HOMEM JOVEM, SEQUELAR DE AVC, EM COMA COM SUBITAS MODIFICAÇÕES DA REPOLARIZAÇÃO VENTRICULAR

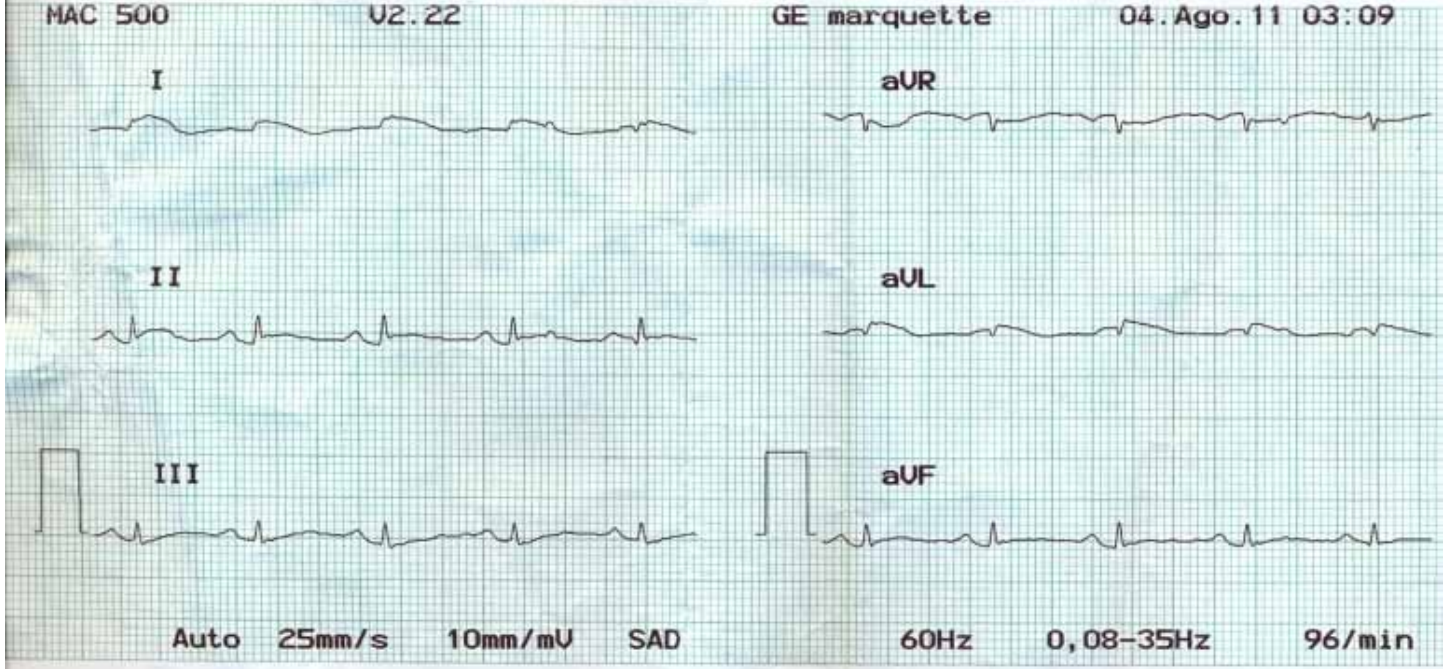
YOUNG MAN, STROKE SEQUELAE, IN STATE OF COMA WITH SUDDEN MODIFICATIONS ON VENTRICULAR REPOLARIZAÇÃO

HOMBRE JOVEN SEQUELAR DE AVC, COMATOSO CON SÚBITAS MODIFICACIONES EN LA REPOLARIZACIÓN VENTRICULAR

Case report from Dr Raimundo Barbosa Barros MD " the fox"
Coronary center Hospital de Messejana Dr. Carlos Alberto Studart Gomes
Fortaleza-Ceará-Brazil

Prezado Dr Andrés
Eu recebi esta trazado há pouco no Congresso. Não tenho maiores detalhes.
Trata-se de um paciente do sexo masculino, de 43 anos com sequela de AVC internado com pneumonia e insuficiência respiratória sob ventilação mecânica. Atualmente comatoso.
A enfermeira notou súbitas alterações no monitor e realizou este ECG. Foi rotulado como infarto do miocardio agudo.
O que voce acha desta distorção na porção final do QRS com elevação do ponto J e segmento ST
Sindrome coronariana aguda? Onda de Osborne? Hipotermia?
Estou aguardando mais detalhes pois eu não examinei o paciente.
RBB

Dear Dr Andrés
I received this recently brought in Congress. I have no details.
It is a youmg male patient, 43 yo, with sequelae of stroke hospitalized with pneumonia and respiratory failure on mechanical ventilation. Currently comatose.
The nurse noticed sudden changes in the ECG monitor and realized this ECG. It was labeled as acute myocardial infarction.
What do you think about this distortion in the final portion of the QRS with J point and ST segment elevation?
Acute coronary syndrome? Osborne wave? Hypothermia?
I'm waiting for more details because I have not examined the patient.
RBB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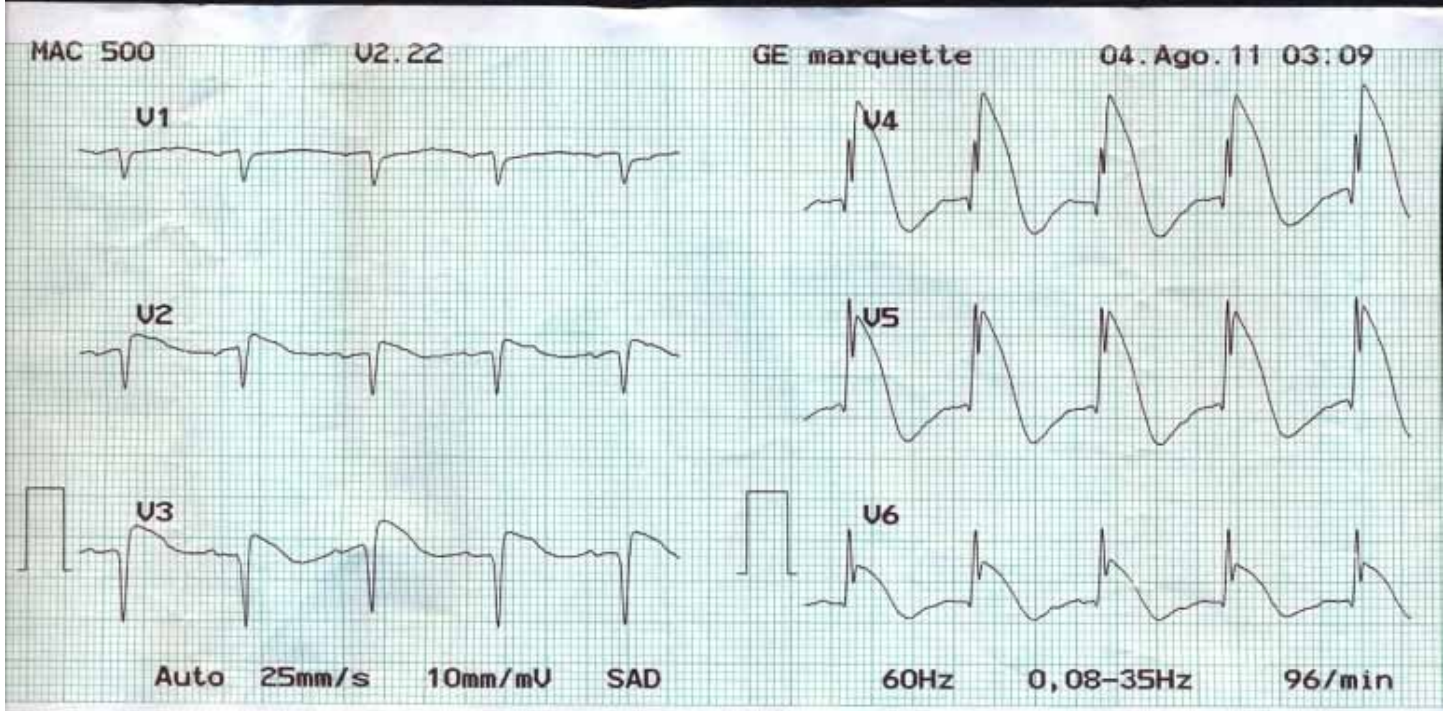
MAC 500
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V1
V4
V2
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V3
V6
Auto 25mm/s 10mm/mV SAD
60Hz 0,08-35Hz 96/min

Colleagues opinion

Con relación al caso del hombre joven con secuela de AVC, opino que el trastorno de la repolarizacion es un evento primario (síndrome coronario agudo) por la marcada elevación del ST de V2 aV6 y I-aVL, correspondiente imagen recíproca en inferior evocativas del territorio de la circunfleja.
Bajo voltaje en las derivaciones de los miembros.

Juanico Cedano

Related to the case of young man with stroke sequelae, I think that the J point and ST segment elevation are primary events (acute coronary syndrome) by the marked ST segment elevation from V2 to V6 and I-aVL, corresponding reciprocal image inferior wall evocative of the left circumflex territory. Additionally, a low QRS voltage is observed exclusively in limb leads. Cause?.

Cedano Juanico MD

Queridos Raimuindo y Andrés

Que interesante ECG, lastima no poder contar con el trazado sin esta imagen tan interesante (alguno antes o despues!). Yo analizaria este ECG de la siguiente manera:
Esta alteración de la repolarización es FISIOLÓGICA o no FISIOLÓGICA?
Por fisiologica me refiero a cualquier proceso fisiopatologico que pueda alterar la repolarización y por no-fisiologica me refiero a interferencia de cualqueir tipo no generada en el organismo sino por le metodo de deteccion.
En este caso, se me ocurren algunos diagnósticos diferenciales:

CAUSAS FISIOLOGICAS:

1. Isquemia

2. Hipotermia: ver reciente ECG publicado por Andrés en la Rev FAC y consecuente carta al editor publicada por mi en el siguiente numero

3. Alteración electrolitica: una combinacion de hipokalemia e hipomagnesemia, por ejemplo

4. Alteraciones de los canales de sodio, por ejemplo inducidas por el uso de propofol para la sedacion de la ventilacion mecanica. Sin embrago esperariamos las precordiales derechas estar mas envueltas en este fenomeno.

5. Las alteraciones del segmento ST-T en pacientes con ACV fue ampliamente descripta y debe ser tenida en cuenta (Ver Baranchuk Morillo Cardiol J 2009). Se deben a alteraciones a nivel central que modulan la actividad neuroendocrina. El envolvimeinto de la insula genera mayor alteracion ECG.

CAUSAS NO FISIOLOGICAS

1. Interferencia electromagnética: por ejemplo inducida por el ventilador mecánico (estamos estudiando esto sistematicamente en Queen's) o por otro equipo. Sin embargo, llama la atención la distribucion siguiendo el territorio de la DA, en caso de interferencia deberiamos verla en todas las derivaciones.

2. Registro arterial en el ECG, ver caso recientemente recuperado en J Electrocardiol. Pero esto se descarta porque sucede en la mayoria de las precordiales.

Resumen
Las causas pueden ser variadas, pero una combinacion de alteraciones centrales, hipotermia y trastornos electroliticos podrian justificar este cuadro.

SAlud y espero otros comentarios

AB

Paciente con historia de infarto anterolateral con presencia de onda J en V4,V5,V6. Llama la atención la presentación de las ondas patológicas en V4,V5. Con el dato de AVC hemorrágico y la hipotermia severa coincide con esta onda.

Gregorio Maslivar

Estimados amigos mi opinion

Siendo el paciente joven, con ACV (en ningun momento dice ser hemorrágico) con asistencia respiratoria mecánica por depresión de la conciencia (comatoso) con cambios súbitos de la repolarización ventricular (supradesnivel del segmento ST tipo corriente del lesión subepicárdica) simulando un potencial de acción en precordiales pensaria en:

1) Vasoespasmo coronario tipo Angina vasoespástica de Prinzmetal provocada por hipocapnia[1] secundário a hiperventilación mecánica. La hiperventilación es el aumento da cantidad de aire que ventilan los pulmones, por causas a variadas Ej. ejercício físico, fiebre, hipoxia, respiración mecánica etc., pudiendo traducirse por hipocapnia y alcalosis.
2) La posibilidad grande de aparición de arritmias ventriculares complejas: TV, TV polimorfas, FV con potencial de provocar múerte subita, y que de abortarse pueden ser causa de encefalopatia anóxica como lo presenta el paciente
3) Seria interesante saber :1) si en los cambios súbitos de la repolarización ventricular ceden con la infusión de nitroglicerina para descartar el vasoespasmo 2) El nivel de PCO2 (hipocapnia).

Saludos

Juan José Sirena Santiago del Estero Argentina.

1. **Shteĭngardt IuN, Mel'nik TG, Porovskiĭ IaV. Pseudo-ischemic changes in the ECG caused by hyperventilation. Kardiologiia. 1983 Oct;23(10):54-6.**
2. **Feldskov T, Gude AB, Højgaard MV. Severe hyperventilation as a differential diagnosis of acute coronary syndrome. Ugeskr Laeger. 2007 Jan 8;169(2):142-3.**

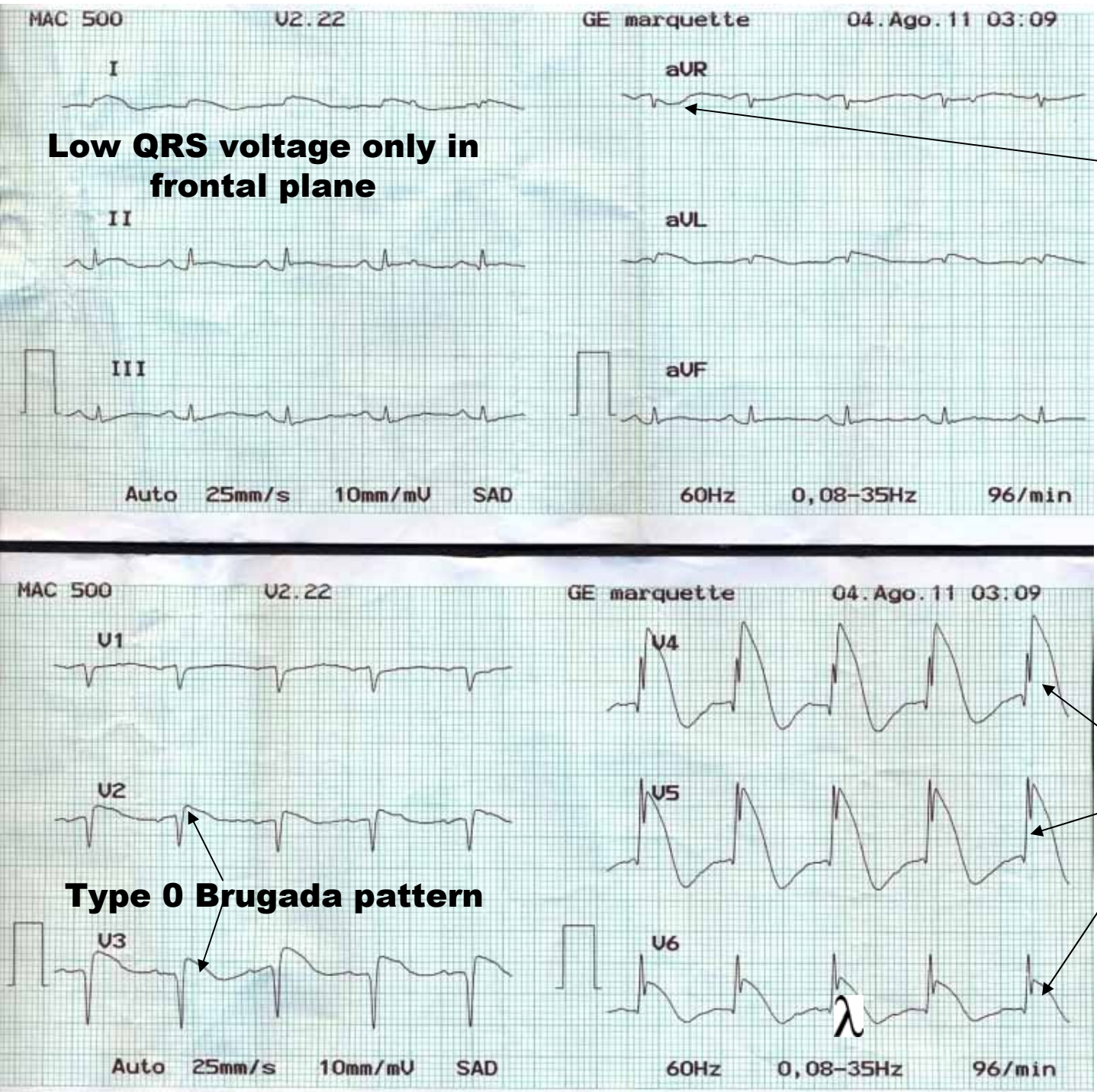
Ours conclusions

ECG analysis:

1)Sinus Rhythm; 2) Low QRS voltage only in frontal plane; 3) J points-ST segments elevation from V_4 to V_6 with monophasic action potential-like pattern. This shape is very similar with the labeled Gussak or Lambda-like wave [1;2;3.] This pattern was recently described by Kukla et al[3].in acute myocardial infarction scenario. The authors conclude that the '**lambda**-like' ST segment elevation in AMI may identify patients with increased risk of VF or SCD. 4) Type 0 Brugada-like pattern[4] from V_2 to V_3 (coved-type ST elevation without a negative T wave, which represents the existence of loss-of-dome type action potentials.).5) ST segment depression in aVR (reciprocal change or mirror image).

Diagnosis hypothesis: Hyperventilation-induced ST segment elevation mimicking acute myocardial infarction in a comatose patient. Controlled hyperventilation leading to respiratory alkalosis may induce coronary artery spasm. This maneuver is currently used in the diagnosis of Prinzmetal's angina. de Gregorio et al[5] describe the case of a comatose patient with tracheostomy in whom hyperventilation, caused by excessive bronchial secretion resulting in partial obstruction of the tracheal cannula, was followed by ST segment elevation mimicking acute myocardial infarction. Exactly as the present case.

1. **Riera AR, Ferreira C, Schapachnik E, et al. Brugada syndrome with atypical ECG: downsloping ST-segment elevation in inferior leads. J Electrocardiol. 2004 Apr;37:101-104.**
2. **Gussak I, Bjerregaard P, Kostis J. Electrocardiographic "lambda" wave and primary idiopathic cardiac asystole: a new clinical syndrome? J Electrocardiol. 2004 Apr;37(2):105-7.**
3. **Kukla P, Jastrzebski M, Sacha J, et al. Lambda-like ST segment elevation in acute myocardial infarction - a new risk marker for ventricular fibrillation? Three case reports. Kardiol Pol. 2008 Aug;66(8):873-7; discussion 877-8.**
4. **Take Y, Morita H, Wu J, et al. Spontaneous electrocardiogram alterations predict ventricular fibrillation in Brugada syndrome. Heart Rhythm 2011 Jul;8:1014-1021.**
5. **de Gregorio C, Saporito F, Andò G, Hyperventilation-induced ST segment elevation mimicking acute myocardial infarction in a comatose patient with tracheostomy. Int J Cardiol. 2011 Jun 2;149:e47-49.**



Low QRS voltage only in frontal plane

ST segment depression in aVR: reciprocal change or mirror image.

Type 0 Brugada pattern

Gussak or Lambda-like wave

λ

J point and ST segment:
An Electrocardiographic Up-date

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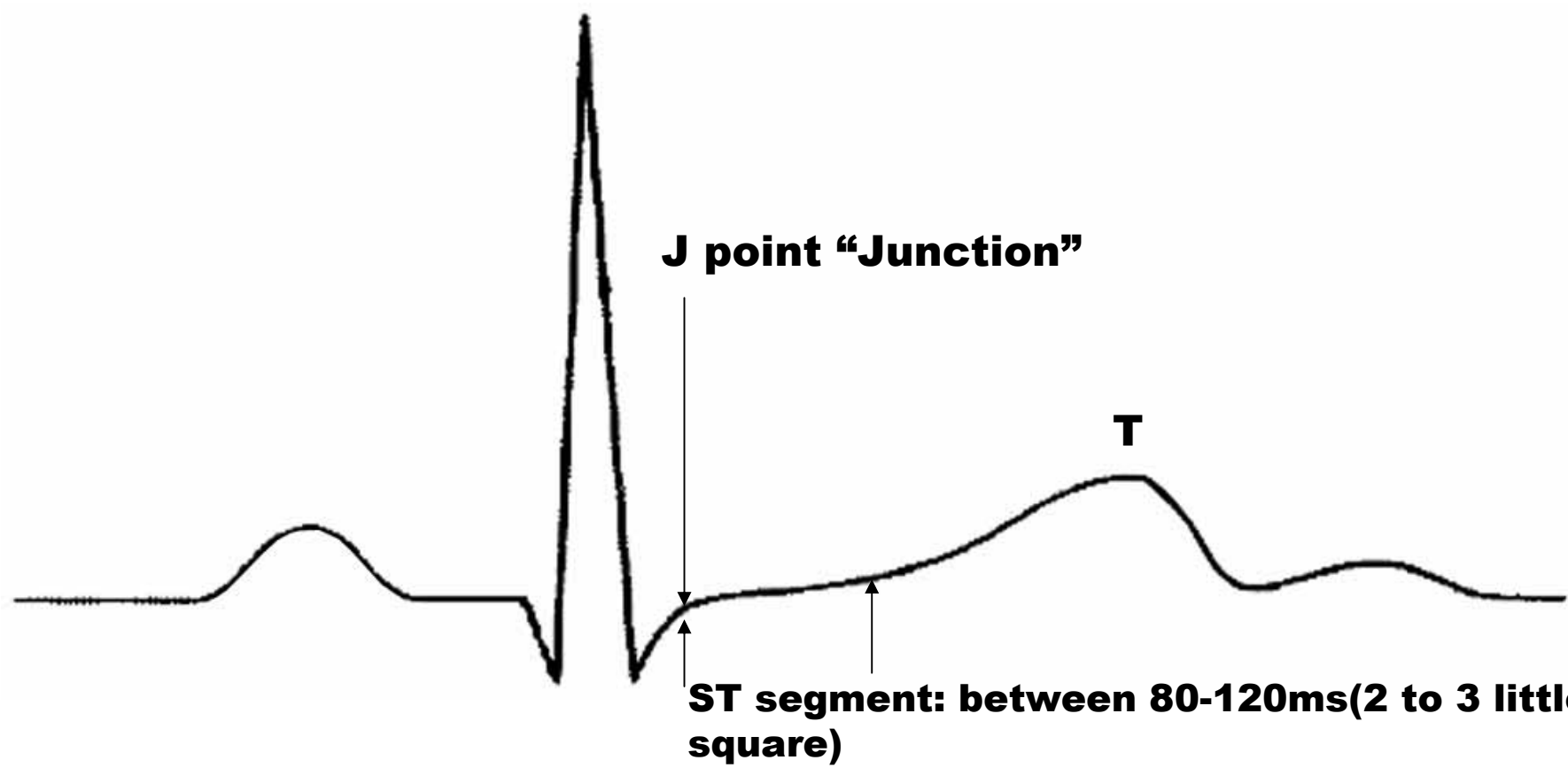
The J point is the point of convergence between the end of QRS complex and the onset of ST segment.

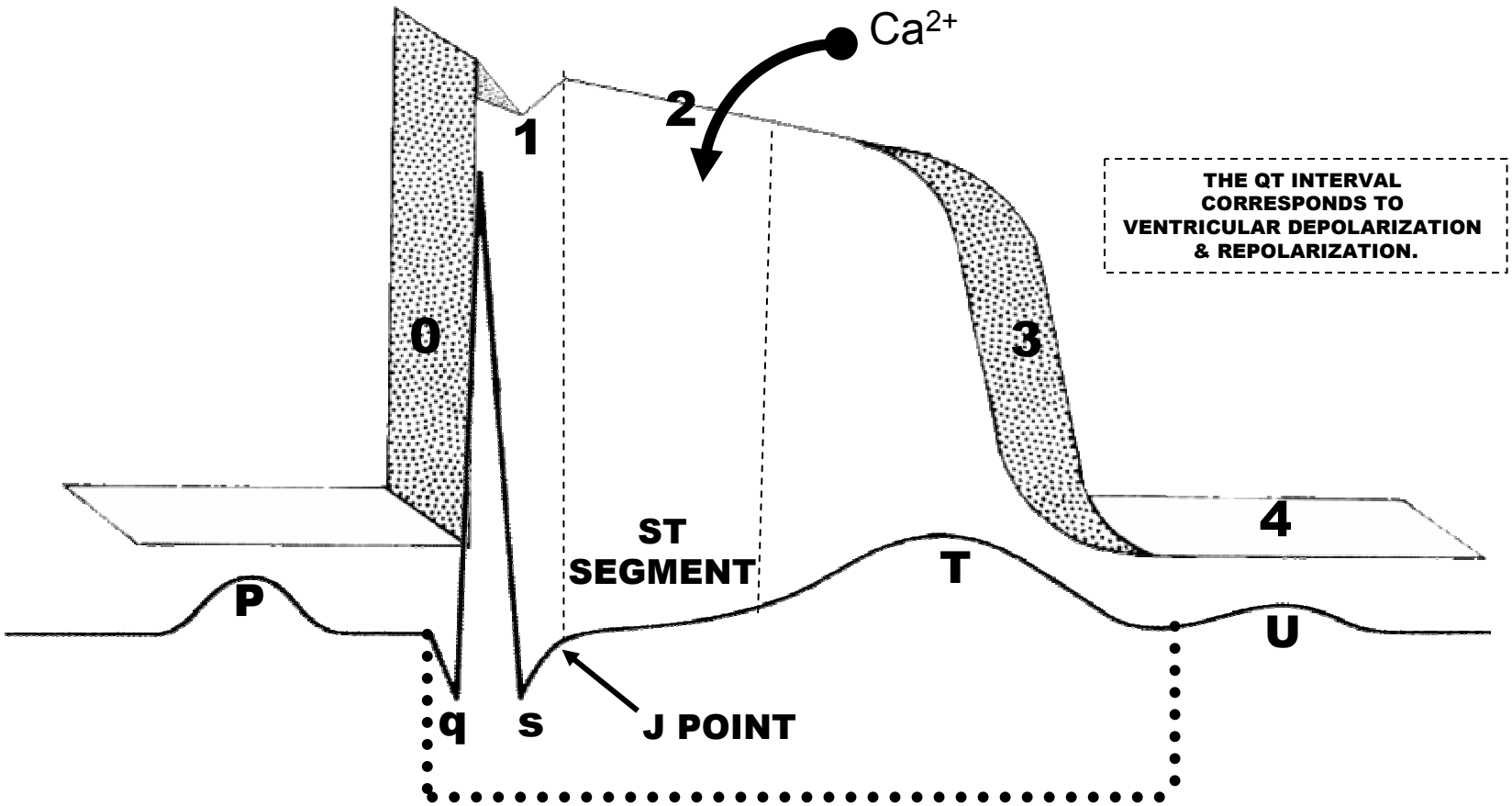
Prolonged plateau (e. i. congenital LQT3 and LQT8 variants and hypercalcaemia) are associated with a lengthening of the ST segment and late apparition of the T wave, and a shortened plateau (e.i. hypocalcaemia and Brugada Syndrome types 3 and 4) with shortening of the ST segment.

The normal ST segment duration is between 80 to 120ms

The ST segment stretches from the J point (union of ST with the end of QRS complex) up to the onset of the T wave which is usually hard to determine.



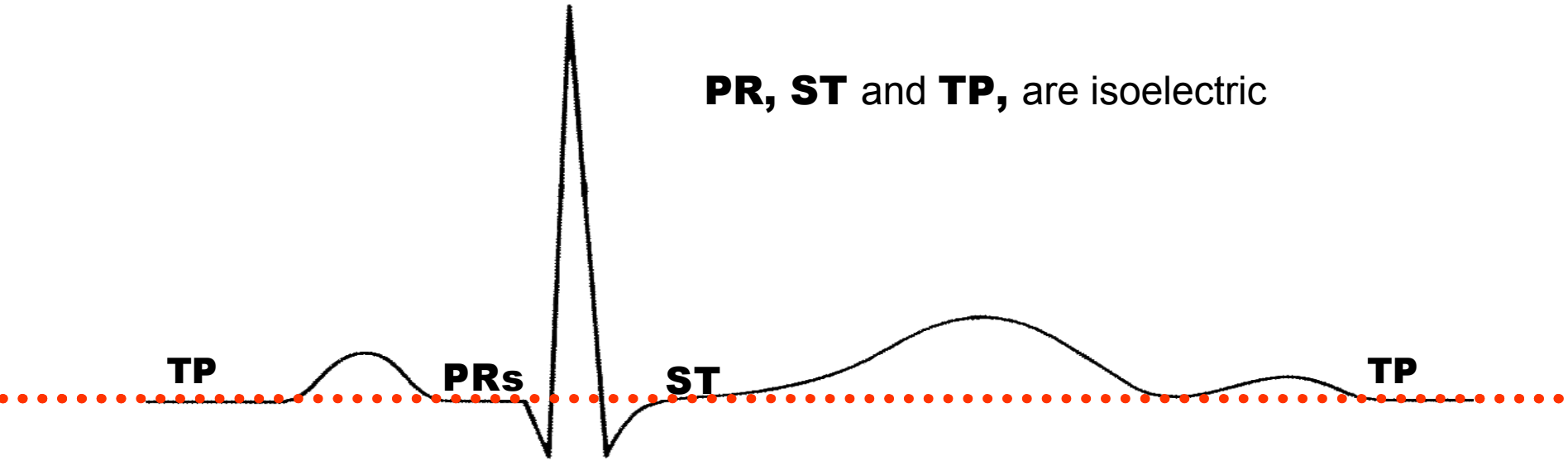
ST segment corresponds to phase 2, plateau, or dome of monophasic action potential (AP). Dome or "plateau" coinciding with the ST segment of surface ECG corresponding to slow entrance of Ca^{2+} by slow channels or I_{Ca2+-L}



QT interval or electric systole

Normal value: 350 to 440 ms or 446 ± 15%:

Correlation between monophasic action potential and surface ECG. We observe in it that phase 0 corresponds to QRS, phase 1 to the J point, phase 2 to the ST segment, phase 3 to the T wave and phase 4 to the U wave.



Regarding the level of ST segment, in normal conditions is at the same level as **PR** segment (isoelectric) fo the same complex. Usually, **PR** (end of P wave up to QRS complex onset), **ST** segment (from J point or the end of QRS up to the beginning of the T wave) and (from the end of the T wave up to the P wave of the following cycle **TP**) segments are at the same level. The figure shows a normal ECG and a line of dots pointing out the level of the three segments: **PR**, **ST** and **TP**[1].

In the limb leads the ST segment is isoelectric in 75% of normal adults[2].

In Precordial leads ST segment elevation is seen in 90% of cases of normal people[3].

ST segment elevation or depression up to 1mm is considered a normal variant.

1. **Riera AR. Correlation of levels between PRS or PQ, ST segment and TP. Cardiol J. 2008; 15: 204-205.**
2. **Hiss RG, Lamb LE, Allen MF. Electrocardiographic findings in 67,375 asymptomatic subjects. X. Normal values. Am J Cardiol. 1960 Jul;6:200-231.**

Types of J point and ST segment displacements (elevations and depressions)

I) Elevation

a) Upwardly convex (convex to the top)
b) Downwardly convex or concave to the top

II) Depression

a) Depression and upwardly convex or downsloping
b) Depression and upwardly concave
c) Depression and horizontal

Clinical causes of J point and ST segment elevation upwardly convex or convex to the top

1. **Acute Coronary Syndromes (ACSs): STE-ACS[1].**
   - **ST segment elevation myocardial infarction (STEMI) Acute Myocardial Infarction (30%)**
   - **ST segment elevation Unstable Angina (UASTE) 38%**
   - **Lambda-like ST segment elevation in AMI[2]** CAD is the major determinant of SCD, and its predisposing genetic background is complex. Very recently, a first genome-wide association study on primary VF was published (See next slide).
2. **Percutaneous Coronary Intervention (PCI)** enhanced P2Y12 inhibition (protein is found on the surface of blood platelet cells and is an important regulator in blood clotting) with either higher clopidogrel dosing or new oral antiplatelet agents, including prasugrel and ticagrelor, in the setting of STEMI, focusing on results in the setting of primary PCI[3].
3. **Prinzmetal's angina, *variant angina* or angina inversa[4].** Hypocapnia induzed ST segment elevation[5].

1. **Nikus K, Pahlm O, Wagner G, Birnbaum Y, Cinca J, Clemmensen P, et al. J Electrocardiographic classification of acute coronary syndromes: a review by a committee of the International Society for Holter and Non-Invasive Electrocardiology.Electrocardiol. 2010 Mar-Apr;43:91-103.**
2. **Kukla P, Jastrzebski M, Sacha J, Bryniarski L. Lambda-like ST segment elevation in acute myocardial infarction - a new risk marker for ventricular fibrillation? Three case reports. Kardiol Pol. 2008 Aug;66(8):873-7;**
3. **Capranzano P, Mehran R, Tamburino C, Stone GW, Dangas G. Clinical Impact of Enhanced Inhibition of P2Y 12-Mediated Platelet Aggregation in Patients with ST-Segment Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention. Hosp Pract (Minneap). 2010 Nov;38:38-43.**
4. **Shah RV, Januzzi JL Jr. Images in cardiovascular medicine. ST-elevation alternans and nonsustained polymorphic ventricular tachycardia in a patient with Prinzmetal (variant) angina.Circulation. 2010 Mar 23;121:1371-1373.**
5. **de Gregorio C, Saporito F, Andò G, Hyperventilation-induced ST segment elevation mimicking acute myocardial infarction in a comatose patient with tracheostomy. Int J Cardiol. 2011 Jun 2;149:e47-49.**

The cost of genomic information has fallen steeply, but the clinical translation of genetic risk estimates remains unclear. Ashley et al[1] aimed to undertake an integrated analysis of a complete human genome in a clinical context. The authors assessed a patient with a family history of vascular disease and early SD. Clinical assessment included analysis of this patient's full genome sequence, risk prediction for CAD, screening for causes of SCD, and genetic counseling. Genetic analysis included the development of novel methods for the integration of whole genome and clinical risk. Disease and risk analysis focused on prediction of genetic risk of variants associated with Mendelian disease, recognized drug responses, and pathogenicity for novel variants. They queried disease-specific mutation databases and pharmacogenomics databases to identify genes and mutations with known associations with disease and drug response.

The authors estimated post-test probabilities of disease by applying likelihood ratios derived from integration of multiple common variants to age-appropriate and sex-appropriate pre-test probabilities. They also accounted for gene-environment interactions and conditionally dependent risks.

Analysis of 2.6 million single nucleotide polymorphisms and 752 copy number variations showed increased genetic risk for MI, type 2 diabetes, and some cancers.

The authors discovered rare variants in three genes that are clinically associated with SCD - TMEM43, DSP, and MYBPC3. A variant in LPA was consistent with a family history of CAD. The patient had a heterozygous null mutation in CYP2C19 suggesting probable clopidogrel resistance, several variants associated with a positive response to lipid-lowering therapy, and variants in CYP4F2 and VKORC1 that suggest he might have a low initial dosing requirement for warfarin. Many variants of uncertain importance were reported. These results suggest that whole-genome sequencing can yield useful and clinically relevant information for individual patients.

1. **Ashley EA, Butte AJ, Wheeler MT, Chen R, Klein TE, Dewey FE, et al. Clinical assessment incorporating a personal genome. Lancet. 2010 May 1;375: 1525-1535.**

4. **ST elevation during exercise treadmill testing:**
    - Suggests extremely tight coronary artery stenosis or spasm[1] (transmural ischemia)
    - ST elevation in the lead aVR during exercise treadmill testing may indicate left main coronary artery disease[2].

5. **Tako-Tsubo Cardiomyopathy (TTC)[3]**

6. **Kounis syndrome[4].** associated with the Greek physician Nicholas Kounis, is defined as "the concurrence of ACS with conditions associated with mast cell activation, involving interrelated and interacting inflammatory cells, and including allergic or hypersensitivity and anaphylactic or anaphylactoid insults." "It is caused by inflammatory mediators such as histamine, neutral proteases, arachidonic acid products, platelet activating factor and a variety of cytokines and chemokines released during the activation process.

1. **Norgaz T, Gorgulu S. ST elevation on the exercise ECG: only severe stenosis? Heart. 2010 Jun;96(12):995; author reply 995-6.**
2. **Ozmen N, Yiginer O, Uz O, Kardesoglu E, Aparci M, Isilak Z, et al. ST elevation in the lead aVR during exercise treadmill testing may indicate left main coronary artery disease. Kardiol Pol. 2010 Oct;68:1107-1111.**
3. **Bielecka-Dabrowa A, Mikhailidis DP, Hannam S, Rysz J, Michalska M, Akashi YJ,et al. Takotsubo cardiomyopathy--the current state of knowledge.Int J Cardiol. 2010 Jul 9;142:120-125.**
4. **Biteker M. Current understanding of Kounis syndrome. Expert Rev Clin Immunol. 2010 Sep;6:777-788.**

7. **Persistent ST-segment elevation after anterior myocardial infarction consequence of left ventricular aneurysm development**[1]
8. **Massive Pulmonary Embolism**[2]
9. **Severe hypothermia (Osborn wave**[3]**)**
10. **Idiopathic Ventricular Fibrillation or atypical BrS: Lambda wave**[4]
11. **Brugada syndrome**[5]
12. **Brugada phenocopyes, Brugada-like patterns, or acquired Brugada syndrome**[6]
13. **Congenital Short QT associated with BrS**[5]**. Overlap? Or BrS type 4?**[7]
14. **Hypertrophic cardiomyopathy (HCM).** the ECG finding of convex ST-segment elevation and abnormal Q waves could be valuable for detection of disease progression in patients with HCM[8].

1. Napodano M, Tarantini G, Ramondo A, Cacciavillani L, Corbetti F, Marra MP, et al. Myocardial abnormalities underlying persistent ST-segment elevation after anterior myocardial infarction. J Cardiovasc Med (Hagerstown). 2009 Jan;10:44-50.
2. Lin JF, Li YC, Yang PL. A case of massive pulmonary embolism with ST elevation in leads V1-4.Circ J. 2009 Jun;73:1157-9.
3. Pavlidis AN, Giannakopoulos A, Manolis AJ. Iatrogenic giant Osborn waves. Circulation. 2010 Oct 12;122(15):1519.
4. Gussak I, Bjerregaard P, Kostis J. Electrocardiographic "lambda" wave and primary idiopathic cardiac asystole: a new clinical syndrome?J Electrocardiol. 2004 Apr;37:105-107.
5. Wilde AA, Antzelevitch C, Borggrefe M, Brugada J, Brugada R, Brugada P, et al. ; Study Group on the Molecular Basis of Arrhythmias of the European Society of Cardiology. Proposed diagnostic criteria for the Brugada syndrome. Eur Heart J 2002;23:1648-1654.
6. Riera AR, Uchida AH, Schapachnik E, Dubner S, Filho CF, Ferreira C.Propofol infusion syndrome and Brugada syndrome electrocardiographic phenocopy.Cardiol J. 2010;17(2):130-5.
7. Antzelevitch C, Pollevick GD, Cordeiro JM, Casis O, Sanguinetti MC, Aizawa Y, Loss-of-function mutations in the cardiac calcium channel underlie a new clinical entity characterized by ST-segment elevation, short QT intervals, and sudden cardiac death..Circulation. 2007 Jan 30;115(4):442-9.
8. Furuki M, Kawai H, Onishi T, Hirata K. Value of convex-type ST-segment elevation and abnormal Q waves for electrocardiographic-based identification of left ventricular remodeling in hypertrophic cardiomyopathy. Kobe J Med Sci. 2009 Jun 5;55:E16-29.

The J-wave syndrome causes

I) Hypothermic J wave[1]

II) Non-hypothermic J wave: The J wave syndrome is characterized by a prominent J wave accompanied by ST-segment elevation in the absence of structural heart disease. It includes the benign early repolarization pattern, the highly arrhythmogenic BrS and IVF.

- **Classical Early repolarization Pattern (ERP) or Early Repolarization Variant (ERV)** or type 1, which displays an ERP predominantly in the lateral precordial leads, is prevalent among healthy male athletes and is rarely seen in VF survivors.

- **Early repolarization syndrome as a new electrical disorder associated with SCD** this can include the type 2, which displays an ERP predominantly in the inferior or inferolateral leads, is associated with a higher level of risk; and type 3, which displays an ERP globally in the inferior, lateral, and right precordial leads, is associated with the highest level of risk for development of malignant arrhythmias and is often associated with VF storms[2].

- **Early repolarization in short QT syndrome[3].**

1. **de Souza D, Riera AR, Bombig MT, et al. Electrocardiographic changes by accidental hypothermia in an urban and a tropical region. J Electrocardiol. 2007 Jan;40:47-52.**
2. **Antzelevitch C, Yan GX. J wave syndromes. Heart Rhythm. 2010 Apr;7: 549-58.**
3. **Watanabe H, Makiyama T, Koyama T, Kannankeril PJ, Seto S, Okamura K, et al. High prevalence of early repolarization in short QT syndrome. Heart Rhythm. 2010 May; 7: 647-65**

I) **Classical Early Repolarization Pattern[1;2](ERP):** It is not always linked with benign clinical course and can sometimes lead to repeated syncope, torsade de pointes VT/VF. Pedigree research is of importance for ERP. The association between ERP on ECGs and risk of IVF reported by Haïssaguerre et al. raises questions about the generally held concept that ERP is a benign ECG pattern. Although the association reported is strong enough to suggest validity, the data do not permit distinction between the following two possibilities: that ERP is a single pathophysiological entity with variable expression, or that ERP is a nonspecific ECG pattern that might be associated with specific high-risk or low-risk entities. Physicians should continue to view this common ECG variant as generally benign. Careful attention should, however, be paid to patients with ERP and J-point elevations ≥ 2 mm with unexplained arrhythmias or a family history of unexplained SCD[3].

1. **J Shu J, Zhu T, Yang L, Cui C, Yan GX. ST-segment elevation in the early repolarization syndrome, idiopathic ventricular fibrillation, and the Brugada syndrome: cellular and clinical linkage. Electrocardiol. 2005 Oct;38(4 Suppl):26-32.**
2. **Riera AR, Uchida AH, Schapachnik E, Dubner S, Zhang L, Celso Ferreira Filho, Ferreira C. Early repolarization variant: epidemiological aspects, mechanism, and differential diagnosis. Cardiol J. 2008;15(1):4-16.**
3. **Myerburg RJ, Castellanos A.Early repolarization and sudden cardiac arrest: theme or variation on a theme? Nat Clin Pract Cardiovasc Med. 2008 Dec;5:760-761.**

• **Severe hypercalcemia:** Electrocardiographically, relatively short QT interval (mean QTc of 340 ms) , ST segment is depressed, and T wave becomes negative in hypercalcemia. In severe cases is possible to observe rarely a J wave and Brugada type1 phenotype or mimicking acute myocardial infarction with prominent J-waves in the inferior leads.

1. **Zeb M, McKenzie DB, Naheed B, Gazis T, Morgan JM, Staniforth AD. Hypercalcaemia and a Brugada-like ECG: An independent risk factor for fatal arrhythmias. Resuscitation. 2010 Aug;81:1048-1050.**
2. **Mehta S, Parameswaran AC, Greenspan A, Figueredo VM. Hypercalcemia due to rhabdomyolysis mimicking Brugada syndrome. Pacing Clin Electrophysiol. 2009 Nov;32:e14-25.**
3. **Falk RH. Severe hypercalcaemia mimicking acute myocardial infarction. Clin Med. 2009 Oct;9:503-504.**
4. **Sado DM, Greaves K. Severe hypercalcaemia mimicking acute myocardial infarction. Clin Med. 2009 Oct;9:503.**
5. **Wesson LC, Suresh V, Parry RG. Severe hypercalcaemia mimicking acute myocardial infarction. Clin Med. 2009 Apr;9:186-187.**
6. **Namboodiri N, Bohora S, Dora SK, Tharakan JA. Electrocardiographical case. J wave and presyncope in a middle-aged woman. Singapore Med J. 2008 Feb;49:160-163.**
7. **Topsakal R, Sağlam H, Arinç H, Eryol NK, Cetin S. Electrocardiographic J wave as a result of hypercalcemia aggravated by thiazide diuretics in a case of primary hyperparathyroidism. Jpn Heart J. 2003 Nov;44:1033-1037.**
8. **Jenkins JK, Best TR, Nicks SA, Murphy FY, Bussell KL, Vesely DL. Milk-alkali syndrome with a serum calcium level of 22 mg/dl and J waves on the ECG.South Med J. 1987 Nov;80:1444-1449.**
9. **Sridharan MR, Horan LG. Electrocardiographic J wave of hypercalcemia.Am J Cardiol. 1984 Sep 1;5:672-673.**
10. **Douglas PS, Carmichael KA, Palevsky PM. Extreme hypercalcemia and electrocardiographic changes. Am J Cardiol. 1984 Sep 1;54:674-675.**

Injuries in the central nervous system: Subarachnoid hemorrhage, post-heart arrest and in cervical sympathetic system dysfunction**.**
Brugada "entities": result of a preferential abbreviation of the right ventricular epicardial action potential, With mutation cases (≈17%): true Brugada disease (autosomal dominant pattern). Sporadic cases (≈63%): Brugada syndrome.
Others Brugada phenotypes, Brugada phenocopies, Brugada-like ECG pattern or acquired Brugada syndrome: they are those clinico-pharmacological entities or circumstances, where Brugada phenotype or sign in ECG, may be found as a consequence of causing increase in Ito channel function in the ventricular epicardium or decrease of slow calcium channel5. Concealed forms of arrhythmogenic dysplasia of the right ventricle6;
Idiopathic ventricular fibrillation related to a prominent J wave in the inferior/lateral leads, variant of BrS or atypical BrS: These forms are distinguished by ECG abnormalities of the J wave, and ST-segment elevation appeared in the inferior and lateral leads.

Early repolarization syndrome as a new electrical disorder associated with SCD: gain-of-function mutation s422l in the KCN8-encoded cardiac ATP-sensitive potassium channel K_{ATP} channel kir6.1 as a pathogenic substrate (Haïssaguerre syndrome[1]).

CACNA2D1 as possible novel ERS susceptibility genes[2].

Early repolarization in short QT syndrome. There is a high prevalence of early repolarization in patients with SQTS. Early repolarization may be useful in identifying risk of cardiac events in SQTS[3].

Family IVF with mutation on DPP6 (dipeptidyl-peptidase 6) gene on chromosome 7 has not early repolarization on ECG[4].

Eventually, vagally mediated VF initiated by PVCs arising from the RVOT[5].

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EXPERIMENTAL BACKGROUND

1. Yan GX, Antzelevitch C. Cellular basis for the electrocardiographic J wave. Circulation. 1996 Jan 15;93:372-379.
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HYPOTERMIC-J WAVE

1. **Clements SD Jr, Hurst JW. Diagnostic value of electrocardiographic abnormalities observed in subjects accidentally exposed to cold. Am J Cardiol. 1972 May; 29:729-734.**
2. **Gavaliatis IP. Electrocardiographic issues related to action potential phases 1 and 2 on the occasion of a case of accidental mild hypothermia. Int J Cardiol. 2001 Jan; 77:81-86.**
3. **Noda T, Shimizu W, Tanaka K, Chayama K. Prominent J wave and ST segment elevation: serial electrocardiographic changes in accidental hypothermiaJ Cardiovasc Electrophysiol. 2003 Feb;14:223.**
4. **Kanna B, Wani S. Giant J wave on 12-lead electrocardiogram in hypothermia. Ann Noninvasive Electrocardiol. 2003 Jul;8:262-5.**
5. ***RuDusky BM. The electrocardiogram in hypothermia-the J wave and the Brugada syndrome. Am J Cardiol. 2004 Mar 1;93:671-672.***
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ATYPICAL BRUGADA PATTERN IDIOPATHIC VENTRICULAR FIBRILLATION RELATED TO A PROMINENT J WAVE IN THE INFERIOR LEADS, OR VARIANT OF BRUGADA SYNDROME

1. Kalla H, Yan GX, Marinchak R. Ventricular fibrillation in a patient with prominent J (Osborn) waves and ST segment elevation in the inferior electrocardiographic leads: a Brugada syndrome variant? J Cardiovasc Electrophysiol. 2000 Jan;11:95-98.
2. Sahara M, Sagara K, Yamashita T, Abe T, Kirigaya H, Nakada M, et al. J wave and ST segment elevation in the inferior leads: a latent type of variant Brugada syndrome? Jpn Heart J. 2002 Jan;43:55-60.
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5. Takeuchi T, Sato N, Kawamura Y, Takahashi F, Sato M, Kikuchi K, et al. A case of a short-coupled variant of torsades de Pointes with electrical storm. Pacing Clin Electrophysiol. 2003 Feb;26:632-636.
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7. Tsunoda Y, Takeishi Y, Nozaki N, Kitahara T, Kubota I. Presence of intermittent J waves in multiple leads in relation to episode of atrial and ventricular fibrillation. J Electrocardiol. 2004 Oct;37:311-314.
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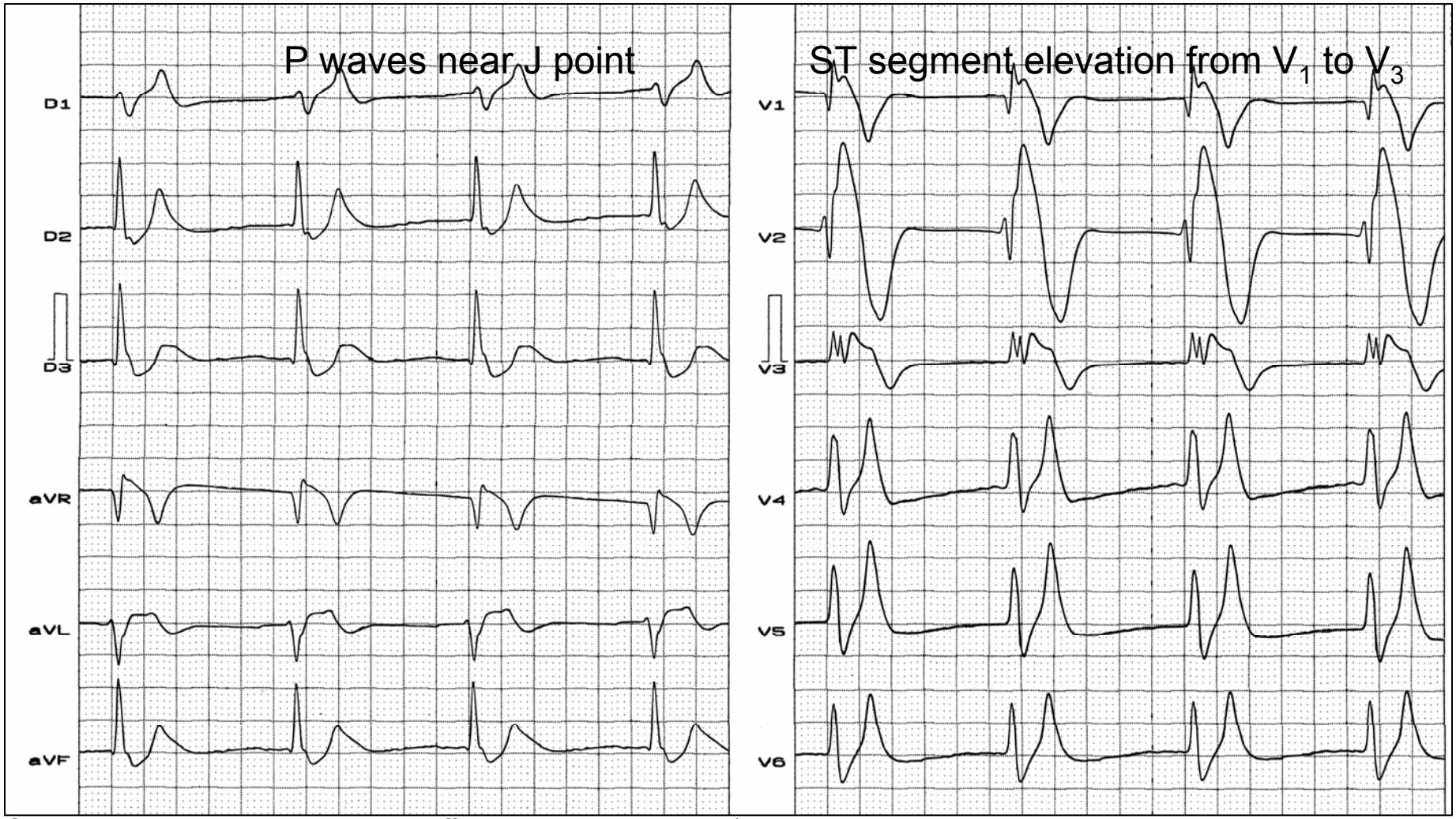
ELECTROLYTES DISTURBANCES I) HYPERKALEMIA



Clinical diagnosis: terminal renal insufficiency. Hypercalemia: 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 Brugada syndrome, which some authors call "Acquired Brugada Pattern"or acquired ECG Brugada pattern.

Typical T waves in "tent", pointed, and with a narrow base classical of hyperkalemia.

1. **McIntyre WF, Femenía F, Arce M, Pérez-Riera AR, Baranchuk A. Importance of early electrocardiographic recognition and timely management of hyperkalemia in geriatric patients. Exp Clin Cardiol. 2011 Summer;16(2):47-50.**
2. **Ortega-Carnicer J, Benezet J, Ruiz-Lorenzo F, Alcázar R. Transient Brugada-type electrocardiographic abnormalities in renal failure reversed by dialysis. Resuscitation. 2002 Nov;55:215-219**

SUBARACHNOID HEMORRHAGE

1. Carrillo-Esper R, Limón-Camacho L, Vallejo-Mora HL, Contreras-Domínguez V, Hernández-Aguilar C, et al. Non-hypothermic J wave in subarachnoid hemorrhageCir Cir. 2004 Mar-Apr;72(2):125-9.

ACUTE BRAIN INJURY
CARDIAC ARREST
DYSFUNCTION OF CERVICAL SYMPATHETIC SYSTEM

COCAINE INTOXICATION

1. **Ortega-Carnicer J, Bertos-Polo J, Gutiérrez-Tirado C. Aborted sudden death, transient Brugada pattern, and wide QRS dysrrhythmias after massive cocaine ingestion. J Electrocardiol. 2001 Oct;34:345-349.**

ELECTROCARDIOGRAPHIC IN ACS

With ST segment elevation (STEMI)

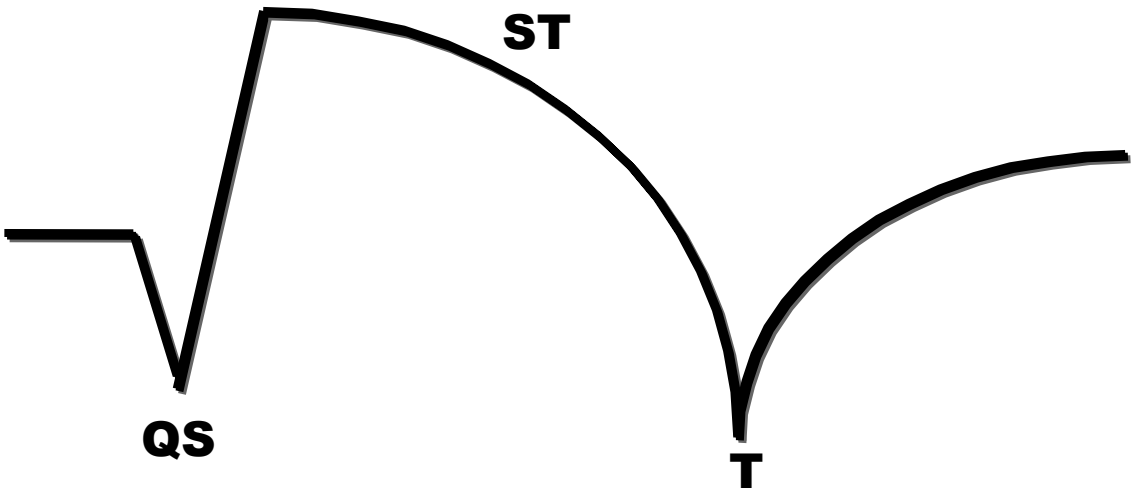
- New or presumably recent J point and ST segment elevation in 2 or more adjacent leads $\geq$ 2 mm in V_1, V_2 or V_3 or $\geq$ 1 mm in other leads

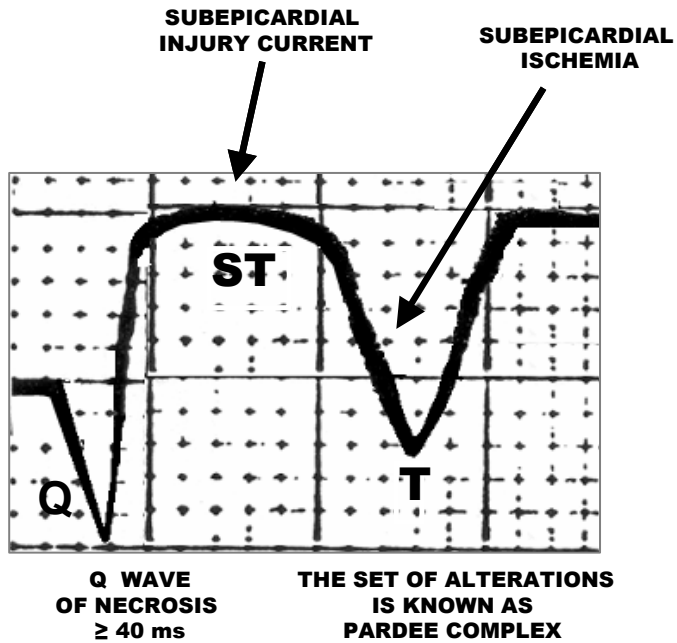
Without ST segment elevation (NSTEMI)

- ST segment depression
- Isolated alterations of the T wave

1. **Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined--a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol. 2000 Sep;36:959-969. Erratum in: J Am Coll Cardiol 2001 Mar 1;37:973.**

ACUTE PHASE OF MI ECG COMPONETS





Why phenocopy is the more appropriate term for Type 1 Brugada ECG pattern?

Many pharmacological agents and others clinical pathological circumstances not related to class I anti-arrhythmic agents have been reported to induce Brugada ECG patterns including tricyclic antidepressants, fluoxetine, lithium, trifluoperazine, tramadol, antihistamines, propanolol, mesalazine6, cocaine, hyperkalemia and cocaine in association and others. Additionally electrolytes disturbances, cardiomyopaties, acute pericarditis7, compression of RVOT, etc. can to produce the Brugada phenotype. The drug-induced Brugada sign or Brugada phenotype have become increasingly prevalent. There is growing interest in the mechanisms responsible for this acquired ECG pattern and its clinical significance. It is possible that drug-induced Brugada ECG patterns or others clinical pathological circumstances such as cardiomyopaties, myocarditis, acute pericarditis, etc may be due eventually to an individual susceptibility that favours drug-induced ECG abnormalities and, possibly as a result of an increase in a latent ion channel dysfunction similar to that in drug-induced long QT syndrome. However, further evidences are needed to confirm this hypothesis. Consequently, until to day the more appropriate denomination is Brugada phenocopy. It is an environmental condition that imitates (copies) one produced by a gene. In others words, the person who has an environmentally-produced condition that mimics one produced by a gene or a phenotype that is not genetically controlled but looks like a genetically controlled phenotype. An environmentally induced phenotype that resembles the phenotype produced by a mutation.

Here, we will review the cases and evidence of drug-induced Brugada syndrome and others clinical pathological circumstances reported in the literature.

Drugs

1. Tricyclic Antidepressants
2. Fluoxetine,
3. Lithium,
4. Trifluoperazine
5. Antihistamines
6. Cocaine.
7. Propranolol intoxication
8. Mesalazine
9. Tramadol Overdose

Electrolytes disturbances

- Hyperkalemia (see next slide)
- Hypercalcaemia

Associations

Cardiomyopaties

References

1.Rennyson SL, Littmann L. Brugada-pattern electrocardiogram in propranolol intoxication. Am J Emerg Med. 2010 Feb;28(2):256.e7-8.

2.Cole JB, Sattiraju S, Bilden EF, Asinger RW, Bertog SC. Isolated Tramadol Overdose Associated with Brugada ECG Pattern. Pacing Clin Electrophysiol. 2010 Oct 7. doi: 10.1111/j.1540-8159.2010.02924.

3.Littmann L, Monroe MH, Taylor L 3rd, Brearley WD Jr. The hyperkalemic Brugada sign. J Electrocardiol. 2007 Jan;40:53-59.

4.Nayyar S, Nair M. Brugada pattern in toxic myocarditis due to severe aluminum phosphide poisoning.Pacing Clin Electrophysiol. 2009 Nov;32(11):e16-7.

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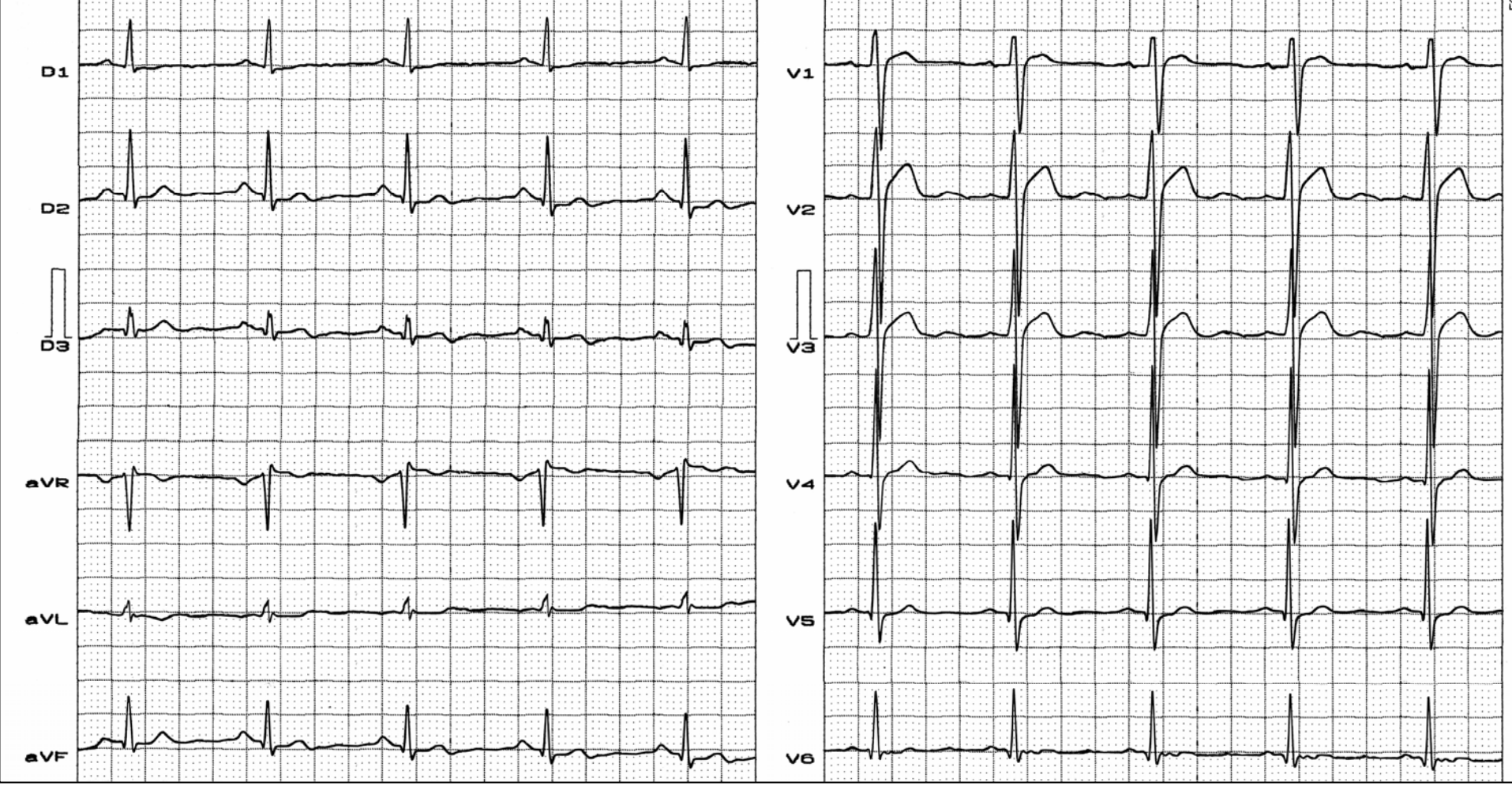
6.Hermida JS, Six I, Jarry G. Drug-induced pericarditis mimicking Brugada syndrome. Europace. 2007 Jan;9(1):66-8.

7.Ozeke O, Selcuk MT, Topaloglu S, Maden O, Aras D. Brugada-like early repolarisation pattern associated with acute pericarditis. Emerg Med J. 2006 Dec;23(12):e64.

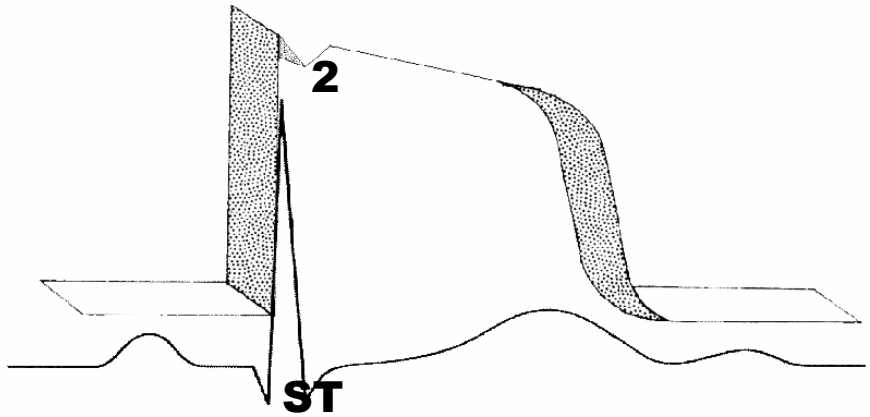
8.Matsuki M, Sato N, Matsuda K, Yamaki M, Nakagawa N, Sakamoto N, ET AL. Brugada syndrome whose ST-segment changes were enhanced by antihistamines and antiallergenic drugs. Intern Med. 2009;48(12):1009-13.



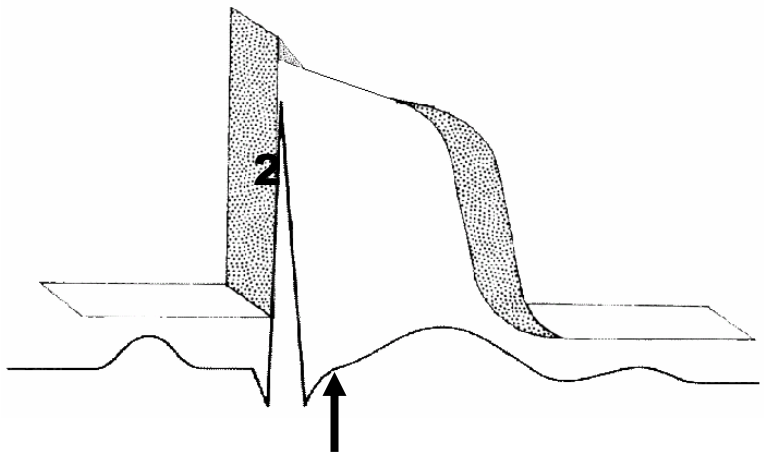
Clinical diagnosis: 16-year-old teenager with osteosarcoma. High ionized serum calcium: 3.5 mEq/l (normal: 2.2 to 2.7 mEq/l).
ECG diagnosis: sinus rhythm, HR: 75 bpm, QTc interval: 346 ms, short Q-oTc and Q-aT, almost non existent ST segment, T wave follows immediately after QRS complex. J point elevation =2mm in V_2 and 1mm in V_3, very short ST segment and followed by a positive T wave. ST-segment elevation is a common finding in severe hypercalcemia[1]. Eventually could mimicking acute myocardial infarction[2].

1. **Littmann L, Taylor L 3rd, Brearley WD Jr. ST-segment elevation: a common finding in severe hypercalcemia. J Electrocardiol. 2007 Jan; 40:60-62.**
2. **Nishi SP, Barbagelata NA, Atar S, Birnbaum Y, Tuero E. Hypercalcemia-induced ST-segment elevation mimicking acute myocardial infarction. J Electrocardiol. 2006 Jul;39:298-300.**

NORMAL



HYPERCALCEMIA



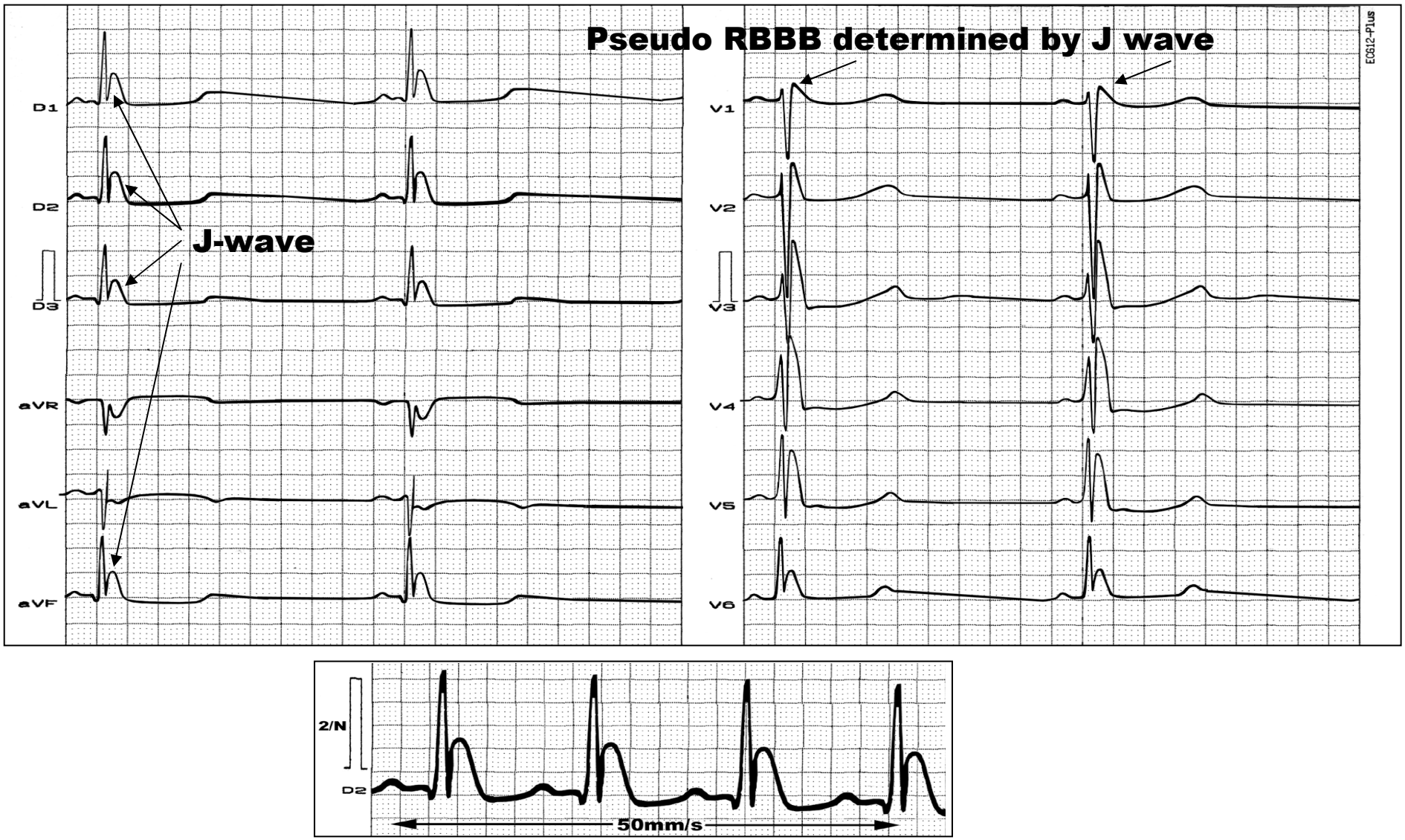
ALMOST ABSENT ST SEGMENT

QTc interval shortening, Q-oTc interval shortening: interval from Q wave onset to T wave onset corrected according to HR.Q-aT interval decrease: interval between QRS onset to T wave apex. Values below 270 ms are diagnostic.

The ECG manifestations of Brugada syndrome are often dynamic or concealed and may be unmasked or modulated among others by the hypercalcemia[1].

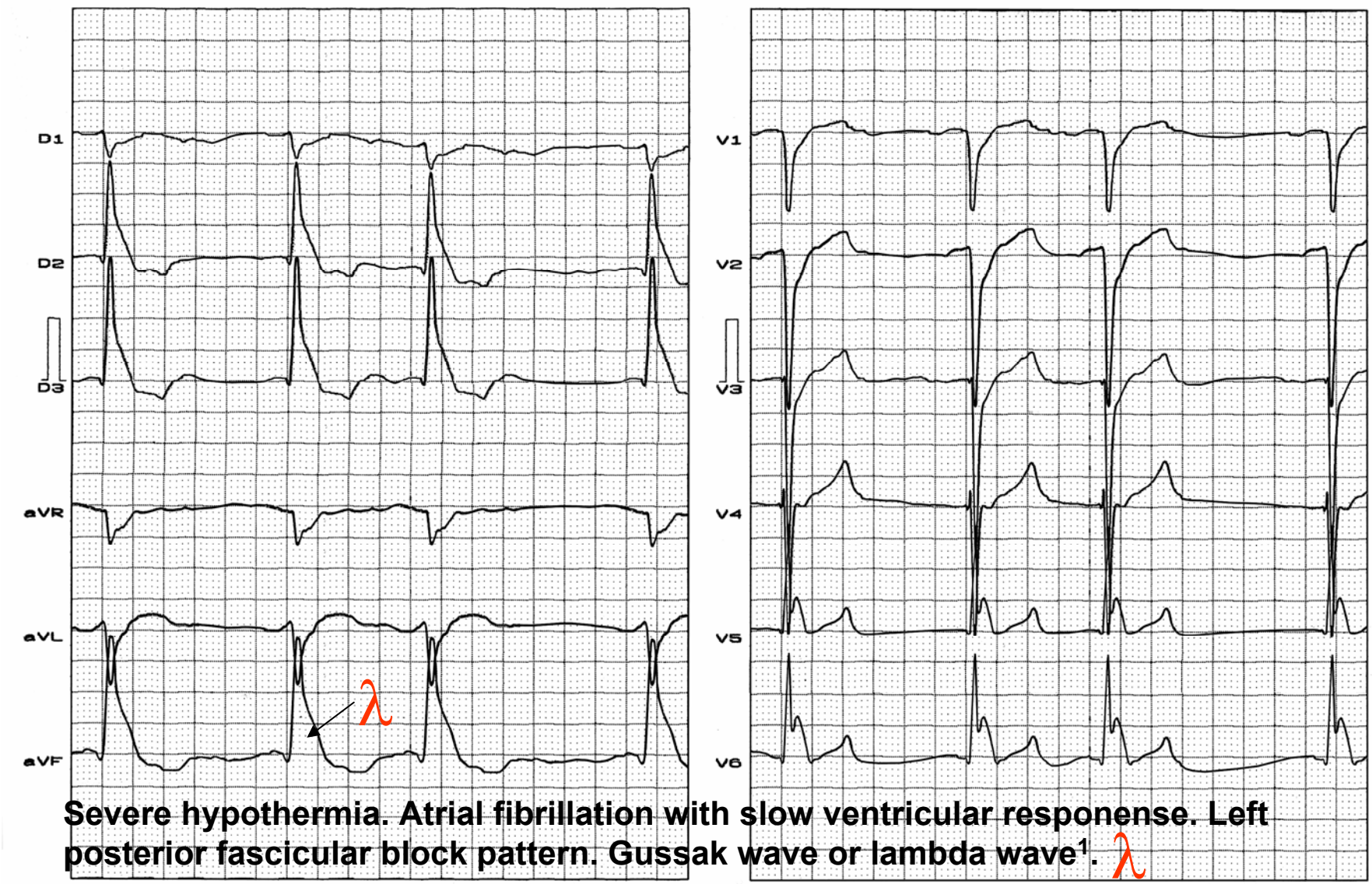
1. **Antzelevitch C, Brugada P, Borggrefe M, Brugada J, Brugada R, Corrado D, Gussak I, LeMarec H, Nademanee K, Perez Riera AR, Shimizu W, Schulze-Bahr E, Tan H, WildeBrugada syndrome: report of the second consensus conference. AHeart Rhythm. 2005 Apr;2:429-440.**

Name: ADS; **Gender:** Male; **Age:** 32 y.o; **Ethnic group**: mulatto; **Weight:** 68 Kg; **Height:** 1.64 m; **Date:** 03/04/2002; Steps to increase body temperature.



Characteristic ECG of a patient during severe hypothermia: Sinus bradycardia HR 30bpl, prominent J-waves evident in inferior leads and I. Pseudo RBBB determined by J wave, which is not part of QRS complex

Name: PASA; **Gender:** Male; **Age:** 47 y.o.; **Ethnic group**: Afro-descendent; **Weight:** 61Kg; **Height:** 1.68 m; **Date:** 03/07/2008; Central body temperature 29ºC.



Severe hypothermia. Atrial fibrillation with slow ventricular responense. Left posterior fascicular block pattern. Gussak wave or lambda wave[1]. λ

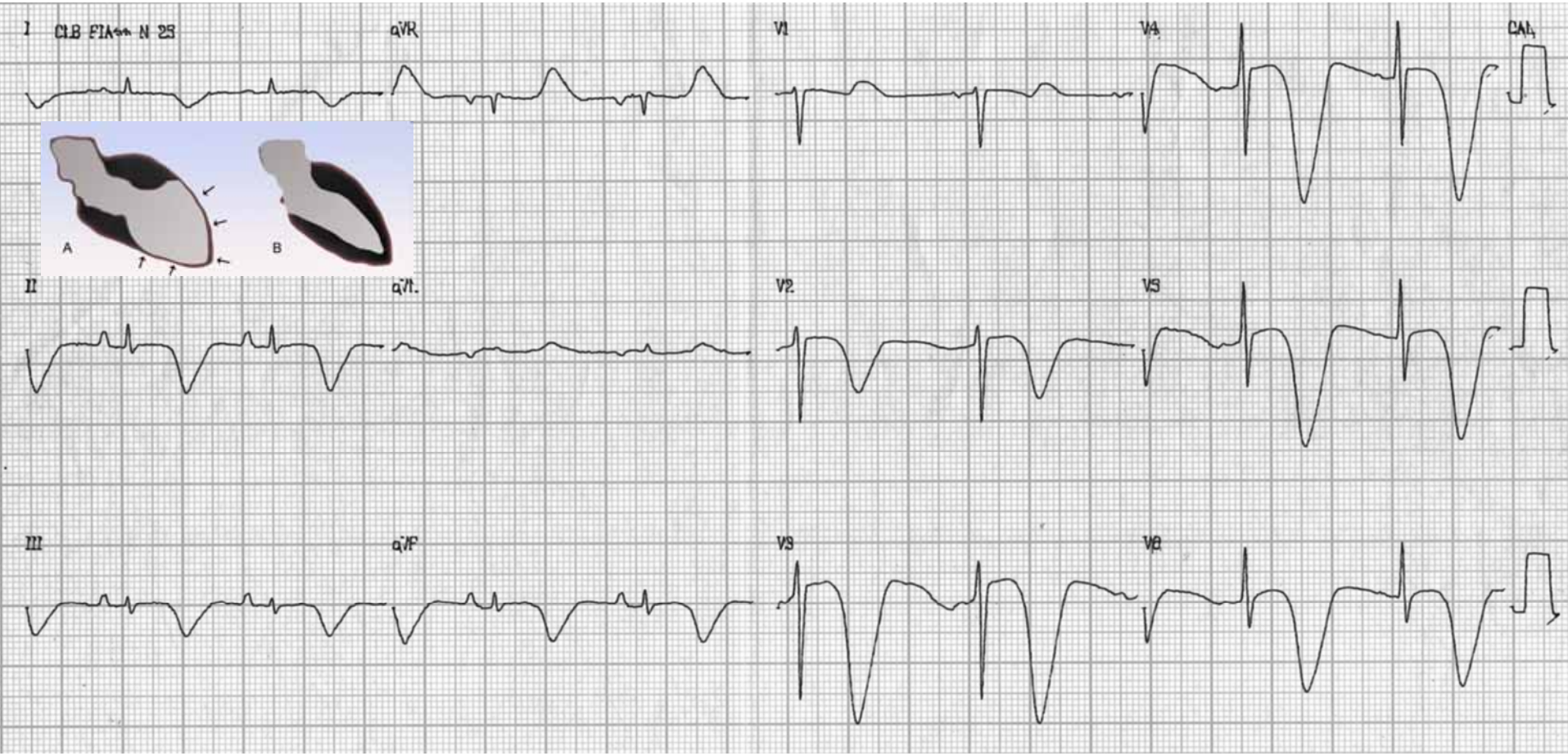
1. **Gussak I, Bjerregaard P, Kostis J. Electrocardiographic "lambda" wave and primary idiopathic cardiac asystole: a new clinical syndrome? J Electrocardiol. 2004 Apr;37(2:105-7.**

Tako-Tsubo Cardiomyopathy (TTC), stress-induced cardiomyopathy, apical ballooning syndrome, "broken heart" syndrome, Gebrochenes-Herz-Syndrome

- Is found in 1.7–2.2% of patients presenting with ACS[1]
- Especially, older women in the postmenopause are affected.
- Precipitated by a stressful event. History of a recent severe emotional or physical stress
- Acute chest symptoms mimicking ACS with ST elevation myocardial infarction (STEMI) sudden onset of congestive heart failure or syncope,
- New ischemic ECG changes with ST-segment elevation ± T-wave inversion,
- Reversible or transient nature of left ventricular regional wall dysfuction motion abnormality not corresponding to a single coronary artery territory
- high circulating levels of catecholamines (mainly adrenaline/epinephrine).
- Absence of significant coronary artery stenoses. (unobstructed coronaries)
- The prognosis of this condition is generally excellent with almost all patients returning to normal within a few weeks.

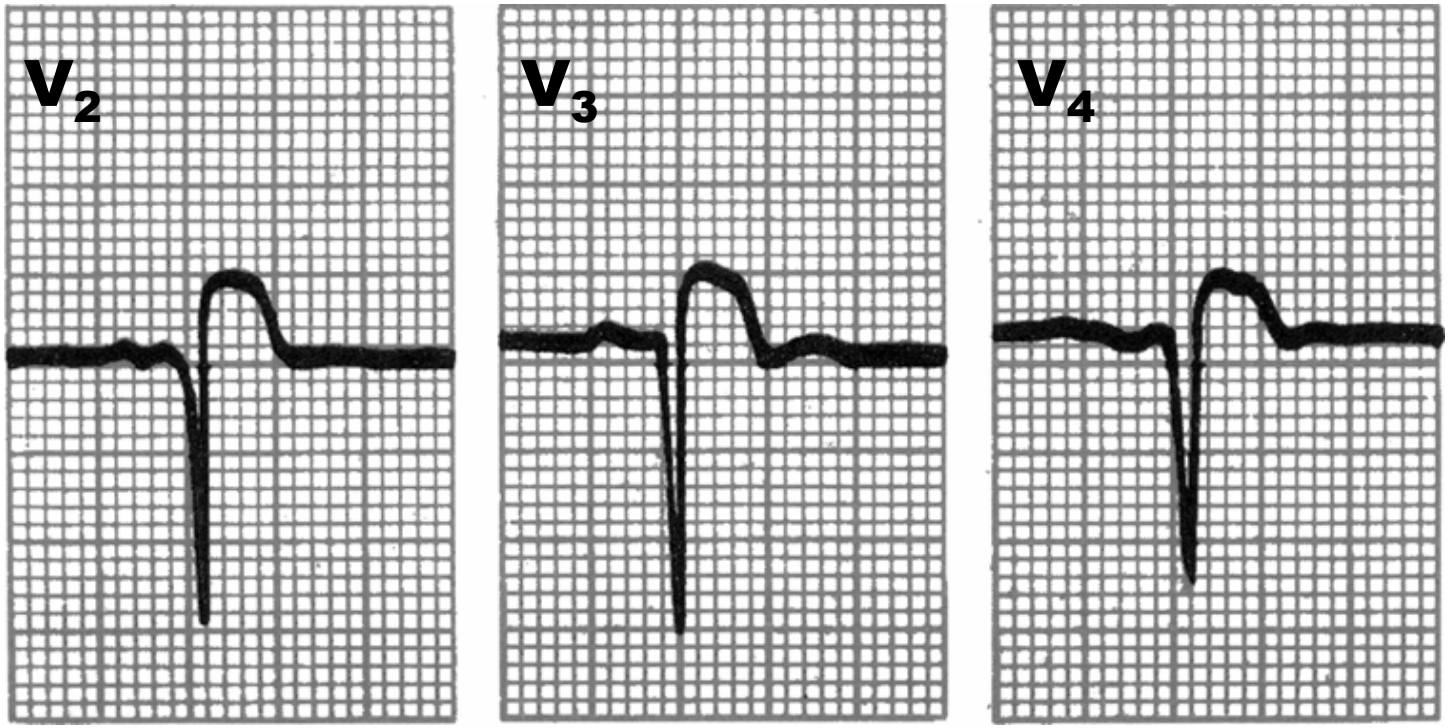
1. **Eshtehardi P, Koestner SC, Adorjan P, Windecker S, Meier B, Hess OM, et. al. Transient apical ballooning syndrome--clinical characteristics, ballooning pattern, and long-term follow-up in a Swiss population. Int J Cardiol. 2009 Jul 10;135:370-375.**

TAKOTSUBO CARDIOMYOPATHY



Takotsubo cardiomyopathy, transient apical ballooning syndrome, apical ballooning cardiomyopathy, stress-induced cardiomyopathy, broken-heart-syndrome, and simply stress cardiomyopathy, is a type of non-ischemic cardiomyopathy in which there is a sudden temporary weakening of the myocardium (the muscle of the heart). Because this weakening can be triggered by emotional stress, such as the death of a loved one, a break-up, or constant rejection, the condition is also known as broken heart syndrome. Stress cardiomyopathy is a well-recognized cause of acute HF, lethal ventricular arrhythmias, and ventricular rupture.

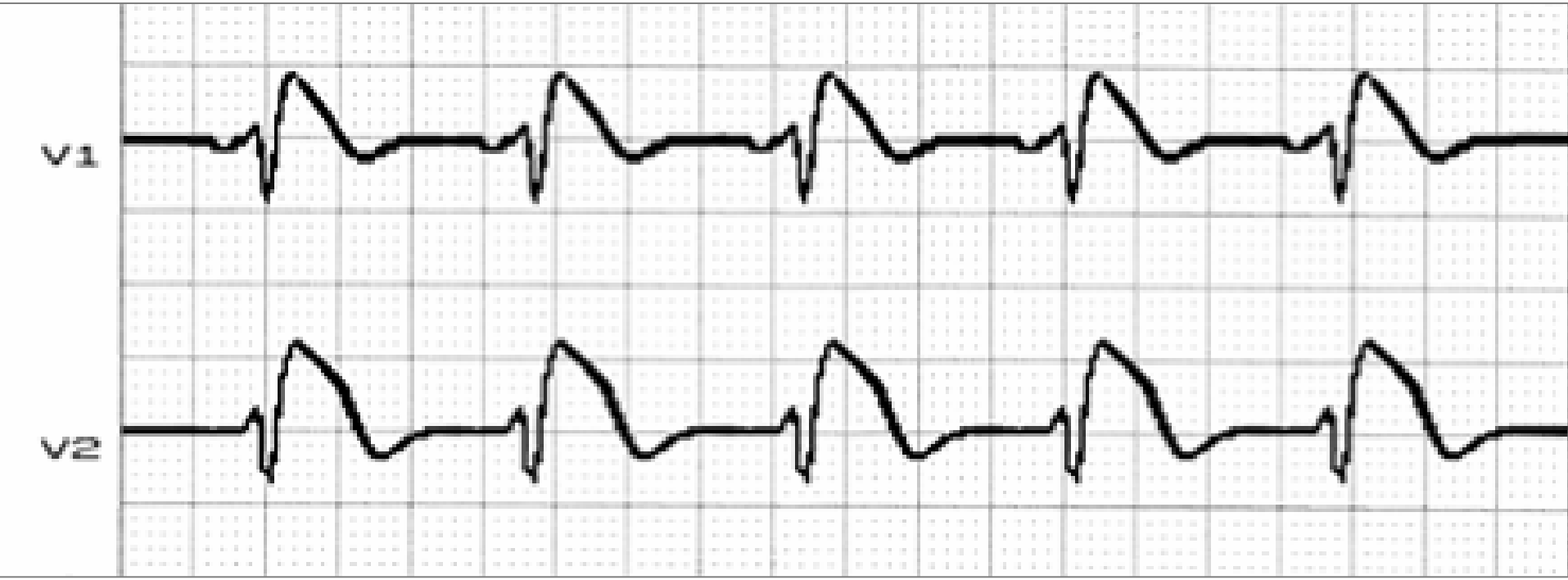
ANEURYSM OF LEFT VENTRICLE ANTERIOR WALL



Example of an ECG of aneurysm of antero-septal wall in the chronic phase of myocardial infarction (MI) (after 3 months of the acute event). This location is the most frequent (65%), apical (21, 3%), posteroinferior 9%, lateral 5%. Left ventricular aneurysm is an important complication of acute transmural myocardial infarction (MI) that bears great clinical significance because of high mortality. Persistent subepicardial injury current remains, indicating the possibility of residual aneurysm. Persistent ST-segment elevation after anterior MI is related to a larger extent of transmural necrosis and persistent microvascular damage as assessed by contrast-enhanced magnetic resonance imaging[1]. The presence of microvascular damage seems to be the most powerful determinant of persistent ST-segment elevation. Heart Rate Variability analysis supplies parameters with high predictive value for left ventricular aneurism formation in the early period after acute anterior MI. The higher sympathetic activity and reduced heart rate variability may be associated with a higher incidence of complications such as ventricular arrhythmias and increased mortality in patients with left ventricular aneurism[2].

1. **Napodano M, Tarantini G, Ramondo A, Cacciavillani L, Corbetti F, Marra MP, Myocardial abnormalities underlying persistent ST-segment elevation after anterior myocardial infarction. Cardiovasc Med (Hagerstown). 2009 Jan;10:44-50.**
2. **Yildirim A, Soylu O, Dağdeviren B, Eksik A, Tezel T. Sympathetic overactivity in patients with left ventricular aneurysm in early period after anterior myocardial infarction: does sympathetic activity predict aneurysm formation? Angiology. 2007 Jun-Jul;58:275-282.**

Type 1 ECG Brugada pattern coved-type, Brugada phenotype, Brugada sign.



J point and ST segment elevation ≥ 2mm followed by a negative T wave.
In a large patient cohort[2] reevaluate the appropriateness of the diagnostic consensus criteria. The authors concluded that Lead V_3 does not yield diagnostic information in BrS. Individuals with ECGs displaying only one diagnostic right precordial leads have a similar clinical profile and arrhythmic risk as Brugada patients with ECGs displaying >1 diagnostic right precordial leads . This work suggests that revision of the consensus criteria should be considered.ECG manifestations are intermittent in more than $^3/_4$ of the affected patients[1]. Spontaneous type ECG 1 phenotype manifestation of BrS was more frequent in older symptomatic patients, absent in children, and related with low body mass index (BMI)[4].

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4. **Santos LF, Correia E, Rodrigues B, Nunes L, Costa A, Carvalho JL, Spontaneous fluctuations between diagnostic and nondiagnostic ECGs in Brugada syndrome screening: Portuguese family with Brugada syndrome. Ann Noninvasive Electrocardiol. 2010 Oct; 15: 337-343**.