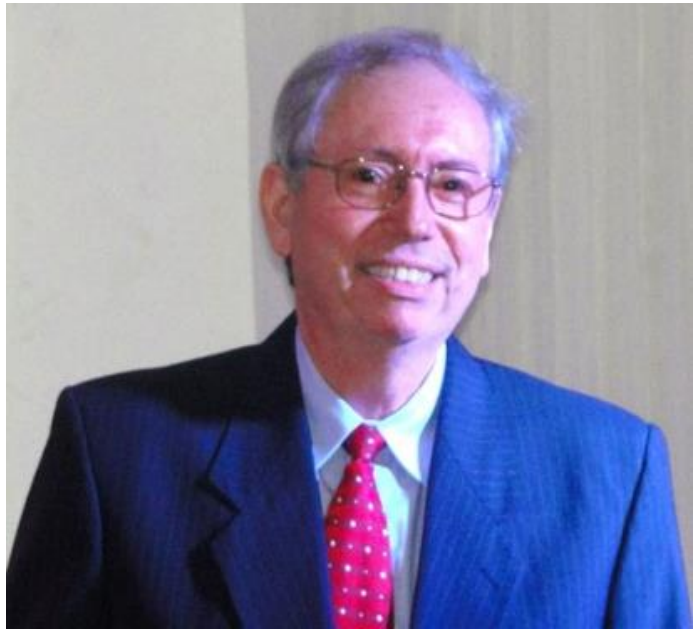
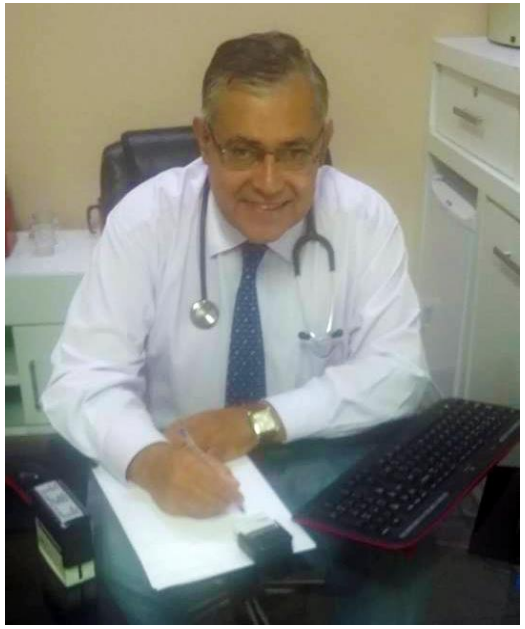
Súbito bloqueio atrioventricular avançado em octogenário hipertenso durante prova de esforço

Suddenly advanced atrioventricular block in octogenarian hypertensive during stress test





https://ekgvcg.wordpress.com/

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2. Post-Graduates Advisor at Design of Studies and Scientific Writing Laboratory in the ABC Faculty of Medicine - ABC Foundation - Santo André – São Paulo – Brazil
3. Visiting Scientist at Program in Molecular and Integrative Physiological Sciences (MIPS), Department of Environmental Health | Harvard T.H. Chan School of Public Health.

Reporte de caso

Homem, 83 anos, branco, assintomático aposentado. Hipertenso conhecido de longa data em uso regular de captopril 25mg 3 x dia. Sem saber o motivo o médico de sua confiança solicitou-lhe um teste ergométrico (motivo?). Durante a fase de recuperação apresentou súbito bloqueio atrioventricular (AV) avançado com manifestação de baixo fluxo cerebral (pré-síncope).

Encaminhado para nosso hospital onde implantou um MP provisório e posteriormente definitivo.

Ritmo cardíaco lento A2 hiperfonético; sopro sistólico +/4 em foco mitral e aórtico.

Pulmões limpos.

O Ecocardiograma exibia apenas hipertrofia ventricular esquerda concêntrica moderada e espessamento com calcificação mitro-aórtica e discreta Insuficiência mitral.

Coronariografia: lesão discreta da artéria coronária descendente anterior distal avaliada em 40%.

Pergunta: Qual o diagnóstico da sequência eletrocardiográfica?

Case Report

Male, white, 83-year-old patient, with no symptoms, retired. Long-standing, known hypertension, using captopril 25 mg, 3 x day, regularly. His family doctor requested an ergometer test apparently for no known reason (reason?). During the recovery phase, he presented sudden advanced atrioventricular (AV) block, with symptoms of low brain flow (pre-syncope).

He was referred to our hospital where temporary pacemaker(PM) was implanted, and later a permanent PM.

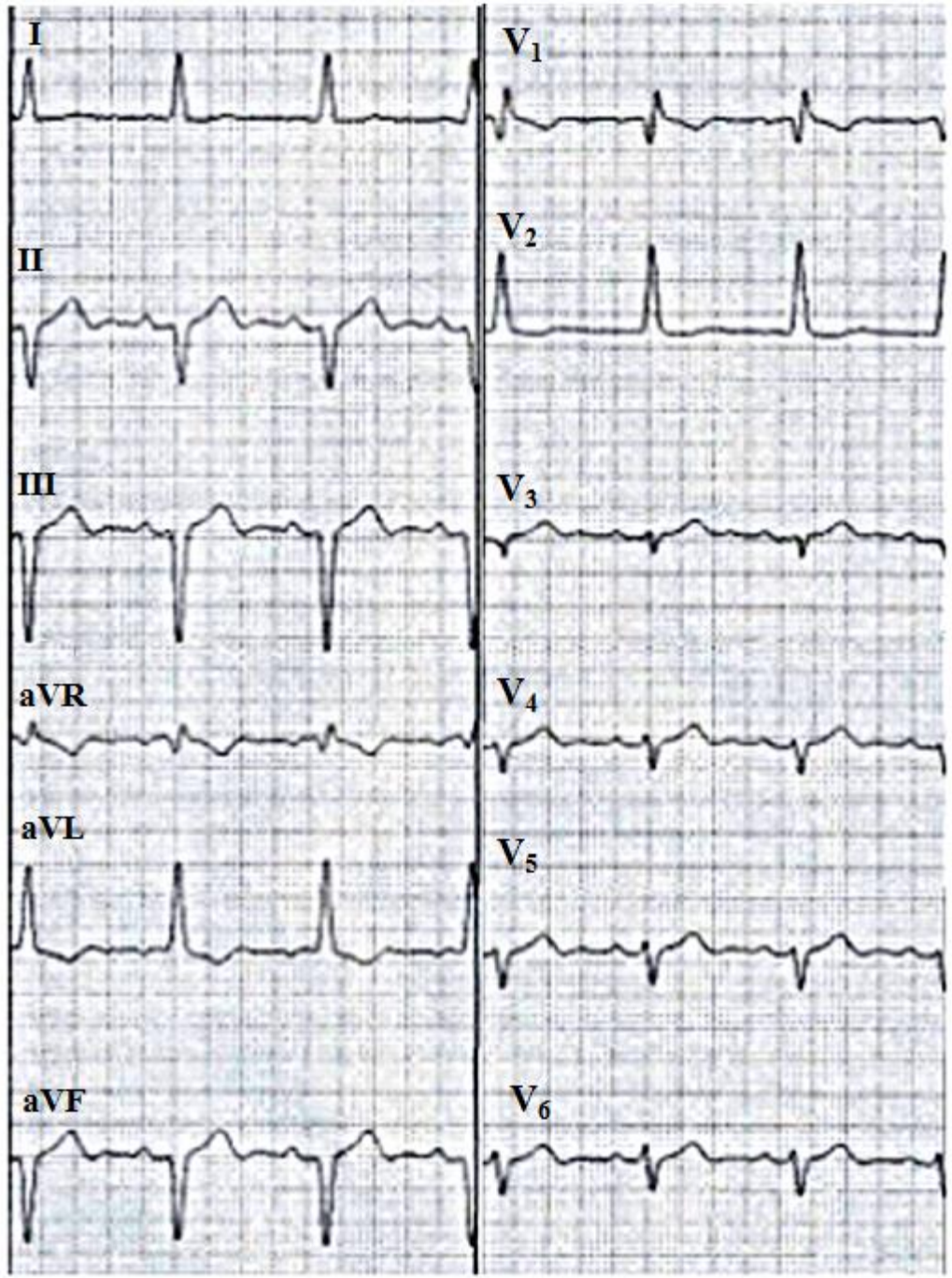
Slow heart rhythm, hyper resonant A2, systolic murmur +/4 in mitral and aortic focus. Clean lungs.

Echocardiogram exhibited only moderate concentric left ventricular hypertrophy and thickening with calcification of the mitral-aortic junction and discrete mitral valve failure.

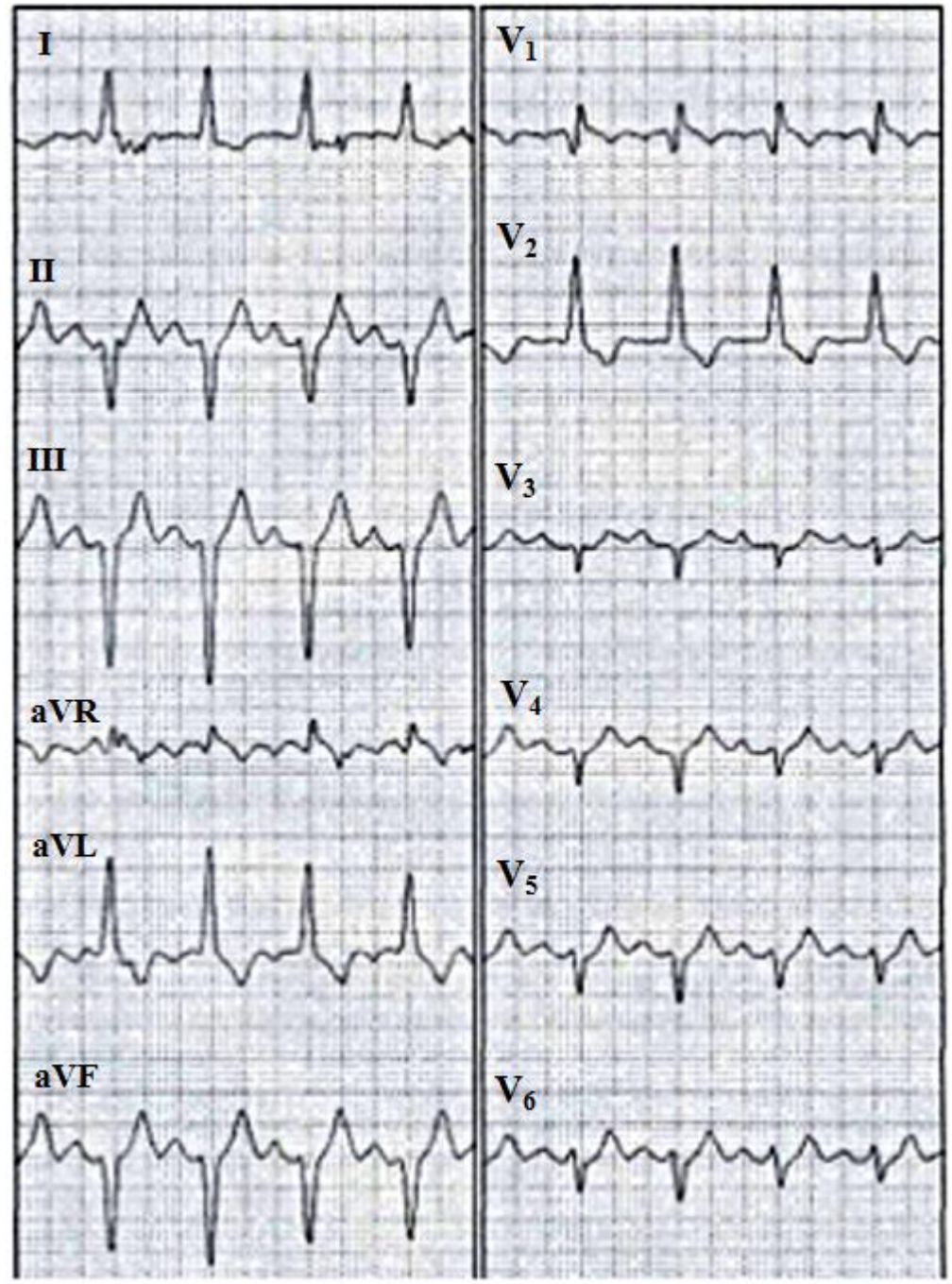
Coronary angiography; discrete lesion of the distal LADA evaluated in 40%.

Question: What is the diagnosis of the electrocardiographic sequence?

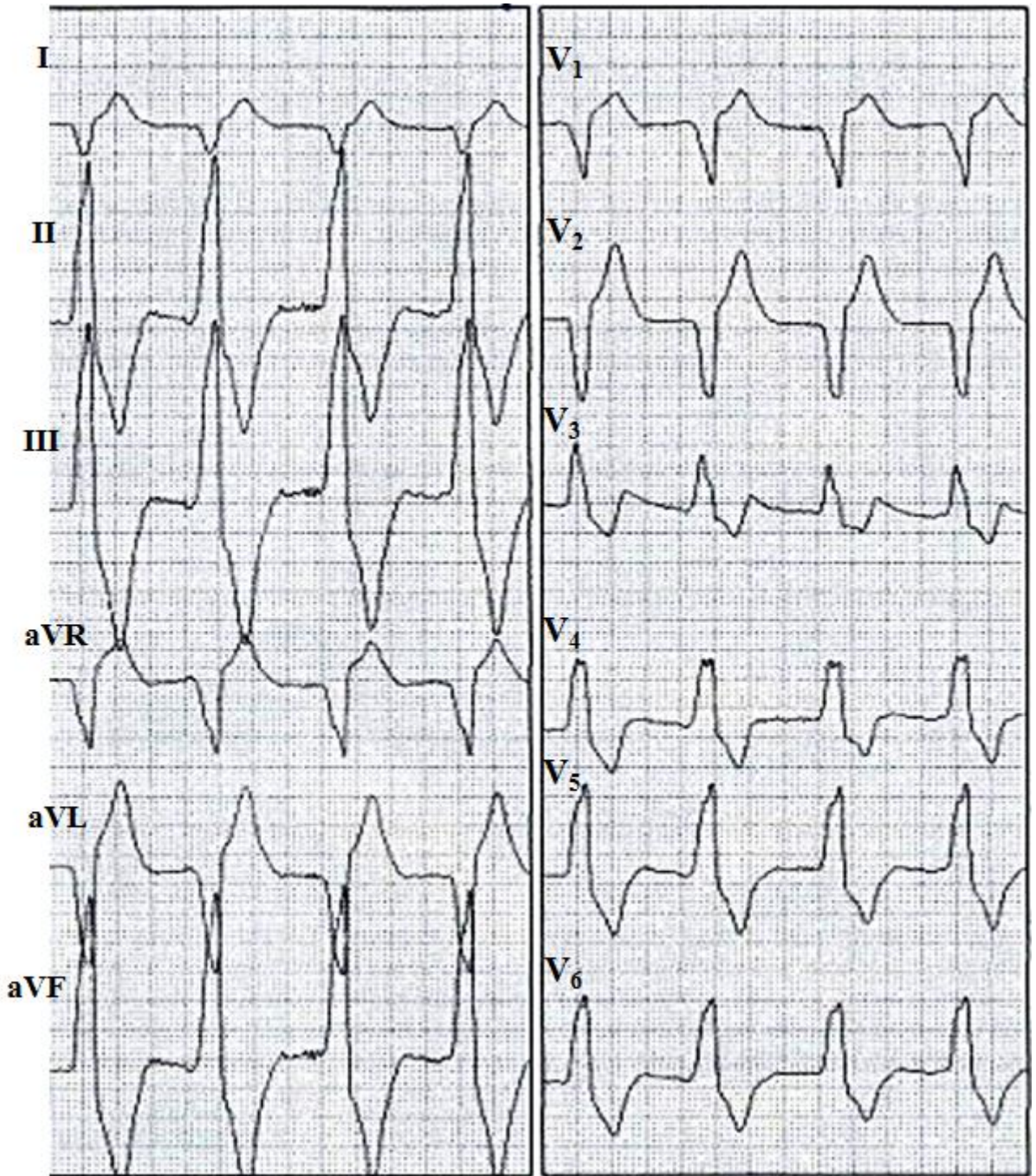
ECG-1 Performed at rest before the effort



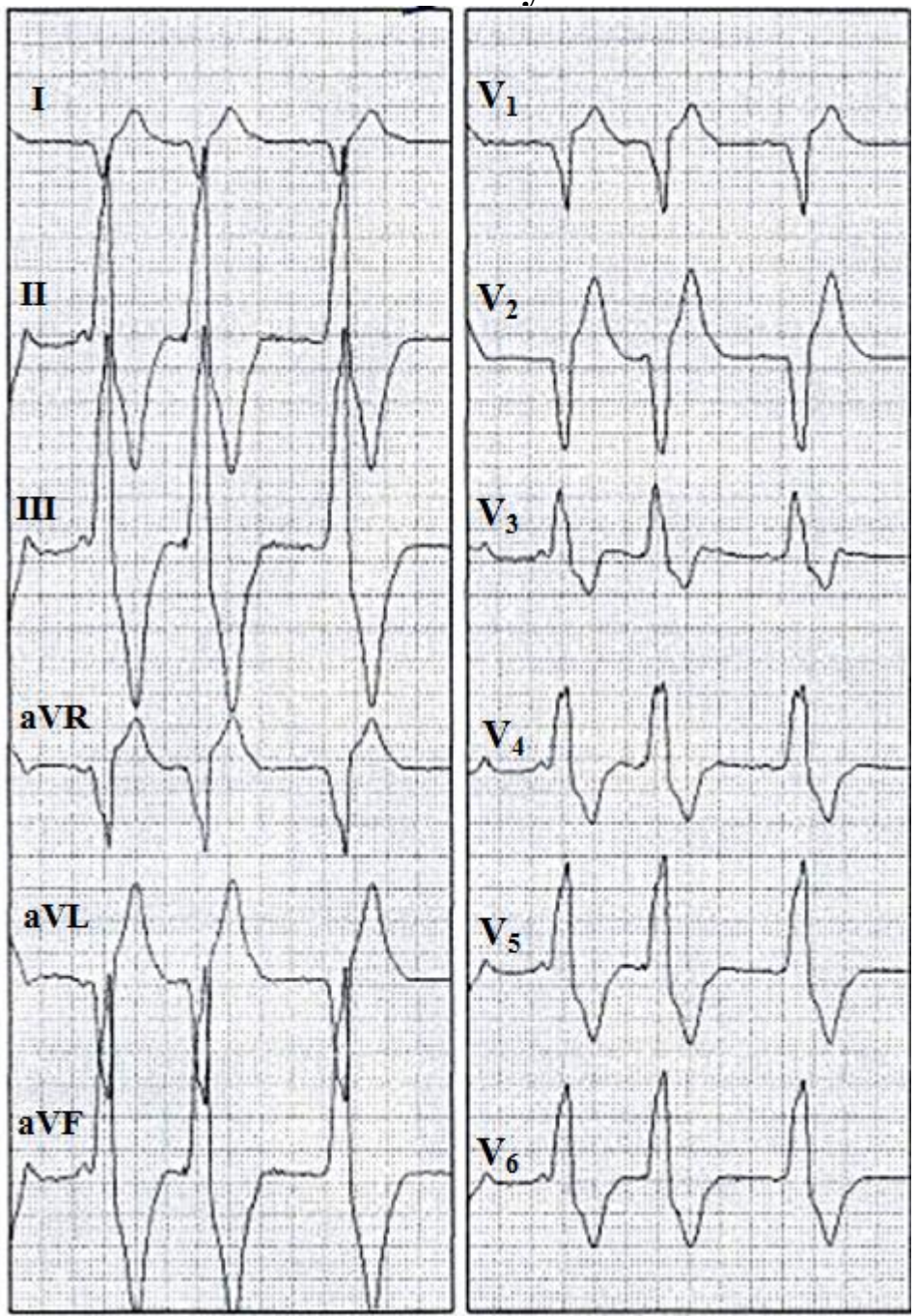
ECG-2 Performed at the beginning of the effort



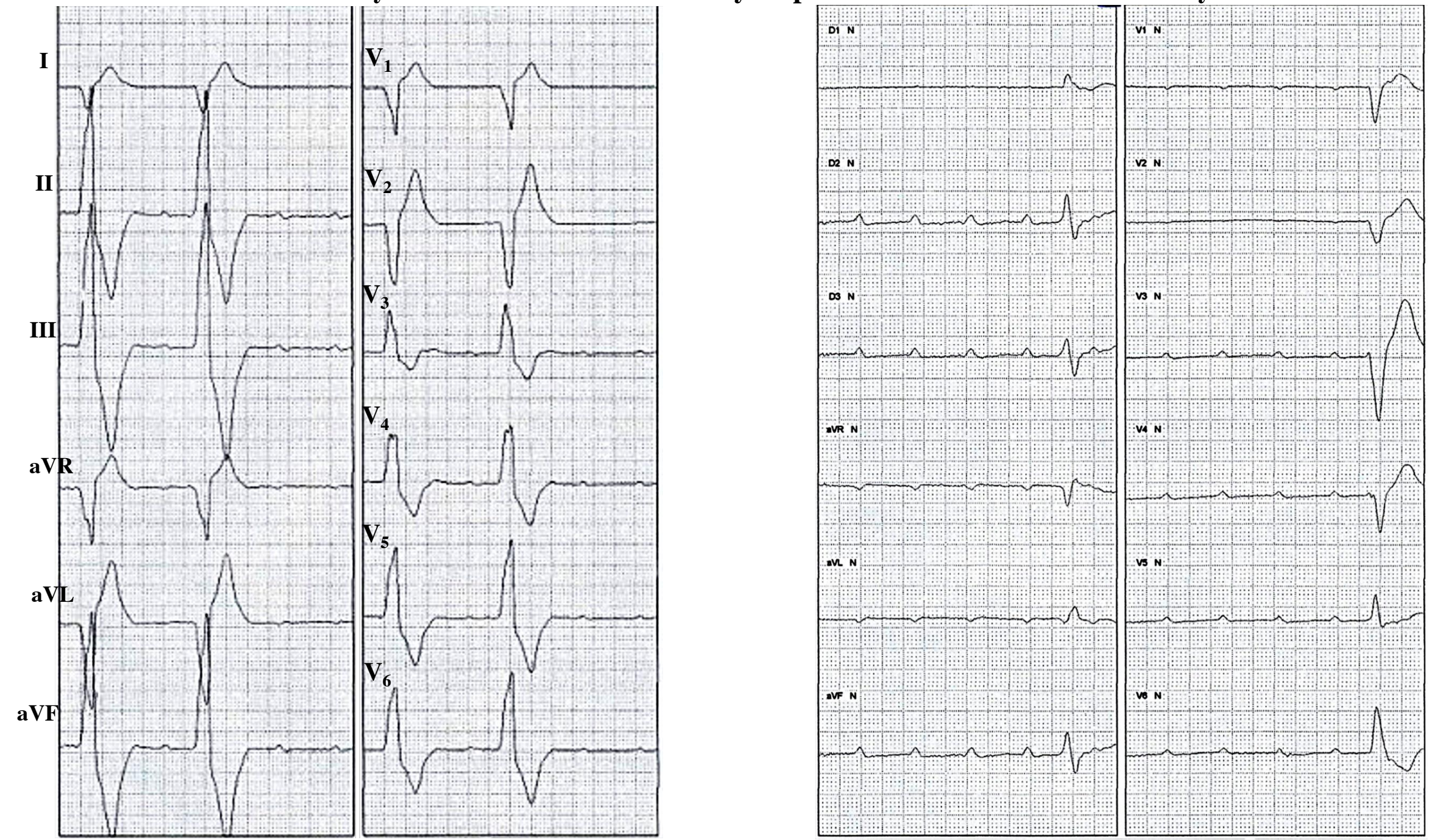
Recovery 1’

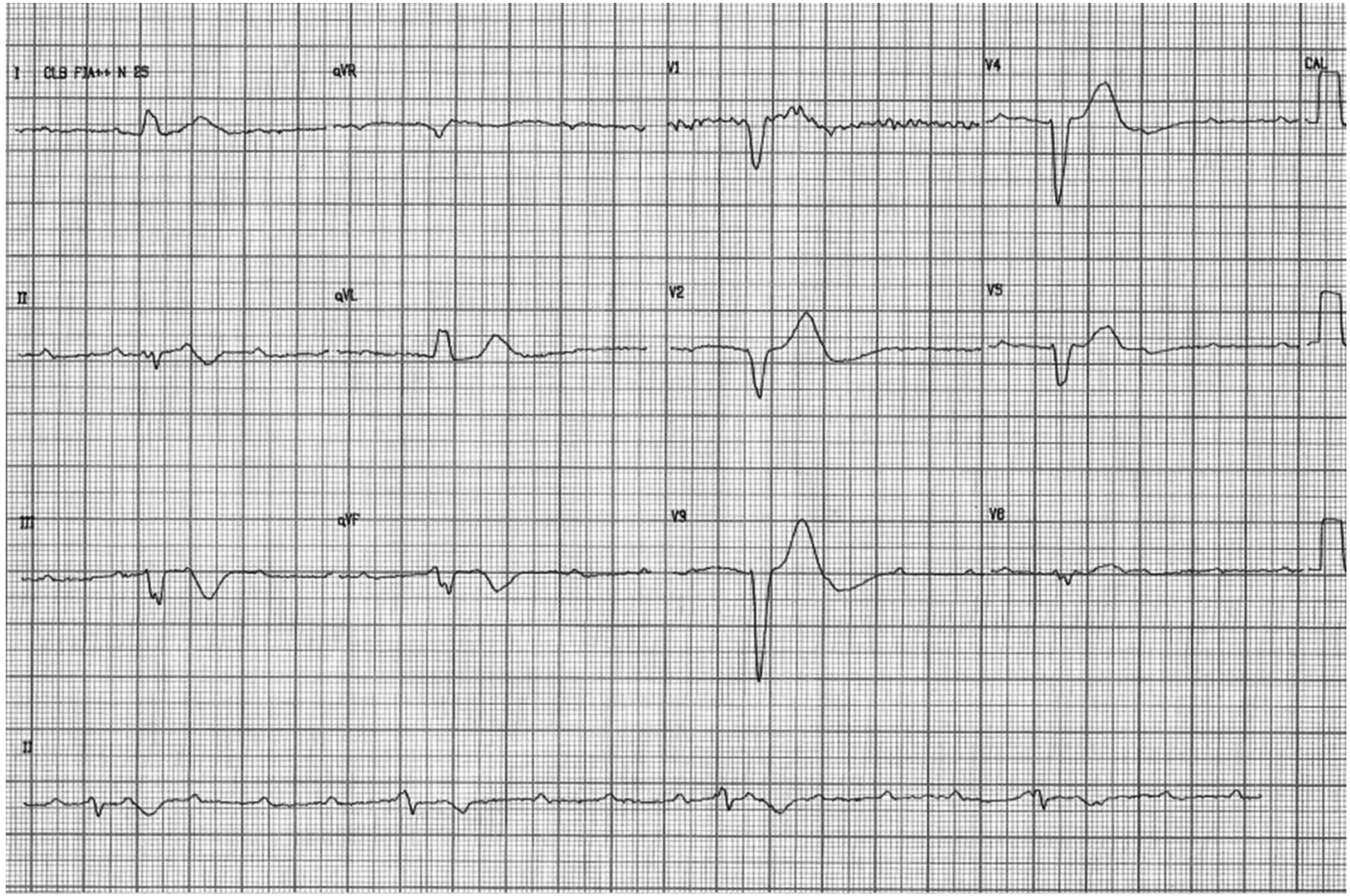


Recovery 2’



Recovery 3’ Pre-syncope Recovery 4’




I CLB F3A++ N 25
aVR
V1
V4
CAL
II
aVL
V2
V5
III
aVF
V3
V6
II

Colleagues opinions

English

Dear friends, Andrés, Raimundo, and Luiz Carlos,

This is a case of aborted sudden cardiac death, with great clinical and electrophysiological significance, in a hypertensive, 80-year-old patient. This evolution occurred in the left ventricular outflow tract, in a patient who for many years had a persistent left ventricular enlargement.

ECG1: left systolic overload of the heart base (pattern of baseline hypertrophy, frequent after 60 years of age in males and 50 years in females) manifest by deep S waves in III and concomitant high R waves in aVL (>10 mm), that in this case are accompanied by wide R waves in V2, expressing hypertrophy in the high anterior-superior septum. There is an embryological, anatomical and circulatory relation between both areas. Cardiac magnetic resonance and ECG are the only methods capable of studying the heart base and the upper septum (echo cannot study these areas).

Inverted T wave in I and aVL associated to depressed ST segment followed by positive T wave in III, suggesting fibrosis and calcification of these areas.

Left ventricular horizontalization and aorto-ventricular angulation cause basal hypertrophy.

The decrease in voltage in the precordial leads is due to left anterior hemiblock, which in 90% of the cases is accompanied by basal hypertrophy.

ECG2: it shows a pattern similar to ECG1, worsened by sinus tachycardia and increase in blood pressure values, which affect the left ventricular outflow tract.

ECG3: idioventricular rhythm with left bundle branch block pattern, which exhausts progressively (complete block by exhaustion). This phenomenon was described in the 1970s in experimentation labs, and I myself heard it explained in the clinic of the late master Pablo Chiale.

Approximately 5 years ago, a paper on sudden cardiac death in hypertensive patients with first-degree AV block was published in Circulation. The mechanism would be this: elongated His bundle, which is part of the outflow tract in a chronic hypertensive patient, that would cause calcification and fibrosis of the valvular annuli, affecting the fibrous body affecting the His bundle, inducing complete LBBB, which may progress in hypertensive, elderly patients.

Warm regards,

Samuel **Sclarovsky** MD Israel

Spanish

Queridos amigos Andrés, Raimundo y Luiz Carlos: este es um caso de muerte súbita abortada de gran importancia clínica y electrofisiológica em um octogenário hipertenso. Esta evolución se procesa en el tracto de salida del ventrículo izquierdo en um paciente que durante muchos años tuvo sobrecarga ventricular izquierda persistente.

ECG-1: Sobrecarga sistólica de la base cardíaca(patrón de hipertrofia basal frecuente después de los 60 años en el hombre y de los 50 años en la mujer) manifestada por ondas S profundas en III y concomitante ondas R altas en aVL(> 10mm) que en este caso se acompaña de R amplias em V2 que expresa hipertrofia del septo antero-superior alto. Existe uma relación embriológica, anatómica y circulatória entre ambas áreas. La resonancia magnética cardiaca y el ECG son los unicos métodos capaces estudiar la base cardiaca y el septo superior. (El ecocardiograma no consigue estudiar estas áreas).

La onda T invertida en I y aVL asociada a segmento ST deprimido seguido de T positiva em III sugiere fibrosis y calcificación de estas áreas.

La horizontalización del ventrículo izquierdo y la angulación aorta/ventrículo ocasionan la hipertrofia basal.

La disminución del voltaje em las precordiales se debe a hemibloqueo anterior izquierdo el cual en el 90% de los casos se acompaña de hipertrofia basal.

ECG-2: muestra un patrón semejante al ECG-1 agravado por la taquicardia sinusal y aumento de las cifras de presión arterial que afectan el tracto de salida del ventrículo izquierdo.

ECG-3: ritmo idioventricular con patrón de bloqueo de rama izquierda que progresivamente se va agotando(bloqueo completo por agotamiento) Este fenómeno fue descripto en los años 70 em laboratório de experimentación siendo que yo lo escuché explicado en la clínica por el malogrado maestro Pablo Chiale.

Hace aproximadamente 5 años se publicó en Circulation un trabajo de muerte súbita em hipertensos con bloqueo AV de primer grado. El mecanismo seria el siguiente um haz de His alargado formando parte del tracto de salida en um hipertenso crónico ocasionaria calcificación y fibrosis de los anillos valvares comprometiendo el cuerpo fibroso afectando el haz de His induciendo a bloqueo completo de rama izquierda que puede progresar em ancianos hipertensos.

Um faternal abrazo

Samuel Sclarovsky

Dear colleagues,

This is an older patient with long standing hypertension and calcification at the mitral-aortic junction which can explain the conduction disturbances.
The initial ECG shows sinus rhythm, right bundle branch block, and left anterior hemiblock. During exercise he probably developed paroxysmal A-V block (the tracings showing the transition form 1:1 conduction to A-V block is not shown). During A-V block we observe a ventricular escape with left bundle inferior axis morphology. This escape has an irregular cycle length and slows down during recovery, suggesting that it was maintained by the increased adrenergic tone associated with exercise.
At rest his escape was too slow and temporary pacing was required.

Thank you for the nice tracings!

Mario González
Penn State Hershey Heart and Vascular Institute
500 University Drive
Hershey, PA 17033Tel: 800-243-1455Fax: 717-531-4077

mgonzalez@hmc.psu.edu

ECG-1 basal: ritmo sinusal, atraso de condução pelo ramo direito e bloqueio divisional anterossuperior esquerdo (BDAS). ECG 2: Durante esforço: padrão eletrocardiográfico mantido. ECG-3: Primeiro e segundo minutos da recuperação: Ritmo idioventricular acelerado. ECG-4: Terceiro minuto da recuperação: : diminuição do automatismo do ritmo idioventricular. ECG-5: Quarto minuto da recuperação: bloqueio AV total com escape de morfologia de bloqueio de ramo esquerdo.
Conclusão: Paciente com doença binodal (Distúrbio de condução pelo ramo direito e BDAS) com bloqueio de fase III durante esforço e presença de RIVA, mascarando BAVT na fase inicial de recuperação.
Os achados indicam doença importante no sistema de condução e justificam o implante de marcapasso definitivo.
Dr. José Grindler e col. Acácio F. Cardoso, Marco A. B de Lima, Isaac Valdemiro, Larissa B. Talharo, Gabriel A. D. Kreling e Layara Lipari.
Diretor de Serviço: Eletrocardiologia HC
Faculdade de Medicina USP

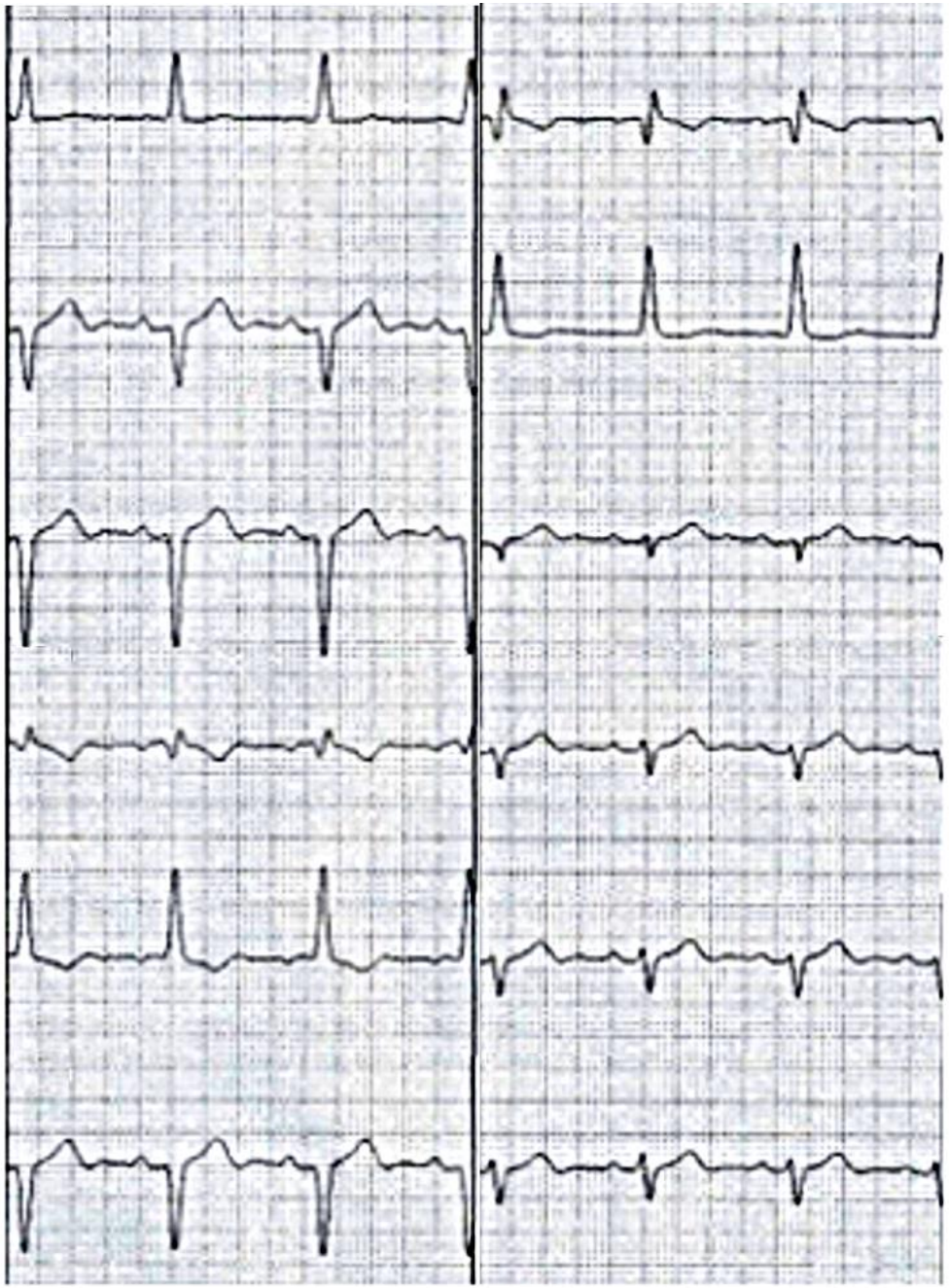
English

ECG-1 baseline: sinus rhythm, right end conduction delay in the right branch and left anterior divisional/fascicular block (LAFB).
ECG 2: During effort: Similar electrocardiographic pattern (maintained pattern).
ECG-3: First and second minutes of recovery: Accelerated idioventricular rhythm (AIVR)
ECG-4: third minute of recovery:: decreased automaticity of AIVR.
ECG-5: Fourth minute of recovery: complete AV block with escape rhythm with left bundle branch block morphology.
Conclusion: Patient with intraventricular conduction disease (conduction disorder in the right bundle branch and left anterior fascicle) with phase III block during exertion and presence of AIVR, masking a total AV block in the early stage of recovery.
The findings indicate severe disease in the intraventricular conduction system and justify a permanent pacemaker implantation.
Dr. José Grindler e col. Acácio F. Cardoso, Marco A. B de Lima, Isaac Valdemiro, Larissa B. Talharo, Gabriel A. D. Kreling e Layara Lipari.
Diretor de Serviço: Eletrocardiologia HC
Faculdade de Medicina USP

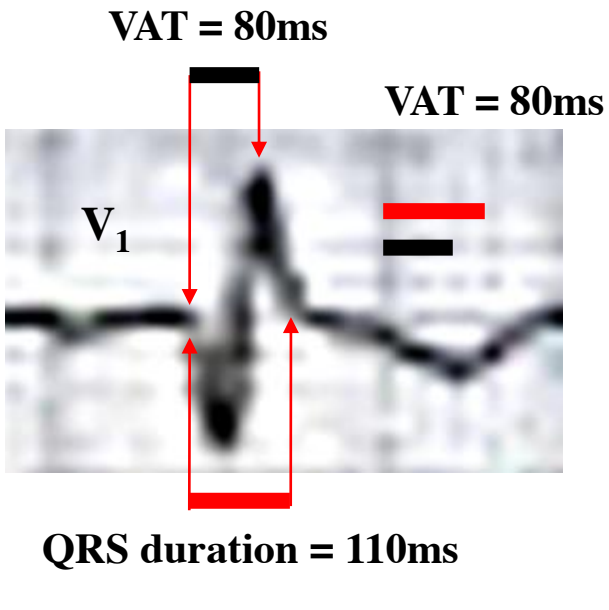
Dr. José Grindler

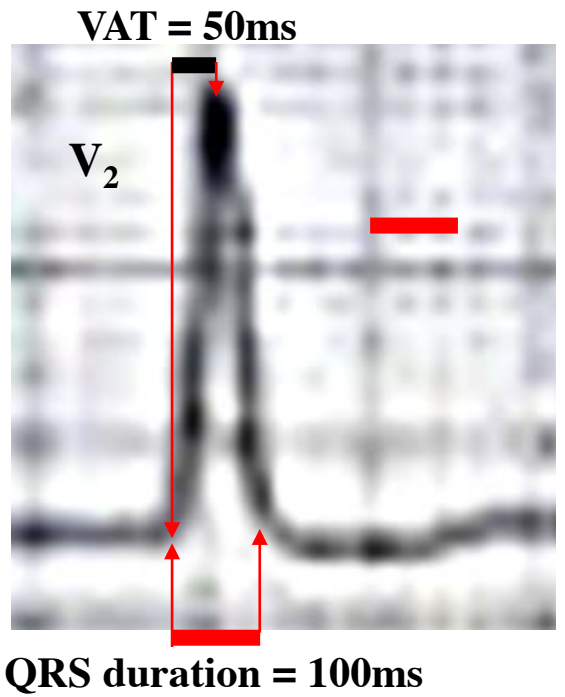
Final Comments

ECG-1 Performed at rest before the effort



ECG diagnose: Extreme left axis deviation: (QRS axis in - 60°), small and sharp r wave in II, III and aVF followed by deeper S waves rS. Also rS pattern leads is recorded in leads V5-V6 as a result of the superiorly directed forces. Accordingly, S waves tend to disappear in leads above the normal level and are deeper when the electrodes are placed below the normal level (**Elizari 2007**): left anterior fascicular block (LAFB).
Qr in V_1, prolonged Ventricular Activation Time (VAT) in V_1-V_2 (VAT V_1 = 80ms and V_2 = 50ms).

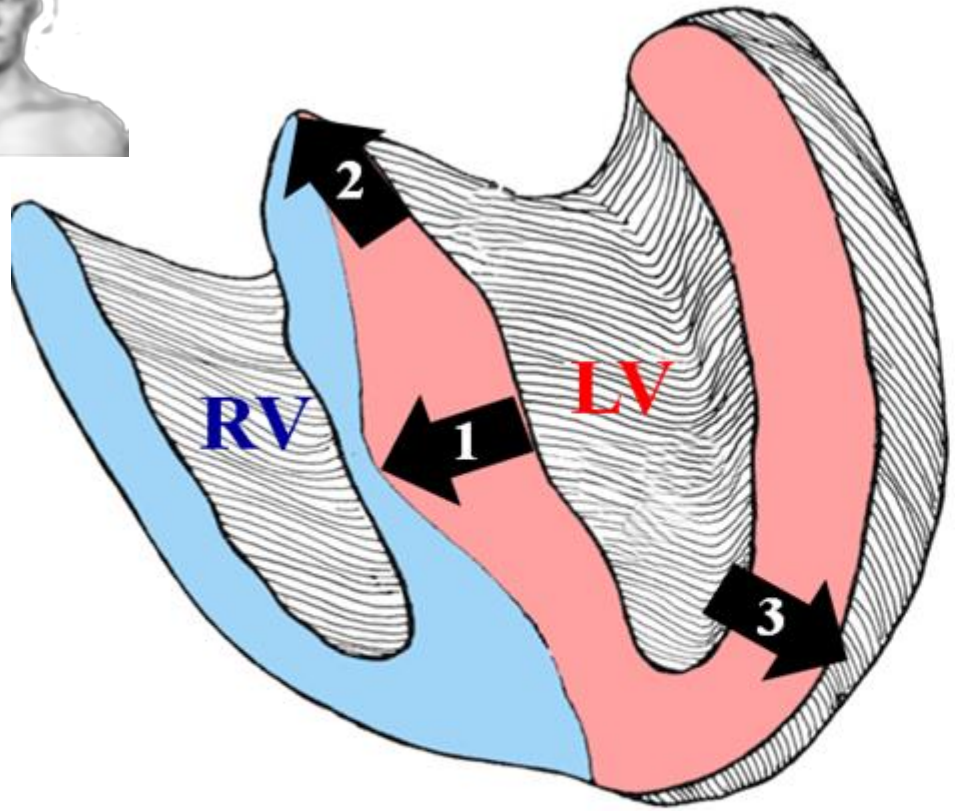




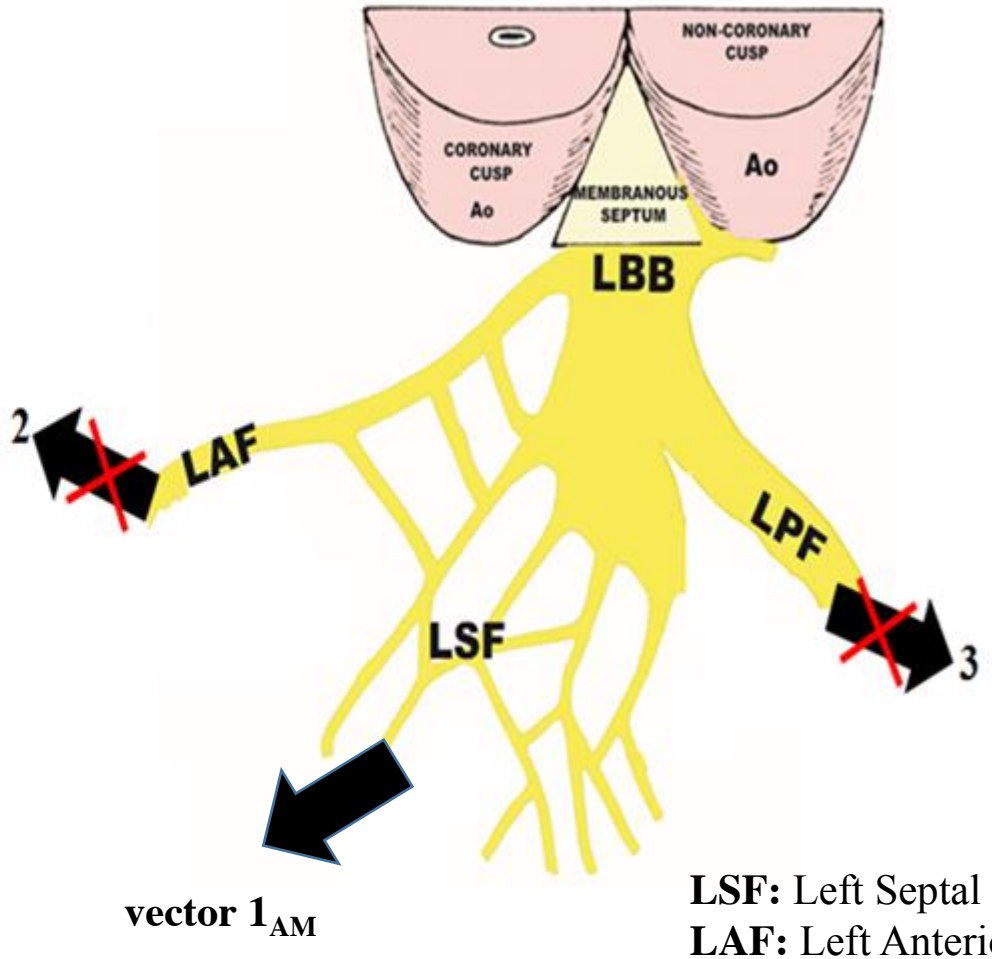
▬ Prolonged Ventricular Activation Time (VAT) in V1-V2= 80-50ms. Normal values of VAT < 50ms in V5 or V6 < 30ms in V1-V2 (**Pérez-Riera 2016**).

▬ QRS duration = 100ms. R wave voltage in V2 ≥ 15mm, absence of initial q wave in left leads I, aVL, V5-V6 (consequence of absence of the first left middle septal vector, first anteromedial vector (1_{AM}) or Penaloza and Tranchesi vector (**Penaloza 1965**)). **Conclusion:** Left Anterior Fascicular Block (LAFB) + Left Septal Fascicular Block (LSFB): Left bifascicular block.

Sequential representation of normal initial 10-20ms ventricular activation in the frontal plane



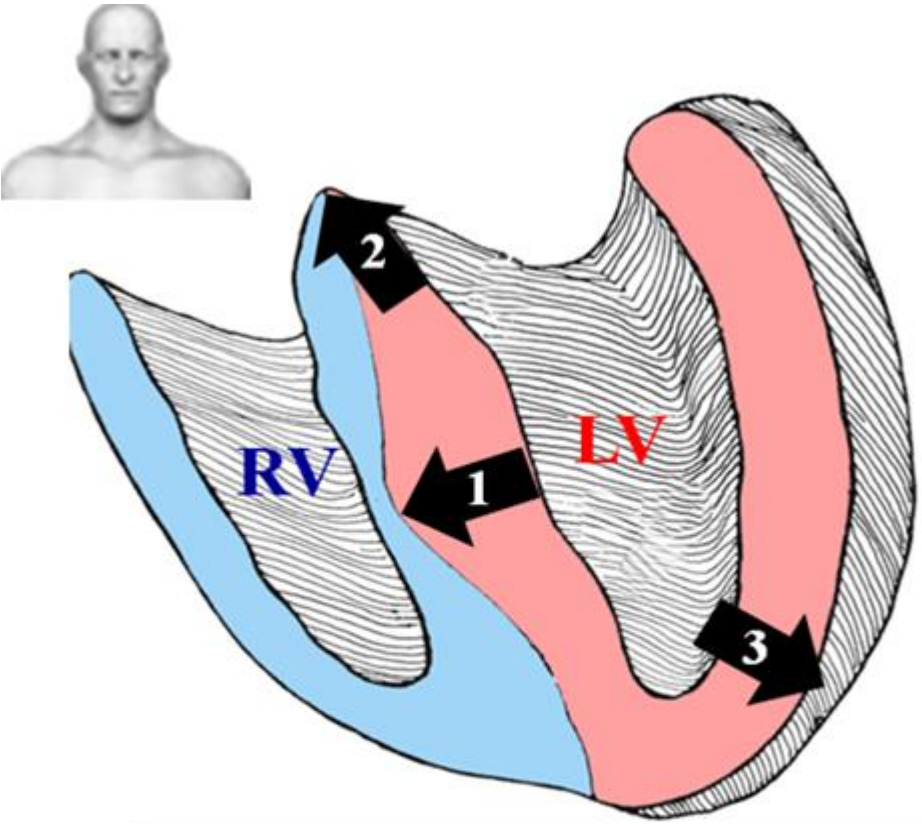
Initial ventricular despolarization from 0 to 10 ms
1) Central & apical region dependent of LSF 2) Anterosuperior region dependent of LAF 3) Posteroinferior region dependent of LPF



LSF: Left Septal Fascicle
LAF: Left Anterior Fascicle
LPF: Left Posterior Fascicle

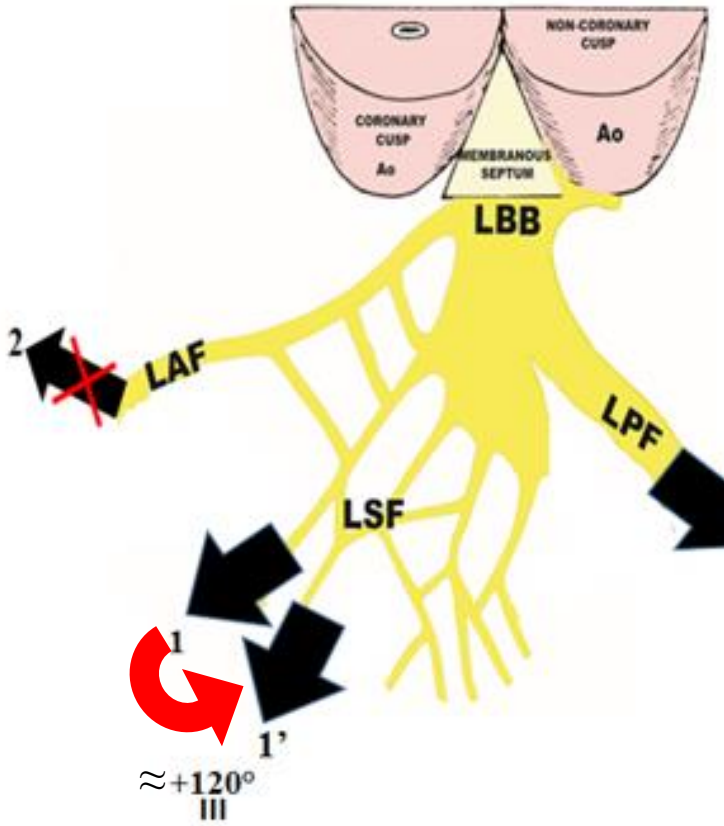
Notes: In normal conditions vectors 2 (**LAF**) and 3 (**LPF**) have opposite directions, and consequently cancel each other. So, the only vector that expresses is vector 1 (**LSF**) of the left middle third of the left interventricular septum surface, vector 1_{AM} (anteromedial) or Peñaloza and Tranchesi vector (**Penaloza 1955**) which is directed downward and rightward (80% of cases) or leftward (remaining 20%).

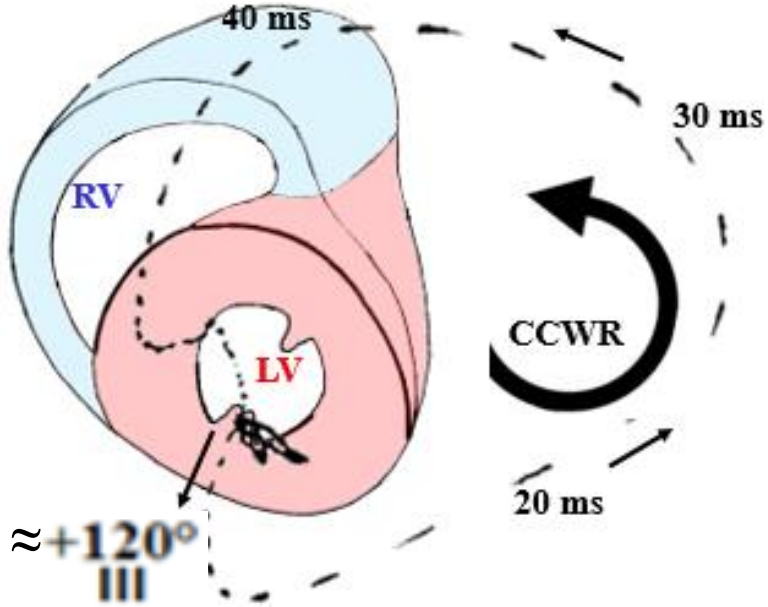
Sequential representation of initial 10 to 20ms ventricular activation in the FP in isolated left anterior fascicular block



Initial ventricular despolarization from 0 to 10 ms

1) Central & apical region dependent of LSF
2) Anterosuperior region dependent of LAF
3) Posteroinferior region dependent of LPF



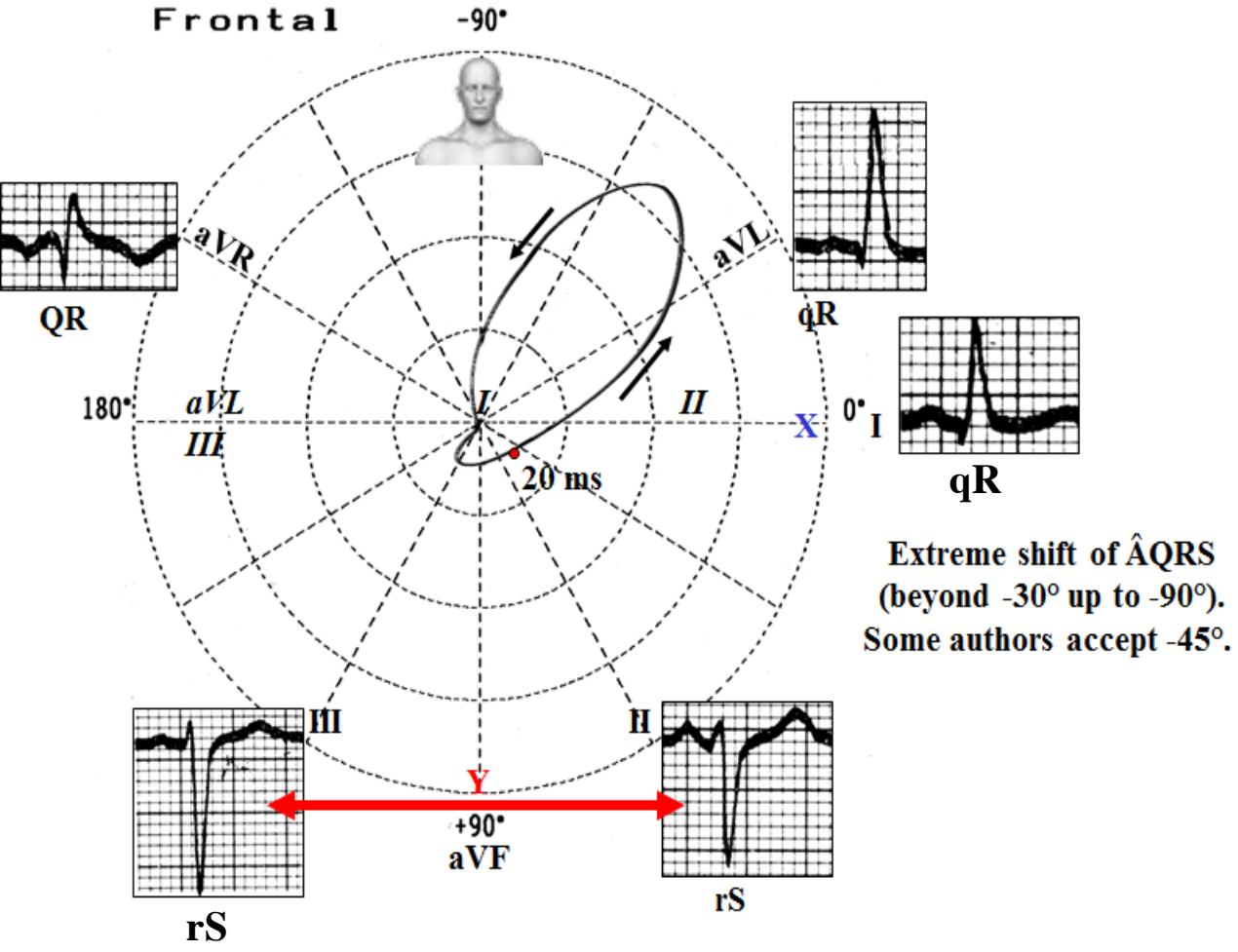


LSF: Left Septal Fascicle
LAF: Left Anterior Fascicle
LPF: Left Posterior Fascicle
LBB: Left Bundle Branch
RV: Right Ventricle
LV: Left Ventricle
CCWR: Counterclockwise rotation

The first 10-20ms QRS vector depicts an inferior and rightward shift in the frontal plane (≈+120° /III lead) (**Elizari 2007**) responsible for the presence of a small initial q wave in leads I and aVL and a small and sharp r wave in III, aVF and II.

Differential diagnosis between isolated LAFB and LAFB associated with LSFB

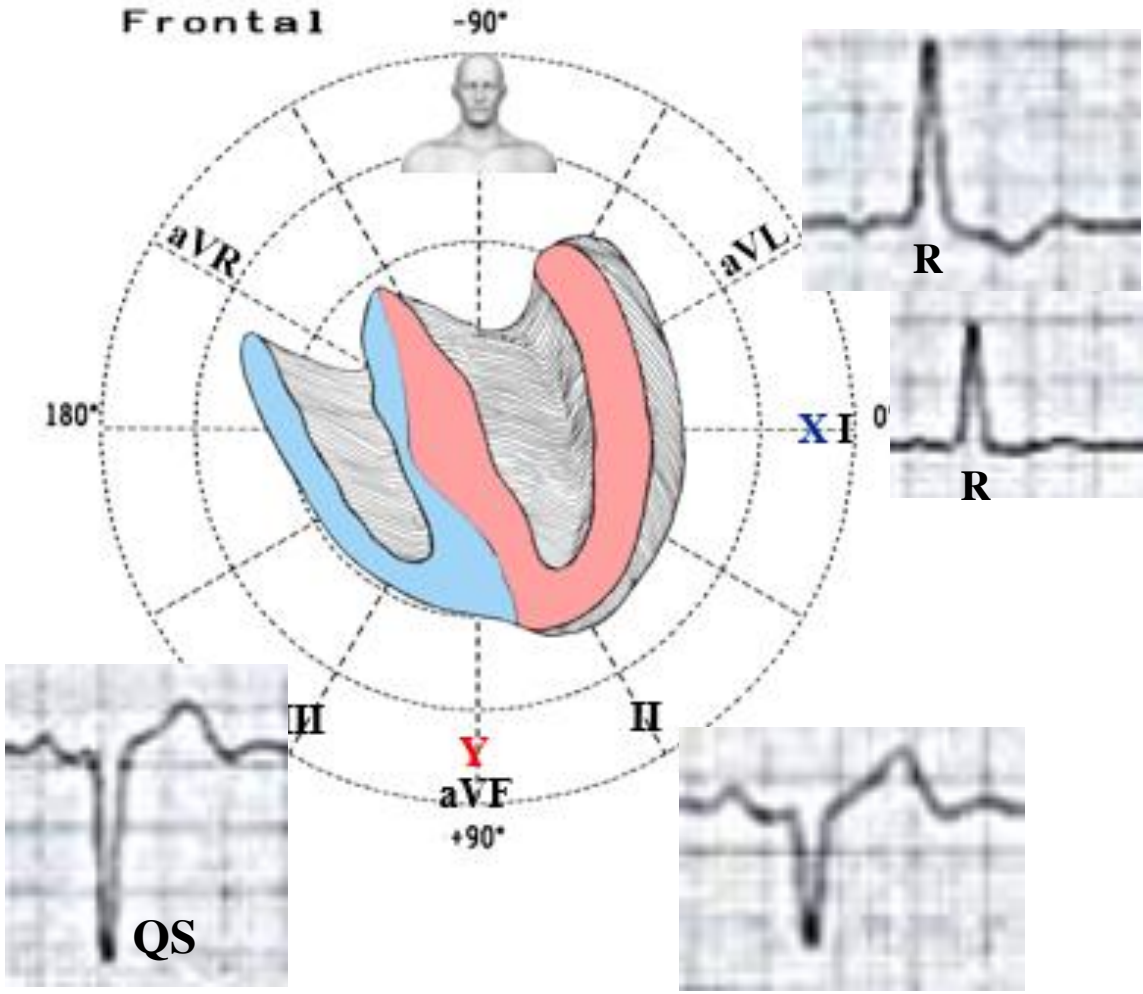
Isolated LAFB in Frontal Plane



Extreme shift of ÂQRS (beyond -30° up to -90°). Some authors accept -45°.

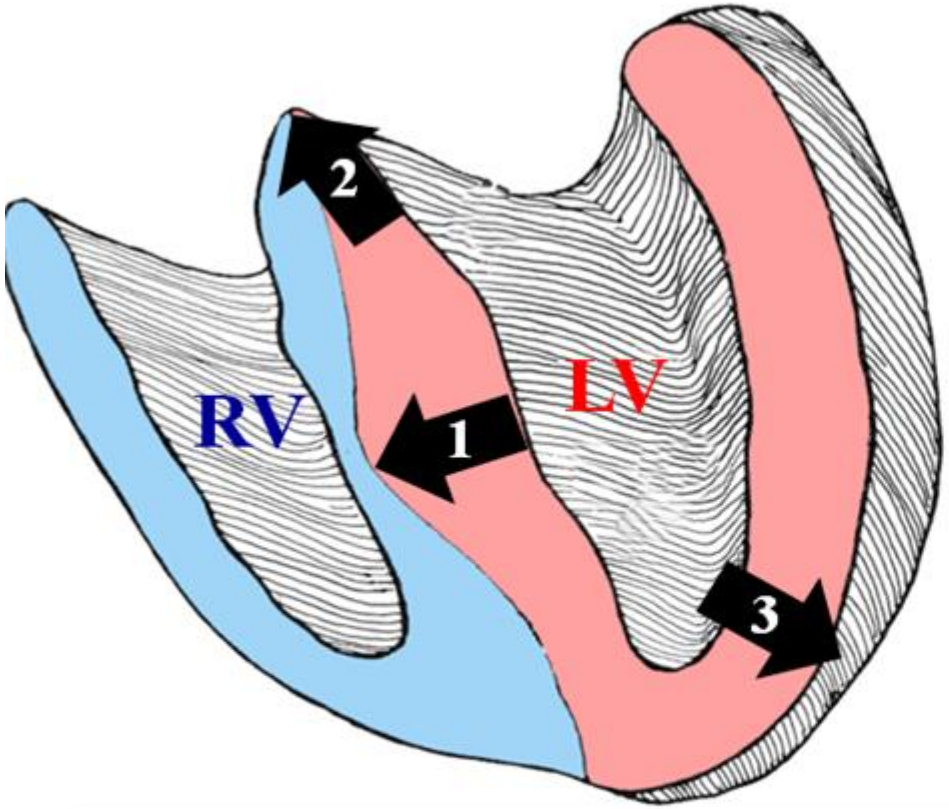
ECG/VCG correlation in the frontal plane in the typical LAFB. The following stand out: extreme deviation of QRS axis in the left superior quadrant beyond 30º (or -45º); vector from initial 10 to 20 ms heading below and rightward; QRS loop of CCW rotation; rS pattern in inferior leads; SIII > SII; rIII > rII; qR pattern in I and aVL.

LAFB + LSFB in Frontal Plane

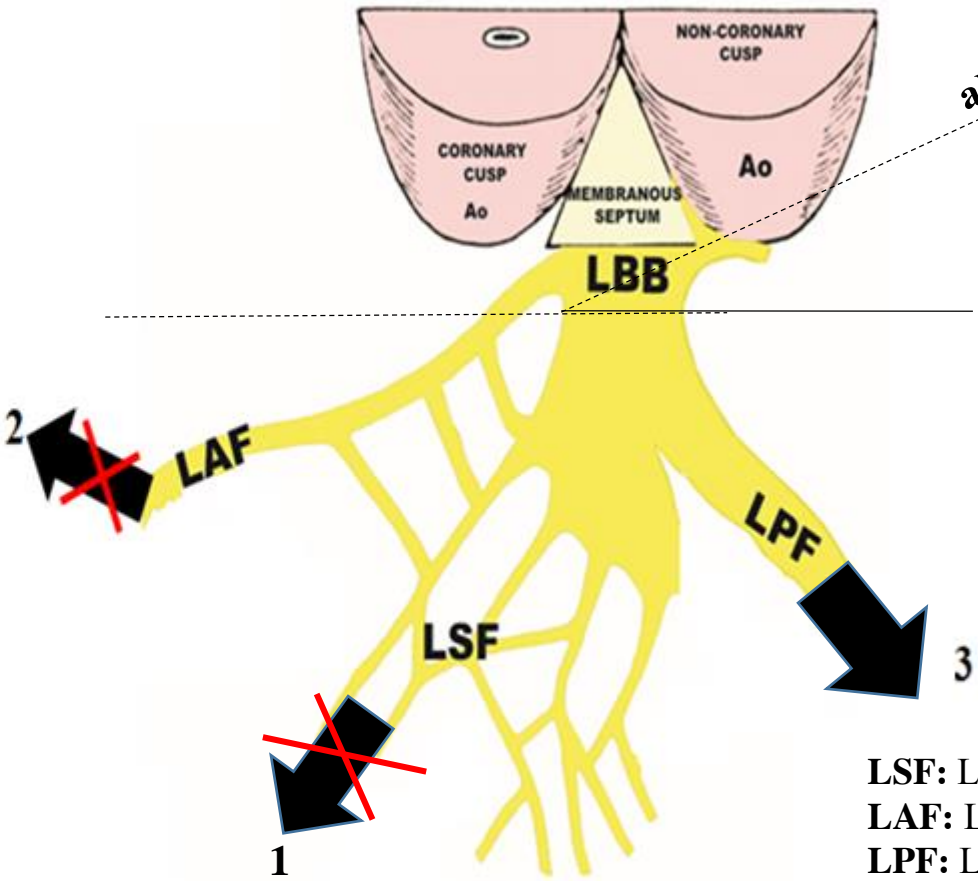


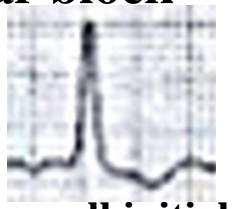
Concomitant blockade of the LAF and LSF causes initial activation in the posterior-inferior region dependent of the LPF; consequently, the initial activation is directed to the left and below, disappearing the small initial q wave I and aVL and the initial small r wave in leads III, aVF and embryonic r wave in II dependent of not blocked LPF.

Sequential representation of initial 20ms ventricular activation in the frontal plane in left anterior fascicular block(LAFB) associated with left septal fascicular block(LSFB) . It is a variety of left bifascicular block

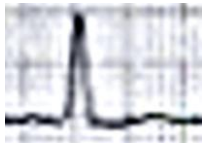


Initial ventricular despolarization from 0 to 10 ms
1) Central & apical region dependent of LSF 2) Anterosuperior region dependent of LAF 3) Posteroinferior region dependent of LPF





The small initial q wave disappear



LSF: Left Septal Fascicle
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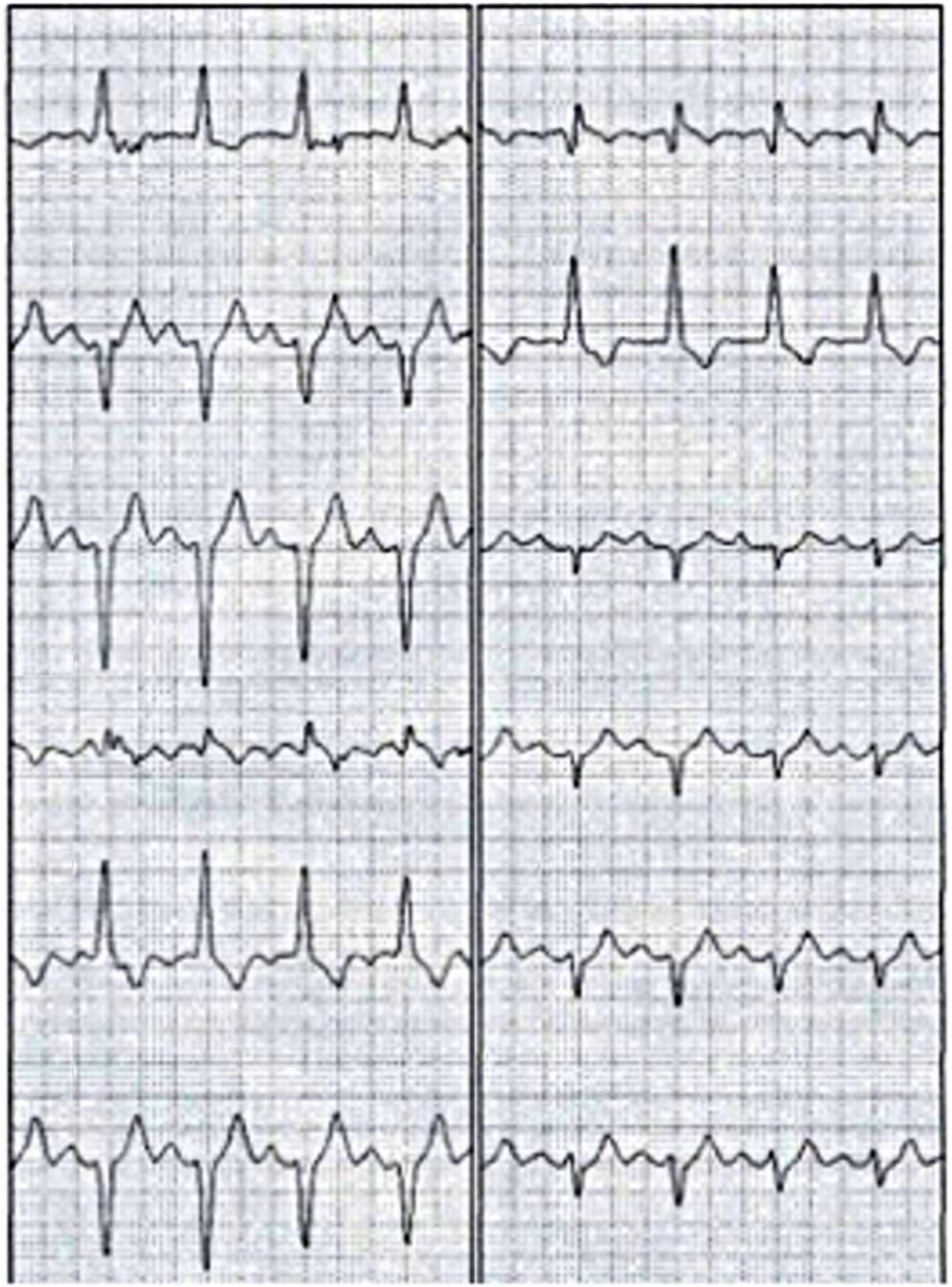
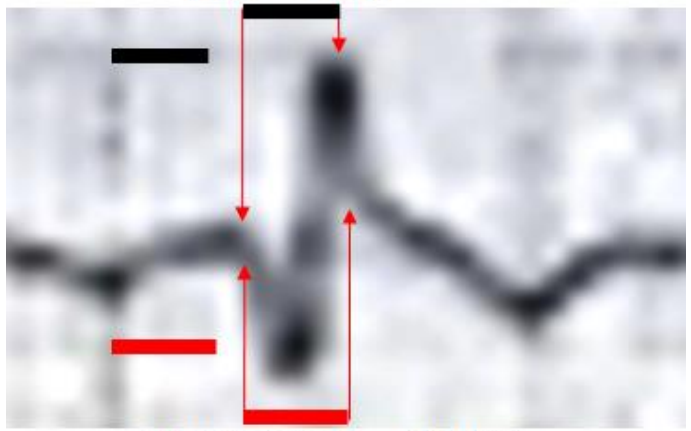
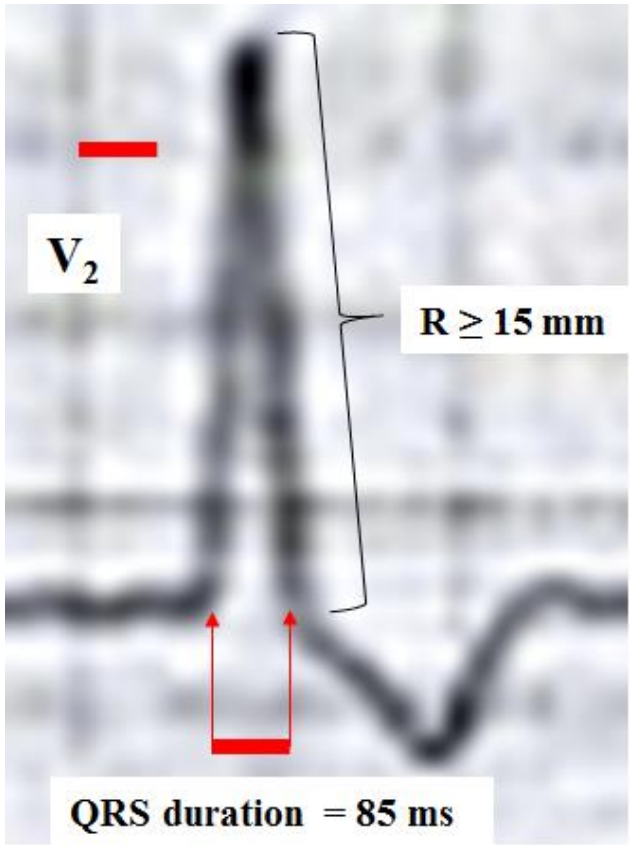
LBB: Left Bundle Branch
RV: Right Ventricle
LV: Left Ventricle

Concomitant blockade of LAF and LSF causes initial activation in the posterior-inferior region dependent of the LPF; consequently, the initial activation is directed to the left and below, disappearing the small initial q wave I and aVL and the initial small r wave in inferior leads III and aVF. Eventually an embryonic initial r wave is registered in II dependent of not blocked LPF.

ECG-2 Performed at the beginning of the effort







ECG diagnose: Extreme left axis deviation: (QRS axis in - 60°), small and sharp r wave in II, III and aVF followed by deeper S waves rS. Also rS pattern leads is recorded in leads V5-V6 as a result of the superiorly directed forces. Accordingly, S waves tend to disappear in leads above the normal level and are deeper when the electrodes are placed below the normal level (**Elizari 2007**): left anterior fascicular block (LAFB).

Qr in V_1, very prolonged Ventricular Activation Time (VAT) in V_1 (VAT = 90ms). Normal values of VAT < 50ms in V5 or V6 < 30ms in V1-V2 (**Pérez-Riera 2016**). QRSd = 100ms. R wave voltage in V2 ≥ 15mm, absence of initial q wave in left leads I, aVL, V5-V6 (consequence of absence of the first left middle septal vector, first anteromedial vector (1_{AM}) or Penaloza and Tranchesi vector (**Penaloza 1965**). **Conclusion:** Left Anterior Fascicular Block (LAFB+ Left Septal Fascicular Block (LSFB): Left bifascicular block.

Electrocardiographic characterization of isolated Left Septal Fascicular Block

(MacAlpin 2002-2003; Dabrowska 1978; Abrahao 1979; Tranchesi 1979; Riera 2008a,b; Uchida 2006; Pastore 2009; Pérez-Riera 2011; 2013; 2015a,b; 2016a,b; Ibarrola 2014)

I. Normal QRS duration or with a minor increase (up to 110 ms). When associated with other fascicular or bundle blocks it could be ≥ 120 ms.
II. FP leads with no modifications: normal QRS.
III. Increased ventricular activation time or intrinsic deflection V1 and V2: ≥ 35 ms.
IV. R wave voltage of V1 ≥ 5 mm;
V. R/S ratio in V1 > 2;
VI. R/S ratio in V2 > 2;
VII. S wave depth in V1 < 5 mm;
VIII. Possible initial Q wave in V2 and V3 or V1 and/or V2;
IX. R wave of V2 > 15 mm;
X. RS or Rs pattern in V2 and V3 (frequent rS in V1) with R wave "in crescendo" from V1 through V3 and decreasing from V5 to V6;
XI. Absence of q wave in left precordial leads V_5, V_6 and I (by absence of vector 1_{AM}). One first needs to exclude ILBBB, CLBBB and WPW;
XII. Intermittent PAF during hyperacute phase of myocardial infarction (**Madias 1993**), or during an exercise stress test in patients with severe myocardial ischemia (**Gambetta 1973; Moffa 1997; Uchida 2006**) and during early atrial extra stimuli with some degree of ventricular aberration (**Hoffman 1976**);
XIII. Appearance of intermittent, rate-dependent initial q/Q wave in V_1 and/or V_2;
XIV. The last Brazilian Guidelines for Interpreting Rest Electrocardiogram (**Pastore 2016**) provided the following criteria: QRS duration < 120 ms, in general, close to 100 ms. The appearance of LSFB does not increase QRSD by more than 25 ms, due to multiple interconnections between the fascicles of the LBB ("passageway zone" of Rosenbaum). The QRS complex is slightly prolonged between 100 to 115 ms. Thus, LSFB pattern with a prolonged QRSD indicates the presence of additional conduction disturbances such as other fascicular blocks, RBBB, MI, focal block, or a combination of these; ≥15 mm voltage R waves in V_2 and/or V_3 or from V_1; increasing for all intermediary precordial leads and decreasing from V_5 to V_6; "r" wave jump may occur from V_1 to V_2 ("rS" in V_1 for R in V_2);
XV. Absence of QRS axis shift in the frontal plane;
XVI. T wave polarity most of the times, negative in right precordial leads.

Note: all these criteria are valid in absence of RVH, septal hypertrophy or lateral-wall MI (old dorsal), normal variant, misplace of precordial electrodes, athlete heart, RBBB, type A WPW, LVH, Duchenne-Erb myopathy, pseudo-dextrocardia, endomyocardiofibrosis, and other causes of prominent QRS anterior forces (PAF).

Vectorcardiographic characterization (all in the HP)

(De Pádua 1976-1976-1977-1977-1978; Alboni 1979; Inoue 1983; Young 1975; Nakaya 1978; Tranchesi 1979):

I. QRS loop in the HP with an area predominantly located in the left anterior quadrant ($\geq {}^{2}/_{3}$ of the loop area facing the orthogonal X lead: 0º to ±180º);

II. Absence of normal convexity to the right of the initial 20 ms of the QRS loop;

III. Discrete rightward-orientation with moderate delay of the vector from 20 to 30 ms;

IV. Anterior location of the 40 to 50 ms vector;

V. Posterior location with a reduced magnitude of the vector from 60 to 70 ms;

VI. Maximal vector of the QRS loop located to the right of +30º;

VII. Intermittent or transient anterior displacement of QRS loop (**Moffa 1997; Pérez-Riera 2015**);

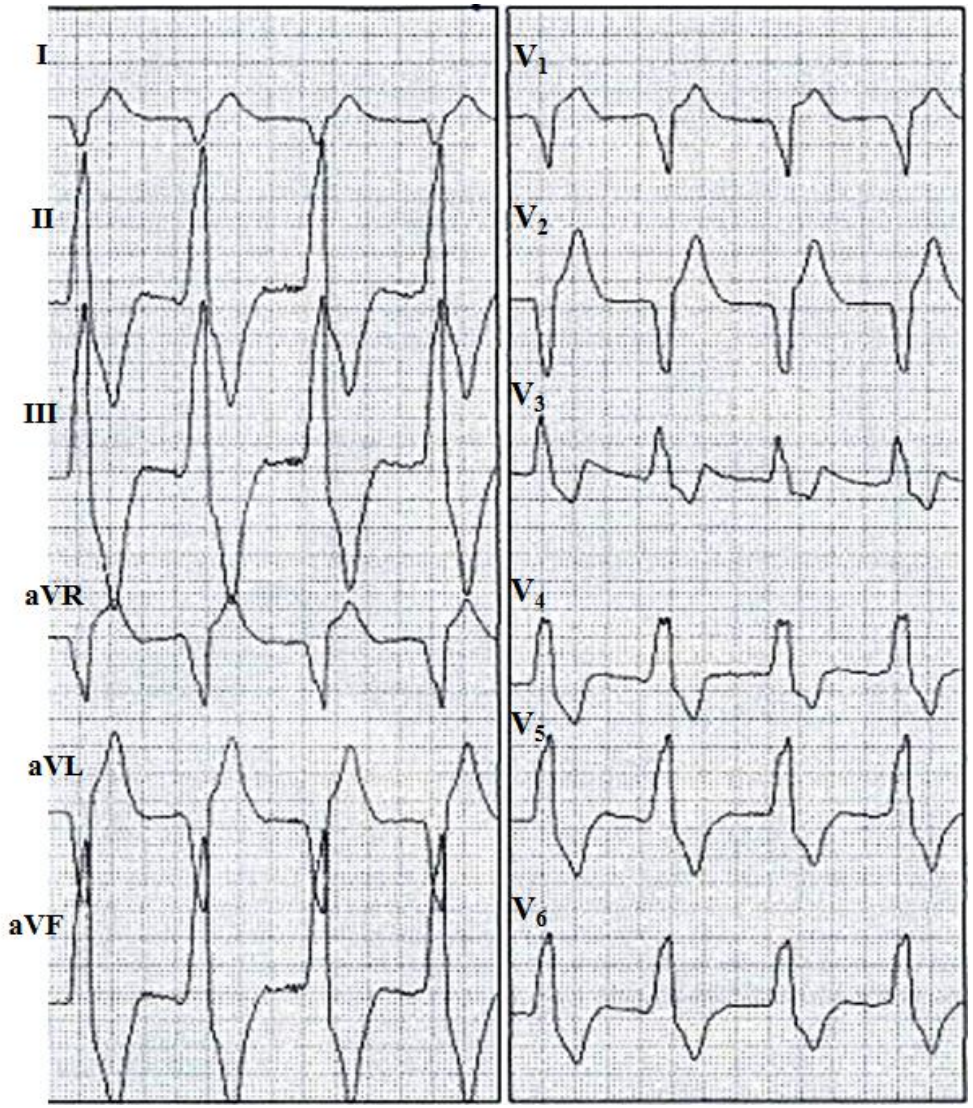
VIII. T loop with posterior orientation tendency (useful for the differential diagnosis with lateral MI);

IX. The QRS loop rotation may be:

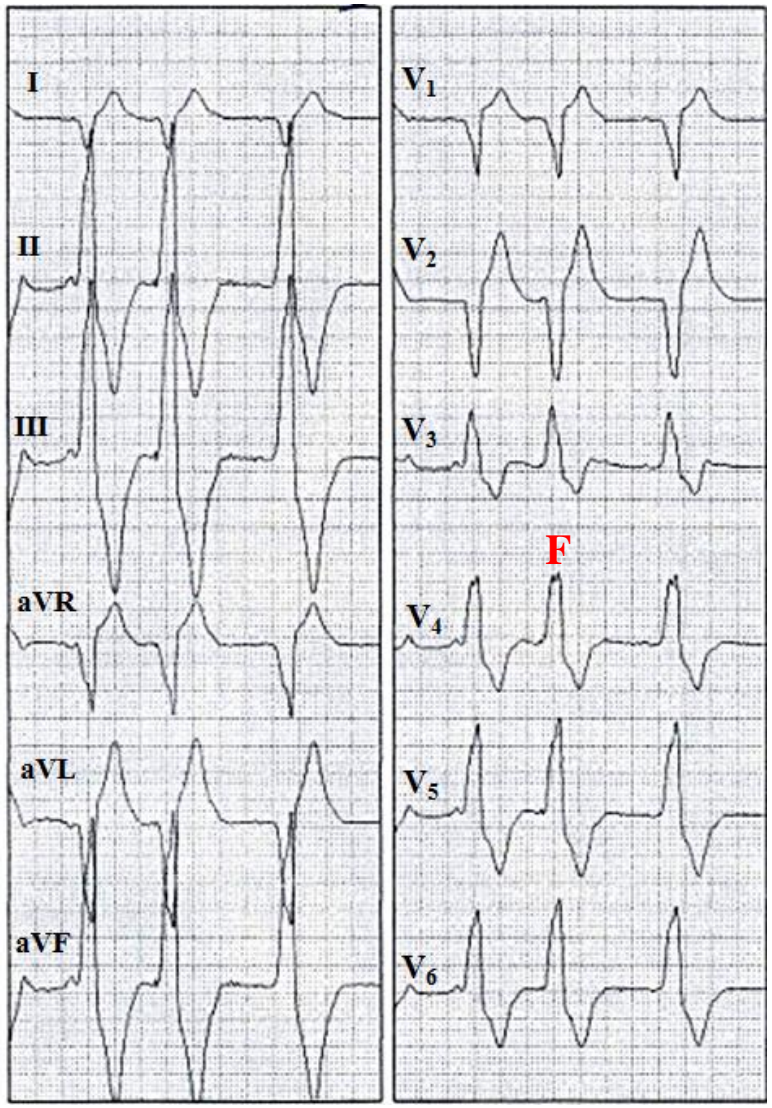
1) Counterclockwise: incomplete LSFB.

2) Clockwise: advanced or complete LSFB or in association with complete RBBB, LAFB, or LPFB.

Recovery 1’



Recovery 2’

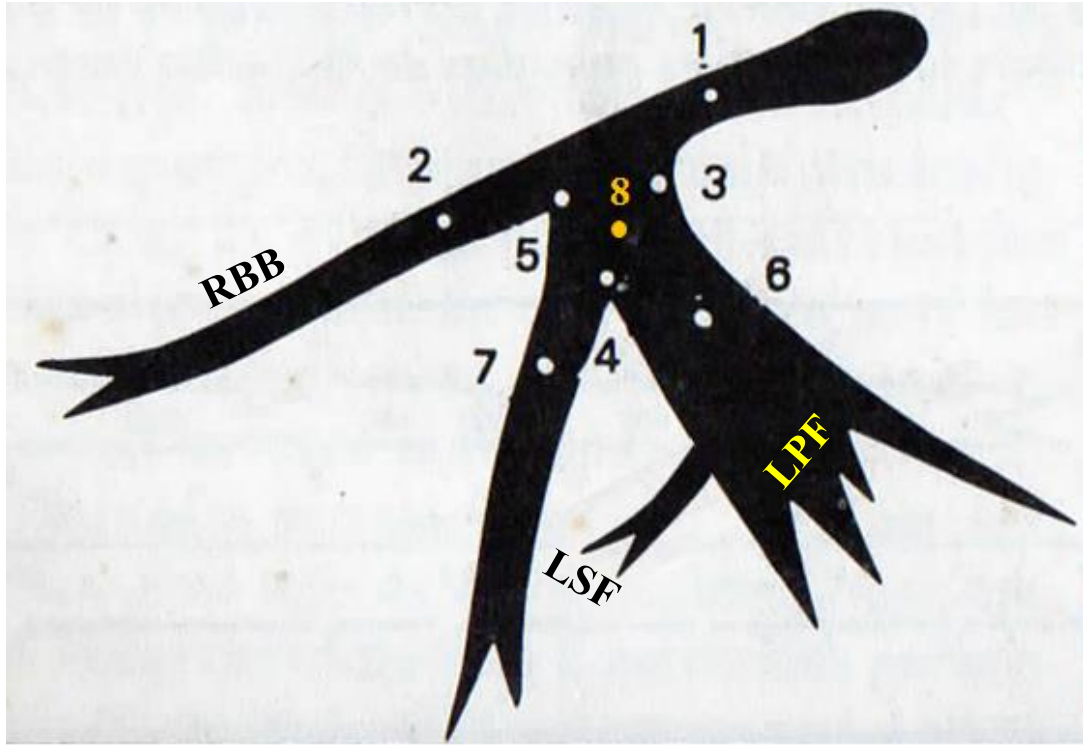


Sustained Accelerated Idioventricular Rhythm (AIVR): wide QRS complexes (≥ 120ms) near regular rhythm, HR between 50-110bpm* and presence of fusion beats (**F**) without capture beats.

*Heart Rates < 50 bpm consistent with a ventricular escape (idioventricular) rhythm

*Heart Rates > 100 bpm consistent with ventricular tachycardia (≥ 3 consecutive QRS complexes at a heart rate faster than 100 bpm)

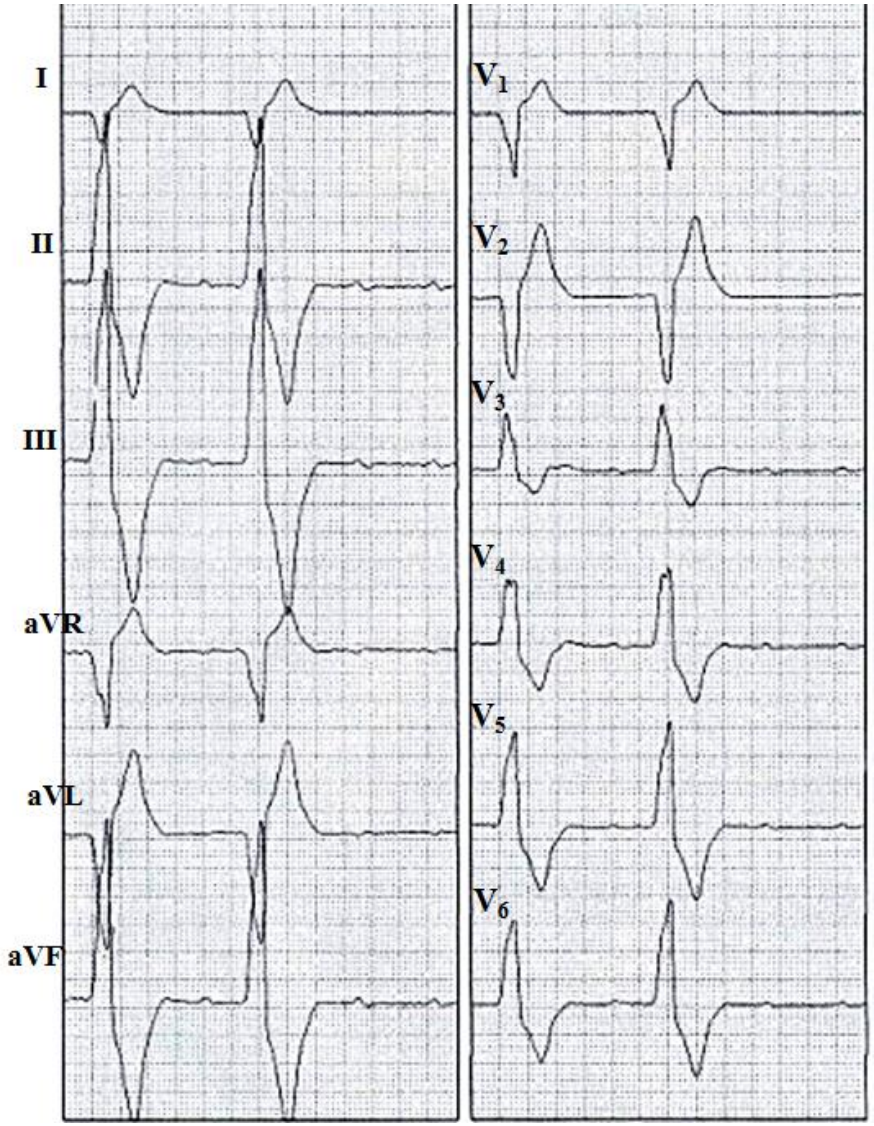
Modified from (**Elizari 1978**)



LAF

Focus 1: Normal QRS
Focus 2: Incomplete LBBB pattern
Focus 3: Incomplete RBBB and minimal degree of LAFB
Focus 4: Incomplete RBBB
Focus 5: Incomplete LPFB
Focus 6: Incomplete LAFB + incomplete RBBB
Focus 7: LPFB + incomplete RBBB
Focus 8: The present case has complete LBBB + LPFB pattern. Where is the focus? Answer: We think that the focus is in the point 8 and the stimulus has major degree of dromotropic disturbance in LPF related LAF.

Recovery 3'
Accelerated Idioventricular Rhythm (AIVR)

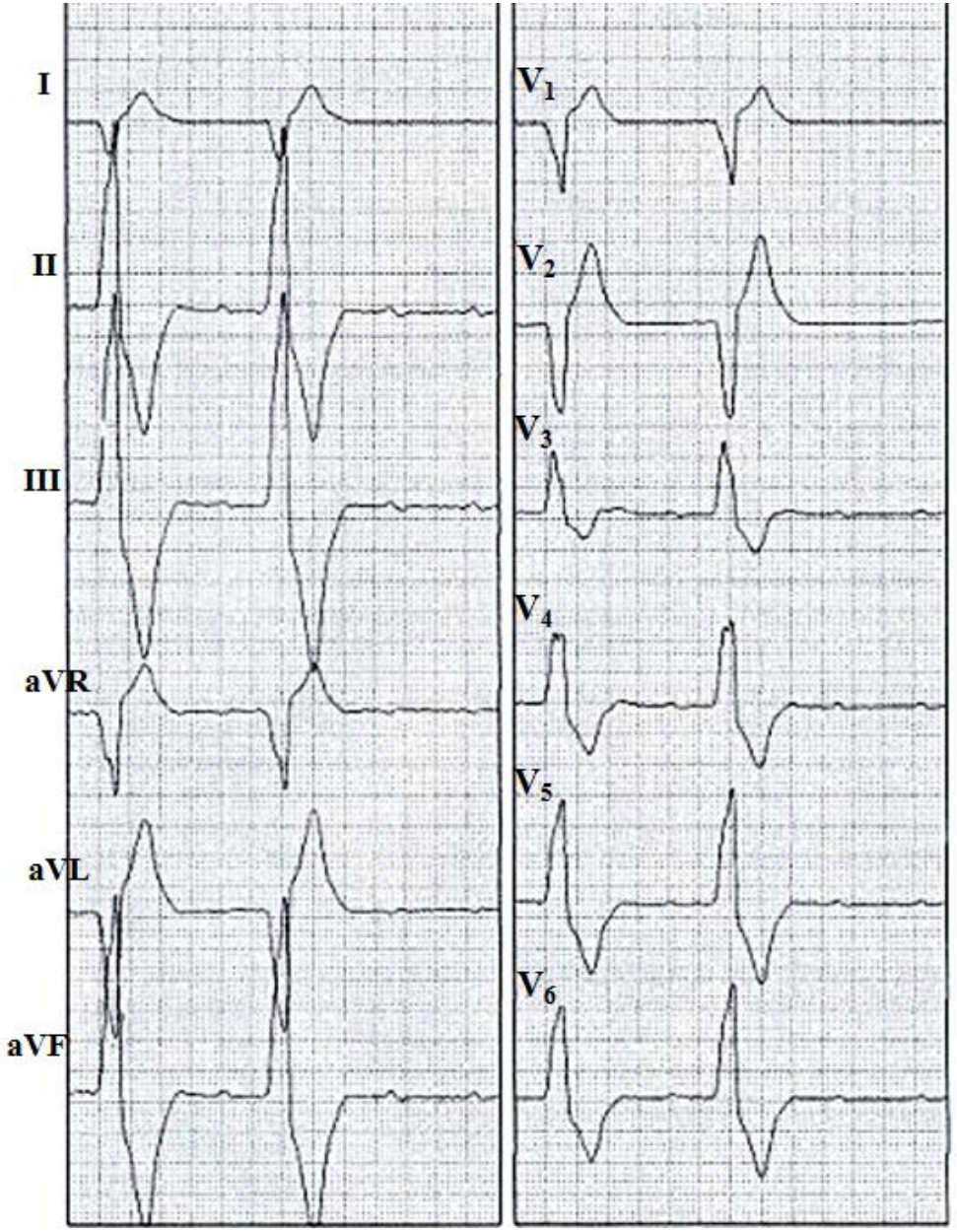


AIVR with lower automaticity

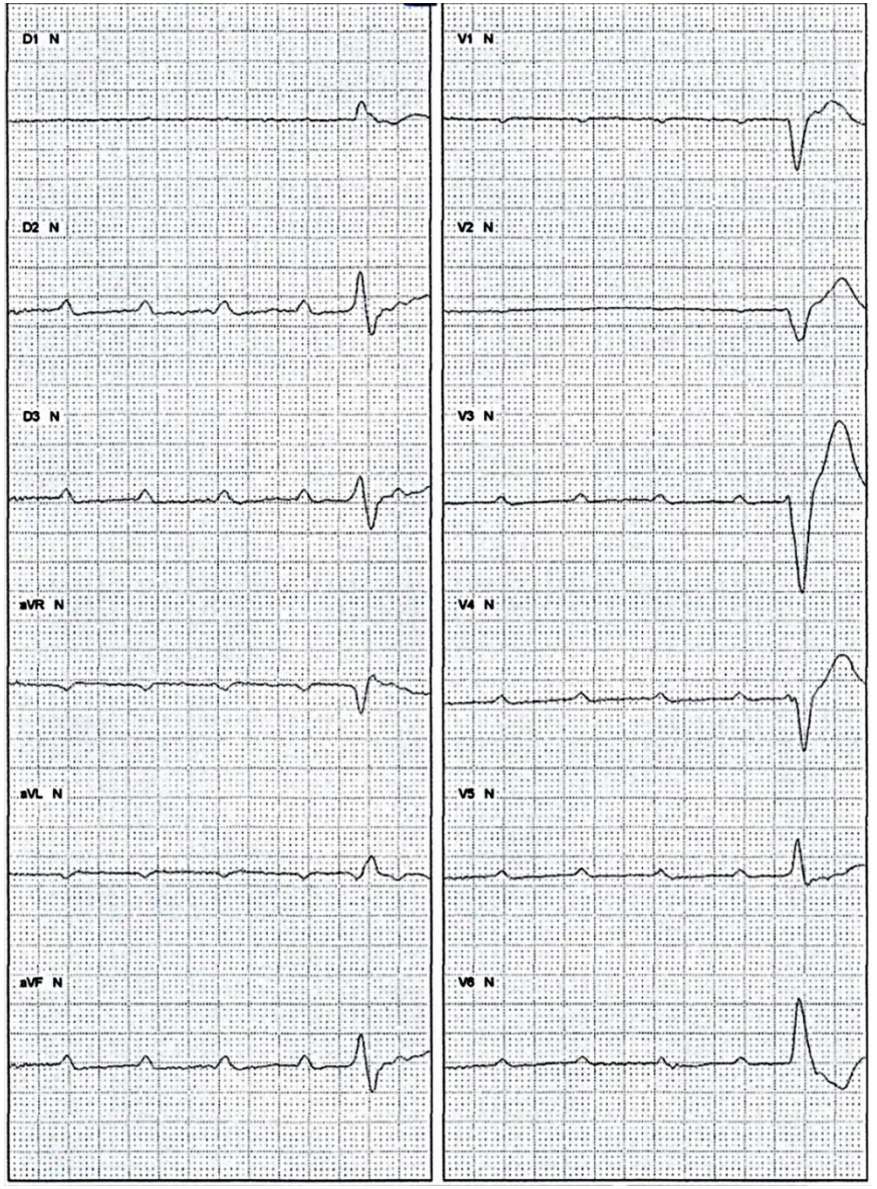
Recovery 3’

Pre-syncope

Recovery 4’

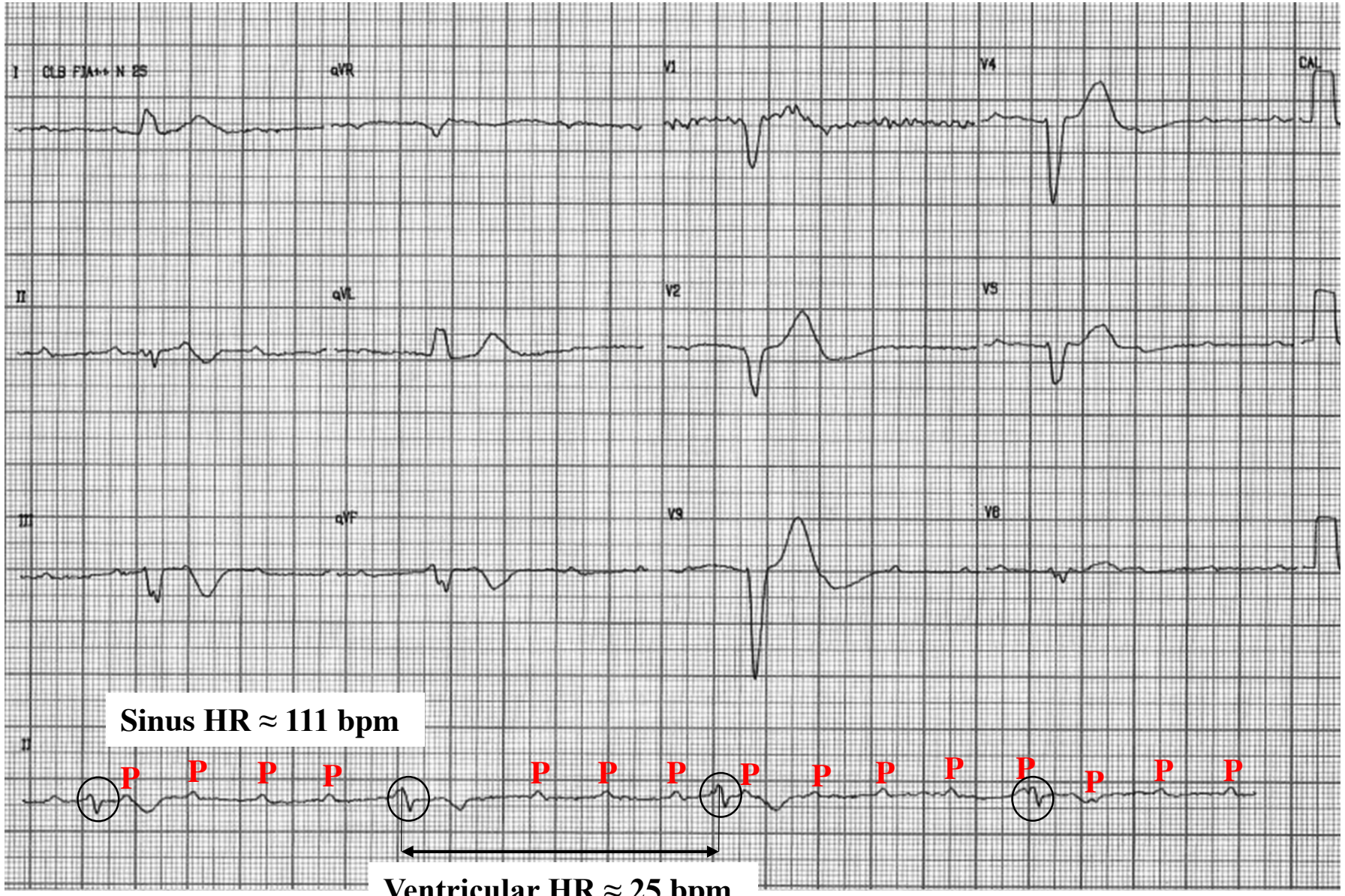


AIVR with lower automaticity



Third-degree atrioventricular (AV) block, also referred to as third-degree heart block or complete heart block

Third-degree atrioventricular (AV) block, also referred to as third-degree heart block, complete heart block or total AV block

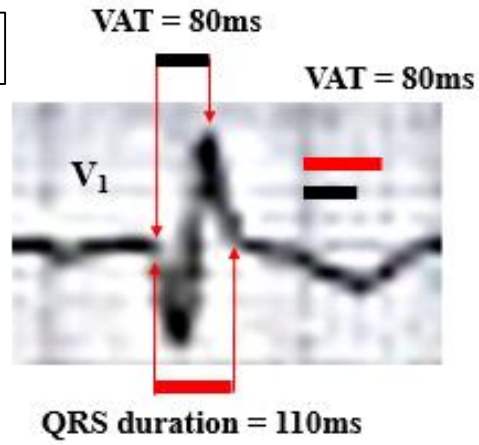


Final commentaries on the diagnostic disagreements between the participants of the Forum

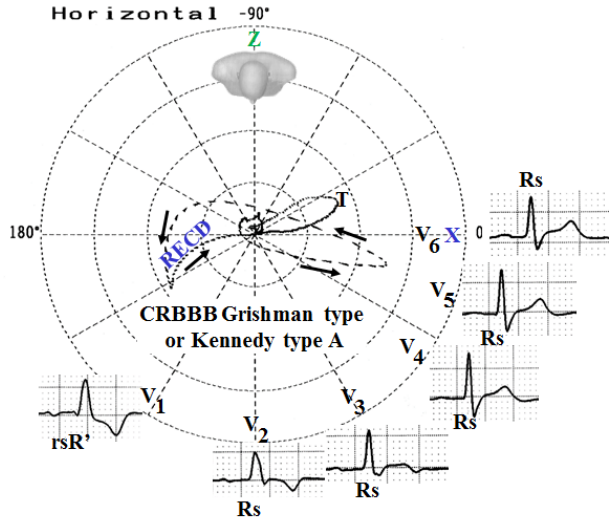
There was a partial disagreement in the commentaries by the colleagues that expressed their opinion on this case. All agreed on the existence of left anterior fascicular block (LAFB); however, none of the participants established the reason for the atypical pattern observed in I and aVL; i.e. pure R in I and aVL, and not qR as is characteristic on LAFB. We are certain that the absence of initial q in these leads is due to the concomitance of LSFB, the presence of which is responsible by the absence of the first vector, vector 1AM, left mid-septal surface vector or Peñaloza and Tranchesi vector, heading below and to the right ≈ +120°; i.e. pointing to III. Two of the contributors mentioned the presence of right bundle branch block or "conduction delay by the right branch" (RBBB associated to LAFB), probably led by the QR pattern of V1 and wide R of V2, associated to extreme shift to the left of the QRS electrical axis in the frontal plane. We believe that in this case there is no RBBB, based on the following factors:

- In RBBB, conduction delay within QRS is mandatorily final. In this case, the total duration of QRS is 110 ms, since the initial part of QRS, "R peak time", holds no less than 80 ms, and the final part only 30 ms (A). On the other hand, in RBBB the conduction delay (RECD) is final (B).

A



B



RECD: Right End Conduction Delay

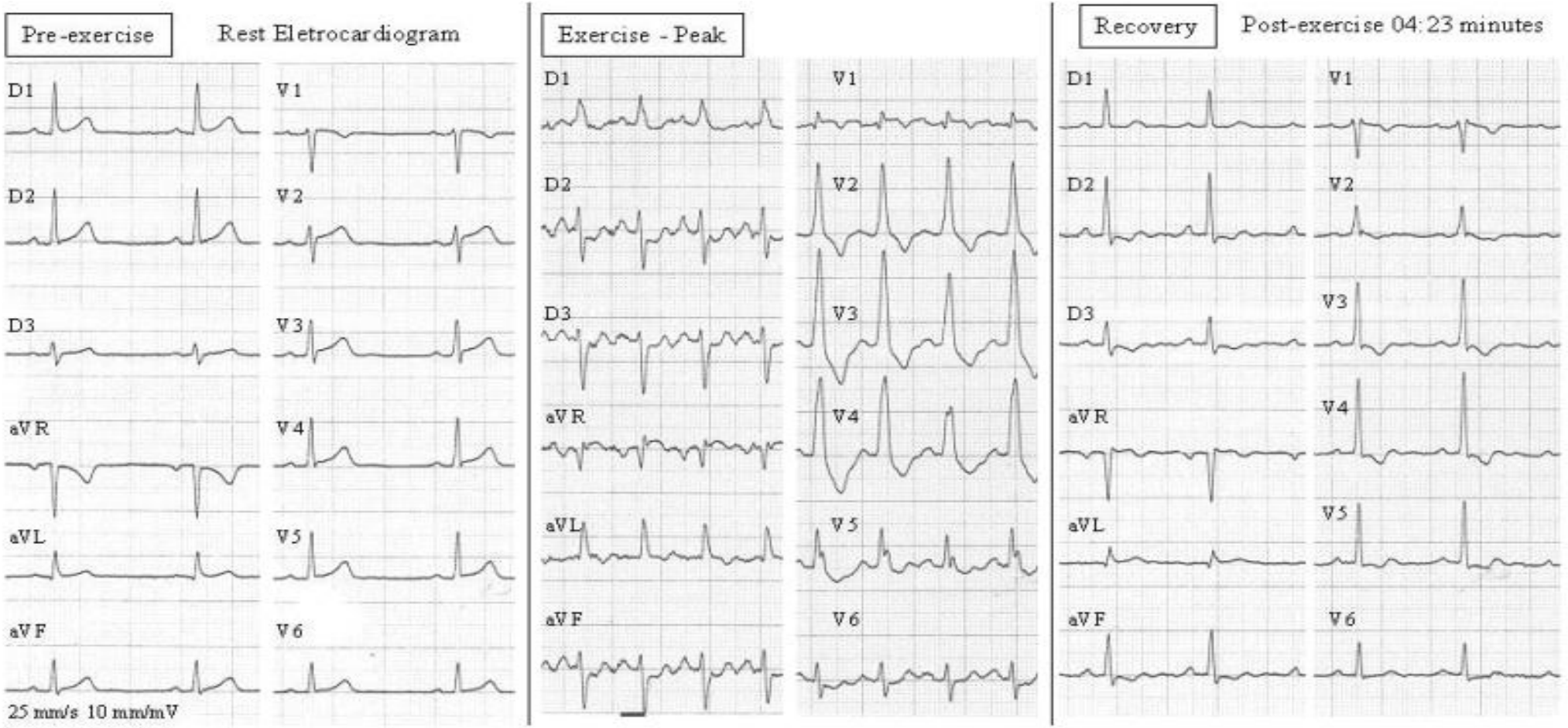
- QR pattern in V1 could be found in the case of LSFB.
- R wave in V2 of voltage ≥15 mm is one of the LSFB criteria.
- I and aVL do not have a final wide S, as it would be expected in RBBB. The RS pattern observed in V5-V6 is clearly caused by the presence of LAFB (**Elizari 2007**).
- The final r wave of aVR is not wide, as it would be expected in the presence of RBBB or end conduction delay through this branch.

Similar examples of transient LAFB + LSFB by…

Raimundo Barbosa-Barros (nickname The Fox) and his wife Dra Niobe Maria Ribeiro Furtado Barbosa

Andrés and his wife Helena Akemi Watanabe “my Yoko Ono”

Adrian Baranchuk, his wife Barbara Raimondi and his daughter Gala

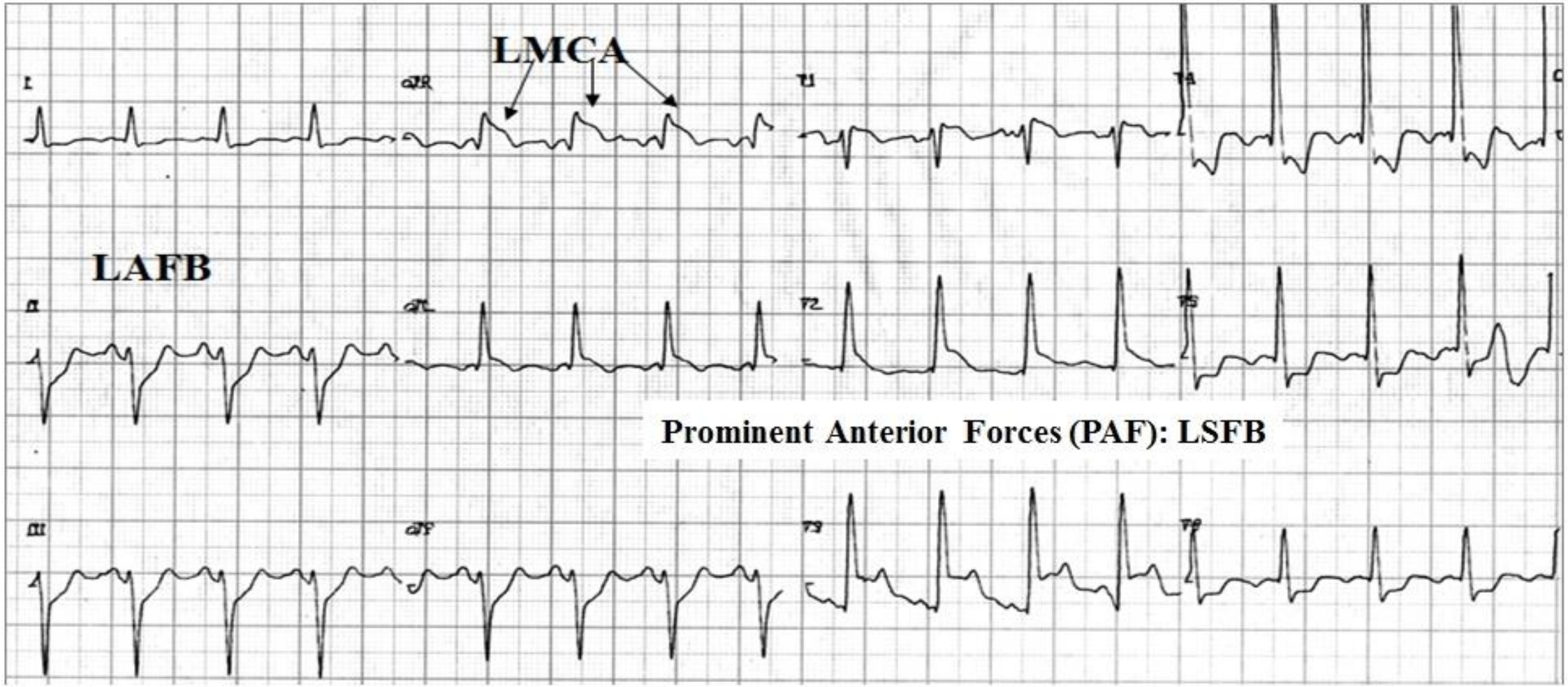


We presented a case very similar (**Uchida 2007**): a 54-year-old male, with a history of systemic hypertension, hyperlipidemia and typical chest pain during exercise. During the exercise stress test, ECG demonstrated abrupt prominent anterior QRS forces, an increase in R wave amplitude from V1 to V4, extreme left axis deviation and minor ST segment depression in II, III and aVF. The post-exercise period showed progressive return of the QRS axis in both frontal and horizontal planes and the ST depression worsened by 1 mm. Coronary angiogram showed a critical proximal LAD critical occlusion. During peak of exercise we observe tall R waves in V1-V4. It is a hallmark ECG finding in LSFB. The proposed ECG criteria for LSFB are: prominent R waves in V1-V3, minimal QRS prolongation (QRS < 120 ms), T wave morphologic alteration (flat or inversion), frequent initial embryonic q wave in right and/or middle precordial leads, absence of initial q wave in left lateral leads consequence of absence of 1_{AM} vector and clinical absence of other causes of prominent anterior QRS forces. During exercise peak we also observe LAFB, consequently we have left bifascicular block (LAFB + LSFB).

ECG of LMCA obstruction associated with LAFB and LSFB

Clinical features: ACS: 72-year-old male patient, admitted in the emergency room with typical precordial pain that yielded after the administration of IV nitroglycerin. Coronary angiography revealed LMCA spasm + proximal critical lesion of the LAD. Management: the patient was urgently revascularized, successfully (Coronary Artery Bypass Graft).

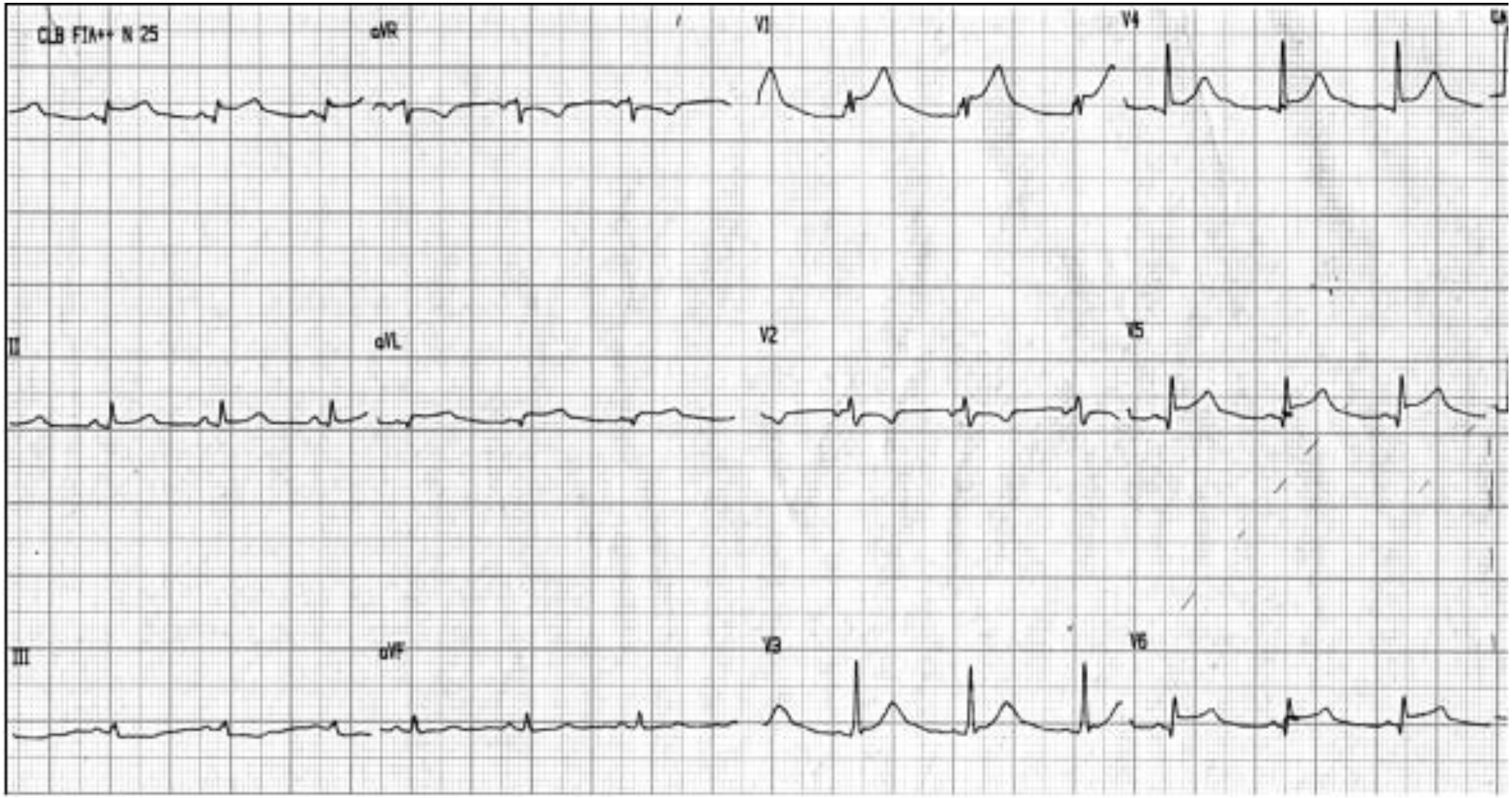
ECG at admission - Name: AR.; **Date:** 02/01/2009.; **Age:** 72 y/o; **Gender:** Male; **Ethnic Group:** Caucasian; **Weight:** 72 Kg.; **Height:** 1.74 m.



ECG diagnosis: 1) LAFB + 2) LSFB: PAF + Injury block + aVR lead with ST segment elevation suggestive of obstruction in the LMCA. **Laboratory:** There was no increase of necrosis markers (CK-MB/troponin).

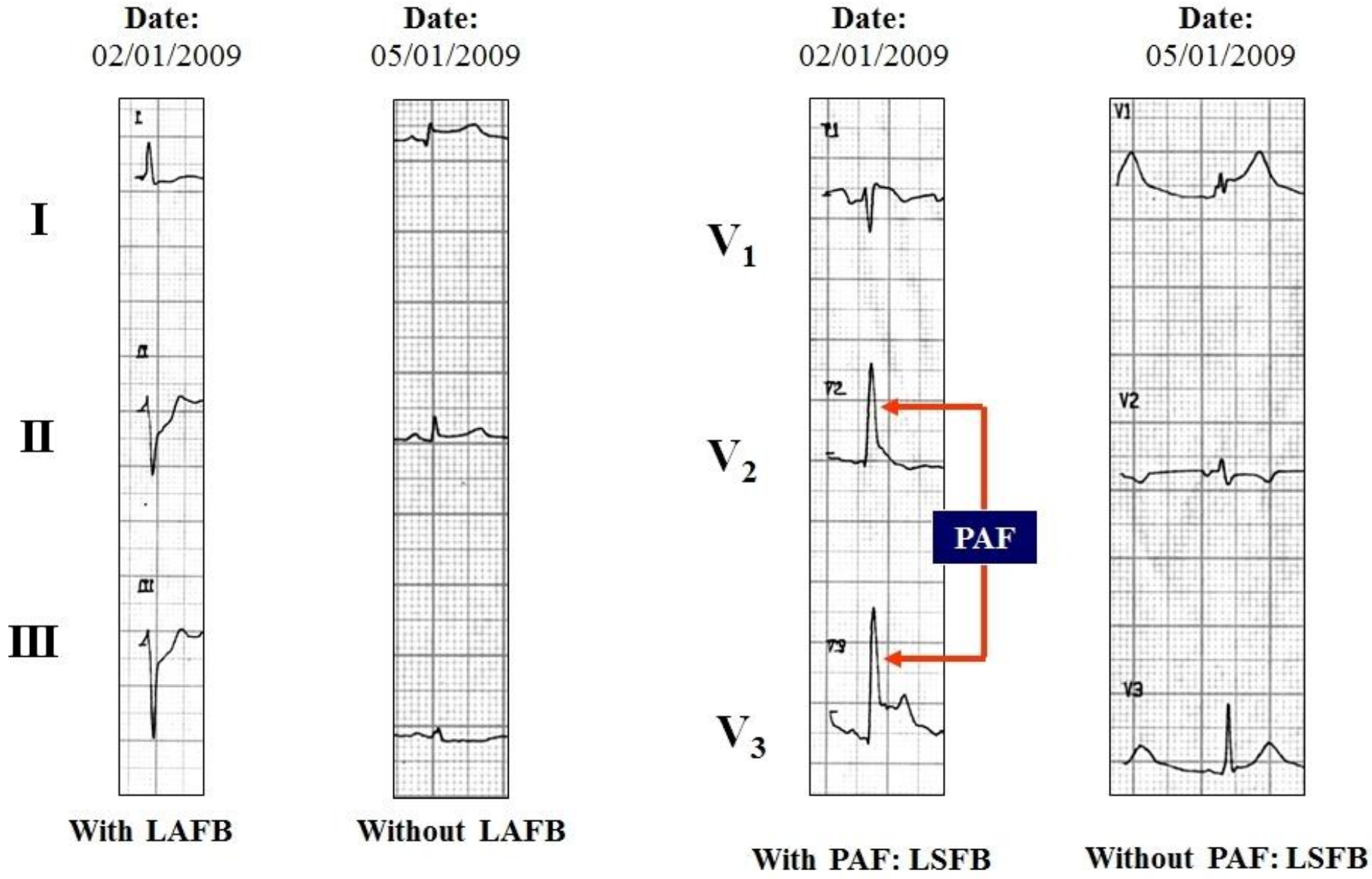
ECG performed on the third day after successful Coronary Artery Bypass Graft

Name: AR; **Date:** 05/01/2009; **Age:** 72 y/o; **Gender:** Male; **Ethnic:** Caucasian; **Weight:** 72 Kg; **Height:** 1.74 m; **Biotype:** Mesomorphic; **Management:** Coronary Artery Bypass Graft (CABG) 72 hours before.



ECG diagnosis: Both fascicular and divisional blocks have disappeared; the extreme shift of QRS electric axis to the left in the frontal plane (LAFB) is not seen, and prominent anterior forces (LSFB) disappeared.

Comparison among inferior and right precordial leads with/without left bifascicular block (LAFB + LSFB)



PAF: Prominent Anterior Forces

Theoretical consideration of Mitral Annular Calcification isolated or associated with aortic valve calcification

Mitral Annular Calcification (MAC)

It is a chronic, degenerative process in the fibrous base of the mitral valve. Although MAC was initially thought to be an age-related degenerative process, there is accumulating evidence that other mechanisms, such as atherosclerosis and abnormal calcium-phosphorus metabolism, also contribute to the development of MAC. Despite its frequency, the clinical relevance of MAC is grossly underappreciated. Indeed, MAC is associated with an increased incidence of cardiovascular disease, mitral valve disease, arrhythmias, and mortality. MAC also influences the outcomes of cardiac surgery and interventions, and its clinical relevance may well increase substantially in the forthcoming era of transcatheter mitral valve replacement (**Abramowitz 2015**). Calcification of various cardiovascular structures is associated with aging (**Barasch 2006; Aronow 1991**). MAC is a chronic degenerative process of the mitral valve ring; it was first described by Bonninger (**Bonninger1908**) as associated with complete atrioventricular block. Calcification of the annulus fibrosus of the mitral valve was commonly found in older people at autopsy and was considered to be a sequela of rheumatic heart disease (**Korn1962; Roberts1983**). However, evidence of previous disease was often absent and the lesion is now generally regarded as the end stage of an inflammatory process. MAC and atherosclerosis share similar risk factors, and the presence of MAC may reflect the intensity and duration of exposure to these risk factors (**Adler2001; Allison 2006**). MAC has been proposed as a visible barometer of the burden of atherosclerotic disease (**Pressman 2011**; **Holtz 2012**). Furthermore, studies have suggested that the presence of MAC is independently associated with a higher incidence of cardiovascular disease and cardiovascular death (**Holtz 2012; Fox 2003; Kohsaka 2008**). HIV infection is an independent predictor of MAC and AVC. Whether these calcifications predict mortality in HIV+ patients (**Rezaeian 2016**). MAC may be related to diabetes, hypertension, hyperlipidemia, and secondary hyperparathyroidism from renal failure (**Klink 2015**). Degenerative mitral valve disease with severe MAC is significantly associated with flail mitral leaflet (**Zemer Wassercug 2015**).

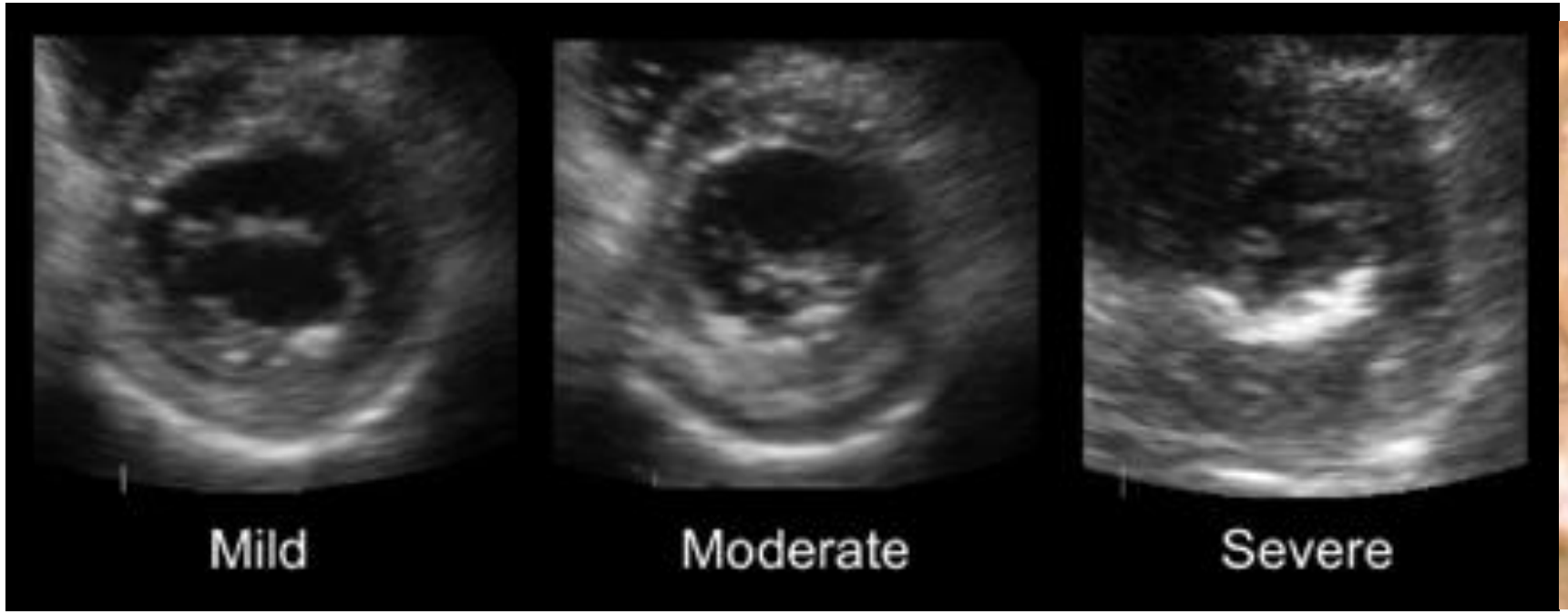
Pathophysiology and Etiology

The main effects of aging on heart are Increased atrial chamber size, decreased left ventricle cavity size, sigmoid shape of interventricular septum, calcification of aortic and mitral valves, thickening of leaflets, tortuousities of coronary arteries, increased lumina, calcifications, and atherosclerosis plaques, increased subepicardial fat, brown atrophy, lipofuscin deposition, basophilic degeneration, decreased myocytes, increased collagen, intraventricular conduction system fibrosis, infiltration of calcium into the conduction system, aortic changes (dilated ascending aorta and rightward shift, tortuous thoracic aorta, elastic tissue fragmentation and deposition of collage and atherosclerosis), previously thought to

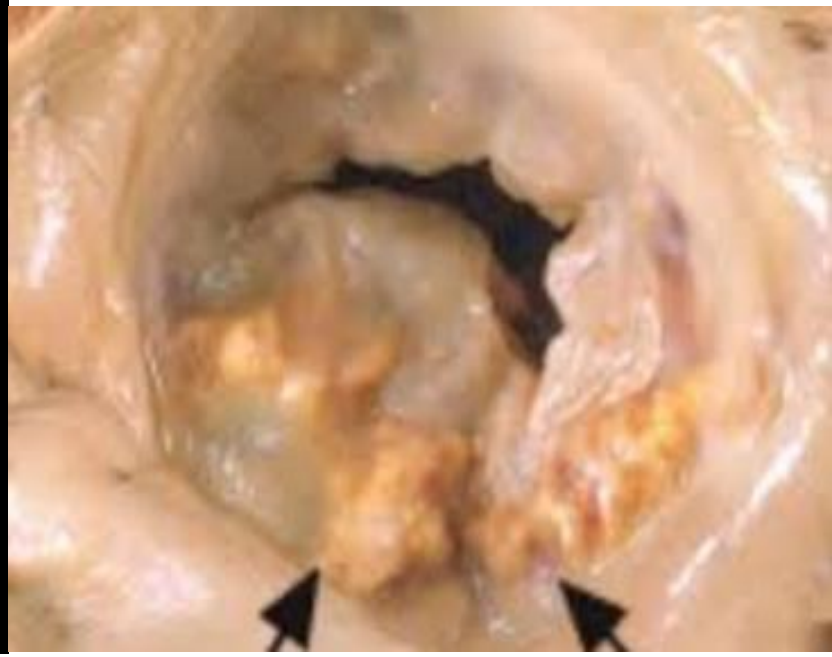
reflect a passive process. Cardiac valve calcification is actively regulated and potentially modifiable (**Parker 2001; Thanassoulis 2015; Ix 2007**). Moreover, cardiac valves express markers of osteoblastic differentiation and calcify in a manner similar to normal osteogenesis, with lamellar bone evident in the majority of pathological specimens examined (**Mohler2001**). The prevalence of MAC in patients with end-stage renal disease is higher than in age-matched control subjects (**Maher 1987; Goodman 2000; Cohen1987; Movva 2013**). The calcium-phosphate product correlates directly with the prevalence of MAC (**Aronow 1987**). Although it was initially believed that high phosphate concentrations trigger vascular calcification simply by exceeding the calcium-phosphate solubility product (causing precipitation). High phosphate levels induce vascular smooth muscle cells to differentiate into an osteoblastic phenotype (**Jono 2000**). Caseous calcification of the mitral valve is a rare form of MAC that typically affects the posterior annulus. The contents of the cavity are composed of a mixture of calcium, fatty acid, and cholesterol, with a ‘‘toothpaste-like’’ texture, and may present as an intracardiac mass or cavity (**Harpaz 2001; Chahal2011; Elgendy I2013**).

Effects of Hypertensive Heart Disease, Left Sided heart disease

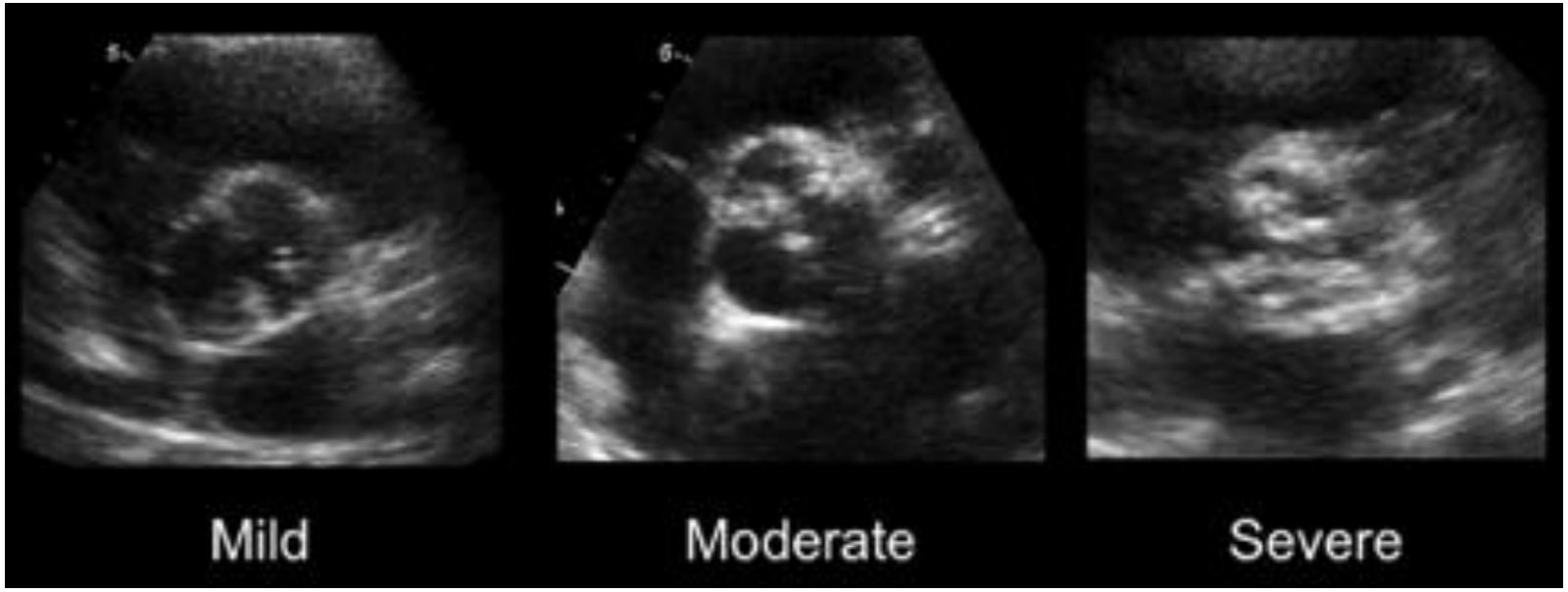
- Response of the heart to increased pressure in the systemic circulation.
- Thickening and Enlargement of the Heart: Concentric hypertrophy develops as a compensatory phenomenon which may lead to cardiac dilatation, CHF and other cardiac dysfunctions.
- Diastolic dysfunction related to hypertensive left ventricular hypertrophy (LVH) has been shown to affect right-sided cardiac morphology and haemodynamics. Pulmonary hypertension (PH) denotes a poor prognosis in patients with left-sided heart disease.
- Morphology: initially there may be circumferential hypertrophy without increase in heart size, may exceed above 2 cm, weight may increase 500 gm.
- Left atrial enlargement (LAE) is a marker of chronically elevated LV filling pressure and diastolic dysfunction. LAE is associated with RVH (**Cuspid I 2013**).
- Microscopically: increased transverse myocyte diameter, followed by increased size variation and interstitial fibrosis.



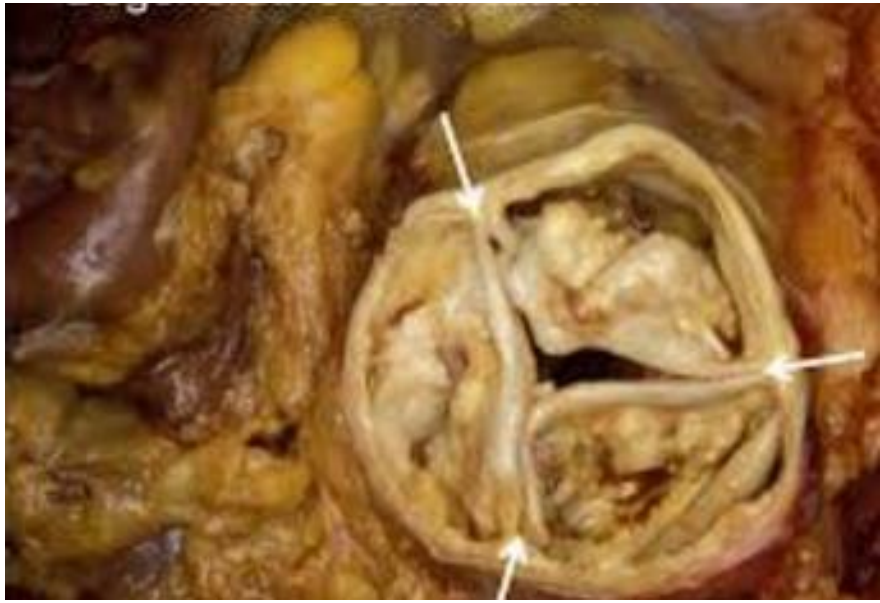
Mild, moderate, and severe mitral annular calcification.



Severe mitral valve calcification



Mild, moderate, and severe aortic valve calcification.



Severe aortic valve calcification

Epidemiology: The prevalence of MAC varies significantly among different populations and is also influenced by differences in age and the presence of comorbidities. In the Framingham study with an elderly population, the prevalence of MAC was 14% (**Fox 2003**). Allison et al studied middle-aged and elderly patients seen in a ”preventive health” clinic found a prevalence of 8% (**Allison 2006**). Other studies have shown lower prevalence rates, especially those including asymptomatic patients free of clinical CAD (**Savage 1983**).

Age: In elderly people, the prevalence of MAC is significantly higher, as described in the Cardiovascular Health Study (CHS), a community-based cohort study of elderly individuals (mean age, 76 yo) (**Barasch 2006**). The prevalence of MAC in this study was 42% and was strongly associated with the presence of cardiovascular disease. Among patients older than 85 years, the prevalence of MAC was 60%.
In the Framingham Heart Study, MAC was not found in those younger than 40 years (**Savage1983**). In the study by Allison et al (**Allison 2006**), each 10-year increase in age was associated with a 3.7-fold increase in the likelihood of MAC being present.
The prevalence increased with age; at age 70 years, 10% of women and 15% of men were found to have MAC.

Sex: Conflicting evidence exists regarding the occurrence of MAC between males and females. While the Framingham Heart Study found that 72% of subjects with MAC were female (**Fox 2003**), the Allison study observed a trend towards lower prevalence of MAC in women versus men (difference not statistically significant) (**Allison 2006**).
The population-based Atherosclerosis Risk in Communities (ARIC) study found a similar overall prevalence of MAC between sexes (4.6% in women and 5.6% in men, with a mean age of 59 y) (**Fox 2004**).
The Multi-Ethnic Study of Atherosclerosis (MESA) found a female predominance for MAC, observing a prevalence of 12% in women and 8% in men aged 45-84 years (**Kanjanauthai 2010**).

Race: Data on the prevalence of MAC in different racial groups are limited. A cohort that included a majority of Hispanic patients (mean age, 68 y) showed a prevalence of 26% (**Kohsaka 2008**). The prevalence in a cohort of ARIC patients that included only African Americans (mean age, 59 y) was 4.9% (**Fox 2004**). According to data from the MESA cohort of patients aged 45-84 years, the prevalence of MAC was highest in whites (12%), followed by Hispanics (10%) and then African Americans (7%), and was lowest in Chinese subjects (5%) (**Kanjanauthai 2010**). Racial differences were not only observed in MAC but also in other valvular calcifications in a prior study (**Potpara 2011**).

Prognosis: Several studies have looked at associations between the presence of MAC and cardiovascular events. The Framingham Study followed 1197 subjects for 16 years and showed an association between MAC and cardiovascular disease (CVD), CVD death, and all-cause death. Moreover, for each 1 mm increase in MAC, the risk of CVD, CVD death, and all-cause death increased by approximately 10% (**Fox 2004**).
In the ARIC substudy restricted to African Americans, MAC was associated with incident CVD events, defined as fatal coronary event, hospitalized MI, or cardiac procedure.
Mortality data in patients with MAC and nonvalvular atrial fibrillation was examined in the Belgrade Atrial Fibrillation Study. This prospective study followed 1056 middle-aged subjects for a mean of 9.9 years. Significant associations were found between MAC and all-cause death, CVD death, and the composite endpoint of ischemic stroke, myocardial infarction, and all-cause death (**Potpara 20011**).
In the Northern Manhattan Study of 1955 subjects with a mean follow up of 7.4 years, MAC was associated with an increased risk of myocardial infarction and vascular death but not ischemic stroke (**Kohsaka 2008**).

History: Patients with MAC may have multiple associated comorbidities. The comorbidities with the strongest association with MAC are the following:

Stroke: The association of MAC and stroke was initially proposed by Rytand (**Rytand 1946**). One of the first observational studies on the subject was a prospective study in 1989 by Nair et al (**Nair 1989**), in which patients with MAC were found to be at increased risk for stroke. Benjamin et al (**Benjamin 1992**) presented a prospective study from the Framingham group; 1159 subjects were studied and followed for an average of 8 years. After adjusting for known risk factors for cerebrovascular events, subjects with MAC still had a higher risk of stroke. Moreover, the multivariate analysis showed that for every additional millimeter of MAC width, the relative risk of stroke increased by approximately 25%. However, it remains uncertain whether the increased risk for stroke is caused by MAC itself or merely through its relationship with risk factors for cerebrovascular disease (**Thanassoulis 2010**). MAC has been associated with carotid stenosis, aortic atheroma, markers of inflammation, and other biomarkers. While embolic events in MAC patients might be due to calcific material that dislodges from the annulus, the more common scenario is that of associated conditions that are the direct cause of stroke. Further, the association between MAC and stroke is not present in all studies. The Strong Heart Study found that MAC was associated with an increased stroke risk (**Kizer 2005**), while the Boston Area Anticoagulation Trial for AF and the Cardiovascular Health Study (**Boon 1997**) did not.

Atherosclerosis disease: It has a tendency to initiate in areas with decreased shear stress or increased turbulence of blood flow, both of which are present at the attachment points of the aortic and mitral leaflets to their annuli. In animal studies, induced atherosclerosis produces plaque formation in the posterior leaflet of the mitral valve (**Thubrikar 1985**). Clinical studies have observed an association between MAC and risk factors for atherosclerosis (**Fulkerson 1979**). The association between MAC and atherosclerosis has been found in different vascular beds: the coronary tree (**Thanassoulis 2010**), the aorta (**Adler1998**), and the carotid arteries (**Adler 2000**). Thus, it seems feasible that MAC and atherosclerosis represent two facets of the same disease (**Adler1998; Roberts 1983**).

MAC is a predictor of coronary artery disease (**Thanassoulis 2010; Lazaros 2013**). Moreover, its presence has been related to vulnerable plaque (**Acarturk 2003**) and a greater burden of coronary disease (more than 1 vessel involved) (**Utsunomiya 2010**).

Chronic kidney disease: In a community-based sample from the Framingham Heart Study, MAC was more common in patients with chronic kidney disease (CKD) versus patients with normal kidney function (**Kannam 2008**). Furthermore, participants with CKD were 50% more likely to have at least one calcified valve. This relationship was attenuated by adjustment for cardiovascular risk factors, suggesting that shared risk factors partially mediate the increased prevalence. In the Chronic Renal Insufficiency Cohort (CRIC) in a cross-sectional study. CRIC population, presence of MAC was independently associated with age, Caucasian race, decreased GFR, and elevated phosphate. African American and Hispanic race, as well as former smoking status were protective against MAC. These results are suggested by mechanisms of dysregulation of inflammation, hormones, and electrolytes in subjects with renal disease (**Abd Alamir 2015**).

In another study of patients with severe MAC, nearly 60% had clinically significant CKD. The authors suggested that severe MAC on echocardiography should alert the physician to the likely presence not only of atherosclerosis but also CKD (**Fox 2006**).

Among dialysis patients, prevalence rates for MAC are 4-5 times higher than in the general population (**Jesri 2008**). Moreover, calcium-phosphorus product and parathyroid hormone levels are higher in patients with MAC (**Raggi 2002; Ribeiro 1998**). For CKD and dialysis patients, some (**Wang 2003; Straumann1992**) but not all studies (**Takahashi2013; Panuccio 2004**) have found that MAC correlates with higher total and cardiovascular mortality. In addition, MAC serves as a marker for left ventricular systolic dysfunction in these patients, with or without end-stage renal disease (**Al-Absi 2006; Hüting 1994**).

Mitral regurgitation: Mitral regurgitation is a hemodynamic abnormality commonly associated with MAC, with a prevalence of up to 63% (**Rao 2006**). Calcium infiltration of the base of the posterior leaflet reduces leaflet mobility, increases traction on the chordae, and elevates the leaflets, which facilitates chordal elongation or rupture, causing secondary mitral regurgitation (**Aronow 1987**). Another proposed mechanism is failure of the calcified annulus to contract at the end of diastole (**Labovitz 1985**). MAC has been reported to lead to regurgitation severe enough to require surgery in some cases (**Aronow 1987**).

Mitral stenosis: Degenerative mitral stenosis (DMS) is an important cause of mitral stenosis, developing secondary to severe mitral annular calcification. These patients are generally elderly with multiple comorbidities and often are high-risk candidates for surgery. The mainstay of therapy in DMS patients is medical management with heart rate control and diuretic therapy. Surgical intervention might be delayed until symptoms are severely limiting and cannot be managed by medical therapy. Mitral valve surgery is also challenging in these patients because of the presence of extensive calcification. Hence, there is a need to develop an alternative percutaneous treatment approach for patients with DMS who are otherwise inoperable or at high risk for surgery (**Sud 2016**). Mitral stenosis is a rare complication of MAC (**Carpentier 1996; Osterberger 1981**). However, MAC can occasionally cause mitral stenosis severe enough to warrant valve replacement (**Korn1962**). The pathophysiology is thought to be an absence of normal annular dilatation during diastole, resulting in functional mitral stenosis (**Labovitz 1985**). Alternatively, decreased mobility of the valve when annular calcium limits leaflet excursion, particularly of the anterior leaflet, may be responsible (**Ramirez1980**).

Arrhythmias: MAC is associated with a high frequency of conduction defects, including atrioventricular block, bundle branch block, and intraventricular conduction delay, especially in more severe cases (**Turakhi 1987**). MAC is also associated with symptomatic bradyarrhythmias requiring pacemaker implantation (**Muddassir 2007; Mellino 1982**). This is likely secondary to infiltration of calcium into the conduction system. Data from the Framingham cohort show that MAC is associated with an increased risk of incident AF, even when adjusted for atrial size (**Nair 1982**). Nair et al found a similar association (**Mainigi 2012**). This is not surprising given that MAC is more prevalent in elderly people and that MAC, atherosclerosis, and AF all share common risk factors.

Endocarditis: infective endocarditis is a possible complication of MAC (**Fox 2004**). One prospective study of 976 elderly patients demonstrated a higher incidence of infective endocarditis in patients with MAC (3% vs 1%) (**Nair 1984**).

Aortic valve disease: In a retrospective study among 24,380 patients, Movahed et al found that MAC was present in 15% of patients with aortic stenosis, compared with only 6% of patients without aortic stenosis (**Movahed 2007**). In another study that included 219 patients with a mean age of 57 years, MAC was strongly associated with aortic valve calcification (**Aronow 1990**). MAC has also been found to be associated with more severe aortic stenosis in a study by Michel et al (**Michel 1988**).

Complications of MAC include: stroke (associated with MAC but, in most cases, probably not directly caused by it), MI (associated with MAC but probably not directly caused by it), atherosclerosis (associated with MAC but probably not directly caused by it), mitral regurgitation, mitral stenosis, arrhythmias (conduction disease may be associated with cardiac calcification generally) and infective endocarditis.

Diagnosis considerations: MAC often takes unusual configurations, which can raise concerns about neoplasm, abscess, or thrombus. Any prominent echo-bright abnormality in the posterior annulus region is likely to be MAC. Tumor, infection, and clot are distinctly unusual in this location. Caseous annular calcification is an unusual form of MAC in which there is a prominent mass in the annulus with a liquid or gelatinous center. At surgery, the contents have been described as having the texture of gruel or toothpaste. Caseous MAC has an estimated prevalence of approximately 0.6% of all cases of MAC (**Jassal 2008**). At times MAC can also be mobile or produce mobile projections, which can embolize and be a source of stroke.

Differential Diagnosis: With atrial myxoma, benign cardiac tumors, thrombus and vegetation.

Imagen studies: MAC is usually an incidental finding on cardiac imaging. With transthoracic echocardiography, on the parasternal or apical views, MAC is identified as an echodense band or mass in the atrioventricular groove. MAC is seen all the way through systole and diastole, distinguishable from the posterior mitral valve leaflet (**Benjamin 1992**). While most commonly affecting the posterior annulus, it can occasionally involve the anterior annulus, or interannular fibrosa. Calcification can extend from the annulus onto the leaflets, limiting their mobility. It is not unusual to find the posterior leaflet encased in calcium and completely immobilized. This usually has no physiologic consequences. However, calcification extending onto the anterior leaflet and limiting its mobility may be associated with transmitral gradients (**Ramirez 1980**). Caseous calcification is less echodense than typical MAC; a central echolucent zone is usually present and acoustic shadowing is generally absent. Cardiac MRI and CT scanning have also been used in the evaluation of MAC (**Michel 1988; Deluca 2008**) and can be particularly helpful in differentiating caseous MAC, cardiac tumor, and thrombus when poor quality images are seen on echocardiography (**Gulati 2011**).

Histologic finding: Biopsy is never needed for the diagnosis of MAC. In its most characteristic configuration, it forms a semilunar deposit of calcium within the annulus fibrosus, with limited extension to the leaflet tissue. This is different from the calcification seen in rheumatic valvular disease, which usually involves the commissures and the leaflet tissue with only late extension to the annulus. Carpentier et al studied pathologic specimens of 68 patients (mean age, 62 y) with extensive MAC and significant mitral regurgitation. They found calcification of at least one third of the posterior annulus in 88% of cases, with calcification of the entire posterior annulus in 10% (**Carpentier 1996**).Calcium formation was generally encapsulated in a fibrous sheath. However, fibrous encapsulation was not found in areas of myocardium infiltrated by the calcific process. Beyond the limits of the calcification, the remaining annulus fibrosus usually displayed fissures and zones of dehiscence. These defects were filled with lipoid substances, platelets, and red blood cell aggregates. In caseous MAC in particular, the histopathologic findings are characterized by central liquefaction necrosis and scattered calcifications that are predominantly located in the peripheral regions (**Harpaz2001**).

Staging: In general, no standard grading system by echocardiography is recognized. Many studies have classified the severity of MAC by measuring its thickness on M-mode echocardiography at the point of greatest width. Thickness greater than 1 mm but less than 4 mm has been

considered mild to moderate, whereas thickness greater than 4 mm has been considered severe. MAC greater than 4 mm has been found to be an independent predictor of myocardial infarction and valvular disease (**Kohsaka 2008**). Other investigators have graded the severity of MAC by dividing the posterior annulus in thirds and adding up the number of thirds involved. Still others have looked at annular calcification in the context of overall cardiac calcification, using semiquantitative systems to grade calcification in the aortic and mitral valves, aortic root, and submitral apparatus, as well as the mitral annulus (**Movva 2013; Aronow 1987**).

Treatment

The presence of asymptomatic MAC does not require specific medical therapy. Because of the association between MAC and atherosclerosis, valvular disease, stroke, and other vascular diseases, appropriate medical management of concomitant cardiovascular risk factors is recommended (**Blankstein 2009**). Interestingly, a study from the MESA cohort determined that while several cardiovascular risk factors predicted incident MAC, the severity of MAC at the time of first detection was the primary predictor of MAC progression. This would suggest that while atherosclerotic processes may initiate MAC, they are only modestly associated with its progression (**Di Bella 2006**).Indeed, the potential regression of MAC with medical therapy has not been examined, but studies done with aortic valve calcification have shown no regression despite treatment with ACE inhibitors and statins (**Bonow 2008; Elmariah 2013**). MAC has also been associated with CKD, and its presence on echocardiography should alert the physician to the possible presence of decreased renal function (**Kannam 2008; Fox 2006**). No endocarditis prophylaxis is indicated in patients with isolated MAC (**Blankstein 2009**). According to the 2008 American College of Chest Physicians guidelines for valvar and structural heart disease, antithrombotic therapy with aspirin is recommended in patients with MAC but without AF who have experienced systemic embolism, ischemic stroke, or transient ischemic attack (**Elmariah2013**). For recurrent events despite aspirin therapy, anticoagulation with a vitamin K antagonist is suggested (target INR, 2.5; range, 2-3). In patients with MAC who have a single embolus documented to be calcific, data are not sufficient to recommend either for or against antithrombotic therapy. Patients with isolated MAC do not require hospitalization. However, these patients are at increased risk for major cardiovascular events (eg, stroke, MI). Given the strong association with atherosclerosis, cardiovascular risk factor modification (eg, hypertension, hyperlipidemia) and appropriate follow-up is important. No surgical treatment is indicated for MAC, unless correction of concomitant mitral regurgitation or mitral stenosis is needed. In fact, severe MAC makes valve surgery more difficult. Risks and benefits of surgery must be carefully assessed in patients with significant MAC, as increased surgical mortality has been observed in these patients. Patients with MAC have high surgical risk for mitral valve replacement due to associated comorbidities and technical challenges related to calcium burden, precluding surgery in many patients. Transcatheter mitral valve replacement (TMVR) with the compassionate use of balloon expandable aortic transcatheter heart valves has been used in this clinical scenario. TMVR might evolve into an acceptable alternative for selected

patients with severe MAC who are not candidates for conventional mitral valve surgery. However, this field is at a very early stage and the progress will be significantly slower than the development of transcatheter aortic valve replacement due to the complexity of the mitral valve anatomy and its pathology. Optimizing patient selection process by using multimodality imaging tools to accurately measure the mitral valve annulus and evaluate the risk of left ventricular outflow tract obstruction is essential to minimize complications. Strategies for treating and preventing LVOT are being tested. Similarly, carefully selecting candidates avoiding patients at the end of their disease process, might improve the overall outcomes (**Guerrero 2016**).

Transcatheter mitral valve repair with a MitraClip device is also producing good outcomes in patients with primary mitral regurgitation who are at high surgical risk. Findings from clinical trials of MitraClip versus surgery in patients of intermediate surgical risk are expected to be initiated in the next few years.

In patients with secondary mitral regurgitation, mainly a disease of the left ventricle, the vision for the next 5 years is not nearly as clear. Outcomes from ongoing clinical trials will greatly inform this field.

Use of transcatheter techniques, both repair and replacement, is expected to substantially expand.

Mitral annular calcification is an increasing problem in elderly people, causing both mitral stenosis and regurgitation which are difficult to treat (**Nishimura 2016**).

For those patients with documented calcific emboli or repeated thromboembolism despite anticoagulation, valve replacement may be considered.

The 8th edition of the American College of Chest Physicians guidelines recommends antithrombotic therapy with aspirin (50-100 mg/day) (**Salem 2008**). Warfarin therapy (target INR, 2.5; range, 2-3) may be considered under certain circumstances for long-term stroke prevention (**Rosenhek 2004**). Start with caution, especially in elderly patients and those with hepatic impairment, poor nutrition, CHF, severe CKD, or a high risk of bleeding. Treatment of associated cardiovascular conditions should be addressed as per respective guidelines. Aspirin is an odorless, white, powdery substance available in 81 mg, 325 mg, and 500 mg for oral use. Aspirin is a stronger inhibitor of both prostaglandin synthesis and platelet aggregation than other salicylic acid derivatives. It can be used in low doses to inhibit platelet aggregation and improve complications of venous stasis and thrombosis. Aspirin reduces the likelihood of MI and is also very effective in reducing risk of stroke. Early administration of aspirin in patients with acute MI may reduce cardiac mortality in the first month. Warfarin inhibits the synthesis of 6 vitamin K-dependent proteins involved in coagulation system (factors II, VII, IX, X; proteins C, S). Many other Coumadin derivatives are used worldwide.

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