Transient alternating infrahisian system conduction defects

Martín Ibarrola, MD,
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Spanish: Reporte de un caso

Paciente masculino de 59 años concurre a la consulta por presentar cuadro diarreico de 5 días de evolución.
Antecedentes personales: Hipertenso leve en uso de Losartan 25 mg 2x por dia, refiere ser portador de enfermedad de Chagas. História familiar negativo para morte subita o arrritmias cardiacas. História social nega tabaco o alcohol
Examen físico: Presión arterial: 130-80 mmHg, nada digno de nota. Fueron realizados varios ECGs en el momento de la consulta. Traía con él dos ECGs realizados en Diciembre de 2015. Los exámenes de laboratorio de urgencia revelaron apenas moderada hipokalemia (nivel de potasio sérico 2,8 mEq/L). **Ecocardiograma:** Leve hipertrofia ventricular izquierda excéntrica con función ventricular conservada, fracción de eyección normal (55%), patrón diastólico de relajación prolongado, diámetro telediastólico del ventrículo izquierdo normal (55 mm), aurícula izquierda con leve dilatación (48 mm). Ventrículo derecho con función sistólica y diámetro normal. Diámetro de la raíz de la aorta normal (36 mm).
Preguntas:

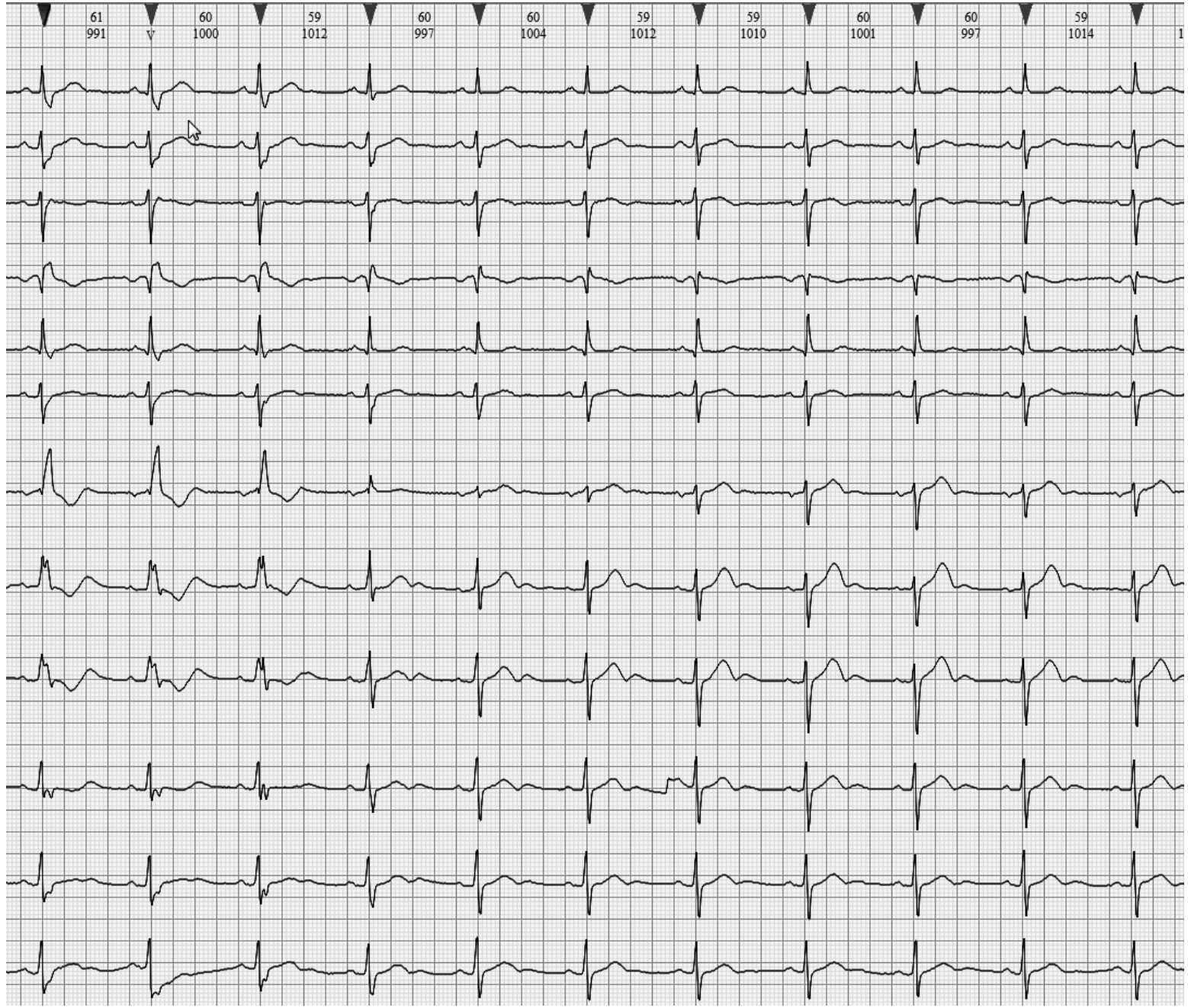
1. Describir la evolución de los trastornos dromótropos intraventriculares. 2) ¿Cuál es la más probable causa(s) de los mismos?; 3. ¿Existe riesgo de muerte súbita?. 4. ¿Cuál es la conducta más adecuada a seguir?

English: Case report

59 male patient presented for consultation due to diarrheic scenario with 5 days of evolution.
Personal history: Mild hypertension, in use of Losartan 25 mg, 2x per day. He refers to be carrier of Chagas disease.
Family history: Negative for sudden cardiac death or cardiac arrhythmias.
Social history: Negative for tobacco, alcohol abuse or illicit drugs.
Physical examination: Blood Pressure: 130-80 mmHg. Nothing worthy of note.
Several ECGs were performed at the consultation. He brought with him two ECGs performed in December 2015.
Emergency laboratory tests were requested that revealed just moderate hypokalemia (potassium serum level 2.8 mEq/L).
Echocardiogram: Mild eccentric left ventricular hypertrophy with preserved ventricular function, normal LV ejection fraction (55%), LV with diastolic dysfunction pattern, normal left ventricular diastolic diameter (55 mm). Left atrium with mild dilatation (48 mm). Right ventricular with normal systolic function and diameter. Normal root diameter of the aorta (36 mm).
Questions:

1. Describe the evolution of intraventricular dromotropic disorders; 2. What is the most probable cause(s) of these dromotropic disorders?; 3. Is there a risk of sudden death?; 4. What are the most appropriate approach steps?

ECG performed in 2016



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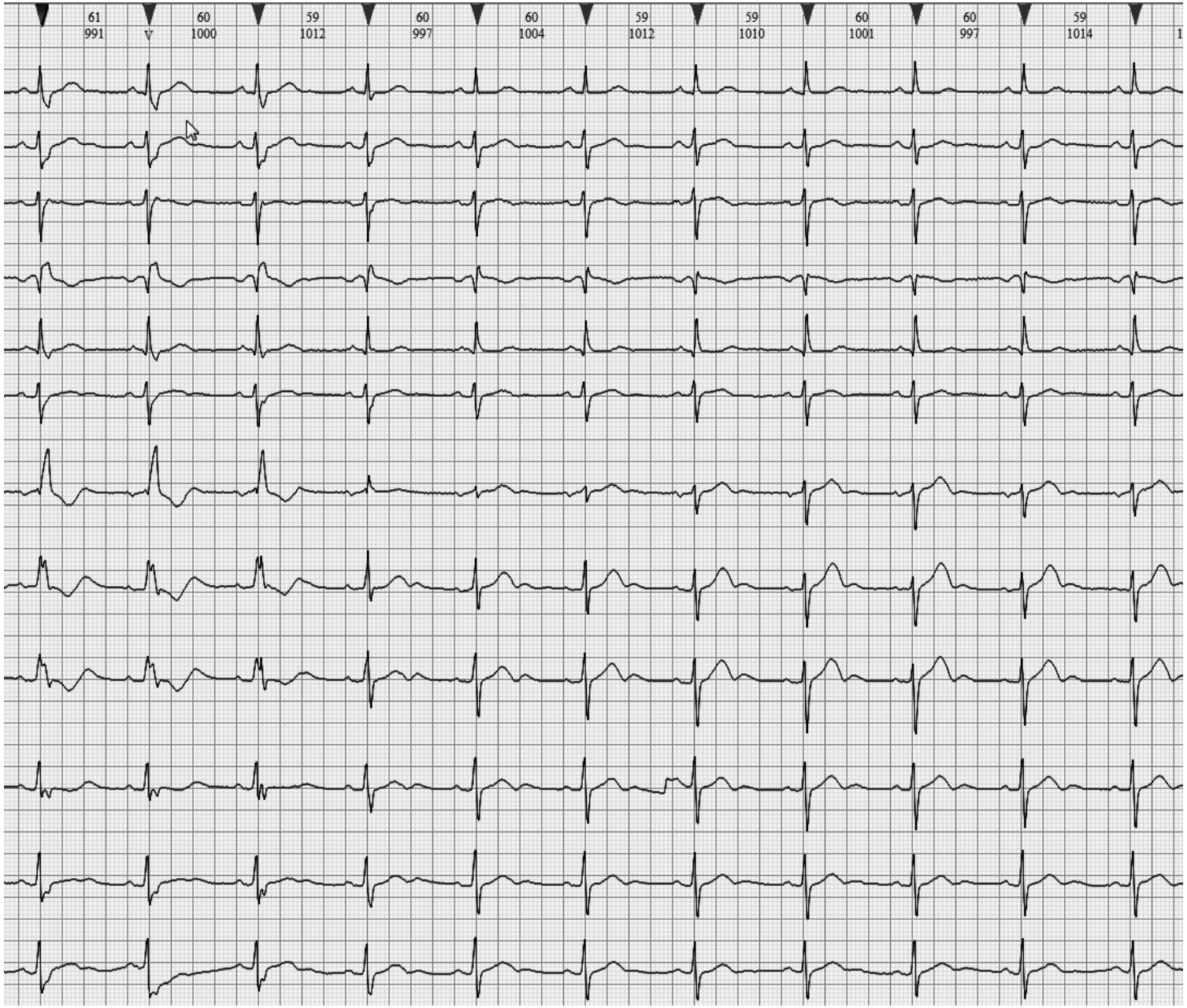

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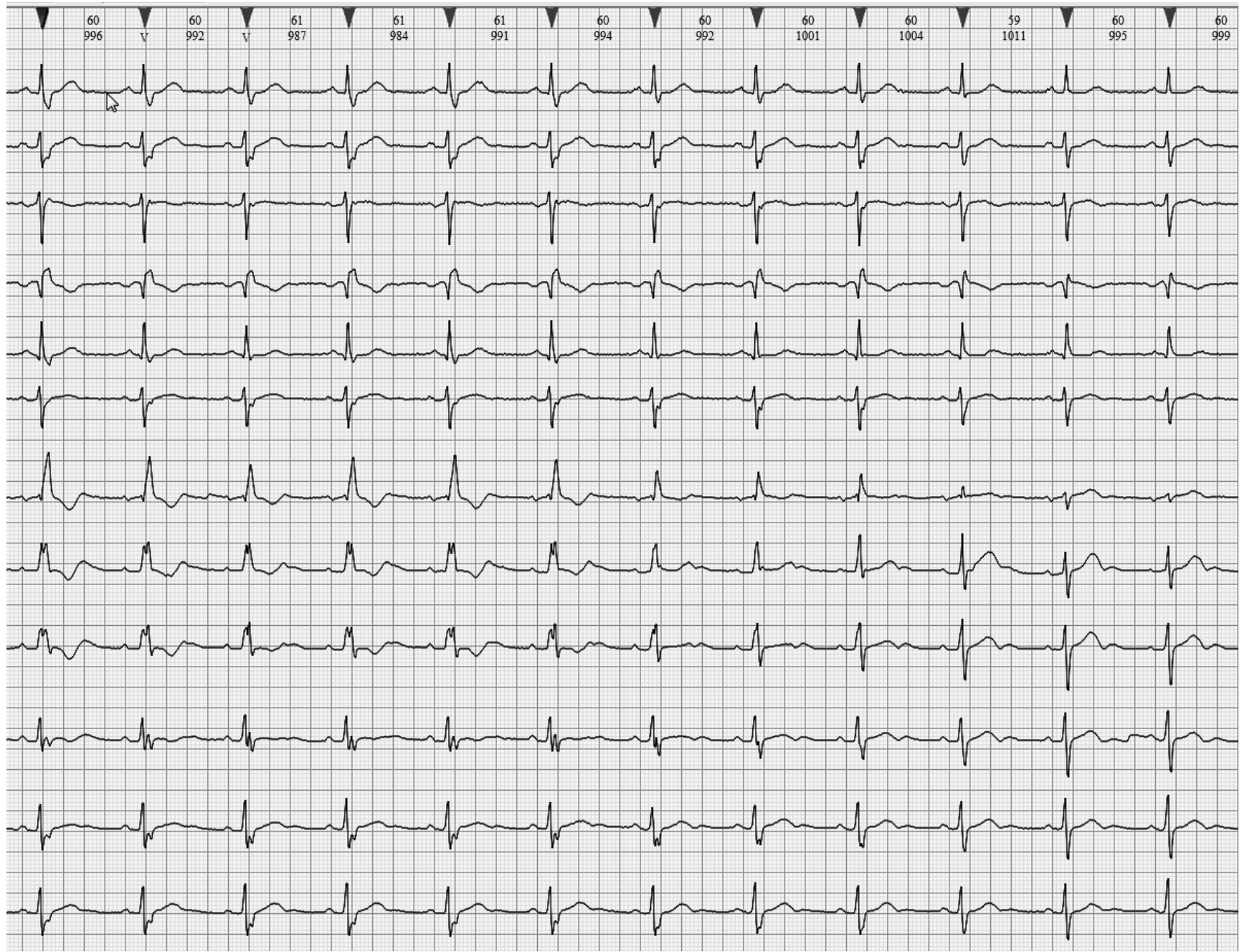

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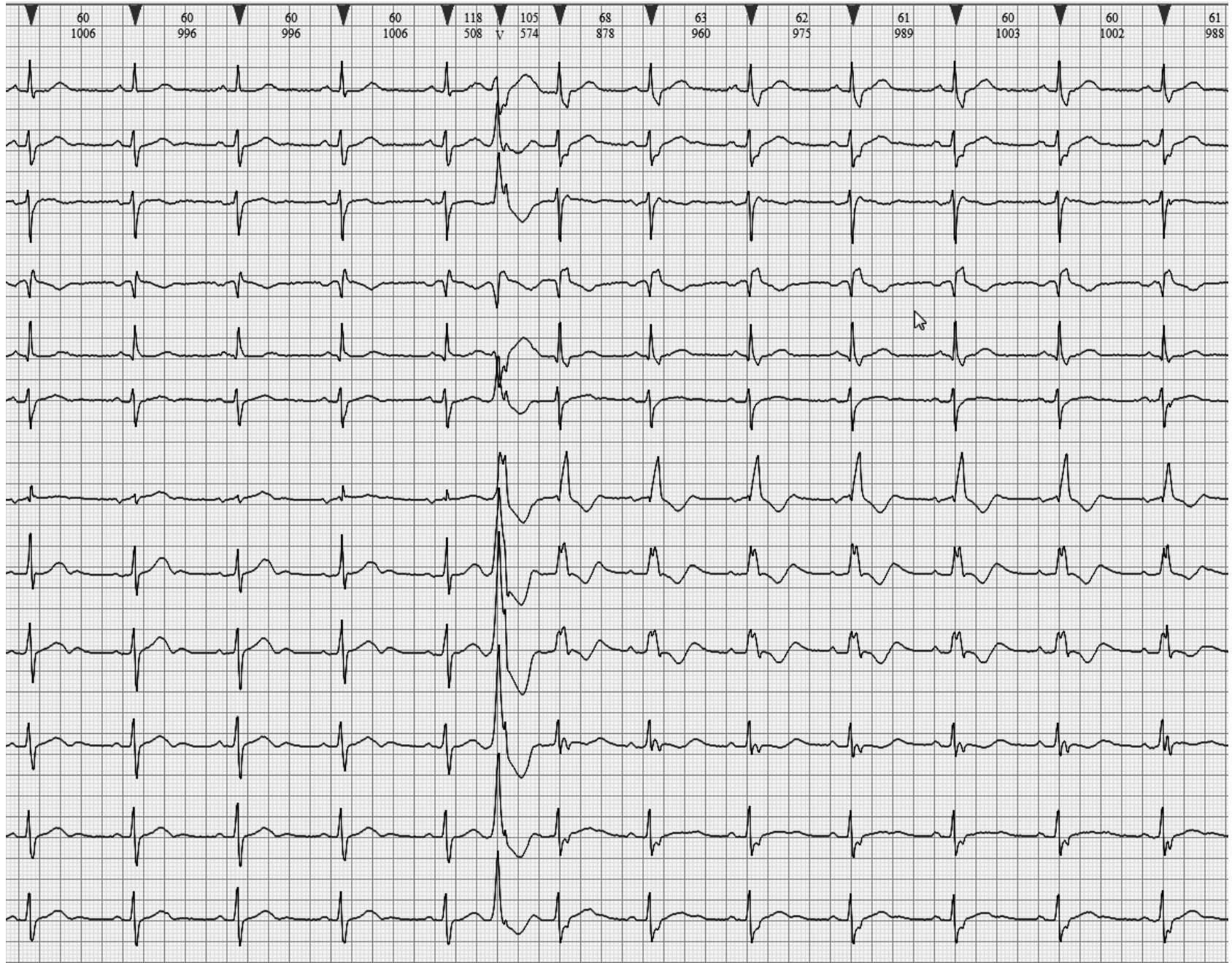

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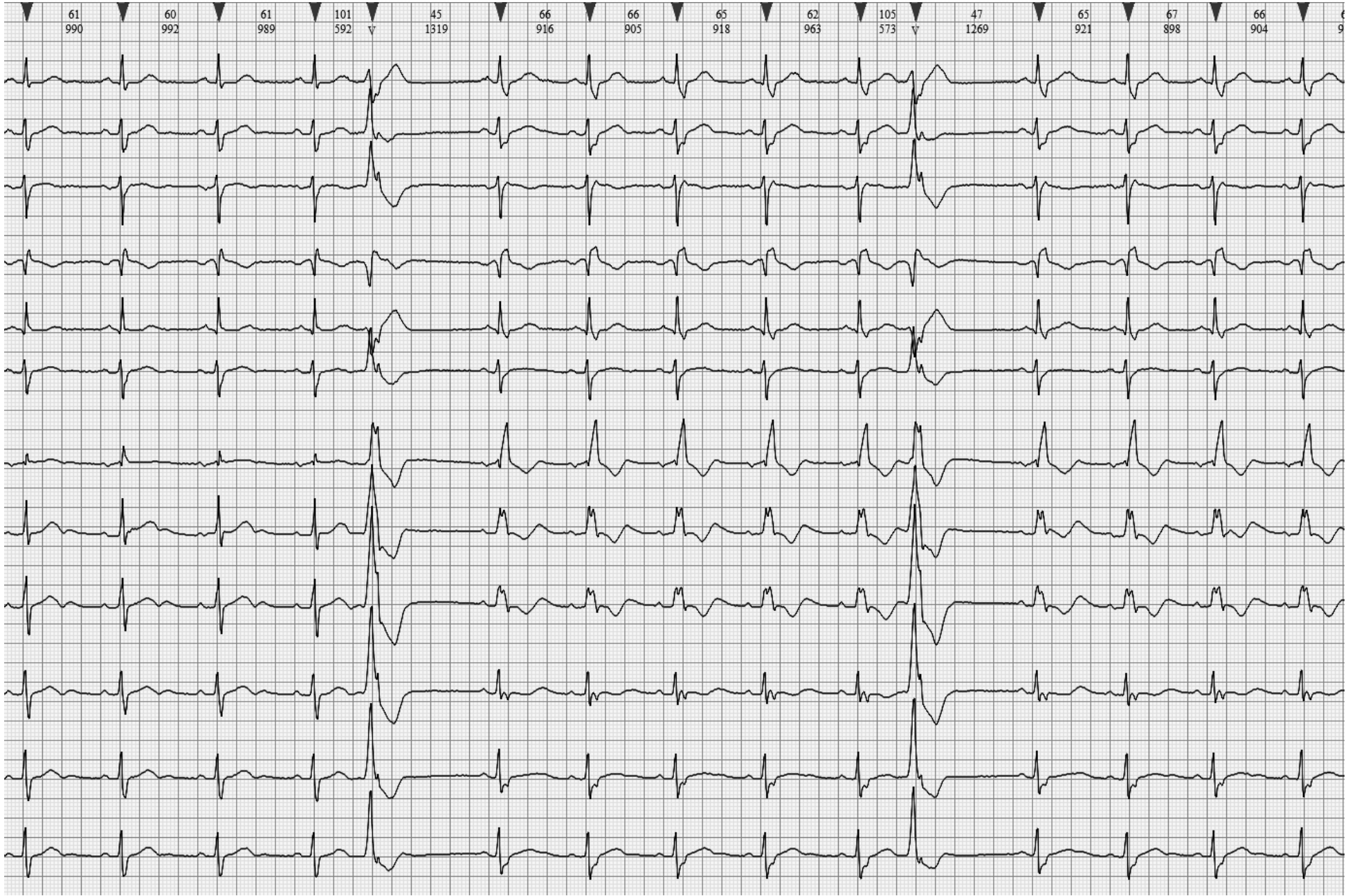
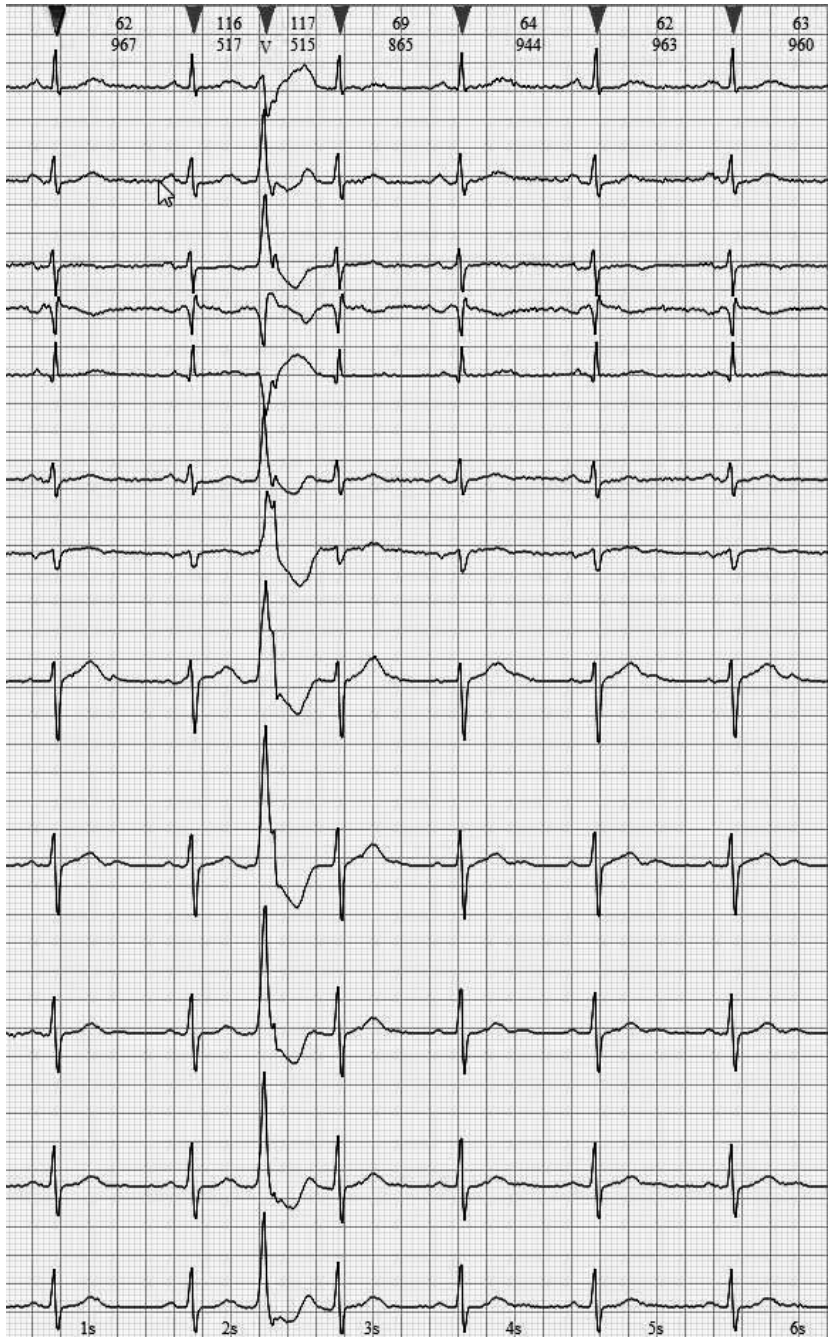
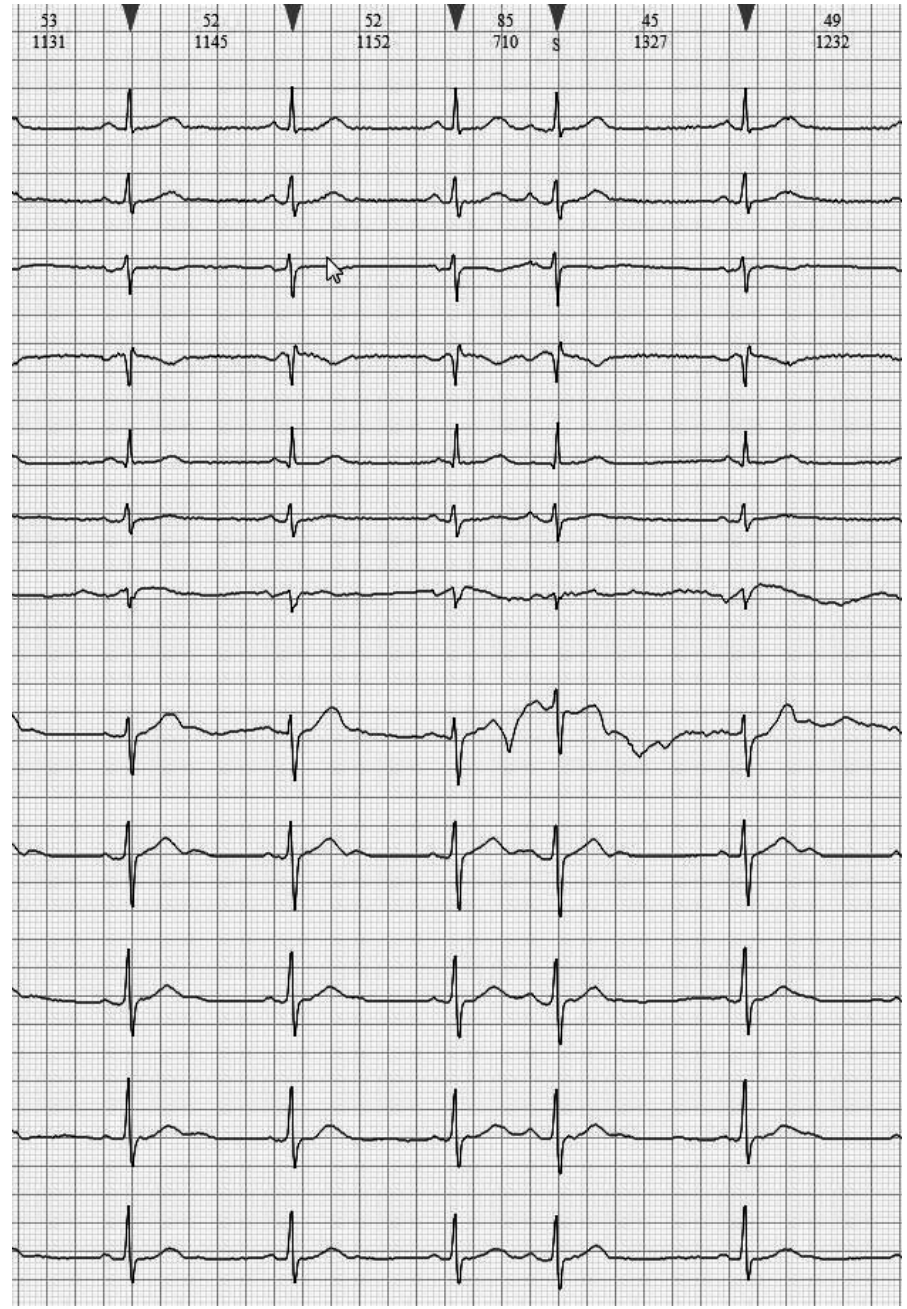


ECG December 2015





Dec 2015 normal ECG, neither PVC or APC is associated with RBBB. In 2016 there is phasic RBBB (non rate related) as well as LAFB pattern. An interpolated PVC (from the anterior apical LV) produces the RBBB pattern perhaps due to trans septal concealed conduction into the RBB which is perpetuated perhaps due to the same mechanism. Another PVC associated with near compensatory pause is also associated with RBBB pattern perhaps due to phase 4 block in a diseased RBB. Wonder whether bifascicular block is related to either Chagas disease or hypertrophic myopathy. An EP study with overdrive atrial pacing would define presence of HP disease and if H-V is very prolonged would suggest use of pacemaker.

Spanish

Dic. 2015. ECG normal, ni extrasístoles ventriculares o auriculares asociadas con BRD. En el 2016 hay BRD fásico (no relacionado a la frecuencia) así como patrón de BDASI. Extrasístole ventricular interpolada desde el VI apical anterior, que produce el patrón de BRD, talvez por conducción transeptal oculta en el BRD, que se perpetúa, probablemente por el mismo mecanismo. Otra ESV asociada con pausa casi compensatoria, también se asocia a patrón de BRD, probablemente por bloqueo en fase 4 en una rama derecha enferma.Me pregunto si el bloqueo bifascicular se relaciona con enfermedad de Chagas o miopatía hipertrófica.Un EEF con sobreestimulación auricular definiría la presencia de hipertrofia y si H-V está muy prolongado, sugeriría el uso de marcapasos.

Melvin N. Scheinman, MD

Overview

Dr. Melvin Scheinman is Professor of Medicine, Walter H. Shorenstein Endowed Chair in Cardiology, and one of the founding fathers of the field of cardiac electrophysiology. Dr. Melvin Scheinman is one of the founding pioneers of clinical cardiac electrophysiology. He grew up in Brooklyn, New York and took his undergraduate degree at Johns Hopkins University where he graduated first in his class. Postgraduate medical education included Albert Einstein College of Medicine, residency training at the University of North Carolina (Chapel Hill) and cardiology training at the University of California, San Francisco Medical Center.

Dr. Scheinman is best known as the first person to have performed catheter ablation in humans.
We are very pround with his participation in our virtual discusions.

Hola Martin y Andres,

There is a significant change in the electrocardiogram between 2015 and 2016. Both are in sinus rhythm, but now he has developed a left anterior fascicular block and intermittent right bundle branch block. Most ECGs also show premature ventricular complexes of a single morphology (right bundle inferior axis) originating in the anterior (superior) wall of the LV close to the mitral annulus. Some of these PVCs are interpolated. Others have a compensatory pause.

We see RBBB at cycle lengths equal or less than 1000 msec and normal or minimally degree of delay in the right bundle with cycle lengths equal or longer than 1012 msec. This suggest phase-3 RBBB. There are two beats with RBBB after a PVC with longer cycle lengths (1269 and 1319 msec). This is more difficult to analyze because the previous PVC may have had retrograde concealed conduction into the right bundle resulting in aberrancy. It is impossible to determine the timing of such retrograde concealed conduction. Certainly it would be quire delayed since the PVC originated from the LV and has to cross the septum before reaching the right bundle branch retrogradely.

This progression of conduction abnormalities indicate that the patient has Chagas cardiomyopathy. His systolic left ventricular function is preserved, which is a good finding.

I would performed an exercise stress test and obtain Holter recording to see if he has more malignant arrhythmias. If possible, I would obtain an MRA with late enhancement to look for areas of fibrosis. This information will help us to better determine his risk of sudden death.

Un abrazo,

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Spanish

Hay un cambio significativo en el electrocardiograma entre 2015 y 2016. Ambos están en ritmo sinusal, pero ahora el paciente ha desarrollado bloqueo divisional antero-superior izquierdo y bloqueo de rama derecha intermitente. La mayoría de los ECG también muestran extrasístoles ventriculares de morfología única (eje inferior de la rama derecha), que se originan en la pared anterior (superior) del VI cerca del anillo mitral.Algunas de las extrasístoles ventriculares son interpoladas. Otras presentan una pausa compensatoria. Vemos BRD a longitudes de ciclo iguales o menores a 1000 ms, y una conducción normal o mínimo de retardo en la rama derecha con longitudes de ciclo iguales o mayores a 1012 ms. Esto sugiere BRD en fase 3. También hay dos latidos con BRD luego de extrasístoles ventriculares con mayores longitudes de ciclo (1269 y 1319 ms). Esto es más difícil de analizar porque la extrasístoles ventriculares previa podría haber presentado conducción retrógrada oculta hacia la rama derecha, resultando en aberración. Es imposible determinar el momento de tal conducción retrógrada oculta. Ciertamente estaría bastante atrasada, puesto que la extrasístoles ventriculares se originaron en el ventrículo izquierdo y debe cruzar el septo antes de alcanzar la rama derecha en forma retrógrada. Esta progresión de anormalidades de conducción indica que el paciente tiene miocardiopatía chagásica. Su función sistólica del VI está preservada, lo que es un buen hallazgo. Yo realizaría una prueba de esfuerzo y obtendría un registro Holter para verificar si presenta arritmias malignas. De ser posible obtendría una resonancia magnética con realce tardío para procurar eventuales áreas con fibrosis. Esta información nos ayudaría a determinar mejor su riesgo de muerte súbita.

Mario Gonzalez MD

Guest of Honor, College of Medicine, National University of Rosario, Argentina Invited Visiting Professor, College of Medicine, Pontifical Catholic University of Argentina, Buenos. Distinguish International Educator. University of Florida

Português

Há uma mudança significativa no eletrocardiograma entre 2015 e 2016. Ambos estão em ritmo sinusal, porém, atualmente o paciente desenvolveu BDAS e BRD intermitente. A maioria dos ECG também mostram extra-sístoles ventriculares com morfologia única (eixo inferior do ramo direito), que se originam na parede anterior superior do VE perto do anel mitral. Algumas extra-sístoles ventriculares são interpoladas. Outras apresentam pausa compensatória.

Vemos BRD com comprimentos de ciclos $\leq$ 1000 ms, e uma condução normal ou atraso mínimo no ramo direito com o ciclo de comprimento igual ou superior a 1012 ms. Isto sugere BRD na fase 3. Há também duas batidas com BRD após extra-sístoles ventriculares com ciclos de comprimentos maiores (de 1269 e 1319 ms). Isso é mais difícil de analisar, porque as extra-sístoles anteriores poderiam haver apresentado condução retrógrada oculta, resultando em aberração. É impossível determinar o tempo de tal condução oculta retrógrada. Certamente seriam bastante tardias, uma vez que as extra-sístoles ventriculares originadas no VE e devem atravessar o septo antes de chegar ao ramo direito em retrógrada. Esta progressão de anormalidades de condução indica que o paciente possui cardiomiopatia miocardiopatia chagásica. A função sistólica do VE é preservada, o que é um bom sinal. Eu solicitaria um teste de esforço e um registro de Holter para verificar se aparecem arritmias malignas. Se possível faria uma ressonância nuclear magnética cardíaca com MRI realce tardio na procura de eventuais áreas com fibrose. Esta informação nos ajudará a determinar melhor o risco de morte súbita.

Mario Gonzalez MD
Penn State Hershey Heart and Vascular Institute

Spanish

Queridos colegas: El paciente tiene ritmo sinusal con interval PR normal, extrasístoles ventriculares aisladas (de cara anterior del VI). BRD intermitente (no transitorio) con diferentes grados de BIRD llegando hasta la conducción normal en los últimos latidos del primer trazado. Es frecuencia-dependiente (diferente para cada fecha). Una vez instalado el BRD tiende a perpetuarse por activación retrograda de la rama derecha desde el VI que desplaza el periodo refractario de la rama derecha hacia la derecha.
Clásicamente el BRD transitorio ocurre cuando persiste a través de un cierto tiempo independiente de la frecuencia.
BRD alternante ocurre cuando la conducción alterna con la normal o con BRI (conducción 2:1).Por ahora no requiere marcapaso.
Lindo trazado, gracias.
Les deseo un lindo domingo
Gerardo Nau MD Argentine

English

Dear colleagues: The patient has sinus rhythm with normal PR interval, isolated premature ventricular contraction from LV anterior face. BRD intermittent (non-transient) with different degrees of BIRD reaching normal driving in the last heartbeat first tracing. It is frequency-dependent (different for each date). Once installed RBBB tends to perpetuate itself by retrograde activation of the right bundle branch from the sixth shifting the refractory period of the right bundle branch to the right.
Classically it occurs when the transitional RBB persists through some time independent of frequency.
Alternating RBBB driving occurs when alternating with normal or BRI (conduction 2: 1) .For now requires pacemaker.
Nice ECGs, thanks.
I wish you a nice Sunday
Gerardo Nau MD from Argentine

Interesante ECG!!!. la EV que emerge de una onda U (algunas interpoladas y otra con pausa compensadora) provoca BCRD intermitente pero haciéndolo de una manera gradual (pasando del BCRD al BIRD y normalización de la conducción). La penetración retrógrada de la EV (del VI pared anterior/apical) en la rama modifica el período refractario provocando el trastorno de conducción. Es interesante que existan dos posibles mecanismos, uno de ellos cuando la EV es interpolada (linking?) y la otra cuando existe pausa compensadora (en F4?). un EEF sería académicamente bonito para demostrar esto. Seguiremos esperando las opiniones de las maestros de este
abrazos.
Oscar Pellizón MD PhD.

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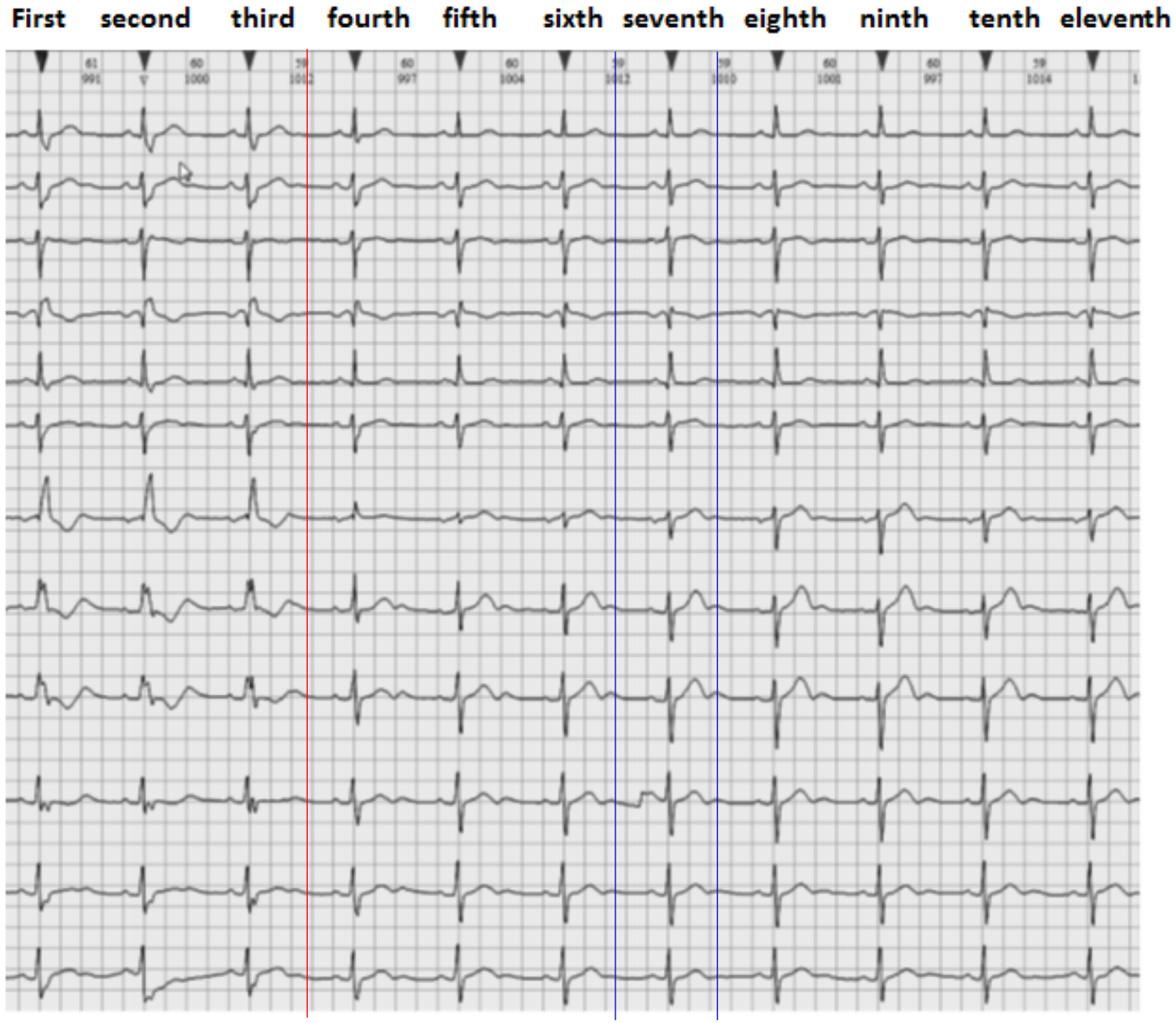
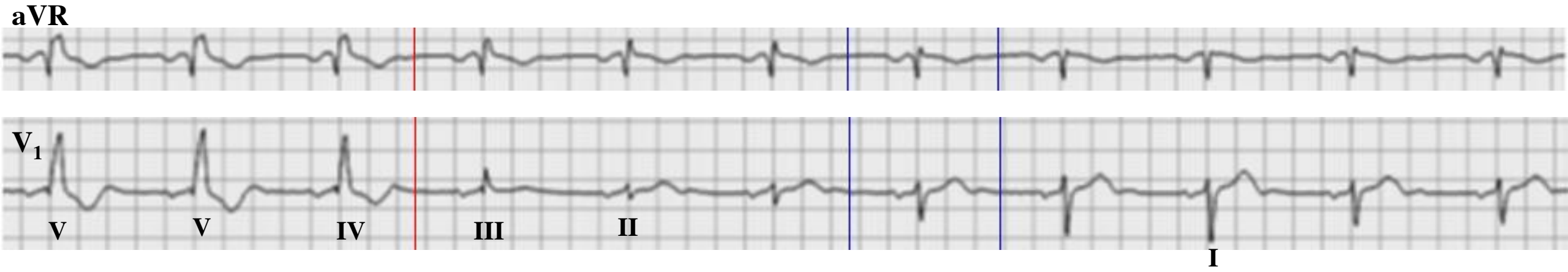
English
Interesting ECG!!! The PVC that originates at the U wave (some interpolated and another with compensatory pause) causes intermittent CRBBB, but gradually (going from CRBBB to IRBBB and conduction normalization). The retrograde penetration of the PVC (from the anterior/apical LV wall) in the branch modified the refractory PR causing conduction disorder. It is interesting that there may be two possible mechanisms; one of them when the PVC is interpolated (linking?) and the other when there is compensatory pause ((Bradycardia-dependent or in phase 4?). EPS would be academically pretty to show this. We will continue waiting for the opinions of the masters in this forum.
Warm regards

Final comments

ECG performed in 2016



The first three beats have RBBB + LAFB pattern; the fourth, fifth and sixth beats show a lower degree of LAFB + minimal IRBBB and the seventh one has lower degree of IRBBB. From eighth to eleventh beats, the degree of LAFB is still smaller and the RBBB disappears. This dromotropic modification occurs without heart rate variations. Small degrees of block in the left anterior fascicle of LBB totally overlap normal variants (**Elizari 2012**).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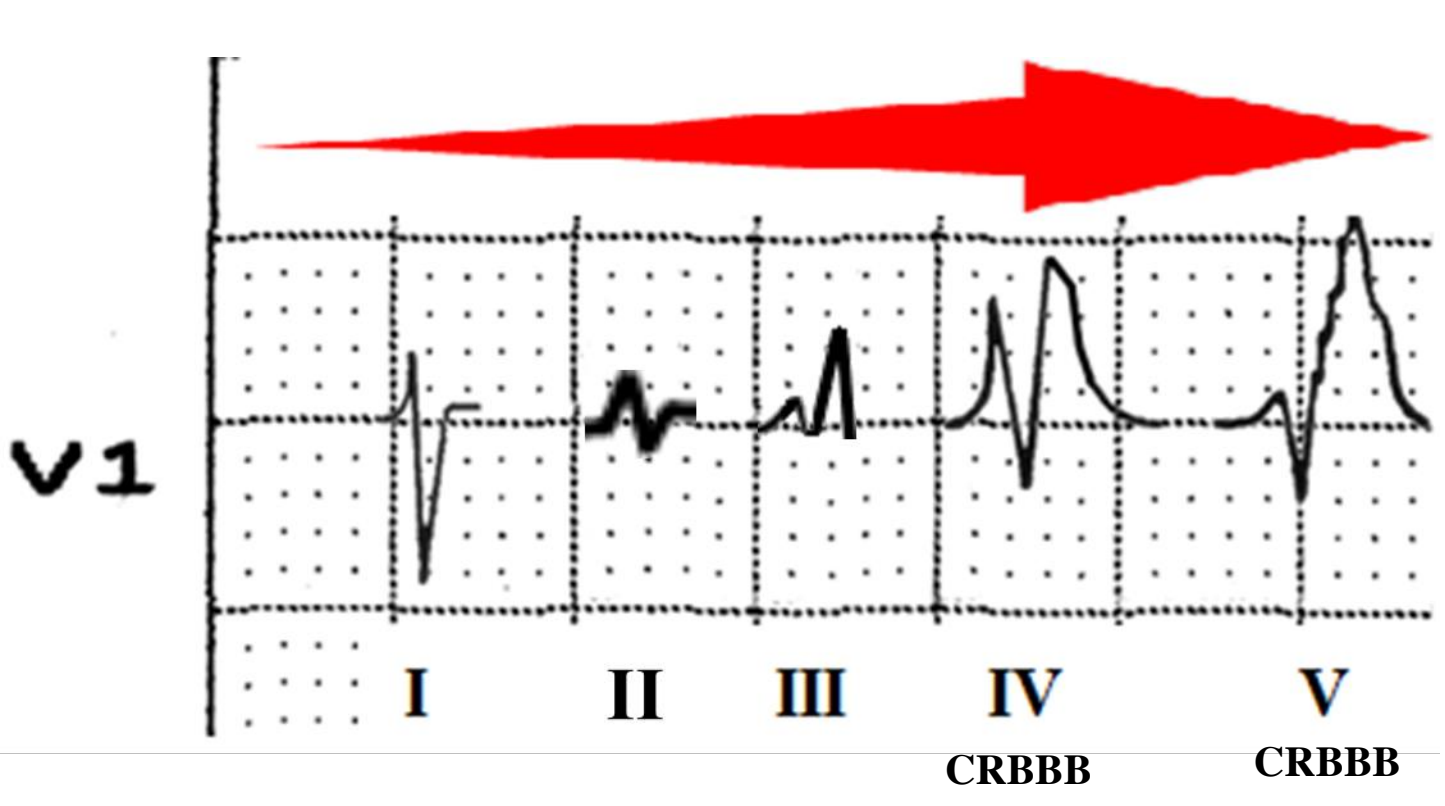
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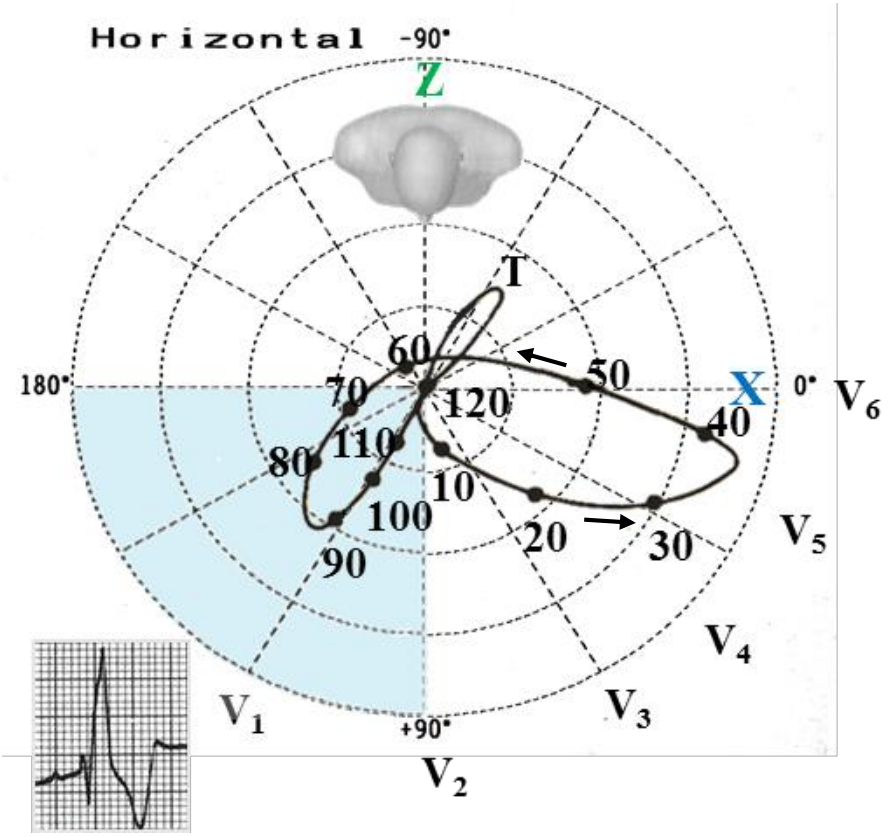
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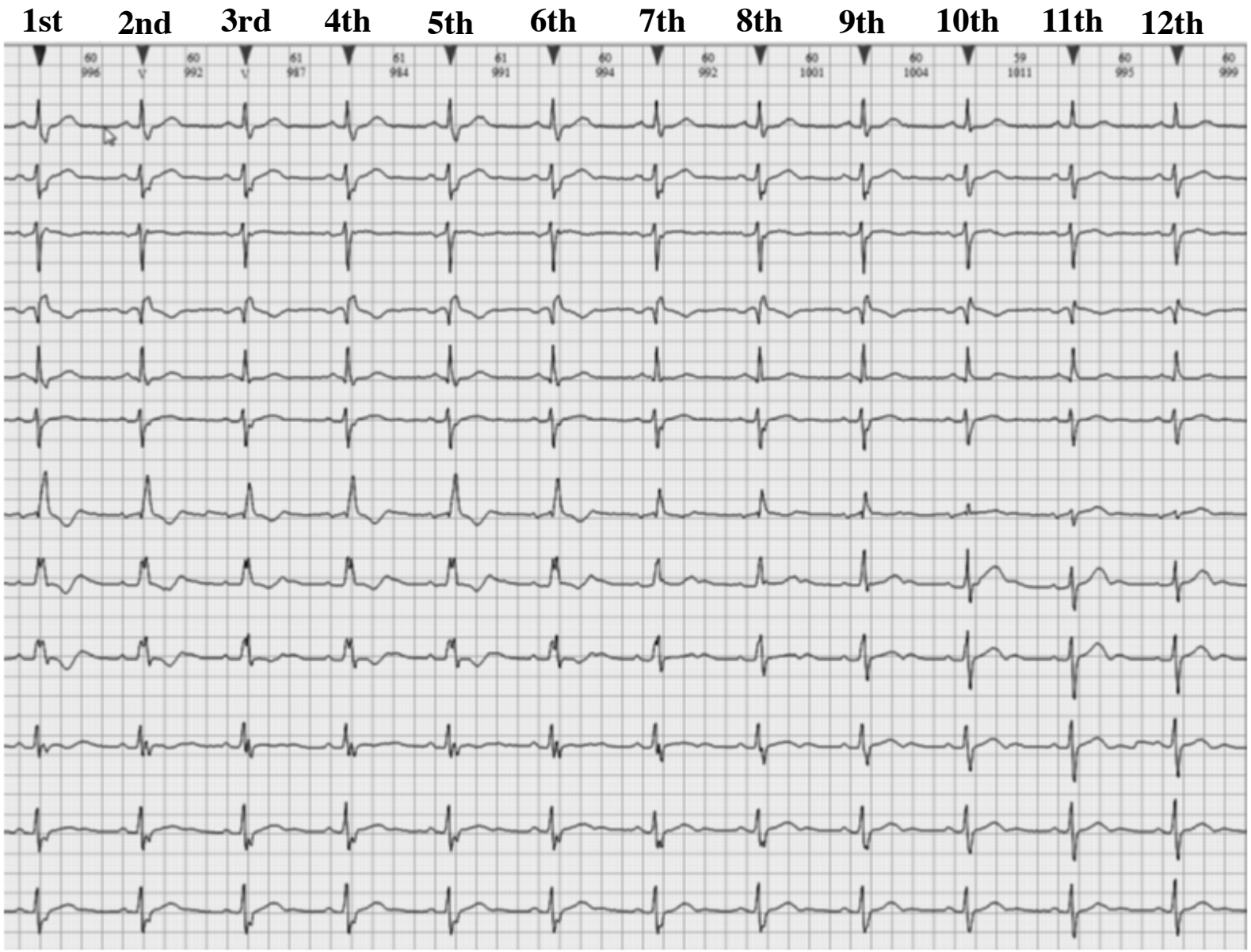
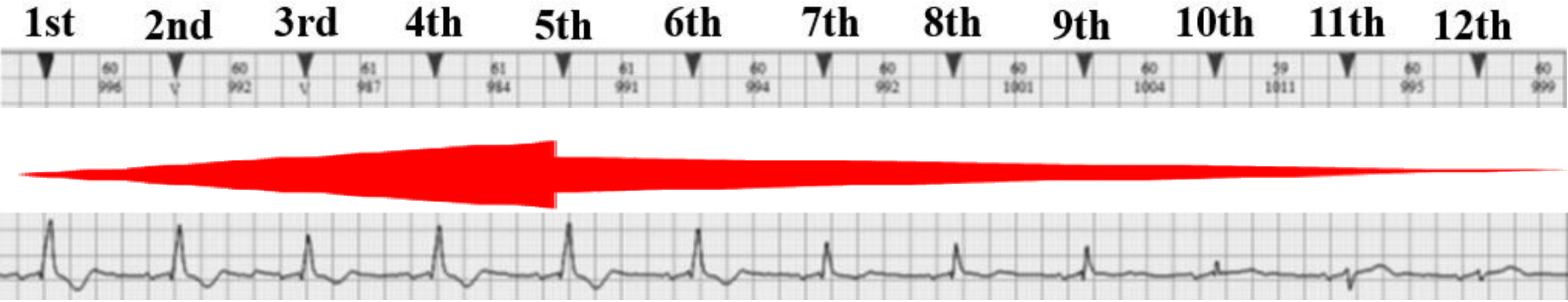
ECG performed in 2016



Graus variáveis de BDAS associado a graus decrescentes de BRD

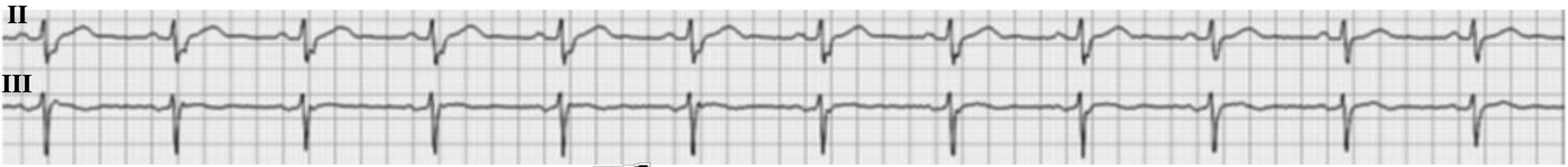
Variable degrees of LAFB associated with decreasing degrees of RBBB without modification in heart rate.



Decreasing degrees of RBBB without modification in heart rate.

Classification of RBBB by steadiness:

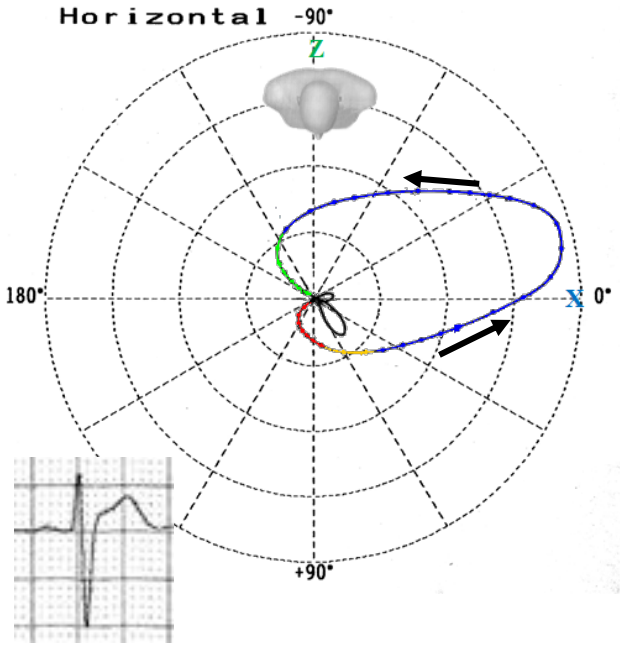
- Permanent;
- Temporary, transient or transitory (see next slide);
- Intermittent (Okajima 1980):
  - Dependent on heart rate:
    - ✓ Tachycardia-dependent or in phase 3 (Izumi 1996);
    - ✓ Bradycardia-dependent (Kinoshita 2003) or in phase 4: by mild or moderate hypopolarization.
  - Independent from hear rate:
    - ✓ By severe hypopolarization: the present case?



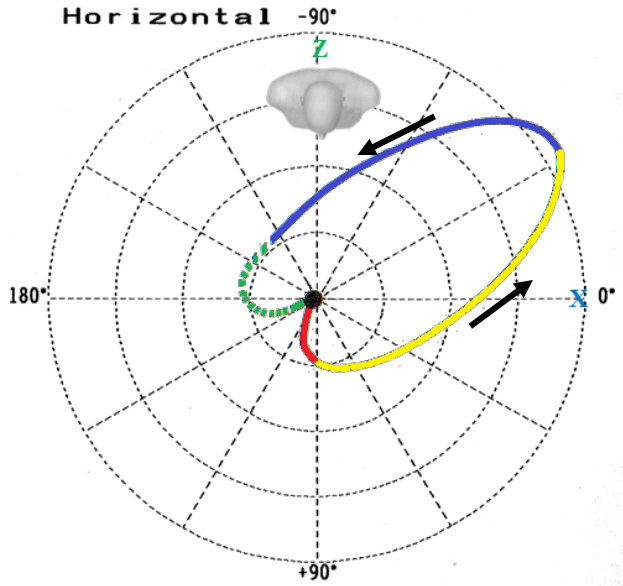
Mayor degree of LAFB **Minor degree of LAFB**

The figure below shows the effect on the configuration of the horizontal QRS loop produced by development of RBBB during cardiac catheterization. With onset of the block, a rightward anterior final appendage was produced, which gradually went away has the transient BBB cleared. A slight increase in the leftward forces, which were partially uncancelled because of the delay in activation of the RV, occurred with the block and gradually cleared.

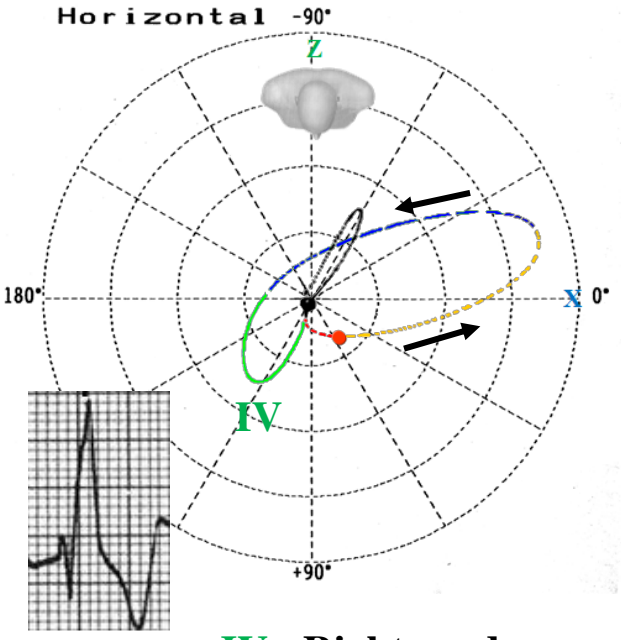
Normal



Transition

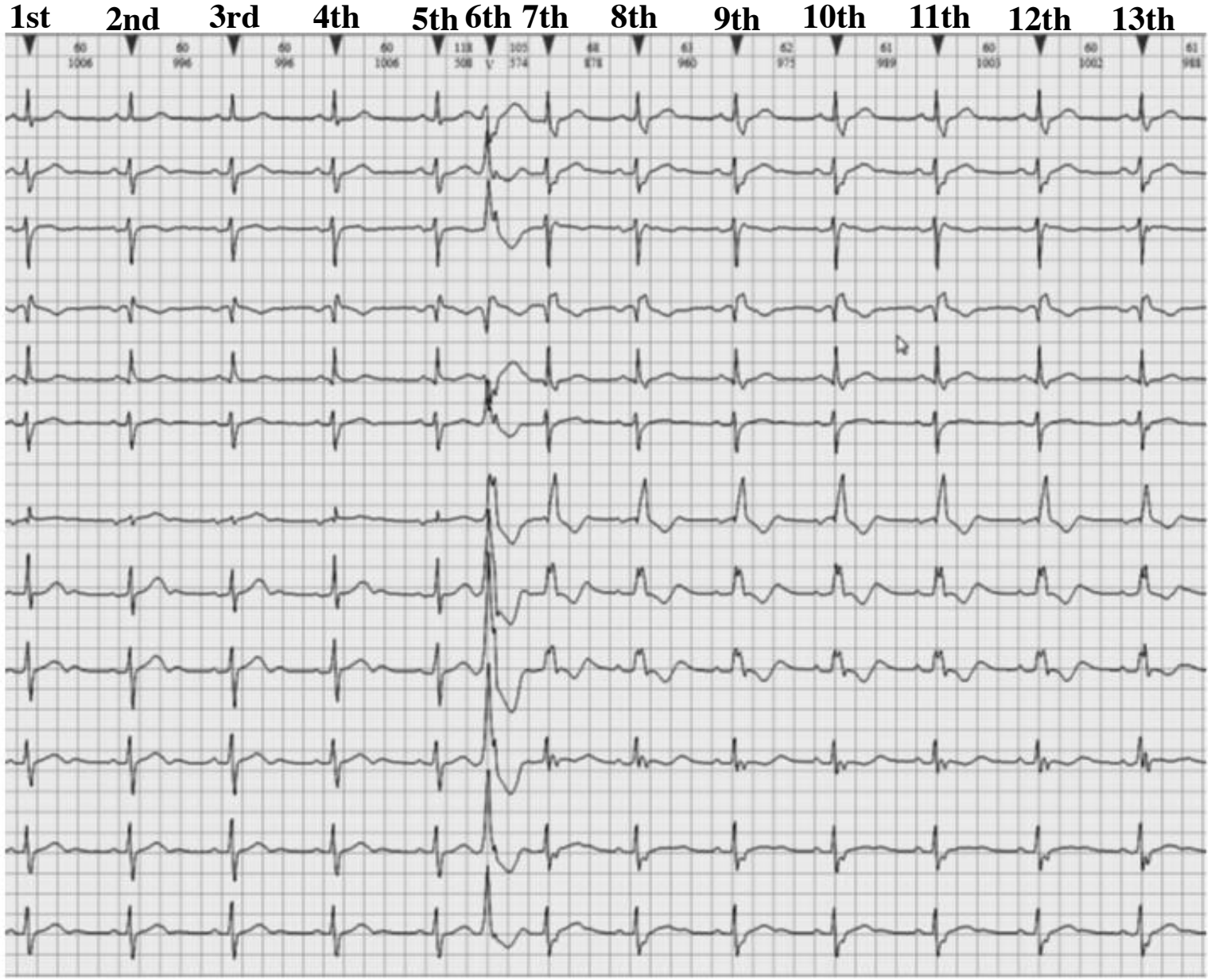


CRBBB

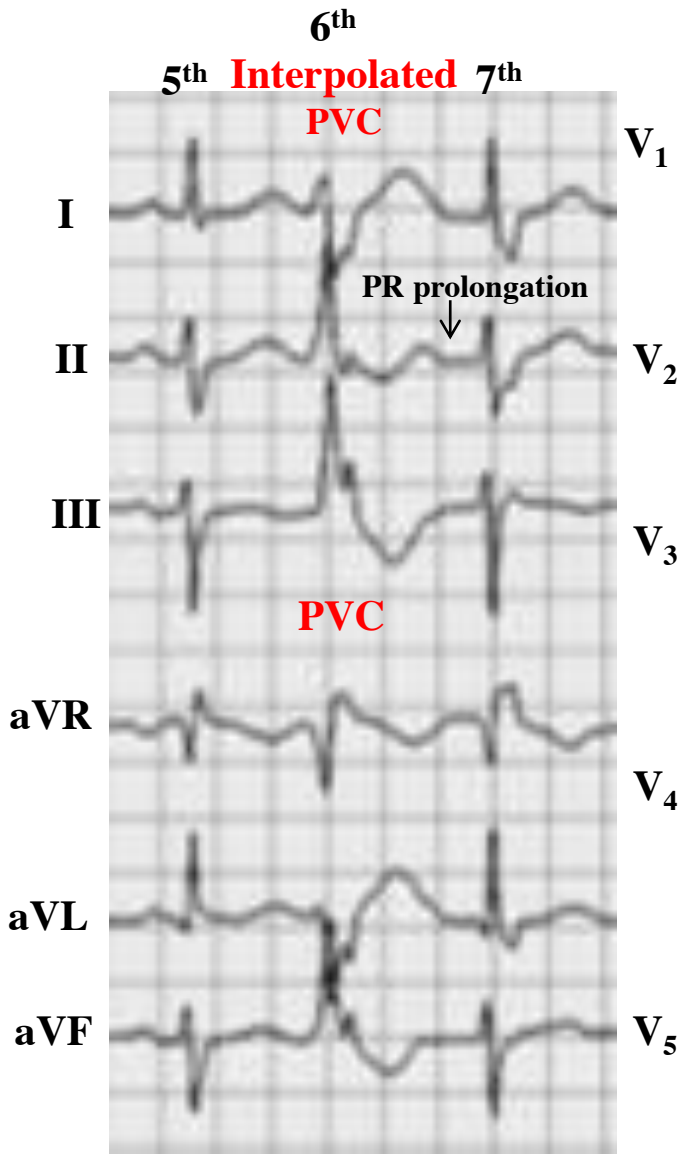


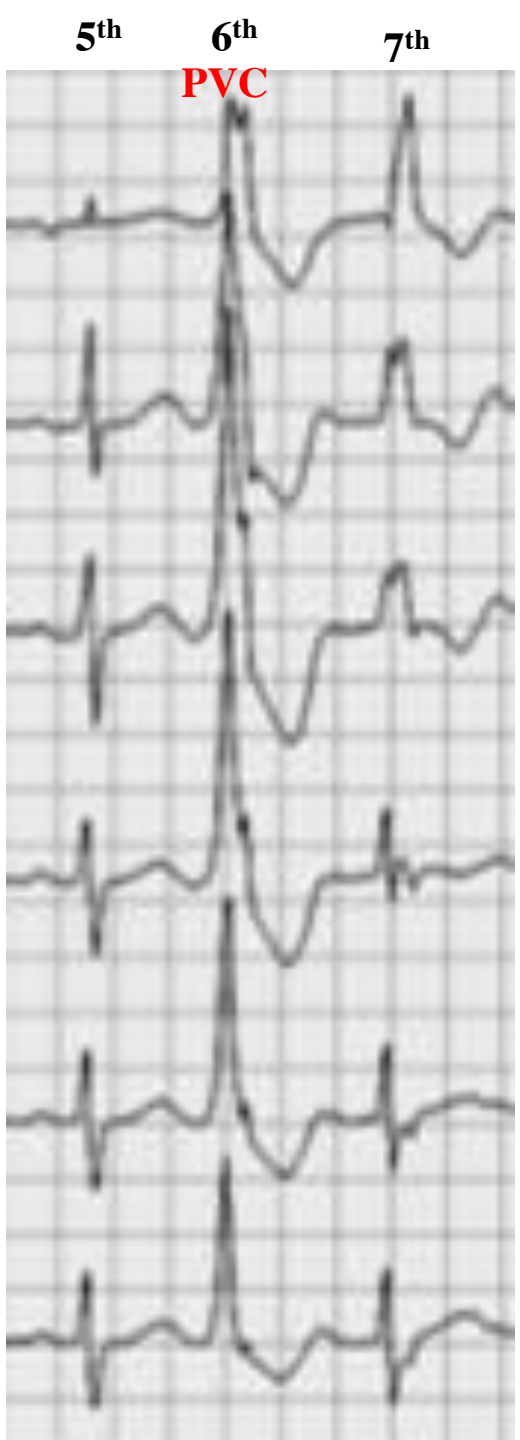
IV - Rightward anterior final appendage

ECG performed in 2016



The first five beats have LAFB associated with minimum degree of RBBB. The sixth beat is a premature ventricular contraction with focus shows LPFB + CRBBB. Seventh beat on register LAHB + CRBBB. Since the seventh beat forward LAFB + CRBBB pattern.





The 6th beat is an interpolated PVC that occurs between two consecutive sinus-conducted beats (5th and 7th beats). This nomenclature (***"interpolated"***) is used because they occur *sandwiched* in between two normal sinus beats *without* the *compensatory* pause that typically follows a PVC. Additionally, the 7th beat has a prolonged PR interval typical of interpolated PVCs. Such PR interval prolongation is the result of **concealed conduction.** Concealed conduction commonly occurs when a retrogradely conducted interpolated PVC enters the atrioventricular (AV) node; thus, the next sinus beat is not conducted to the ventricle or conducted with a prolonged PR interval because of increased refractoriness of AV conduction system (**Langendorf 1956**). PVC occurs mostly when the bradycardic sinus rate and the PVC is early. The PR interval of the following beat after the PVC is prolonged because the canceled retrograde conduction of the ectopic beat, which renders the AV Junction partially refractory to the closely following sinus impulse. Disturbances of AV conduction caused by an interpolated PVC affect the conduction not only of the first but also fo the second postextasystolic complex as a result of changing the RP-PR relation. This accounts for a postponed compensatory pause (**Langendorf 1956**). But this is a misnomer because, by definition, interpolated PVCs do not have compensatory pauses. Thus, it follows that what does not exist cannot be postponed. In reality, the basic manifest feature is a prolongation of the first RR interval that follows the interpolated beat. However, in view of its use for more than half a century, it is probably best to continue using this terminology, but only as long as its underlying mechanism and fundamental manifestations are properly understood (**Castellanos 2006**).

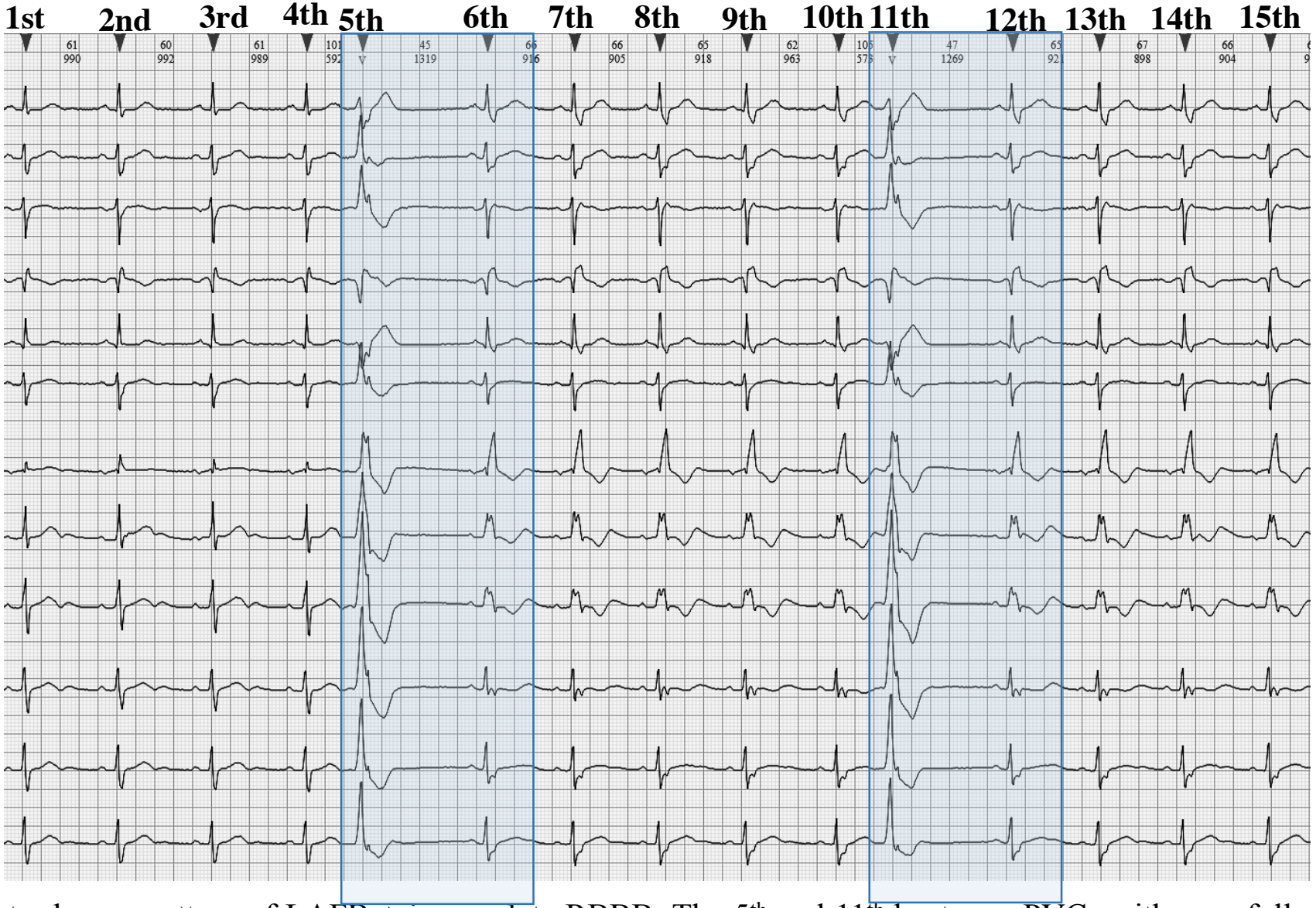
The focus of the PVC is located in the in the anterosuperior wall (RBBB+LAFB) (**Rosenbaum 1968**). Most PVCs are associated with *retrograde* conduction of the impulse back toward the AV node. If this retrograde conduction extends far enough to reach the atria, a *negative* P wave may be seen in lead II *after* the PVC. Even when retrograde conduction from a PVC does not extend all the way back to the atria — retrograde conduction usually lasts long enough to *prevent* forward conduction of the next sinus P wave. (**Chung 1972**).

An interpolated PVC may produce either delayed AV nodal conduction or complete block of the next sinus impulse or depression of AV nodal conduction with a prolonged AH interval (**Bissett 1977**) or pseudo-AV dissociation in the presence of dual atrioventricular nodal pathway(**Luzza 1994**). This accounts for the ***Compensatory pause"*** that is usually seen following a PVC (*as occurs for the PVCs with full compensatory pause*). If the timing is just right — a PVC may occur at moment when *enough* recovery of the conduction system has occurred to *allow* forward conduction of this next sinus beat. This is what happens with interpolated PVCs. In cases of bigeminy repetitive interpolated PVCs, these are occasioned by strongly modulated ventricular pacemaker accelerated by an intervening normal QRS (**Takayanagi 2013**).

The presence of ventriculoatrial block at a ventricular pacing cycle length of 600 ms correlated with the presence of interpolation. Patients with interpolation had a longer mean ventriculoatrial block cycle length than patients without interpolated PVCs (520 ± 110 ms vs. 394 ± 92 ms; P = .01).

The presence of interpolated PVCs is predictive of the presence of PVC cardiomyopathy. Interpolation may play an important role in the generation of PVC-induced cardiomyopathy (**Olgun 2011**).

ECG performed in 2016

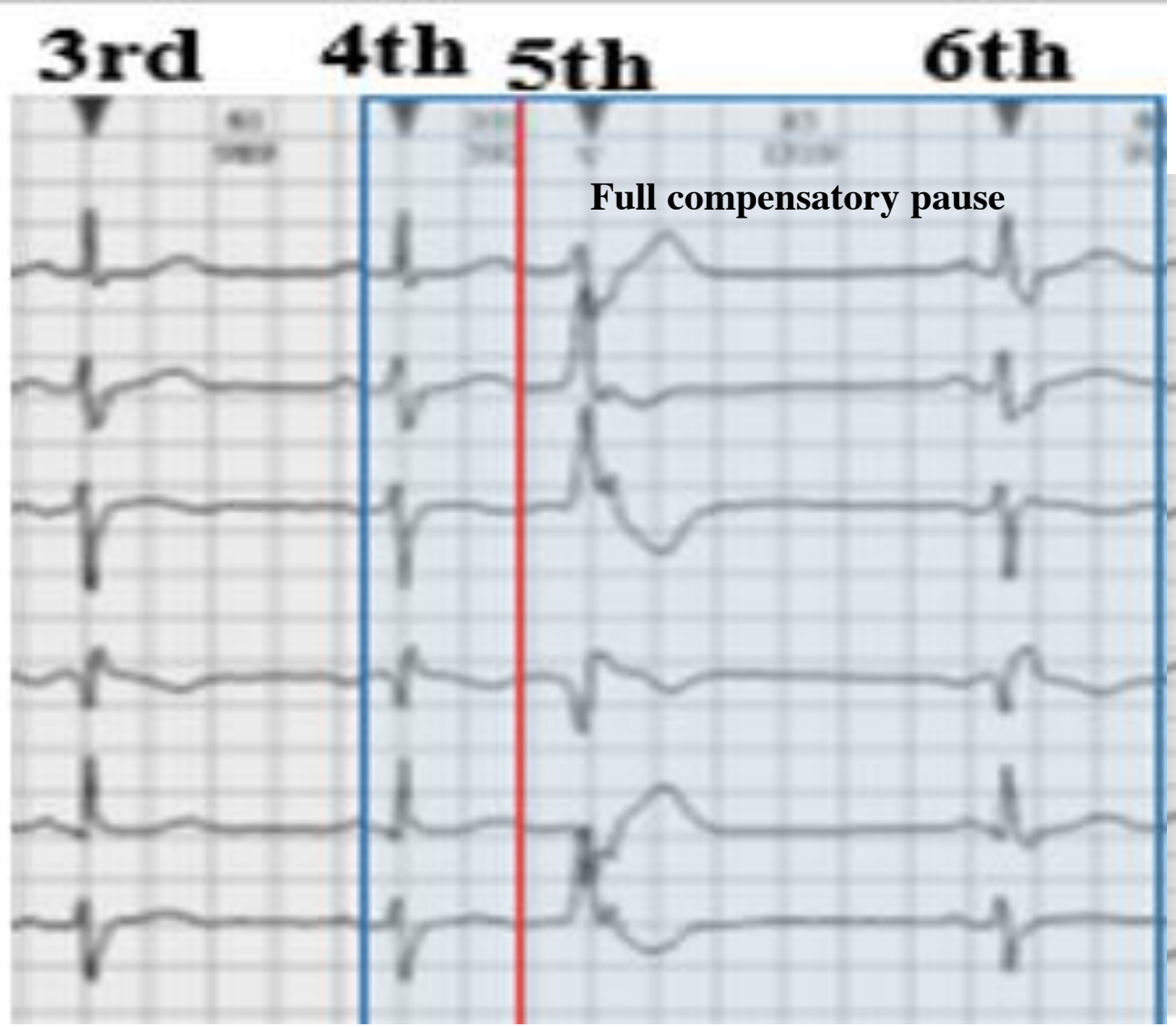


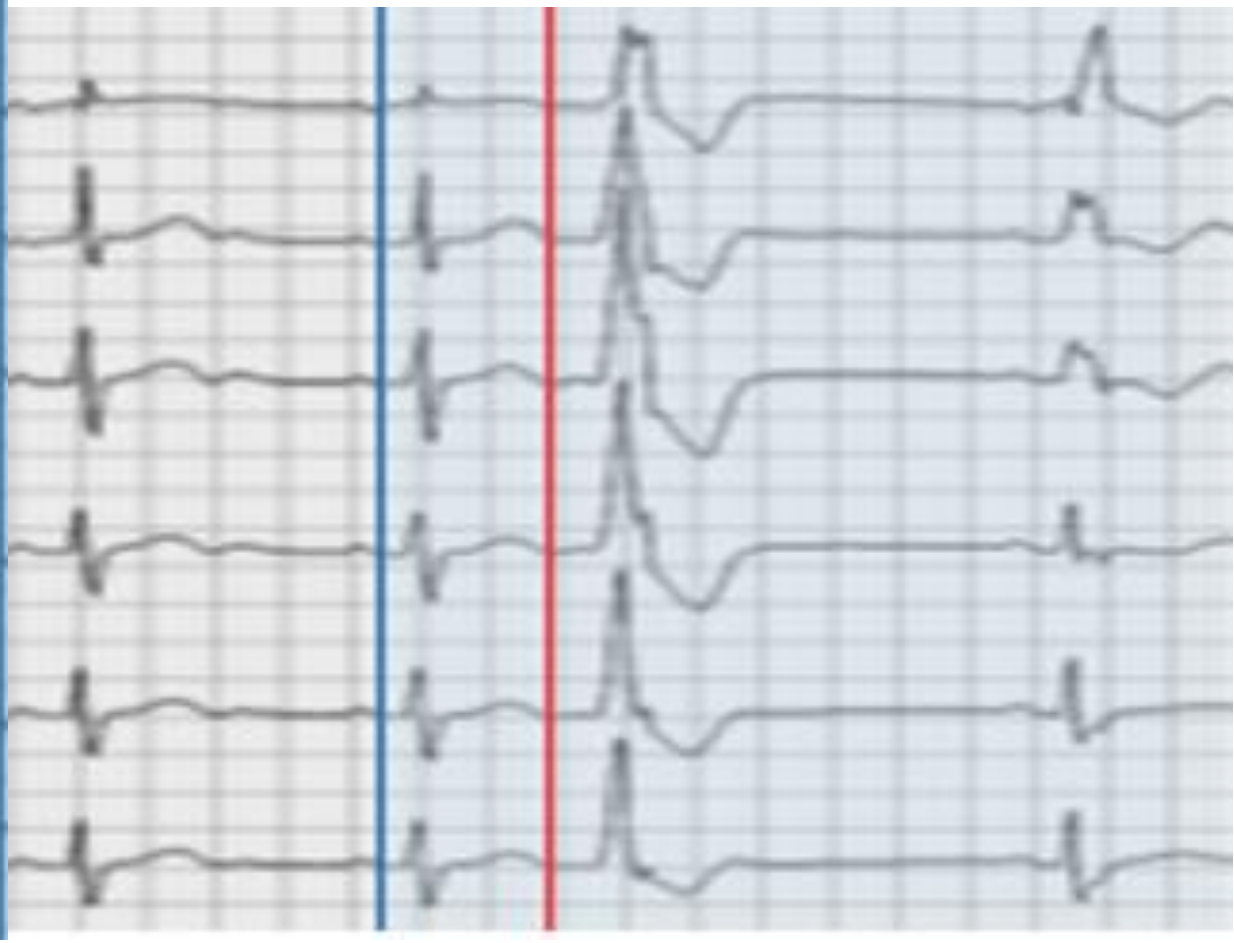
The 11th beat is a PVC because:

1. **Wide QRS complex:** (≥ 120 ms) with abnormal morphology
2. **Premature:** occur earlier than would be expected for te next sinus beat;
3. **Has discordant ST segment and T wave** changes
4. **Full compensatory pause**
5. **Retrograde capture of the atria** may or may not occur

Additionally, Arising from a same ectopic focus; that interpolated PVC because has the same pattern.

The first four beats show a pattern of LAFB + incomplete RBBB. The 5th and 11th beats are PVCs with near full compensatory pause (light blue rectangles). The focus of PVCs is located in the anterosuperior wall of the LV (RBBB morphology + LAFB) (**Rosenbaum 1968**). From the 6th to the 10th beats and from de 12th to the end, the pattern is LAFB + CRBBB. Additionally, Arising from a same ectopic focus; that interpolated PVC because has the same pattern that interpolated PVCs.





One of the characteristic features of PVCs is the full compensatory pause which follows. A full compensatory pause is said to exist when the R-R interval containing the VPC is two times the R-R interval of the basal rhythm,

In 1977, the researchers of Argentinean school of the great master Mauricio B. Rosenbaum and his favorite pupil, Marcelo Victor Elizari, analyzed thoroughly the diagnosis and management of active ventricular rhythms, especially premature PVCs. This legendary group of investigators divided monomorphic PVCs into the following types:

A) Narrow PVCs: QRS duration <120 ms. These PVCs could originate in the His bundle, branches, or the main fascicles or divisions of the His system. The authors differentiate seven patterns within this group:

1. **PVCs originating at the penetrating portion of the His bundle: QRS with pattern identical to the base complex (normal).**
2. **PVCs that originate in the right bundle: QRS with ILBBB pattern.**
3. **PVCs that originate in the left branch truncus: CRBBB pattern + minimal degree of LAFB.**
4. **PVCs that originate in the contact area between the right branch and the left anterior fascicle: QRS with IRBBB pattern.**
5. **PVCs that originate in the anterosuperior fascicle: pure LPFB pattern.**
6. **PVCs that originate in the left posterior fascicle: QRS complex with ILAFB + IRBBB.**
7. **PVCs that originate in the left anterior fascicle: QRS with ILPFB and IRBBB pattern**.

Clinical notes: all narrow PVCs are characterized by a variable coupling, that could be confused with parasystole. This coupling could reach 100 ms. The constant pattern of beats rules out aberrancy. Such variable coupling suggests that the mechanism is not reentry, but variations in Purkinje cells automatism by a variation in phase 4 slope (variable diastolic depolarization of rapid fibers). The narrow PVCs are observed in healthy young individuals, without heart disease, and they are nearly always asymptomatic. They should not be treated. There was scant therapeutic response in those who did receive medications.

B) Broad PVCs: when QRS ≥ 120 ms.

1. **PVCs from the base of the ventricles or Wolffian:** They are characterized by displaying positive QRS complexes in the precordial leads from V1 through V6, thus making them similar to Wolffian beats. The initial part of the QRS complex is broad, resembling a δwave. This initial broadening indicates its basal origin, where there are few Purkinje cells and conduction is slower. SAQRS could be either superior or inferior, depending on whether the source is on the anterior or posterior wall. They appear in healthy individuals. They should not be treated.
2. **PVCs from the tip of the ventricles or PVCs of the tip:** They have a CLBBB pattern.
3. **PVCs that originate in the base of the anterior papillary muscle of the right ventricle:** They appear in healthy individuals. They should not be treated!!!! All of those that originate in the RV are considered to appear to healthy individuals and display a CLBBB pattern, with inferior axis between +60 and +120 degrees, except for the rare ARVc/D. In these PVCs there are certain atypical features worthy of note: initial forces from 10 to 20 ms heading to the front in the horizontal plane and of slow inscription; VCG with clockwise rotation in the HP,

unlike the typical counterclockwise rotation of typical CLBBB; and frequent variable coupling. In 50% of the cases, there is no underlying structural heart disease. Probably the papillary muscle stretching by the tendinous chords during the mechanical activity of the heart, participates in the genesis of these PVCs. The rest of the PVCs that originate in the right ventricle, except the Wolffian ones, have a CLBBB pattern.

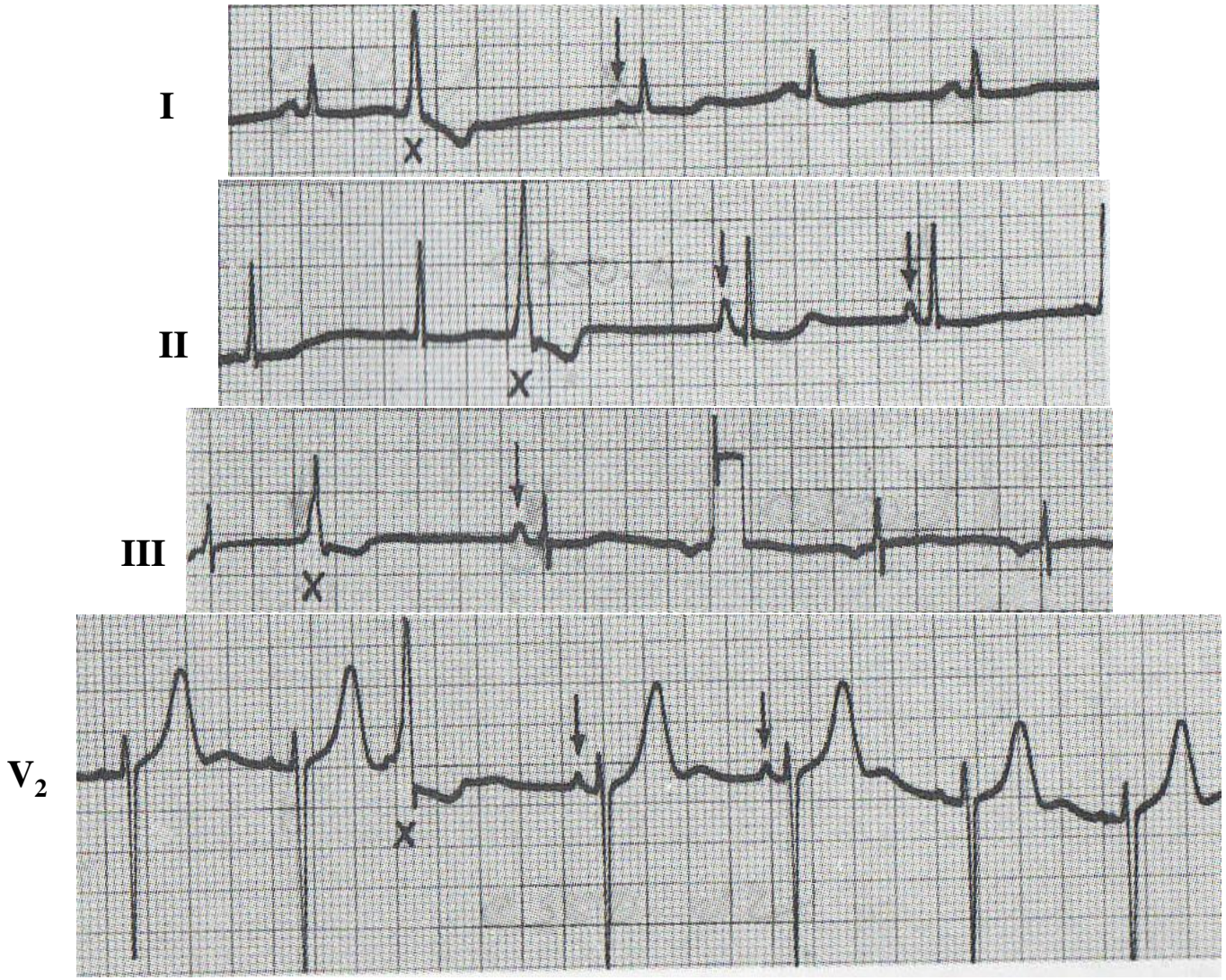
Two revolutionary Electrocardiographers of the Southern Hemisphere

Mauricio B. Rosenbaum

Marcelo Víctor Elizari

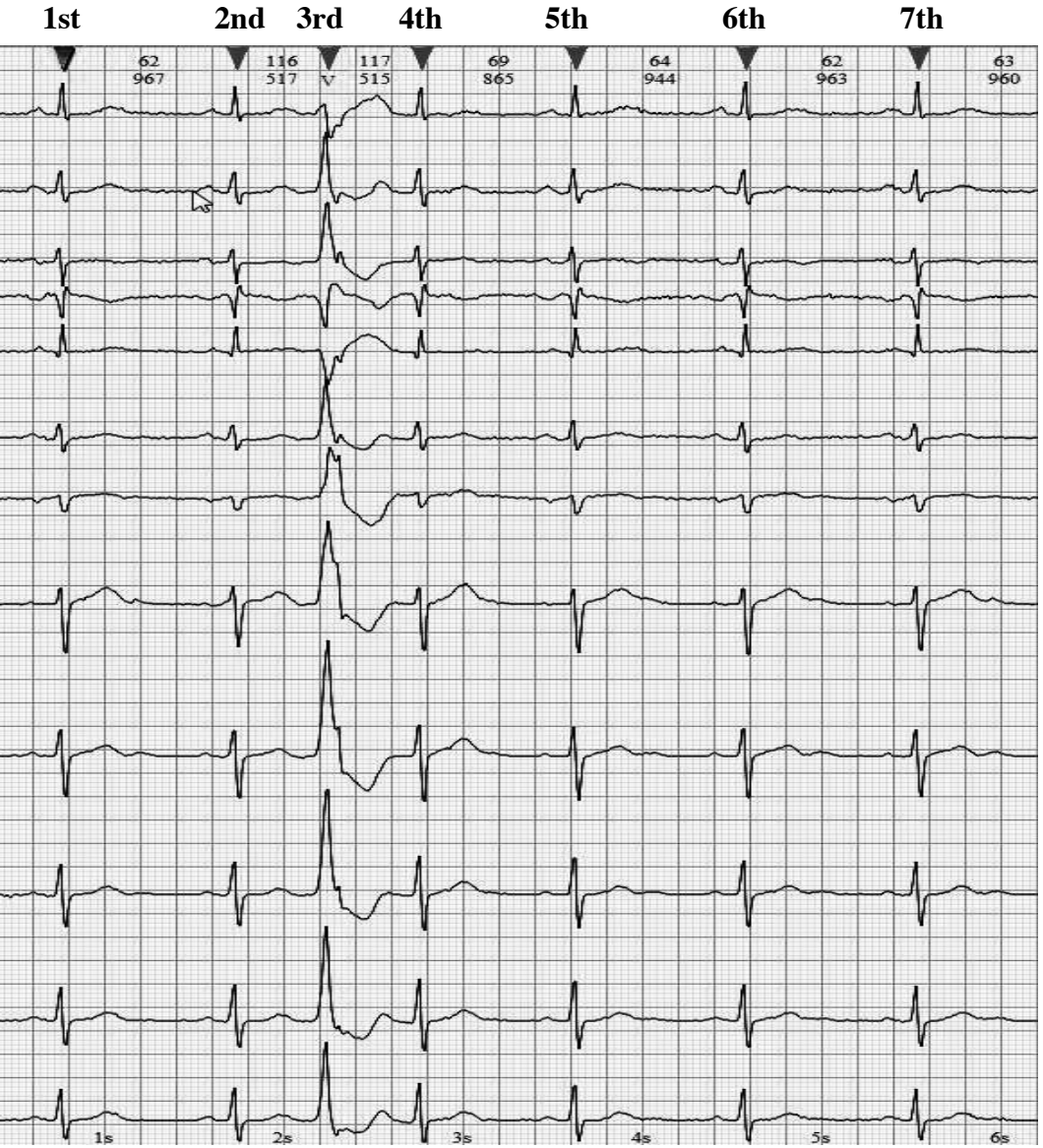
Electrocardiographic characteristics of premature ventricular contraction

1. QRS duration: wide QRS complex (≥ 120 ms) with abnormal morphology because of the abnormal propagation of the ectopic impulse in the ventricles due to the asynchronous onset of the excitation in the two ventricles.
2. Premature: occur earlier than would be expected for the next sinus beat;
3. Compensatory pause: a full compensatory pause almost always follows this arrhythmia when the basic rhythm is sinus.
4. Constant coupling interval: the coupling interval of the unifocal PVCs is usually constant because the impulse formation in the ventricle is dependent upon the preceding beat of the basic rhythm. Different coupling intervals are indicatives of multifocal origin or parasystole.
5. Retrograde capture of the atria may or may not occur
6. Postectopic pause: one of the characteristic features of PVCs is the full compensatory pause is said to exist when the R-R interval is two times the R-R interval of the basic rhythm. A full compensatory pause is observed when the PVC meets with the sinus impulse at the SA junction (sinus atrial interference), in the atria (atrial interference), at the AV junction (AV interference), and in the ventricles (ventricular interference).
7. Discordant ST segment and T wave changes: occasionally the T wave of the sinus beat immediately following a PVC may show alteration of its contour, amplitude, and/or direction. This phenomenon is termed “postectopic T wave changes”. The postectopic T wave changes are much more common following an interpolated PVC than PVC with full compensatory pause. The recognition of postectopic T wave changes is important clinically because it almost always indicates organic heart disease.
8. Post ectopic aberrant ventricular and aberrant atrial conduction (Chung’s phenomenon): the QRS complex of the sinus beat following an interpolated PVC occasionally shows a slightly or markedly deformed configuration, considered to be due to the fact that ventricular activation by the sinus impulse immediately following the interpolated PVC is carried out during a partial refractory period. This form of aberrant ventricular conduction commonly is associated with postectopic T wave changes. Extremely rarely , the P wave of the sinus beat following a PVC may have a deformed configuration. This is termed “aberrant atrial conduction” (Chung’s phenomenon). This is analogous of ventricular conduction.

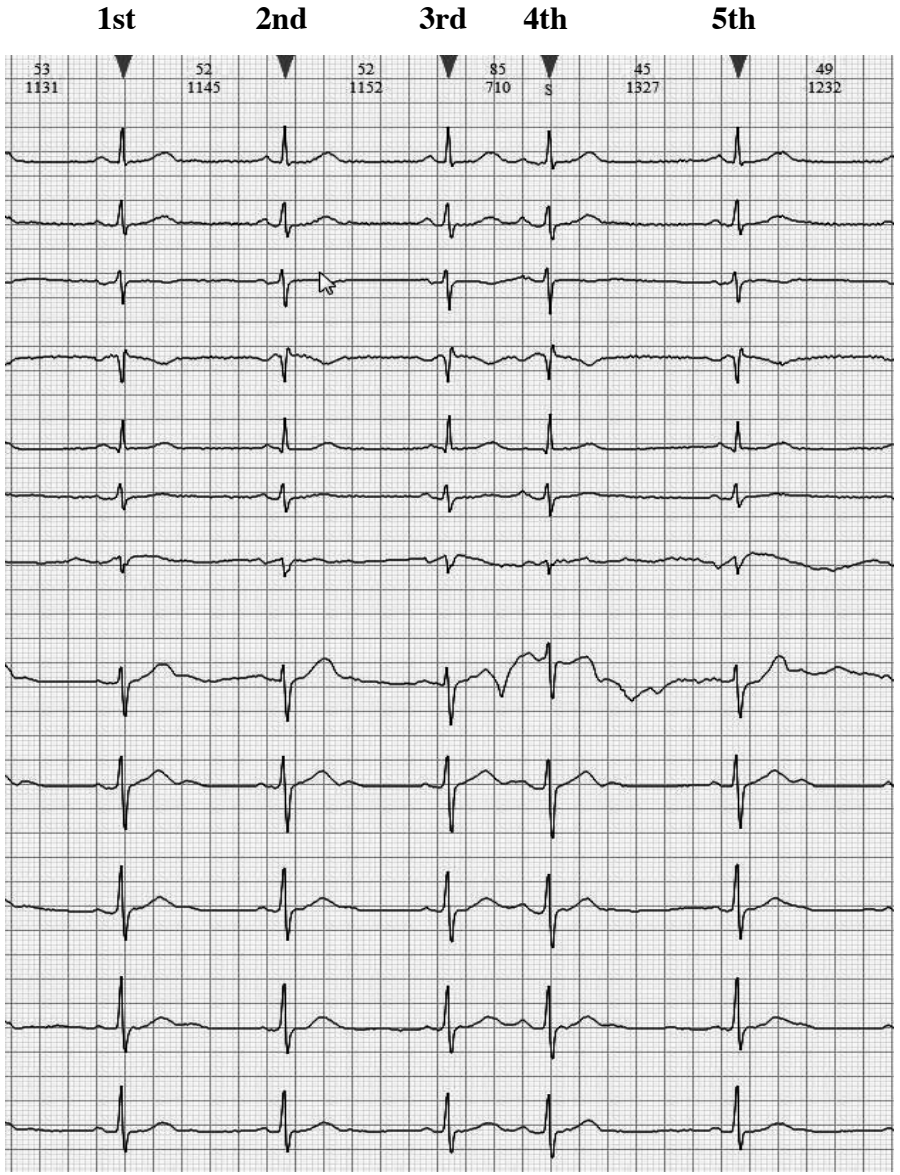


Sinus rhythm with left axis deviation of P wave (P axis -15°) and PVCs (X) followed by aberrant atrial conduction. Note that the configuration of the P wave in the sinus beats (indicated by arrows) following the PVC (X) is bizarre. This finding is called aberrant atrial conduction (Chung's phenomenon) (**Chung 1977**).

ECG December 2015



The 1st, 2nd , 4th 5th 6th and 7th beats show possible minimal degree of LAFB or without conduction disturbance. The 3rd beat is an interpolated PVC with LPFB+CRBBB pattern.



The 1st, 2nd, 3th and 5th beats have normal interventricular conduction. The 4th beat is a premature atrial beat.

Clinical significance of ventricular premature contractions

1. When the PVCs are provoked by mild exercise (with less than 70% of maximum heart rate), the finding often indicates the presence of organic heart disease mainly coronary artery disease. In the other hand, PVCs often disappear with exercise in healthy subjects.
2. PVC with QRS duration ≥ 180 ms suggests myocardial abnormality.
3. Multiform or multifocal PVCs are always indicative of abnormality.
4. PVC with variable coupling and variable interectopic intervals are more apt to be associated with cardiac disease.
5. PVCs with LBBB and vertical or rightward axis occur most frequently in normal person.
6. PVCs of bizarre configuration with multiple notching and slurring or both are considered always associated with heart disease.
7. Bidirectional PVCs are usually are indicative of digitalis intoxication.
8. PVC with bigeminy are often, but not Always, a sign of digitalis toxicity.
9. PVC occurring during the vulnerable phase (at or near the peak of T wave) of the preceding beat may result in VT/VF and sudden death.
10. Postectopic T wave changes are usually indicative of organic heart disease.

Conclusion: Transient alternating infrahisian system conduction defects. The term bilateral bundle-branch block, bifascicular block, is not recommended (**Surawicz 2009**) because of the great variation in anatomy and pathology producing such patterns. The international committee (USA and European) recommends that each conduction defect be described separately in terms of the structure or structures involved instead of as bifascicular, trifascicular, or multifascicular block. Because a great majority of patients with chronic complete heart block have bilateral bundle-branch lesions, it becomes important to recognize earlier degrees of bilateral bundle-branch block (BBB). The H-V interval in the His bundle electrogram during unilateral bundle-branch block reflects the conduction primarily through the contralateral bundle branch, and thus the His bundle electrogram in BBB provides information regarding the functional status of the contralateral bundle branch in addition to helping in the localization of defects elsewhere in the conduction system. Lichstein et al (**Lichstein 1978**) presented a similar case which had an ECG pattern of complete RBBB with alternating periods of LAFB and LPFB. During one of the periods of alternating fascicular block, an His bundle electrogram was recorded and the His Purkinje (H-V interval) conduction time was within normal limits. In a second episode of alternating fascicular block, periods of Mobitz type II second-degree A-V block were noted. It is postulated that this case provides clinical evidence that incomplete block of a fascicle may occur in spite of an ECG pattern of complete fascicular block. It is thought that the periods of alternating fascicular block result from a changing relationship between conduction velocity and refractory period.

The intraventricular conduction defects started observed some 10 years after the introduction of the string galvanometer by Einthoven. As early as 1910, it was known that conduction blockade could occur along either branch of the intraventricular conducting pathway. It took some 20 years to identify properly the ECG manifestations of RBBB and LBBB. A further 30 years were needed to obtain a sound correlation between these functional disorders and the presence of anatomical lesions. The introduction of the concept of left hemiblocks by Argentinian Rosenbaum's School further improved our understanding of intraventricular conduction defects. The latter concept is based on the hypothesis of the anatomical and functional bifascicularity of the LBB, a hypothesis which cannot be accepted to day because the left bundle branch in most of cases is trifascicular. Later developments indicated that left fascicular block (LAFB, LPFB and LSFB) associated with RBBB represent manifestations of bilateral conduction disturbances (incomplete bilateral bundle branch block). Such an association may constitute a forerunner of complete atrioventricular block, or an indicator of the possibility of sudden death. Whether these complications occur frequently or unfrequently in the setting of incomplete bilateral bundle branch block remains an unsettled question (**Kulbertus 1978**). Developments of left fascicular blocks associated with RRBB represent manifestations of bilateral conduction disturbances (incomplete bilateral BBB). Definitive diagnosis of bilateral bundle-branch delay/block may be made when catheter-induced RBBB develops in patients with baseline LBBB. An ECG pattern of RBBB in lead V1 with absent S wave in leads I and aVL indicates concomitant LBB delay. Pure RBBB and bifascicular blocks are associated with S waves in leads I and aVL.

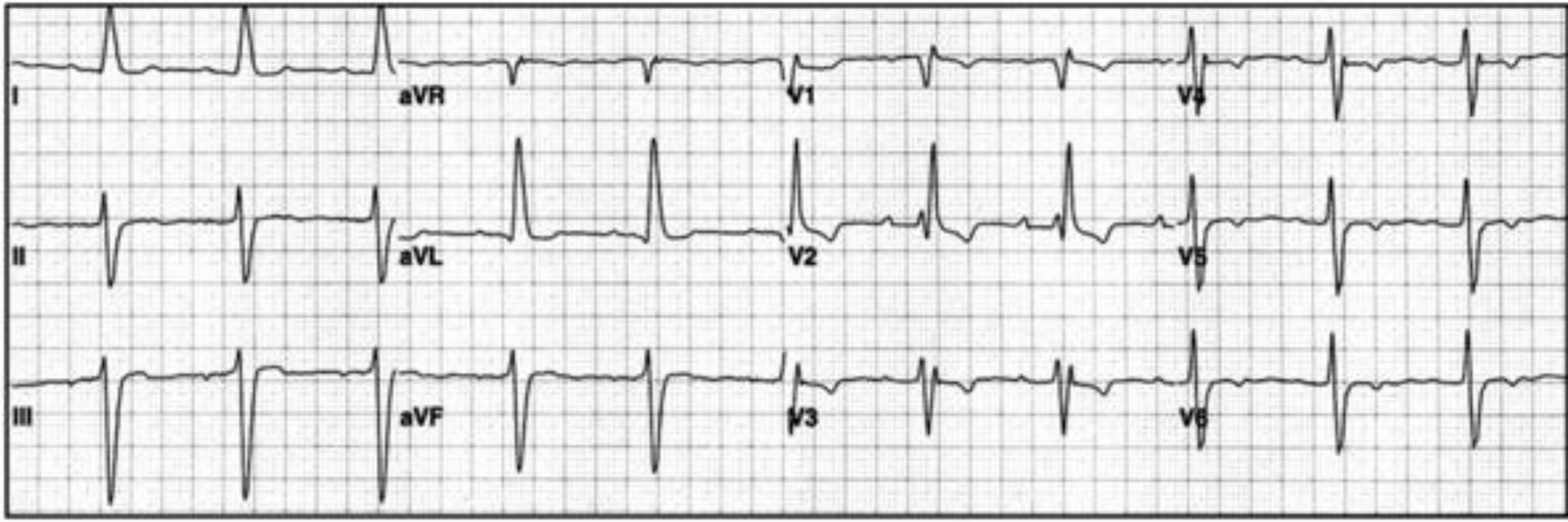
This pattern was named in the past masquerading bundle-branch block, it has been postulated to be secondary to either septal myocardial infarction or bilateral bundle-branch disease (**Richman 1954; Unger 1958**).
Since the seminal Rosembaum et al studies we recognize two masquerading ECG types (**Rosenbaum 1973**):

- The "standard type" ("standard masquerading right bundle-branch block") and
- The "precordial type" ("precordial masquerading right bundle-branch block")

In the "standard type" the LAFB obscured totally or partially the diagnosis of CRBBB only in the frontal plane leads by abolishing (or becoming very small) the final broad S wave in the left leads I and aVL and the precordial leads remain the typical CRBBB pattern.
In the standard type in the frontal plane, there are four main developmental phases that do not necessarily occur in the chronological sequence. The table below shows the four main developmental ECG patterns of masquerading standard type.

The four main developmental ECG patters of masquerading standard type

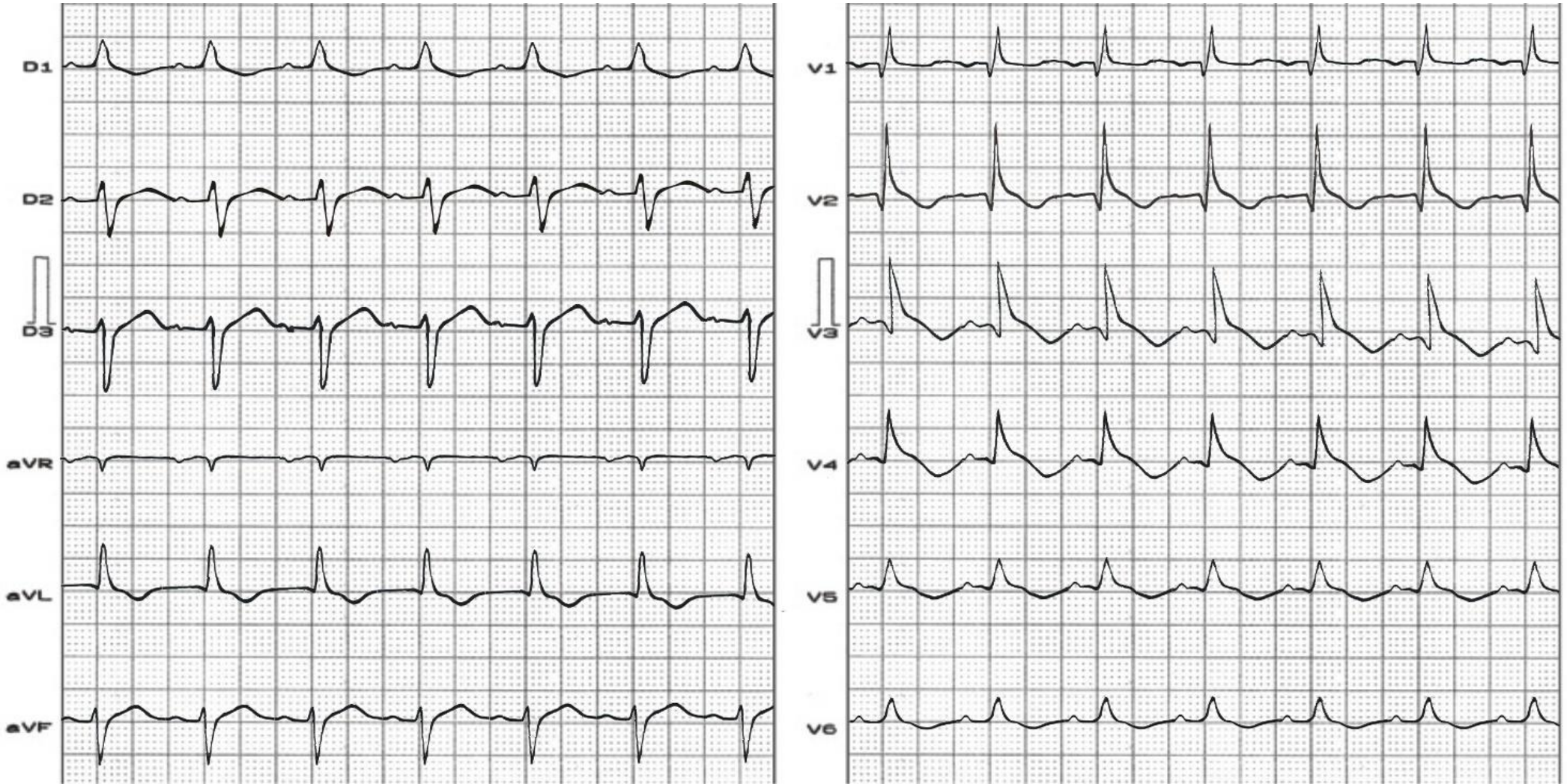
	aVL	I	II	III
Uncomplicated LAFB: QRS duration < 120ms	qR	qR	rS	Rs SIII>SII
LAFB with CRBBB: QRS duration ≥120ms	qRS	qRS	rS with notch on the ascending ramp of S	rS with notch on the ascending ramp of S
LAFB with CRBBB and diminution of the final QRS vectors. QRS duration ≥120ms	qR	qR	rS	rS
LAFB with CRBBB and diminution of the final and initial QRS vectors	R	R	QS	QS



Electrocardiographic pattern of bilateral bundle-branch block. Note the absence of S waves in leads I and aVL: formerly called "Standard masquerading Right Bundle Branch Block". Association RBBB + LAFB. The "standard type" or "standard masquerading right bundle-branch block", has been postulated to be secondary to either septal myocardial infarction or bilateral bundle-branch disease (**Richman 1954; Unger 1958**). In the "standard type" the LAFB obscured totally or partially the diagnosis of Complete RBBB only in the frontal plane leads by abolishing (or becoming very small) the final broad S wave in the left leads 1 and aVL and the precordial leads remain the typical CRBBB pattern.

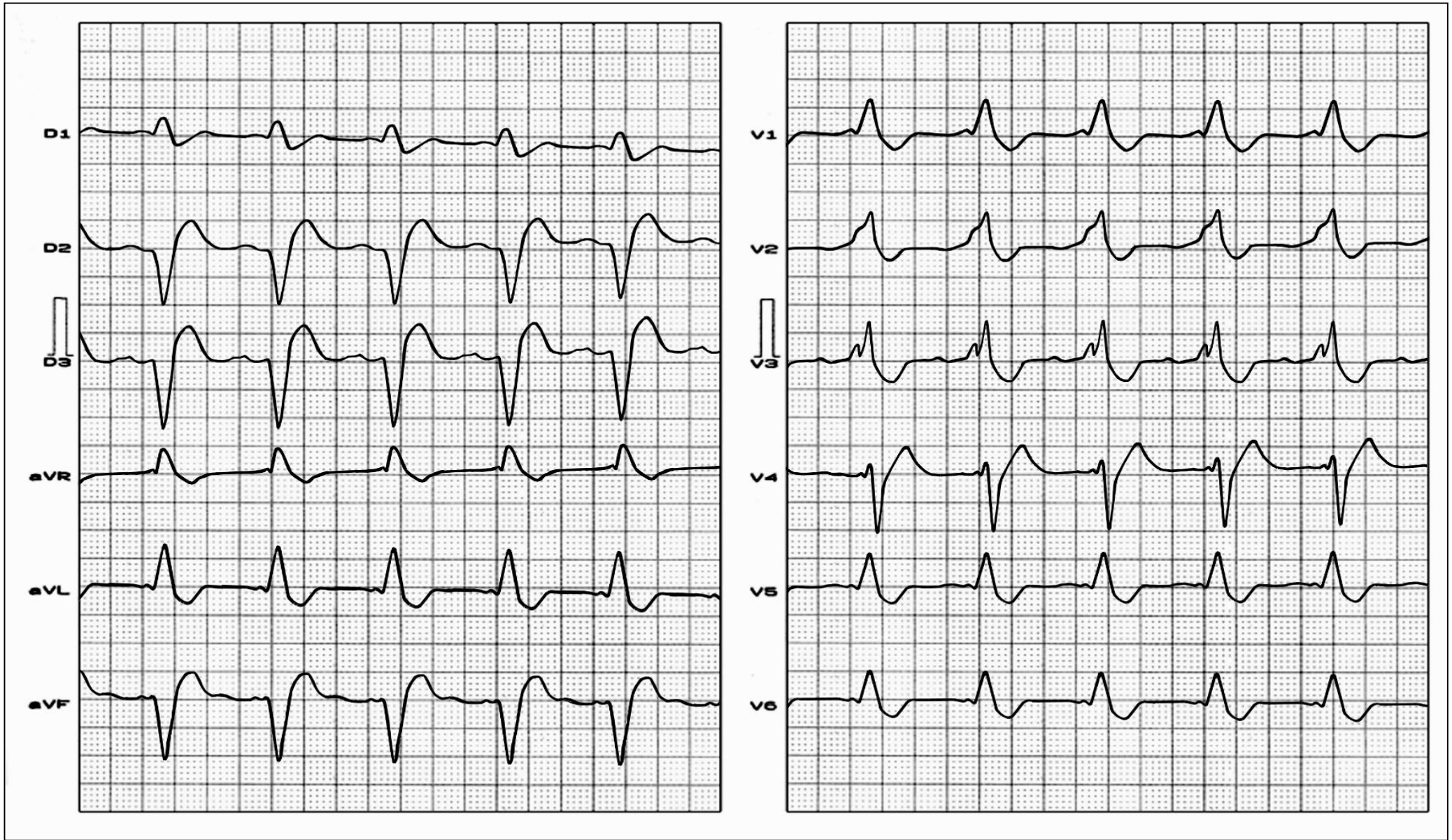
II. The precordial type (*"precordial masquerading right bundle-branch block")*

This type shows the pattern of CRBBB in the right precordial leads and complete left branch block pattern (CLBBB) in the left-side precordial leads. This result from CRBBB associated with severe left ventricular hypertrophy/enlargement (LVH/LVE), a localized block in the anterolateral wall of the left ventricle often due to myocardial infarction, and usually LAFB. Presumably, the intramural left ventricular block, together with the LVH or the LAFB, or both, produce predominant leftward forces which tend to cancel out the late rightward forces of the RBBB in the left precordial leads. Finally, masquerading bundle-branch block can be associated with severe and diffuse conduction system disease, and patients with this finding may require permanent pacemaker implantation, especially if they are symptomatic (**Kowey 1989**).



III. The Standard and Precordial masquerading bundle-branch block in association

In this case the limb leads show an apparent Left bundle-branch block pattern with extreme left axis deviation (LAFB) and the precordial leads exhibit the pattern of CRBBB in the right precordial leads and LBBB pattern in left precordial leads V5-V6. Additionally, an abnormal Q waves are frequently present on right precordial leads.



Cardiac Magnetic resonance imaging (CMRI) in chronic Chagasic myocarditis

Cardiac magnetic resonance imaging (CMRI) after gadolinium infusion seems also a promising technique to obtain a better regional characterization of myocardial tissue, and may be important in the non-invasive diagnosis of active myocarditis in patients with chronic Chagasic myocarditis such us the present case. CMRI seems to be a good diagnostic method to detect myocarditis in chronic Chagasic myocarditis. Its use in the diagnosis of chronic Chagas' heart disease myocarditis is promising and it has the potential to be a useful alternative to endomyocardial biopsy. An important advantage of CMRI is the ease of performance of serial studies as may be necessary in long-term follow up. Further observations on larger number of patients will be of interest to confirm these results and determine the sensitivity and specificity of CMRI in the detection of chronic Chagasic myocarditis.

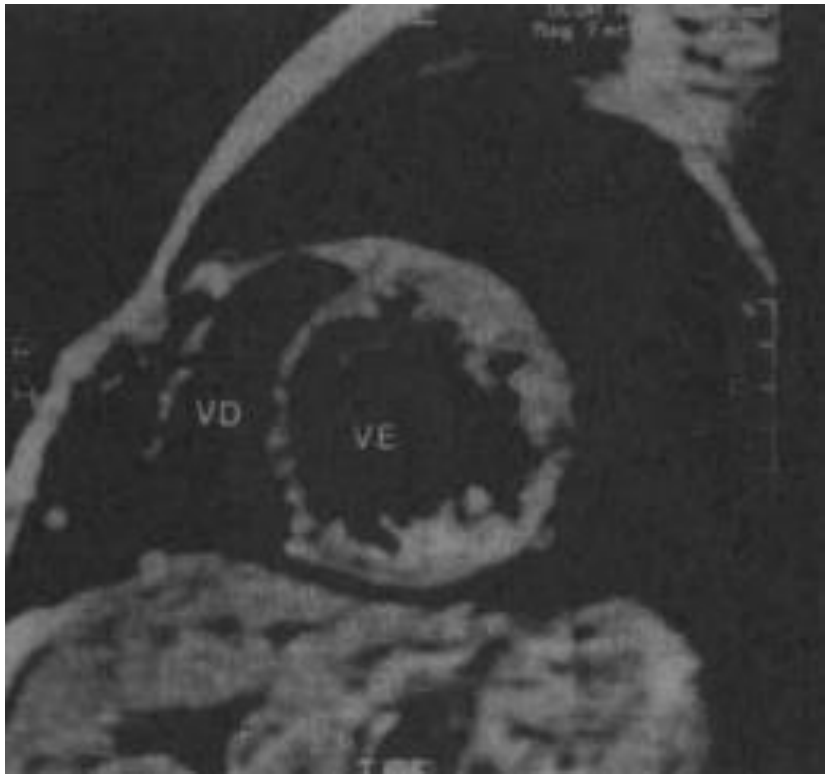
The gold standard for validation of the CMRI technique or for any other method used for the diagnosis and distribution of myocarditis should be the realization of multiple biopsies in many segments of the heart or a post-mortem pathological examination of the whole heart, which was clearly not possible. The association of endomyocardial biopsy, Gallium-67 myocardial uptake and CMRI in this study is an alternative to improve the analysis of the role of each method. Kalil filho (**Kalil Filho 1995**) used regional cardiac CMRI for the assessment of the inflammatory process in chronic Chagasic myocarditis. Cardiac signal intensity from the septal and free wall myocardial regions was compared with that from skeletal muscle before and after a bolus injection of gadolinium. Increased relative signal intensity was observed in the LV free wall and in the septum.

Researches of Heart Institute (InCor SP/Brazil) have seriously studied chronic Chagasic myocarditis pathophysiology. They clearly demonstrated differences between chronic Chagasic myocarditis and idiopathic dilated cardiomyopathy. These researches have shown that hearts with chronic Chagasic myocarditis exhibited severe diffuse fibrosis and arteriolar dilatation with organized thrombi (**Higuchi 1999**). Those findings led to the hypothesis that ischemic myocardial lesions could explain the severity of diffuse fibrosis and lesions like the aneurysm of LV apex and inferior-basal LV wall.

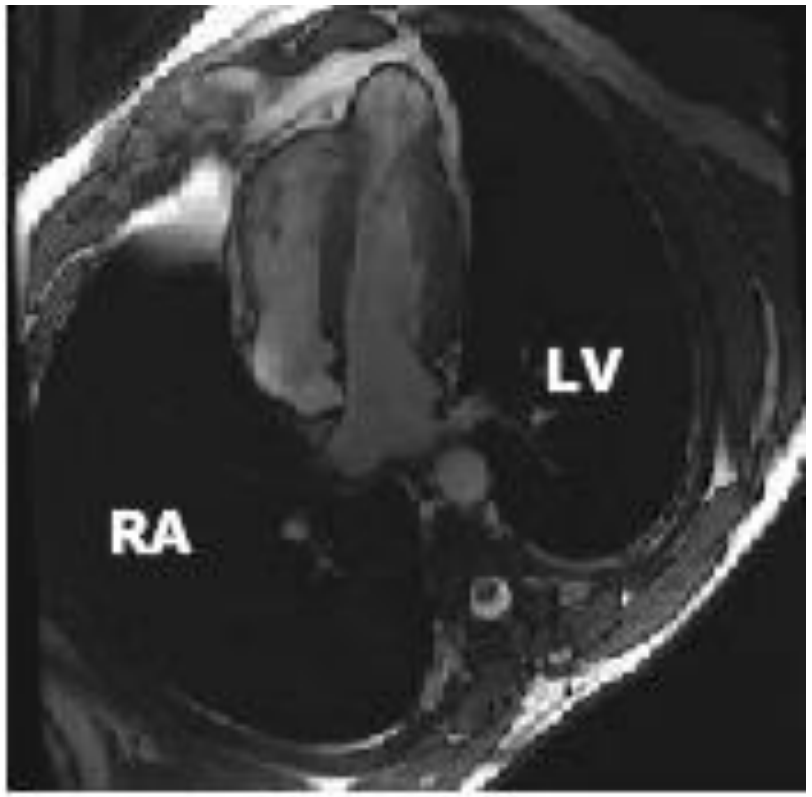
In chronic Chagasic myocarditis, the presence of two or more contiguous segments with transmural fibrosis was an independent predictor of VT (4.1-fold greater VT risk) (**Melo 2012**). The identification of two or more segments of transmural delayed enhancement by use of CMRI is associated with the occurrence of clinical VT in patients with chronic Chagas myocarditis. Thus, CMRI improved risk stratification. However, there are not enough data supporting the role of LGE for VT prediction in viral or autoimmune myocarditis.

Increase in T2-weighted (T2W) myocardial signal intensity and T1-weighted myocardial early gadolinium enhancement (MEGE) can be detected by CMRI in patients throughout all phases of chronic Chagasic myocarditis, including its subclinical presentation. Moreover, those findings were parallel to myocardial fibrosis (LGE) in extent and location and also correlated with the degree of chronic chagasic myocarditis clinical severity. These findings might have therapeutic and prognostic usefulness in the future (**Torreão 2015**).

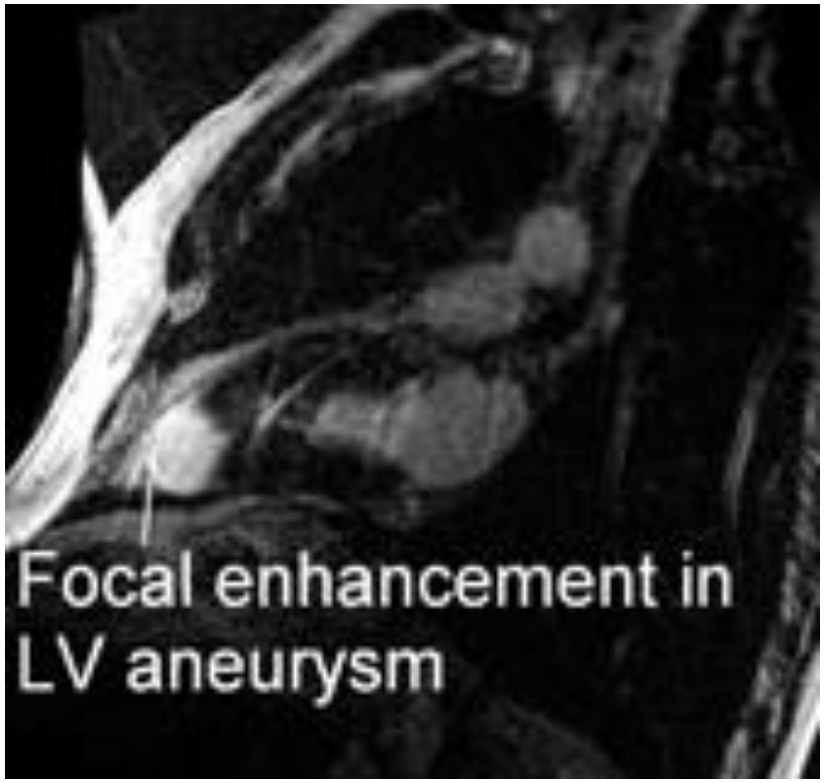
Cardiac Magnetic Resonance Imaging in chronic Chagasic myocarditis



A typical example of a short axis nuclear magnetic imaging view of the heart at the level of the papillary muscles after the infusion of Gadolinium of a patient with chronic Chagasic myocarditis and biopsy proved significant myocarditis. Note the greater signal intensity of the lateral and posterior walls of the LV.



Four-chamber CMRI reveals normal left ventricular size with marked thinning and focal aneurysm at the apex. The aneurysm measures 3.6 x 3.2 x 3.1 cm. Overall left ventricular systolic function was preserved with focal apical dyskinesis on cine images.



CMR delayed images revealed focal myocardial hyper-enhancement within the thinned wall of the aneurysm. The remainder of the myocardium demonstrated no abnormal delayed enhancement. The renal infarcts are thought to be due to emboli from thrombus in the LV aneurysm.

Important definitions/criteria: Right Bundle Branch Block

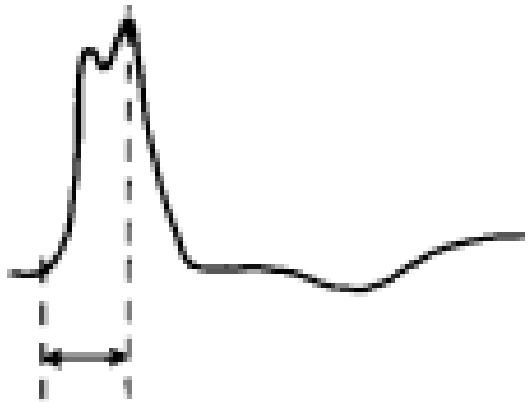
a. Supraventricular cardiac command
b. If the rhythm is sinus, PR ≥ 120 ms (0.12 s);
c. QRS duration ≥100 and <120 ms (IRBBB) or ≥120 ms (CRBBB). Incomplete RBBB (IRBBB): QRS duration between 100 and < 120 ms in adults, between 90 and 100ms in children between 4 and 16 years old, and between 86 and 90 ms in children less than 8 years old. Complete RBBB (CRBBB): advanced or of 3º degree: QRS duration ≥120 ms, greater than 100 ms in children from 4 to 16 years old, and greater than 90 ms in children less than 4 years old. It is considered complete RBBB when the QRS duration is ≥ 120 ms or ≥ 60 comets in vectorcardiography.
d. Terminal broad R wave of the QRS complex in lead V_1 or V_1 and V_2 and in aVR. Right precordial leads (V3R, V1 or V1 and V2) with rsr′, rSR' or rsR' pattern. The R′or r′ deflection is usually wider than the initial R wave. The final R' wave wide and sometimes notched: triphasic QRS complex called "M complex". In a few cases, a wide an often notched pure R wave pattern may be seen in lead V1 and/or V2. When a pure dominant R wave with or without a notch is present in V1, R-peak time ≥50ms in lead V1 is present.
e. Slurred wide final S wave in left leads: I, aVL, V_5, and V_6. S waves were not required in ECG leads I, aVL, and V6. S wave of greater duration than R wave or grater than 40 ms in leads I and V6 in adults.
f. A delay in the appearance of the ventricular activation time, "R-peak time or intrinsicoid deflection > 50 to 80 ms (**Lerecouvreux 2005**) may also be observed in the right precordial leads and normal in V5-V6.
g. Ventricular repolarization (ST/T) with opposite direction to the terminal deflection of the QRS complex: T wave polarity opposite to the polarity of the last deflection of QRS complex, ST segment and T wave: Opposite to the terminal deflection of the QRS complex.
h. Asymmetrical T wave: With an ascending slow slope with superior concavity and faster descending slope. The evidence presented by Moore and his colleagues that the IRBBB pattern may be due to a heritable focal hypertrophy of the RV, and not consequence of delayed conduction within the right bundle branch, should stimulate us to reappraise the validity of our electrocardiographic vocabulary. Continued anatomic and electrophysiologic research is vital to verify or disprove our current electrocardiographic concepts, so that the words accurately reflect the best known facts about electrical activity of the heart (**Massing 1972; Barker 1949**). IRBBB may be present in the absence of heart disease, particularly when the V1 lead is recorded higher than or to the right of normal position and r′ is less than 20 ms. In children, IRBBB may be diagnosed when the terminal rightward deflection is < 40ms but ≥20ms. QRS duration < 120ms associated with rS pattern in V1 with S presenting notch in ascending slope is called atypical IRBBB (**Schamroth 1985**).

Left Bundle Branch Block (LBBB)

a) **QRS duration:** ≥120 ms. Stricter criteria for complete LBBB (CLBBB): QRS duration ≥ 140 ms for men and ≥ 130 ms for women, along with mid-QRS notching or slurring in ≥ 2 contiguous leads. This new values are used for Cardiac Resynchronization Therapy (CRT) (**Strauss 2011**). Up to one-third of patients diagnosed with LBBB by conventional ECG criteria are misdiagnosed. 1/3 of patients diagnosed with LBBB by conventional ECG criteria may not have true CLBBB, but likely have a combination of left ventricular hypertrophy and left anterior fascicular block. Strict LBBB shows decreased left ventricular pumping efficiency compared with nonstrict LBBB (**Strauss 2011**). Stricter criteria for CLBBB include a QRS duration ≥ 140 ms for men and ≥ 130 ms for women, along with mid-QRS notching or slurring in ≥ 2 contiguous leads. Almost all patients who developed evidence of LBBB after transcatheter aortic valve replacement (TAVR) met the new strict criteria, indicating probable procedural injury to the left bundle branch. Preprocedural QRS duration did not predict the development of strict LBBB (**Sundh 2015**).

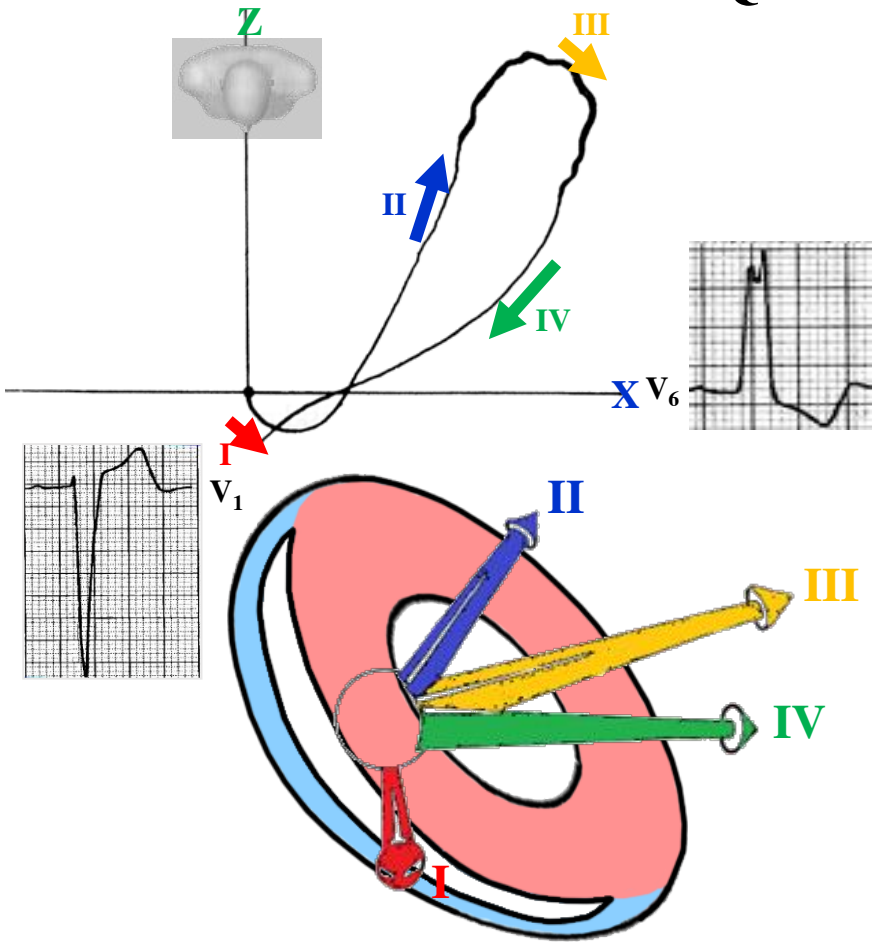
b. **QRS pattern**: rS or QS deflection in ECG leads V1 and V2; and monophasic, broad notched or slurred R wave, recorded slowly in the left leads: I, aVL, V5 and V6. Since the aVL lead is higher, it can rarely show qR pattern in absence of complicated LBBB. When the left septal division emerges before the blocked area, preserving septal vector I as normal, heading to the right and the front: qR in left leads (atypical CLBBB). Occasional Rs or RS pattern in V_5 and V_6. In this case, it may indicate: displaced transition of QRS complex to left; associated right ventricularhypertrophy or RVE; associated LAFB or association with myocardial infarction on LV free wall.

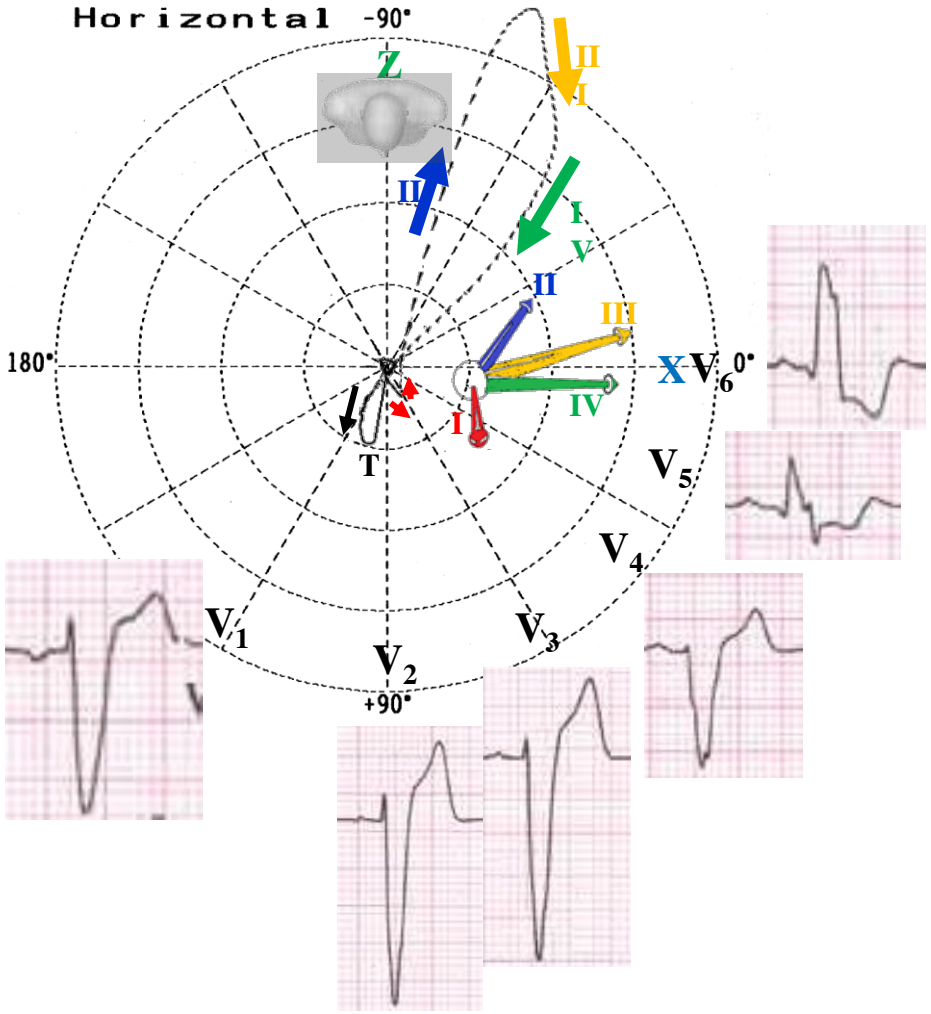
c. **Ventricular Activation Time, R-peak time** ≥ 50 ms in I and V5-V6, but normal in V1-V2 and V3, when small initial r waves can be discerned in the above leads.



The "R peak time" is the interval elapsed since the beginning of the QRS complex preferably measured in multiple simultaneous leads up to the summit of R or R‘ if the latter is present. If the R-wave has a notch the "R peak time" should be measured to the second peak according to the recommendations of the Minnesota code (**Pineas 1982**)

Outline that shows the four depolarization-activation vectors in CLBBB in the HP. There is an ECG/VCG correlation of the QRS loop and the leads V1 and V6

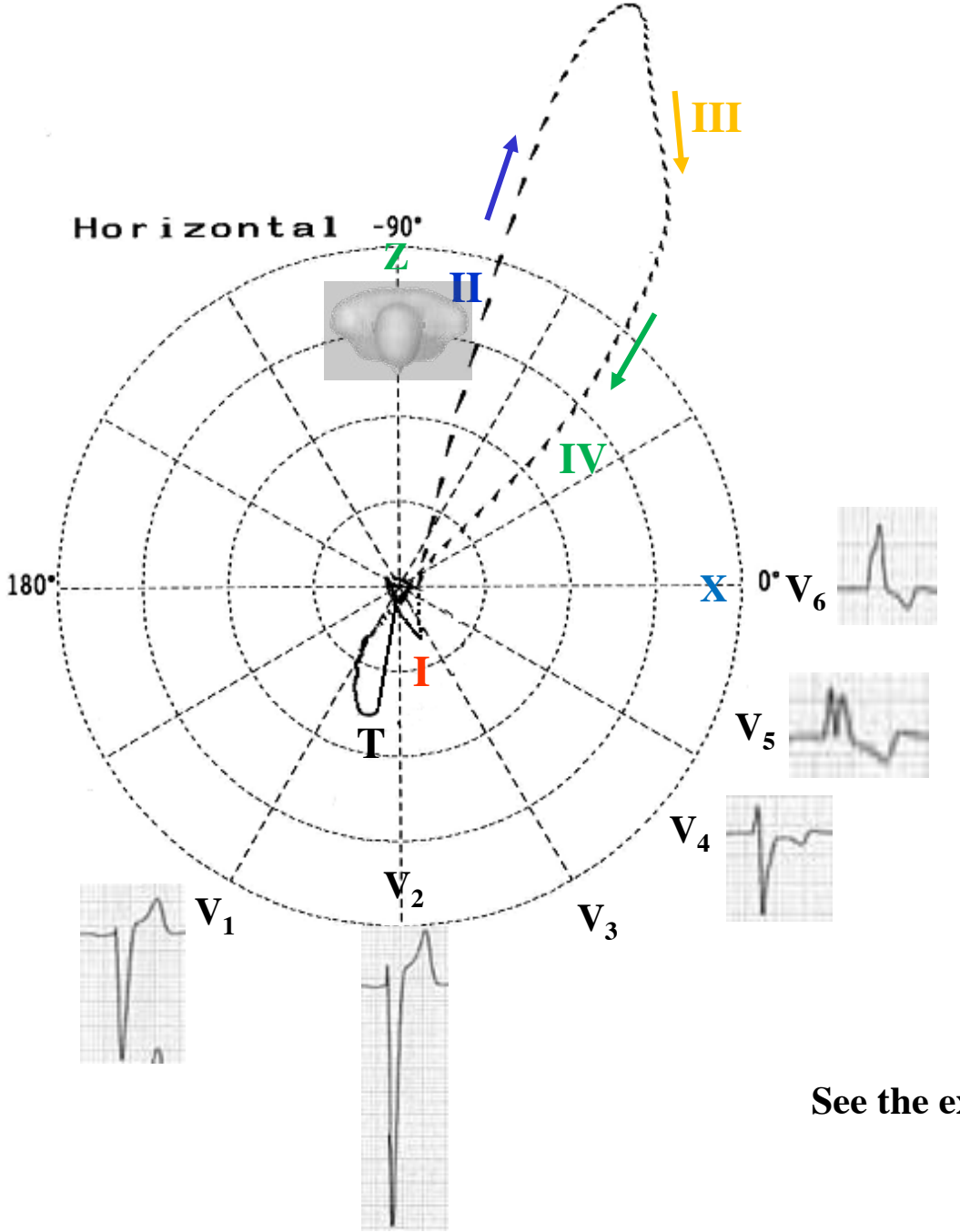


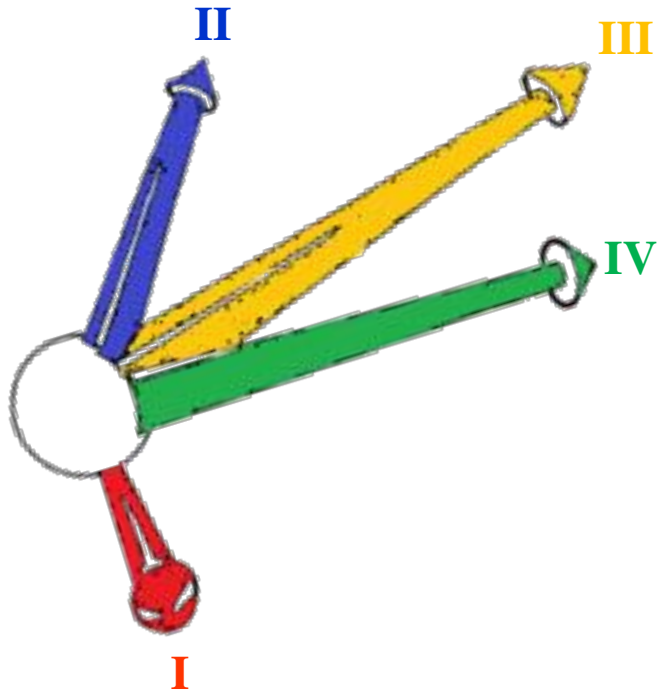


- ✓ The QRS loop duration is ≥ 120ms
- ✓ The QRS loop shape is elongated and narrow
- ✓ The main body of the QRS loop is inscribed posteriorly and to the left within -90 and -40°.
- ✓ Conduction delay noted in the mid and terminal portion
- ✓ The main body of QRS loop is inscribed clockwise (CW)
- ✓ The magnitude of the max QRS vector is increased above normal exceeding 2mV.
- ✓ ST segment and T wave vector are directed rightward and anteriorly (opposite to QRS loop)

d. **Abnormalities in the ST segment and T wave:** that occur as the direct result of changes in the sequence and/or duration of ventricular depolarization, manifested electrocardiographically as changes in QRS shape and/or duration. These abnormalities are referred to as secondary repolarization abnormalities. Recognition of secondary repolarization abnormalities is usually not difficult. In LBBB, the ST- segment and T-wave vectors are generally directed opposite to the mean QRS vector. Depressed ST segment and/or negative T wave in leads V1-V2 with negative QRS (negative concordance) are abnormal (**Sgarbossa 1996; Gunnarsson 2001**). Positive T waves in leads with upright QRS (V5-V6) may be normal (positive concordance). Depression upwardly convex of ST segment in left leads (I, aVL, V_5 and V_6) is called secondary repolarization abnormalities. The distinction between primary and secondary repolarization abnormalities is clinically relevant because primary abnormalities indicate changes in the repolarization characteristics of ventricular myocytes whereas secondary changes do not. The designation of the ST and T-wave abnormalities as primary or secondary is appropriate, and it is recommended that automated interpretative algorithms be programmed to identify them. The ST segment and T-wave vectors opposite to a greater deflection of QRS: positive from V_1 to V_3 and negative in left leads I, aVL, V_5 and V_6. These are Secondary Repolarization Abnormalities with wide QRS-ST-T angle and normal ventricular gradient. The classic ventricular gradient concept introduced by Wilson et al (**Wilson 1931**) in 1931 is of some theoretical interest concerning primary versus secondary repolarization abnormalities. Ventricular gradient in a single ECG lead is the net time integral of the ECG voltage from the beginning of the P wave to the end of the U wave. Its spatial counterpart is the ventricular gradient vector determined from the orthogonal XYZ leads. The practical utility of the ventricular gradient in differentiating primary from secondary repolarization abnormalities has not been demonstrated. When the direction of the QRS axis is normal, an abnormal direction of the T-wave axis is generally an indication of primary repolarization abnormalities (**Wilson 1931; Surawicz 1988**).

ECG/VCG correlation of CLBBB in the Horizontal Plane (HP)





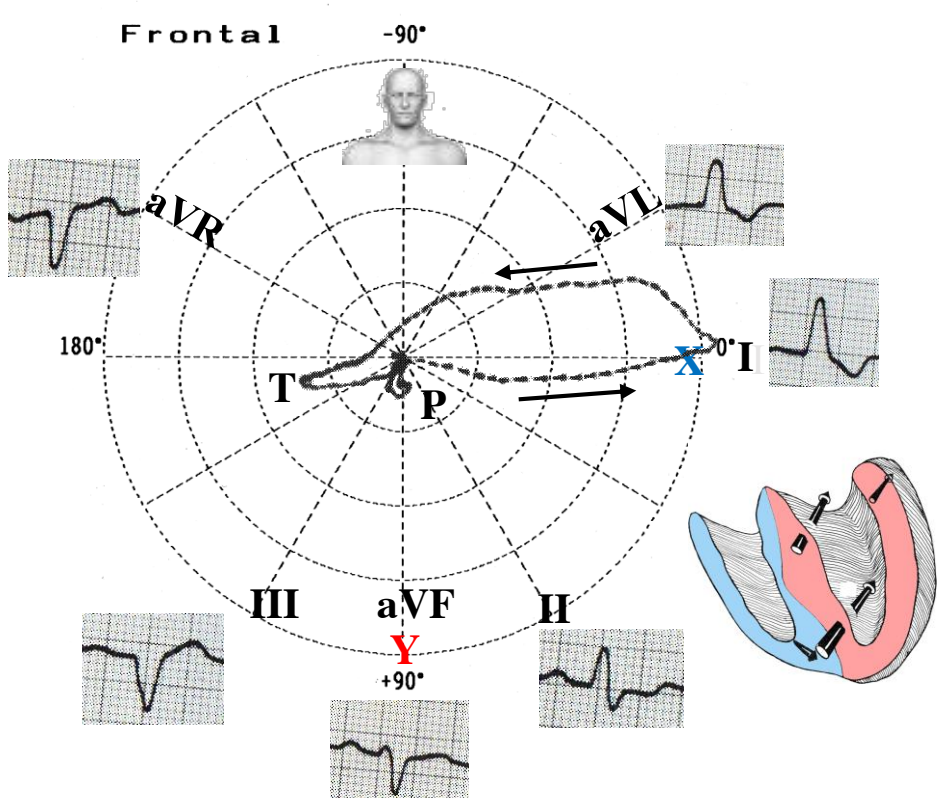
See the explanation in the next slide.

Vectocardiographic criteria of CLBBB not complicated in the HP

- Narrow, long QRS loop, and with morphology usually in 8.
- The QRS loop duration is ≥ 120ms.
- The QRS loop shape is elongated and narrow.
- The main body of the QRS loop is inscribed posteriorly and to the left within -90 and -40°.
- Maximal vector of QRS located in the left posterior quadrant (between –40º to -80º) and with increased magnitude (>2 mV).
- Main portions of QRS loop with clockwise rotation. CCW rotation may indicate parietal CLBBB or complicated with lateral infarction or severe left ventricular hypertrophy (LVH).
- Vector of initial 10 ms directed to the left and anteriorly (**I**)
- The efferent limb (**II**) located to right related afferent limb (**III** and **IV**).
- Conduction delay noted in the mid and terminal portion
- The main body of QRS loop is inscribed clockwise (CW)
- The magnitude of the max QRS vector is increased above normal exceeding 2mV.
- ST segment and T wave vector are directed rightward and anteriorly.
- T loop of counterclockwise recording. The clockwise rotation of T wave in this plane suggests CLBBB complicated with infarction or LVH.

Vectocardiographic criteria of CLBBB not complicated in the FP

QRS and T loop in the LBBB



- Vector of initial 10 ms directed to the left and inferior; rarely to the left and superior;
- QRS loop with counterclockwise rotation or in eight;
- QRS loop with characteristic middle final delay;
- Direction of maximal vector usually between +30 and –30º;
- Vectors of ST and T opposite to QRS (angle around 180º) and with counterclockwise rotation.

ECG diagnostic criteria of isolated LAFB (Willems 1985; Ioan 1988; Elizari 2007; Surawicz 2009)

Frontal plane

1) Extreme shift of SÂQRS in the left superior quadrant (beyond 30 up to -90°). Some authors accept between -45 and –90° (**Elizari 2012**); frontal plane axis between −45 and −90°, qR pattern in lead aVL, R-peak time in lead aVL ≥ 45 ms, and QRS duration <120 ms (**Surawicz 2009**).
2) rS in II, III and aVF. If SÂQRS was in -30°, II would be R = S;
3) r III > r II (it indicates CCW rotation in the FP). The voltage of the r waves is 3 to 5 mm in average;
4) SIII > SII: this criterion differentiates it from RECD of the right branch and SI-SII-SIII syndrome, where SII > SIII;
5) qR pattern in I and aVL;
6) Frequent notch of the descending limb of R wave in I and aVL (this sign would be present in 80% of the cases);
7) R-peak time in aVL ≥ 45 ms;
8) aVR always begins with q or Q wave: qR, QR or Qr. QS is rare;
9) Possible notch in R wave of aVR;
10) QRS duration < 120 ms.

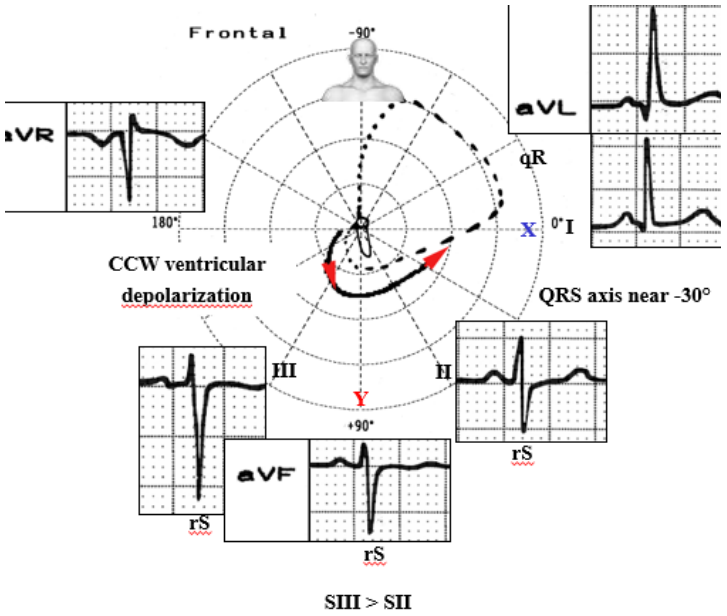
Horizontal plane (Elizari 2007)

1) This plane is very little affected when compared to the frontal plane;
2) Possible dislocation to the left of the transition area: normally it is in V3 and V4. In LAFB it may be in V5 and V6;
3) Voltage decrease of R wave and concomitant increase in S wave depth in V5 and V6, as a consequence of the superior dislocation of the forces;
4) Possible pattern of pseudo anterior infarction with appearance of q wave in the right precordial leads, as a consequence of the initial forces heading below and back. In case of doubt, recording one intercostal space below removes the q wave from pseudo infarction (**McHenry 1971**).

VCG criteria of LAFB (Longo 1981)

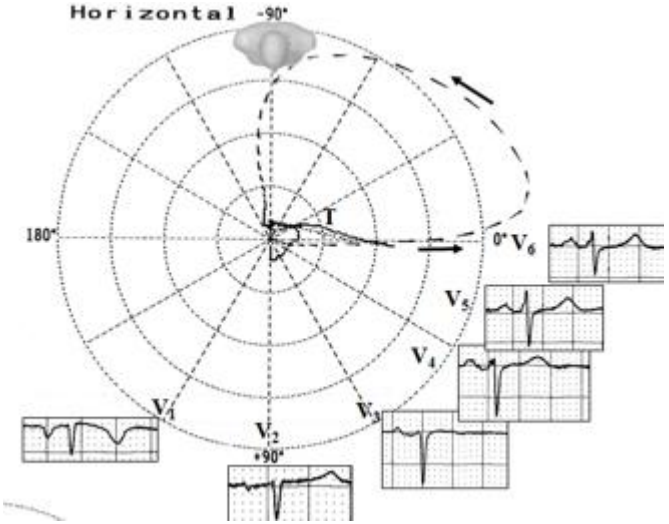
Frontal Plane (Ramalhão 1976):

1) QRS loop ≤ 100 ms. When intermittent, the increase does not exceed 20 ms;
2) Constant counterclockwise rotation of QRS loop when not associated to other diseases; in the presence of LVH or Acute MI, the rotation of the initial 20 ms may change;
3. Vector of initial 10 to 20 ms heading below and rightward;
4. Maximal vector of QRS heading above around -20º;
5. QRS loop located predominantly in the left superior quadrant;
6. ST/T loop always normal in non-complicated LAFB.



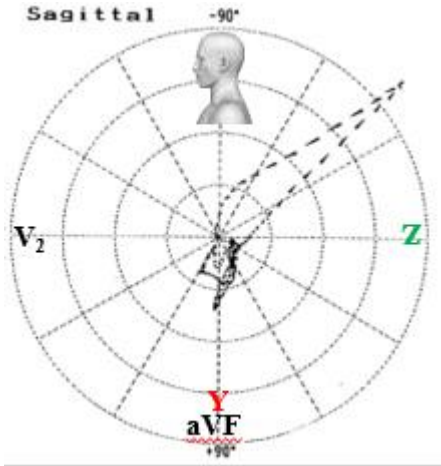
Horizontal Plane

1) QRS loop with counterclockwise rotation;
2) Vector of initial 10 to 20 ms heading to the right and the front;
3) QRS loop of location slightly posterior than normal;
4) Maximal middle vector of QRS near –40º.



Left Sagittal Plane

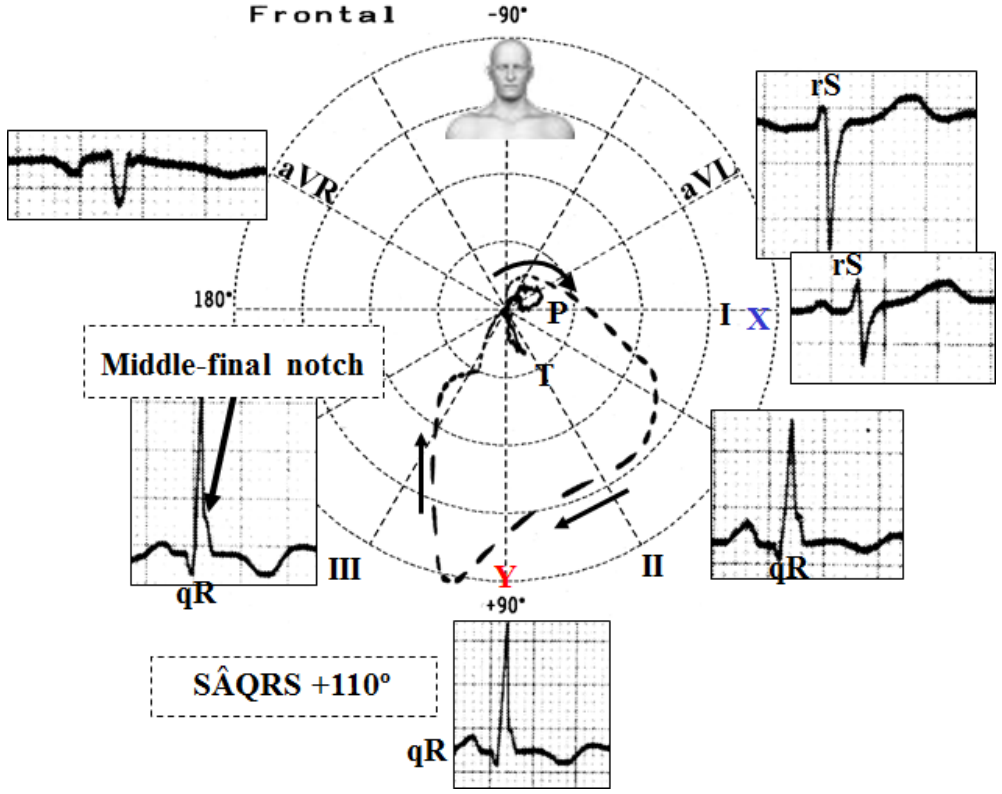
1) Vector of initial 10 to 20 ms heading to the front and below;
2) Most area of QRS loop located in the posterior and superior quadrant;
3) Maximal middle vector of QRS around –145º.
4) Vector of 40 to 80 ms in the posterosuperior quadrant.



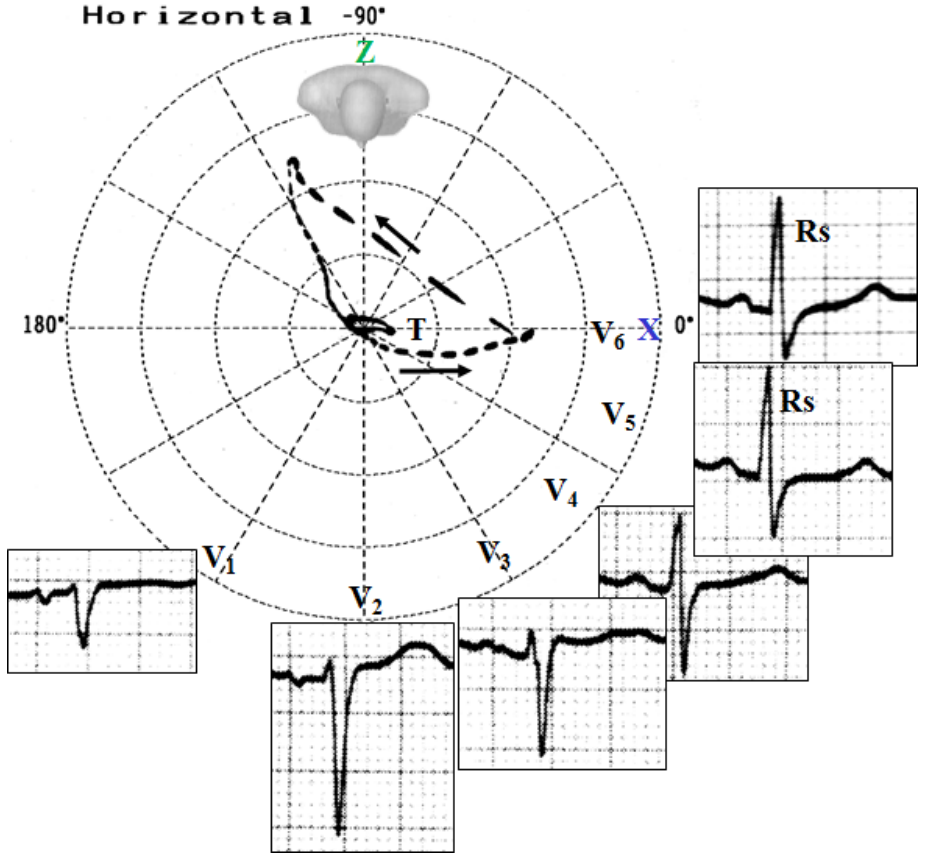
Isolated Left posterior fascicular block electrocardiographic criteria

1. Frontal plane axis between +90° and ±180° (predominantly ≥ +120°): The diagnosis is clinical-electrocardiographic because it is necessary the absence of right atrial enlargement and RVH, vertical heart in a slender person, large lateral MI, tricyclic antidepressant overdose(non-specific intraventricular conduction delay, right axis deviation of the terminal QRS, terminal R wave > 3 mm in aVR and R/S ratio > 0.7 in aVR), etc. In summary, not evidence of any other clinical cause for right axis deviation
2. rS pattern in leads I and aVL
3. qR pattern in leads III and aVF. LPFB. When associated with MI reduces the Q waves in leads III, aVF, and II and produces tall R waves in the inferior leads by a delayed excitation of preserved myocardium of inferolateral portions of the left ventricle, thereby masking MI.(**Castellanos 1987**). The development of RBBB + LPFB during acute myocardial infarction is a sign of poor prognosis. RBBB + LPFB has a high probability to turn into complete AV block.
4. Increased R voltage in III and II leads
5. Prolonged R wave peak time in aVF: ≥ 45ms
6. The pattern can appears similar to the $S_1Q_3T_3$ pattern sometimes present in a patient with an acute pulmonary embolus.
7. Therefore, instead of the expected broad and deep Q waves or QS waves in leads III and aVF leading generally to left axis deviation, the clinician meets a small Q wave and tall R waves in the same leads, with a AQRSF. Moreover, the T waves are asymmetrically negative, rather than symmetrically negative as in simple IMI. When associated with inferior MI severe two- and three-vessel disease is the rule.
8. S1Q3 pattern in the limb leads
9. Deep S waves in V_2 -V_3 by posterior dislocation and to the right of the final forces.
10. QRS duration <120 ms. QRS duration normal or slightly prolonged (80-110ms). 20 milliseconds longer than normal conduction
11. Persistent S waves in low lateral leads V5-V6
12. Scant progression of growth of r wave in precordial leads: dislocation to the left of the transition precordial zone.
13. V_5 and V_6: qRs or Rs patterns.
14. Increased R peak time of V_5 and V_6 (> 45 ms to 50 ms)
15. Disappearance of q wave in V5 and V6 when LPFB occurs
16. It is extremely rare to see LPFB in isolation. It usually occurs associated with RBBB. The rarity of LPFB is attributed to the thickness of the left posterior fascicle and to the vascular immunity secondary to its dual blood supply from the first septal perforator branch of the left anterior descending artery and from the AV node artery arising from the dominant artery, either the right or the circumflex coronary artery.

ECG/VCG correlation of isolated LPFB

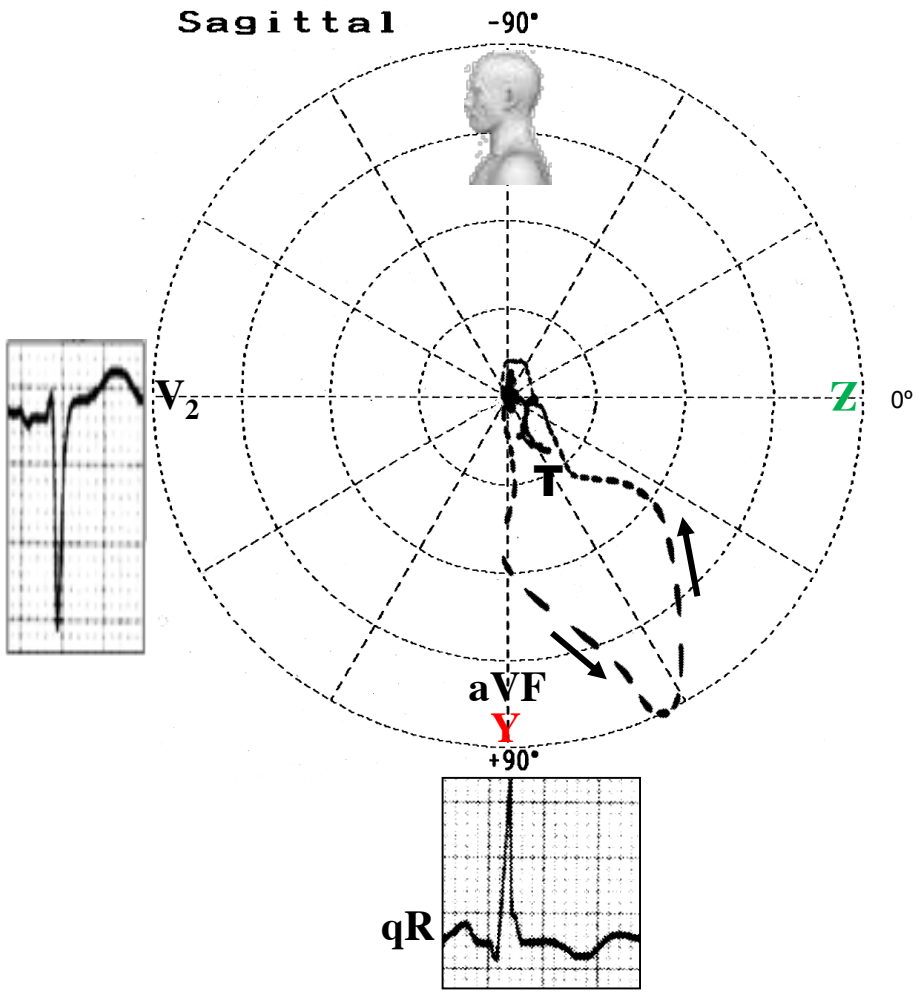


ECG/VCG correlation in the frontal plane of a typical case of LPFB: vector of initial 10 to 20 ms heading upward and to the left; rS pattern in I and aVL; qR in inferior leads; R in III > R in II; middle final notch in ascending limb of R wave of III; QRS loop of clockwise rotation and broadened morphology in clinical absence of RVH, vertical heart or lateral infarction (the diagnosis of LPFB must obligatorily be clinico-electrocardiographic). Only diagnosis if there is clinical absence of RVH, “vertical heart” or lateral infarction.



ECG/VCG correlation in the horizontal plane of a typical case of LPFB: vector of initial 10 to 20 ms heading to the front and the left; counterclockwise rotation; > 20% of the area of QRS loop located in the right posterior quadrant; deep S waves in V2 by posterior dislocation of final forces; dislocation to the left of the transition area in precordial leads; RS complexes in V5 and V6.

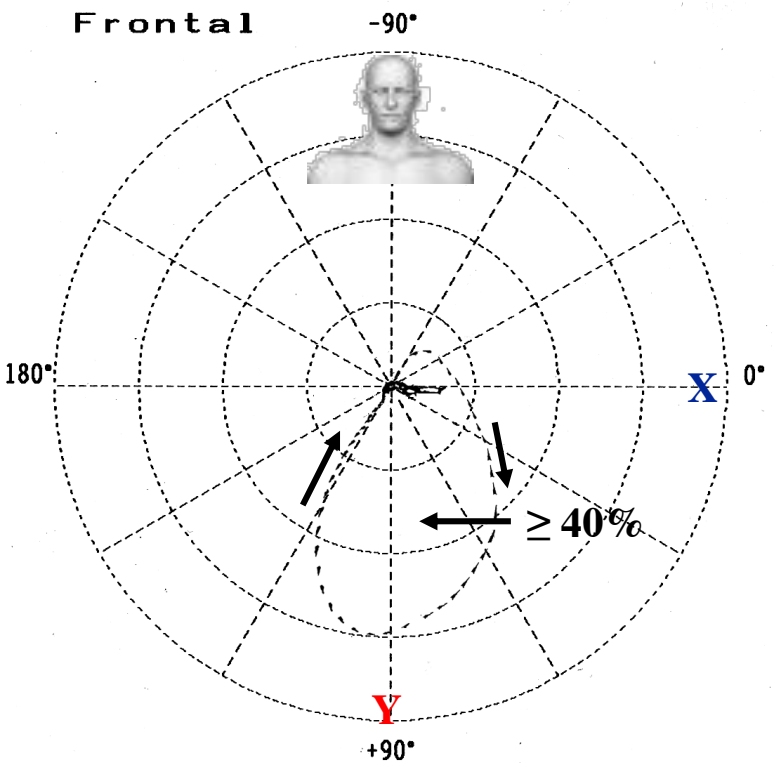
ECG/VCG correlation in the LSP



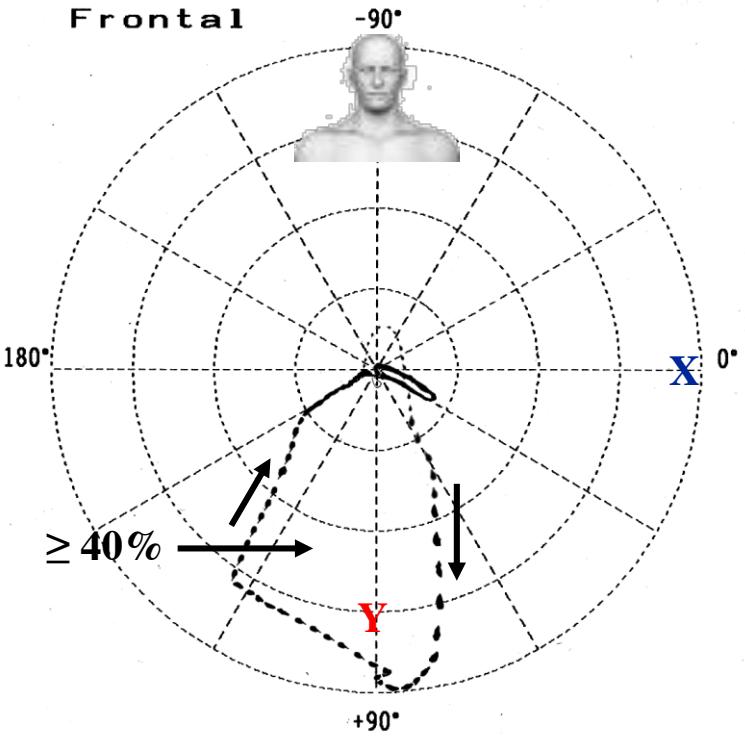
ECG/VCG correlation in the left sagittal plane of a typical case of LPFB: QRS loop of counterclockwise rotation and totally located in the postero-inferior quadrant. In aVR a qR pattern is observed, as well as middle final notch in the ascending limb of the R wave. The presence of the initial q wave points out that the vectors of the initial 20 ms are heading above.

Differences in the FP between isolated LPFB and in association to CRBBB

	Isolated LPFB	LPFB + CRBBB
QRS duration	90 to 110 ms	≥120 ms
Location of QRS loop	≥ 40% left of Y line	≥ 40% to the right of the Y line
Vector of final 20 ms	There might be delay, but discrete.	With important delay to the right.

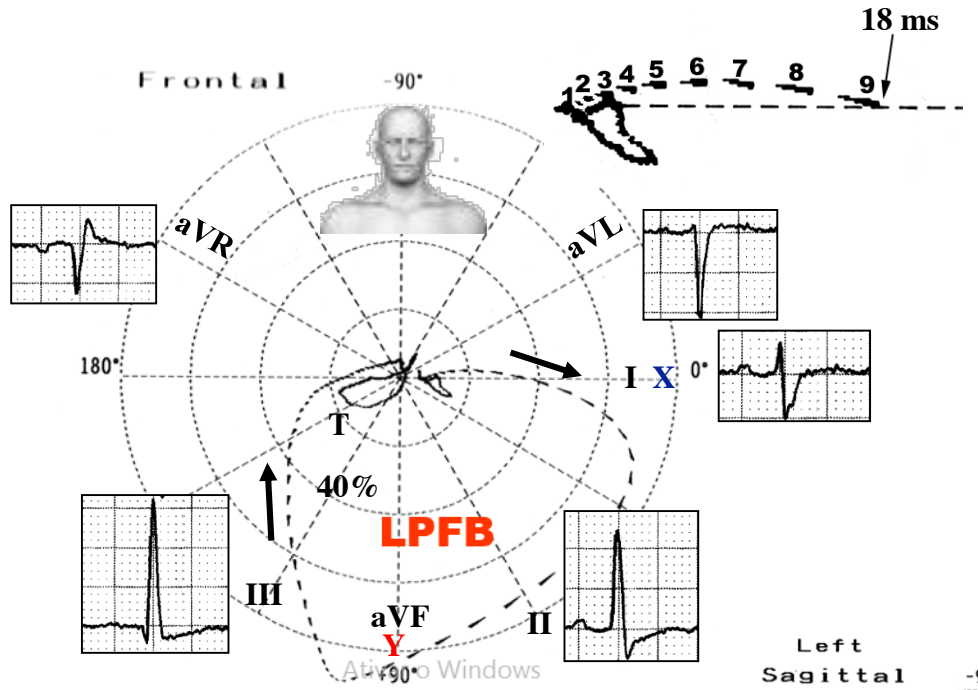


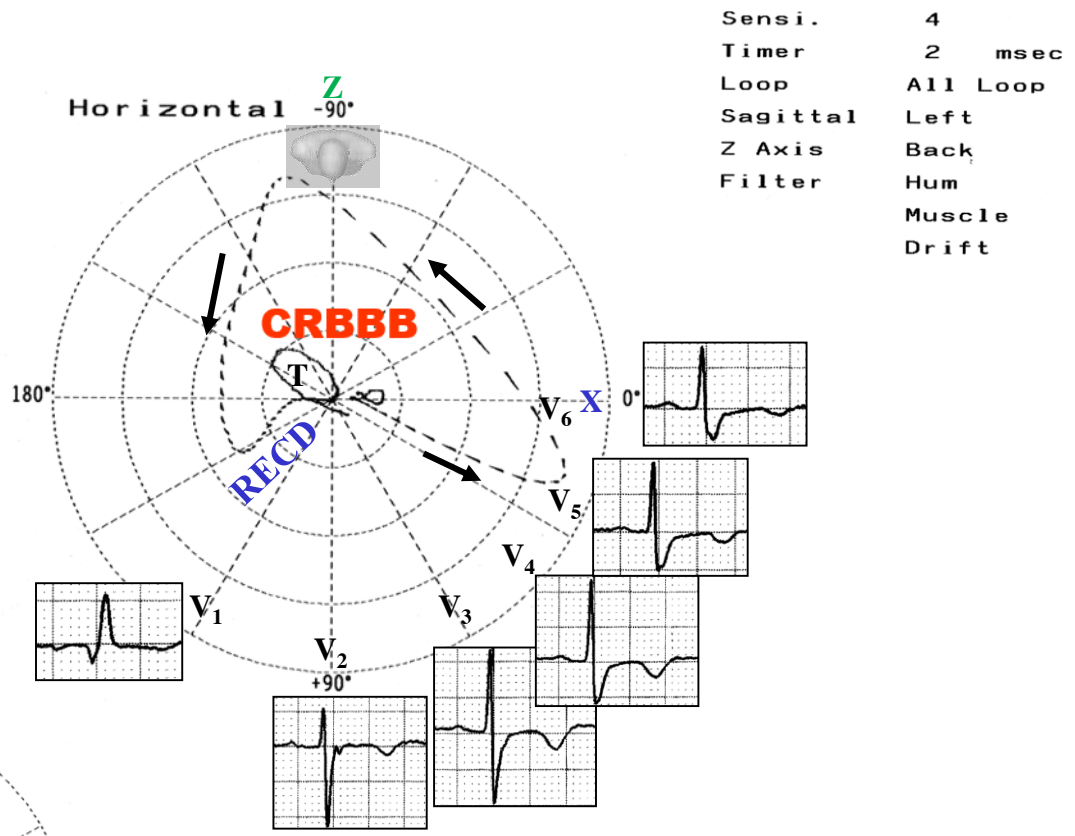
45 to 50 dashes in QRS loop: 1 dash = 2 ms

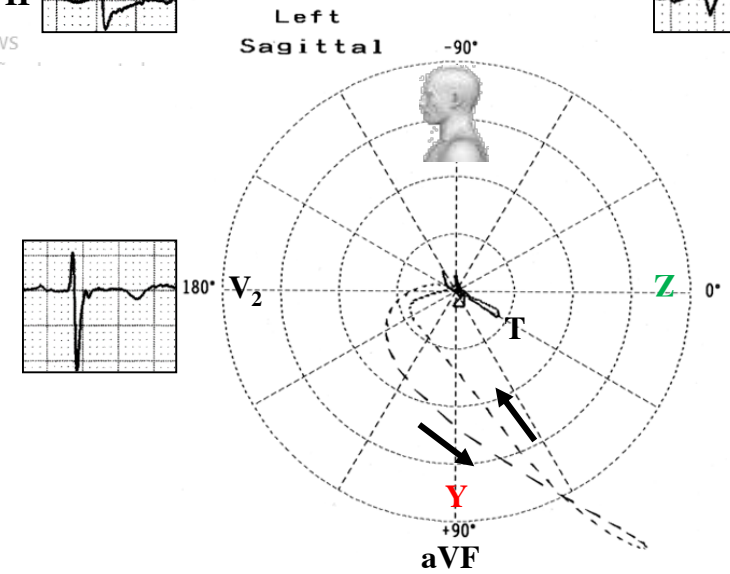


≥ 60 dashes in QRS loop: 1 dash = 2 ms

ECG/VCG correlation of LPFB + CRBBB







ECG/VCG correlation in the frontal plane where the following stands out: rS in I and aVL; qR in III; voltage of R wave of III >15 mm and > R wave of II; vector of initial 18 ms above the X line; QRS loop of CW rotation; aspect of "fat" QRS loop; ≥ 40% of the QRS loop located to the right: LPFB associated to CRBBB.

ECG/VCG correlation in the HP where the following stand out: qR pattern in V1 (it may be observed in CRBBB associated to LPFB even in absence of septal infarction); "broad" S wave of left leads: CRBBB; right end conduction delay in "glove finger" located in the right anterior quadrant: CRBBB; afferent limb of the QRS loop located behind the orthogonal X lead: CRBBB of the VCG Grishman type or Kennedy type I.

VCG criteria for LPFB (Brohet 1977)

Frontal Plane:

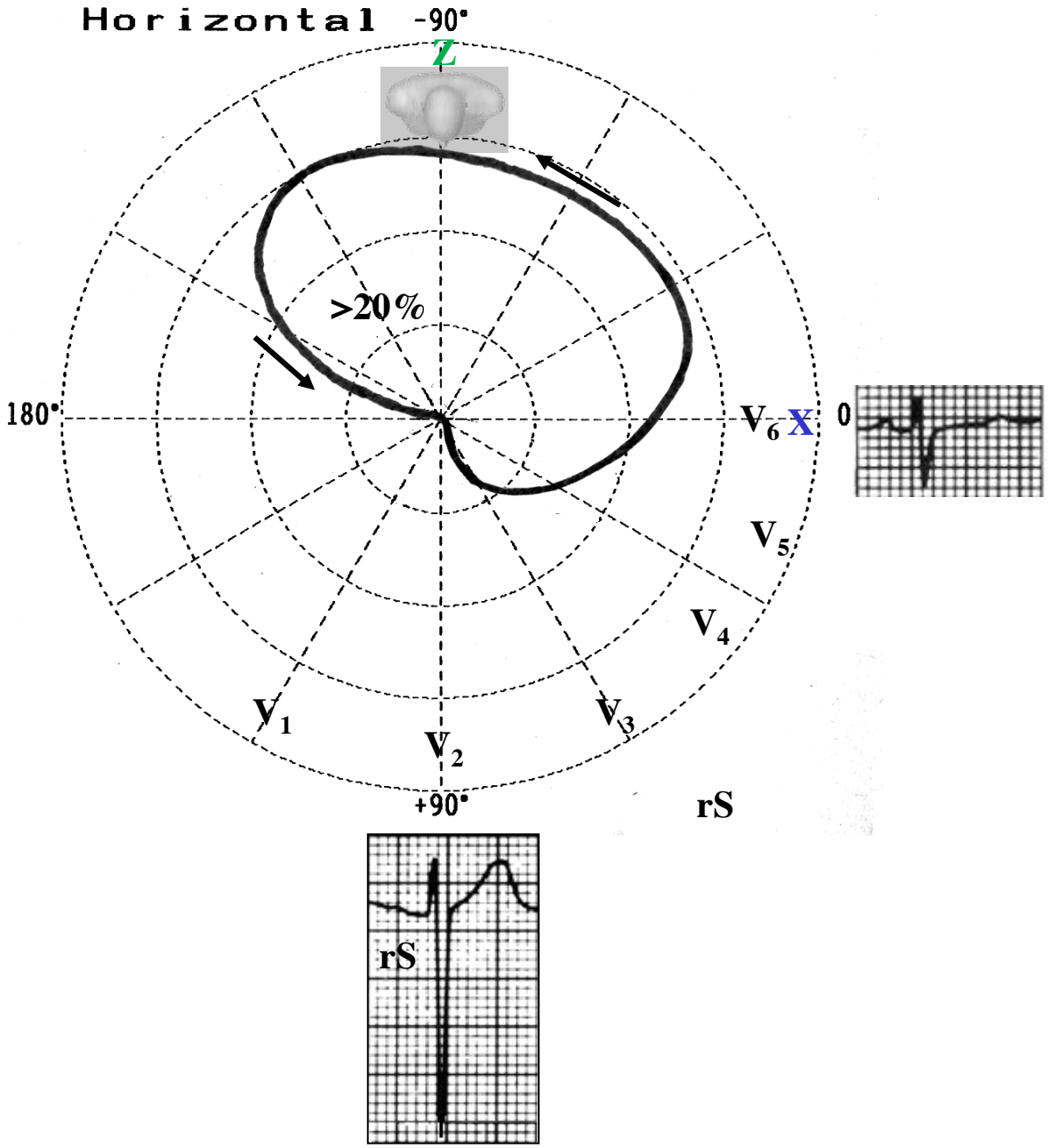
- Vector of initial 10 to 20 ms heading above and to the left (near -45°) with possible delay (initial 10 to 25 ms). If associated to inferior infarction, superior initial forces of 25 ms or more (more than 12.5 dashes above the orthogonal X lead. 1 dash = 2 ms) (Castellanos 1972).
- Broad QRS loop, with clockwise rotation. Cooksey, Dunn and Massie said that occasionally, it may be in "eight" with a counterclockwise terminal portion (10%).
- Maximal vector near +110º (+80º to +140º)
- Almost all the loop is located below the X line (0 to ±1800) in the inferior quadrants
- 20% of the loop located in the right inferior quadrant. If there is association to CRBBB, 40% or more
- Afferent limb heading below and slightly to the left, and the efferent one to the right.
- Middle-terminal portion of the QRS loop (vector of 60 ms to 100 ms) with delay. It may possibly reach the right superior quadrant
- QRS loop duration up to 110 ms if in isolation. In association to Complete RBBB > 120 ms
- Normal ST-T vectors in isolated LPFB: T loop with clockwise rotation, heading below and to the left. If in association to Complete RBBB: alteration secondary to ventricular repolarization.

Horizontal Plane:

- QRS loop very similar to RVH of type C;
- QRS loop of counterclockwise rotation. It is admitted that the rotation could be in "eight";
- Vector of initial 10 to 20 ms heading to the front and the right or left;
- Greater area of QRS loop located in the left posterior quadrant;
- Maximal vector of QRS around -60^0 to -110^0;
- Final portions with delay (60 ms to 100 ms) and located in the right posterior quadrant;
- 20% or more of the area of the QRS loop located in the right posterior quadrant;
- T loop to the front and the left ($+60^0$) and clockwise rotation.

Vectorial representation of QRS loop of ventricular activation in LPFB in the HP

Typical QRS loop in the LPFB in the horizontal plane. The following stand out: vector from the initial 10 to 20 ms heading to the front and the left or right; precordial transition area dislocated to the left; deep S wave in V2 or V2 and V3; frequent RS in left leads V5 and V6; QRS loop similar to RVE type C; QRS loop of CCW rotation; 20% or more of the QRS loop area located in the right posterior quadrant; left precordial leads with RS pattern similar to RVH type C.



Nonspecific or unspecified Intraventricular Conduction Delay/Disturbance (NICD)”

This term applies to any pattern of intraventricular conduction disturbance that cannot be ascribed to block in the bundle branches or fascicles of left bundle of the specialized conduction system. In other words when a prolonged QRS duration QRS duration >110 ms in adults, >90 ms in children 8 to 16 years of age, and > 80 ms in children less than 8 years of age exists, but does not satisfy the criteria for either LBBB or RBBB or pre-excitation pattern, the diagnosis of nonspecific (unspecified) intraventricular block or conduction delay is referred. without criteria for RBBB, LBBB or Wolff-Parkinson-White. The definition may also be applied to a pattern with RBBB criteria in the precordial leads and LBBB criteria in the limb leads (old standard masquerading bundle branch block) and vice versa leads (old precordial masquerading bundle branch block) (**Bonner 1978**; **Robles de Medina 1978**). Prolonged QRS duration in a standard 12-lead ECG is associated with increased mortality in a general population, with intraventricular conduction delay being most strongly associated with an increased risk of arrhythmic death (**Aro 2011**). Tang et al (**Tang 2010**) randomized 1798 patients with LVEF of ≤ 30%, QRSd of ≥ 120 ms (or paced QRS ≥ 200 ms), and NYHA class II or III heart failure to receive an ICD or an ICD-CRT. After a mean follow-up of 40 months, there was a 25% relative reduction both in the primary outcome of death or heart failure hospitalization, as well as in the secondary outcome of total mortality. This trial adds evidence to the efficacy of CRT in selected patients with mild-to-moderate heart failure, at the time of implementation of new guidelines.

The concept of intraventricular conduction defects is those anomalies of supraventricular impulses in intraventricular propagation. In turn, these originate changes in QRS complexes shape and/or duration. The mentioned changes may present as: intermittent (dependent on bradycardia or tachycardia) or present in all heart rates. Additionally, they can be caused by structural disease of the heart or to belong to functional nature:

Structural heart diseases: of the intraventricular conduction system or ventricular myocardium consequence of necrosis, calcification, infiltrative lesions, fibrosis, impaired vascular supply, all may cause structural anomalies in the ventricular myocardium or His-Purkinje system, which originate such disturbances.

Functional: On the other hand, the definition of “aberrant ventricular conduction” refers to those functional disturbances occurring in a portion of the conducting system, caused by a supraventricular impulse reaching the branch during the relative refractory period.

This last recommendation for Nonspecific or Unspecified Intraventricular Conduction Disturbance settles down the following concept: “QRS duration .110 ms in adults, > 90 ms in children 8 to 16 years of age, and > 80 ms in children less than 8 years of age without criteria for RBBB or LBBB. The definition may also be applied to a pattern with RBBB criteria in the precordial leads and LBBB criteria in the limb leads, and vice versa”: The ECG complex coined by Richman a long time ago as “masquerading bundle-branch block” (**Richman 1954**).

Today we know that is essentially a complete RBBB and LAFB, with further modifications of the initial and final QRS vectors, so that standard leads, and at times the left precordial leads, resemble LBBB.

NSIVCD is used when no characteristic pattern of RBBB or LBBB exists, although QRS duration is prolonged. Such abnormalities are frequently seen with previous MI and scar formation. If characteristics abnormalities of the initial QRS portion (Q waves) are present associated with abnormal terminal QRS forces directed toward the infarct, with an angle of ≥100º between the initial and the terminal QRS forces with little or no prolongation of the QRS complexes, these can be called peri-infarction block (**Grant 1959;Vassallo 1986**).

The term *possible peri-infarction block* is recommended when, in the presence of an abnormal Q wave generated by a myocardial infarction in the inferior or lateral leads, the terminal portion of the QRS complex is wide and directed opposite to the Q wave (ie, a QR complex in the inferior or lateral leads).

Peri-ischemic block is term recommended when a transient increase in QRS duration accompanies the ST-segment deviation seen with acute injury. Reversible QRS changes during AMI are attributed to passive pull by the ST-segment shift and intraventricular conduction disturbance (**Surawicz 1998**). Prolonged QRS duration without a specific bundle branch block pattern can also occur due to intramyocardial conduction slowing by drug-induced block of the sodium channels such as tricyclic-antidepressants (TCAs) overdose (e. i. amitriptyline, nortriptyline, trimipramine, despiramine, protriptyline, and dothiepin poisoning), class Ia antiarrhythmic drugs of Vaughan-Williams classification - sodium channel blockers with intermediate association/dissociation, prolongation of action potential duration and effective refractory period - know as fast-channel blockers-affect QRS complex (quinidine, procainamide, and dysopiramide), infrequently, Class Ic antiarrhythmic drugs -sodium channel blockers with slow association/dissociation, pronounced reduction in phase 0 slope; no effect on action potential duration or effective refractory period (flecainide, propafenone, and moricizine), hypothermia, left ventricular enlargement/hypertrophy and very elevated serum potassium levels. The QRS duration prolongation secondary to drugs or electrolyte disturbances frequently have acute clinical presentation. If a drug like quinidine is being taken and can be related temporally to the **NSIVCD** then increasing dosage is not indicated, and in specific case of this drug, a QRS complex prolongation for values ≥140 ms or >35% of the baseline tracing, constitutes absolute indication of interruption of the drug (**Heissenbuttel 1970**).

NSIVCD can be a normal variant and is not always associated with cardiac pathology. Clinical correlation (history and physical examination) is needed to identify associated cardiac abnormalities.

If conduction delay is uniform, the QRS complex is uniformly widened and The QRS-T angle remains normal. Not all delays, however, can be explained by factors known to slow conduction uniformly in the ventricular muscle. Atypical QRS widening that does not fit the criteria for either LBBB or RBBB may be caused by complex delays within the conduction system, regional conduction slowing within the myocardium, or a combination of both. No systematic exploration or classification of such patterns has been attempted (**Surawicz 1995**).

Characteristic of Non-specific Intra-ventricular Conduction Defect caused by Tricyclic-antidepressants (TCAs)

TCAs is a group of drugs used for the depression treatment. One of the effects of these drugs is sodium channel blocking ability causing severe arrhythmias such as ventricular tachycardia (VT) and Torsades de pointes (TdP). Tricyclics have a narrow therapeutic index, *i.e.*, the therapeutic dose is close to the toxic dose. In the medical literature the lowest reported toxic dose is 6.7 mg per kg body weight. Although there are differences in toxicity with the drug class, ingestions of 10 to 20 mg per kilogram of body weight are a risk for moderate to severe poisoning, however, doses ranging from 1.5 to 5 mg/kg may even present a risk. For all TCAs except desipramine, nortriptyline, trimipramine, and protriptyline, this dose is >5 mg/kg. For despiramine it is >2.5 mg/kg; for nortriptyline it is >2.5 mg/kg; for trimipramine it is >2.5 mg/kg; and for protriptyline it is >1 mg/kg (**Woolf 2007**).

Main Electrocardiographic changes of TCA toxicity

- Sinus tachycardia: it is the most common arrhythmia due to anticholinergic activity and inhibition of norepinephrine uptake by TCAs.
- PR interval prolongation
- QRS interval prolongation: QRS duration >100 ms TCA levels >1000 ng/ml are associated with QT and QRS interval prolongation and convulsions (**Koegelenberg 2012**).
- • Right axis deviation of the terminal 40 ms vector of the QRS complex in the frontal plane (T 40 ms axis) Maximal changes in the QRS duration and the T 40 ms axis are usually present within 12 hours of ingestion but may take up to a week to resolve. Although a QRS duration >100 ms and a rightward T 40 ms axis appear to be better predictors of cardiovascular toxicity than the plasma tricyclic drug concentration, they have at best moderate sensitivity and specificity for predicting complications.
- Increased R wave and R/S ratio in lead aVR. serial monitoring of R wave and R/S ratio in lead aVR might be informative in predicting recovery from toxicity following TCA overdose (**Choi 2008**).
- QT/QTc intervals prolongation
- Type 1 ECG Brugada phenocopy pattern (**Meert 2010**).
- Brugada phenocopy ECG pattern with simultaneous ST-segment elevation in the inferior as well as the right precordial leads following ingestion of TCAs (**Sheikh 2010**).
- Nonspecific ST segment and T wave changes
- Atrioventricular block with consequently bradyarrhythmias
- Supraventricular and ventricular tachyarrhythmias may occur. Torsade de pointes occurs uncommonly.

Amitriptyline overdose

Case report

A 49-year-old woman with a history of depression, bipolar disorder, and chronic back pain was brought to the emergency department unresponsive after having taken an unknown quantity of amitriptyline tablets.

On arrival, she was comatose, with a score of 3 (the lowest possible score) on the 15-point Glasgow Coma Scale. Her blood pressure was 65/22 mm Hg, heart rate 121 beats per minute, respiratory rate 14 per minute, and oxygen saturation 88% on room air. The rest of the initial physical examination was normal. She was immediately intubated, put on mechanical ventilation, and given an infusion of a 1-L bolus of normal saline and 50 mmol (1 mmol/kg) of sodium bicarbonate. Norepinephrine infusion was started. Gastric lavage was not done. Results of initial laboratory testing showed a serum potassium of 2.9 mmol/L (reference range 3.5–5.0) and a serum magnesium of 1.6 mmol/L (1.7–2.6), which were corrected with infusion of 60 mmol of potassium chloride and 2 g of magnesium sulfate. The serum amitriptyline measurement was ordered at the time of her presentation to the emergency department.

She remained hypotensive, with regular wide-complex tachycardia on the ECG. She was given an additional 1-L bolus of normal saline and 100 mmol (2 mmol/kg) of sodium bicarbonate, and within 1 minute the wide-complex tachycardia resolved to narrow-complex sinus tachycardia. At this point, an infusion of 150 mmol/L of sodium bicarbonate in dextrose 5% in water was started, with serial ECGs to monitor the QRS duration and serial arterial blood gas monitoring to maintain the pH between 7.45 and 7.55.

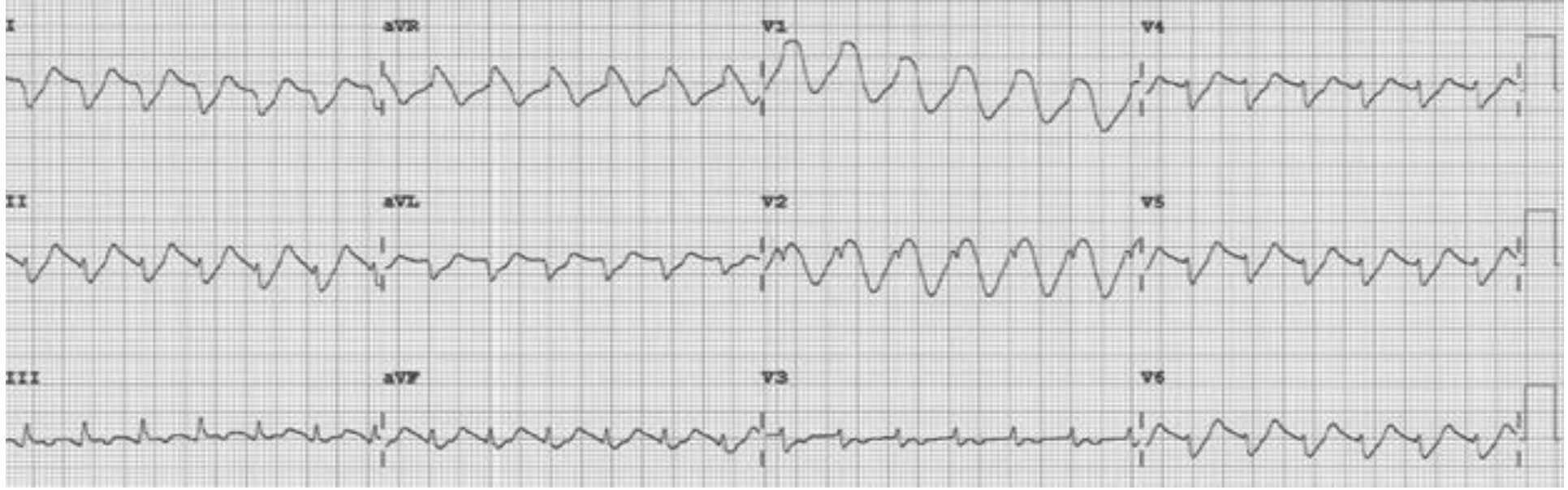
Arterial blood gas analysis showed:

pH 7.15 (normal range 7.35–7.45)

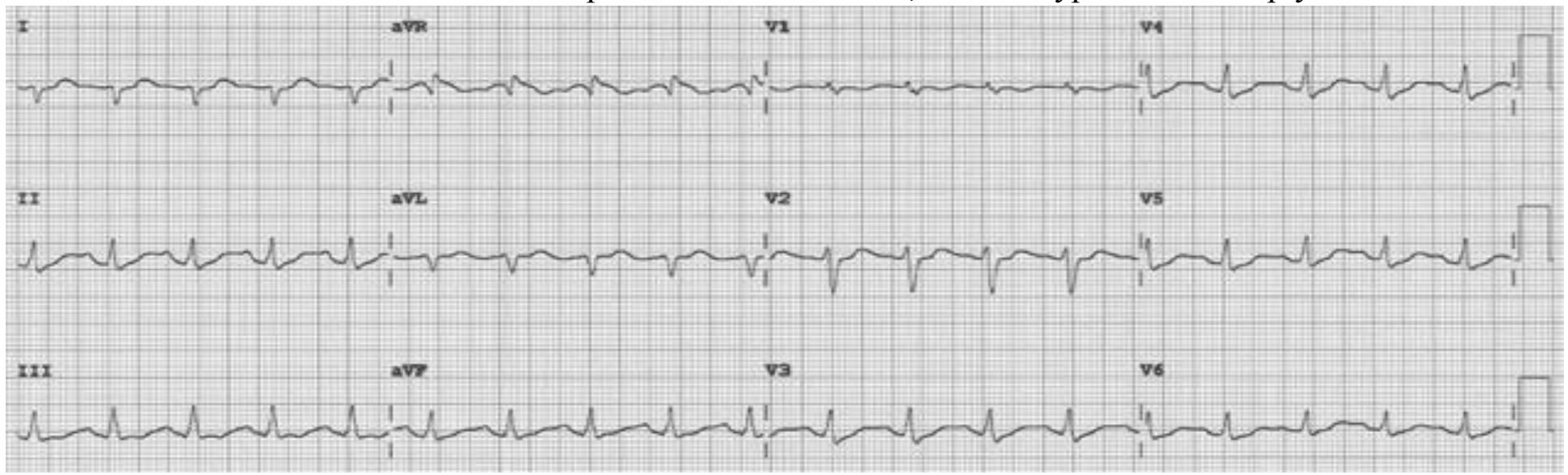
$Pa_{CO}2$ 66 mm Hg (34–46)

$Pa_{O}2$ 229 mm Hg (85–95)

Bicarbonate 22 mmol/L (22–26).



The ECG shows regular wide-complex tachycardia with a ventricular rate of 157 bpm, a QRS duration of 198 ms, a corrected QT interval of 505 ms, and a QRS axis of +179°. Note the negative QRS complexes in leads I and aVL and the final R wave amplitude > 3 mm in aVR, features typical of amitriptyline overdose.

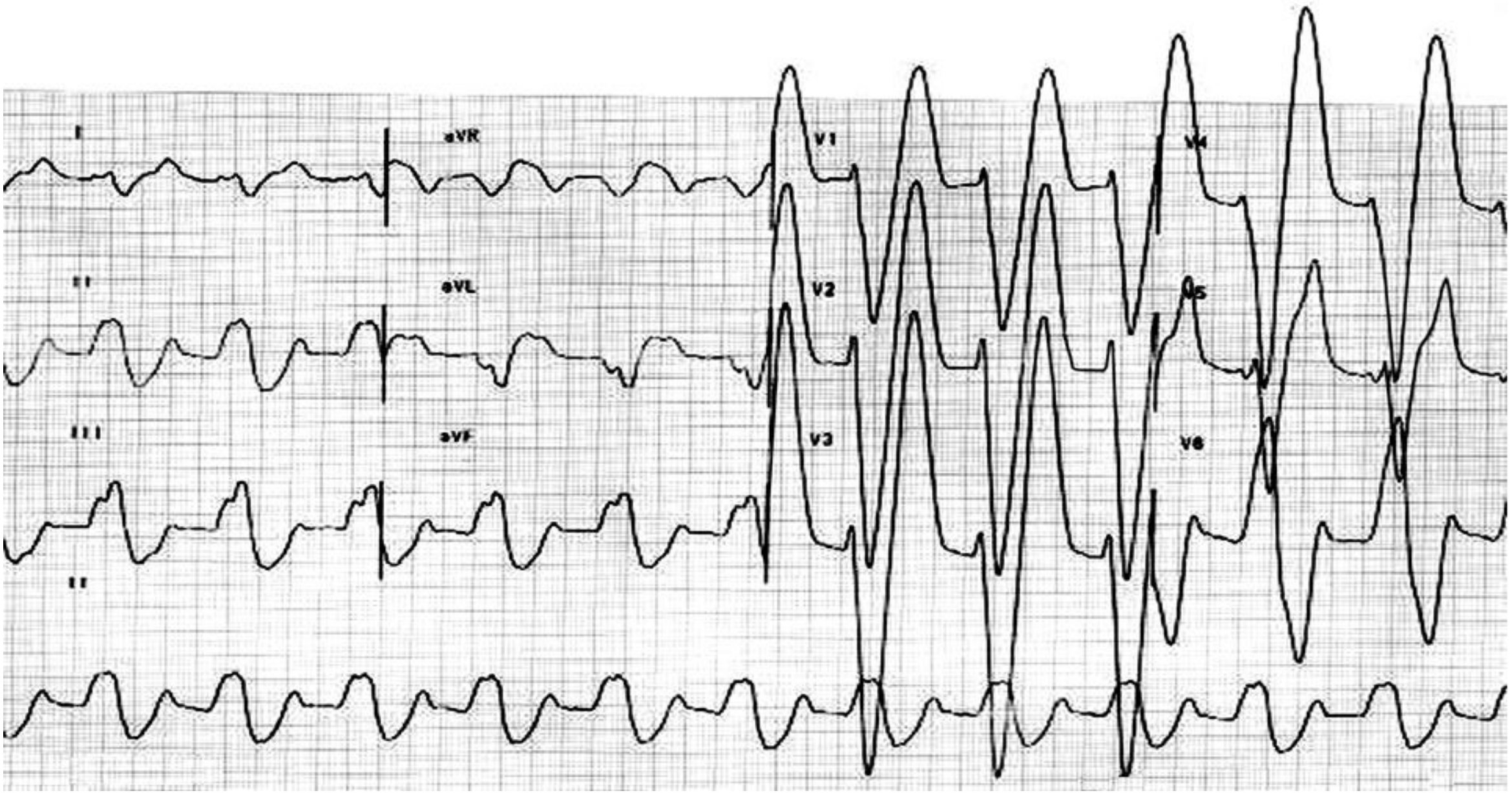


The ECG performed few minutes after infusion of 100 mmol of sodium bicarbonate. Sinus tachycardia (HR = 113 bpm), QRSd of 116 ms, QTc of 478 ms, and QRS axis of +112°. The R wave in lead aVR < 3 mm.

She was then transferred to the intensive care unit (ICU), where she remained for 2 weeks. While in the ICU, she had a single recurrence of wide-complex tachycardia that resolved immediately with an infusion of 100 mmol of sodium bicarbonate. A urine toxicology screen was negative, and the serum amitriptyline measurement, returned from the laboratory 48 hours after her initial presentation, was 594 ng/mL (reference range 100–250 ng/mL). She was eventually weaned off the norepinephrine infusion after 20 hours, the sodium bicarbonate infusion was discontinued after 4 days, and she was taken off mechanical ventilation after 10 days. Also during her ICU stay, she had seizures on day 3 and developed aspiration pneumonia.

From the ICU, she was transferred to a regular floor, where she stayed for another week and then was transferred to a rehabilitation center. This patient was known to have clinical depression and to have attempted suicide once before. She had recently been under additional psychosocial stresses, which likely prompted this second attempt. She reportedly had no neurologic or cardiovascular sequelae after her discharge from the hospital.

Comments: Amitriptyline causes a relatively high number of fatal overdoses, at 34 per 1 million prescriptions (**Henry 1995**). Death is usually from hypotension and VT caused by blockage of cardiac fast sodium channels leading to disturbances of cardiac conduction such as wide-complex tachycardia. Other manifestations of amitriptyline overdose include seizures, sedation, and anticholinergic toxicity from variable blockade of gamma-aminobutyric acid receptors, histamine 1 receptors, and alpha receptors (**Shannon 1988**). Of the various changes on ECG described with amitriptyline overdose, sinus tachycardia is the most common. A QRS duration greater than 100 ms, right to extreme-right axis deviation with negative QRS complexes in leads I and aVL, and an R-wave amplitude greater than 3 mm in lead aVR are indications for sodium bicarbonate infusion, especially in hemodynamically unstable patients (**Liebelt 1995**). Sodium bicarbonate increases the serum concentration of sodium and thereby overcomes the sodium channel blockade. It also alkalinizes the serum, favoring an electrically neutral form of amitriptyline that binds less to receptors and binds more to alpha-1-acid glycoprotein, decreasing the fraction of free drug available for toxicity (**Sayniuk 1984**). In patients with amitriptyline overdose, wide-complex VT and hypotension refractory to sodium bicarbonate infusion can be treated with lidocaine, magnesium sulfate, direct-current cardioversion, and lipid resuscitation (**Kiberd 2012; Harvey 2012**). Treatment with class IA, IC, and III antiarrhythmics is contraindicated, as they block sodium channels and thus can worsen conduction disturbances.



Nonspecific or Unspecified Intraventricular Conduction Defect/Disturbance or Nonspecific intraventricular conduction delay (NSIVCD). Very prolonged QRS duration without a specific bundle branch block pattern can also occur due to intramyocardial conduction slowing by severe hyperkalemia. Lead I suggest RBBB (rS pattern) and precordial leads LBBB. A "sine QRS wave" appearance is observed in II.

Possible etiologies of intraventricular conduction defects

A. Sclerosis left cardiac skeleton (Lev's disease) (Lev 1964 a, Lev b; Lev c)

It is characterized by fibrosis and calcification of the mitral annulus, the central fibrous body, the base of the aorta and the cusp of the interventricular septum may be accelerated by pathologies such as hypertension or unavoidable biological processes involution in old age. *Idiopathic fibrosis or esclerodegenerative involvement of both bundles branches* **(Schloff 1967; Bharati 1976):** Degenerative changes in the AVN or bundle branches (eg, fibrosis, calcification, or infiltration) is the most common cause of nonischemic AV block. Lev syndrome is an acquired complete heart block due to idiopathic fibrosis and calcification of the electrical conduction system of the heart. It is most commonly seen in the elderly and is often described as senile degeneration of the conduction system and may lead to third-degree AV block.

B. Familial Progressive Cardiac Conduction Defect (PCCD) (Lenègre Syndrome)

Progressive cardiac conduction disorder (PCCD) is an inherited cardiac disease that may present as a primary electrical disease or be associated with structural heart disease (**Baruteau 2015**). Familial PCCD is either asymptomatic or manifests as dyspnea, dizziness, syncopal episodes, abdominal pain, heart failure or sudden death when complete AV block develops. The age of disease onset is variable. Syncope during exertion has been reported and the disease can progress from a normal ECG to RBBB and from the latter to complete heart block. In 1999, degenerative changes in the AV conduction system were linked to mutations of the *SCN5A* sodium channel gene (mutations of the same gene may lead to congenital long QT syndrome type 3(LQT3) and overlapping progressive cardiac conduction defect or Brugada syndrome (**Schott 1999; Kyndt 2001; Li 2016**) and to Brugada syndrome. Familial PCCD is a degenerative process affecting the His-Purkinje system. Mutations in several genes have been identified as disease-causing: *SCN5A*, *SCN1B TRPM4*, SCN10A, KCNK17, connexin proteins genes. and CLCA2 (**Tan 2016**). Mutations in the genes *NKX2-5*, *TBX5*, *PRKAG2* and *LMNA* have been identified when familial PCCD is accompanied by congenital heart disease. Isolated PCCD has also been described in families with carriers of a mutation in one of these genes. A candidate gene, *GJA5*, has been associated with severe, early onset PCCD and has been described in 2 blood relatives. Diagnosis of familial PCCD relies on family history of syncope, pacemaker implantation, and SCD as well as on echocardiogram (ECG) findings showing a major conduction defect (CRBBB, CLBBB, LAFB / LPFB, prolonged PR interval or complete AV block with broad QRS complexes). In most cases, normal cardiac structure and contractile function are observed, but in some, complete AV block can lead to dilation of the LV and HF. VT and torsade de pointes may be recorded during the recovery phase of an exercise stress test or during complete AV block.

Potential congenital heart disease or cardiomyopathy is investigated by ECG or CMRI. Screening of the genes involved in familial PCCD should be achieved even in cases of isolated PCCD at a young age. The differential diagnosis includes Brugada syndrome, idiopathic ventricular fibrillation, long QT syndrome, lupus neonatal, progressive familial heart block type II, and sudden infant death syndrome. Transmission is autosomal dominant with incomplete penetrance and variable expressivity. Transmission is autosomal dominant with incomplete penetrance and variable expressivity. Recessive or sporadic forms are rare. Treatment of PCCD includes the timely implantation of a permanent pacemaker. Follow-up at 6-month intervals is recommended in patients with any degree of heart block and at least a yearly examination is recommended in members of the affected families with a normal ECG. Medications with conduction-slowing properties should be restricted, and fever, an aggravating trigger in individuals with *SCN5A* mutations, should be preemptively treated. When a clinical diagnosis of PCCD is established in an index case, clinical investigation of first-degree family members is necessary. There is no genotype-based risk stratification for patients with PCCD. A high incidence of sudden death is observed in patients with either first-degree AV block in association with bifascicular block or in those with symptomatic advanced AV block. In patients who receive pacemaker implantation, the prognosis is excellent and is very close to that of the general population, except in those with *LMNA* mutations that can lead to ventricular tachycardia and sudden cardiac death. In this population, ICD implantation is recommended in case of severe cardiac conduction defect.

C. Progressive familial heart block type II

In type II, the heart block originates in the atrioventricular node. The different types of progressive familial heart block have similar signs and symptoms. Progressive familial heart block type II (PFHB2) is an autosomal dominant disorder, similar to type I progressive familial heart block (PFHB1; 113900). The pattern of PFHB2, however, tends to develop along the lines of a sinus bradycardia with a LPFB, presenting clinically as syncopal episodes, Stokes-Adams seizures, or sudden death when complete heart block supervenes (**Brink and Torrington, 1977**).

Clinical Features

Brink and Torrington (**Brink 1977**) described a large 4-generation South African family of Dutch ancestry with a strong history of sudden death. Of 24 family members who underwent electrocardiography, 10 had conduction abnormalities, including 3 with sinus bradycardia, 3 with isolated LPFB, 1 with AF and a slow ventricular response, and 2 with complete heart block (the latter 2 had pacemakers implanted). Three other family members had died at the relatively young ages of 41, 39, and 16 years, respectively, despite having had pacemakers implanted. The average age of affected family members was progressively lower in more recent generations, and there was an autosomal dominant pattern of inheritance.

Brink et al. (**Brik 1995**) described ECG features differentiating PFHB1 from PFHB2. PFHB1 is characterized by evidence of bundle branch disease, i.e., RBBB, LAFB, LPFB , or complete AV block, with broad QRS complexes. Progression has been shown from a normal ECG to RBBB and from the latter to complete heart block. These ECG features differentiate PFHB1 from PFHB2, in which the onset of complete heart block is associated with narrow QRS complexes.

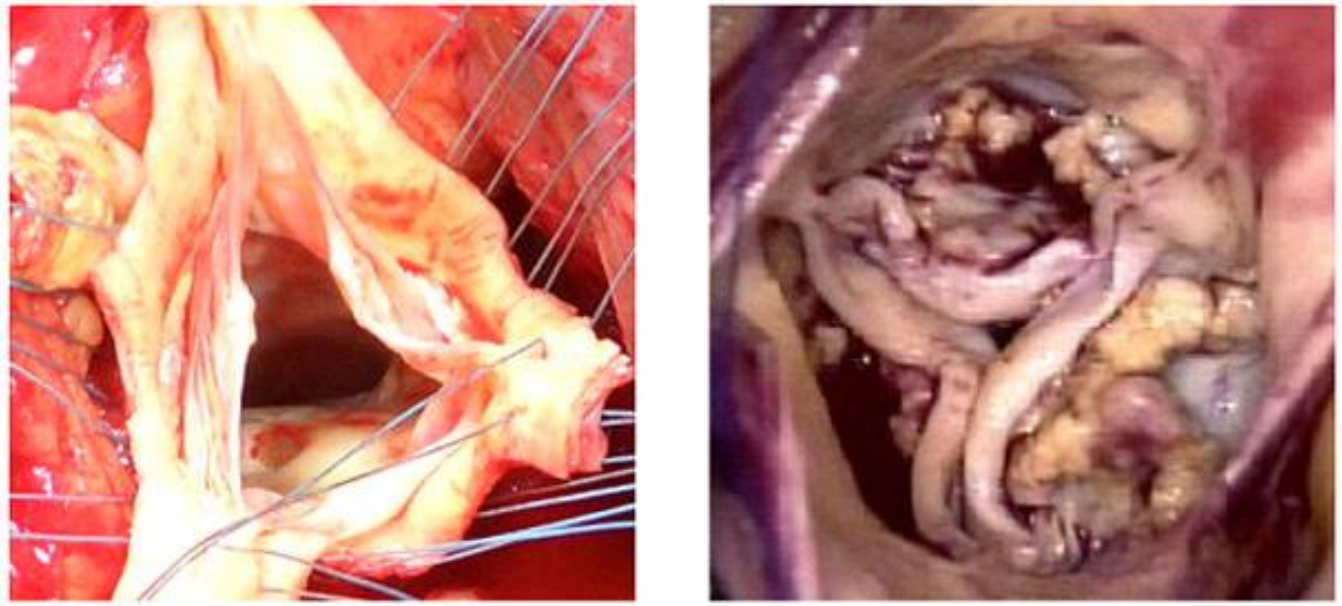
Sarachek et al (**Sarachek 1972**) reviewed 19 reports of familial bradycardia. Ten families had pure AV block, 6 had members with AV block or sinus bradycardia, and 3 had pure sinus bradycardia. Eight families had congenital heart block and 8 had onset in adulthood.

Mapping

Fernandez et al. (**Fernandez 2005**) performed linkage analysis in 26 individuals from the South African family of Dutch descent with PFHB2 originally reported by Brink (**Brink 1977**) and obtained a maximum multipoint lode score of 3.7 on chromosome 1q32. Fine mapping and haplotype analysis narrowed the disease region to a 3.9-cM (2.85-Mb) interval flanked by D1S70 and D1S505. No mutations were found in the plausible candidate genes in that region, KCNH1 (603305), KIAA0205, LAMB3 (150310), and PPP2R5A (601643).

D. Progressive calcification related to mitral or aortic valve annular calcification

Calcific aortic valve disease is a slowly progressive disorder with a disease continuum that ranges from mild valve thickening without obstruction of blood flow, termed aortic sclerosis, to severe calcification with impaired leaflet motion, or aortic stenosis. In the past, this process was thought to be “degenerative” because of time-dependent wear-and-tear of the leaflets with passive calcium deposition. Now, there is compelling histopathologic and clinical data suggesting that calcific valve disease is an active disease process akin to atherosclerosis with lipoprotein deposition, chronic inflammation, and active leaflet calcification. The overlap in the clinical factors associated with calcific valve disease and atherosclerosis and the correlation between the severity of coronary artery and aortic valve calcification provide further support for a shared disease process.



Macroscopic appearance of a healthy and a diseased aortic valve. The left panel shows normal aortic valve leaflets with no calcification or sclerosis, the right panel displays a stenosed valve with leaflet and annular fibrosis and heavy leaflet calcification

Mitral annular calcification (MAC) is a common degenerative process involving the fibrous annulus of the mitral valve. It is generally an incidental finding associated with aging, although it occasionally is prominent enough to cause significant left ventricular inflow obstruction and symptomatic mitral stenosis. In addition, MAC is associated with atrial fibrillation, conduction system disease, atherosclerotic disease and adverse cardiovascular events, including stroke and increased mortality. Mitral annular calcification (MAC) is caused by progressive calcium deposition

along and beneath the mitral valve annulus (**Fulerson1979**). MAC generally follows the C-shape of the mitral annulus, so the base of the anterior mitral leaflet is generally (but not always (Roberts 1981)spared. MAC is most commonly visualized by echocardiography as an echodense, irregular shelf-like structure involving the mitral valve annulus with associated acoustic shadowing). Although mitral valve leaflets and chordae tendineae are generally not involved, calcification may progressively accumulate in the subvalvular region beneath the posterior leaflet with encroachment on the leaflet. Relative sparing of the leaflet commissures and anterior leaflet distinguishes MAC from rheumatic mitral disease.

E. Coronary artery disease (CAD) (**Kawata 1999**)

Coronary artery disease(CAD) is responsible for ≈ 20% of all cases of intraventricular conduction defects (**Lenègre 1964**). In subjects without proven CAD who had been referred for stress echocardiography the presence RBBB with LAFB is an independent predictor of mortality in patients with suspected CAD undergoing stress echocardiography, whereas isolated RBBB is associated with outcomes similar to those observed in patients with no conduction defects (**Cortigiani 2003**). During AMI observed in a CCU patients with intraventricular conduction defects had a higher mean age and death occurred at a younger age than in patients without such defects. The most common isolated defect is LAFB (≈ 9 %). The next most common conduction defect was incomplete bilateral bundle branch block (incidence 7.5%); more than half of these patients had RBBB with LAFB. Far less frequent is isolated CRBBB and CLBBB. LPFB Is rare and is not seen in patients without other intraventricular conduction defects either transient or permanent. Isolate LPFB is a very rare but clinically important intraventricular conduction disturbance. Its appearance is reliably connected with inferior MI and generally reflects severe three-vessel CAD, requiring invasive investigation (**Godat 1993**). The hospital mortality rate is ≈20%. The mortality rate among patients with intraventricular conduction defects is ≈ 40% which is significantly different from that for the entire series and from a series matched by sex and age. The most innocuous intraventricular conduction defect is LAFB (in-hospital mortality rate 25 %). This is statistically not different from the mortality rate in the total series. Higher mortality rates are associated with other conduction defects which produced QRS prolongation and bifascicular block. To determine the incidence and significance of transient intraventricular conduction abnormalities occurring in association with myocardial ischemia during exercise testing, the recordings of 2,200 consecutive exercise tests were reviewed. Ten patients (0.45%) were identified as having both ischemia and intraventricular conduction abnormalities that developed transiently during the exercise test. In all 10 patients both typical angina and ECG evidence of ischemia developed during exercise. Among the 10 patients, LAFB developed in 4, LPFB in 2, RBBB in 2, RBBB with left axis deviation in 1, and LAFB progressing to complete LBBB in 1. All 10 patients had cardiac catheterization showing significant obstruction of the proximal LAD coronary artery at or before the origin of the first septal perforator branch. Eight patients were treated surgically and 2 medically, all with relief of ischemic symptoms. Nine of the 10 had repeat exercise stress testing without angina or ECG evidence of ischemia and without

recurrence of the transient intraventricular conduction disturbance. It is concluded that the development of transient intraventricular conduction abnormalities associated with myocardial ischemia during exercise testing is an uncommon occurrence (0.45%). When such conduction disturbances develop, the existence of significant disease in the proximal obstruction of the LAD coronary artery is strongly suggested. With control of myocardial ischemia, the transient conduction disturbances during exercise are ameliorated (**Boran 1983**).

Domenighetti et al (**Domenighetti 1980**) analyzed the short- and long-term prognosis of 59 patients admitted in the CCU with an AMI, complicated with acute intraventricular conduction defects (AIVCD). In-hospital mortality of patients with AIVCD was more than twice (30%) the mortality of patients without AIVCD. Mortality rate was very high among patients with all forms of incomplete trifascicular block or complete RBBB. Among survivors of the group with AIVCD, late death rate was significantly higher than in survivors of the group without AIVCD (25 vs 8%). Short-term prognosis of conduction defects in MI depends on the extent of the necrosis. The conflicting results in long-term prognosis could be ascribed to variations in patient material and to different criteria used to define the acute nature of a block. The main cause of poor prognosis during the hospital period in patients with AMI and BBB was not arrhythmia or AIVCD but severe pump failure due to extensive myocardial necrosis. Prophylactic temporary pacemaker insertion did not improve the hospital mortality rate of these patients, and patients with AMI and BBB who survive the in-hospital phase after AMI have a good prognosis during the following 15 months (**Alpman1993**).

F. Dilated cardiomyopathy (Xiao 1994)

A combination of increasing PR interval and QRS duration, particularly when associated to rightwards shift of QRS axis, appears to be a marker of high risk in patients with dilated cardiomyopathy (**Xiao 1996**).

G. Chronic Chagasic myocarditis

It is the main cause of BBB and AV block in endemic areas. At the ventricular level, both conduction disturbances and arrhythmias are conspicuous expressions of the myocardial damage. RBBB alone or in combination with LAFB are the most common conduction defects (**Elizari 1993; Femenia 2009**).

H. Hemochromatosis

I. Cardiac sarcoidosis (Bharati 1980)

J. Primary cardiac amyloidosis (Bharati 1980)

K. Myxedema heart

It is characterized by an enlargement of all four chambers, bradycardia, generalized (in precordial and limb leads) low QRS voltage, notching and widening QRS complexes and nonspecific S-T segment and T-wave changes (flat or inverted). The myxedema heart was first described in 1918 by Zondek, who observed the cardiac hypertrophy and demonstrated the reduction in size after giving thyroid substance., and have been described. Low-voltages are known to occur. All these characteristics usually disappear after thyroid medication.

L. Autoimmune rheumatic diseases (ARDs) (Seferović 2006).

M. Ankylosing spondylitis

N. Reiter syndrome: may affect the AV nodal conducting tissue

O. Lyme disease with active infiltration of the AV conduction system, may lead to varying degrees of AV block

P. Kearns-Sayre syndrome (Riera 2008)

Q. Defects of long-chain fatty acid transport across the inner mitochondrial membrane (carnitine palmitoyl transferase type II deficiency and carnitine acylcarnitine translocase deficiency) and in patients with trifunctional protein deficiency (Bonnet 1999)

R. Fahr's disease (FD): It is a rare neurodegenerative disorder of unknown cause characterized by sporadic or familial idiopathic basal ganglia calcification that is associated with neuropsychiatric and cognitive impairment **(Panduranga2012)**

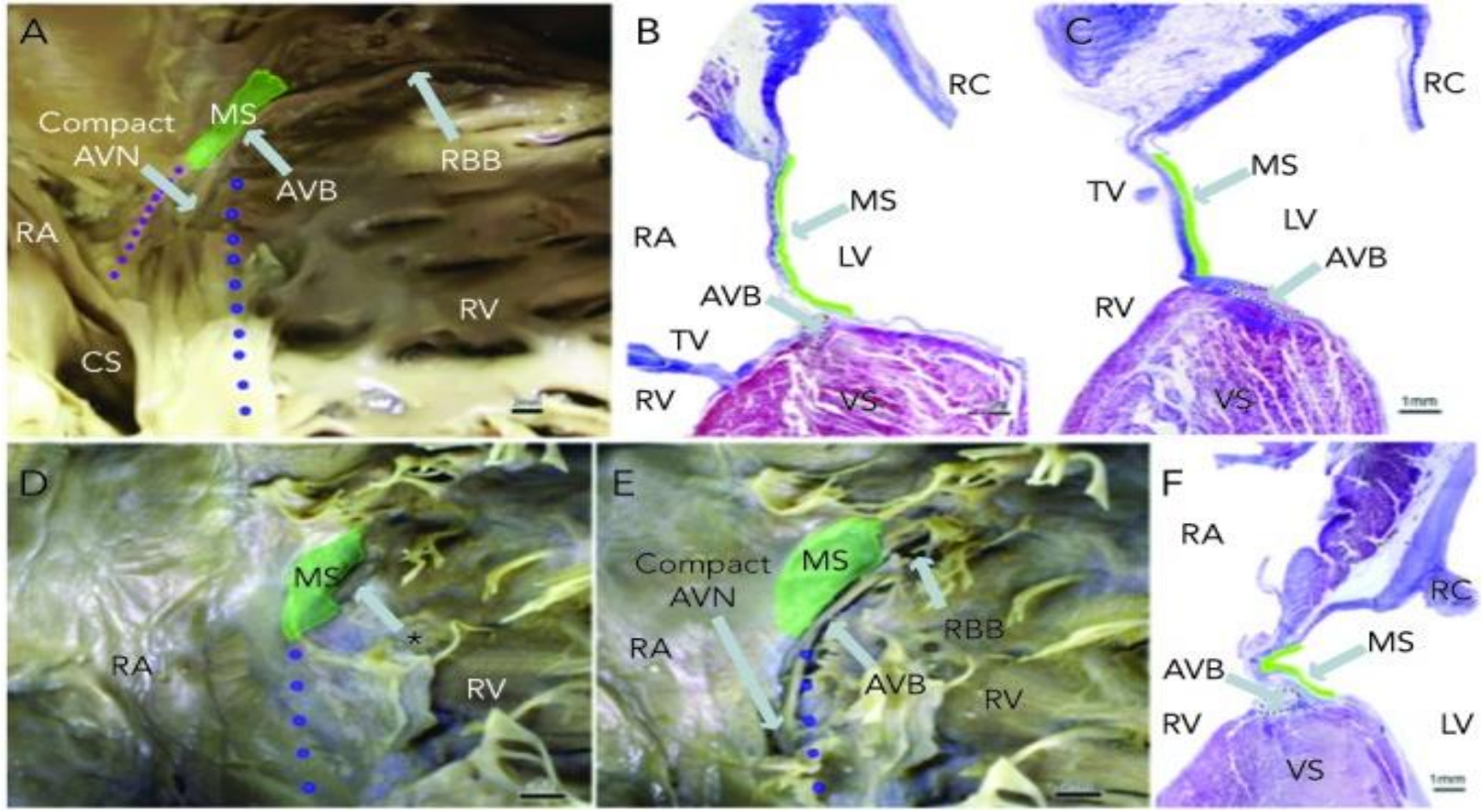
S. Aortic valve replacement (Lehmann1999)

T. Lesions of the atrioventricular conduction system after repair congenital heart disease

After correction of ventricular septal defect(VSD) (**Titus 1963: Allison 1964**), tetralogy of Fallot, atrioventricular canal defect (**Vetter 1982**) and corrected transposition of the great vessels have anterior displacement of the AVN and are prone to develop complete heart block during right heart catheterization or surgical manipulation. The incidences of complete heart block, bilateral bundle-branch block, and ventricular tachyarrhythmia have decreased significantly since the establishment of cold cardioplegia. This has certainly contributed to the remarkable improvement in late follow-up results of postoperative patients with VSD or tetralogy of Fallot. Atrioventricular septal defect and tetralogy of Fallot can be repaired with low mortality by the transatrial-transpulmonary approach without the use of a conduit (**Hoohenkerk 2008**).

U. After transcatheter aortic valve replacement (TAVR)

TAVR has emerged as a valuable, minimally invasive treatment option in patients with symptomatic severe aortic stenosis at prohibitive or increased risk for conventional surgical replacement. Consequently, patients undergoing TAVR are prone to peri-procedural complications including cardiac conduction disturbances, Male sex, baseline conduction disturbances, and intraprocedural AV block emerged as predictors of PPM implantation after TAVR (**Siontis 2014: Young Lee 2015**). Within the right atrium, the AV node is positioned at the base of the atrial septum and is located using landmarks that form the triangle of Koch – the tendon of Todaro, the orifice of the coronary sinus and the insertion point of the tricuspid valve septal leaflet. The antero-posterior relationship of the AV node with respect to the apex of the triangle of Koch varies between individuals as does the length of the non-penetrating (or most proximal) portion of the His bundle. The non-penetrating portion of the His bundle traverses the membranous septum to become the penetrating His bundle, which then physically divides into the respective bundle branches. Inter-individual variation in the penetrating bundle length and depth of septal penetration and variation in the location of the proximal portion of left bundle determine how susceptible these structures are to injury during TAVR. These anatomical variations have been characterized by Kawashima et al (**Kawashima 2014**). Specifically, they describe three major variants in these anatomical relationships that, depending on which is present, determine the susceptibility of a patient to developing complete or LBBB. In an autopsy series of 115 elderly patients, 50 % were found to have a relatively right-sided AV bundle, 30 % a left-sided AV bundle, and in around 20 % the bundle coursed under the membranous septum just below the endocardium. In the latter two variants, the AV bundle is particularly exposed and susceptible to injury. LBBB susceptibility is determined by how soon the left bundle appears on the left side of the septum, and injury to both is further affected by the relative positioning of the membranous septum with respect to the aortic cusps.



Kawashima T, Sasaki H. Gross anatomy of the human cardiac conduction system with comparative morphological and developmental implications for human application.* Ann Anat*2011;193:1–12. Reprinted from Kawashima T, et al. 2014

Positional Variation of the Atrioventricular Conduction Axis A: Typical positions of the compact atrioventricular node in the triangle of Koch, which is defined by the tendon of Todaro (purple dots), the tricuspid valve (blue dots) and the ostium of the coronary sinus, and the atrioventricular bundle in the infra-anterior border of the membranous septum. Right chamber view in the corrected anatomical position. B–C: Positional variation of the atrioventricular bundle within the ventricular septum just below the membranous septum. The atrioventricular bundle positioned in the right and left halves of the ventricular septum, respectively. Sections through the center of the membranous septum. D–F: The exposed atrioventricular bundle before (D) and after (E) dissection, and histological findings (F), respectively. AVB = atrioventricular bundle; AVN = atrioventricular node; CS = coronary sinus; LV = left ventricle; MS = membranous septum; RA = right atrium; RBB = right bundle branch; RC = right coronary cusp; RV = right ventricle; TT = tendon of Todaro; TV = tricuspid valve; VS = ventricular septum.

Predictors of Permanent Pacemaker Implantation Following TAVR Based on Literature Review

Author	Predictors of PPM insertion *	Valve type	Number of patients (% of new PPMs)
(Nazif 2015)	• RBBB (OR 7.03) • LVED diameter per 1 cm increment (OR 0.68) • Prosthesis to LVOT diameter per 0.1 increment (OR 1.29)	SAPIEN valve	n=1,973 (8.8 %)
(Siontis 2014)	• Male gender (RR 1.23) • 1st degree AV delay (RR 1.52) • Left anterior hemi-block (RR 1.62) • Intraprocedural AV block (RR 3.49) • RBBB (RR 2.89) • CoreValve valve (RR 2.54)	CoreValve SAPIEN valve	n=11,210 (SAPIEN valve 6 %, CoreValve 28 %)

PPM – permanent pacemaker; RBBB – right bundle branch block. * P<0.01

V. After alcohol septal ablation in patients with severe obstructive pharmacological non-responsive hypertrophic cardiomyopathy

These patients should therefore have temporary pacing support for ≥ 48 hours after alcohol septal ablation (ASA) or the last occurrence of acute and subacute complete heart block (CHB). Patients without acute CHB during ASA or new IVCDs after ASA are at low risk for subacute CHB (**Chen 2006**).

W. Drugs

*D*igitalis glycosides, beta-blockers, calcium channel blockers, adenosine, and other antiarrhythmic agents. Treatment with amitriptyline (**Kramarz 2013**).

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