Woman with intermittent LBBB and oppressive precordial pain

Raimundo Barbosa-Barros & Andrés Ricardo Pérez-Riera

English

Case report: Caucasian female patient, 61 years of age, with history of presenting in her successive electrocardiograms, left bundle branch block (LBBB) of intermittent presentation (she brought previous tracings with her) and old coronary angiography was normal (1990). Readmitted with oppressive precordial pain started 3 hours before with no irradiation or concomitant symptoms.

Physical examination: normal.

Normal biochemical markers of necrosis.

In the emergency room, she was medicated with acetylsalicylic acid, sublingual nitrate, clopidrogel, simvastatin, and enoxaparin.

We requested new coronary angiography.
Questions:

- Which is the diagnosis of ECG at admission and the previous ECG?
- Which is the explanation for the ECG changes between both traces?

Português

Reporte de caso: Paciente branca do sexo feminino, 61 anos, com antecedentes de apresentar nos seus eletrocardiogramas sucessivos um padrão de bloqueio de ramo esquerdo (BRE) de forma intermitente (trazia consigo traçados anteriores) e coronariografia antiga normal (1990). Readmitida com dor precordial opressiva iniciada há 3 horas atrás sem irradiação nem concomitantes.

Exame físico normal.

Os marcadores bioquímicos de necrose normais.

Na sala de emergência foi medicada com ácido acetil salicílico, nitrato sublingual, clopidrogrel, sinvastatina e enoxaparina.

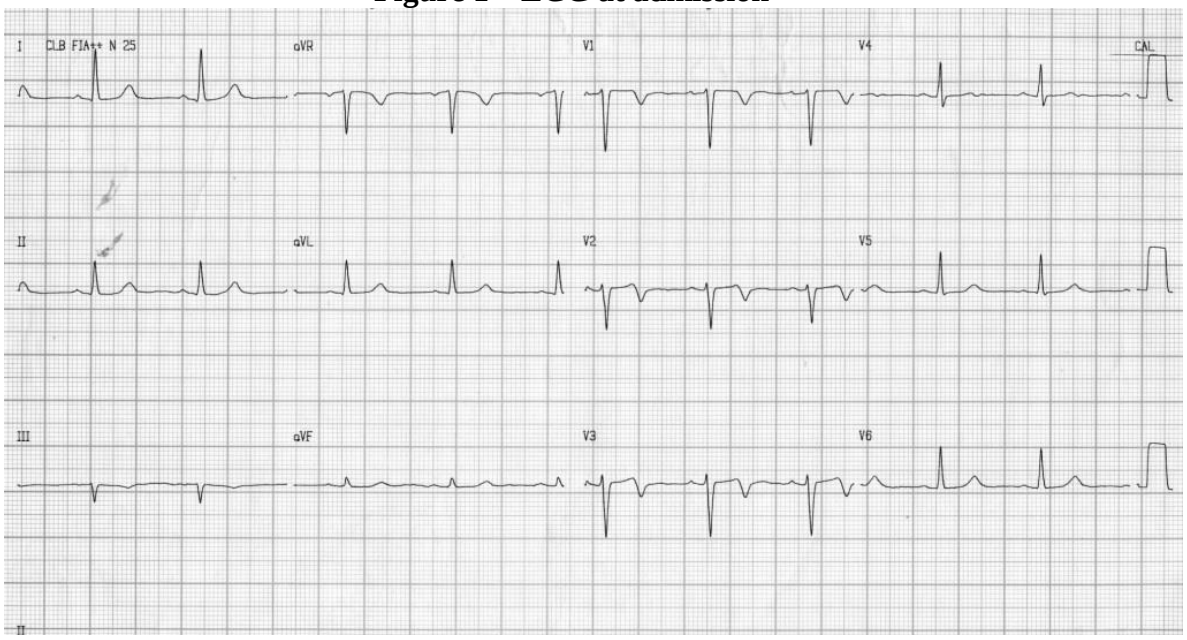
Ecocardiograma normal. Foi solicitado novo cateterismo cardíaco.

Perguntas:

- Qual é o diagnóstico do ECG de admissão e o anterior?

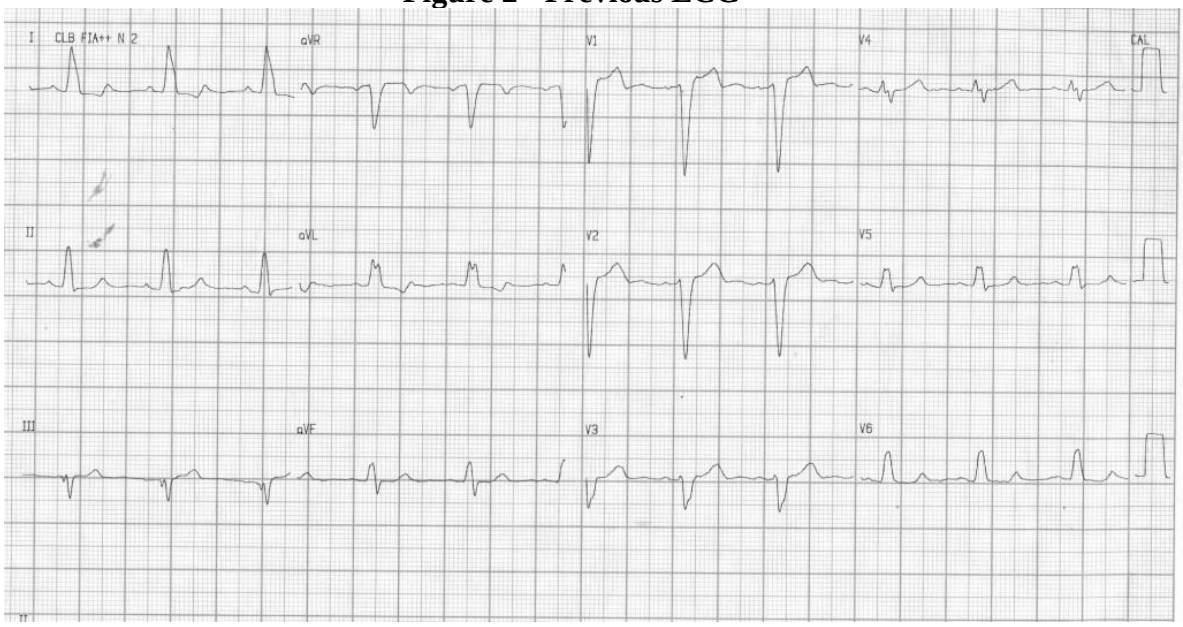
- Qual a explicação das mudanças eletrocardiográficas entre ambos os traçados?

Figure 1 – ECG at admission



Electrocardiographic diagnosis:

Figure 2 - Previous ECG



Electrocardiographic diagnosis:

Colleagues' opinions

Memory.....our ECG will never suffer from Alzheimer. So we will never forget the works of Mauricio Rosenbaum and his staff. The most fascinating finding that should be discussed. Besides the memory phenomenon, Is the Painful LBBB...is there any relationship between pains and intermittent LBBB. I do know about a series of cases from Mark Josephson lab highly supporting this assumption. Many other similar cases have been reported in the literature of these last 3 decades. Cardiac memory is associated with alterations in the cAMP responsive element binding protein and its phosphorylation form.(4)

Bernard Belhassen M.D Israel

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Dear friends.

ECG 1: inverted/biphasic T waves in V2-V4 could indicate acute coronary syndrome with the culprit artery in the LAD ("post-ischemic" T-wave inversion). It could also be cardiac memory (inverted T waves in the same leads that show negative QRS complexes during LBBB). Echocardiography should have shown some abnormality if there was an acute lesion in the LAD.

ECG 2: typical LBBB.

Angiography is indicated, but this is probably cardiac memory.

Best regards

Kjell Nikus MD PhD.

Tampere Finland

Português
Prezado amigo Master "The Cordobés Mustang", Andrés Riera
ECG 1: Ritmo Sinusal FC: 63 bpm. Ausência de progressão de ondas R nas precordiais direitas Onda T invertidas bifásicas tipo “plus minus” de V1 a V3 - Padrão comum em insuficiência coronária.
ECG 2: bloqueio completo do ramo esquerdo. Pequeno entalhe no ramo ascendente do S em V3 (Sinal de Cabrera?)
Lembrando que BCRE do FEixe de His usualmente significa patologia miocárdica mormente distúrbios de condução, as possíveis causas do presente caso (intermitente) incluem:
Trauma cardíaco
Coronariopatia Aterosclerotica - Infarto do Miocárdio
Exercício induzido
Vasoespasmo coronario - Angina de Prinzmetal
Abraços e bom domingo
Adail

Adail Paixão Almeida MD Vitoria da Conquista Bahia Brasil. Saravá!!

English

Dear friend Master "The Cordovan Mustang" Andrés Pérez-Riera

ECG 1: Sinus Rhythm: HR63 bpm. Absence OF Progression of R wave on right precordial leads. Biphasic T wave inverted type "plus minus" from V1 to V3 – It is a common pattern in coronary artery disease.

ECG 2: Complete left bundle branch block. Notch is observed on descendent ramp of S wave in V3 precordial unipolar lead (Cabrera signal?)

Let us remember that LBBB usually means myocardial damage especially conduction disease.
The possible causes for the present case (intermittent) include:

- Cardiac Trauma
- Arterioesclerotic Coronariopathy – Myocardial infarction
- Induced by exercise
- Vasospastic angina or Prinzmetal angina

Hugs and good Sunday
Adail Paixão Almeida MD Vitoria da Conquista Bahia Brazil. Saravá !!

Los bloqueos de rama izquierda intermitentes, en algunos casos inducen dolor anginoso por ocasionar contracción disquinético del septo (de la izquierda hacia la derecha.). La inversión de las ondas T obedece a isquémia y memoria Los bloqueos de rama izquierdos tronculares son frecuentes en mujeres menopáusicas porque la osteopontina **(OPN)**, o bone sialoprotein I (BSP-1 or BNSP),, que controla el metabolismo del calcio, obliga al catión a depositarse en los osteocitos La osteopontina existe en altas concentraciones en el músculo cardiaco. A su vez el estrógeno controla que la osteopontina evitando el depósito del calcio en el corazón. Especialmente durante el embarazo hay alta cantidad de esta en el corazón. En la menopausia por el descenso de receptores estrogénicos alfa y beta se ve facilitado el depósito de calcio en el tejido conectivo El 75% de calcificaciones de los anillos mitrales y aórticos existen en mujeres menopaúsicas y cuando si el tronco de la rama izquierda se encuentra anatómicamente cercano a estos anillos también se calcifica

El fenómeno de dolor anginoso con signos clásicos de isquemia anteroseptal ocurre en algunas mujeres y en otras no. Existe dolor cuando la arteria descendente anterior es anatómicamente corta sin llegar a la punta cardiaca Yo le llamo el tercer mecanismo de isquemia disquinesia o hiperquinesia en áreas con circulación disminuida por arteria descendente anterior corta normales o patológicas

Un fraternal abrazo

Samuel Sclarovsky Israel

English
The intermittent left bundle branch blocks, in some cases induce chest angina pain consequence of dyskinesia contraction of interventricular septum (from left to right.).
The T-wave inversion is due to ischemia and cardiac memory.
Stem LBBB are common in menopausal women because osteopontin (OPN) or bone sialoprotein I (BSP-1 or BNSP), which controls calcium metabolism, forces deposited of the cation on osteocytes. Osteopontin exists in high concentration in human heart muscle. In turn estrogen controls that osteopontin preventing the deposit of calcium in the heart. Especially during pregnancy there is a high amount of this glycoprotein in the heart. At menopause by declining estrogen receptor α and β is facilitated calcium deposition in connective tissue, consequently ≈ 75% of calcifications of the mitral and aortic rings exist in menopausal women as if the trunk of the left bundle branch is anatomically close to these rings is also calcify
The phenomenon of angina pain with classic signs of anteroseptal ischemia occurs in some women and not others. There is pain when the left anterior descending artery (LDA) is anatomically short without reaching the heart apex. I call this mechanism third mechanism dyskinesia or hyperkinesia ischemia in areas with decreased movement for short LAD normal or pathological
A fraternal Hugh
Samuel Sclarovsky Israel MD

Português
Caso interessante de memória miocárdica. As ondas T ficam negativas nas derivações em que o QRS era negativo enquanto durava o QRS largo do BRE.
A dor, certamente, não era isquêmica, mas a presença da memória miocárdica com suas T negativas leva muitas vezes à indicação, desnecessária, de cinecoronariografia.
Abraços a todos

Jose Claudio Kruse MD Porto Alegre Brasil.

Very interesting case of myocardial memory. The T waves are negative in leads in which QRS is negative while it lasts wide QRS left bundle branch block.
Certainly the pain was not ischemic but consequence of the myocardial memory with their negative T-wave often leads to unnecessary indication, coronary angiography
Hugs to all
Jose Claudio Lupi Kruse MD from Porto Alegre Brazil.

"O bonitão"

Spanish Estimado Andres Mi opinión

ECG 1: T negativas plus -minus de V1 a V3 orientando a isquemia subepicardica anterior sugestivo de estenosis critica de coronaria descendente anterior proximal ATE (antes de primera diagonal ("Sind WELLENS? en contexto de no cambios de marcadores daño miocárdico y SCA)

ECG 2: Patrón de BCRI con ondas T que no se oponen al QRS sugiriendo también isquemia de la cara anterior. El porqué del BCRI intermitente ?... por isquemia de la rama izquierda, por compromiso ramos "sinistri " y posiblemente asociado también a compromiso de algún ramo proveniente de una CD comprometida

Posiblemente nuevo cateterismo muestre obstrucción aguda de porción proximal de DA y crónica de la CD

Un gran abrazo

Juan José Sirena Santiago del Estero Argentina

English **Dear Andres My opinion**

ECG 1: -Minus plus and negative T-waves from V1 to V3 suggesting subepicardial ischemia by critical proximal obstruction of LAD (before the first diagonal (Wellens syndrome? Because normal biomarkers in context of ACS ?

ECG 2: LBBB pattern with T waves do not oppose the QRS also suggesting ischemia of the anterior surface. Intermittent LBBB why? ... Ischemia of truncus of the left bundle branch-, by obstruction of "sinistri ramus" and possibly associated with chronic concomitant obstruction of ramus of the RCA

New catheterization possibly show acute obstruction of the proximal portion of LAD and chronic of RCA.

A big hug

Juan José Sirena M.D. Santiago del Estero Argentina

Estimado Andrés: Como referí.
Tiene 25 años de evolución de sus episodios anginosos, porque comenzó a los 36 años.
Habría que definir si el BRI es taquicárdico dependiente o solo aparece relacionado con los episodios anginosos.
Las ondas T negativas son pseudo-primarias o de memoria cardiaca ya que tienen la misma polaridad de la onda T durante el episodio de BRI, que interpreto está relacionado con las crisis anginosas.
Mi diagnóstico presuntivo es vaso espasmo coronario en territorio de descendente anterior. Cateterismo cardiaco y prueba de provocación de la misma para confirmar el diagnóstico.
Optimizar el tratamiento para el vaso espasmo coronario y prueba ergometría para descartar BRI taquicardico dependiente y T negativas de memoria cardiaca.
Un cordial saludo
Martin Ibarrola

English
Dear Andrés: As I mentioned.
It has 25 years of evolution of her angina episodes that began at 36 y/o.
It should be defined if the LBBB is tachycardia-dependent or only appears related to angina episodes.
Negative T waves are pseudo-primary or due to cardiac memory as they have the same polarity of the T wave during the LBBB, which I interpret is linked to angina attacks.
My presumptive diagnosis is coronary vessel spasm (Prinzmetal) of left anterior descending artery territory. Cardiac catheterization and spasm provocation test to confirm the diagnosis.
Optimizing treatment for coronary vasospasm and stress test to discard LBBB tachycardia-dependent and negative T waves of cardiac memory.
Best regards
Martin Ibarrola

Hola foristas,
Estoy de acuerdo con los comentarios de K Nikus y Martin Ibarrola. Si el dolor no es típico y además los marcadores de necrosis son negativos hay que pensar en memoria post BRI (estan descritas molestias precordiales en caso de bloqueo de rama izquierda intermitente). Si el dolor es anginoso típico hay que repetir coronariografia y descartar espasmo coronario y disección coronaria espontánea (a veces se requiere IVUS para descartar el diagnóstico) y se trataría de una onda T negativa postisquemica. Saludos

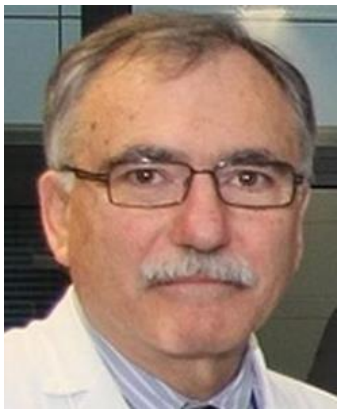
English

Hello forum members,

I agree with the comments from K Nikus and Martin Ibarrola. If pain is not typical and also necrosis biomarkers are negative, you should think about post LBBB memory phenomenon (it is described with chest discomfort in cases of intermittent LBBB). If pain is typical of angina, coronary angiography should be repeated and discard coronary spasm and spontaneous coronary dissection (sometimes Intravascular Ultrasound (IVUS) is required to exclude the diagnosis) and would be a post ischemic negative T wave.

Greetings

Miquel Fiol Sala, M.D.Ph.D., Balearic Islands, Spain



Spanish

Estimado Andrés: doy mi humilde opinión: el bloqueo de la rama izquierda no es de muy alto grado, tiene características tronculares y es intermitente, hallazgos que no son tan frecuente en la enfermedad coronaria crónica sino más en la miocardiopatía dilatada idiopática, enfermedad de Lev o valvulopatía. El dolor precordial opresivo siempre asusta aunque, si no responde a nitritos y no presentó marcadores puede que no sea de origen coronario. El trastorno de la repolarización puede obedecer al fenómeno de memoria cardiaca. De todos modos quedaría a criterio médico realizar una CCG o esperar y hacer un SPECT

Cordialmente

English

Dear Andrés: I give my humble opinion: the left bundle branch block is not very high degree (advanced or complete), has truncal features and is intermittent, findings that are not so common in chronic CAD but in idiopathic dilated cardiomyopathy, Lev disease or valve disease. The oppressive chest pain is always scary though, does not meet nitrites and markers can not submit non-coronary origin. Repolarization disturbance may be due to the phenomenon of cardiac memory. Anyway medical judgment would be to conduct a coronary angiography or wait and perform a Single Photon Emission Computed Tomography (SPECT).

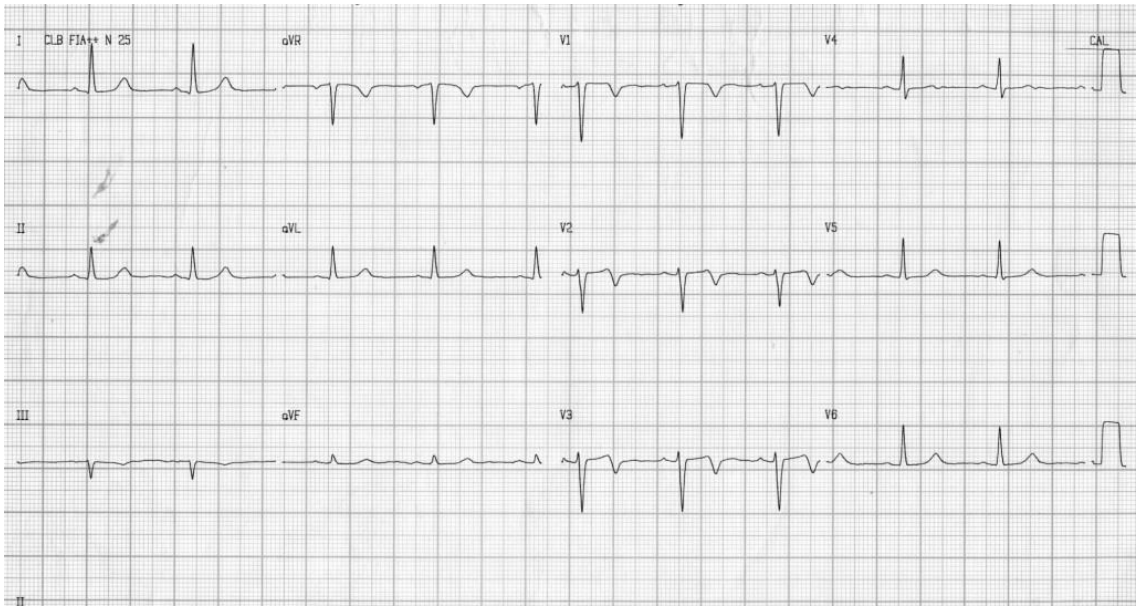
Cordially

Daniel Dasso, División Cardiología. Sección Electrofisiología. Hospital Juan A. Fernandez. CABA., Buenos Aires, Argentina

Final comments by Raimundo Barbosa-Barros & Andrés Ricardo Pérez-Riera

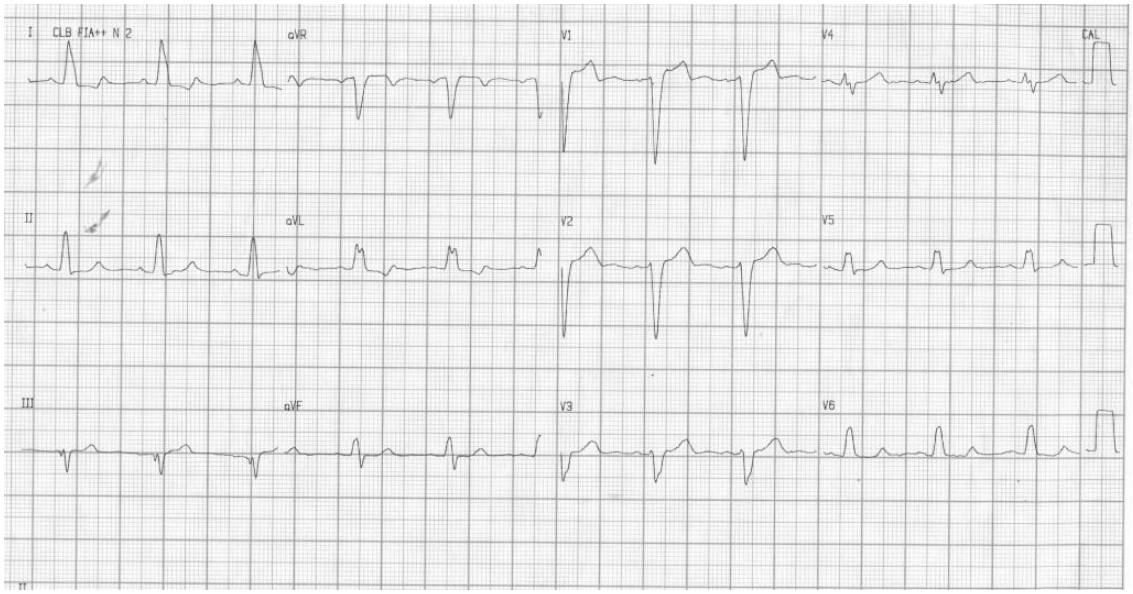
Woman with intermittent LBBB and oppressive precordial pain: electric cardiac memory mimicking myocardial ischemia or Chatterjee phenomenon (1): residual changes in the T wave after regression of abnormalities of ventricular activation

Figure 1 – ECG at admission



Electrocardiographic diagnosis: sinus rhythm, HR 65 bpm, SAP +55° and to the front, PR interval 140 ms, SAQRS +10° and backward, QRS duration 90 ms, SAT +30° in the FP and backward and the left in the HP with negative T wave from V1 through V3. **Note:** In normal adults invariably, the ventricular repolarization vector (T vector) is heading to the left and below, and usually discretely to the front around +10° in the HP. Consequently, normal T wave polarity is always positive from V3 to V6; generally positive in V2 and frequently negative in V1. In the frontal plane, normal SAT in the FP is between +15° and +80° consequently, T wave will always be positive in II and aVF and I; variable (biphasic or inverted) in aVL and III; and negative in aVR. **Conclusion:** negative T wave in the three right precordial leads. The previous ECG showed CLBBB pattern (**Figure 2**).

Figure 2 - Previous ECG



Electrocardiographic diagnosis: Sinus rhythm, HR 74 bpm, PR interval 140 ms, SAQRS +10°, QRS duration 120 ms, QRS complexes of right precordial leads (V1 to V3), predominantly negative of the rS type, pure and monophasic R waves of slow inscription in the left leads: I, aVL and V6, QRS complex of the QS type in aVR, ST-T opposite to greater QRS deflection: positive from V1 to V3, but not opposite in the left leads I, aVL, V5 and V6. Positive T wave in aVL and positive or minus-plus in I, constitutes a criterion that leans in favor of cardiac memory (CM) (2). Conceptually, by presenting QRS duration = 120 ms from the merely morphological point of view she meets the concept of complete left bundle branch block (CLBBB) or advanced left bundle branch block (ALBBB); however, this is incomplete second degree block. Why? Answer: because following the concept of Professor Antoni Bayés de Luna, any intermittent left bundle branch block is necessarily of a second degree, even when reaching the arbitrary criterion of 120 ms for QRS duration (3). Thus, according to permanence, left bundle branch blocks could be classified in the following manner:

- **Permanent or definitive:** most of them. These are troncular or of a third degree, advanced or complete (ALBBB or CLBBB).
- **Intermittent or of the second degree:** which in turn, could be:
  1) Dependent on heart rate:
     - Tachycardia-dependent or in “phase 3”;
     - Bradycardia-dependent or in “phase 4”.
  2) Independent from heart rate:
     - Mobitz type I;
     - Mobitz type II by Wenckebach phenomenon;
     - By significant hypopolarization.

In this group of intermittent or transient blocks, the phenomenon of Cardiac Memory (CM) or T-wave memory may occasionally be observed, manifested by changes in T wave polarity, following the intermittent alterations of ventricular activation or depolarization in a given time after conduction without dromotropic disorder.

Normal echocardiogram

New cardiac catheterization revealed normal coronary arteries and ventriculography.

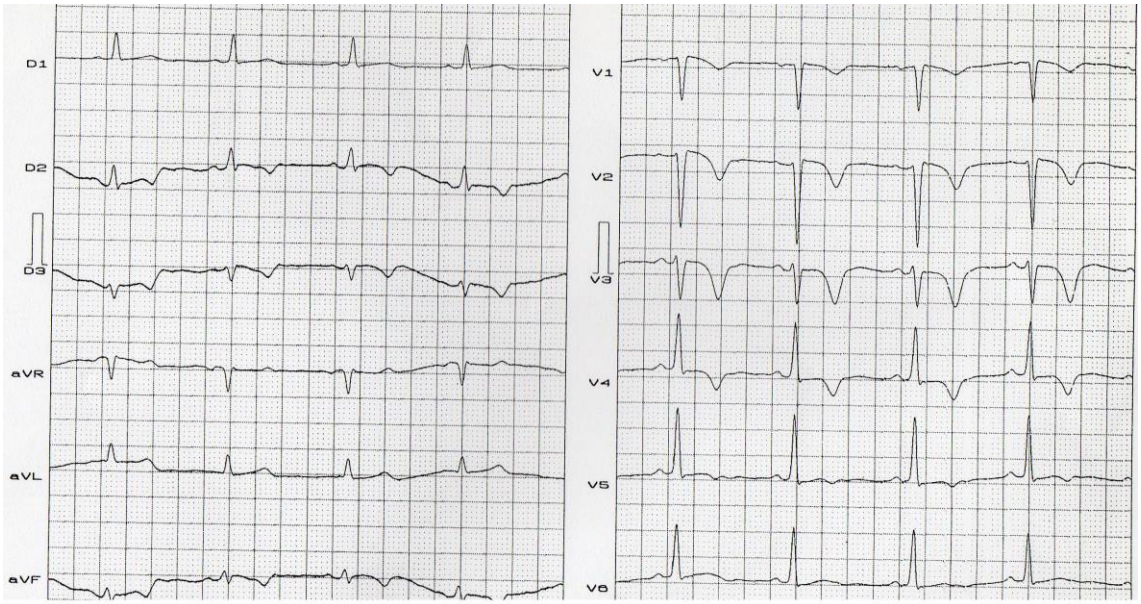
The most convincing and studied example with ECG and cardiogram vector (VCG) is shown in Figures 3, 4, 5, 6 and 7A, all belonging to the same patient. The ECG of Figure 3 was made approximately 3 days before the ECG/VCG of the tracings in Figures 4, 5, 6 and 7A, all made at the same time.

This is a 38-year-old lady, who came to our clinic 3 days before and our colleague made the ECG in Figure 3, with the aim of a pre-participation evaluation for a gym academy. Negative and irrelevant family history, novices, she denies having any previous disease. She always had normal blood pressure.

Normal transthoracic echocardiogram and a tomography of the coronary arteries made later, revealed normal calcium score and permeable coronary arteries with no anomalies.

Figure 3

Date: Feb 27, 2013; time: 17 h; Age: 38 years old; Sex: Female; Race: Caucasian.



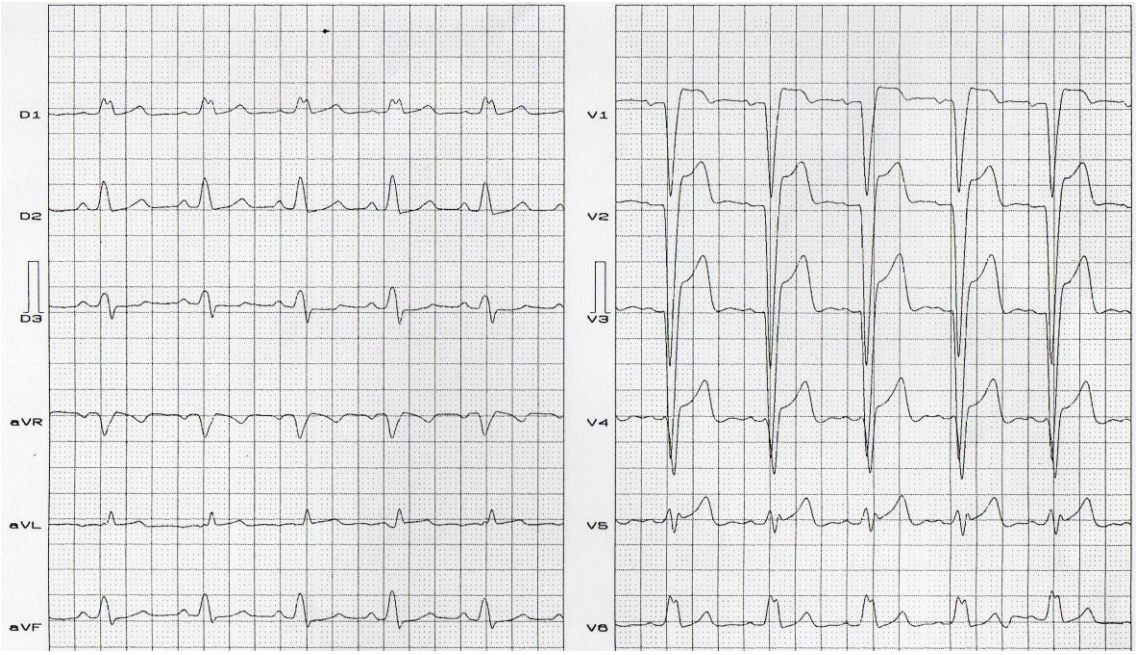
Electrocardiographic diagnosis: Sinus rhythm, heart rate 83 bpm; SAQRS +15° and backward with QRS complexes of the QS type in V1 and rS with small initial r in V2-V3 and sudden passage of the transition area in V4, where the QRS complex is of the pure R or Rs type. This sudden passage from complexes of the rS type to complexes of the Rs type from V3 to V4 without recording R/S transition complex, eventually occurs in the presence of left ventricular enlargement (LVE) by posterior shift of the QRS loop in the horizontal plane.

Negative T waves in II, III and aVF and in V1 and deeply negative from V2 though V4, lead to the doubt of anterior and inferior subepicardial ischemia or a chance of non-obstructive apical hypertrophic cardiomyopathy by the presence of deep, giant, negative T waves from V2 to V4 in a totally asymptomatic person.

In athletes with anamnesis and normal physical examination, the presence of deep, inverted T waves in ≥2 or more contiguous leads in the anterior or lateral wall should lead to the suspicion of hypertrophic cardiomyopathy or arrhythmogenic right ventricular dysplasia/cardiomyopathy (4).

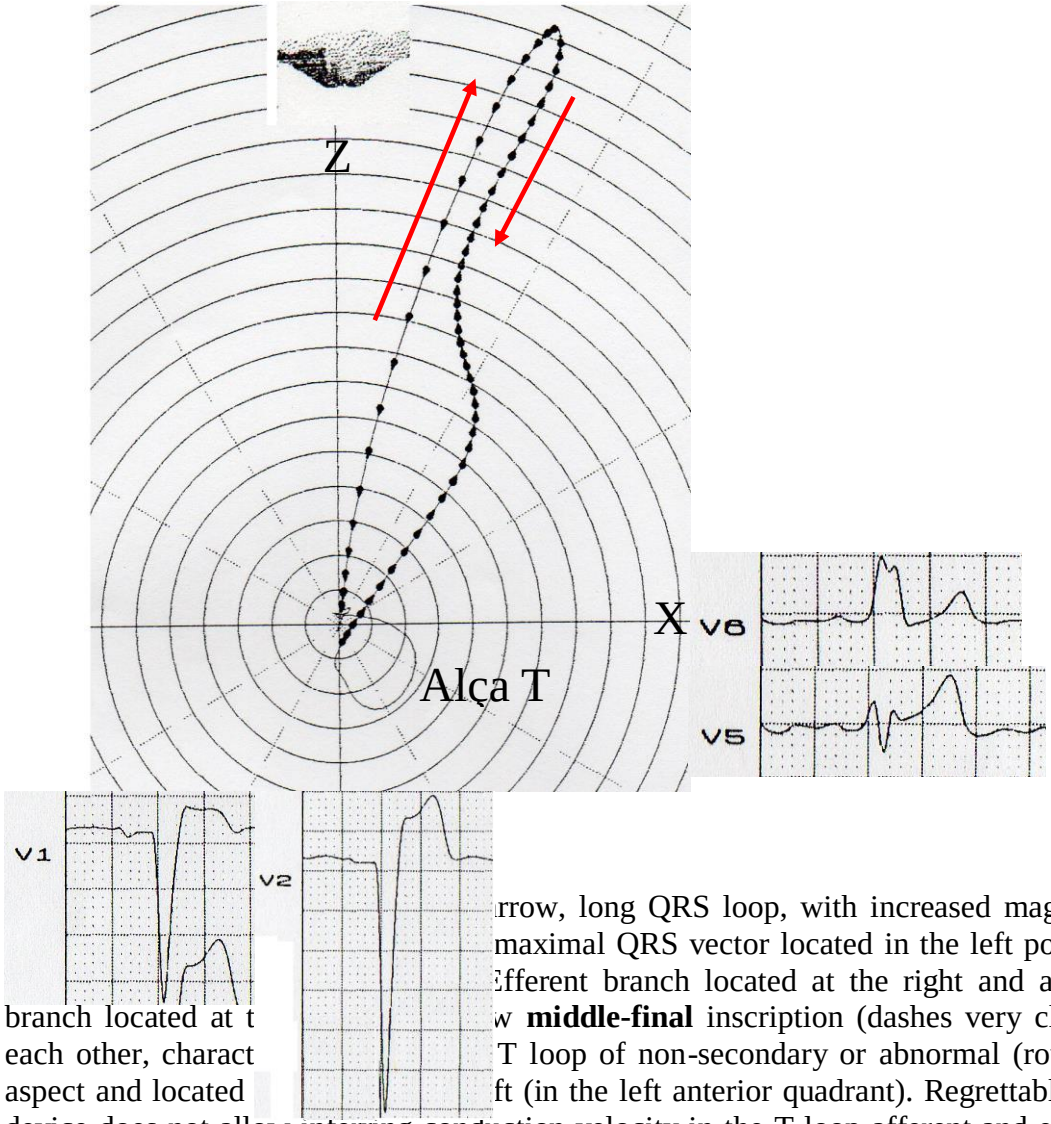
Figure 4

Date March 2, 2013; time: 17 h; age: 38 years old; Sex: female; Race: Caucasian.



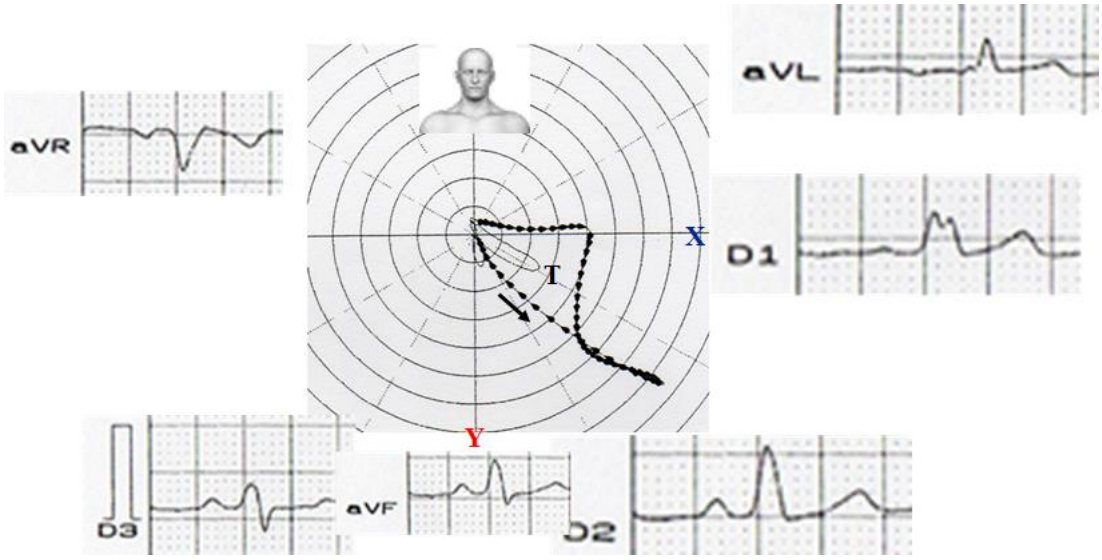
Electrocardiographic diagnosis: Typical CLBBB pattern by QRS duration of 120 ms and characteristic pattern; however, followed by positive T waves in left precordial leads.

Figure 5 Horizontal Plane. Electro/vectorcardiographic correlation.



rrow, long QRS loop, with increased magnitude maximal QRS vector located in the left posterior fferent branch located at the right and afferent branch located at t w **middle-final** inscription (dashes very close to each other, charact T loop of non-secondary or abnormal (rounded) aspect and located ft (in the left anterior quadrant). Regrettably, this device does not allow inferring conduction velocity in the T loop afferent and efferent branches. **Electrocardiographic:** QRS complexes of the QS type in V1 and V2 and pure monophasic R in V6 with wider QRS. Ventricular repolarization opposite to depolarization only in the right precordial leads and matching in V5-V6.

Figure 6 - ECG/VCG correlation in the Frontal Plane

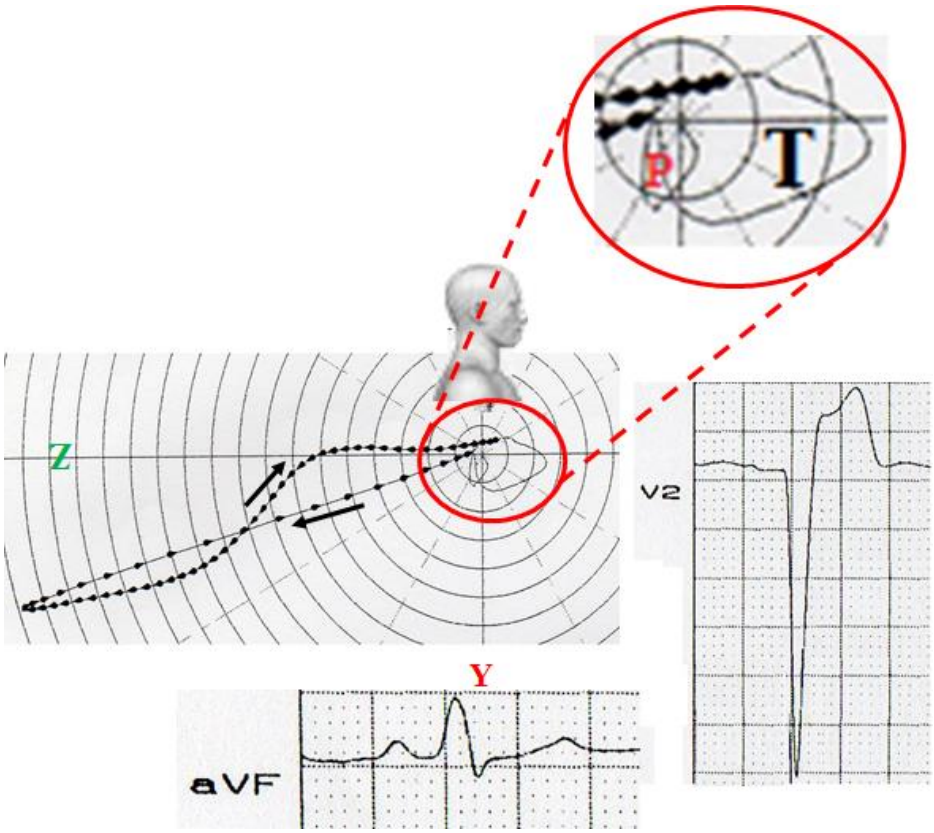


Diagnosis: Vectorcardiographic: P loop in +70°, SAQRS close to +35° and QRS loop of counterclockwise rotation.

T loop not opposite to QRS loop, a fact considered atypical in classical CLBBB. (T loop located in +30° and matching QRS loop in +35°).

Electrocardiographic: SAP +70°, PR interval 140 ms, duration of QRS 120 ms, pure, wide and monophasic R wave "in tower", with notch in I, aVL time of ventricular activation or intrinsicoid deflection >50 ms in I, SAT in +30°; i.e. not opposite to QRS.

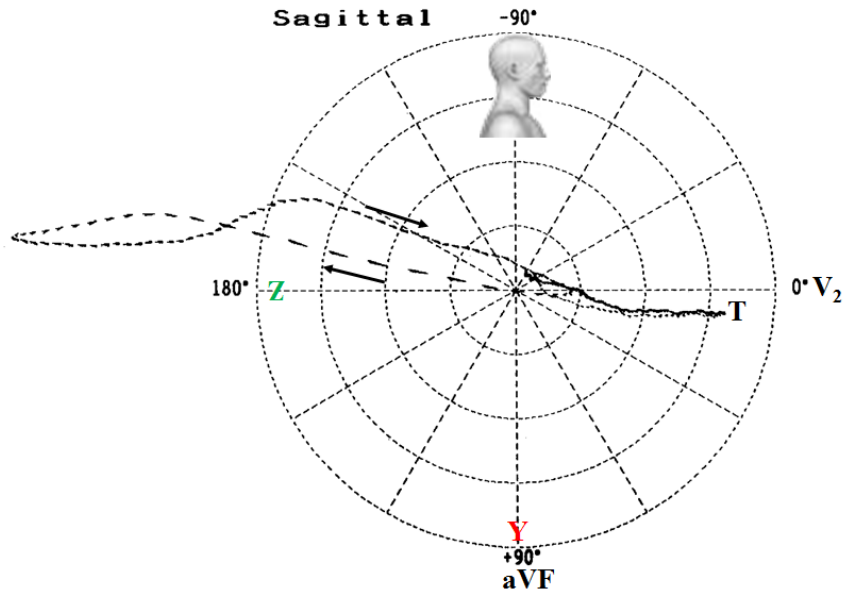
Figure 7A - Right Sagittal Plane. ECG/VCG correlation



Vectorcardiographic diagnosis: QRS loop located in the posterior-inferior quadrant, rotation in eight, and with afferent loop of slow **middle-final** conduction.

T loop of opposite direction to QRS loop heading to the front and with altered (rounded) morphology. In normal conditions in uncomplicated CLBBB, T loop is fusiform or elongated as shown in Figure 7B.

Figure 7B



VCG of a patient carrier of uncomplicated CLBBB in the right sagittal plane. Check the thin and long aspect of the T loop heading to the front, close to +3°. In this case, the device allows seeing that the efferent branch of the T loop presents a slower recording than the afferent branch. This T loop is very different from the T loop aspect of the 7A figure, which is rounded.

Possible causes for Cardiac Memory

The phenomenon of cardiac memory (CM) is characterized by the presence of negative T waves preceded by normal QRS complexes after a conditioning period of abnormal ventricular depolarization in the same ECG leads. The term CM was coined by Mauricio Rosenbaum and his school (5) in an experimental fashion in dogs to describe electrocardiographic alterations in ventricular repolarization induced by abnormal ventricular activation by:

1. Intermittent left bundle branch block (6).
2. After ventricular pacemaker (7). In this case, CM that induces negative T waves, is caused by the presence of transmural gradients of repolarization manifest during atrial pacing, which is maximum near the site of ventricular stimulation (8).
3. Following an episode of ventricular tachyarrhythmia (9).
4. After ablation of anomalous pathway in Wolff-Parkinson-White or transitorily in an intermittent fashion. T wave inversion in II, III and aVF associated to delta

wave disappearance of delta wave after ablation of anomalous accessory pathway in patients carriers of Wolff-Parkinson-White syndrome, is a powerful marker of success of ablation procedure (10).

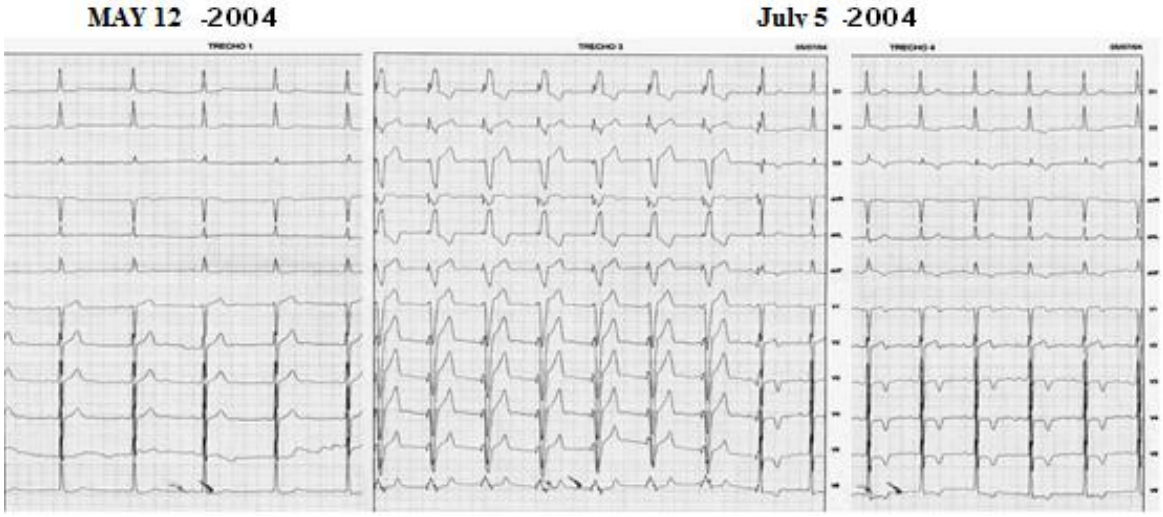
The great interest for investigating this topic is due to the impact that recognizing this phenomenon has when making decisions in cardiological clinical practice, since it manifests with T wave alterations generally interpreted mistakenly as of ischemic origin (**pseudo-primary T waves**) observed in multiple scenarios, mainly in the presence of precordial pain in the ER, as in the first case.

Concept of CM accumulation

Accumulation: duration and frequency of depolarization alteration is a predictor in relation to the time of the phenomenon of CM, which will remain present after the end of ventricular depolarization alteration. Consequently, when CM is observed after a short event of tachyarrhythmia, the phenomenon of CM will last shortly, and on the contrary, when depolarization alteration was prolonged as it happens after preexcitation removed by ablation, T wave changes are observed for a long period of hours or days (11). Inden et al (12) found that the prolongation in the duration of action potential of the epicardium was present before, and persisted after preexcitation ablation. Gradual changes on repolarization properties include action potential prolongation that continues after ablation procedure and may be justified by the phenomenon of accumulation proper of CM.

In the following example (Figure 8) we show the case of a male patient, carrier of single-chamber permanent pacemaker, implanted by sinus node disease, who was admitted in the ER with atypical precordial pain and ECG displaying PM rhythm in VVI mode, alternating with his own rhythm, with T wave inversion in II, III, aVF and V1-V6, that were mistakenly interpreted as being of ischemic origin. In spite of the negative markers (troponin), the patient was referred for coronary angiography that revealed normal coronary arteries. Check that these alterations in ventricular repolarization occur after a period of ventricular stimulation, in the leads where QRS was negative. Moreover, the previous ECG shows normal QRS without repolarization alterations. This electrocardiographic evolution clearly configures the presence of CM.

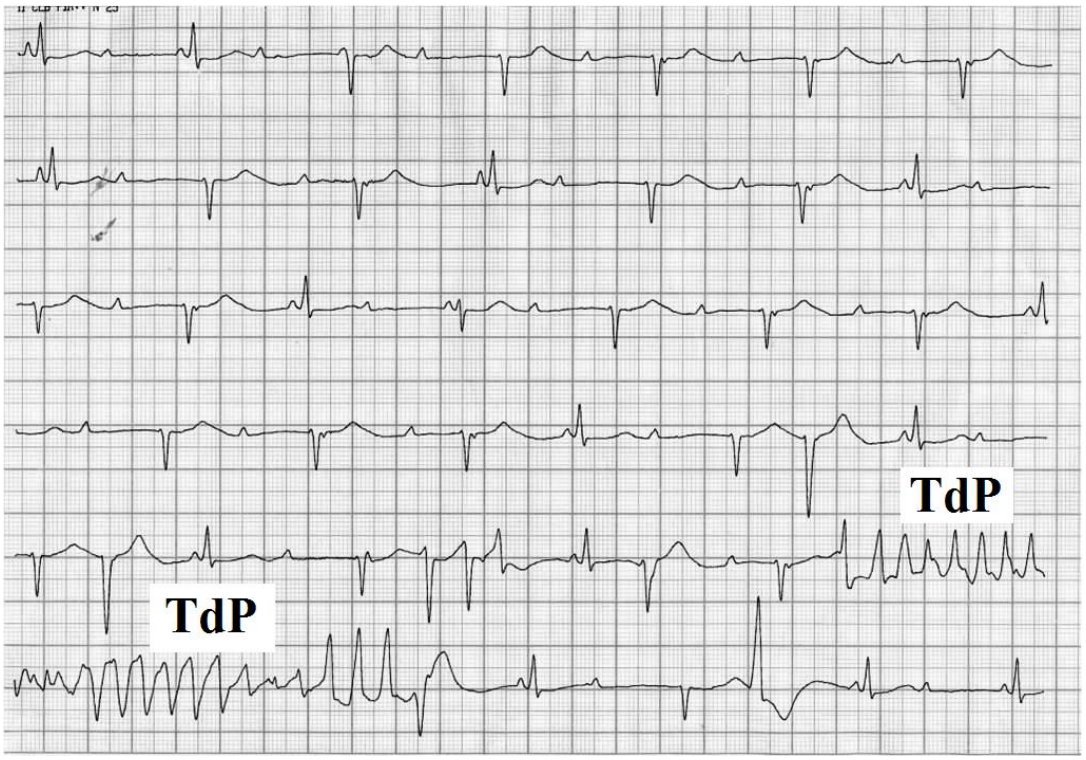
Figure 8



Although these electrocardiographic findings are attributed to ischemia, T wave inversion in the case of CM, does not correlate to myocardial ischemia. These alterations may arise early, and may persist for weeks after the onset of abnormal ventricular depolarization. Although the exact time relation has not been figured out yet, new investigations have shown that the time of permanence of T wave alterations depend on the so-called accumulation phenomenon.

The phenomenon of CM may also occur after a brief period of temporary ventricular stimulation, as in the case of Figure 9, in which ventricular repolarization alterations appeared after 24 hours of cardiac pacing in a patient admitted with syncope and ECG displaying the presence of complete AVB and runs of Torsades des pointes (Figures 9, 10 and 11).

Figure 9



ECG long/continuous DII in admittance.

Figure 10

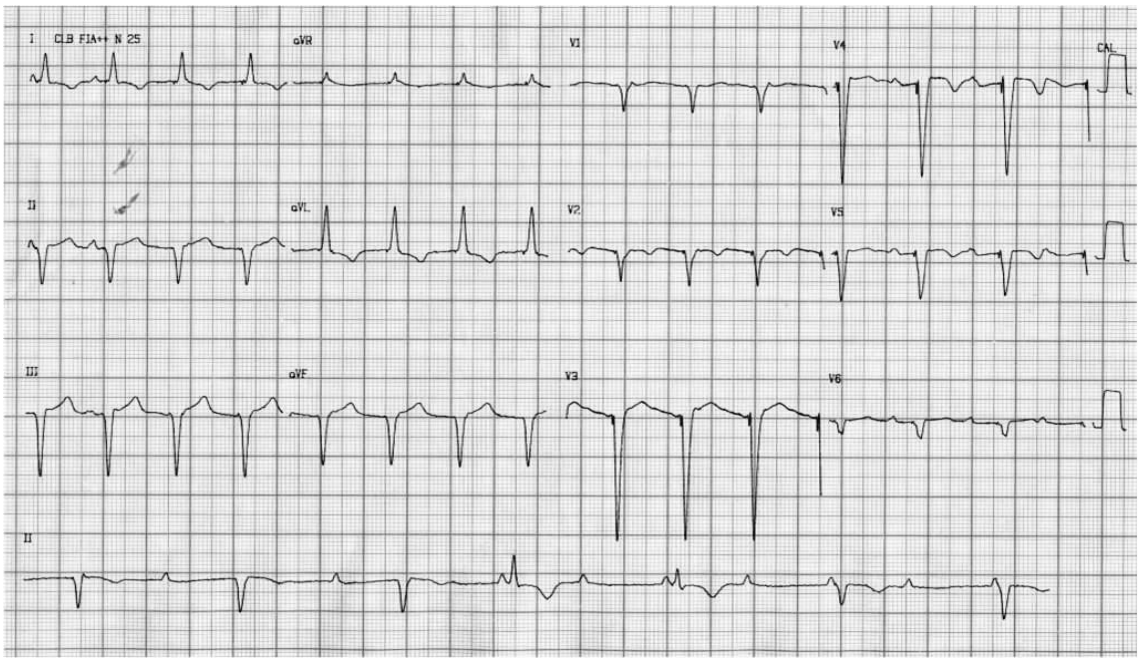
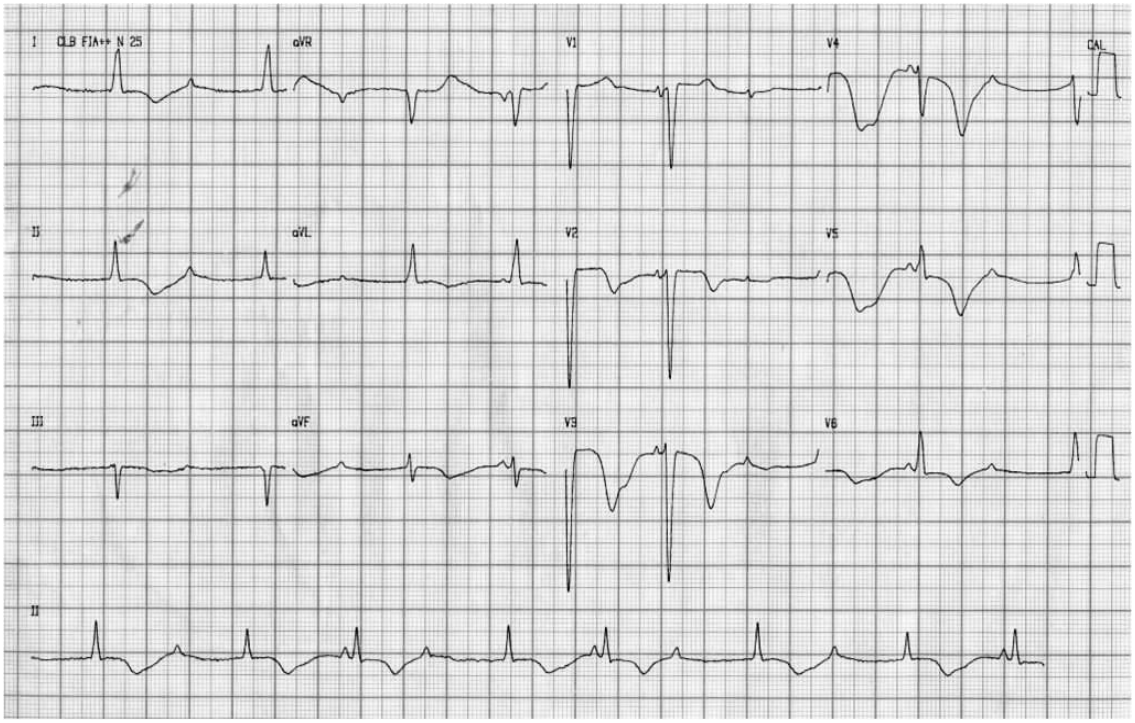


Fig 10: ECG after temporary pacemaker implant. Inferior tracing (long II) was recorded with the PM off.

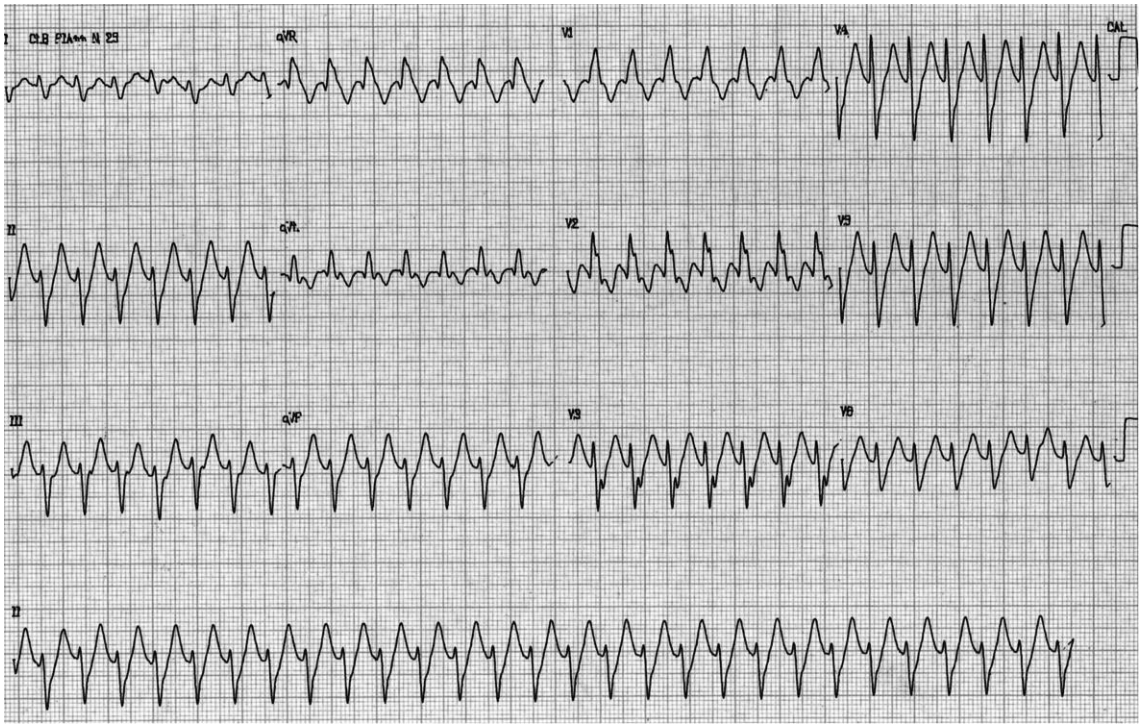
Figure 11



ECG diagnosis: Complete ECG with PM off after 24 hours, showing AV dissociation rhythm with long QT, ventricular repolarization alterations (negative T waves) in the same leads where QRS complexes were previously negative (II, III, aVF and V2-V6), configuring the effect of CM.

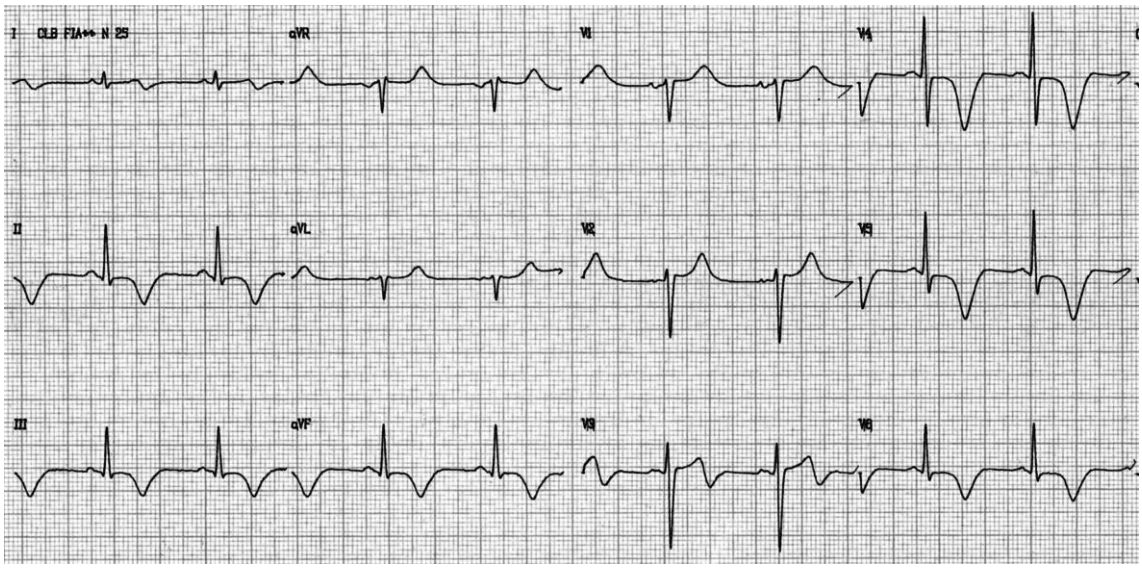
In another example (Figures 12, 13 and 14) we observed the case of a young male, 22-year-old patient, admitted during event of fascicular ventricular tachycardia, in whom ECG after reversion with IV verapamil, shows negative T waves suggesting CM. Such alterations normalized after 1 week, according to the electrocardiographic evolution described below.

Figure 12



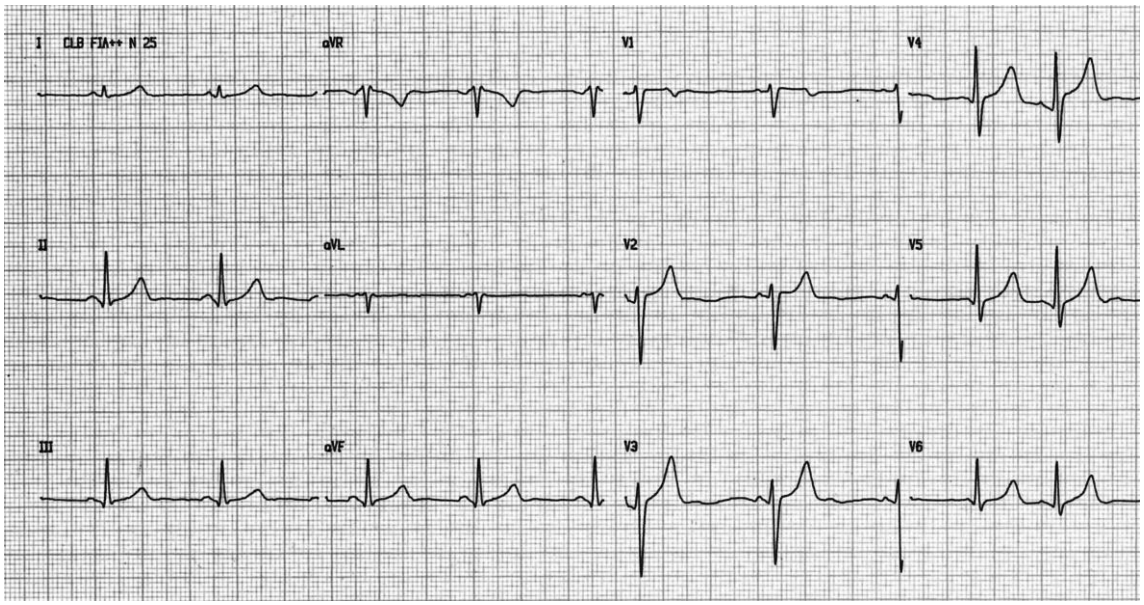
Admission ECG showing fascicular VT of Belhassen.

Figure 13



ECG after reversion to sinus rhythm with verapamil, showing negative T waves in II, III, aVF and from V4 through V6 and plus-minus in I, typical of CM phenomenon.

Figure 14



ECG made after 1 week, showing normalization of alterations in ventricular repolarization.

Mechanisms attempting to explain the phenomenon of cardiac memory.

A) Hypothesis of modification in the expression of sarcolemmal ion channels, of connexin 43 and calcium percentage in the intracellular sarcoplasmic reticulum.

In CM, two early and late regions could be activated.

I) Region of early activation located proximally to the site of altered activation, causing changes in the electrotonic flow, mediated by angiotensin II receptors. The block of angiotensin I receptor attenuates short-term CM, which in the last case modifies the sarcolemmal potential. Three important channels have been identified as being responsible for the early CM phenomenon and the expression of connexin 43:

   a. Decrease in transient outward potassium channel activity in phase 1, causing decrease in notch of epicardial cells. This decrease is due to the regulation in the expression of Kv4 channels and stability of Kv4.3 mRNA channel. LV pacing causes a loss in the epicardium notch and T vector shift mentioned as CM initiated by local increase in angiotensin I in the Hek293 cells, in which the Kv4.3 and KchlP3 subunits contribute to a greater Ito expression with the angiotensin I receptor (AT1R) (13).

The CM phenomenon could be abolished using the transient outward potassium channel blocker, Ito 4-aminopyridine (4-AP) channel (14). Changes in Ito concentration affect action potential, modify vulnerability to arrhythmias and influence excitation-contraction coupling. A decrease in Ito density is observed in immature hearts, in elderly people, cardiomyopathies and heart failure. A decrease in Ito density causes action potential duration prolongation, and less calcium efflux by the Na^+/Ca^{2+} exchanger channel. Both facts favor calcium increase in the sarcoplasmic reticulum with accumulation of this cation in the intracellular medium, thus favoring triggered arrhythmias.

b. Decrease in activity of the L-type calcium current. Pharmacological block of the slow calcium channel attenuates the appearance of CM, both early and late. On the other hand, and rapidly, it decreases the activation of the delayed outward-rectifier I_{Kr} channel.

c. Decrease in the activation of the delayed rapid rectifier I_{Kr} channel in phase 3, and consequently reduction in I_{Kr} transmural gradient (15).

d. Reduction in the expression of connexin 43. The proteins that make up Gap junctions are known as connexins. The most numerous connexin found in the heart is connexin 43, and in a lower number, connexins 40 and 45. In the ventricles, there is a large amount of connexins 43 and 45, and very little of connexin 40. In the atria, there is a large amount of the three types. Connexin 43 is the greatest determinant of the electrical properties of the cardiac muscle. The closure of gap junction is at the level of this connexin, causes negative dromotropism and its decrease may contribute to the CM phenomenon (16).

II) Late-activated region, distal to the site of altered activation. Characterized by significant prolongation of action potential due to increase in mechanical strain. In spite of a marked action potential duration (APD) prolongation, there was a surprisingly minimum variation in the densities of ion channels in the sarcolemma and a significant increase in cytosolic calcium concentration (twice the concentration of cytosolic CA) responsible for the prolongation in APD in the region of late activation, increasing the activity

of the Na^{+}/Ca^{2+} exchanger channel (17). In summary, the basis for memory is caused by an increase in the electrophysiological regional gradients.

B) Hypothesis that supports the basis of CM as the presence of a slow acting mechano-electric feedback mechanism.

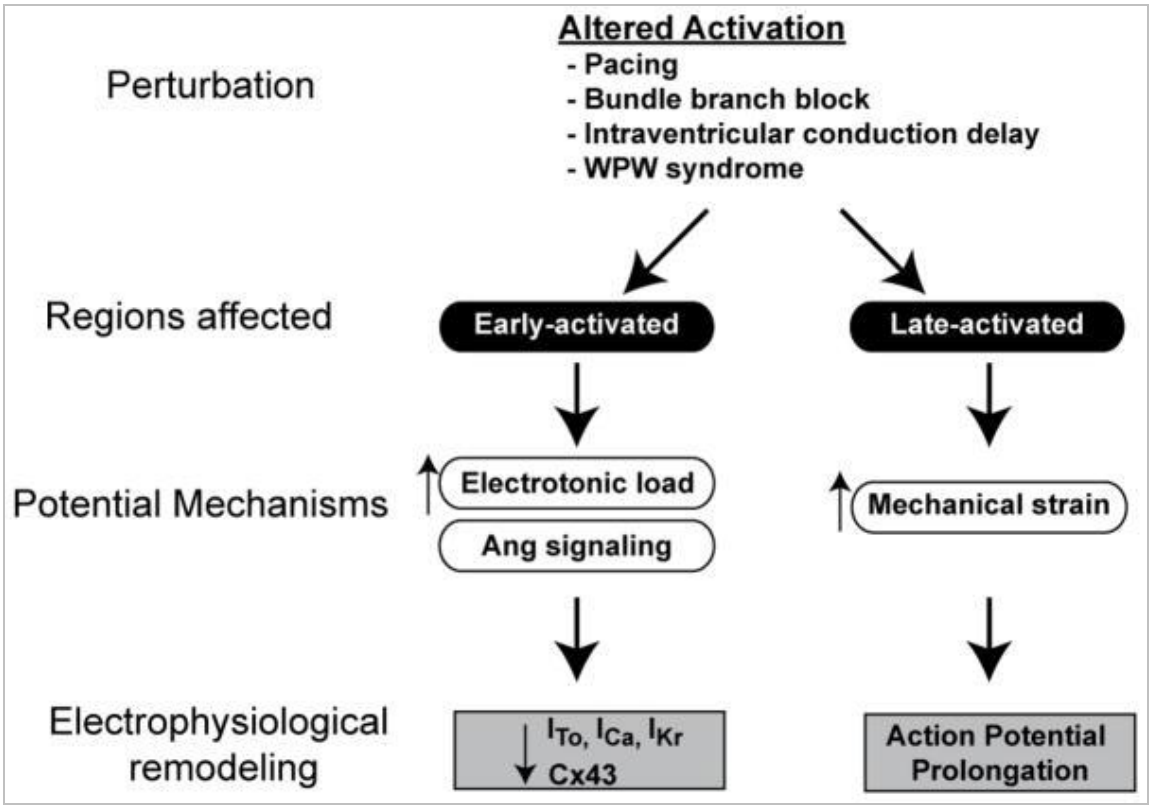
C) In ECG, T and R waves are matching during normal sinus rhythm, but mismatching after a period of ventricular pacing. This phenomenon called CM, could be mediated by mechanic stimulus. Hermeling et al (18), using a mathematical model investigated if this phenomenon of slow acting mechano-electric feedback explains CM. The authors built a model that resembled the behavior of the left ventricle using serial coupled mechanic and electric segments. Every segment was equipped with ion currents of the membrane, of calcium handling channels and slow excitation-contraction coupling of slow acting mechano-electric feedback. The model showed T wave concordance with R wave in normal sinus rhythm and acute mismatching T waves after restoration of sinus rhythm. These results of LV simulation indicate that the slow coupling of excitation-contraction of mechano-electric feedback in the LV may explain:

   a. The relatively small differences in systolic shortening and mechanic work during sinus rhythm;
   b. The small dispersion in repolarization time;
   c. Matching T waves during sinus rhythm;
   d. The phenomenon of CM.

The physiological distribution in the electrophysiology properties, reflected by matching T waves, may be useful to optimize the cardiac pump function.

Table 1 summarizes the main mechanisms of CM.

Table 1



How to suspect in the daily clinical practice, that we are facing an effect of CM?

First, we should bear in minds which are the circumstances in which this phenomenon occurs (LBBB, cardiac stimulation, presence of accessory pathways and ventricular arrhythmias). If there was presence of precordial pain associated to some of the previously mentioned conditions, the diagnosis of this phenomenon becomes more complex. In this situation, it is imperative to make a clinical analysis of the characteristic of the pain (typical or atypical), along with T wave morphology, and whenever possible, to make a comparison with previous tracings. The analysis of cardiovascular risk factors is important too, since we have to rule out the presence of true ischemic episode. Diffuse T wave inversion may be frequently observed in the presence of lesion in the anterior descending artery, but also in the CM effect after ventricular pacing, making the differential diagnosis between these 2 phenomena difficult and complex. A recent study (5) proposes a series of criteria that favor the diagnosis of CM and not of myocardial ischemia in this scenario:

- Positive T wave in aVL

- Positive or isodiphasic T wave in DI
- T waves with maximum negativity in precordial leads in relation to III.
- In the case of being secondary to CLBBB, a duration not much greater than 120 ms is a constant, as well as repolarization in the left leads, not opposite to the preceding R waves.
- T loop of VCG in the case of CLBBB during CM is shown as rounded, unlike the T loop of uncomplicated CLBBB, which is fusiform or elongated.

The results showed a sensibility of 92% and specificity of 100% for the diagnosis of CM. Although not yet validated, this tool could be very helpful in the differentiation between a benign condition (CM) from another potentially severe, such as myocardial ischemia.

Altered mechanical load of the heart leads to ventricular hypertrophy, decompensated heart failure and fatal arrhythmias. Nevertheless, the molecular mechanisms that point to mechanic and electric dysfunction remain very little known. Increasing evidence suggest that ventricular electrical remodeling is a process that could be induced by altered mechanic stress, creating persistent electrophysiological alterations that predispose the heart to fatal arrhythmias. As to ventricular electrical remodeling, it is clearly a physiological property of the human heart manifest by T-wave memory and a variety of pathological states associated to altered ventricular activation, as bundle branch block, preexcitation, pacemaking, etc. Animal models that are being used to investigate ventricular electrical remodeling induced by stretching, present significant limitations. The model of the zebra-fish recently arose as an attractive animal model to study cardiovascular diseases and could overcome some of such limitations. The zebra-fish model could provide new clarifications on the molecular mechanisms that lead to negative electrical remodeling in response to stretching and mechano-electric feedback. The data suggest that the model of the zebra-fish is a powerful platform to investigate the molecular mechanisms of mechano-electric feedback in the heart (19).

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