

ST segment Elevation *Myocardial Infarction*
(STEMI) with Brugada ECG pattern

Infarto Agudo do miocárdio com elevação do
segmento ST e padrão Brugada de ECG

From Raimundo Barbosa Barros MD

Coronary Center Hospital de Messejana Dr. Carlos Alberto Studart Gomes Fortaleza-Ceará-Brazil

Final Comments by Andrés Ricardo Pérez-Riera M.D. Ph.D.

ID: ARER, 56 anos, masculino. Admitido na sala de emergencia em 19/01/12 às 13:00 com quadro dor torácica de caráter em queimor que iniciara há 8 horas. A dor era constante, irradiava-se para pescoço e membro superior esquerdo até cotovelo, sem fatores precipitantes, de melhora ou piora e associada a náuseas e vômitos.

Nega síncope prévia, dispnéia ou outras queixas.

Antecedentes: Ex-tabagista (de 45maços por ano), etilista.

Nega diabetes, hipertensão arterial, cirurgias ou co-morbidades conhecidas. Nega uso de medicações.

História familiar negativa.

Qual o diagnóstico?

Raimundo

ID: ARER, 56 year old male. Admitted to the Emergency room on January /19/2012 at 13:00 with a picture of chest pain burning in cartáter that started 8 hours erlier. The pain was constant, radiating to the neck and left arm until the elbow, without precipitating factors, improving or worsening, and associated with nausea and vomiting.

Denies prior syncope, dyspnea or other complaints.

Background: Ex-smoker (45packet per year) alcoholic.

Deny diabetes, hypertension, surgeries, or known comorbidities. Denies use of medications.

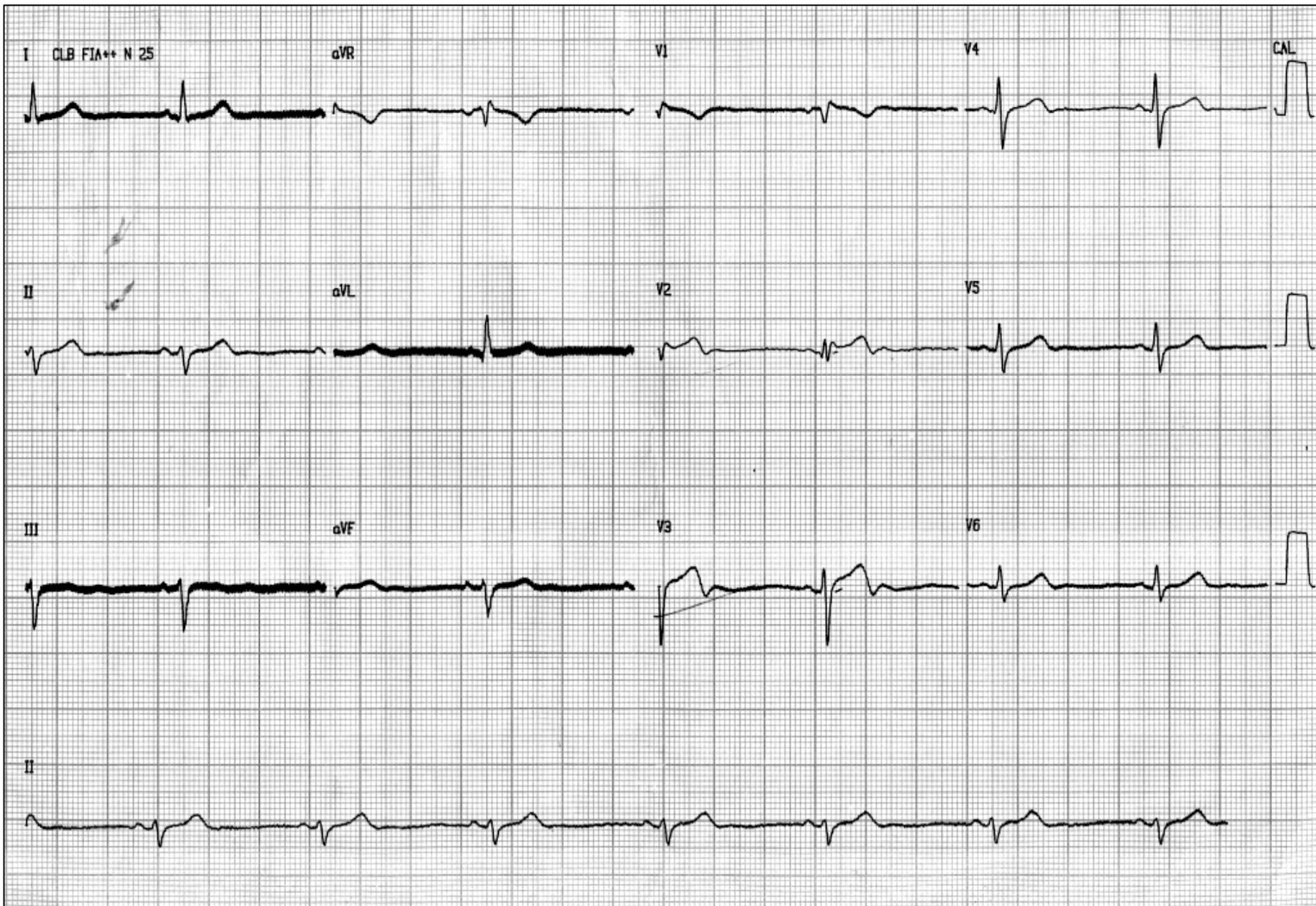
Negative family history.

Which the diagnosis?

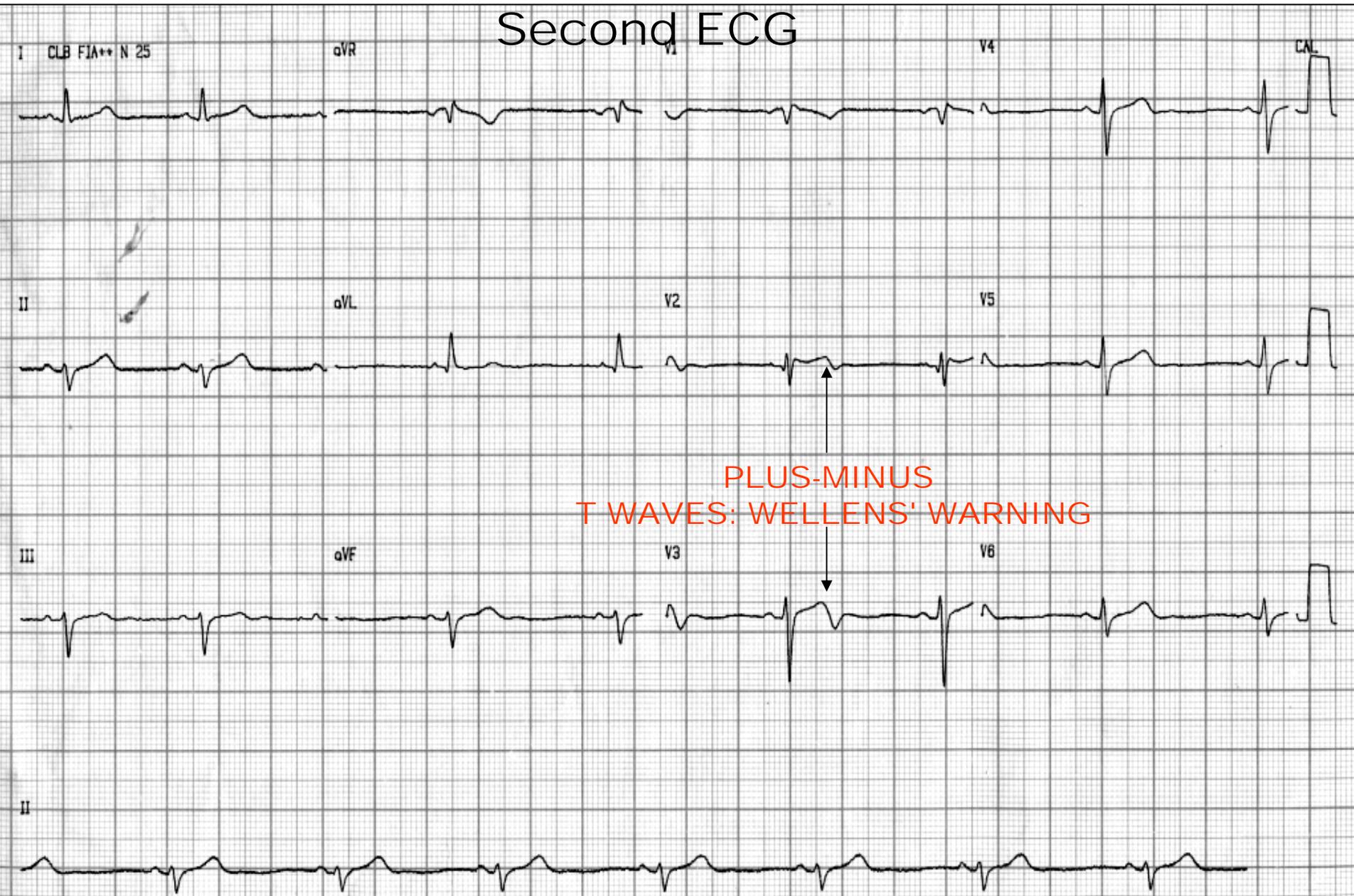
Raimundo

ECG admission January, 19/2012

First ECG

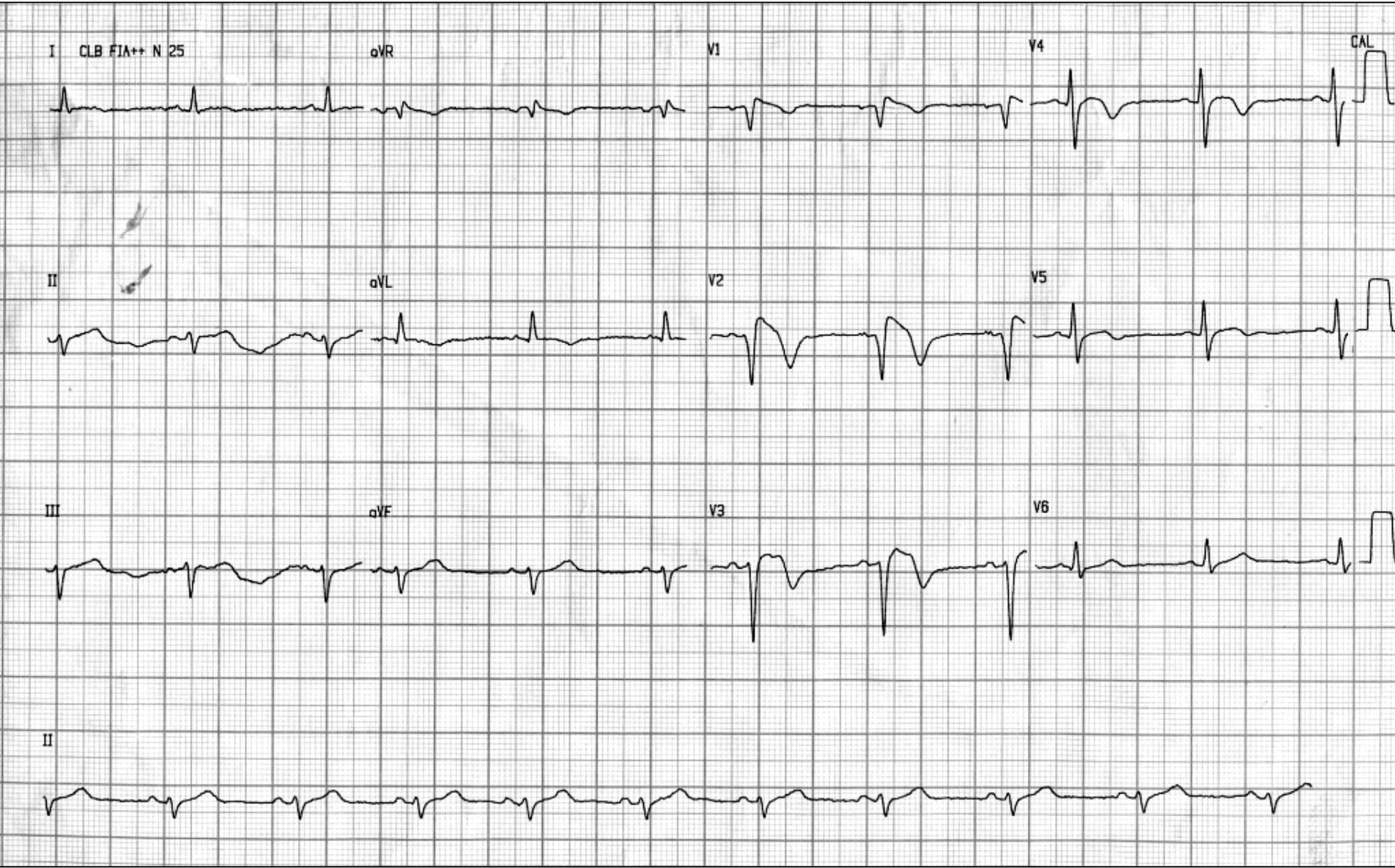


Second ECG



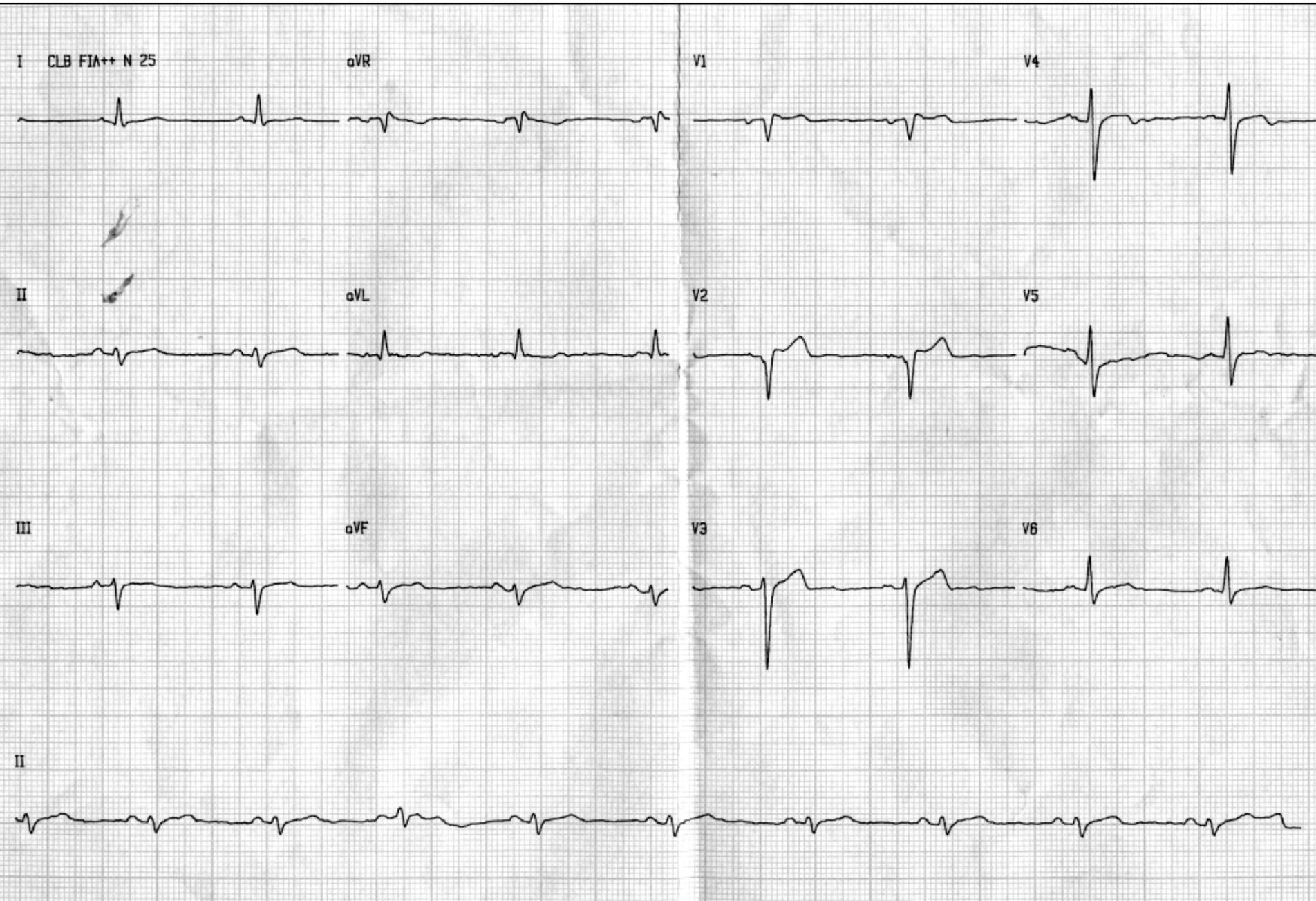
January 20/ 2012 asymptomatic

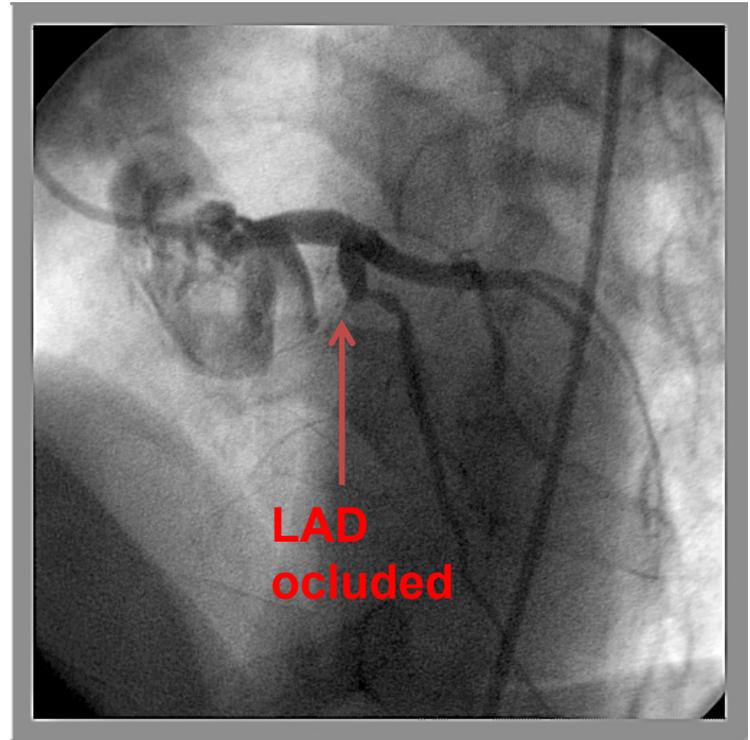
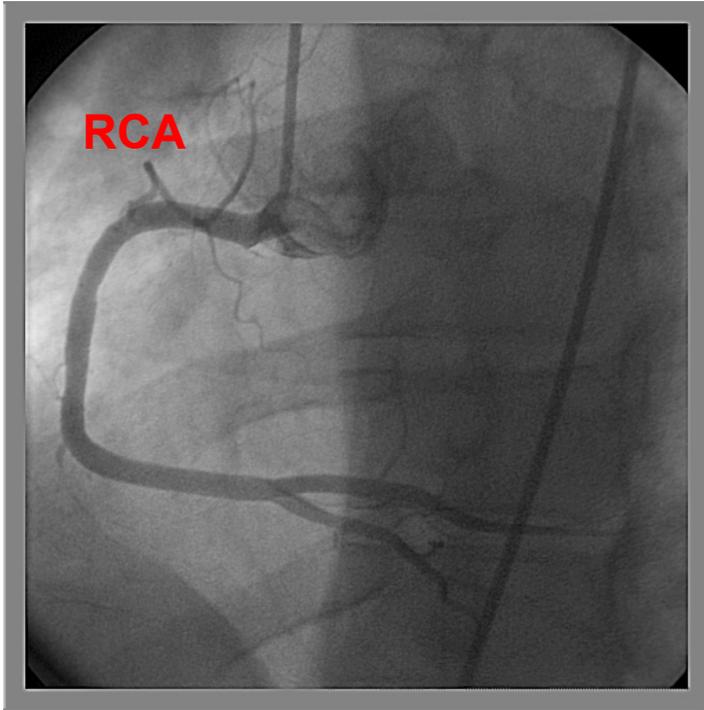
Third ECG

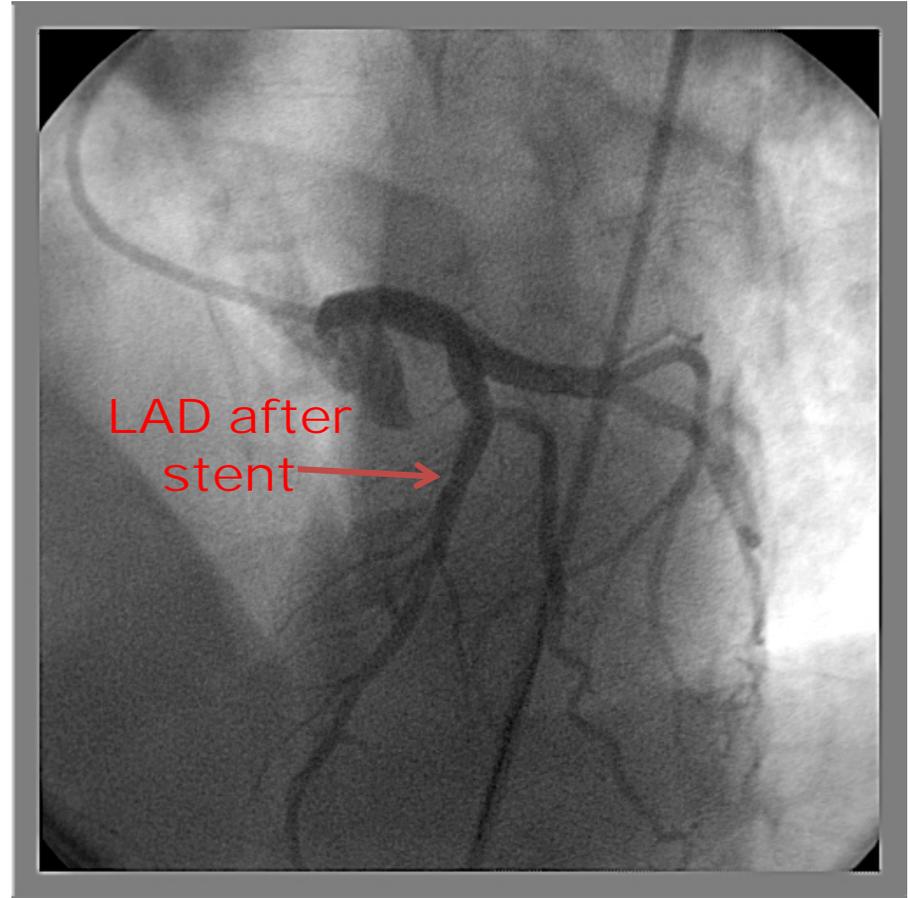
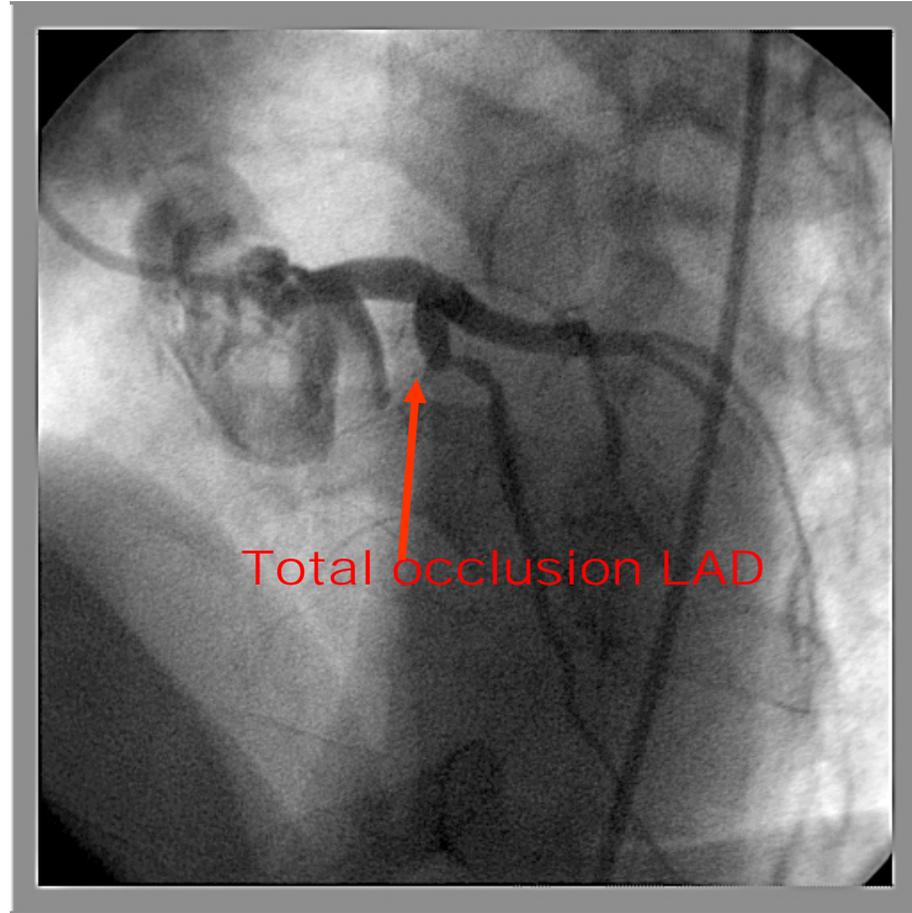


January, 25/2012 asymptomatic

Fourth ECG







COLLEAGUES OPINIONS

This is actually a very interesting case of a patient with both acute ischemic event and Brugada syndrome.

The complete normalization of the ECG 5 days after the one showing type 1 Brugada pattern is intriguing.

What happens during the following days ???

Why type 1 Brugada-ECG type was observed the day following the PCI and not before or late after ??

I think you should ask Charlie Antzelevitch. I am sure we will learn a lot from his comments.

Prof. Bernard Belhassen

Director, Cardiac Electrophysiology Laboratory

Tel-Aviv Sourasky Medical Center

Tel-Aviv 64239, Israel

Tel/Fax: 00.972.3.697.4418

bernardb@tasmc.health.gov.il

Este é realmente um caso muito interessante de um paciente com ambos: um evento isquêmico agudo e síndrome de Brugada.

A normalização completa do ECG 5 dias após mostrar o padrão eletrocardiográfico Brugada tipo 1 é intrigante.

O que aconteceu durante os dias seguintes?

Porque o padrão ECG tipo 1 tipo Brugada foi observado no dia seguinte ao PCI e não antes ou depois de tarde?

Eu acho que você deveria perguntar a Charlie Antzelevitch. Estou certo de que vamos aprender muito com seus comentários.

Prezados amigos do Forum , e especialíssimos The Fox e El Potro:

ECG1: Ritmo Sinusal FC = 48 bp Eixos: P = + 40° QRS = -45° T = +30° Duração: P = 0,08” PR = 0,16” QRS = 0,08” Análise morfológica :1. Desvio eixo elétrico a esquerda; 2. q mínima DI e aVL; 3. rSr' em aVR Não configurando sinal de aVR para retardo de condução de ramo direito 4. QSr em V1 5. qRSr' em V25. ST supra desnivelado em V2 e V3, configuração tipo sela de montar em V2, ST apenas de 1 mV e 2mV em V3; 6 .T com T1 positiva em V2 e V3 T2 negativa nestas derivações; 7. Desvio da transição p/ esquerda R/S em V4; 8. S em V5 e V6

Conclusão: 1. bradicardia sinusal. 2. bloqueio divisional ântero-superior esquerdo. 3. infarto ântero – septal. OBS: não vejo padrão de Brugada neste ECG inicial.

ECG2: imediatamente após cat c/ angioplastia: sem modificação em relação ao ECG da admissão exceto pela melhoria técnica.

ECG3: padrão de Brugada tipo 1 caracterizado por elevação do segmento ST de convexidade superior ≥ 2 mm (0.2 mv) seguido de onda T negativa nas precordiais direitas (V1 a V3). Neste caso; chama atenção o padrão isquêmico em V4: ST sem supra T invertida - reperfusão incompleta.

ECG4: V2: Q com entalhe linha de base isoeétrica; reperfusão - onda T aplanada V5,V6 -Aumento de R nestas derivações (com a palavra o Dr. Sclarovsky sobre estes fenômenos da reperfusão.

Conclusão: 1. padrão de Brugada no ECG 3 com isquemia concomitante - 24 horas após angioplastia e stent na artéria descendente anterior. 2. infarto ântero-septal no ECG 5 dias pós intervenção percutânea com reperfusão completa 3. cabe investigar uso de bloqueador de Na⁺ ou de outra droga provocativa de Brugada

Adail – Bahia - Brasil

Dear friends from forum and very special The Fox and “El potro”

ECG1: Sinus rhythm, HR 48bpm. P axis +40°, P duration 80ms. PR interval 160ms, QRS duration 80ms

Morphological analysis

Left axis QRS deviation, embryonic initial q wave in I and aVL, and rSr' in aVR without criterion for right end conduction delay. Qsr in V1 and qRSr'em V2

ST segment elevation in V2-V3 with saddle back shape in V2, 1mm in V1 and 2mV on V3; Negative T waves on right precordial leads. Transition zone deviated to left with R/S pattern in V4 and persistence S wave in V5-V6

Conclusion Sinus bradychardia, left anterior fascicular block, and anteroseptal myocardial infarction

Observation: I don't see ECG Brugada pattern in this first ECG.

ECG2: immediately after cath / angioplasty: no changes in relation to the admission ECG except for technical improvement.

ECG3: type 1 Brugada pattern characterized by convex to the ST segment elevation greater ≥ 2 mm (0.2 mV) followed by negative T wave in right precordial leads (V1 to V3). In this case, calls attention to the standard ischemia in V4: ST without ST inverted T - incomplete reperfusion.

ECG4: V2: Q notched isoelectric baseline; reperfusion - T wave flattened V5, V6-R voltage increase in these leads (with the word Dr. Sclarovsky on these phenomena of reperfusion.

Conclusion: 1. Brugada ECG pattern in 3 with concomitant ischemia - 24 hours after angioplasty and stenting in left anterior descending artery. 2. anteroseptal infarction on ECG five days after percutaneous intervention with complete reperfusion 3. worth investigating with Na⁺ blocker provocative drugs.

Adail - Bahia - Brazil

To Dr Raimundo Barbosa Barros and Professor Andrés Ricardo Pérez Riera: very nice case of reperfused LAD and Brugada syndrome together The amazing phenomenon is that the patient with two high risks ECG pattern he didn't suffered from ventricular fibrillation or reperfusion polymorphic ventricular tachycardia

My sincere congratulation of the two brilliant cardiologist

Samuel Sclarovsky

Para Dr Raimundo Barbosa Barros e Professor André s Ricardo Pérez Riera: caso muito lindo de descendente anterior reperfundida e síndrome de Brugada juntos O fenômeno incrível é que o paciente com dois padrões eletrocardiográficos de elevado risco não sofrera fibrilação ventricular ou taquicardia ventricular polimorfa de reperfusão

Minhas sinceras felicitações a estes dois brilhantes cardiologistas.

Samuel Sclarovsky

Para el Dr. Raimundo Barbosa Barros y el Profesor Andrés Ricardo Pérez Riera: caso muy hermoso de reperfusión de la descendente anterior y síndrome de Brugada concomitante. El fenómeno increíble es que con dos patrones electrocardiográficos de elevado riesgo no sufrirera fibrilación ventricular o TV polimófica de reperfusión

Mis sinceras felicitaciones a estos dos brillantes cardiólogos

Samuel Sclarovsky

Andres Sorry to be so slow to respond. This is an interesting ECG series indeed. As you are aware, there is a great deal of dynamicity in the electrocardiographic (and arrhythmic) manifestation of Brugada syndrome (BrS). This dynamicity is due to fluctuations in autonomic tone, hormone levels (thyroid, testosterone, etc), administration of drugs (particularly psychotropic, narcotics, etc), blood alcohol levels and fever, to mention just a few. There clearly is not enough information to know which, if any, of these contributed to the manifestation of a BrS ECG a day after PCI and marked diminution of the phenotype 5 days later.

In this particular case, the presence of ischemia likely introduces another dimension and that is of ion channel remodeling that may occur as a consequence of the ischemic episode. While we are largely ignorant about the ischemia-mediated ion channel remodeling that can accentuate BrS, we are somewhat knowledgeable about the factors that accentuate ion channel remodeling in the case of post-MI QT prolongation and Torsade de Pointes (Crotti et al, [Torsade de Pointes following Acute Myocardial Infarction: Evidence for a Deadly Link with a Common Genetic Variant](#). Heart Rhythm, In press). Here, a polymorphism in HERG (K897T) or LQTS mutations appear to synergize the electrical remodeling process that occurs following ischemia or MI. Whether a similar interaction occurs between the post-ischemic electrical remodeling and the genetic variants underlying BrS, remains to be demonstrated.

A synergism is thought to exist between BrS and ischemia because both are associated or can be accentuated by a reduction in I_{Na} or I_{Ca} as well as an increase in I_{K-ATP} . This however does not explain the development of a Type I ST segment elevation the day *after* PCI.

Warmest regards

Charlie

Charles Antzelevitch, PhD, FACC, FAHA, FHRS Executive Director/Director of Research
Gordon K. Moe Scholar Professor of Pharmacology Masonic Medical Research Laboratory 2150 Bleecker
Street Utica, NY 13501-1787 Tel: (315) 735-2217 ext. 117 (after 5 PM ext. 129) Fax: (315) 735-5648
ca@mmrl.edu

www.mmrl.edu To view a short movie about the Masonic Medical Research Laboratory, please click on link below:

<http://www.impactmovie.com/mmrl>

Andrés Perdón por ser tan lento para responder. Se trata de una interesante serie de ECG de hecho. Como ustedes saben, hay una gran cantidad de dinamismo en el electrocardiograma (y arrítmico) la manifestación del síndrome de Brugada (BRS). Este dinamismo se debe a fluctuaciones en los niveles autonómicos tono de hormonas, (tiroides, la testosterona, etc), la administración de medicamentos (en particular, psicotrópicas, cocaína, etc), los niveles de alcohol en la sangre y fiebre, por mencionar sólo algunos. Evidentemente, no existe información suficiente para saber que, en su caso, de las cuales contribuyeron a la manifestación de un SBr ECG un día después de disminución PCI y marcado del fenotipo 5 días más tarde.

En este caso particular, la presencia de isquemia probable introduce otra dimensión: “LA REMODELACIÓN DE LOS CANALES IÓNICOS” que puede producirse como consecuencia del episodio isquémico. A pesar de que conoce muy poco acerca de la remodelación de iones isquemia-mediada en el SBr BRS, tenemos buena información acerca de los factores que acentúan la remodelación de los canales iónicos en el caso de post-IAM prolongación del intervalo QT y Torsade de Pointes (**Crotti et al, [Torsade de Pointes following Acute Myocardial Infarction: Evidence for a Deadly Link with a Common Genetic Variant.](#) Heart Rhythm, In press**).. Aquí, un polimorfismo en el gen HERG (K897T) o mutaciones LQTS parecen sinergizar el proceso de remodelación iónica eléctrica que se produce en la isquemia o infarto de miocardio. Si se produce una interacción similar entre el remodelado eléctrico post-isquémica y el SBr con sus variantes genéticas que subyacen, queda por demostrar. Un sinergismo se cree que existe entre SBr y la isquemia, porque ambos están asociados o pueden acentuar una reducción en el I_{Na} o I_{Ca} , así como un aumento en I_{K-ATP} . Sin embargo, esto no explica el desarrollo de un patrón electrocardiográfico tipo I con elevación del segmento ST el día después de la PCI.

Saludos cordiales

Charlie



Charles Antzelevitch, PhD, FACC, FAHA, FHRS Executive Director/Director of Research Gordon K. Moe Scholar Professor of Pharmacology Masonic Medical Research Laboratory

Comments: we are very proud to have in our forum. the opinion of Professor Charlie. He is the main word leader in basic research about the Brugada syndrome

Can be attributed to this researcher and his school from the Masonic Medical Research Laboratory in Utica, NY. the discovery of:

- 1) Mechanism of phase 2 reentry as a cause of PVT / VF;
- 2) Demonstration of heterogeneity in the electrical thickness of the ventricular myocardium;
- 3) Detailed description of M cells and their importance in LQTS;
- 4) Delineation of the ionic and cellular basis of LQTS and Brugada syndrome;
- 5) Understanding the ionic basis of J and T wave of the ECG;
- 6) The role of M cells in the origin of U waves, triggered activity and the Torsade de Pointes;
- 7) Determination of the importance of the apex of the wave T / T wave end point "Tpeak-Tend" as an index of transmural dispersion of repolarization.
- 8) Identification of the genetic basis of congenital short QT syndrome (Ramon Brugada when he was in the Masonic laboratory.

Thank very much dearest teacher for your constant support!!

Andrés.

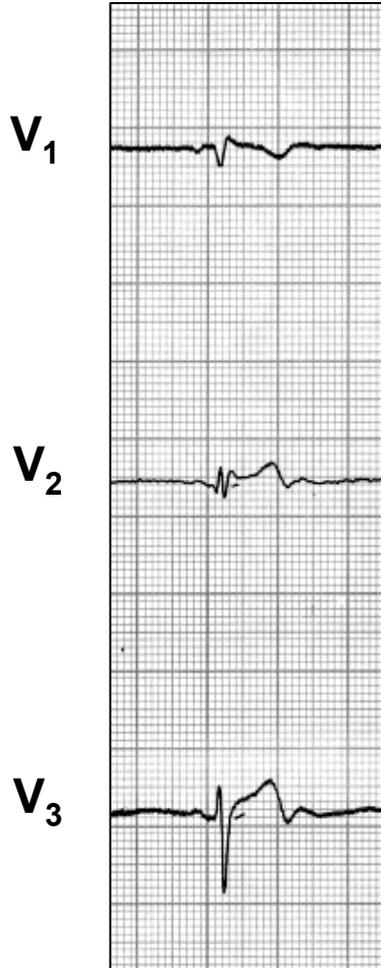
FINAL COMMENTS

By Andrés Pérez-Riera M.D. Ph.D.

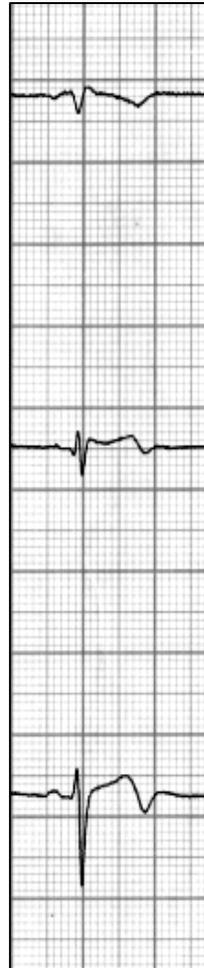
Acute MI and its consequences (death, chronic ischemic coronary artery disease, heart failure) are still the number 1 causes of death and of cardiovascular diseases. In this context, patients with STEMI are at the highest risk. The first-line management of STEMI patients often determines if the outcome is life or death. The current optimal evidence-based management of STEMI patients as a practice-oriented extract according to the latest ESC guidelines, fully published some Months ago <http://www.escardio.org>. All efforts must be made to keep the respective time intervals between the onset of symptoms and the beginning of reperfusion therapy as short as possible, i.e. best within a dedicated STEMI network. Two of the time intervals are particularly essential: the time delay between the onset of symptoms and the first medical contact (FMC) and the time delay between FMC and the beginning of reperfusion. The time delay between the onset of symptoms and FMC depends on the patient as well as on the organization of the emergency medical service (EMS). Unfortunately, too many patients/bystanders still hesitate to immediately call the EMS. More intense measures must therefore be taken to educate the public. The optimal FMC by medical doctors or paramedics reacts quickly and ideally arrives with ECG equipment for immediate diagnosis of STEMI (persistent ST-segment elevation or presumably new LBBB) before hospital admission. Unfortunately in many cases, the FMC is the emergency room of a hospital. Further decisions can be made without laboratory findings. The average time delay between onset of symptoms and FMC is very important. The next critical time interval is that between FMC and the beginning of reperfusion: this interval depends solely on the EMS organization and the distance to the next catheter laboratory with 24 h percutaneous coronary intervention (PCI) availability. The key question for further decisions is whether a primary PCI can be performed within 120 min after FMC. If so, the primary PCI should definitively be preferred. In patients <75 years presenting with a large anterior infarction within 2 h after onset of symptoms, this time interval should not exceed 90 min. For primary PCI an often used measure of quality is the "door-to-balloon" time, which should of course be as short as possible. Therefore, patients with STEMI should be admitted directly to the catheterization laboratory bypassing the ER or intensive care unit. The upper limit of the guideline recommendations is 120minutes. Here we have 8 hours of pain!!!!

European countries report a significantly shorter corresponding time delay. If primary PCI is not possible within 120 min (or 90 min) after FMC, thrombolysis must be initiated within 30 min after FMC, either in the EMS ambulance or in a nearby non-PCI hospital. A thrombolytic therapy, however, even if "successful", is not the final therapy: within 24 h (but not before 3 h) cardiac catheterization has to be performed with PCI, if applicable. PCI in these patients is not indicated. The first-line medication aims at dual antiplatelet therapy (DAPT) and anticoagulation. For DAPT, the combination of ASA with a thienopyridine is mandatory. If primary PCI is feasible, DAPT with prasugrel (loading dose of 60 mg, independent of age and weight) is preferred due to its faster onset of action and superior effectiveness over clopidogrel (loading dose of 600 mg). In patients with STEMI, prasugrel when compared to clopidogrel significantly reduced nonfatal MI after 15 months from 9.0% to 6.8% and stent thrombosis significantly from 2.8% to 1.6% (ARC definite/probable). If, however, there are contraindications against prasugrel (s/p stroke or TIA) or if thrombolysis had to be performed, clopidogrel is the choice for DAPT. The i.v. administration of glycoprotein IIb/IIIa inhibitors (GPI) has been limited to only those patients with a high intracoronary thrombus burden. The upstream application of GPI is not recommended. Recommendations for the mechanical treatment of thrombus burden include manual thrombus aspiration (which was upgraded) and a mesh-based protection stent device (MGuard™). For anticoagulation, unfractionated heparin (UFH) is recommended as always but bivalirudin is an upcoming alternative, either in the catheterization laboratory on top after an EMS-delivered UFH bolus or as a possible first-line monotherapy. Bivalirudin may be preferred in STEMI patients with a high risk of bleeding. To prevent possible thrombotic events after PCI, bivalirudin should be continued for several hours after primary PCI. Regardless of whether PCI or thrombolysis was the first-line therapy and regardless of whether a stent (BMS or DES) was implanted, DAPT should be continued for 12 months with prasugrel 10 mg/day (or 5 mg/day, if ≥ 75 years old and/or < 60 kg body weight) or clopidogrel (75 mg/day). There is no evidence that higher maintenance doses of clopidogrel may circumvent possible clopidogrel resistance. The usefulness of so far non-standardized in-vitro platelet aggregation measurements or the practice-oriented interpretation of genetic tests for CYP2C19 polymorphism is unknown. With the 12 months DAPT the patient is treated not the stent.

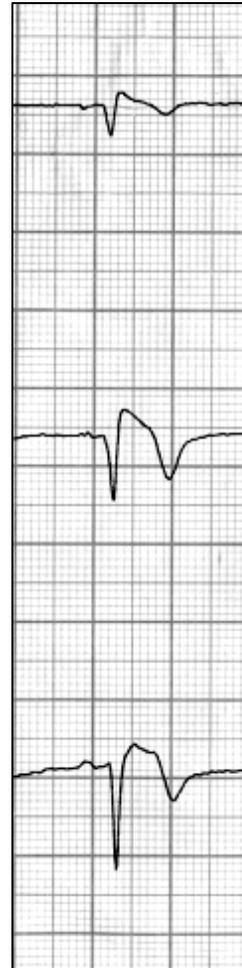
**ECG admission
January, 19/2012**



**Immediately after PCI
January, 19/ 2012**

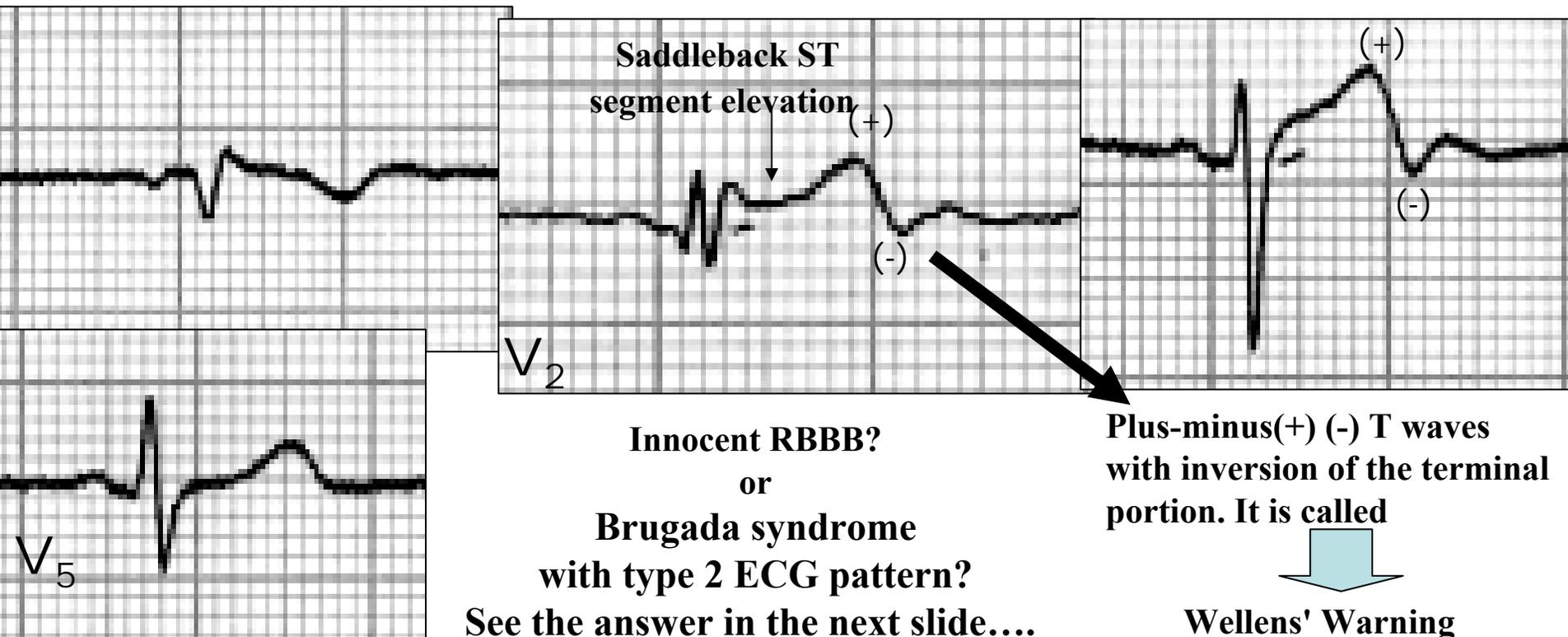


**Asymptomatic
January 20/ 2012**



**Asymptomatic
January, 25/2012**





Innocent RBBB?
or
Brugada syndrome
with type 2 ECG pattern?
See the answer in the next slide....

Plus-minus(+) (-) T waves
with inversion of the terminal
portion. It is called

Wellens' Warning

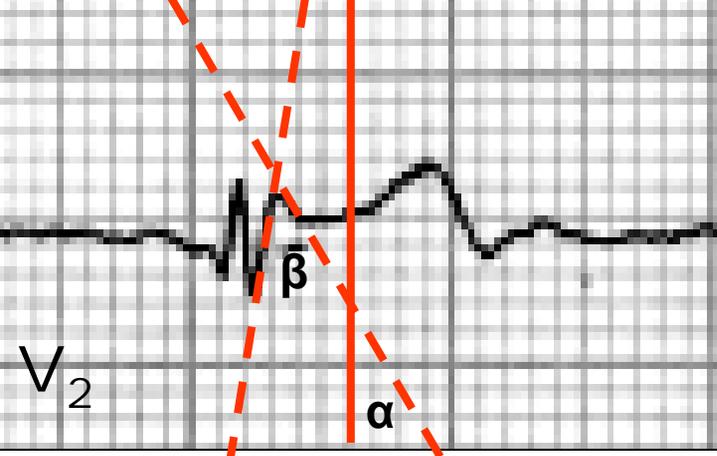
Consistent with
Subepicardial anterior
ischemia

LAD occlusion

Observation: V₂ lead shows a tetraphasic pattern **qRsR'** with broad final R' wave. QRS duration = 150ms in V₂ and < 120ms in left lead V₅ = 110ms. This observation is indicative of **parietal block on right precordial leads**. Parietal block is a typical feature of ARVC/D and BrS(1). Also in Coronary heart disease because negative dromotropic depolarization consequence the affectation of rapid phase 0 sodium channel.

Embryonic initial q wave in V₂ is indicative of electrical necrosis or electrically inactive area.

1. Peter S et al. Diagnosis of arrhythmogenic right ventricular dysplasia-cardiomyopathy: value of standard ECG revisited. Ann Noninvasive Electrocardiol 2003;8:238-245.



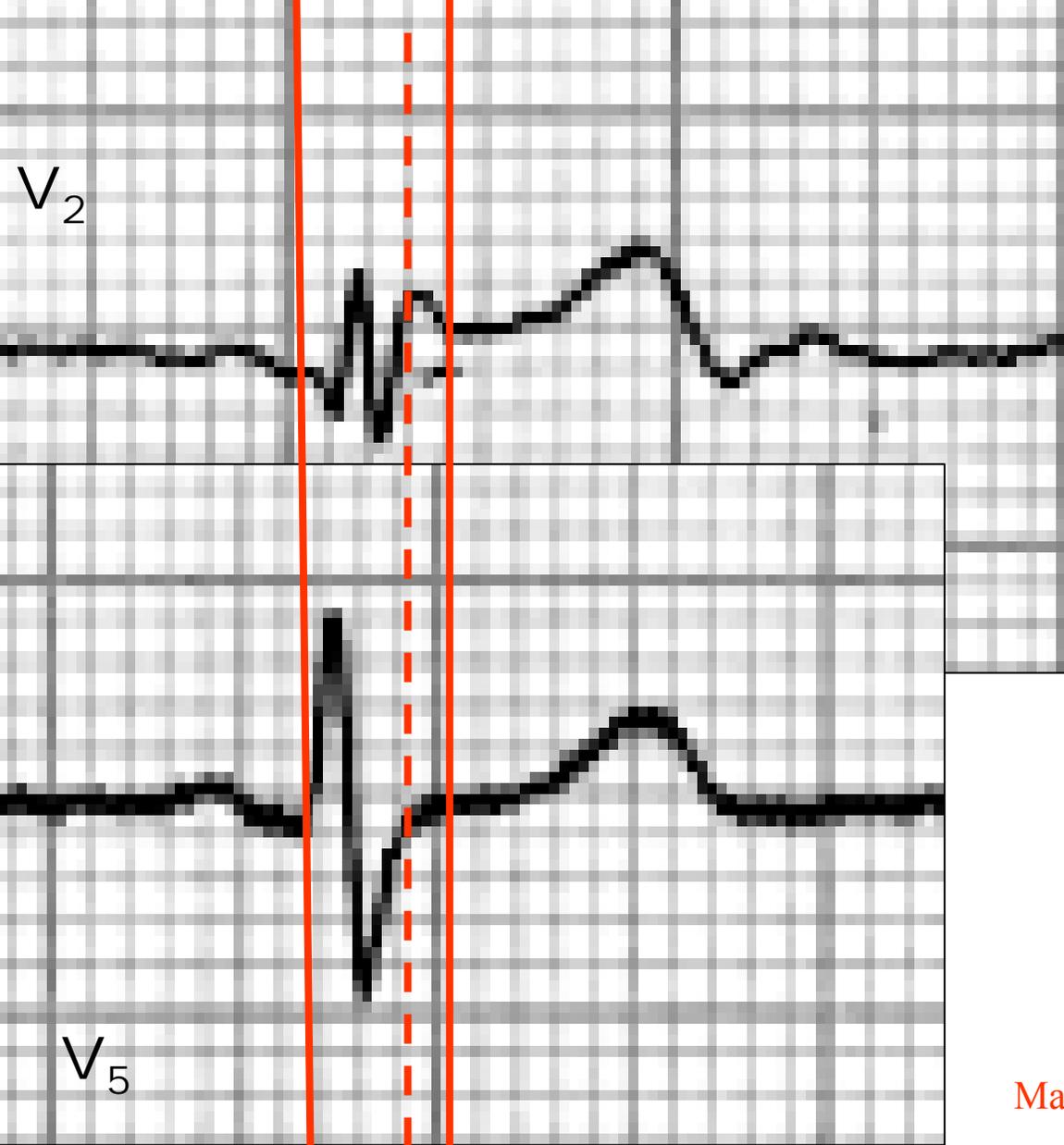
α angle: defined as the angle between a vertical line and the down slope of the r'-wave. In patients with BrS α angle is wider and fall more slowly than innocent incomplete RBBB. α angle was slightly less sensitive and specific compared with β and is clearly related with repolarization (repolarization phenomena) because it is not influenced by depolarization (QRS duration) (1)

β angle: defined as the angle between the upslope of the S-wave and the downslope of the r'-wave. The mean β angle was significantly smaller in the 14 patients with negative results on antiarrhythmic drug challenge (AAD) compared to the 24 patients with positive results on AAD ($36 \pm 20^\circ$ vs. $62 \pm 20^\circ$, $p < 0.01$). Its optimal cutoff value was 58° , which yielded a positive predictive value of 73% and a negative predictive value of 87% for conversion to type 1 pattern on AAD.

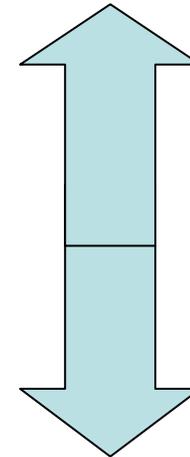
β angle is related to both depolarization and repolarization. A wider QRS complex (slow conduction) and abnormal repolarization both contribute to a wider β angle. (2)

Conclusion: Absence of Brugada syndrome. α and β angles very acute.

1. Chevallier S, Forclaz A, Tenkorang J, et al. New electrocardiographic criteria for discriminating between Brugada types 2 and 3 patterns and incomplete right bundle branch block. J Am Coll Cardiol. 2011 Nov 22;58: 2290-2298.
2. Brugada P. On the Intriguing Phenotypic Manifestations of Brugada Syndrome and the Diagnostic Value of the Electrocardiogram. 2011; 58; 2299-2300.



V₂ QRS duration = 150ms

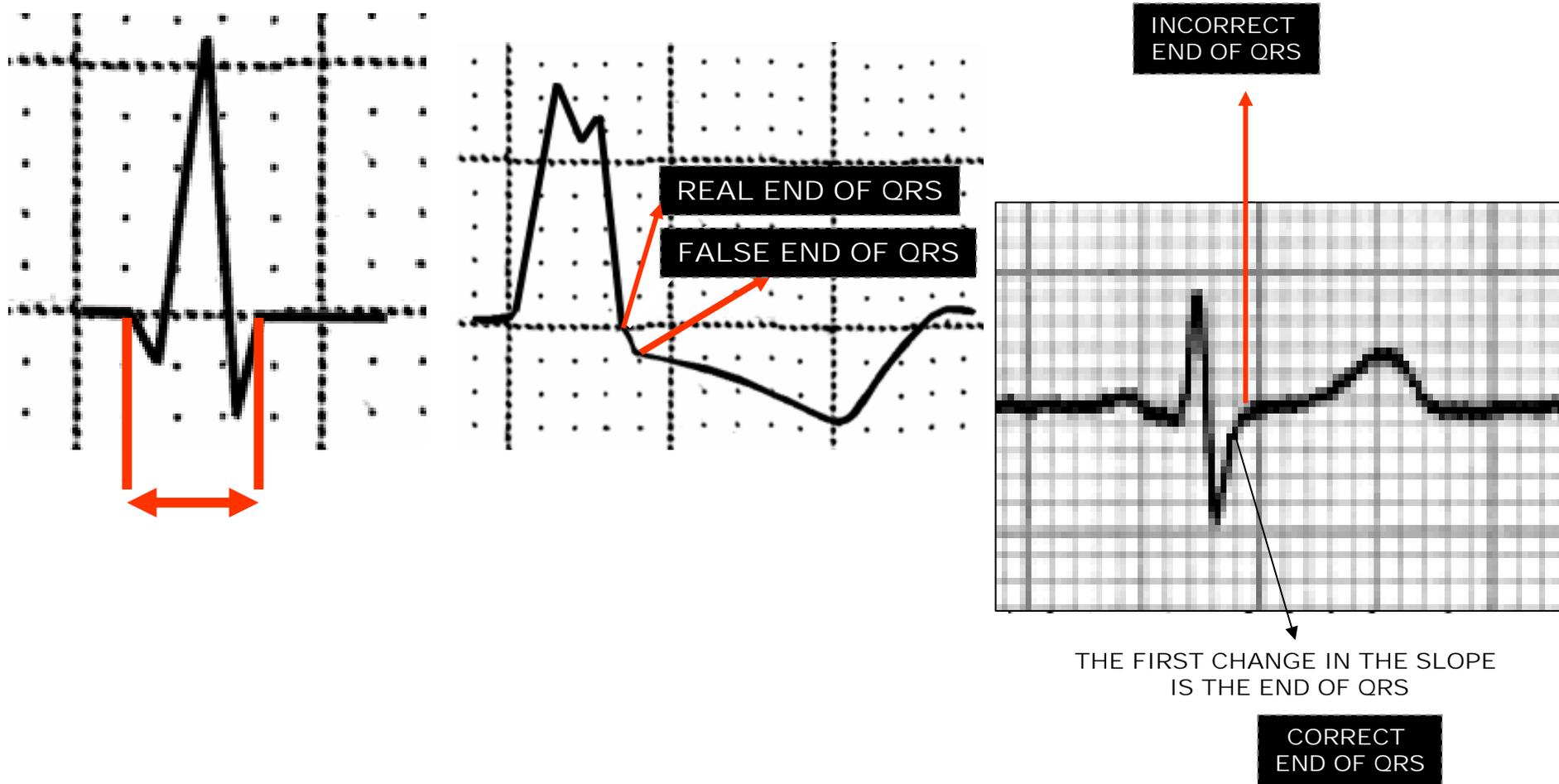


V₅ QRS duration = 110ms

Right parietal block
Marked transmurals conduction delays(1)

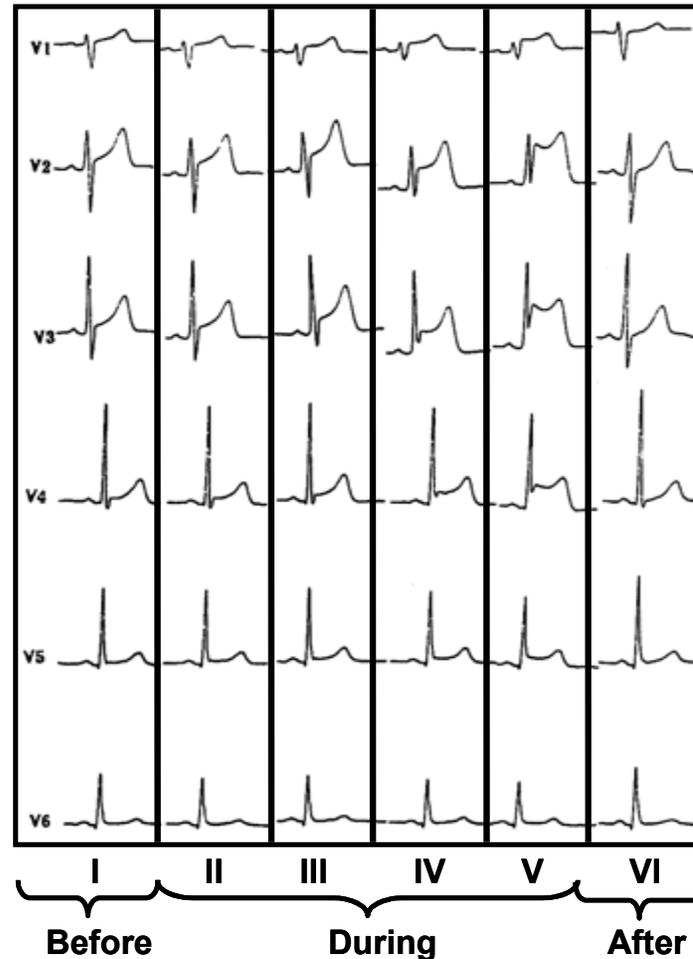
1. Di Diego JM, Fish JM, Antzelevitch C. Brugada syndrome and ischemia-induced ST-segment elevation. Similarities and differences. J Electrocardiol. 2005 Oct;38(4 Suppl):14-7.

PROPER MEASUREMENT OF QRS DURATION



Outline that shows the proper measurement of QRS complex duration.

CHANGES DURING PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY



In a patient in whom ST segment elevation was present in leads V_1 through V_3 during the PTCA procedure, balloon occlusion of the proximal left anterior descending coronary artery was associated with a QRS duration increase in these leads.(1)

References

1. Surawicz B, Orr CM, Hermiller JB, et al: QRS changes during percutaneous transluminal coronary angioplasty and their possible mechanism. *J Am Coll Cardiol* 1997; 30:452

BRUGADA SYNDROME AND ISCHEMIA RELATIONSHIP

Nishizaki et al.(1) presented a 49-year-old man with chest pain and syncope with saddleback or occasionally coved type ST elevation from V1 to V3. Coronary spasm in the left anterior descending artery was induced by acetylcholine injection and ST elevation changed from saddleback to coved type in V2-V3 together with ST depression in V4-V5 (mirror image), whereas acetylcholine injection into the RCA did not provoke spasm, but induced augmented and coved type ST elevation in V2 without ST-T changes in V4-V5. These ECG changes in response to acetylcholine administration into each coronary artery are compatible with pathogenesis of vasospastic angina and Brugada syndrome, respectively.]

Yagihara et al.(2) presented a comorbid case with concomitant BrS (Extrastimuli induced VF.) and Prinzmetal angina (intracoronary ergonovine maleate induced spasms) treated with ICD, Calcium antagonist and isosorbide dinitrate.

In the BrS is observed activation of ATP-regulated potassium current that promote phase 2 reentry (P2R) (3) Activation of I_{k-ATP} , can produce a marked dispersion of repolarization and refractoriness in epicardium as well as between epicardium and endocardium, leading to the development of PVC activity via a mechanism called by Antzelevitch time phase 2 reentry. The blockade of the transient outward current and/or the ATP-regulated potassium channels may be useful antiarrhythmic interventions under ischemic or "ATP depleted" conditions.(4)

1. Nishizaki M, Fujii H, Ashikaga T, Yamawake N, Sakurada H, Hiraoka M. ST-T wave changes in a patient complicated with vasospastic angina and Brugada syndrome: differential responses to acetylcholine in right and left coronary artery. *Heart Vessels*. 2008; 23: 201-205.
2. Yagihara N, Sato A, Furushima H, Chinushi M, Hirono T, Aizawa Y. Ischemia-induced prominent J waves in a patient with Brugada syndrome. *Intern Med*. 2010;49:1979-1982.
3. Antzelevitch C, Di Diego JM: The role of K⁺ channel activators in cardiac electrophysiology and arrhythmias. *Circulation* 1992; 85:1627-1629.
4. Di Diego JM, Antzelevitch C. Pinacidil-induced electrical heterogeneity and extrasystolic activity in canine ventricular tissues: Does activation of ATP-regulated potassium current promote phase 2 reentry? *Circulation* 1993; 88: 1177-1189.

I_{k-ATP} ; ATP-dependent potassium current, ATP-sensitive K^+ (KATP) channels or time-independent K^+

Current through channels activated by a fall in intracellular ATP concentration; inhibited by terfenadine, (1) sulfonylurea drugs, such as the sulphonylurea glibenclamide (2) and activated by acute ischemia due to vasospasm. Vasospasm shortening of the APD increasing dispersion of repolarization between ischemic and non-ischemic myocardium and predisposing to reentrant arrhythmias.(3) This effect is secondary to the depression of L-type Ca^{2+} current and the activation of I_{k-ATP} during ischemia. Patients with BrS may be a higher risk of ischemia-related SCD. In the BrS is observed activation of ATP- regulated potassium current that promote phase 2 reentry phase (P2R). (4) ST-Segment elevation is a common ECG manifestation of acute transmural myocardial ischemia in leads facing the injury. Acute myocardial ischemia involving the RVOT is known to induce a Brugada PHENOCOPY. In the presence of a prominent Ito-mediated AP notch, no-flow ischemia causes true ST-segment elevation because of selective depression and loss of the AP dome at some epicardial sites. In the absence of a prominent AP notch, ischemia ultimately produces an apparent ST-segment elevation, which is secondary to a prolongation of the R wave caused by **marked transmural conduction delays**. Similarly, in the Brs model generated in preparations displaying a large epicardial Ito, ST-segment elevation was due to loss of the epicardial AP dome at some sites but not at others. Transmural conduction delay giving the appearance of ST-segment elevation is also observed in the Brugada model in preparations exhibiting smaller AP notch. In both models, propagation of the dome from the site at which it is maintained to a site at which it is lost may result in closely coupled phase 2 reentrant PVCs.

1. Nishio M, Habuchi Y, Tanaka H, et al. Blockage by terfenadine of the adenosine triphosphate (ATP)-sensitive K^+ current in rabbit ventricular myocytes. *J Pharmacol Exp Ther.* 1998; 287:293-300.
2. Schaffer P, Pelzmann B, Bernhart E, et al. The sulphonylurea glibenclamide inhibits voltage dependent potassium currents in human atrial and ventricular myocytes.*Br J Pharmacol.* 1999;128:1175-1180.
3. Kaab S, Zwermann L, Barth A, et al. Selective block of sarcolemmal IKATP in human cardiomyocytes using HMR 1098. *Cardiovasc Drugs Ther.* 2003; 17:435-441.
4. Antzelevitch C, Di Diego JM: The role of K^+ channel activators in cardiac electrophysiology and arrhythmias. *Circulation* 1992; 85:1627-1629.
5. Di Diego JM, Fish JM, Antzelevitch C. Brugada syndrome and ischemia-induced ST-segment elevation. Similarities and differences. *J Electrocardiol.* 2005 Oct;38(4 Suppl):14-7.

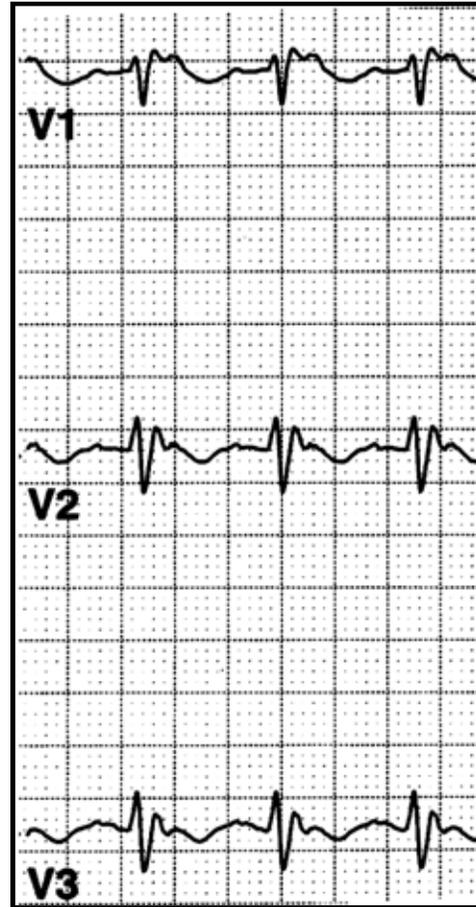
Experimental studies have suggested that a prominent I_{to} -mediated action potential notch and a subsequent loss of the AP dome in the epicardium, but not in the endocardium, give rise to ST-segment elevation and subsequent VF. Noda et al (1) evaluated the frequency of coronary spasm, augmentation (≥ 0.1 mV) of ST-segment elevation in right precordial leads, and induction of VF by intracoronary injection of acetylcholine (ACh) and/or ergonovine maleate (EM) in 27 symptomatic patients with BrS and 30 control subjects.

The coronary spasm was induced in 3 (11%) of the 27 patients with BrS and in 13 (43%) of the 30 control subjects. ST-segment elevation was augmented by 11 (33%) of the 33 RCA injections (ACh: 6/11 [55%]; EM: 5/22 [23%]), without coronary spasm, but not by any of the left coronary injections in patients with BrS. VF was induced by 3 (9%) of the 33 RCA injections (ACh: 2/11 [18%]; EM: 1/22 [5%]), but not by any of the left coronary injections. In contrast, neither ST-segment elevation nor VF was observed in any of the control subjects. These results support the hypothesis that **mild ischemia and vagal influences act additively or synergistically with the substrate responsible for the BrS to elevate the ST-segment and precipitate VF**. These observations suggest that Brugada patients may be at a higher risk for ischemia-related SD.(1)

Yagihara et al(1) presented a 75-year-old man was admitted to the hospital for evaluation of syncope and abnormal ECG. ECG showed type 1 ECG Brugada pattern. During cardiac catheterization, baseline coronary angiography was normal, but intracoronary ergonovine maleate induced spasms of the RCA and left coronary arteries concomitant with chest pain and ST elevation on ECG. J waves were accentuated or newly developed. Soon after an intracoronary injection of nitroglycerin, chest pain was relieved and ischemia-induced J wave disappeared and the ST segment returned to the same morphology as baseline. Extrastimuli induced VF. He received an ICD. He was also treated with Ca antagonist and isosorbide dinitrate and has had an uneventful course for 5 months.(2)

1. Noda T, Shimizu W, Taguchi A, et al. ST-segment elevation and ventricular fibrillation without coronary spasm by intracoronary injection of acetylcholine and/or ergonovine maleate in patients with Brugada syndrome. *J Am Coll Cardiol.* 2002 Nov 20;40:1841-1847.
2. Yagihara N, Sato A, Furushima H, Chinushi M, Hirono T, Aizawa Y. Ischemia-induced prominent J waves in a patient with Brugada syndrome. *Intern Med.* 2010;49:1979-1882.

SURGICAL REPLACEMENT OF THE AORTIC VALVE AND CORONARY BYPASS



Example of a ECG (leads V₁-V₃) simulating the type 2 ECG Brugada pattern during replacement of the aortic valve and coronary bypass.(1)

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1. Surawicz/Knilans Chou' s Electrocardiography in Clinical Practice Adult and Pediatric 5th. Edition 2001 Pg. 136 figure 7-22 Foreword by Douglas P. Zipes W. B. Saunders Company A Harcourt Health Science Company

**BRUGADA SYNDROME
AND
VASOSPASTIC ANGINA RELATIONSHIP**
Andrés R Pérez-Riera creation

BRUGADA SYNDROME AND VASOSPASTIC ANGINA

	BRUGADA SYNDROME	VASOSPASTIC ANGINA
Precordial pain:	No.	Yes.
Tendency to VT/VF:	High.	High.
Structural heart disease:	Absent.	Could exist.
Response to nitrates and nitroglycerine:	Null.	Improves or suppresses clinical/electrocardiographic manifestations.
Permanence of ST segment elevation:	Persistent (or fluctuating) and without pain.	Brief, transitory and accompanied by pain.
Cause:	Genetic alteration of Na ⁺ channel. Esporadic.Others	Possible alteration in production nitrous oxide in vascular wall.
Presence of image in mirror or reciprocal in ECG:	Could be present.	Present.
Topography of ST elevation:	Right precordial leads of V1 to V3; it could rarely be observed in inferior wall and triggered or increased by antiarrhythmic agents of the IC ¹ and IA classes.	Variable. It could alternate between precordial leads and inferior ones. It could be triggered by hyperventilation.

BRUGADA AND VASOSPASTIC ANGINA

BRUGADA SYNDROME

VASOSPASTIC ANGINA

Dromotropic disorders:

AV block of the first degree by extension of H-V in 50% of cases and in carriers of the mutation.

It could happen in a transitory way until a high degree of AV block during the episode; it is associated with a higher risk of arrhythmia and SCD.

Persistent T wave inversion:

Negative T wave in precordial leads from V1 to V3, characteristic of type 1 ECG pattern.

Inverted and deep T waves from V1 to V4 associated to anterior hypokinesia, suggesting myocardial “stunning” that indicates critical lesion of the anterior descending artery: “LAD-T wave pattern”.

Presence of transitory Q wave:

No.

It could happen.

Effort test:

It could normalized the variation during effort.

Variable response.

Myocardial scintigraphy with thallium 201:

Normal.

Transitory transmural hypo -uptake.

BRUGADA SYNDROME AND VASOSPASTIC ANGINA

BRUGADA SYNDROME

VASOSPASTIC ANGINA

Response to test of maleate of ergonovine in doses of 0.05 to 0.40 mg (stimulant of alpha adrenergic and serotoninergic receptor)

There could be a mild diffuse reduction of caliber without spasm when doses are equal to or less than 0.40 mg are used.

Intense coronary spasm accompanied by pain and ST elevation. Possible cardiac block, asystole and VT.

Response to hyperventilation:

It does not modify.

Severe spasm and reproduction of clinical electrocardiographic manifestations.

Response to intracoronary acetylcholine, each dose given in a time above one minute, in doses of 10, 25, 50 and 100 μ g doses separated by five minute intervals:

It could worsen the ST elevation with paradoxical dilation of coronary vessels.

Severe spasm and reproduction of clinical electrocardiographic manifestations.

BRUGADA SYNDROME AND VASOSPASTIC ANGINA

BRUGADA SYNDROME

VASOSPASTIC ANGINA

Response to magnesium sulfate:

Not mentioned.

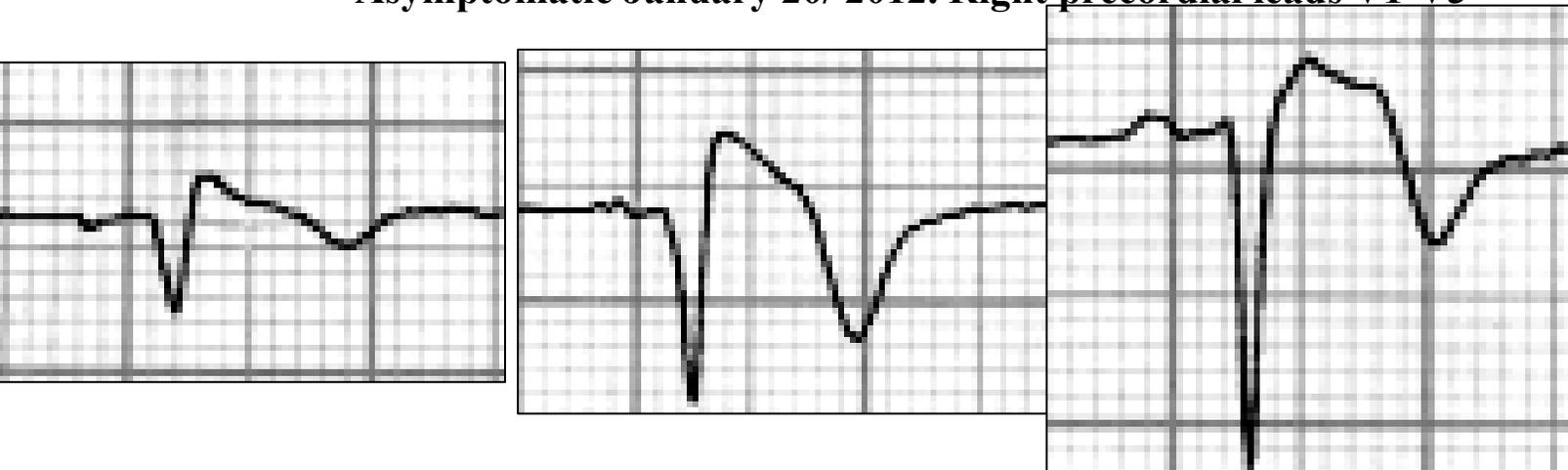
Suppresses attacks induced by hyperventilation and exercise.

Treatment:

Automatic implantable cardioverter defibrillator in association with amiodarone, a drug that contributes to diminish the number of shocks. Isoproterenol indicated in electric storm associated with general anesthesia and cardiopulmonary "bypass" or Amiodarone?

Calcium antagonists, such as nifedipine, diltiazem, verapamil, and felodipine associated to nitrates. Benefit with prazosin is mentioned.

Asymptomatic January 20/ 2012. Right precordial leads V1-V3



This pattern is the classical observed in AMI. These ECG modifications are observed after 20 minutes of experimental LAD coronary occlusion: necrosis, subepicardial injury and ischemia. We observe:

1. **Necrosis Q wave : Q duration ≥ 40 ms**
2. **Subepicardial injury current: ST segment elevation convex to the top**
3. **T wave of subepicardial ischemia. Negative symmetrical broad base T wave**

Is this pattern a Type 1 ECG Brugada pattern in a patient with BrS ?

Answer: We don't know, but very probably this is a mere ischemic-mediated Brugada phenocopy (1;2;3;4)

1. Baranchuk A, Nguyen T, Ryu MH, Femenía F, Zareba W, Wilde AAM, Shimizu W, Brugada P, Pérez-Riera AR. Brugada Phenocopy: New terminology and proposed classification. *Ann Noninvasive Electrocardiol* 2012(in press)
2. Wang JG, McIntyre WF, Kong W, Baranchuk A. Electrocutation-induced Brugada phenocopy. *Int J Cardiol.* 2012 Feb 9. [Epub ahead of print]
3. Nguyen T, Smythe J, Baranchuk A. Rhabdomyoma of the interventricular septum presenting as a Brugada phenocopy. *Cardiol Young.* 2011 Oct;21:591-594.
4. Arce M, Riera AR, Femenía F, Baranchuk A. Brugada electrocardiographic phenocopy in a patient with chronic Chagasic cardiomyopathy. *Cardiol J.* 2010;17:525-527.

After 20 minutes of experimental or natural total obstruction of a coronary branch, three concentric areas are delimited in the affected myocardium:

- 1) Peripheral or ischemic area: it modifies the T wave. In it, there is a discrete circulatory deficit, and only metabolic and functional alterations without ultrastructural injuries.
- 2) Intermediate injury area: it modifies the ST segment. There is a greater circulatory deficit than in the previous one, and ultrastructural modifications; however, without cell death and still reversible.
- 3) Central or necrosis area: it modifies the QRS complex (Q wave > 40 ms). There is maximal circulatory deficit and structural injuries, nearly always irreversible.

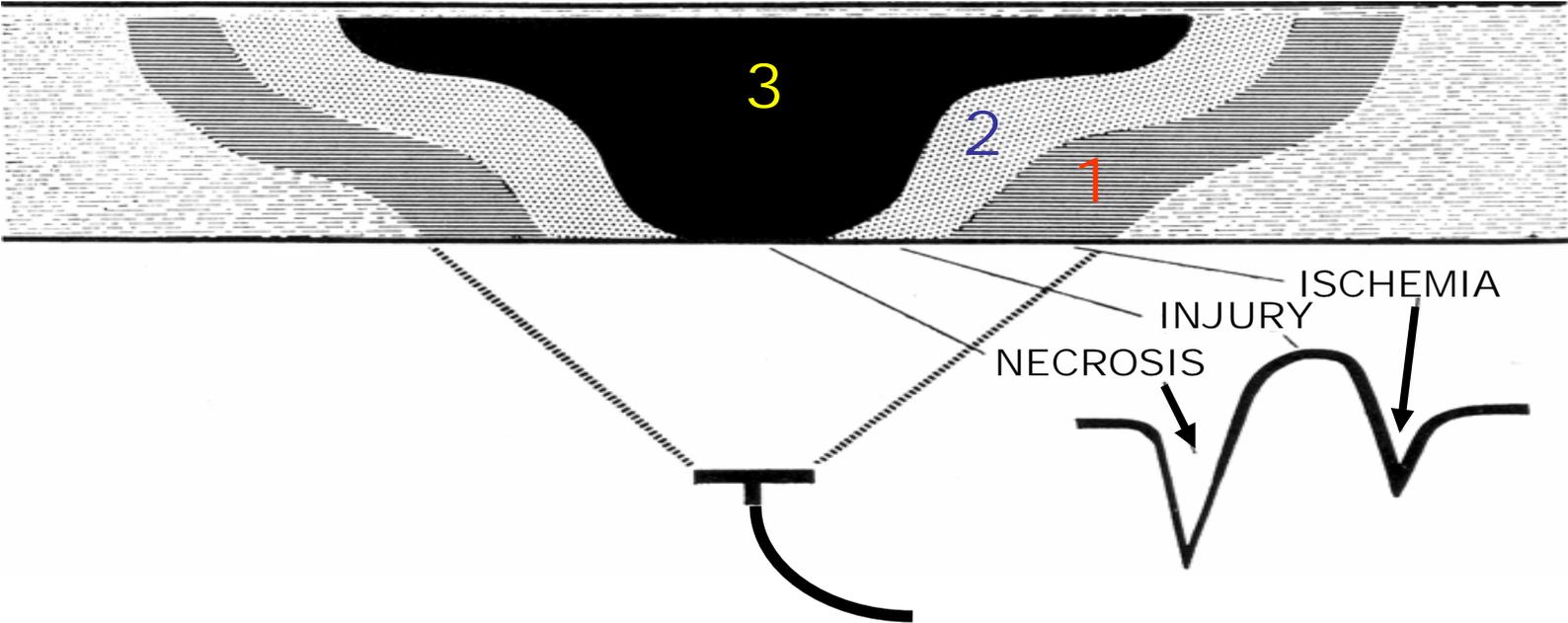
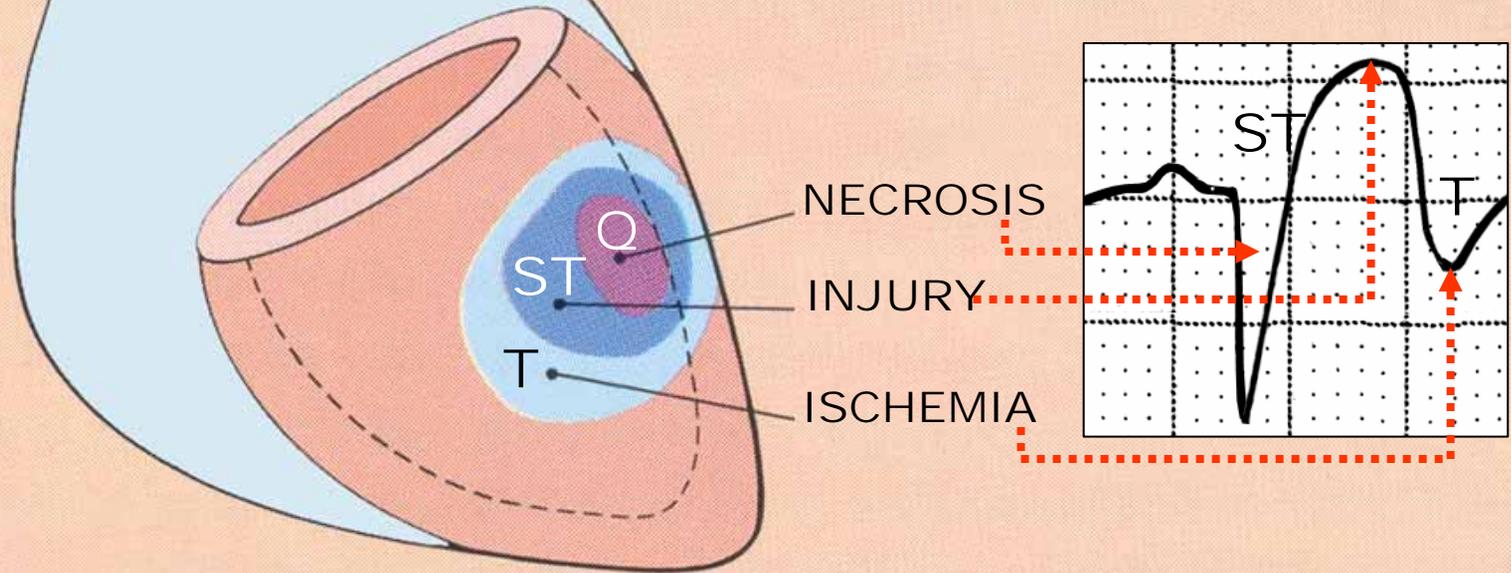


Illustration of the three areas that occur after 20 minutes of total occlusion: central area of necrosis or electric death, intermediary injury area or peripheral or ischemic area that influences on the T wave.

NECROSIS-INJURY-ISCHEMIA



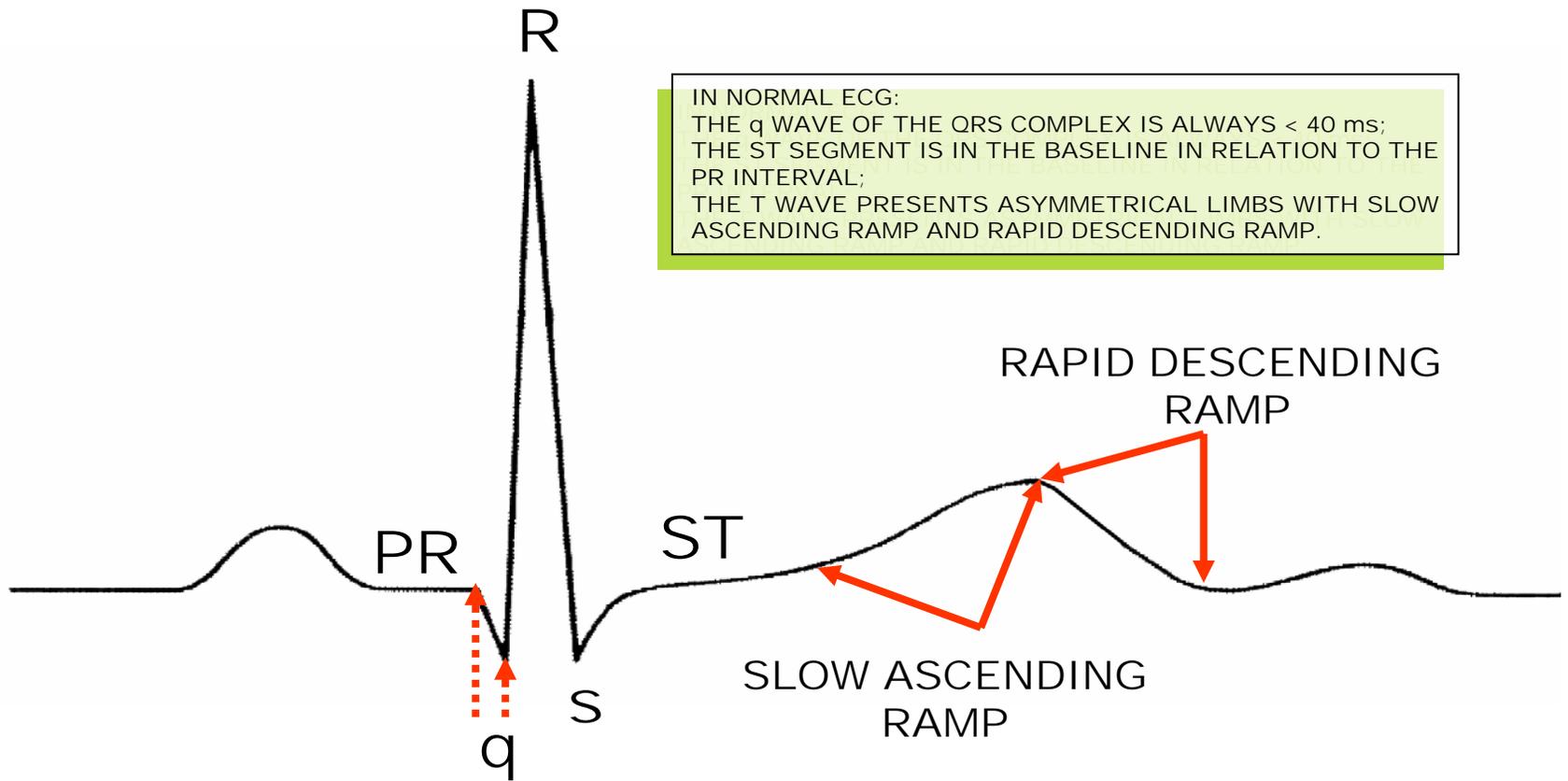
Note: the electrical death not necessarily coincides with the cell death. The first one occurs when the action potential (AP) reaches -50 mV (normal: -90 mV).

The cell does not respond and it behaves from the functional point of view, as a dead tissue, even though biologically the cell is still alive.

The acute myocardial infarction (AMI) without Q wave of necrosis in the ECG, is called non-Q or subendocardial infarction, and it represents 29% of AMI.

Hospital mortality of this type of AMI is lower than the AMI with Q wave; however, the latter one is similar, indicating that hospital survivors have a greater mortality than AMI with Q wave in the ECG.

Illustration of the necrosis-injury-ischemia in the ventricular cone.

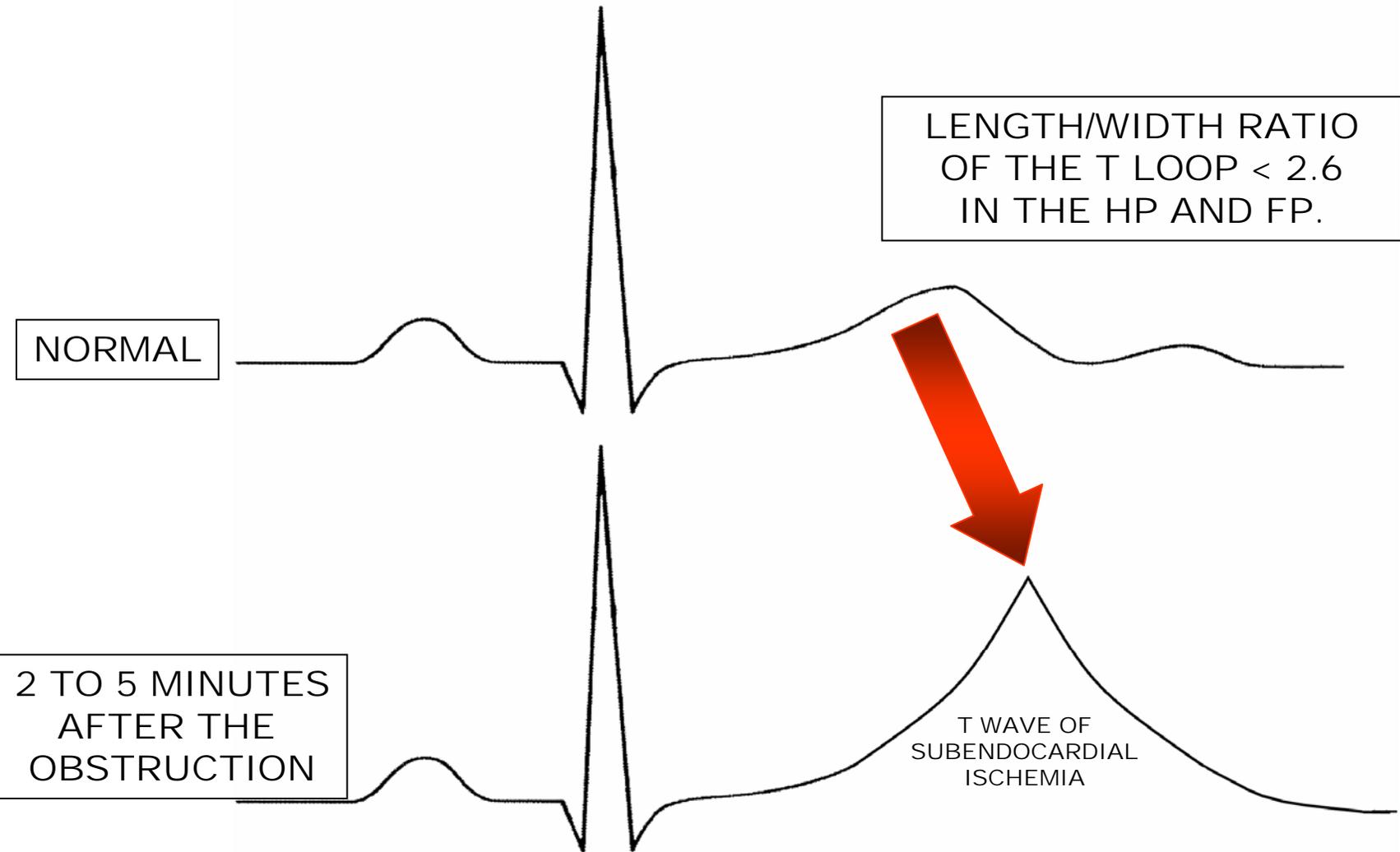


**Duration of
 q wave < 40 ms**

When the classical symptoms of acute myocardial infarction by obstruction of some coronary artery occurs, or if we experimentally fastened the left anterior descending artery of a dog, we would observe in the leads that explore the area irrigated by the vessel obstructed in a sequential/temporal way, the following modifications:

Normal ECG profile showing: Q wave (first wave of the QRS complex), the duration of which is always < 40 ms; That the ST segment is at the same level as the PR segment; T wave of asymmetrical limbs with slow ascending ramp and one rapid descending ramp

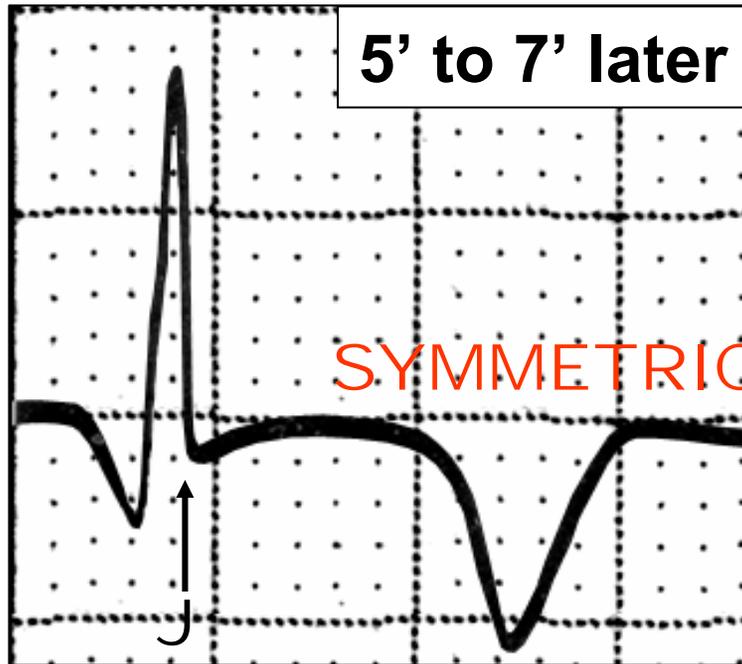
2 to 5 minutes after the obstruction or experimental fastening: the T wave becomes wider, symmetrical, with a wider base and pointy: it is the image of subendocardial ischemia.



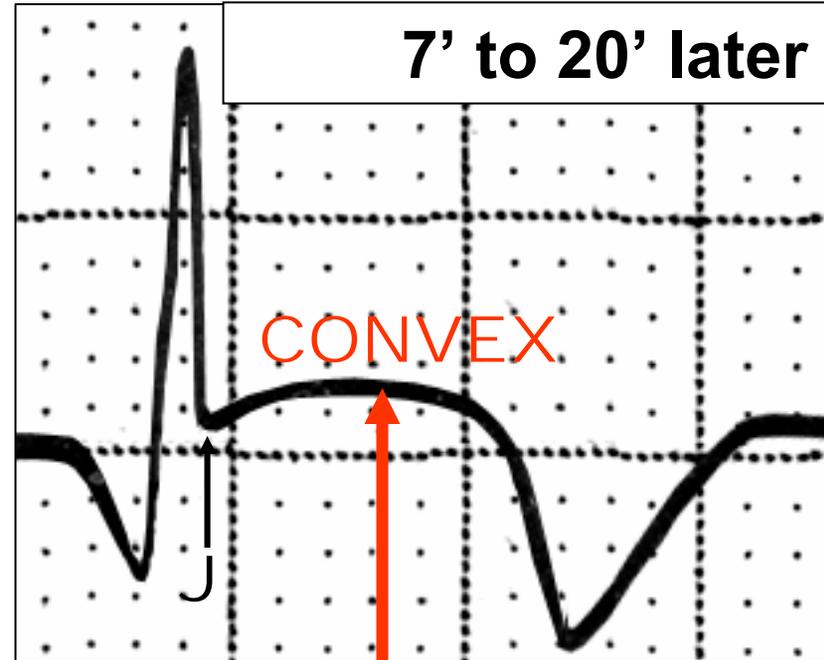
The T loop of VCG presents a uniform inscription velocity in both limbs

Outline of ECG modifications that occur between 2 and 5 minutes since the obstruction; the T wave becomes symmetrical with a broad base. The T loop of VCG presents a uniform inscription velocity in both branches and the length/width ratio of the T loop < 2.6 in the HP and the FP

5 to 7 minutes after the obstruction: we observe T wave with polarity inversion, a wide base and symmetrical limbs: it is the T wave of subepicardial ischemia or in “seagull” waves



T WAVE OF SUBEPICARDIAL ISCHEMIA

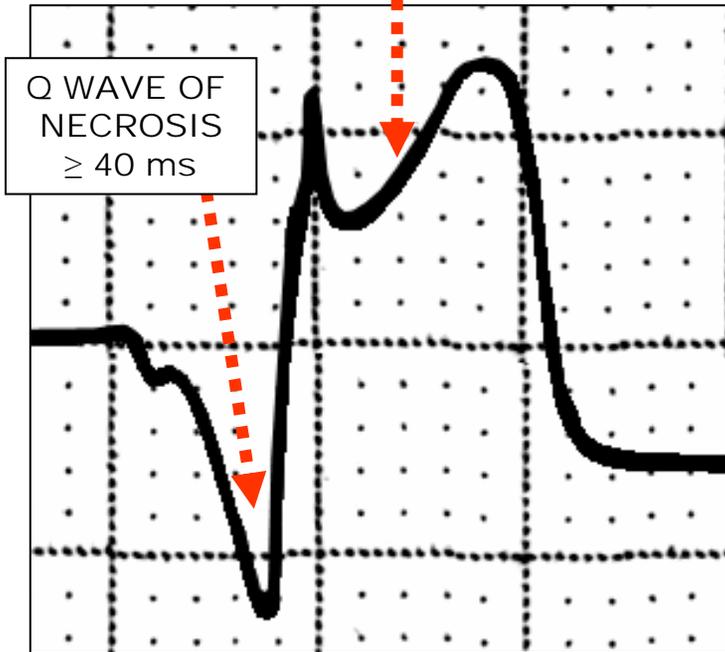


SUBEPICARDIAL INJURY CURRENT: ST

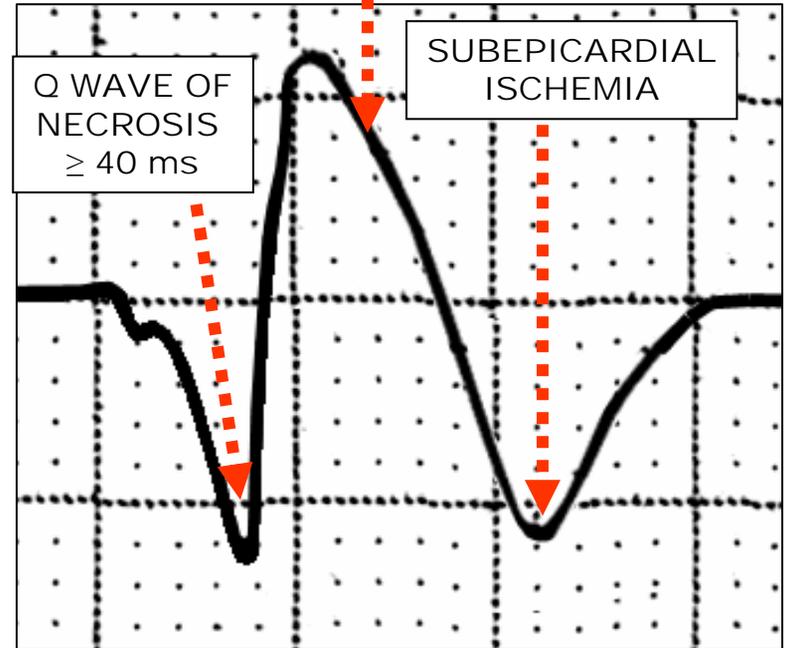
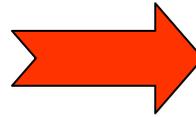
Modifications that occur between 5 and 7 minutes after the occlusion: ischemic subepicardial T wave; i.e. inverted and with symmetrical limbs. Between 7 and 20 minutes, J point and ST segment elevation convex to the top is associated to the abovementioned

AFTER 20 MINUTES

SUBEPICARDIAL INJURY CURRENT



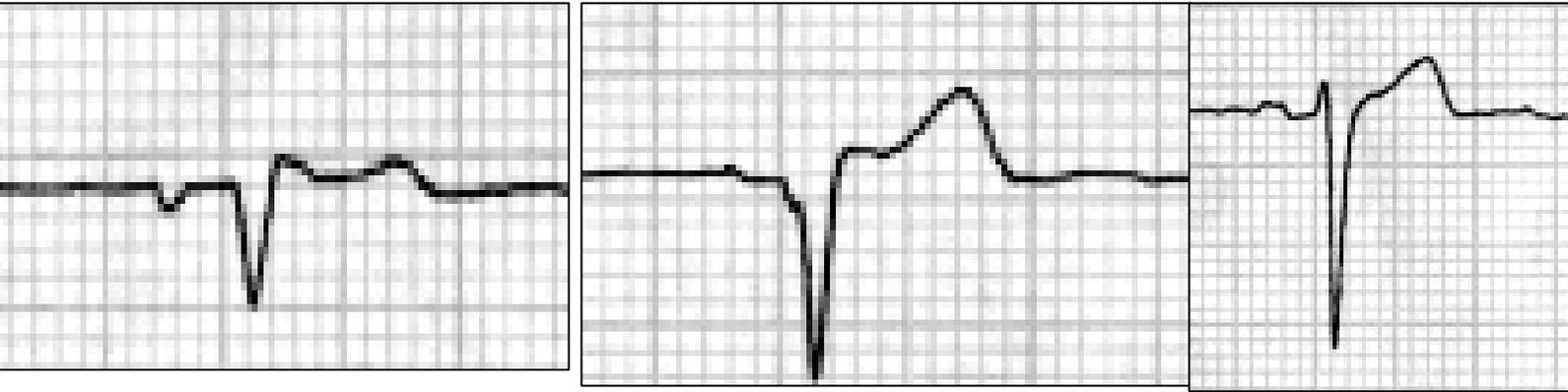
SUBEPICARDIAL INJURY CURRENT: ST



THE SET OF ALTERATIONS IS KNOWN AS PARDEE'S COMPLEX

Modifications that occur after 20 minutes of coronary occlusion, necrosis, subepicardial injury and ischemia.

Asymptomatic January, 25/2012



Only residual septal wall myocardial infarction (V_1 - V_2) In this phase we have not more chest pain.



ELECTROCARDIOGRAPHIC TOPOGRAPHIC CLASSIFICATION OF MYOCARDIAL INFARCTIONS

Wall Affected	Leads Showing ST Segment Elevation	Leads Showing Reciprocal ST Segment Depression	Suspected Culprit Artery
Septal	V1, V2	None	Left Anterior Descending (LAD)
Anterior	V3, V4	None	LAD
Anteroseptal	V1, V2, V3, V4	None	LAD
Anterolateral	V3, V4, V5, V6, I, aVL	II, III, aVF	LAD, LCX, or Obtuse Marginal
Extensive anterior (Sometimes called Anteroseptal with Lateral extension)	V1,V2,V3, V4, V5, V6, I, aVL	II, III, aVF	Left main coronary artery (LCA)
Inferior	II, III, aVF	I, aVL	RCA or (LCX)
Lateral	I, aVL, V5, V6	II, III, aVF	LCX) or Obtuse Marginal
Posterior (Usually associated with Inferior or Lateral but can be isolated)	V7, V8, V9	V1,V2,V3, V4	Posterior Descending (PDA) (branch of the RCA or LCX))

The Brugada-type 1 ECG is characterized by ST-segment elevation in the right precordial ECG leads and has been reported to have the potential of sudden death.

The right coronary artery (RCA) originates above the right cusp of the aortic valve. It travels down the right atrioventricular groove, towards the crux of the heart. At the origin of the RCA is the conus artery. The conus artery (third coronary artery) is a coronary artery that is present in only 45 percent of human hearts.(1) The conus artery may provide collateral blood flow to the heart when the left anterior descending artery is occluded.(2) In one study, 305 cadaveric specimens were examined to determine the origin of the conus coronary artery. The authors found that the conus artery could arise independently from the aorta or from a common ostium with the RCA. Right ventricular outflow tract supplied from the conus artery of the RCA is considered as the anatomopathologic substrate of BrS.

Ogano et al (3) presented two asymptomatic patients with a type 2 Brugada ECG pattern (saddleback Brugada-type ECG) who exhibited a dynamic ECG conversion to type 1 Brugada ECG pattern following a VT/VF episode when myocardial ischemia occurred exclusively at the conus artery. Some types of BrS might be caused VT/VF by selective myocardial ischemia at the conus artery.

- 1. Schlesinger MJ, Zoll PM, Wessler S (1949). "The conus artery: a third coronary artery". *American Heart Journal* 38 (6): 823–38.**
- 2. Wynn GJ, Noronha B, Burgess MI. Functional significance of the conus artery as a collateral to an occluded left anterior descending artery demonstrated by stress echocardiography. *Int J Cardiol.* 2010 Apr 1;140:e14-15.**
- 3. Ogano M, Iwasaki YK, Morita N, et al Proarrhythmic ECG deterioration caused by myocardial ischemia of the conus branch artery in patients with a Brugada ECG pattern. *Pacing Clin Electrophysiol.* 2011 Mar;34(3):e26-29.**

CONCLUSION:

Ischemic-mediated Brugada phenocopy. What is a phenocopy?

Answer: An environmental condition (in this case ischemia) that imitates (copies) one produced by a gene. Recently, (1) we proposed a new terminology that remove to the literature - together with professor Shimizu the confuse terms Brugada like ST segment elevation, and acquired forms of BrS.(2)

Why?

Because

1. Classical picture of Myocardial infarction: chest pain associated with concomitant manifestations nausea and vomiting.
2. Typical irradiation pain (radiating to the neck and left arm until the elbow, without precipitating factors,
3. The pain was constant, improving or worsening,
4. Absence of prior syncope.(asymptomatic)
5. Coronary artery disease risk factors (smoker (45packet per year) and alcoholic.
6. Negative family history.
7. Classical evolutionary ECG on right precordial leads. (LAD occlusion)

Brugada phenocopy secondary to ischemia that involve RVOT or the anteroseptal wall region is a result of the depression of I_{Ca-L} and the activation of I_{k-ATP} during ischemia.

1. Baranchuk A, Nguyen T, Ryu MH, Femenía F, Zareba W, Wilde AAM, Shimizu W, Brugada P, Pérez-Riera AR. Brugada Phenocopy: New terminology and proposed classification. *Ann Noninvasive Electrocardiol* 2012(in press)
2. Shimizu W. Acquired forms of the Brugada syndrome. *J Electrocardiol*. 2005 Oct;38(4 Suppl):22-25.