ 58° for the β-angle) and the base of the triangle, (≥4mm for the base of the triangle). cannot differentiate the ECG pattern of BrS from Brugada phenocopy (**Gottschalk 2016**) (Figure below).

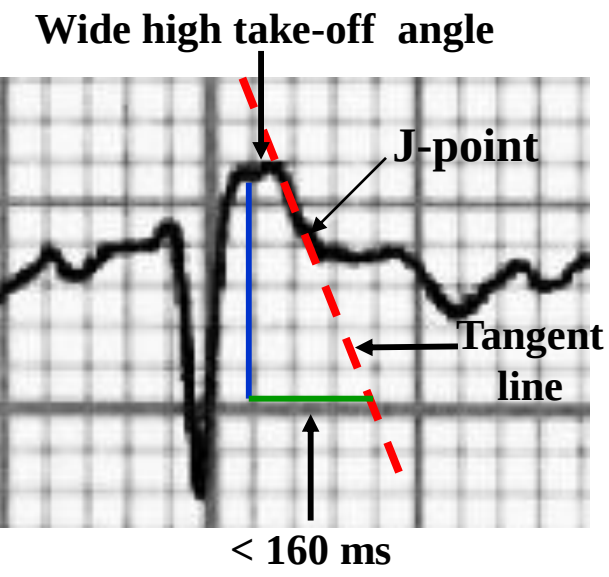


Where is the end of QRS complex?

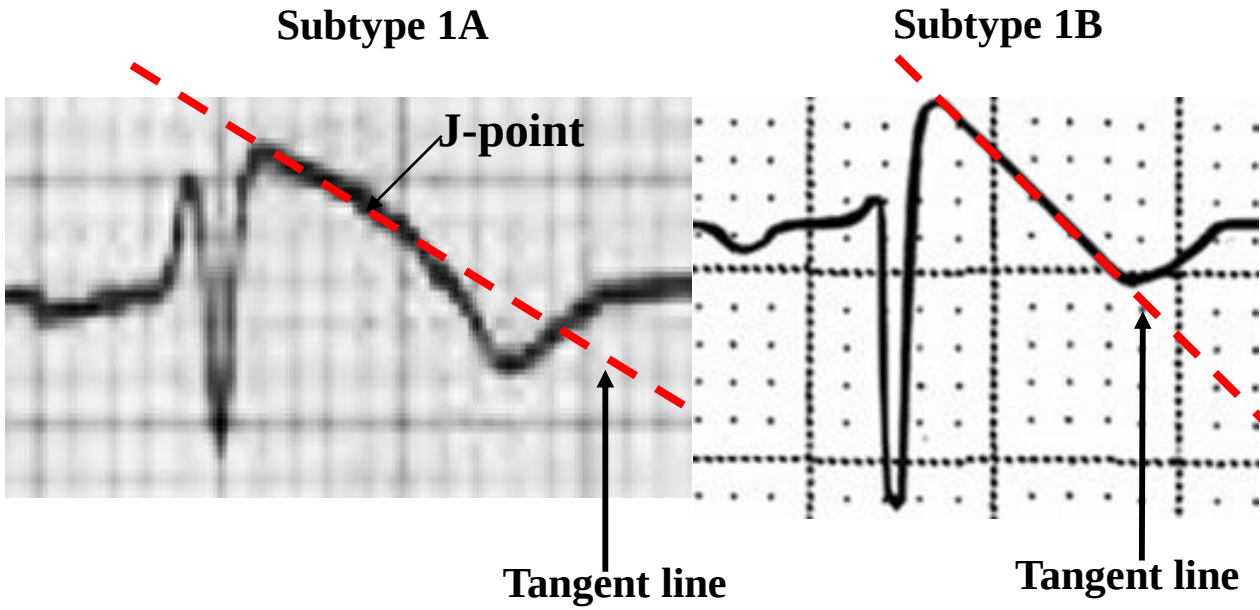


Answer: Point 2 because it is coincident of J-point. It is approximate point of convergence between the end of QRS complex and the onset of ST segment. It is considered the point at which the QRS complex finishes and the ST segment begins. The J-point is an essential landmark for measuring QRS duration and ST segment elevation and/or depression. J-point represents approximate the end of depolarization and the beginning of repolarization as determined by the surface ECG. There is an overlap of ≈10 milliseconds (**Mirvis 1982**).
The J point is used to measure the degree of ST elevation or depression present. It is very important in ACS-ST segment elevation myocardial infarction (STEMI).

V1 the present case



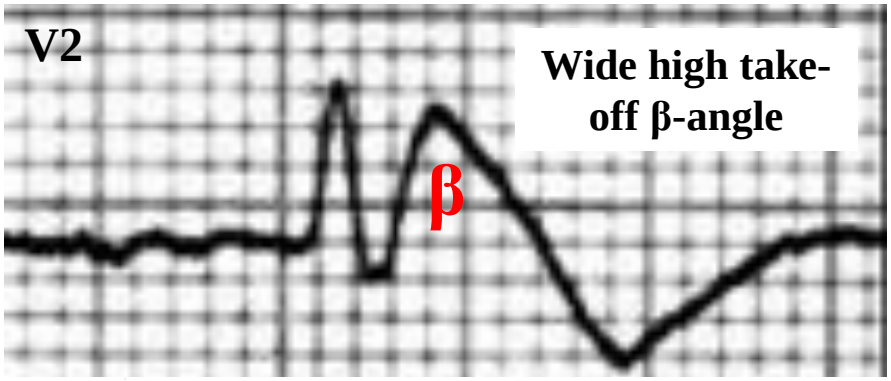
V1 truly Brugada type 1 pattern



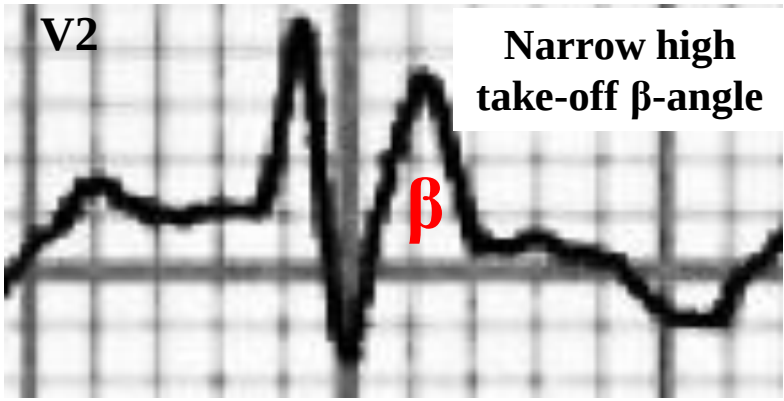
Atypical type 1 Brugada pattern because the tangent line is near the vertical line and the base triangle is < 160 ms.

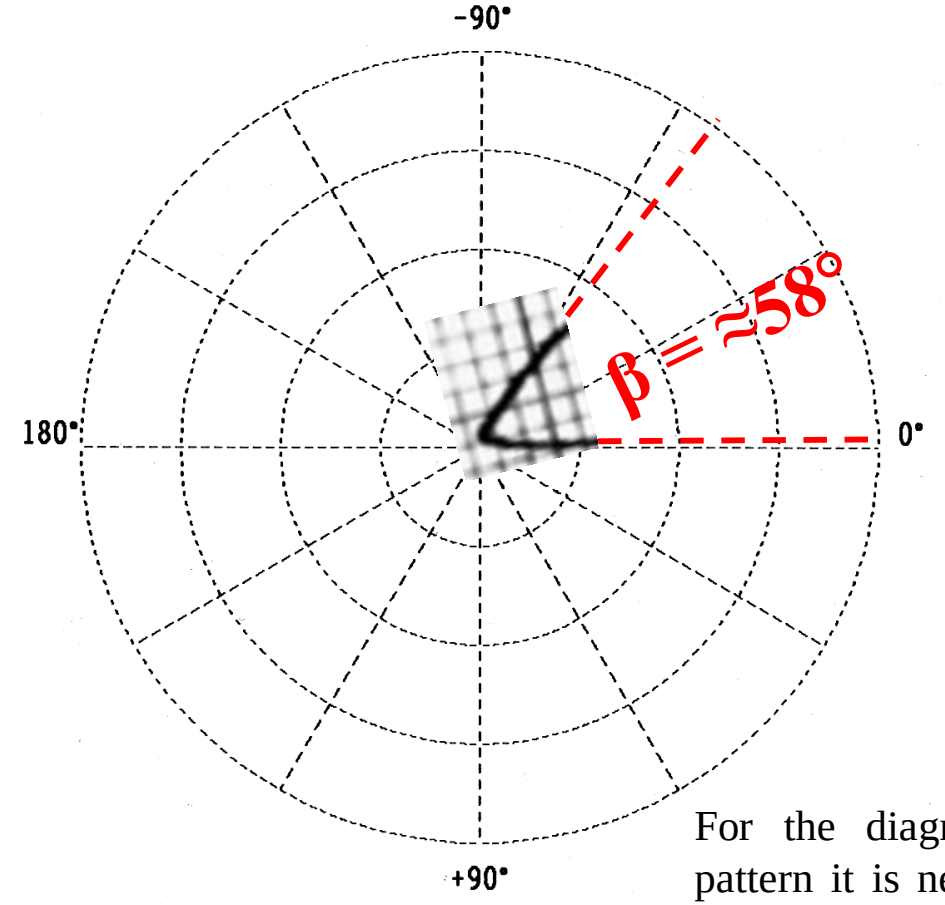
Subtype 1A	Subtype 1B
Wide high take-off angle	Wide high take-off angle
ST segment with convex upward shape	ST segment rectilinear oblique descendant
J-point corresponds to the point where the tangent line moves away from the downward slope of the ST segment	It is impossible to determinate the J-point location

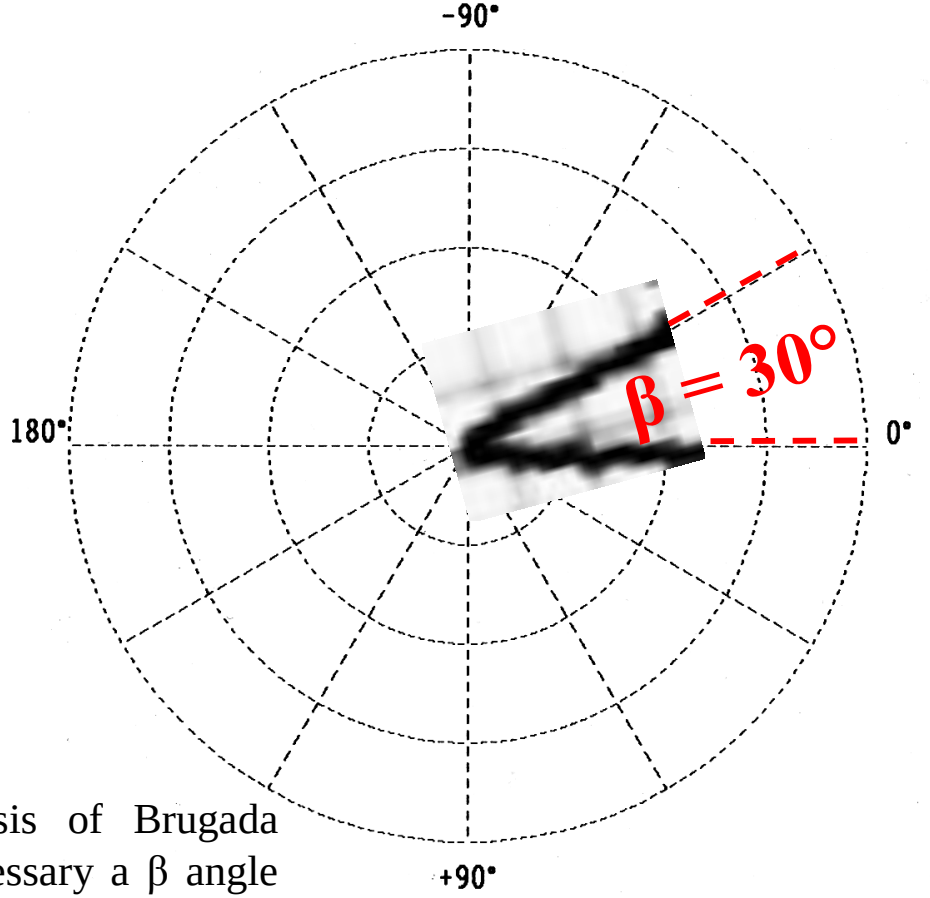
β-angle in truly Brugada syndrome



β-angle in the present case V2 lead







For the diagnosis of Brugada pattern it is necessary a β angle at least 36.8°

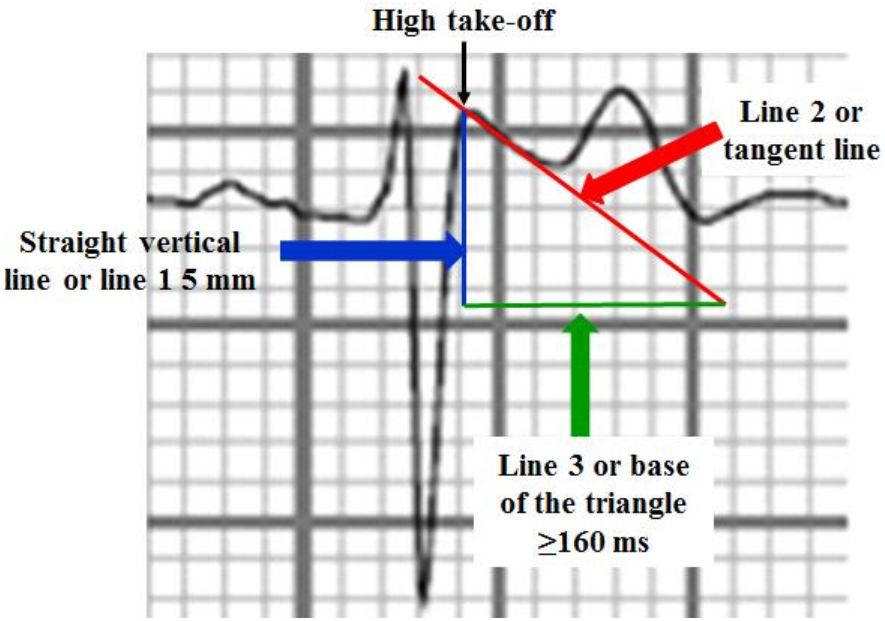
A study published in the Europace Journal helps us with the differential diagnosis between type 2 Brugada pattern and "innocent" ordinary incomplete RBBB, frequently observed in athletes. For such differentiation the best criterion tested is the so-called "measuring the base of the triangle":

- From the apex of r' wave (high take-off) we draw a straight vertical line (blue line) heading down up to 5 mm (this straight line will reach below the isoelectric line). We call this line l in the figure of the next slide.
- Next, we draw a horizontal line parallel to the isoelectric line from the end, of 5 mm, below the peak of r', which is line 3 in the figure of the next slide.
- Finally, we draw a tangent line that follows the descending ramp of the r' wave until meeting line 3. This is line 2 in the figure. When the base of this triangle was ≥ 160 ms, it suggests we are before type 2 Brugada pattern; and when it is <160 ms, it suggests IRBBB. The method shows an 85% sensitivity, 95.6% specificity, 94.4% positive predictive value(PPV), and 87.9% negative predictive value (NPV) (**Serra 2015**).

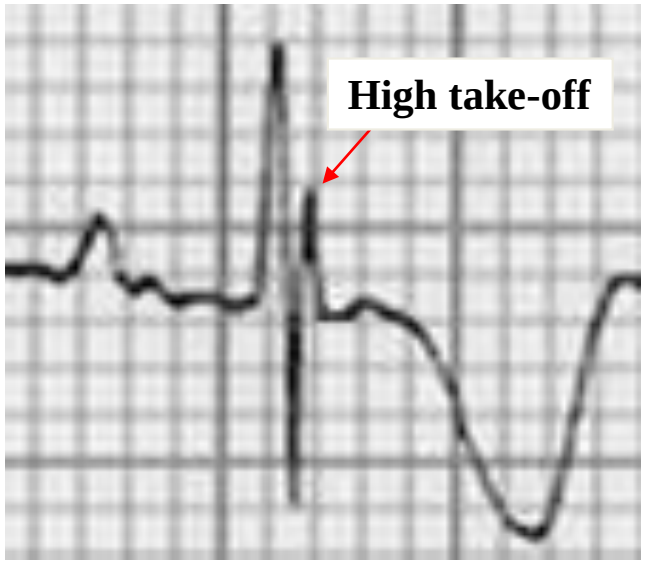
The accuracy of the PPV and NPV will vary according to the prevalence of the disease in the population and therefore are rarely generalizable outside the reported study population. When the prevalence of the disease in low, the PPV decreases and can result in a greater proportion of false positive results. 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 (**Serra 2015**). For the reason, result important that the authors consider reporting the likelihood ratios (LRs) for the new ECG criteria because 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**). LRs 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. 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 likelihood ratios (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

Type 2 Brugada pattern versus ordinary “innocent” incomplete RBBB

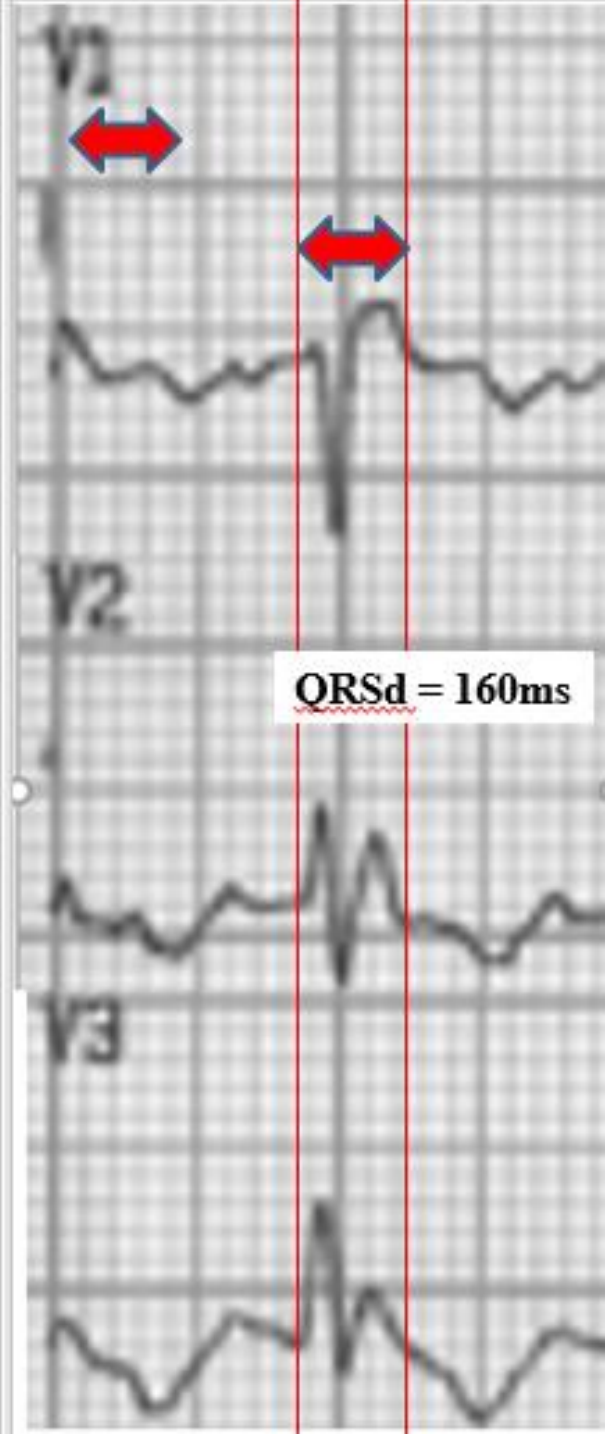
Type 2 Brugada pattern



Ordinary “innocent” incomplete RBBB



	Type 2 Brugada pattern	Ordinary “innocent” IRBBB
β angle	≥ 58° (**Bayés de Luna 2012**) 62 ± 20° (**Chevalier 2011**) β-angle ≥ 36.8° (**Serra 2025**)	Narrower or acute angle: 36 ± 20°(**Chevalier 2011**)
α angle	Mayor	Minor
T-wave	Positive or plane	Negative
Duration of the triangle base from the r´ high take-off at 5mm	> 3.5 mm or 160ms	Minimal
High take-off	Wide or broad	Acute



Located QRSd prolongation from V1 to V3. This feature is characteristic of ARVC/D and is related with the amount of fibrotic tissue in patients with VT that originate in the RV.

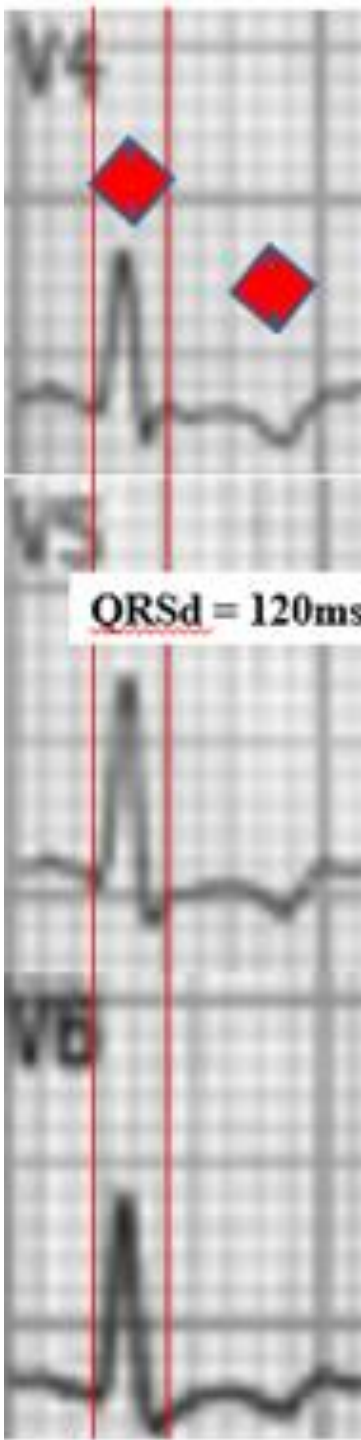
QRSd V1 + V2 + V3 / QRS dV4 + V5 + V6 >1.2.

QRSd of $^{V1+V2+V3}$ / $_{V4, V5 \text{ and } V6}$ $\geq$ 1.2 in approximately 65% of cases. QRS prolongation located in right precordial leads.

QRSD $\geq$ from V1 to V3 with 91% sensitivity, 90% specificity that predicts VT in patients carriers of ARVC/D (**Nasir 2003; Nasir 2003**).

The mechanism of the right conduction defects is not disease of the bundle branch itself but a distal block probably situated in the RV free wall. This hypothesis is supported by the histological appearances of the dysplastic zones (**Fontaine 1984**).

Pitzalis et al. show that parietal bock is not specific of ARVC/D, since it is found in BrS with QT interval prolongation only from V1 to V3 (**Pitzalis 2003**).



Brugada Phenocopy etiological categories

Brugada phenocopies may be induced by a multitude of clinical circumstances that have been characterized into six distinct etiological categories (**Anselm 2014; Baranchuk 2012; Bayés de Luna 2012**):

1. **Electrolyte Disorder:** hyperkalemia (**Ortega-Carnicer 2002; Recasens 2013**), hypokalemia in the context of congenital hypokalemic periodic paralysis (**Gazzoni 2013**), concurrent hypernatremia, hypokalemia, recurrent hypokalemia (**Genaro 2014**), hypophosphatemia (**Meloche 2016**), concurrent hypokalemia and hyponatremia (**Mok 2008: Hunuk 2016**).
2. **Endocrine and Metabolic Disorders:** hypopituitarism (**Anselm 2015**), adrenal crisis (**Dogan 2015**), hypothermia (**Gottschalk 2014**), acidosis (**Kovacic 2004**).
3. **Mechanical compression right ventricular outfow track:** induced by compressive giant mediastinal lipoma (**Asteriou 2013; Gottschalk 2014**), writhing of a reconstructed esophagus resulting in mechanical compression on the heart (**Kaneko 2013**) in the context of pectus excavatum resulting in mechanical mediastinal compression (**Awad 2013; Tarin 1999**).
4. **Ischemia:** acute anterior MI (**Ferrando-Castagnetto 2016; Tomcsányi 2003**), myocardial infarction with right ventricular involvement (**Jastrzebski 2015**), Takotsubo cardiomyopathy (**Kirbas 2016**), during balloon angioplasty (**Gottschalk 2016**), in the context of an acute inferior MI ST-segment elevation, during percutaneous coronary intervention of the right coronary artery (**Peters 2016**), stenosis of the dominant mid right coronary artery (**Agrawal 2015**), coronary anomalies (**Dendramis 2015**).
5. **Massive pulmonary embolism** (**Zhan 2014**).
6. **Myocardial disease:** acute myocarditis due to hyperesinophillic syndrome (**Nayyar 2009**), Chagasic cardiomyopathy (**Arce 2010**), ARVC/D (**Corrado 1996; Peters 2014**).
7. **Pericardial disease:** acute pericarditis (**Ozeke 2006**).
8. **Autonomic modulation:** example exercise-induced (**Enriquez 2016**), intracranial hemorrage (**Labadet 2014**), induced after radiofrequency catheter ablation of atrial fibrillation (**Jiang 2015**).
9. **Miscellaneous:** concomitant ethanol and heroin overdose (**Rambod 2014**), acute cannabis intoxication (**Daccarett 2007**), ketamine intoxication with concurrent acidosis (**Rollin 2011**), electrocution (**Wang 2012**).

Criteria to differentiate the Brugada Phenocopy from and true congenital Brugada syndrome

The great contribution of Dr. Adrian Baranchuk consists in studying the subject in a scientific manner and contributing decisively to the future clarification of nomenclatures. According to our current understanding, the diagnostic criteria for Brugada Phenocopy are (I-V are mandatory) (**Baranchuck 2012: Bayés de Luna 2012; Anselm 2013**):

I. An ECG pattern that has a type-1 or type-2 Brugada pattern following the last consensus (**Bayes 2012**);
II. An underlying identifiable condition;
III. The ECG pattern resolves upon resolution of the underlying condition There is a low clinical pretest probability of true BrS determined by a lack of symptoms, medical history, and family history;
IV. Negative provocative testing with a sodium channel blocker (ajmaline, flecainide, or procainamide) (**Boles 2016**). Provocative testing is not mandatory if surgical RVOT manipulation has occurred within the last 96 hours) because the SCN5A mutation is identified in only 20% to 30% of probands affected by true BrS). Features that suggest true congenital BrS: The ECG pattern has a type 1 or type 2 Brugada morphology. There is a high clinical pretest probability of true congenital BrS determined by presence of symptoms, medical history and family history. Positive provocative testing with sodium channel blockers such as ajmaline, flecainide or procainamide. This indicates sodium channel dysfunction consistent with true BrS Genetic testing is positive in about 20% to 30% of probands (**Probst 2009**);
V. Other clinic ECG differences: absence of ethnicity or racial predominance (in trully BrS male predominance (8:1 ratio male/female). It is a result of the presence of a more prominent, I_{to} channels in males than females), absence of nocturnal agonal breathing(this is characteristic in BrS), absence of family history of SCD in first-degree relatives $\leq$ 45 y.o.(it is frequent in BrS patients), absence of types 1 or 2 ECG BrP in first-degree relatives(if present is indicative of BrS), In BrS the PR interval and the His bundle electrogram is prolonged in ≈50% of the cases. This prolongation of the PR interval is observed predominantly in cases where the SCN5A gene carriers. The presence of a prolonged HV interval intra-His or infra-His block. consequence of HV split or HV prolongation.

The concept of acquired forms (drugs induced) of Brugada syndrome versus Brugada phenocopies

This concept was coined by Wataru Shimizu 11 years ago (**Shimizu 2005-2005**). Differently from Brugada phenocopy, the patients of acquired forms of BrS are hidden carriers of the entity (latent entity), which are similar to the acquired form of LQTS, show the characteristic pattern. For many years, congenital and acquired LQTS were viewed as two different entities with fascinating closeness (**Jackman 1998**). It would take 40 years to finally realize that loss of function of I_{Kr} may be caused by genetic mutations or drugs. The realization that some patients with drug-induced LQTS have underlying subclinical genetic mutations that clinically manifest when treated by QT interval-prolonging drugs, was made by Sesti et al (**Sesti 2000**). The diagnostic use of I_{Kr}-channel blockers to identify patients with underlying LQTS mutations was proposed for the first time by Kaab et al (**Kaab 2003; Viskin 2009**). Experimental studies show us that an intrinsically prominent I_{to} transient outward current-mediated action potential (AP) notch and a subsequent loss of the AP dome in the epicardium but not in the endocardium of the RVOT give rise to a transmural voltage gradient, resulting in type 1 Brugada pattern and phase 2 reentry-induced PVT/VF. Therefore, any intervention that increases I_{to} currents or decreases inward currents (eg, L-type calcium current, fast sodium current) at the end of phase 1 of the AP can accentuate or unmask type 1 Brugada pattern, similar to that found in the BrS, thus producing acquired forms of the BrS. Several drugs in addition to sodium-channel blockers and conditions that induce transient ST-segment elevation, such as that in the BrS, developing acquired forms of the BrS. Theoretically, an acquired intervention that causes a sufficient imbalance of inward and outward currents in the RVOT may induce a BrP in an individual, although the likelihood of arrhythmias is unclear. Whether this requires an underlying genetic predisposition, or represents latent BrS has not been established. Such as Brugada phenocopies, adquired forms of BrS can be caused by **drugs, electrolyte abnormalities, acute ischemia, increased insulin level, febrile state, hypothermia, and mechanical compression of RVOT**. The drugs to be avoided or preferentially avoided are inside the following link: http://www.brugadadrugs.org/. It is is a non-profit initiative developed by physicians (**Postema 2009**) from the University of Amsterdam Academic Medical Center, department of Cardiology, in collaboration with a

panel of world-renowned experts on Brugada syndrome as an aid to physicians who treat patients with BrS and as an aid to patients with BrS and their families with the goal to provide free, worldwide accessible and up-to-date information on safe drug use in BrS. As we can see, both Brugada phenocopies and acquired forms of BrS have the same causes. It so happened that the use of sodium-channel blockers became a widespread means for identifying patients with underlying BrS before the idea of acquired (drug-induced) BrS was accepted. Consequently, the only way to differentiate them is using the provocative test with ajmaline or other Na^+ channel blockers: positive indicates acquired form BrS; negative indicates Brugada phenocopy. **Observation:** the term Brugada-like electrocardiographic pattern should be eliminated because it does not define the underlying cause. The diagnosis of BrS requires the presence of the Brugada ECG type 1 pattern with at least one of the following diagnostic criteria:

1. Syncope
2. Prior cardiac arrest
3. Documented or inducible PVT/VF
4. A family history of sudden death <45 years old
5. Nocturnal agonal respiration.

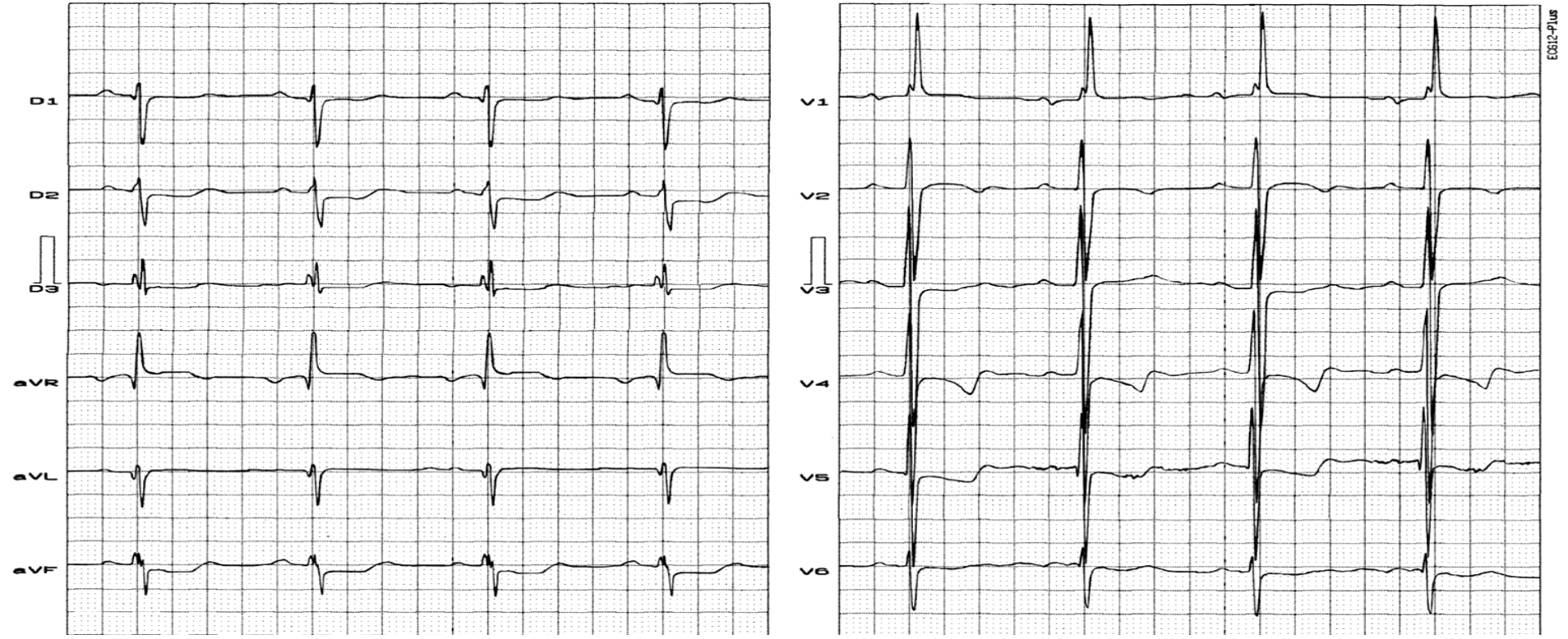
Brugada phenotype is more prevalent in males and is a result of the presence of a more prominent I_{to} channels in males than females. Carriers of the condition are at high risk of PVT/VF, and SCD. Syncopal episodes and paroxysmal palpitations are the only symptoms the patient may have before sudden arrhythmic death occurs. BrS is estimated to be responsible for at least 20% of SDs in patients with structurally normal hearts. In regions of Southeast Asia where it is endemic, the clinical presentation of BrS is distinguished by a male predominance (8:1 ratio of male/female) and the appearance of arrhythmic events at an average age of 40 years (range: 1–77 years).

	Brugada phenocopy	Acquired Brugada syndrome
Structural heart disease	**Possible**	**Absent**
Sex	**Without predominance**	**Male predominance (8:1 ratio of male: female)**
Predominant race	**Without predominance**	**Asian**
Age	**No preference**	**35-40 years old**
Endemic areas	**No**	**Southeast Asia: Thailand "Lai-tai", Japan "Pokkuri", Philippines "Bangungut".**
Family history of SD < 45 yo	**Absent**	**Frequently present**
Genetic screening	**Negative**	**≈ 30% of cases positive**
Identifiable structural cardiac abnormalities	**Possible**	**No**
Na^+ blockers challenge	**Negative (mandatory to perform)**	**Positive**
Nocturnal agonal respiration	**Absent**	**Typical when present**

Examples of Brugada phenocopies

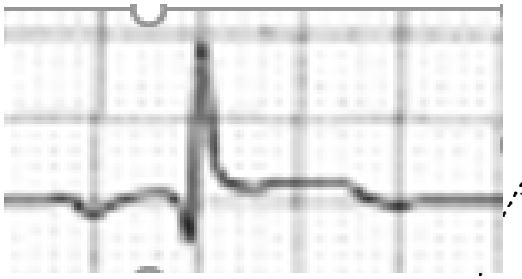
Pre-operative electrocardiogram

Name: RCPL; **Age**: 7 years; **Sex**: female; **Race**: mixed; **Weight**: 23.800Kg; **Height**: 1.21m; **Date**: 08/18/03; **Time**: 14:30; **Medication used**: none stated.

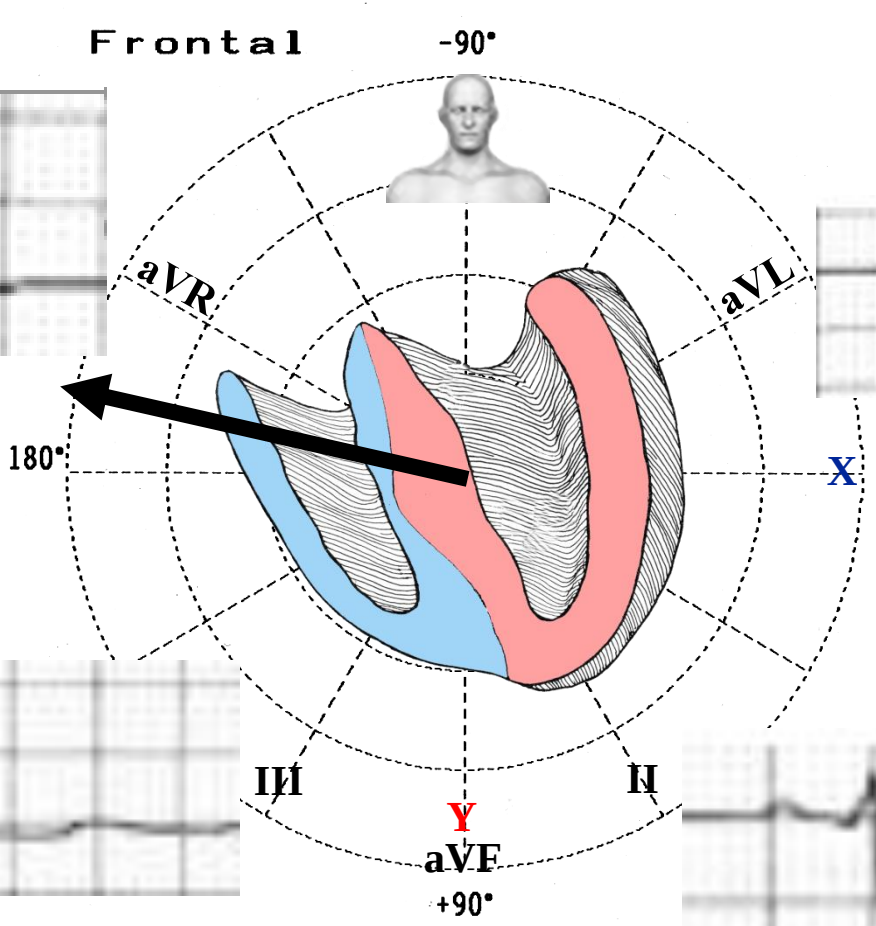


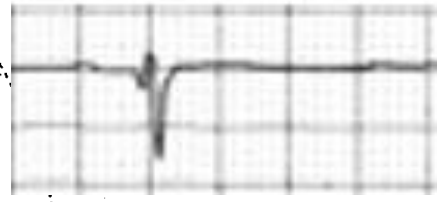
Clinical diagnosis: Fallot pentalogy (Fallot tetralogy + Atrial Septal Defect)

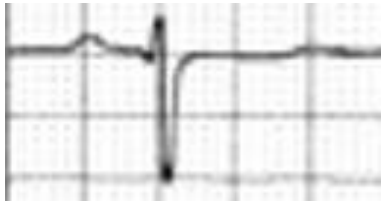
ECG diagnosis: sinus rhythm; HR: 75bpm; **P wave:** P axis: +38° and to the front in HP; P duration: 80ms; P voltage: 1mm; P aspect: rounded; **PR interval:** 167ms; **QRS:** axis -191°(extreme QRS deviation in the right superior quadrant (see next slide); **QRS** duration: 79ms (normal). In V_1 lead, wide monophasic R wave with notch at the bottom of the ascending ramp and abrupt transition from V_1 to V_2: QRS complexes predominantly positive in V_1 to complexes of the rS type in V_2. The sign is considered characteristic of of Fallot's tetralogy and is present in approximately 48% of the cases in this entity (**Pillegi 1960**).The predominant hypertrophy of the lateral-posterior-basal wall of the right ventricle and the crista supraventricularis is responsible for the sudden change in polarity from V_1 to V_2.

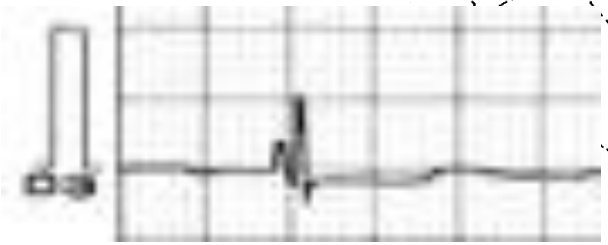


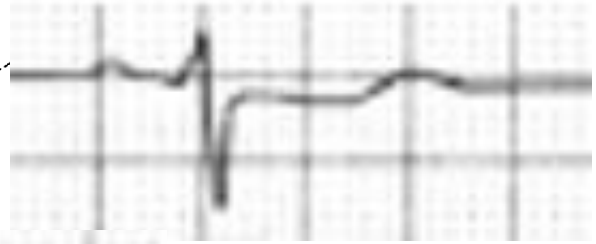
QRS axis on right superior quadrant

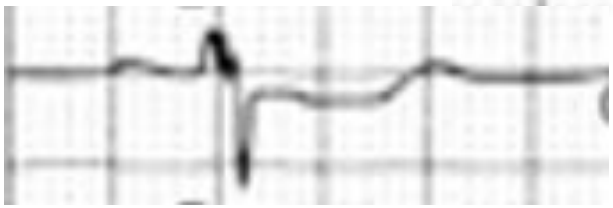












In children between 3 to 8 years old a progressive increase of voltage from R V_1 to V_5 should be observed, as well as a concomitant decrease of S until V_6; "adult progression" of the R/S ratio in the precordial leads. This fact is absent in the present case.

Left precordial leads V_5-V_6: predominantly negative QRS complexes. In 75% of the cases of Fallot's tetralogy an rS or RS pattern in registered in these leads. The voltage of the R wave in V_5 is 8.5mm (in children between 3 and 8 years old, the mean voltage of the R wave in V_5 is 21mm.). In V_6 the voltage of the R wave is 2.5mm. In normal children in this age group, the R wave voltage is 14mm.

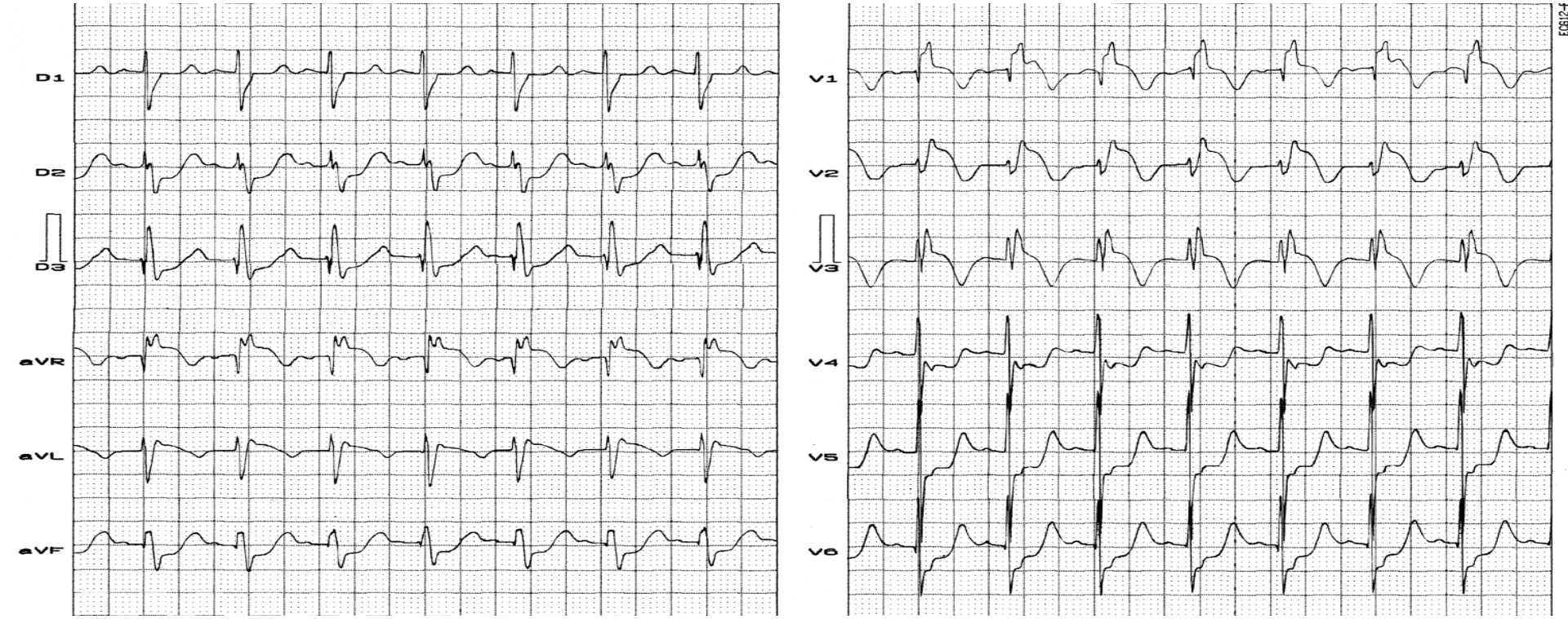
ST/T: SAT 2270 in PF and backwards in PH (negative T wave in V2).

QT: 380ms; **QTc:** 424ms (normal).

Conclusion: right ventricular systolic overload of adaptation; QRS axis with extreme QRS axis deviation in the right superior quadrant, monophasic R wave of great voltage and with initial notch in V_1 and predominantly negative complexes in V_5-V_6 of the qrS type.

Immediate post-operative electrocardiogram

Name: RCPL; **Age:** 7 years old; **Sex:** female; **Race:** mixed; **Weight:** 23.8 Kg; **Height:** 1.21 m;
Date: 08/26/03; **Time:** 20:24; **Medication used:** none stated



ECG diagnosis: sinus rhythm; HR: 18bpm; P wave: SÂP +30°; P duration: 80ms; P voltage: 0.8mV; P aspect: rounded. PRi duration: 130ms; QRS axis: -222°; QRS duration: 116ms (prolonged). ST/T: +88°; QT: 359ms. QTc: 503ms (prolonged). **Conclusion:** Incomplete RBBB pattern, with all the criteria for right anterosuperior fascicular block (RASFB) (**Pastore 1983**): qR in V1, rsR' in V2-V3; SII > SIII; qR in aVR with prominent and broad final R wave, extreme deviation of SÂQRS in the right superior quadrant (between +45° and ± 180° (- 222°)); QRS duration < 120ms (116ms) and S wave in V_5-V_6.
Phenotypic of type 1 ECG Brugada pattern: J point and ST segment elevation ≥ 2mm upwardly convex from V1 to V3 ("coved type") followed by negative T wave: Brugada phenocopy?
QTc: prolonged for heart rate: 503ms.

Echocardiography: Situs solitus. Levocardia. Levoapex. Atrioventricular connection of the concordant biventricular type. Atrioventricular concordance. Presence of atrial septal defect of the fossa ovalis type (=15mm), with a flow from the left to the right.

Anatomically normal atrioventricular valves without dysfunctions.

Wide interventricular septal defect of the anomalous subaortic position type, with aorta passing above the septum in less than 50% and bidirectional flow with left-to-right predominance.

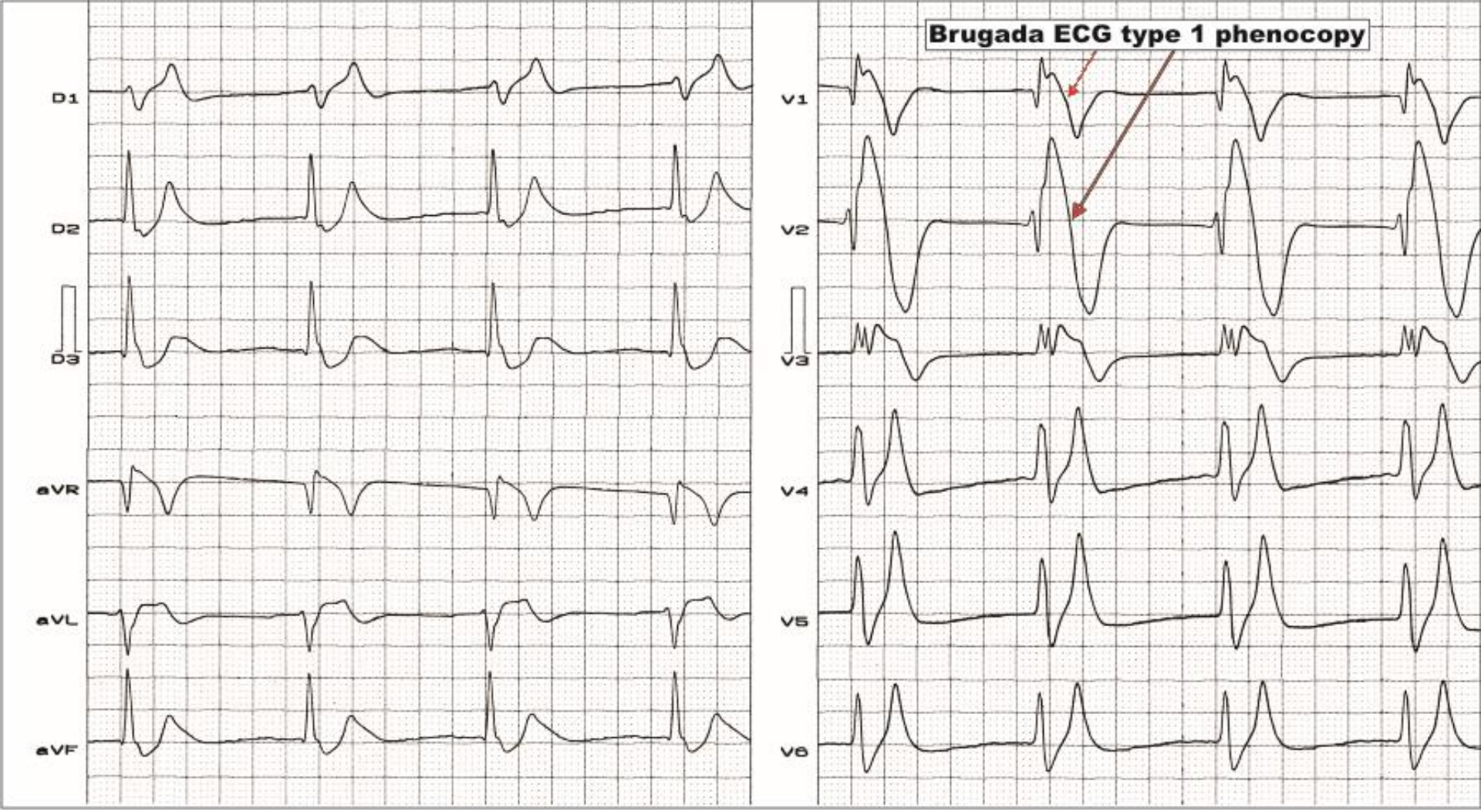
Left chambers with normal dimensions and right chambers with moderate dilatation.

Right ventricle: very significant concentric hypertrophy; anterosuperior deviation of the infundibular septum, causing important narrowing in RVOT.

Pulmonary valve: thickened fascicles and hypoplastic valve ring of 7.7mm. The maximal infundibulum-valvular gradient was 96mmHg.

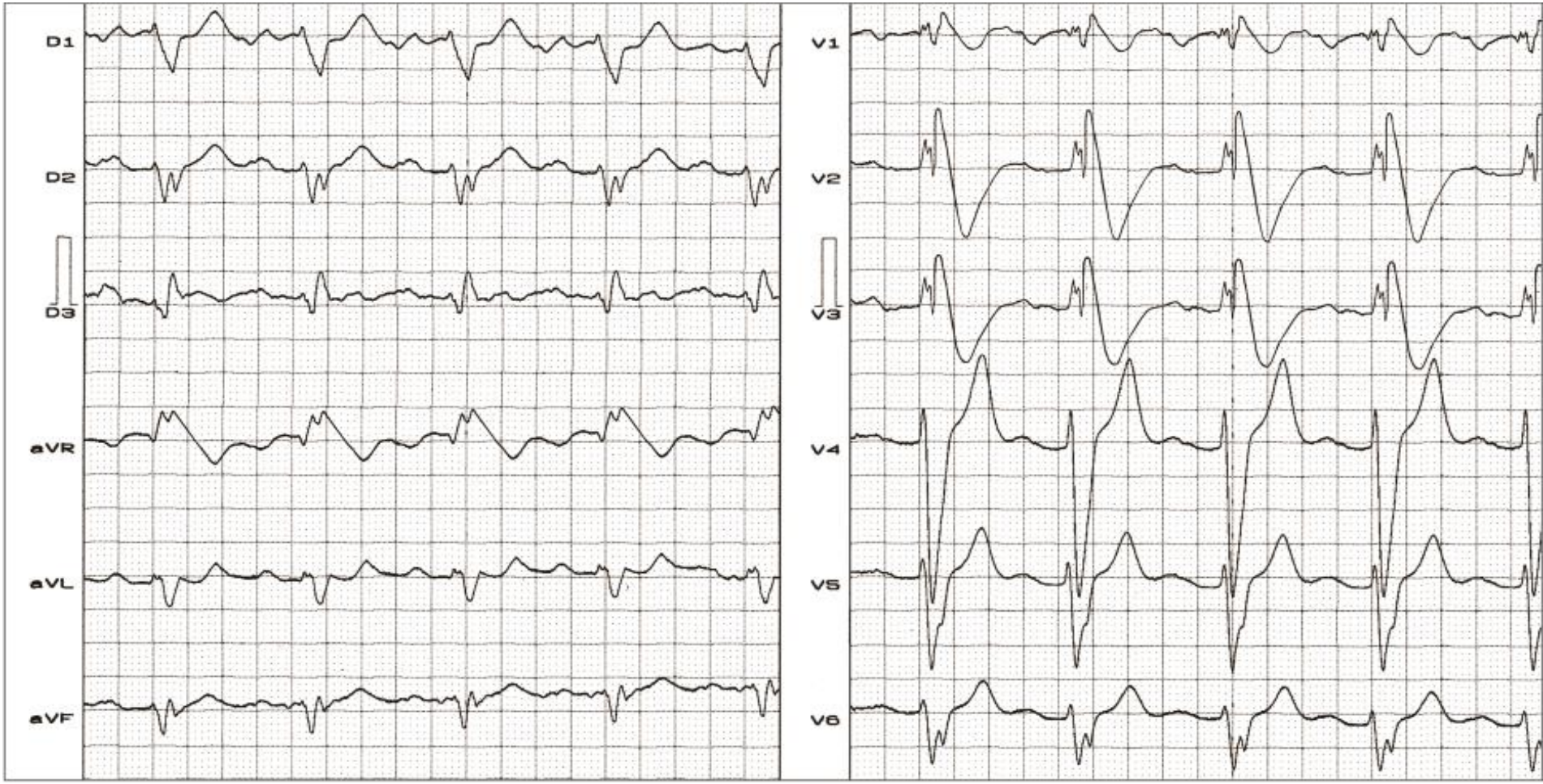
Hypoplastic pulmonary truncus and right and left pulmonary arteries, but confluent. Right pulmonary artery = 6.2mm; left pulmonary artery = 9.4mm. Presence of flow in left pulmonary artery, which suggests small arterial channel. Normal aortic valve. Aortic arch to the left.

Discussion: The sudden change of ECG in the immediate post-operative stage where an incision was made in the RVOT (right ventriculotomy) in the region where the subpulmonary or superior division of the right bundle branch originated the presence of an IRBBB. The incision made in the RVOT probably caused some degree of ischemia in the right ventricle. Several works show that acute infarctions or ischemia involving the RVOT may lead to J point and ST segment elevation similar to BrS or ischemia-induced Brugada phenocopy (**Agrawal 2015**). Surawicz et al (**Surawicz 1997**) report similar circumstances during the procedure of angioplasty by transitory occlusion of the ventricular branch that provides blood supply to the RVOT (anterior descending artery) with spontaneous recovery after rechanneling. This Brugada-pattern is the result of a depression of the slow $I_{Ca^{2+}\text{-L}}$ current and the activation of the $I_{\text{K-ATP}}$ channel during ischemia (**Kataoka 2000**) or induced by predominance of vagal tone, which explains the higher occurrence of tachyarrhythmia events during night rest in BrS. The same phenomenon has been described in variant vasospastic angina when the coronary artery involved is the one that irrigates the region of the RVOT. There are references of coexistence of both entities (**Indik 2002**).



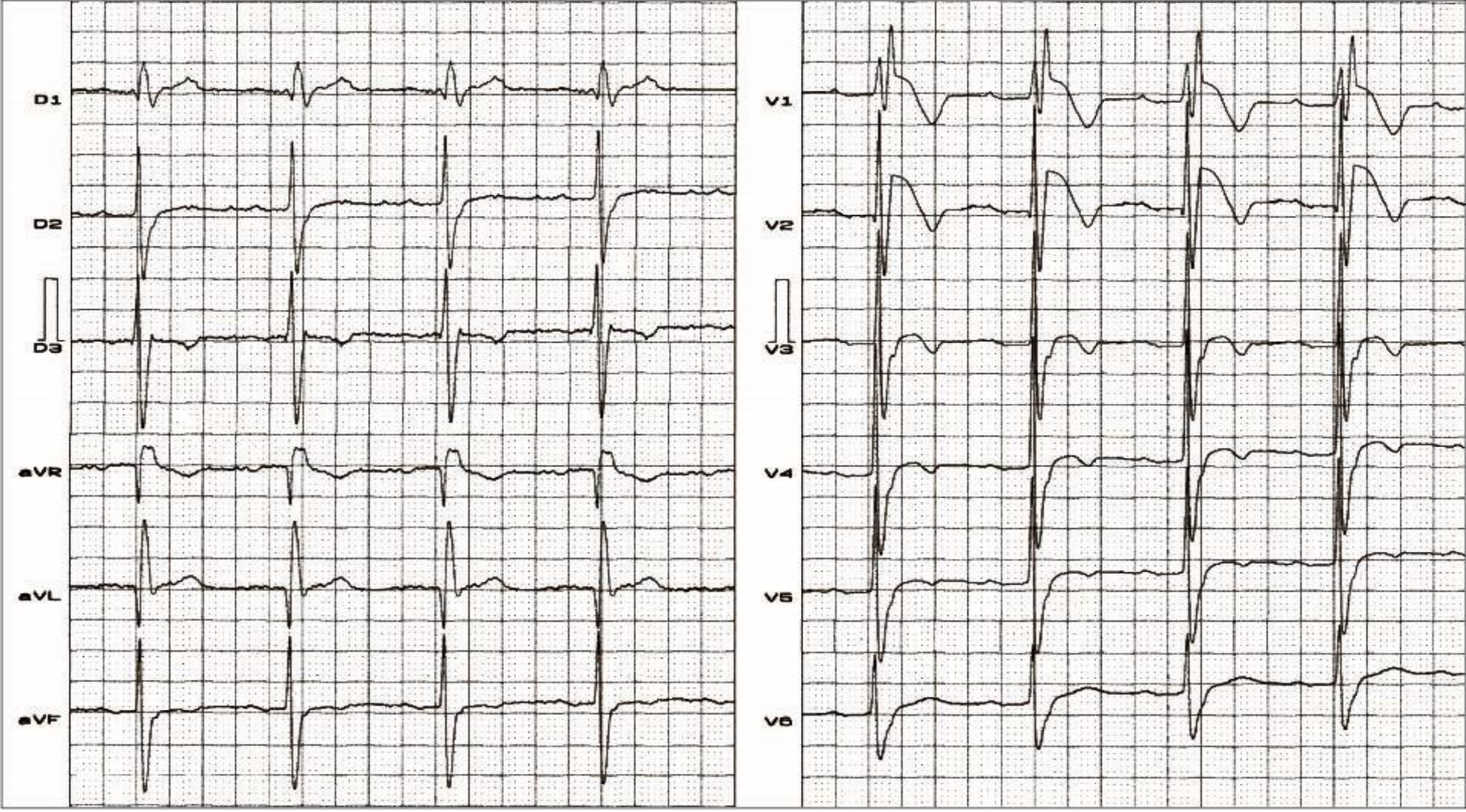
Clinical diagnosis: terminal renal insufficiency. Severe hyperkalemia: K^+ 8.7 mEq/L. This sign is known as dialyzable injury current.

ECG diagnosis: very likely, junctional with P waves near J point, HR: 54 bpm, QRSd: 160 ms, ST segment elevation from V_1 to V_3 and I, aVL and aVR. V_1 to V_3 display ST segment upwardly convex pattern, similar to BrS or Brugada phenocopy", typical T waves in "tent", pointed, and with a narrow base (**Riera 2010**).



Clinical diagnosis: propanone poisoning. Brugada phenocopy secondary to accidental plasma concentrations of propafenone in the toxic range.

ECG diagnosis: Left atrial enlargement, PR interval prolongation or first-degree AV block secondary to augmentation of effective refractory periods of atrioventricular node (> AH interval), His-Purkinje system (> HV interval), nonspecific intraventricular conduction disturbance, (marked abnormal ventricular activation pattern (bizarre): does not satisfy the criteria of either LBBB or RBBB, long QT interval with normal JT interval and Brugada type 1 ECG phenocopy: ST segment elevation convex to the top followed by negative T waves from V_1 to V_3 Induced Brugada-type 1 ECG pattern, is a sign for imminent malignant arrhythmias.

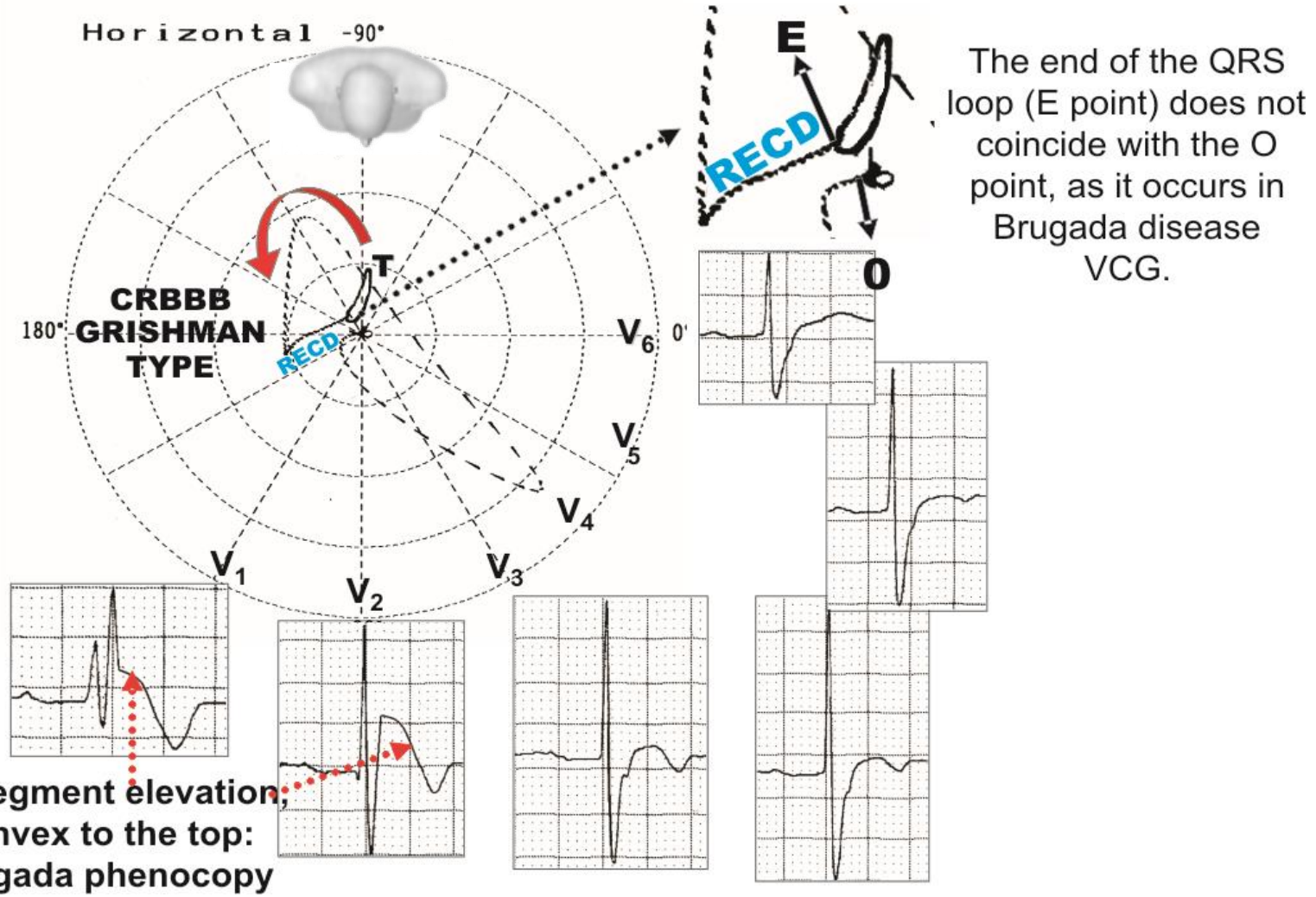


Clinical diagnosis: myotonic muscular dystrophy (Steinert's disease) / type 2 diabetes mellitus / high blood pressure. Brugada phenocopy?

ECG diagnosis: sinus rhythm, HR: 55 bpm, PR interval: 250 ms (first-degree AV block), QRS duration: 165 ms, SÂQRS: near –40º : Complete RBBB + left anterior fascicular block (LAFB), probable trifascicular block.

J point and ST segment elevation≥ 2mm in V_1 and V_2 followed by a negative T wave: Brugada ECG type 1 phenocopy.

ECG/VCG correlation in the horizontal plane

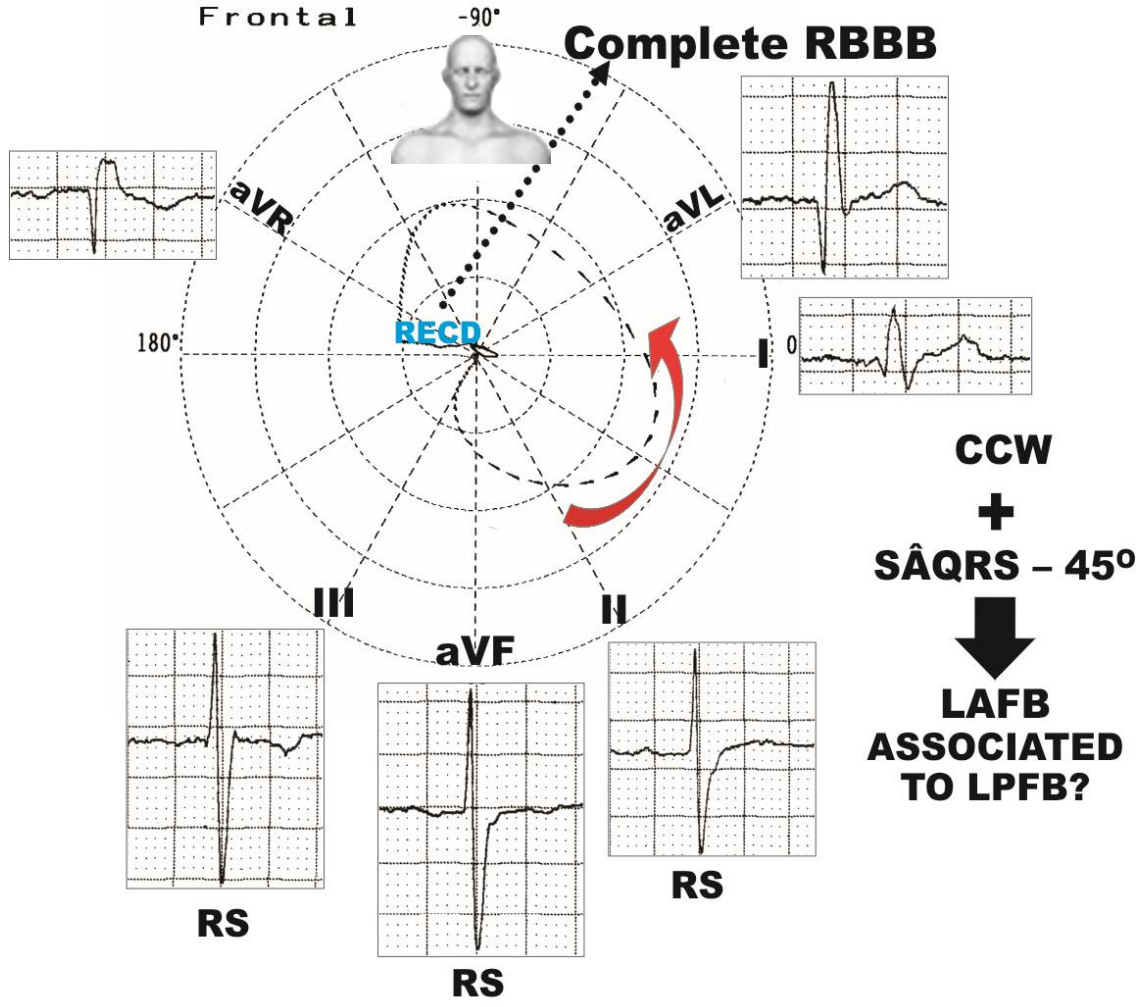


Clinical diagnosis: Myotonic Muscular Dystrophy (Steiner's Disease).

ECG/VCG diagnosis: Complete RBBB Grishman type or Kennedy type I (afferent limb of QRS loop behind X orthogonal line).

J point and ST segment elevation ≥ 2mm convex to the top followed by a negative T wave on right precordial leads: Brugada phenocopy.

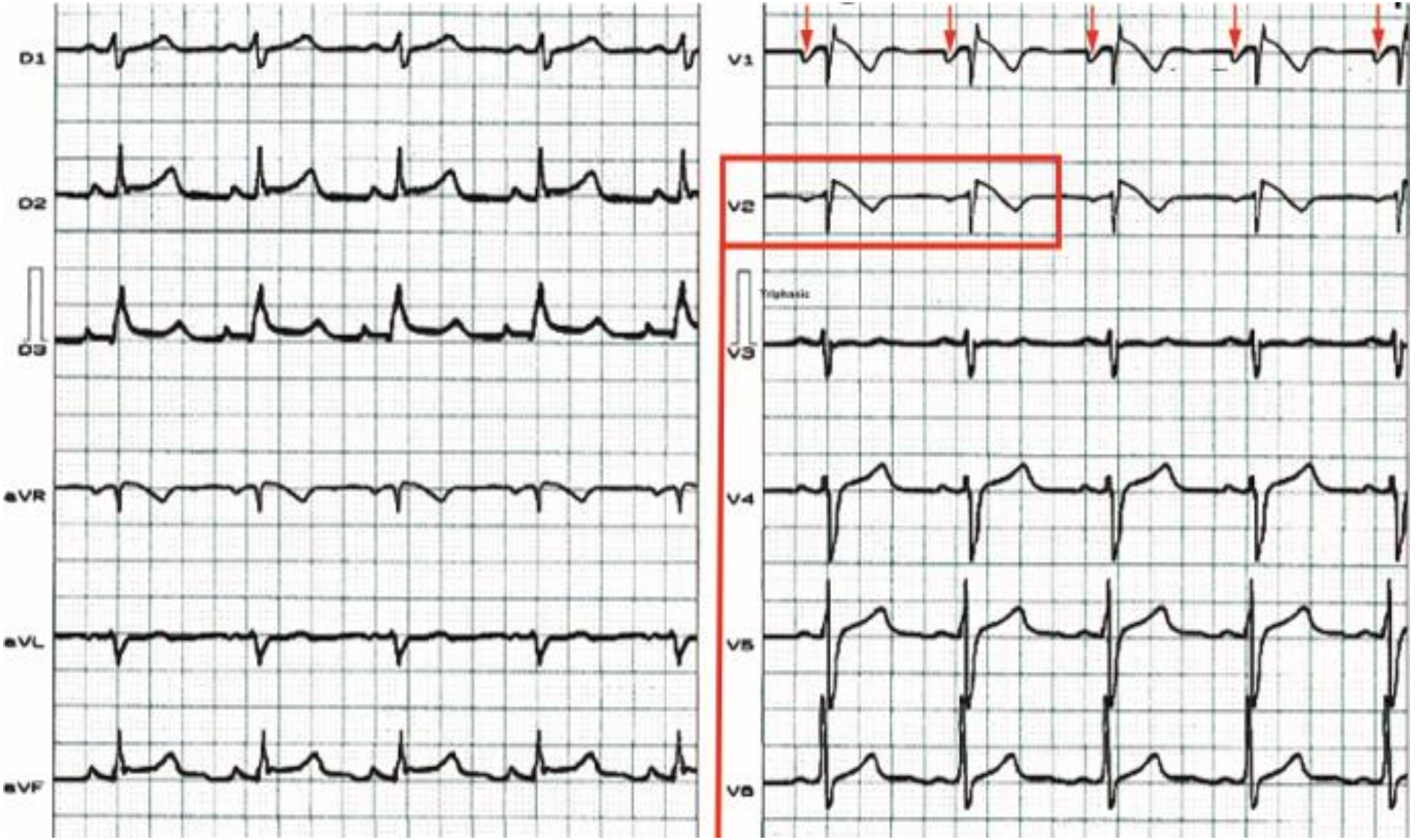
ECG/VCG correlation on frontal plane



CCW: COUNTER CLOCK WISE ROTATION

In classical LAFB, the inferior leads II, III and aVF show rS pattern. In this case, the voltage of R waves in inferior leads are greater, originating RS pattern in these leads. Additionally, QRS loop morphology is rounded and not elliptical as in typical LPFB. Both facts (RS pattern and rounded shape) suggest some degree of associated LPFB. This suspicion is reinforced by the presence of first degree AV block, which may be pointing dromotropic disturbance in the left posterior fascicle.

Negative P waves in V1-V2



Clinical diagnosis: pectus excavatum 18yo male patient.
ECG diagnosis: Negative P waves in V1-V2 Brugada type 1 ECG pattern in V2 : Brugada phenocopy

References

1. Anselm D, Barbosa-Barros R, de Sousa Belém L, Nogueira de Macedo R, Pérez-Riera A, Baranchuk A. Brugada Phenocopy induced by acute inferior ST-segment elevation myocardial infarction with right ventricular involvement. Inn Card Rhythm Manag. 2013;4:1092-4.
2. Anselm DD, Evans JM, Baranchuk A. Brugada phenocopy: A new electrocardiogram phenomenon. World journal of cardiology. 2014;6(3):81.
3. Anselm DD, Baranchuk A.Confirmed Brugada phenocopy in the setting of hypopitutarism. Herz. 2015;40(4):639-40.
4. Arce M1, Riera AR, Femenía F, Baranchuk A. Brugada electrocardiographic phenocopy in a patient with chronic Chagasic cardiomyopathy. Cardiol J. 2010;17(5):525-7.
5. Asteriou C, Lazopoulos A, Giannoulis N, Kalafatis I, Barbetakis N. Brugada-like ECG pattern due to giant mediastinal lipoma. Hippokratia. 2013;17(4):368-9.
6. Awad SF, Barbosa-Barros R, de Sousa Belem L, et al. Brugada phenocopy in a patient with pectus excavatum: Systematic review of the ECG manifestations associated with pectus excavatum. Annals of Noninvasive Electrocardiology. 2013;18(5):415-20.
7. Awad SF, Barbosa-Barros R, Belem Lde S, et al. Ischemia-induced Brugada phenocopy. J Electrocardiol. 2015;48(5):815-7.
8. Baranchuk A. Brugada phenocopy in a patient with pectus excavatum: systematic review of the ECG manifestations associated with pectus excavatum. Ann Noninvasive Electrocardiol. 2013;18(5):415-20.
9. Baranchuk A, Nguyen T, Ryu MH, et al. Brugada phenocopy: new terminology and proposed classification. Annals of Noninvasive Electrocardiology. 2012;17(4):299-314.
10. Bayés de Luna A, Brugada J, Baranchuk A, et al. Current electrocardiographic criteria for diagnosis of Brugada pattern: a consensus report. Journal of electrocardiology. 2012;45(5):433-42.
11. Boles U, Baranchuk A. Brugada Phenocopy or Unmasked Brugada Syndrome? Relevance of the Provocation Test. J Emerg Med. 2016 Feb 20. pii: S0736-4679(16)00115-3. doi: 10.1016/j.jemermed.2015.11.040. [Epub ahead of print]

12. Chevallier S, Forclaz A, Tenkorang J, at al. New electrocardiographic criteria for discriminating between Brugada types 2 and 3 patterns and incomplete right bundle branch block. J Am Coll Cardiol. 2011;58(22):2290-8.
13. Corrado D, Nava A, Buja G, et al. Familial cardiomyopathy underlies syndrome of right bundle branch block, ST segment elevation and sudden death. J Am Coll Cardiol. 1996;27(2):443-8.
14. Daccarett M, Freih M, Machado C. Acute cannabis intoxication mimicking Brugada-like ST segment abnormalities. Intern J Cardiol. 2007;119(2):235-6.
15. Deeks JJ, Altman DG. Diagnostic tests 4: likelihood ratios. BMJ. 2004 ;329(7458):168-9.
16. Dendramis G. Brugada syndrome and Brugada phenocopy. The importance of a differential diagnosis. Int J Cardiol. 2016;210:25-7.
17. Dogan M, Ertem A, Cimen T, Yeter E. Type-1 Brugada-like ECG pattern induced by adrenal crisis. Herz. 2015;40(2):304-6.
18. Enriquez A, Brugada J, Baranchuk A. Exercise-Induced Brugada Phenocopy.J Cardiovasc Electrophysiol. 2016;27(3):360-1
19. Ferrando-Castagnetto F, Garibaldi-Remuñan A, Vignolo G, Ricca-Mallada R, Baranchuk A. Brugada Phenocopy as a Dynamic ECG Pattern during Acute Anterior Myocardial Infarction. Ann Noninvasive Electrocardiol. 2016 Feb 22. doi: 10.1111/anec.12351. [Epub ahead of print]
20. Fontaine G, Frank R, Guiraudon G, et al. Significance of intraventricular conduction disorders observed in arrhythmogenic right ventricular dysplasia. Arch Mal Coeur Vaiss. 1984;77(8):872-9.
21. Gazzoni GF, Borges AP, Bergoli LC, Soares JL, Kalil C, Bartholomay E. Brugada-like electrocardiographic changes induced by hypokalemia. Arq Bras Cardiol. 2013;100(3):e35-7.
22. Genaro NR, Anselm DD, Cervino N, et al. Brugada phenocopy clinical reproducibility demonstrated by recurrent hypokalemia. Ann Noninvasive Electrocardiol. 2014;19(4):387-90.
23. Goldschmidt. R.. Gen und Ausseneigenschaft. I. Abstl. 1935;69: 38-69.
24. Gottschalk B, Anselm D, Baranchuk A. Possible Brugada Phenocopy induced by a giant mediastinal lipoma, Re: Brugada-like ECG pattern due to giant mediastinal lipoma. Hippokratia. 2014;18(2):190.

25. Gottschalk B, Anselm DD, Baranchuk A. Suspected Brugada phenocopy in the context of hypothermia. Acta Cardiol. 2014;69(4):454-5.
26. Gottschalk BH, Baranchuk A. Ischemia-induced Brugada Phenocopy during balloon angioplasty. Int J Cardiol. 2016;205:160.
27. Gottschalk BH, Garcia-Niebla J, Anselm DD, Jaidka A, De Luna AB, Baranchuk A. New methodologies for measuring Brugada ECG patterns cannot differentiate the ECG pattern of Brugada syndrome from Brugada phenocopy. J Electrocardiol. 2016;49(2):187-91.
28. Grimes DA, Schulz KF. Refining clinical diagnosis with likelihood ratio. Lancet. 2005;365(9469):1500-5.
29. Hunuk A, Hunuk B, Kusken O, Onur OE. Brugada Phenocopy Induced by Electrolyte Disorder: A Transient Electrocardiographic Sign. Ann Noninvasive Electrocardiol. 2016 Feb 23. doi: 10.1111/anec.12350. [Epub ahead of print]
25. Indik JH, Ott P, Butman SM. Syncope with ST-segment abnormalities resembling Brugada syndrome due to reversible myocardial ischemia. Pacing Clin Electrophysiol. 2002;25(8):1270-3.
26. Jackman WM, Friday KJ, Anderson JL, Aliot EM, Clark M, Lazzara R. The long QT syndromes: a critical review, new clinical observations and a unifying hypothesis. Prog Cardiovasc Dis. 1988;31(2):115–72.
30. Jastrzebski M, Kukla P, Baranchuk A, Czarnecka D. Right ventricular tombstoning as a Brugada phenocopy. Int J Cardiol. 2015;199:213-4.
31. Jiang C, Wang R, Lu W, Han B. A Brugada-like electrocardiogram pattern induced after radiofrequency catheter ablation of atrial fibrillation. Int J Cardiol. 2015;178:e1-4.
32. Kaab S, Hinterseer M, Nabauer M, Steinbeck G. Sotalol testing unmasks altered repolarization in patients with suspected acquired long-QT-syndrome--a case-control pilot study using i.v. sotalol. Eur Heart J. 2003;24(7):649–57.
33. Kaneko Y, Nakajima T, Irie T, Kurabayashi M. Brugada-type ST-elevation Associated with Writhing of a Reconstructed Esophagus. Intern Med. 2013;52(19):2287-8.

34. Kasamaki Y, Hirayama A. A new criteria differentiating type 2 and 3 Brugada patterns from ordinary incomplete right bundle branch block. Int Heart J. 2011;52(3):159-63.
35. Kataoka H. Electrocardiographic patterns of the Brugada syndrome in right ventricular infarction/ischemia. Am J Cardiol 2000; 86(9):1056.
36. Kirbas O, Ozeke O, Karabulut O, et al. Warm-up Brugada phenocopy associated with takotsubo cardiomyopathy. Am J Emerg Med. 2016 Mar 2. pii: S0735-6757(16)00182-0. doi: 10.1016/j.ajem.2016.02.075. [Epub ahead of print].
37. Kovacic JC, Kuchar DL. Brugada pattern electrocardiographic changes associated with profound electrolyte disturbance. Pacing Clin Electrophysiol. 2004;27(7):1020-3.
38. Labadet C, Gottschalk BH, Rivero M, et al. Brugada phenocopy in the context of intracranial hemorrhage. Int J Cardiol. 2014;177(3):e156-7.
39. McGee S. Simplifying likelihood ratios. J Gen Intern Med. 2002;17(8):646-9.
40. Meloche J, Gottschalk BH, Boles U, LaHaye S, Baranchuk A. Hypophosphatemia as a novel etiology of Brugada Phenocopy. Int J Cardiol. 2016;208:70-1.
41. Mirvis DM. Evaluation of normal variations in S-T segment pattern by body surface mapping: S-T segment elevation in absence of heart disease. Am J Cardiol. 1982;50(1):122-8.
42. Mok NS, Tong CK, Yuen HC. Concomitant-Acquired Long QT and Brugada Syndromes Associated with Indapamide-Induced Hypokalemia and Hyponatremia. Pacing Clin Electrophysiol. 2008;31(6):772-5.
43. Nasir K, Bomma C, Tandri H, et al. Electrocardiographic features of arrhythmogenic right ventricular dysplasia/cardiomyopathy according to disease severity: a need to broaden diagnostic criteria. Circulation. 2004; 110(12):1527-34.
44. Nasir K, Tandri H, Rutberg J, et al. Filtered QRS duration on signal-averaged electrocardiography predicts inducibility of ventricular tachycardia in arrhythmogenic right ventricle dysplasia. Pacing Clin Electrophysiol. 2003;26(10):1955-60.
45. Nayyar S, Nair M. Brugada pattern in toxic myocarditis due to severe aluminum phosphide poisoning. Pacing Clin Electrophysiol. 2009;32(11):e16-7.

46. Ortega-Carnicer J, Benezet J, Ruiz-Lorenzo F, Alcázar R. Transient Brugada-type electrocardiographic abnormalities in renal failure reversed by dialysis. Resuscitation. 2002;55(2):215-9.
47. Ozeke O, Selcuk M, Topaloglu S, Maden O, Aras D. Brugada-like early repolarisation pattern associated with acute pericarditis. Emerg Med J. 2006;23(12):e64.
48. Pastore CA, Moffa PJ, Spiritus MO, et al. Fascicular blocks of the right branch. Standardization of vectorelectrocardiographic findings. Arq Bras Cardiol. 1983;41(3):161-6.
49. Peters S. Brugada phenocopy or Brugada ECG pattern in patients characterized by early repolarization pattern and additional arrhythmogenic right ventricular cardiomyopathy. Int J Cardiol. 2014;172(1):278.
50. Peters S. Brugada phenocopy in percutaneous coronary intervention of the right coronary artery. Int J Cardiol. 2016;203:675.
51. Pillegi F, Bocanegra AJ, Tranchesi J, et al. The electrocardiogram in tetralogy of Fallot. A study of 142 cases. Am Heart J. 1960;59:667-80.
52. Pitzalis MV, Anaclerio M, Lacoviello M, et al. QT-interval prolongation in right precordial leads: an additional electrocardiographic hallmark of Brugada syndrome. J Am Coll Cardiol. 2003; 42(9):1632-7.
53. Postema PG, Wolpert C, Amin AS, et al. Drugs and Brugada Syndrome patients: Review of the literature, recommendations and an up-to-date Website (www.brugadadrugs.org). Heart Rhythm 2009;6(9):1335-41.
54. Probst V, Wilde AA, Barc J, et al. SCN5A mutations and the role of genetic background in the pathophysiology of Brugada syndrome. Cir Cardiovasc Genet. 2009;2(6):552-7.
55. Rambod M, Elhanafi S, Mukherjee D. Brugada phenocopy in concomitant ethanol and heroin overdose. Ann Noninvasive Electrocardiol. 2015;20(1):87-90.
56. Recasens L, Meroño O, Ribas N. Hyperkalemia mimicking a pattern of Brugada syndrome. Rev Esp Cardiol (Engl Ed). 2013;66(4):309.
57. Riera AR, Uchida AH, Schapachnik E, et al. Propofol infusion syndrome and Brugada syndrome electrocardiographic phenocopy. Cardiol J. 2010;17(2):130-5.
58. Rollin A, Maury P, Guilbeau-Frugier C, Brugada J. Transient ST elevation after ketamine intoxication: a new cause of acquired brugada ECG pattern. J Cardiovasc Electrophysiol. 2011;22(1):91-4.

59. Serra G, Baranchuk A, Bayés-De-Luna A, et al. Base of the triangle to determine a Brugada electrocardiogram pattern. Europace. 2015;17(3):505.
60. Sesti F, Abbott GW, Wei J, et al. A common polymorphism associated with antibiotic-induced cardiac arrhythmia. Proc Natl Acad Sci. USA 2000;97(19):10613–8.
61. Shimizu W. Acquired forms of the Brugada syndrome. J Electrocardiol. 2005;38(4 Suppl):22-5.
62. Shimizu W. Acquired forms of Brugada syndrome. In: The Brugada syndrome from bench to bedside. Antzelevitch C, Brugada P, Brugada J, Brugada R, editors. Blackwell-Futura, Massachusetts; 2005. Chapter 14, P. 166-77.
63. Surawicz B, Orr CM, Hermiller JB, et al. QRS changes during percutaneous transluminal coronary angioplasty and their possible mechanism. J Am Coll Cardiol 1997;30(2):452-8.
64. Tarín N, Farré J, Rubio JM, Tuñón J, Castro-Dorticós J. Brugada-like electrocardiographic pattern in a patient with a mediastinal tumor. Pacing Clin Electrophysiol. 1999;22(8):1264-6.
65. Tomcsányi J, Zsoldos A, Bozsik B. Brugada-like acute myocardial infarction. Heart. 2003;89(10):1199.
66. Viskin S, Rosso R, Márquez MF, Antzelevitch C. The acquired Brugada syndrome and the paradox of choice. Heart Rhythm. 2009;6(9):1342-4.
67. Wang JG, McIntyre WF, Kong W, Baranchuk A. Electrocution-induced Brugada phenocopy. Int J Cardiol. 2012;160(3):e35-7.
68. Zhan ZQ, Wang CQ, Nikus KC, Pérez-Riera AR, Baranchuk A. Brugada phenocopy in acute pulmonary embolism. Int J Cardiol. 2014;177(3):e153-5.