Caucasian woman with chest pain and abnormal Electrocardiogram

Caucasian woman, 58 years old, married, housewife, elementary school, from rural area of Bahia, Brazil.

Main complaint: atypical prolonged and recurrent precordial chest discomfort/pain, but with no clear provocative factors.

She refers that approximately three months ago had oppressive chest pain during the night, having consulted an emergency room, where after performing blood tests and an electrocardiogram, was released with the query recommendation cardiologist. At that time, she was treated with acetylsalicylic acid, rosuvastatin daily and sublingual isosorbide dinitrate, if necessary.

Physical examination: within normal limits.(WNL)

General appearance: patient is alert and oriented.

Vital signs: Temp: 36.3°C, respiratory rate 17 breaths per minute, HR 53bpm BP: 110/60mmHg,

Head: Normocephalic, pupils are equal and reactive. Missing numerous dental pieces

Neck: Supple without lymphadenopathy. Neck Veins- JVD at 45° . Normal amplitude and contour of carotid arteries. Not murmurs.

Heart: Regular rate and rhythm without murmurs. S1- heard best at apex, nl intensity S2- heard best at base splitting, A2 > P2 Extra Sounds- S3, S4 absent Absent murmurs

Lungs: vesicular breathing present. Absence of adventitious lung sound: wheezing, rhonchi and crackles.

Abdomen: Soft, nontender, nondistended with good bowel sounds heard, normal. No hepatosplenomegaly.

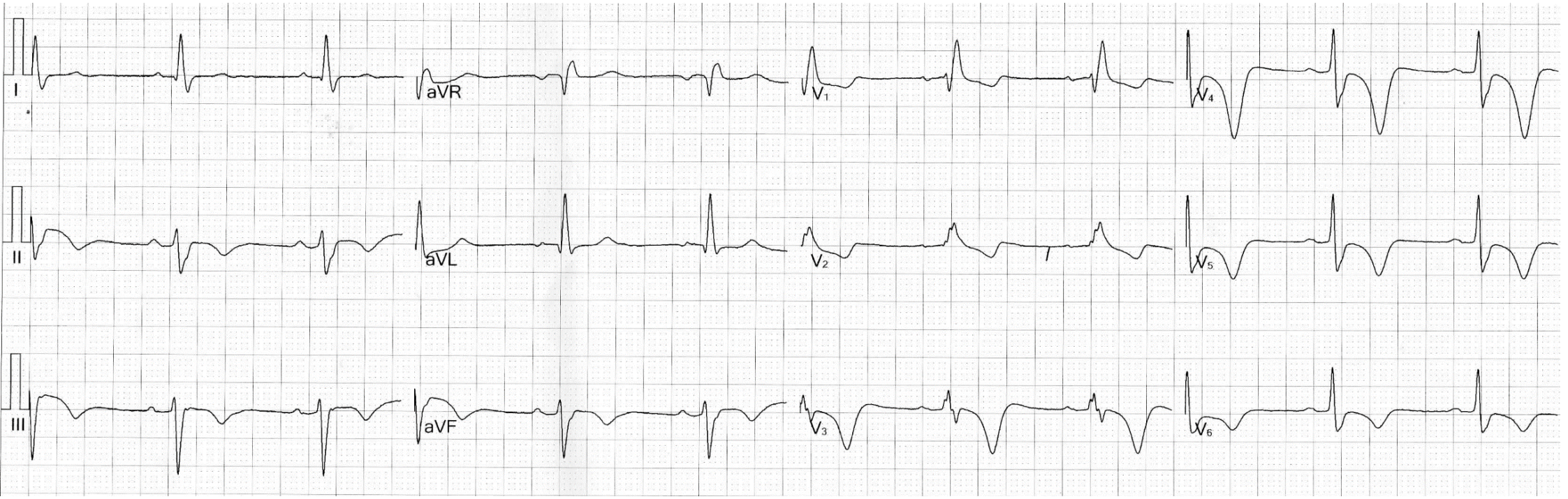
Extremities: Without cyanosis, clubbing or edema.

Neurological: WNL

Skin: Warm and dry without any rash.

Questions:

1. Wich is the ECG/VCG diagnoses?
2. What are the differential diagnosis?


I
aVR
V1
V4
II
aVL
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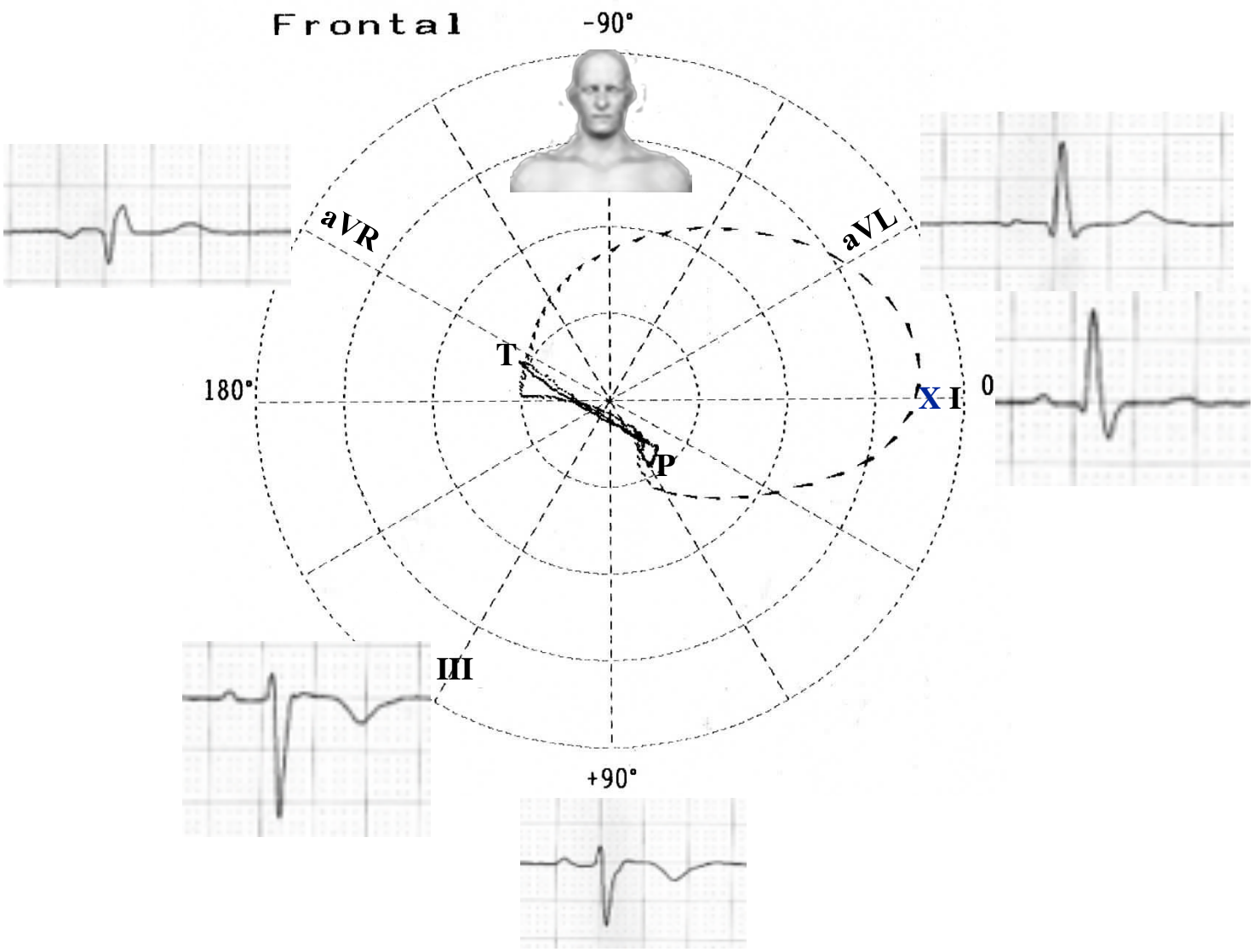
III
aVF
V3
V6


Frontal
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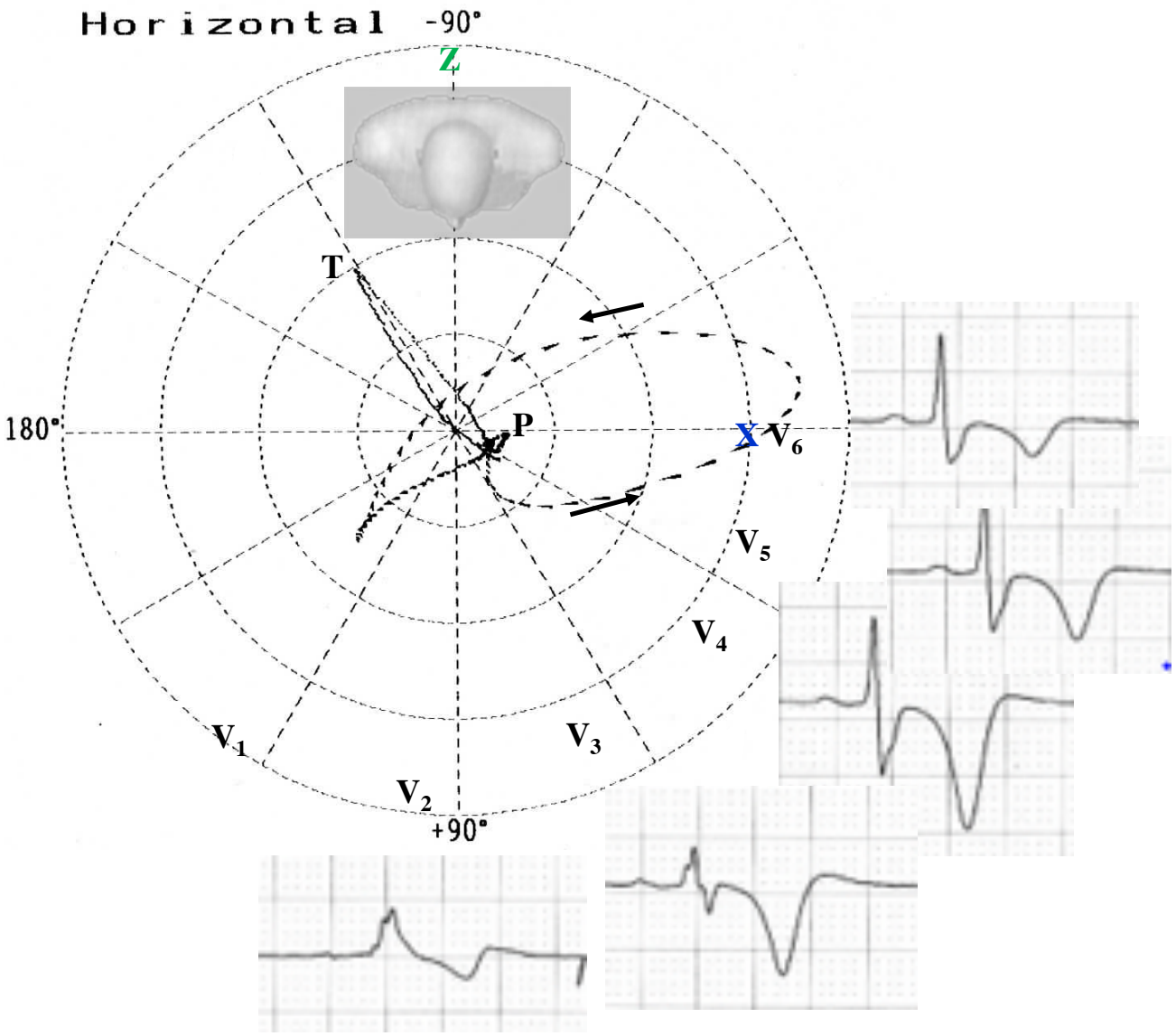
Horizontal
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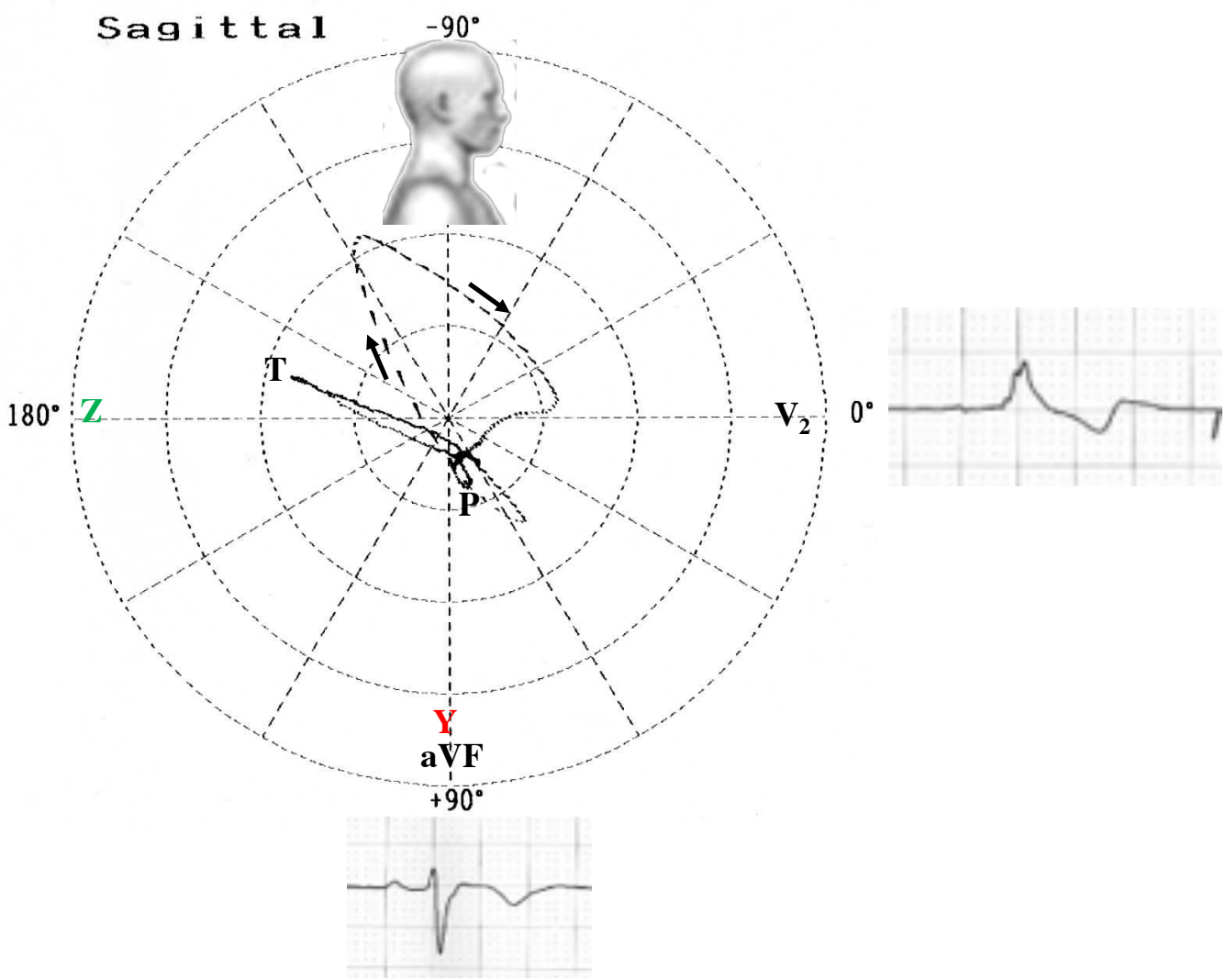
Sagittal
-90°
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Colleagues oppinions

Dear colleagues,

This patient has atypical chest pain and lives in a rural region in Brazil.
The ECG shows sinus rhythm, left anterior fascicular block, right bundle branch block, and abnormal repolarization in anterior and inferior walls.

The most likely diagnosis is Chagas cardiomyopathy. Less likely hypertrophic cardiomyopathy.
Thank you,
Mario Gonzalez MD
Gonzalez@hmc.psu.edu
Penn State Hershey Heart and Vascular Institute
500 University Drive
Hershey, PA 17033 USA

The ECG/Vector shows RBBB and LAFB. The T waves and chest pain are concerning for lateral ischemia and apical hypertrophy should be excluded.
Melvin Sheubman
Professor UCSF School of Medicine 500m Parnassus Avenue, MU San Francisco CA 94143 Melvin.Scheinman@ucsf.edu

Obviamente existe BCRD y HBIA. El bucle de T no es isquémico. En la isquemia el bucle T es redondeado y en esta paciente es alargado y angosto, lo que excluye isquemia. Me llama la atención que si pensamos en Chagas no hayan extrasístoles ventricularer.
Atte
Carlos Lavergne MD Argentina

English
Obviously there CRBBB and LAFB. The T loop is not ischemic, because ischemic T loop is rounded. In the present case it is narrow and long. I draw attention to the absence of PVCs in presence of chronic chagasic myocarditis .
Atte
Carlos Lavergne MD Argentina

Hello. Left anterior fascicular block, right bundle branch block. Atypical T-wave inversions in the inferior leads and the lateral precordial leads. The location of the T-wave inversions could point to myopericarditis. Could also be apical hypertrophic cardiomyopathy, but LVH is missing. Coronary artery disease can't be ruled out. Patient history makes takotsubo unlikely. We don't have Chagas disease, so I can't say anything about that.
Best Regards
Kjell Nikus
Tempere
Finland

Meu caro Andrés: Caso muito interessante. Vamos ás hipóteses

I. O ECG e o VCG mostram BRD+BDASE, provavelmente de etiologia chagásica. o que chama a atenção são as ondas T negativas em DII, DII, aVF e de V4 a V6. O VCG mostra a alça de P orientada para trás, com um aspecto bizarro. Se o diagnóstico for cardiopatia Chagásica crônica, a isquemia fica descartada, porque quando o ECG mostra "isquemia" não há correlação anatomopatológica. Em resumo Cardiopatia chagásica crônica e alteração de T

II. **Variante do normal.** Tenho vários pacientes geralmente mulheres com ondas T negativas e simétricas em várias derivações. A investigação com cintilografia e até cinecoronariografia, resultou normal. Nestes casos forneço às pacientes uma declaração que a negatividade de T corresponde a um padrão normal. Isquemia fica descartada porque a alça de T não é compatível (a T isquêmica possui alça arredondada.).

Outras possibilidades menos prováveis:

III) Hemorragia subaracnóidea

IV) Pericardite crônica.

Um grande abraço e feliz 2016.

Helio Germiniani MD PhD Curitiba Brasil

English

Dear Andrés: very interesting case report. Let's go to hypothesis

I) **Chronic Chagas myocarditis:** The ECG and VCG show RBBB + LAFB probably due to Chagas disease. The negative T wave in DII, DII, aVF and V4 to V6. The VCG shows the P loop driven back, with a bizarre appearance. If the diagnosis is chronic Chagas disease, ischemia is ruled out, because when the ECG shows "ischemia" there is no pathological correlation.

II) **Normal variant.** I have several patients usually women with negative and symmetric T waves in various derivations. The investigation with scintigraphy and to coronary angiography was normal. In these cases the patients we provide a statement that the negativity of T corresponds to a normal pattern. Ischemia is discarded because the T loop of the VCG is not compatible (ischemic T has rounded loop.).

Other less likely possibilities:

III) Subarachnoid hemorrhage

IV) Chronic pericarditis.

Best wishes and happy 2016.

Helio Germiniani MD PhD Curitiba Brazil

Hola amigos potro y zorro Mi opinion Por los antecedentes clinicos mencionados interpretaria el ECG como ritmo sinusal, FC 60bpm, BCRD, BDAS y ondas T negativas gigantes (> 10mm) . Posibles etiologias: 1) Miocardiopatia chagásica forma dromotrópica. Una simple serogia confirmaria . la tiene ?; 2) Cardiopatia isquemica 3) Miocardiopatia hipertrofica apical o forma japonesa de MCH o sindrome de Yamaguchi (me inclino por esta posibilidad) por las o ndas T gigantes negativas (mas de 10mm); 4) Miocardiopatia abalonada apical de -Tako tsubo (mas frecuente en mujeres). Que pruebas indicaria: Serologia para Chagas, Ecocardiograma procurando hipertrofia del segmento apical, Cinecoronariografia con ventriculografia pezquizando imagen tipica de "as pique " en caso de MCH apical y RNM con gadolinio
En espera de los métodos complementarios
Abrazos
Juan Jose Sirena MD Santiago del Estero Argentina

Hello friends Colt and fox My opinion: By case history as mentioned interpret the ECG: sinus rhythm, HR 60bpm, CRBBB, LAFB and giant negative T waves (≥ 10mm). Possible etiologies: 1) Chagas Cardiomyopathy dromotropic would confirm with serogy. It was made?; 2) Ischemic heart disease; 3) apical hypertrophic cardiomyopathy (ApHCM)**, Japanese form or Yamaguchi syndrome (I lean towards this possibility) giant negative T waves (more than 10mm); 4) Apical ballooning cardiomyopathy -Tako tsubo (more common in women). Indicating tests: Serology for Chagas, echocardiogram find tempting apical segment hypertrophy, coronary angiography with ventriculography find tempting spade-like appearance and MRI with gadolinium**
Pending complementary methods
Hugs

Hard to tell. What about blood test? Complete RBBB and widespread negative T waves, symmetric and profound in some leads, without delayed ventricular repolarization. Tako Tsubo? Cardiac memory of a transient acute coronary obstruction, spasm? Transient acute myocardial ischemia? Myocardial stunning? We need more clinical details.

Best,

Philippe Chevalier
Claude Bernard University Lyon 1
Villeurbanne, France

Prezados Maestros: Ritmo sinusal regular, FC = 56bpm, P: duração = 80ms, eixo do: P = +/- 50º , intervalo PR 170ms, eixo do QRS = - 45º, duração do QRS 130ms, padrão rsR´ em V1, R alargado em torre em V2, RS (R em torre com entalhe) V3 RS em V4 e Rs V5,e V6. Ondas T: invertidas em DII, DII, aVF e profundamente invertidas não simétricas de V4 a V6

Conclusão

1, Bloqueio Divisional do Ramo Antero-Superior Esquerdo: Eixo elétrico de QRS ≥ - 45°; rS em D2, D3 e aVF com S3(13mm) >S2; c) Onda S de D3 com amplitude maior que 15 mm (ou área equivalente); no caso apenas 13mv, qR em D1 e aVL com tempo da deflexão intrinsecóide > 50 ms ou qRs com "s" mínima em D1; TDI = 55ms, qR em aVL com R empastado; progressão lenta da onda r de V1 até V3; não avaliável pelo BRD, presença de S de V4 a V6.

2. Bloqueio do Ramo Direito: QRS alargados com duração ≥120 ms como condição fundamental, ondas S empastadas em D1, aVL, V5 e V6; Ondas S presentes não empastadas, padrão qR em aVR com R empastada, rSR' ou rsR' em V1 com R' espessado;, onda T assimétrica negativa em oposição ao retardo final de QRS lateral e inferior, não específica mas sugestivo de componente isquêmico

Não tenho muito conhecimento de VCG mas penso nos seguintes diagnósticos diferenciais:

1. Cardiopatia Chagásica crônica, pela clássica associação de BRD e BDRASE num paciente procedente da América Latina
2. Cardiopatia isquêmica - menos provável
3. Cardiopatia hipertensiva - com mínima possibilidade

Conduta – Ecocardiograma e sorologia

Abraços A|dail

English: Dear Professors: sinus rhythm, HR = 56 bpm, P duration = 80 ms, P axis = +/- 50º, PR interval 170ms, QRS axis = - 45°, QRSd = 130 ms, rsR' in V1, a wide R tower in V2, RS (R tower notched) in V3-V4, and Rs in V5/V6. Inverted T waves in II, II, aVF and deeply inverted asymmetrical T waves from V4 to V6.

Conclusion: 1, LAFB: QRS axis ≥ - 45°; rS in II, III and aVF with SIII (13mm)> SII; c) qR pattern in I and aVL with R-peak time > 50 ms.

2. RBBB: QRSd ≥120 ms, broad S waves in I, aVL, V5 and V6, qR pattern in aVR, triphasic pattern RSR' in V1

Differential diagnosis: Chronic Chagasic myocarditis (classical association RBBB + LAFB) in a patient from Latin America

Ischemic heart disease - less likely; Hypertensive heart disease - minimal possibility

Conduct - echocardiogram and Chagas serology

Hugs

Querido Andrés. Presenta serología positiva para Chagas y cambios ECG que evidencian afectación del sistema de conducción intraventricular (BCRD y HBAI). Por lo que es una paciente con enfermedad de Chagas y angor. Los trastornos de la repolarización no están relacionados a los trastornos de conducción. Los diagnósticos diferenciales son:
1. Isquemia antero-apical sea por enfermedad coronaria o de la microcirculación por su enfermedad de Chagas.
2. Miocardiopatía hipertrófica. No me parece.
3. Aneurisma apical por su enfermedad de Chagas.
4. Takutsubo.
Sería interesante conocer los resultados del ecocardiograma y las enzimas cardíacas.
Cuanto tiempo de evolución tiene el Angor? En que clase funcional está? Mejoró con nitrito sublingual?
Le indicaron nitritos y AAS por lo que pienso que han sospechado de coronariopatía. En ese caso, no debería haber retornado para casa sin ser estudiada.
Un abrazo
Martín Ibarrola MD

Dear Andrés. She has positive serology for Chagas and the ECG shows involvement of the intraventricular conduction system (RBBB and LAFB). So she has Chagas disease and angina. In my opinion, the repolarization disturbances are not related to conduction disturbances.
The differential diagnoses are:
1. Anteroapical ischemia consequence of CAD or microcirculation affectation by Chagas disease.
2. Hypertrophic Cardiomyopathy. I do not think so.
3. Chagas disease with apical aneurysm.
4. Takutsubo.
It would be interesting to know the results of echocardiography and cardiac enzymes.
How long has the Angor evolution? What is the NYHA functional class?
Did she get better the pain with sublingual nitrite?
I think they have suspected CAD because the prescript drugs. In this case the patient should not have returned without coronary angiography.
Hugs

Queridos participantes: mujer de 58 años que hace 3 meses presentó dolor precordial “opresivo” de reposo; se le realizó ECG y enzimas cardíacas para descartar SCA con valores normales. ECG ritmo sinusal, PR de 160 ms, QRSd 140 ms, BRD y HBAI con T negativas bastante simétricas, gigantes anterolateral con segmento ST levemente descendente y negativas inferior con segmento ST rectificado; QTc 480 ms. Onda P +70º, en el PH parecería existir un componente un poco más importante posterior pero el mismo no se observa en el PSD de características normales. Bucle del QRS patrón HBAI + BRD. Asa T atrás arriba y a la derecha, alongada con aumento del voltaje de su vector máximo; (discordante con la T+ de I). Pensaría que la función sistólica y la motilidad del VI están conservadas y normales. Diagnósticos diferenciales: Miocariditis: virales, bacterianas, micóticas, rickettsiósicas, por protozoarios, cardiotoxinas, catecolaminas, antraciclinas, ciclofosfamida, cocaína, metales pesados (cobre, plomo, hierro), alcohol, arsénico, CO, metisergida, cocaina., reacciones de hipersensibilidad: antibióticos (penicilinas, cefalosporinas, sulfonamidas), diuréticos (tiazidas, diuréticos de asa), dobutamina, litio, toxoide tetánico, clozapina, metildopa, picaduras de insectos (abejas, avispas, arañas, escorpiones), mordedura de víboras, enfermedades colágeno-vasculares, sarcoidosis, Kawasaki, hipereosinofilia, granulomatosis de Wegener, tirotoxicosis, radiación, Tako-Tsubo, MCH, cardiopatía isquémica, fistula coronaria, tromboembolia pulmonar aguda, tromboembolia pulmonar crónica recidivante con HP o sin ésta, electro-shocks cerebrales, hipertensión endocraneana, hipersimpaticotonía, alcoholismo, alteraciones hidroelectrolíticas, hiper e hipoparatiroidismos, infartos cerebrales lacunares difusos, modulación electrotónica o “memoria” de la onda T, cambios bruscos de la FC, aumento del estrés parietal meridional sistólico, linfoma de células B, anestesia general, cirugía maxilofacial, bloqueo A-V completo, ondas T negativas gigantes en el síndrome de Guillain-Barré, hemorragia subaracnoidea, terapia con sotalol para revertir FA, aneurisma y seudo aneurisma de la punta del VI. Afectuosamente Isabel Konopka

English: Dear forum participants: 58y/o woman who presented three months ago "crushing" chest pain at rest; He underwent ECG and cardiac enzymes to rule out ACS with normal values. ECG sinus rhythm, PR 160 ms, QRSd 140 ms , RBBB and LAFB rather symmetric negative T, anterolateral giants downward slightly lower ST segment and negative rectified with ST segment; QTc 480 ms. P axis +70°, the PH there seems to be a little further more important component but it is not observed in the right sagittal normal characteristics. QRS loop pattern LAFB + RBBB. T loop to back and right, elongated with increasing peak voltage vector (discordant with the TI). I think that systolic function and motility LV are preserved and normal. Differential diagnosis: Myocarditis: viral, bacterial, fungal, rickettsiosis, protozoal, cardio toxins, catecholamine, anthracyclines, cyclophosphamide, cocaine, heavy metals (copper, lead, iron), alcohol, arsenic, CO, methysergide, cocaine. Hypersensitivity reactions: antibiotics (penicillin, cephalosporin, sulfonamides), diuretics (thiazide diuretics), dobutamine, lithium, tetanus toxoid, clozapine, methyldopa, insect stings (bees, wasps, spiders, scorpions), snake bite, collagen-vascular disease, sarcoidosis, Kawasaki disease, hyper eosinophilia, Wegener granulomatosis, thyrotoxicosis, radiation, Tako-Tsubo, HCM, CHD, coronary fistula, APE, chronic recurrent PE with or without PH, brain electroshocks, intracranial hypertension, hypersimpaticotony, alcoholism, electrolyte, hyper and hypoparatiroidisms disturbances, diffuse lacunar strokes, electrotonic modulation or "memory" of the T wave, sudden changes in HR, increased systolic wall stress southern, B-cell lymphoma, general anesthesia, maxillofacial surgery, complete AV block, Guillain-Barre syndrome giant negative T waves, subarachnoid hemorrhage, sotalol therapy to reverse AF, aneurysm and pseudoaneurysm of the LV apex. Affectionately Isabel Konopka

Final Conclusions

Andrés Ricardo Pérez-Riera, MD, PhD.
Post-Graduates Advisor at Design of Studies and Scientific Writing Laboratory in the ABC Faculty of Medicine - ABC Foundation - Santo André – São Paulo – Brazil
Raimundo Barbosa-Barros, MD.
Chief of the Coronary Center of the Hospital de Messejana Dr. Carlos Alberto Studart Gomes. Fortaleza - Brazil

Conclusion

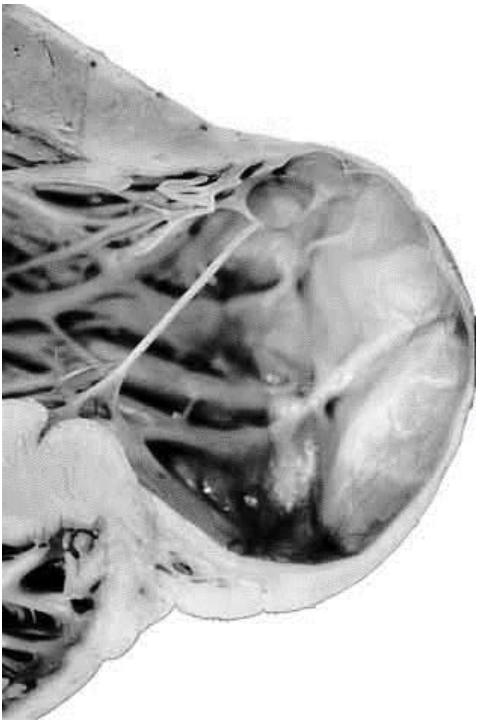
Chronic Chagasic myocarditis

I. **Positive epidemiological** history Woman proceed of endemic rural Area in Brazil. In this country, the classification of *T. cruzi* and their correlation with the clinical manifestations of the chagasic infection have been more detailed in the Reconcavo Baiano-Bahia State (**Andrade 1983**).

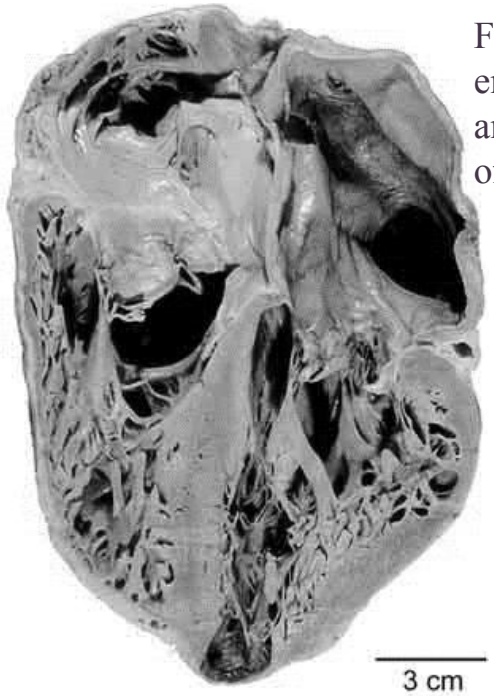
II. **Positive serology:** We evaluated three IgG ELISAs, CeLLabs T. cruzi ELISA, Hemagen Chagas' kit and IVD Research Chagas' Serum Microwell ELISA, and MarDx indirect immunofluorescent assays. All were positive

III. **Echo:** Apical aneurism by transthoracic, two-dimensional echocardiography in long axis view, in apical four-chamber, two-chamber views and in subcostal view.

IV. **Left ventriculography** showed apical aneurism of the LV with "glove's finger" morphology . The lesion appears as an apical akinesia, best seen in left anterior oblique view. Absence of apical thrombi

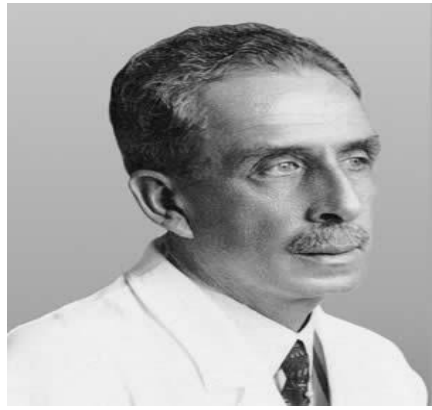


Apical aneurism of the LV with "glove's finger" morphology

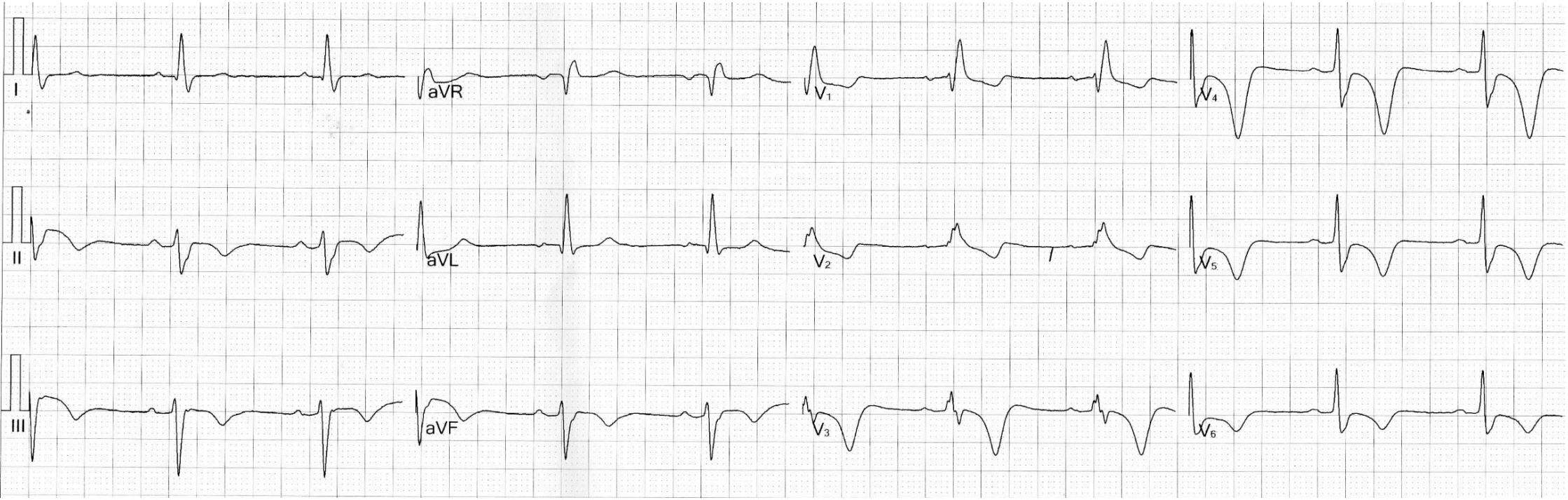


Four-chamber frontal section of globally enlarged chronic chagasic heart (dilatation and hypertrophy) with an apical aneurysm of the left ventricle.

Dr. Carlos Chagas



Name: EMLS; **Age:** 58y/o; **Weight:** 57kg; **Height:** 1.57m; **Date:** Dec 02, 2015; **Medication in use:** acetylsalicylic acid, rosuvastatin 10mg/day, sublingual isosorbide dinitrate 5mg at first sign of chest pain/discomfort.



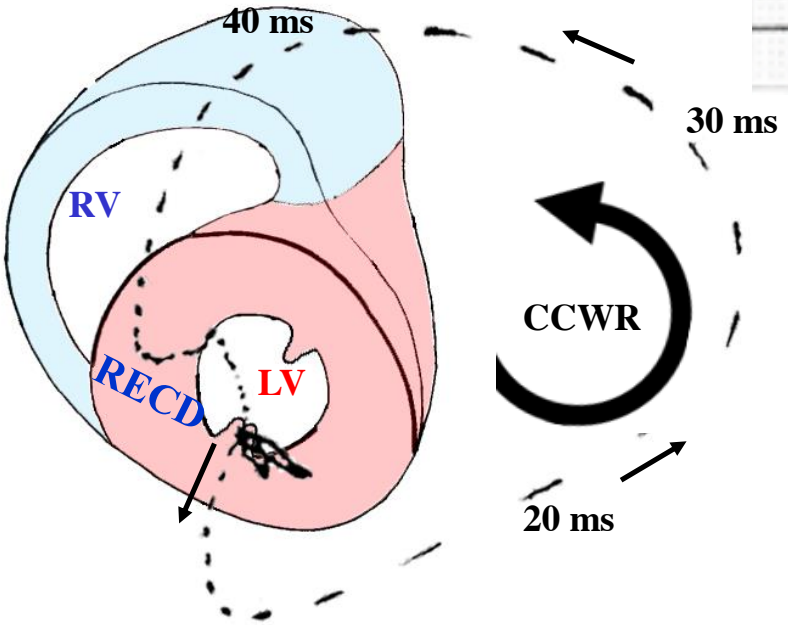
Clinical diagnosis: Chronic chagasic myocarditis with apical aneurism. Minimal augmentation of diastolic and systolic diameters, LVEF 62%
ECG diagnosis: sinus bradycardia, extreme left axis deviation(-72°), SII>SII, qRs pattern in I and aVL , wide QRS duration (130ms), triphasic QRS pattern in V1, qR in aVR, broad final S waves in left leads.
Deep T waves across precordial leads and inferior leads, prolonged QT/QTc (524/483 ms)
Conclusion

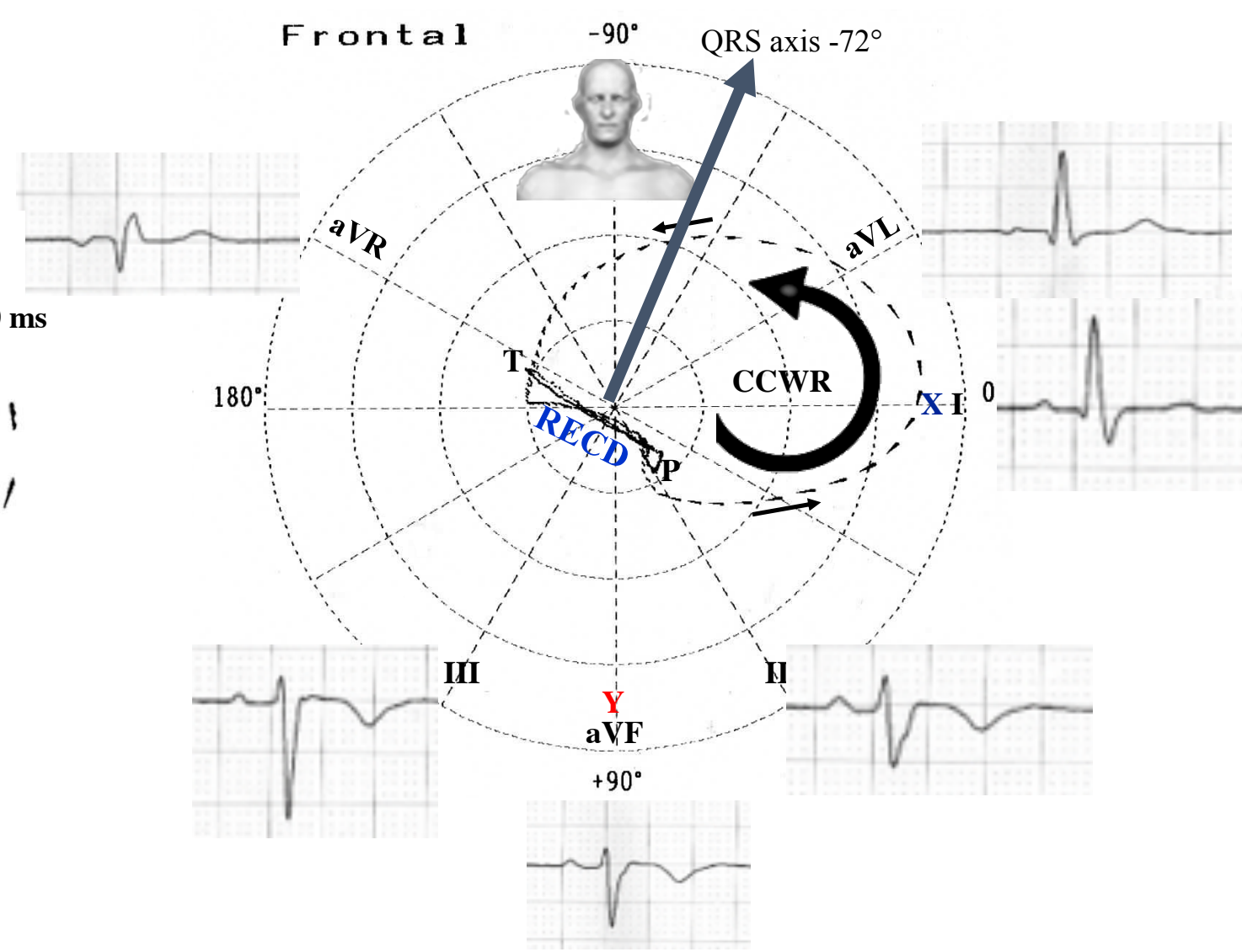
1. Left Anterior Fascicular Block
2. Complete Right Bundle Branch Block

} Right Bundle Branch Block + Left Anterior Fascicular Block (see comments in the next slide)

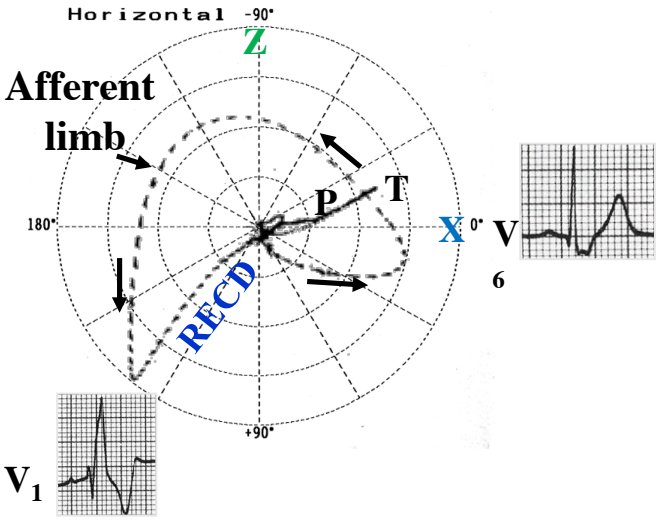
3. Prolonged QT/QTc intervals: 524/483 ms
4. Diffuse near giant negative asymmetrical T wave in anterior and inferior walls

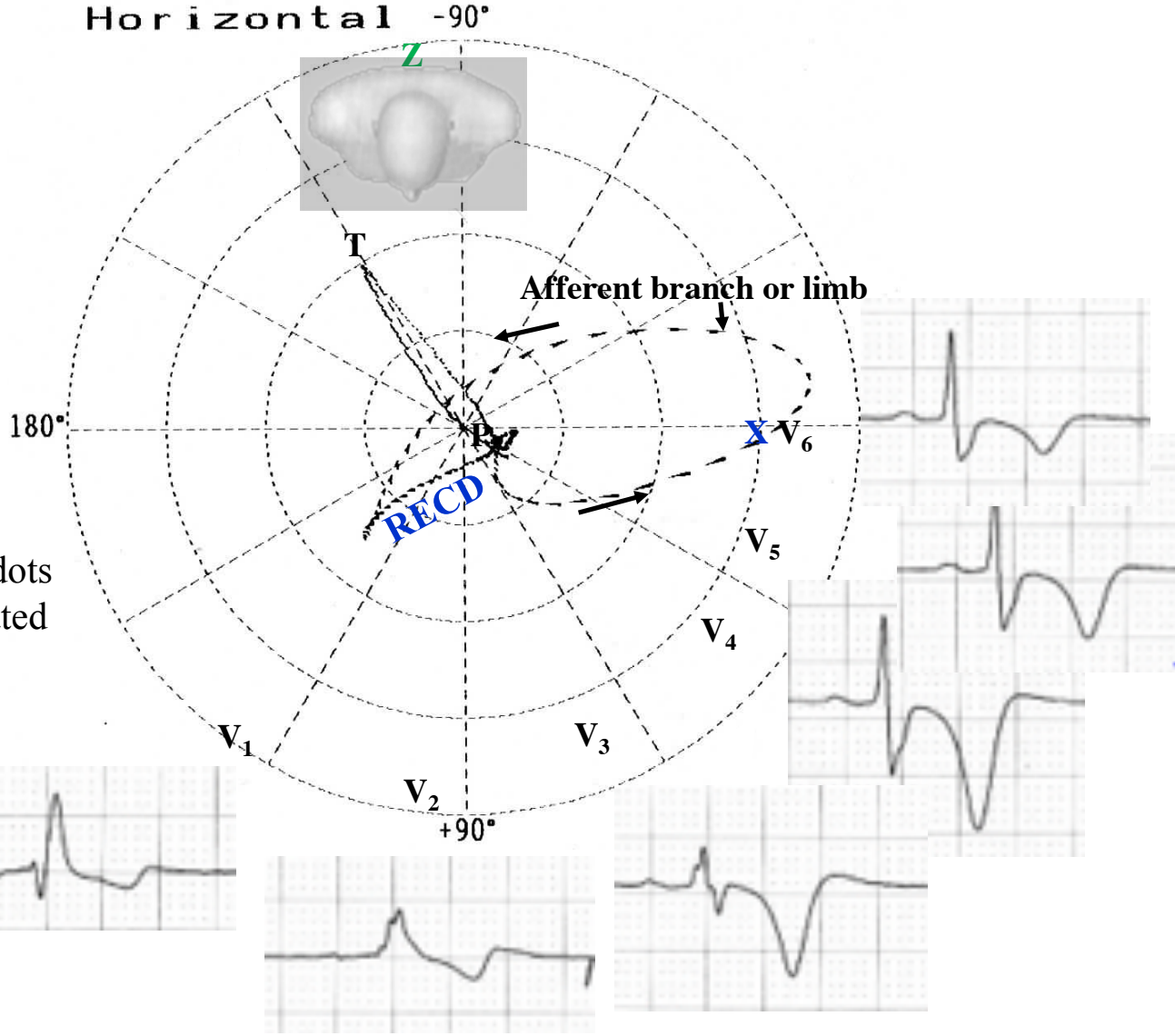
The present case of ECG/VCG correlation in the frontal Plane: LAFB + CRBBB





The present case ECG/VCG correlation on Horizontal Plane

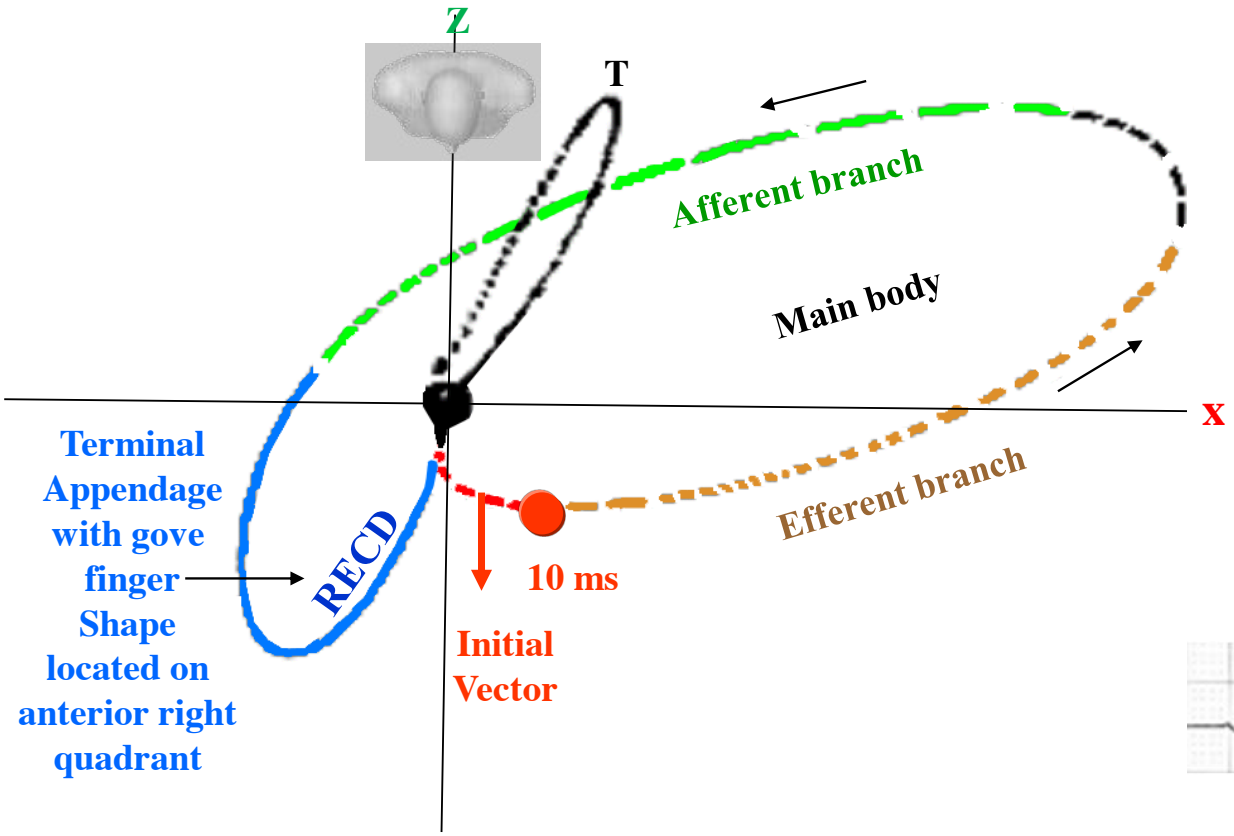


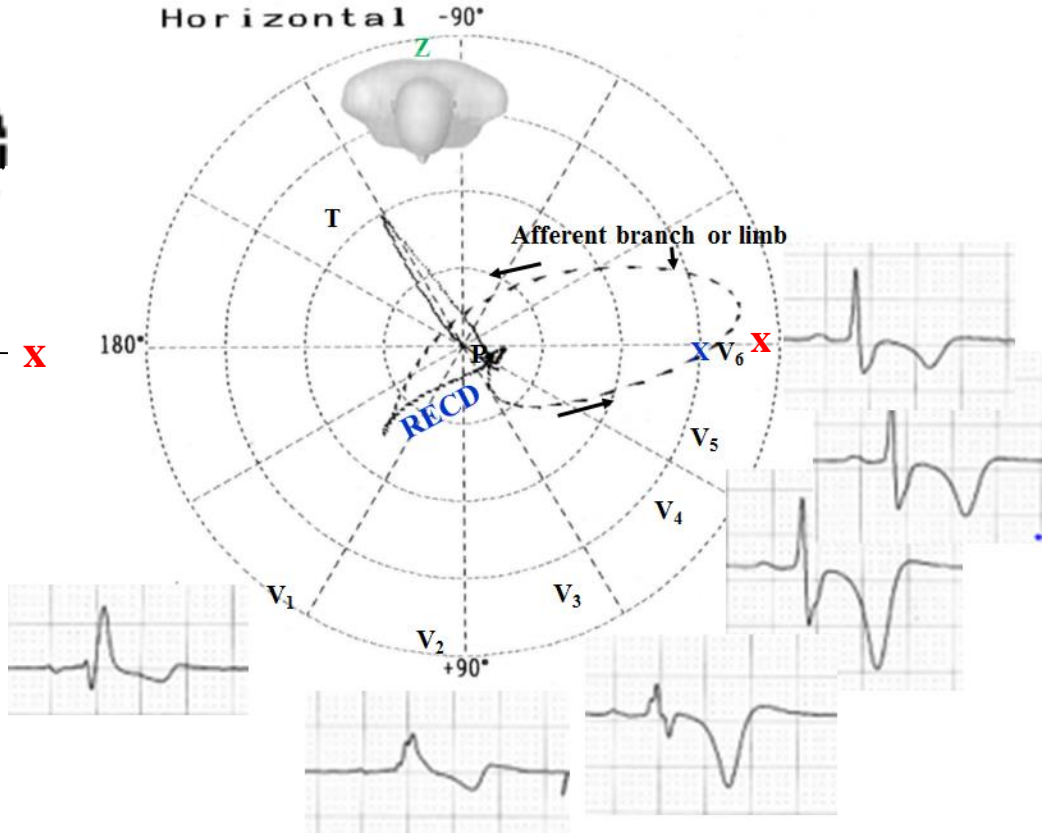


RECD: Right End Conduction Delay: The terminal dots are close together, reflecting end conduction delay located on right anterior quadrant(see next slide).

Complete RBBB Grishman type or Kennedy type I

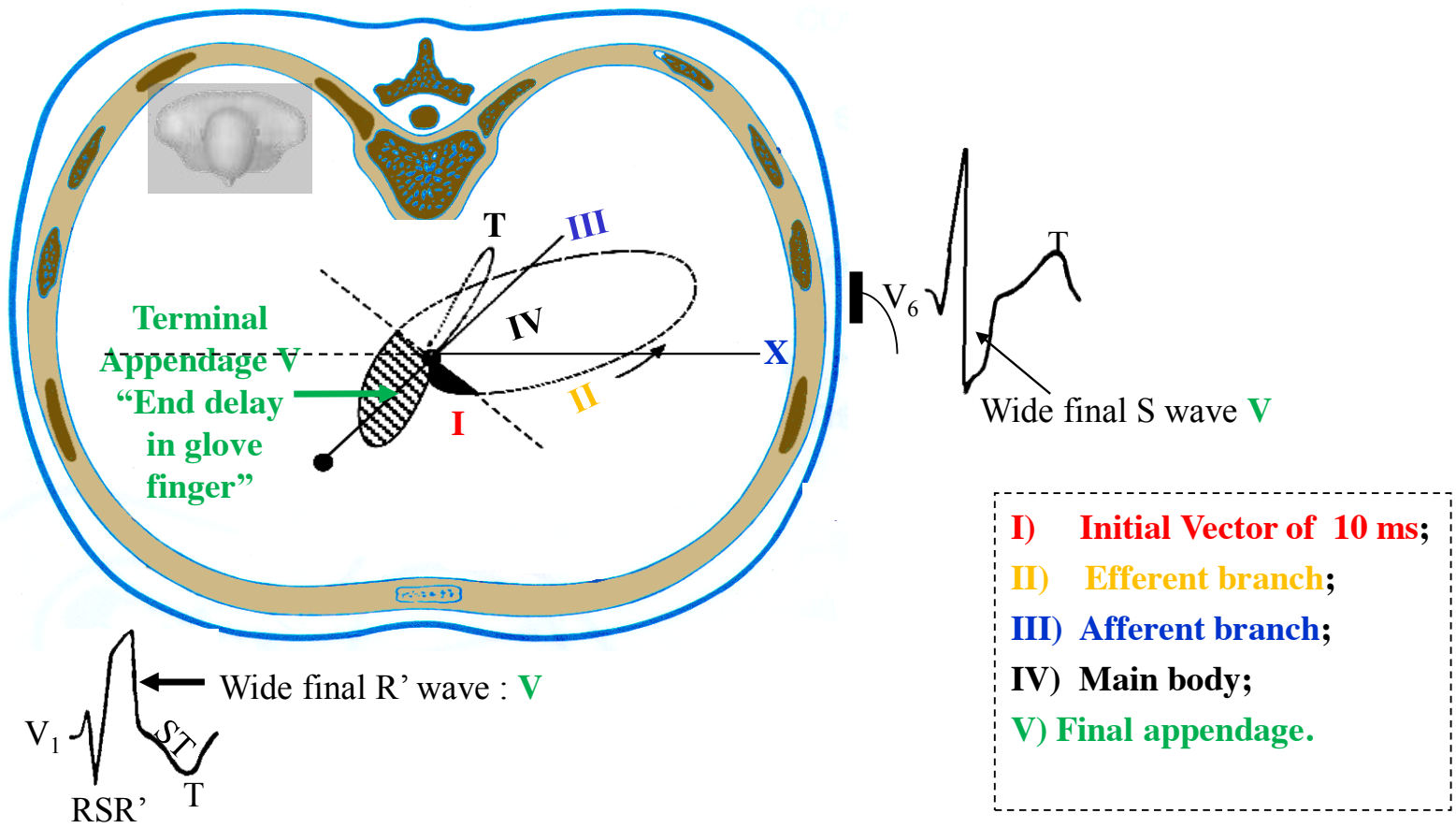
Complete RBBB Grishman or Kennnedy type I: The afferent limb located behind the orthogonal X lead





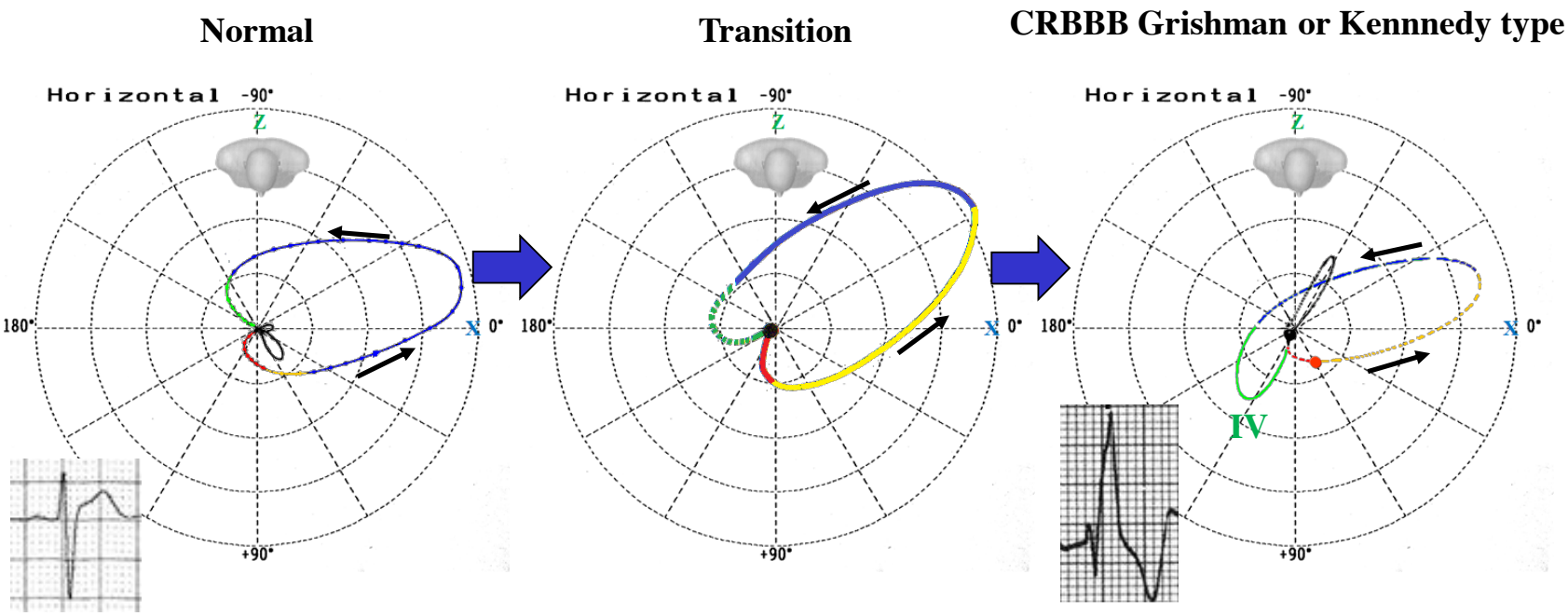
RECD: Right End Conduction Delay: The terminal dots are close together, reflecting end conduction delay

ECG/ VCG correlation in the HP with ECG in uncomplicated CRBBB



QRS/T loops in the horizontal plane showing the 4 components of depolarization: initial vector, efferent branch, afferent branch and terminal appendage and T wave heading to the back and the left, and its correlation with the QRS/ST-T complex in V1 and V6.

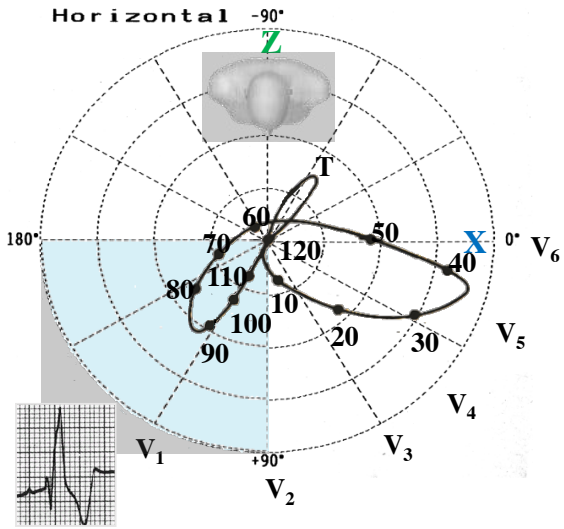
The figure shows the effect on the configuration of the horizontal QRS loop produced by development of RBBB during cardiac catheterization. With onset of the block, a rightward anterior final appendage was produced, which gradually went away has the transient BBB cleared. A slight increase in the leftward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



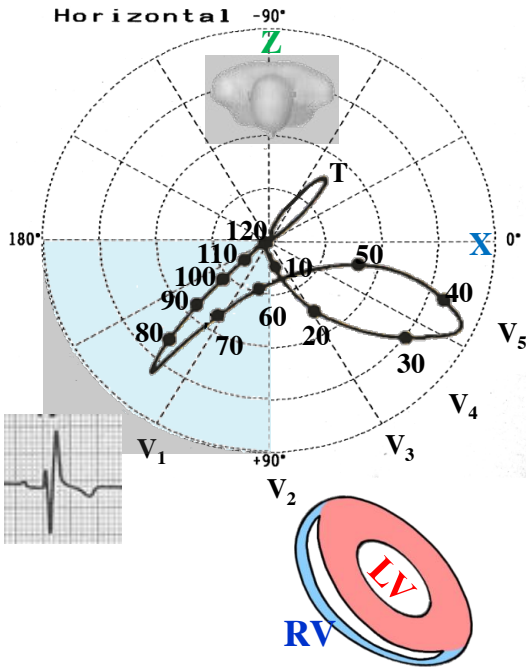
IV - Rightward anterior final appendage
RECD: Right End Conduction Delay: The terminal dots are close together, reflecting end conduction delay located on right anterior quadrant

In three patterns the terminal vector of 60 ≥120ms in "glove finger" (finger-like terminal appendix) located in the right anterior quadrant

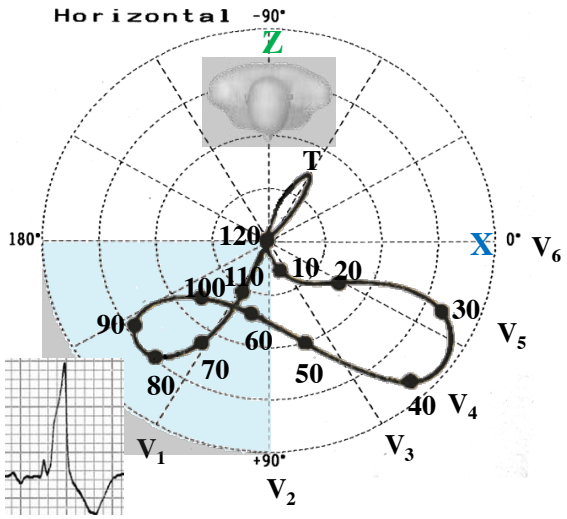
Grishman or Kennnedy type I



Cabrera or Kennedy type II

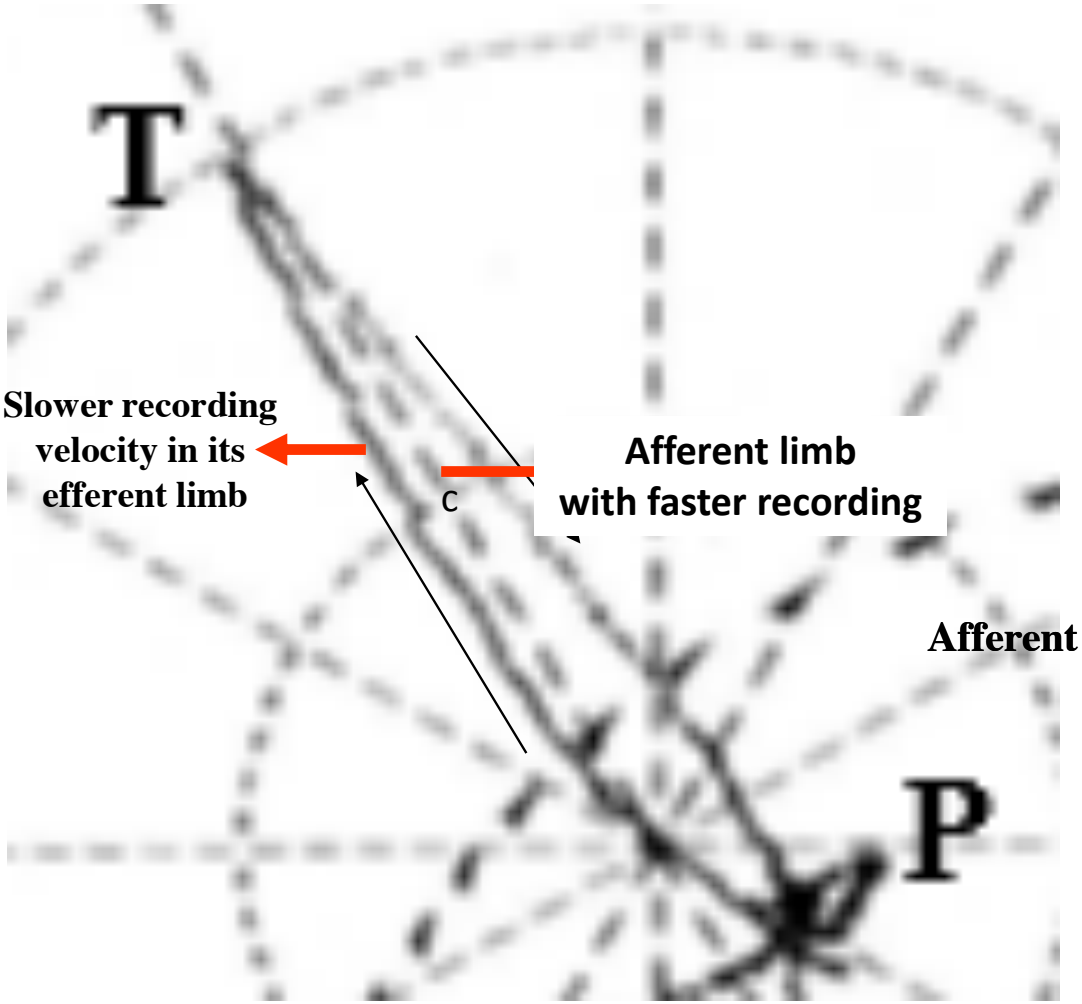


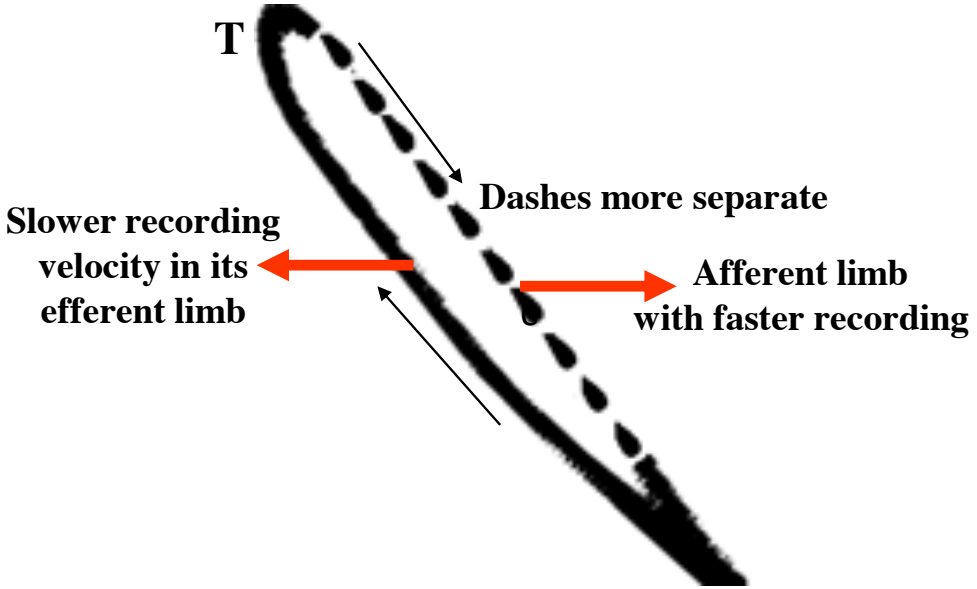
Kennedy type III or C

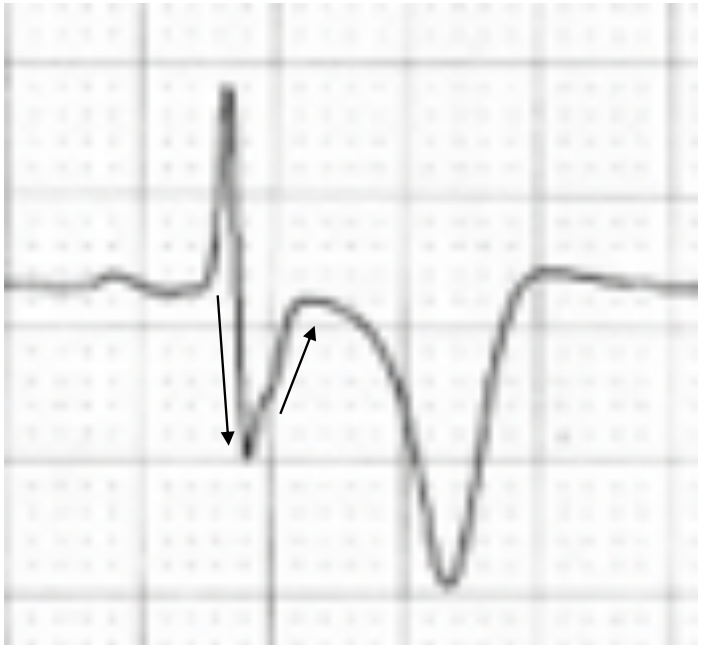


Right anterior quadrant Righ end conduction delay

Observation: The numbers are expressed in miliseconds

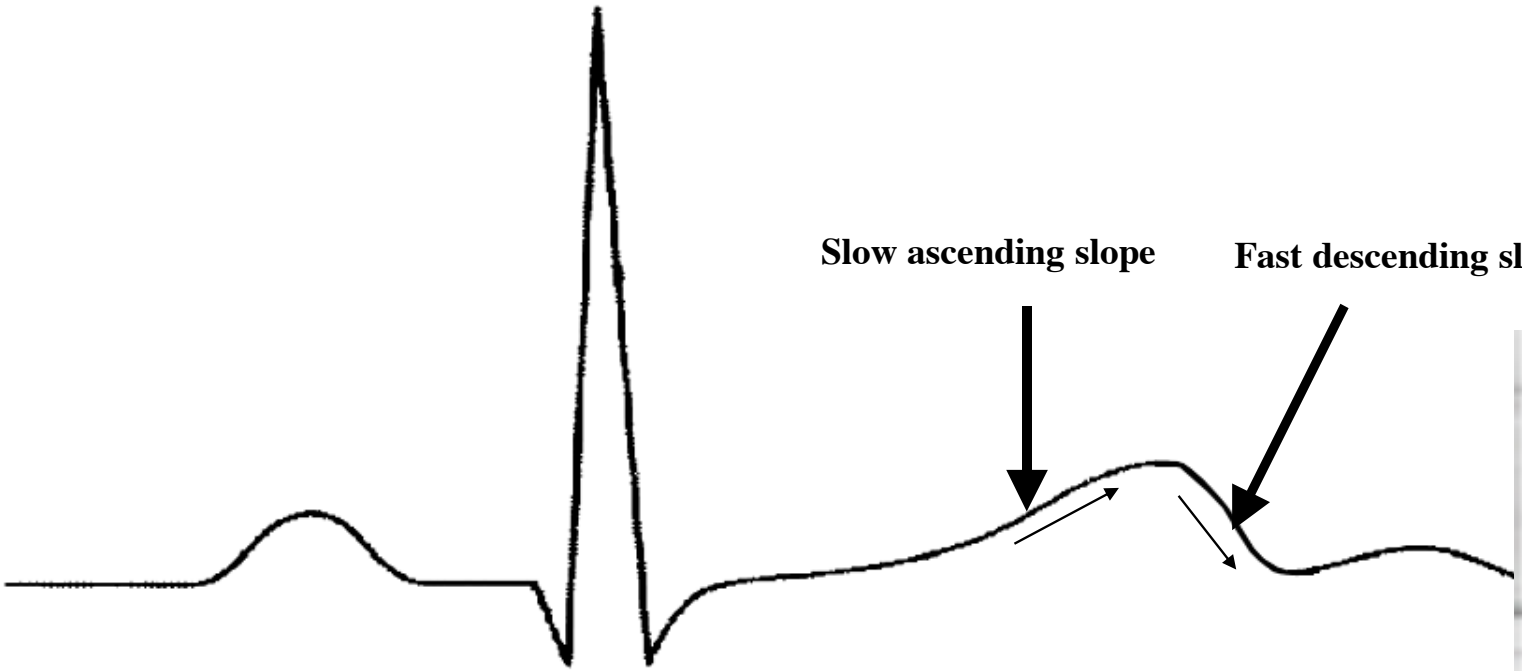


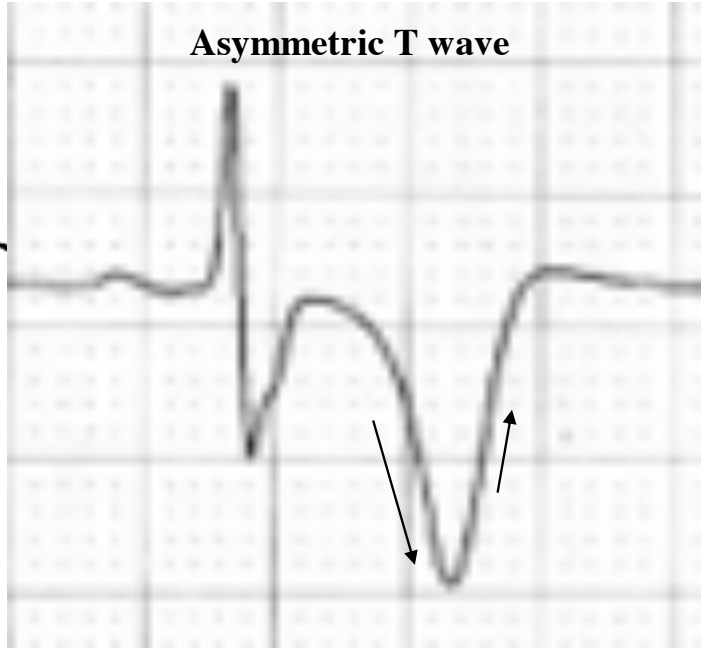




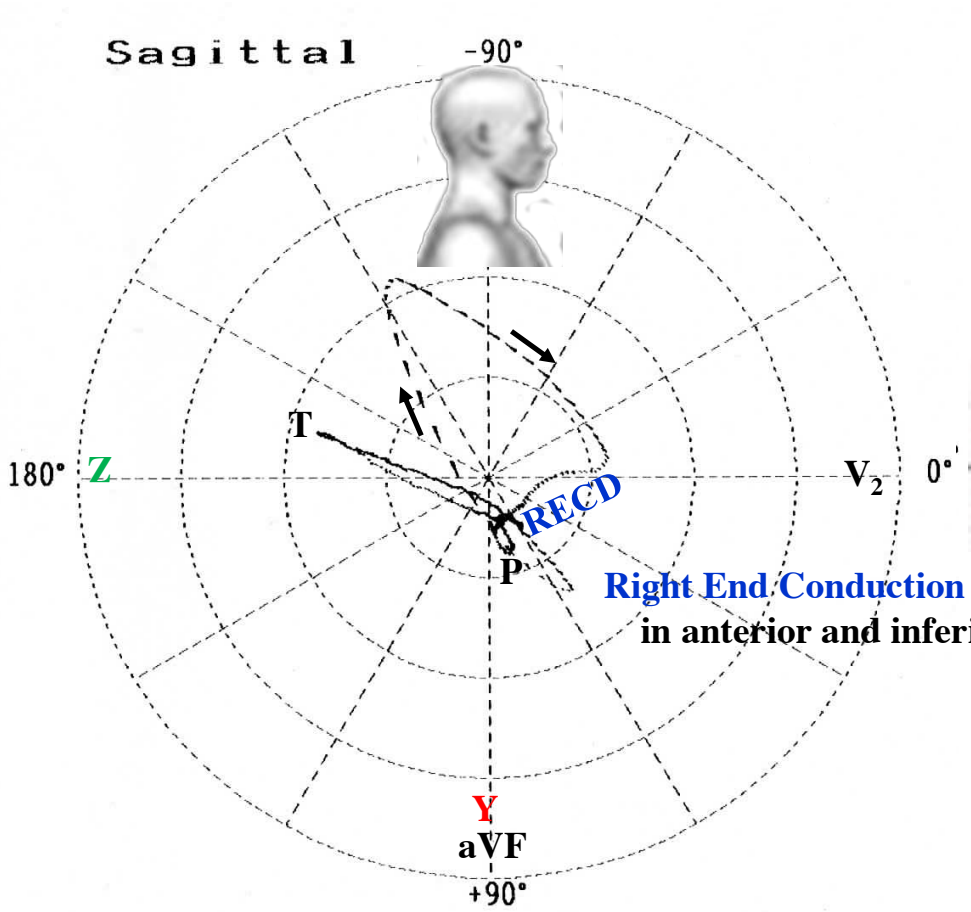
Characteristic normal secondary T loop of VCG and its efferent limb of slow inscription and its faster afferent (dashes more separate).

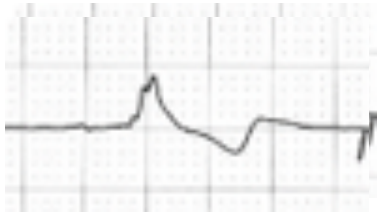
Normal aspect or shape of T wave: assymetric



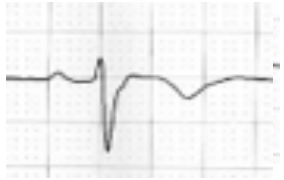


ECG/VCG correlation on Right Sagittal Plane





Right End Conduction Delay (RECD)
in anterior and inferior quadrant



CRBBB associated to LAFB (bifascicular block)

It constitutes the most frequent type of bifascicular block. In the first world it was estimated in 1.4% of all ECGs. In patients that developed complete AV block and had to have a pacemaker implanted, this association was found previously in 35% of the cases.

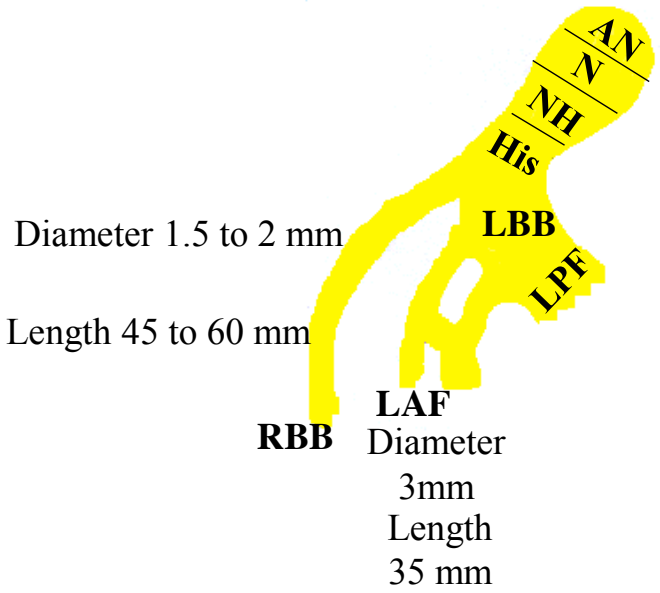
Etiologies

1. **Chronic chagasic myocarditis**: it constitutes the most frequent association in Latin America, where chronic chagasic myocarditis exists from the Argentinean Patagonia up to the frontier with USA. In the CRBBB of chronic chagasic myocarditis, the high association with LAFB stands out: 70% of the cases. In patients younger than 40 years old, from the endemic area, with ECG that shows association of CRBBB and LAFB, there is a high suspicion of chronic chagasic myocarditis, and even more with the additional presence of polymorphic ventricular extrasystole and primary alterations of ventricular repolarization. The association considered typical and most frequent, is complete right bundle branch block (CRBBB) of the His bundle and left anterior fascicular block (LAFB).A longitudinal study of 5,710 infected patients, showed that the presence of CRBBB associated to primary alterations of repolarization and electrically inactive areas, indicates high risk of death. Autopsy studies conducted by Andrade, revealed that most of the patients with chronic chagasic heart disease present a significant involvement of the excito-conductor system at the level of the N-H portion of the AV node, right penetrating and branching portion of the His bundle, proximal portion of the right branch and the anterosuperior division of the left branch. We conclude that CRBBB of chronic chagasic heart disease is of the proximal type (**Shabelman 1961; Rosembaum 1964; Dubner 2008**). The most common ECG changes are the following complete RBBB (35%) and LAFB (35%) (**Marques 2006**). RBBB with LAFB is strongly related to Chagas disease in older patients (**Ribeiro 2014; Garzon 1995**).
2. **Coronary artery disease:** it constitutes the main cause in the first world, where chagas disease does not exist. It is estimated in 1% of the hospital population. It constitutes a complication of acute myocardial infarction of approximately 6%, almost always by obstruction of the LAD artery, since the RBB and the left anterior fascicle are irrigated by the perforator branches of this artery.
3. **Hypertensive heart disease**: 20 to 25% of the cases;
4. Sclero degenerative disease of the His system, Lev disease or sclerosis of the left side of the cardiac skeleton;
5. Chest trauma. The closed trauma of the chest without a cut is frequently accompanied by CRBBB. In this case, the CRBBB frequently disappears after some hours.

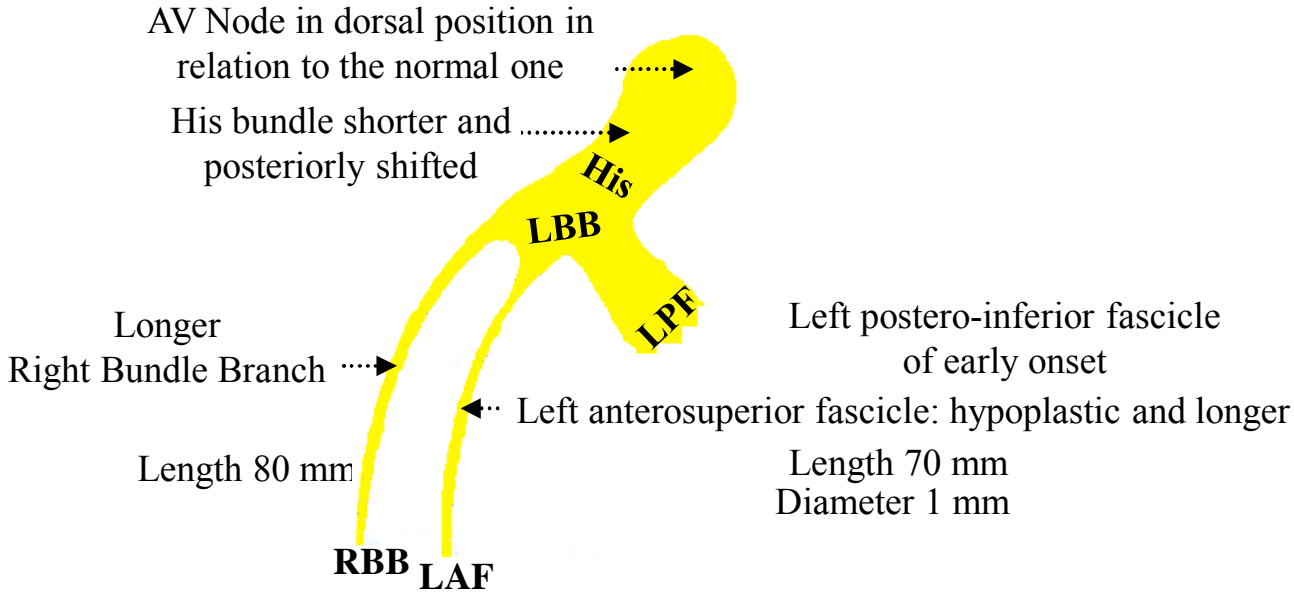
7. Familial with syncope or sudden death genetic Lenègre disease with or without high blood pressure.
8. **Other myocarditis;**
9. **Sarcoidosis;**
10. **Granulomatosis;**
11. **Aortic valve disease;**
12. **Hyperkalemia or hyperpotassemia;**
13. **Congenital isolated;**
14. **Associated to progressive external ophthalmoplegia;**
15. **Post-surgical trauma:** 1) After corrective surgery of Fallot, we may find CRBBB associated to LAFB (7 to 25% of the cases). It is of the truncus and it indicates that the LAF has been injured concomitantly when the surgeon sutured the "patch", placed to increase the RVOT. The patients that remained with bifascicular block after corrective surgery do not present a greater index of late mortality.2) In 4% of the cases after corrective surgery of VSD. 3) After surgery of substitution of tricuspid valve: it has been described as a complication in the exchange of tricuspid valve. 4) After surgery of bypass of internal thoracic and/or saphenous artery, it has been observed in 4% of the cases. The CRBBB in isolation was observed in 6% and LAFB in 6%;
16. **Post-orthotopic heart transplantation:** The most frequent case is CRBBB or IRBBB in isolation (present in 45% to 80%), which may be associated to LAFB in approximately 20%, presenting in most of the cases a permanent nature.
17. **Atrial septal defect of the canal ostium primum type or endocardial cushion defects**: In the horizontal plane we frequently find incomplete RBBB or complete RBBB pattern with sings that suggest RVE and/or BVE. Thus, in the right precordial leads V3R and V1 we can see triphasic patterns of the rsR' or rSR' type with opposite ST and T indicating not very high pressure in the pulmonary artery. In endocardial cushion defects, the right branch is congenitally longer; a fact responsible for the incomplete RBBB or advanced RBBB pattern. In fact, it is a false branch block, since the pattern is due to a delay in RV activation, because the stimulus must go through a longer trajectory. In more than 98% of the cases, extreme deviation of SAQRS is verified concomitantly in the left or right superior quadrants. The latter is more frequent in the total form and showing a pattern of counterclockwise rotation of QRS loop in the frontal plane of the LAFB type. Indeed, there is no true LAFB, but there is early activation of the LV posteroinferior wall by early onset too, of the posteroinferior fascicle of the His bundle, associated to a hypoplasia and extension greater than the anterosuperior fascicle, which delays even more the activation of the anterosuperior wall of the LV.

CRBBB associated to LAFB by endocardial cushion defects: Etiology

Normal intraventricular His system



Intraventricular His system in endocardial cushion defects



It explains RBBB and early posteroinferior activation of the LV
(delayed anterosuperior region activation: Pseudo LAFB.)

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Caro M, Conde D, Pérez-Riera AR, de Almeida AP, Baranchuk A. The electrocardiogram in Down syndrome. Cardiol Young. 2015 Jan;25(1):8-14.

CRBBB associated to LAFB: Electrocardiographic criteria

The criteria for CRBBB are observed in the horizontal plane, while those of LAFB in the frontal plane; on the other hand, LAFB modifies the middle portions of ventricular activation while CRBBB modifies the final ones.

1) QRS complex of duration ≥ 120 ms in the presence of supraventricular command.
2) QRS of duration > 130 ms and SÂQRS from -30° to –90°, which individualize the patients with a greater probability of cardiovascular disease;
3) Extreme deviation of SÂQRS in the superior quadrants: beyond –30°, which may go beyond -90°. The axis between -30° and -45° suggests minor degree of LAFB. If SÂQRS is located in the right superior quadrant, it indicates important participation of CRBBB and/or association with RVE;
4) qR pattern in aVL. qRS or RS morphology may be found. The small initial q wave indicates the first vector heading downward and to the right, produced by the non blocked septal and posterior fascicles. The R wave indicates superior shift of the loop by the LAFB when activating the blocked anterosuperior region;
5) Right precordial leads V3R, V1 and V2: triphasic pattern of the rSR' or rsR' type, with R' greater than r. There may be R with notch ("M shaped") rR' or qR;
6) Broad S wave with a duration ≥ 40 ms in adults in left leads V5, V6 and I by end delay to the right and the front of CRBBB.
7) J point, ST and T opposite to the final deflection of QRS: in the left leads with the J point and the ST segment discretely elevated with positive T and asymmetrical branches (slow ascending and fast descending).

In an 11-year period 209 cases of bilateral BBB (RBBB + LAFB or LPFB). The majority of patients had evidence of CAD or hypertension. A significant number had no clinical evidence of heart disease. The majority of patients had follow-up about 2 years. The incidence of complete heart block was 14.4% (30 of 209). Complete heart block developed more than 10 years after the discovery of bilateral BBB in several patients. It is anticipated that with more complete and longer follow-up the incidence of complete heart block will be even higher (**Scanlon 1970**).

In the presence of LAFB, RBBB shifts the mean QRS axis in CCW manner, first superiorly, then rightward and superiorly, and finally rightward and inferiorly. When the QRS axis shift is moderate (ÂQRS between -60 to -75°, such as the present case) because of the predominance of left ventricular forces resulting in the pattern of "masquerading" BBB. The ECG may also become atypical if the shift is large (ÂQRS between -150 and +150°) because of a predominance of right ventricular forces arising from hypertrophied right ventricle.

When RBBB and LAFB are combined, there are three main directions of the QRS forces in the frontal plane. During the first 20ms of the QRS complexes, the forces point inferiorly and rightward to about +120°, resulting in small Q wave in leads aVL and I, and small initial R wave in inferior leads. During the next 40 to 60ms of the QRS complexes, the forces are directed leftward and superiorly to -45° or more. The two initial vectors are due to the LAFB. The terminal 40 to 60ms QRS vector, produced by RBBB forces, is directed rightward toward ±180°.

1. The initial 20ms QRS vector is directed rightward and inferiorly, producing initial Q waves in leads aVL and I and small initial R waves in leads II, III and aVF.
2. The main vector for the first 60 to 80ms of the QRS complex is oriented leftward and superiorly above -45° axis.
3. The terminal 40 to 60ms QRS vector is directed rightward and anteriorly and either inferiorly, horizontally or superiorly.
4. Thus the limb leads typically show qRS pattern in leads I and rS pattern in inferior leads.
5. The precordial leads show the pattern of RBBB with triphasic complex rsr' in lead V1, and wide S waves in leads V5 and V6.

The pattern of RBBB and LAFB in patients with cardiomyopathy of unknown etiology and epidemiologic risk factors should raise the possibility of Chagas disease and prompt specific diagnostic testing. The combination of RBBB and LAFB had the highest odds ratios for increased prevalence in patients with Chagas' cardiomyopathy compared to non-Chagas disease etiologies (**Cardoso 2016**).

CRBBB associated to LAFB: Vectorcardiographic criteria (Benchimol 1971)

The initial portion of the loop behaves as a LAFB and the final part as a Complete RBBB. The duration of QRS loop ≥ 120 ms.

Frontal plane:

Very similar to isolated LAFB loop:

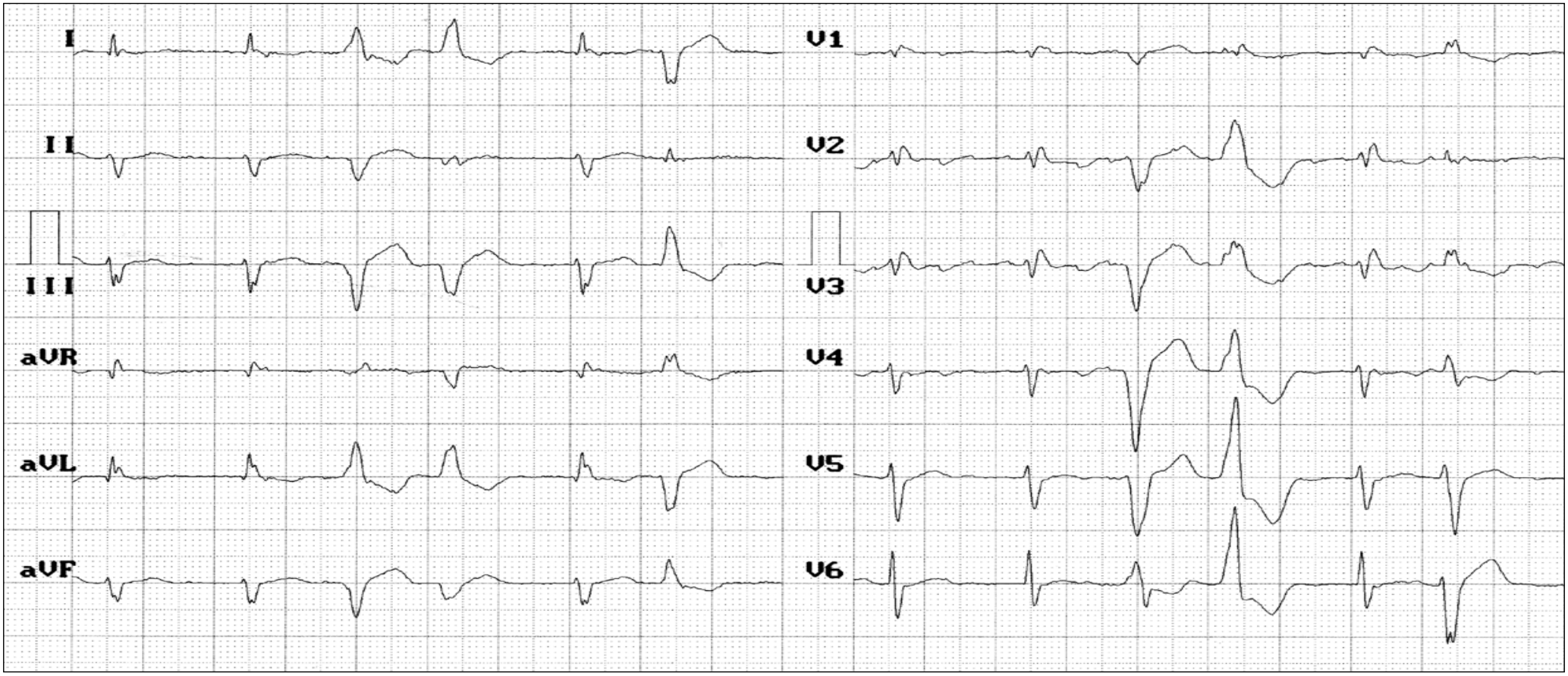
1) Initial vectors from 10 to 20ms heading downward and to the right (type I) or downward and to the left (type II);
2) QRS loop of counterclockwise rotation;
3) SÂQRS with extreme deviation to the left beyond -30°;
4) Efferent branch of QRS loop heading to the left and finally to the left and upward;
5) Afferent branch that begins above and slightly to the left, to finally end in a final appendage of slow recording and located to the right and above.

Horizontal plane:

Typical of QRS loop of isolated Complete RBBB.(**Zamfirescu 1978**)

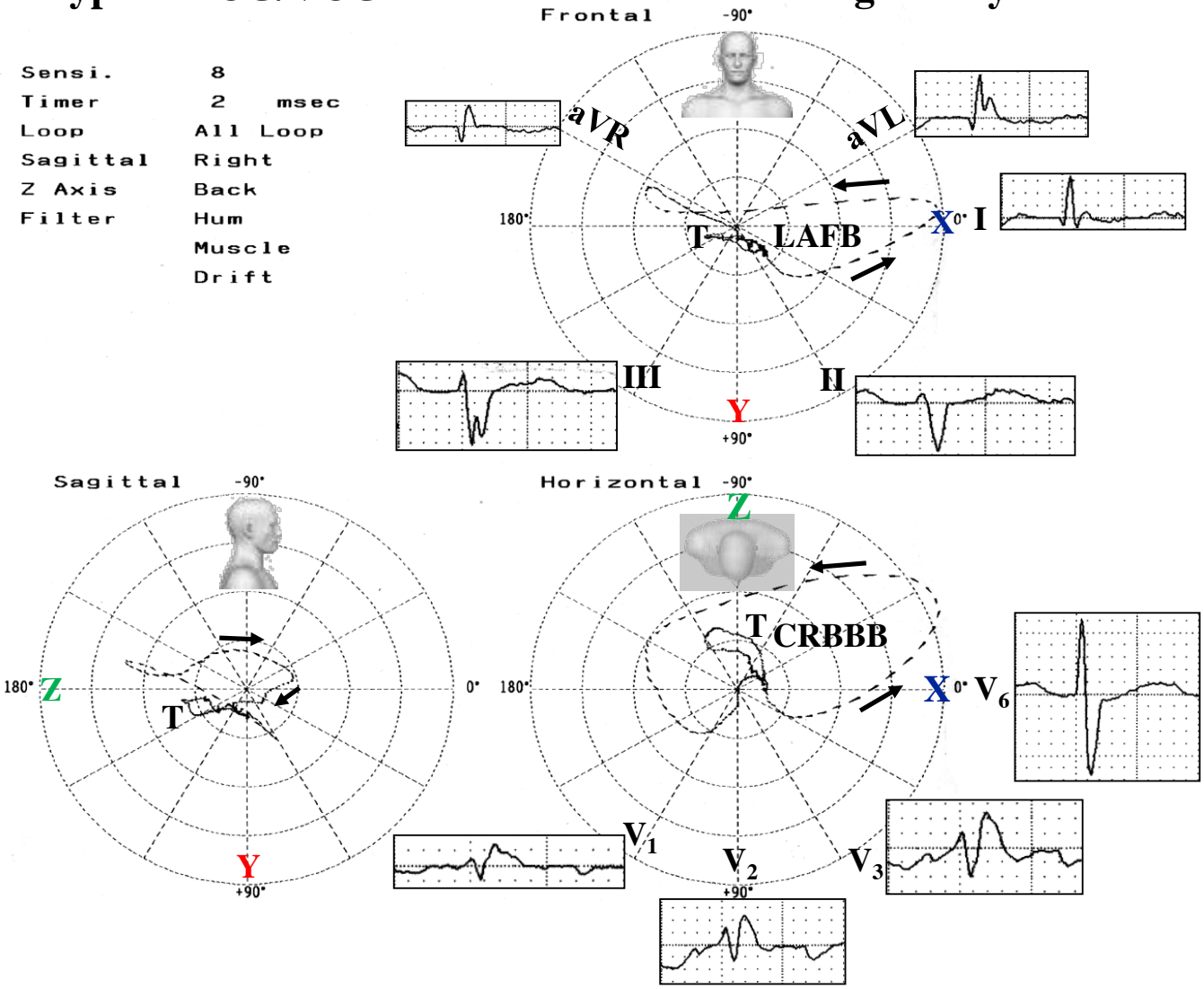
1. Vectors from initial 10 to 20 ms heading to the front and the right or left (**Retamal 1972**)
2. Efferent branch of QRS loop from right to left and with variable degrees of anteriorization;
3. Main body of QRS loop with counterclockwise (type I), eight or clockwise rotation (type II). The type of rotation seems to lack clinical significance; however, type II appears in a greater number of patients in CHF;
4. Afferent branch of QRS loop in front of the X line from left to right;
5. Efferent branch of QRS loop behind or in front of the X line;
6. End delay located in the right anterior quadrant (**Medrano 1969; Cergueira-Gomes 1972**);
7. Ventricular repolarization with T loop opposite to the final portion of the QRS loop to the left, behind and below (**Kukbertus 1970; Lichstein 1973**).

Typical ECG of chronic chagasic myocarditis



Clinical diagnosis: Chronic chagasic myocarditis.
ECG diagnosis: P wave of difficult visualization, indicating intense fibrosis of atrial tissue.
LAFB: extreme deviation of AQRS in the left superior quadrant, around -75°, qR in I and aVL, rS in inferior leads with S in V_5 and V_6
CRBBB: triphasic complex of the rsr' type of V_1 to V_3, wide r of aVR and S in V_5 and V_6
Polymorphic premature ventricular contractions.
Classical triad: CRBBB + LAFB + Polymorphic ventricular premature contractions

Typical ECG/VCG correlation in chronic chagasic myocarditis



VCG in the three planes of the same patient and its correlation with ECG. See the diagnosis of LAFB in the frontal plane and type Grishman VCG CRBBB in the horizontal plane.

The classical electrocardiographic hallmark of chronic chagasic myocarditis includes the association of complete right bundle branch block with left anterior fascicular block.
The ECG complex called since Richman “masquerading bundle-branch block” to day 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.
We present a case of standard masquerading bundle-branch block associated with concomitant hidden right bundle branch block on right precordial leads consequence of low anteroseptal and lateral extensive electrically inactive area.
We think that this is a new type of masquerading bundle branch block.
Chronic Chagasic Myocarditis is an important cause of heart failure in Latin America, but is rare in the United States. Also, due to migratory currents between countries and far-distant regions, chronic chagasic myocarditis is likely to become ubiquitous. A reflection of this tendency is exemplified by the recent growing awareness regarding the occurrence of CCM in the United States. Based on a prevalence of 4.5% of *T. cruzi* serologically detected infection in 205 Latin American immigrants to the USA, and on estimates of the number of such immigrants, approximately half a million infected people are believed to exist now in that country. Conditions for vectorial transmission range between latitudes 42°N and 40°S of the American Continent, from Mexico to Argentina. It is estimated that as many as 8 to 11 million people in Mexico, Central America, and South America have Chagas disease, most of who do not know they are infected. On the basis of limited serological surveys, 4% to 7% of more than 200 million Latin Americans are estimated to be chagasic in extensive areas of 21 countries, and 65-90 million are at risk of becoming infected (**Schmunis 1996**).
Cross-sectional epidemiological studies in Brazil and Venezuela assessed the prevalence of clinical manifestations and mortality due to chronic chagasic myocarditis, However, no clear-cut epidemiological picture of chronic chagasic myocarditis is yet available, due to the lack of appropriately designed large-scale studies to address this serious public health problem in extensive areas of the Latin American. In addition, case reporting is not reliable even in areas of high endemicity. Probably because of marked variations in the genetic background, parasite strain, climate, socio-economic and related hygienic-alimentary conditions, and health care policies, the morbidity and mortality rates ascribed to Chagas' disease are extremely variable even among endemic areas of each country (**Wanderley 1995**). Although the true prevalence of chronic chagasic myocarditis is unknown, these rough estimates clearly indicate that chronic chagasic myocarditis is undoubtedly the most common form of cardiomyopathy in Latin-American countries (**Marin-Neto 1998**). Moreover, rural-urban migration from endemic areas in Brazil is believed to have brought to large cities half a million infected people in the last three decades (**Wanderley 1995**).

Transmission

In Chagas-endemic areas, the main mode of transmission is through an insect vector called a triatomine bug (**http://www.dpd.cdc.gov/dpdx/HTML/TrypanosomiasisAmerican.htm**). A triatomine becomes infected with *T. cruzi* by feeding on the blood of an infected person or animal. During the day, triatomines hide in crevices in the walls and roofs. The bugs emerge at night, when the inhabitants are sleeping. Because they tend to feed on people's faces, triatomine bugs are also known as "kissing bugs". After they bite and ingest blood, they defecate on the person. Triatomines pass *T. cruzi* parasites (called trypomastigotes) in feces left near the site of the bite wound. Scratching the site of the bite causes the trypomastigotes to enter the host through the wound, or through intact mucous membranes, such as the conjunctiva. Once inside the host, the trypomastigotes invade cells, where they differentiate into intracellular amastigotes. The amastigotes multiply by binary fission and differentiate into trypomastigotes, which are then released into the bloodstream. This cycle is repeated in each newly infected cell. Replication resumes only when the parasites enter another cell or are ingested by another vector. The tropical rainforests and urban habitats are not ideal for the establishment of the human transmission cycle.

In regions where the sylvatic habitat and its fauna are thinned by economic exploitation and human habitation, such as in newly deforested areas, piassava palm culture areas, and some parts of the Amazon region, a human transmission cycle may develop as the insects search for new food sources. *T. cruzi* can also be transmitted through **blood transfusions**. With the exception of blood derivatives (such as fractionated antibodies), all blood components are infective. The parasite remains viable at 4°C for at least 18 days or up to 250 days when kept at room temperature. It is unclear whether *T. cruzi* can be transmitted through frozen-thawed blood components. Other modes of transmission include organ transplantation, through breast milk, and by accidental laboratory exposure. Chagas disease can also b e spread congenitally (from a pregnant woman to her baby) through the placenta, and accounts for approximately 13% of stillborn deaths in parts of Brazil (**Teixeira 2001**).

Oral transmission is an unusual route of infection, but has been described. In 1991, farm workers in the state of Paraíba, Brazil, were infected by eating contaminated food; transmission has also occurred via contaminated açaí palm fruit juice and sugar cane juice. A 2007 outbreak in 103 Venezuelan school children was attributed to contaminated guava juice. Chagas Disease is a growing problem in Europe, because the majority of cases with chronic infection are asymptomatic and because of migration from Latin America.

The juice of the "açaí" fruit, when handmade, could be one of the main culprits for outbreaks of Chagas disease in Brazil. Between June 2006 and June 2007, 116 people were contaminated after ingesting the drink in the states of Amapá, Amazonas and Pará. The last state, is where she came from. The contamination of the juice happens when the insect carrier of the protozoan parasite that causes the disease, is grinded jointly with the fruit. According to the parasitologist Aldo Valente, from the Evandro Chagas Institute, an institution linked to the Department of Surveillance in Health of the Ministry of Health, outbreaks of Chagas disease transmitted orally have been occurring since 1968, but it was under-reported, mostly because of the lack of information. Now, as health care agencies have paid more attention to this issue, the number of recorded cases has increased. Besides, Valente reminds us that the ecological imbalance caused by deforestation pushes insects away from their natural habitat and sources of food, contributing in a decisive manner to the occurrence of outbreaks. The main problem brought about by the oral transmission of Chagas disease is that the ingestion implies a large amount of the protozoan parasite that causes the disease, the Trypanosoma cruzi, released in to the blood flow. This fact entails the reduction of the incubation period of the disease: as to conventional transmission, the first symptoms appear between the fourth and eighth week after contagion; in oral transmission, this period reduces to nearly 10 days and the disease can quickly evolve into its more severe forms. So, the violent evolution of this patient could be due to the mentioned mechanism. Let's see what Edgardo has to say about it, since he's the expert.

Açai fruit →

The ECG

The classical electrocardiographic (ECG) hallmark of chronic chagasic cardiomyopathy includes the association of complete right bundle branch block (CRBBB) and left anterior fascicular block (LAFB). The ECG complex coined by the first time in 1954 by Richman et al (**Richman 1954**) as "masquerading bundle-branch block" to day we know that is essentially a CRBBB with LAFB, with further modifications of the initial and final QRS vectors, so that standard leads, and at times the left precordial leads, resemble LBBB.(**Schamroth 1975; Unger 1958**)

Since the pioneer Rosembaum´s et al studies (**Rosembaum 1968; Rosembaum 1973**) we know two ECG types: 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 on frontal plane leads by abolishing (or becomes very small) the final broad S wave in the left leads I and aVL (**Ortega-Carnicer 1986**) and the precordial leads remain the typical CRBBB pattern.

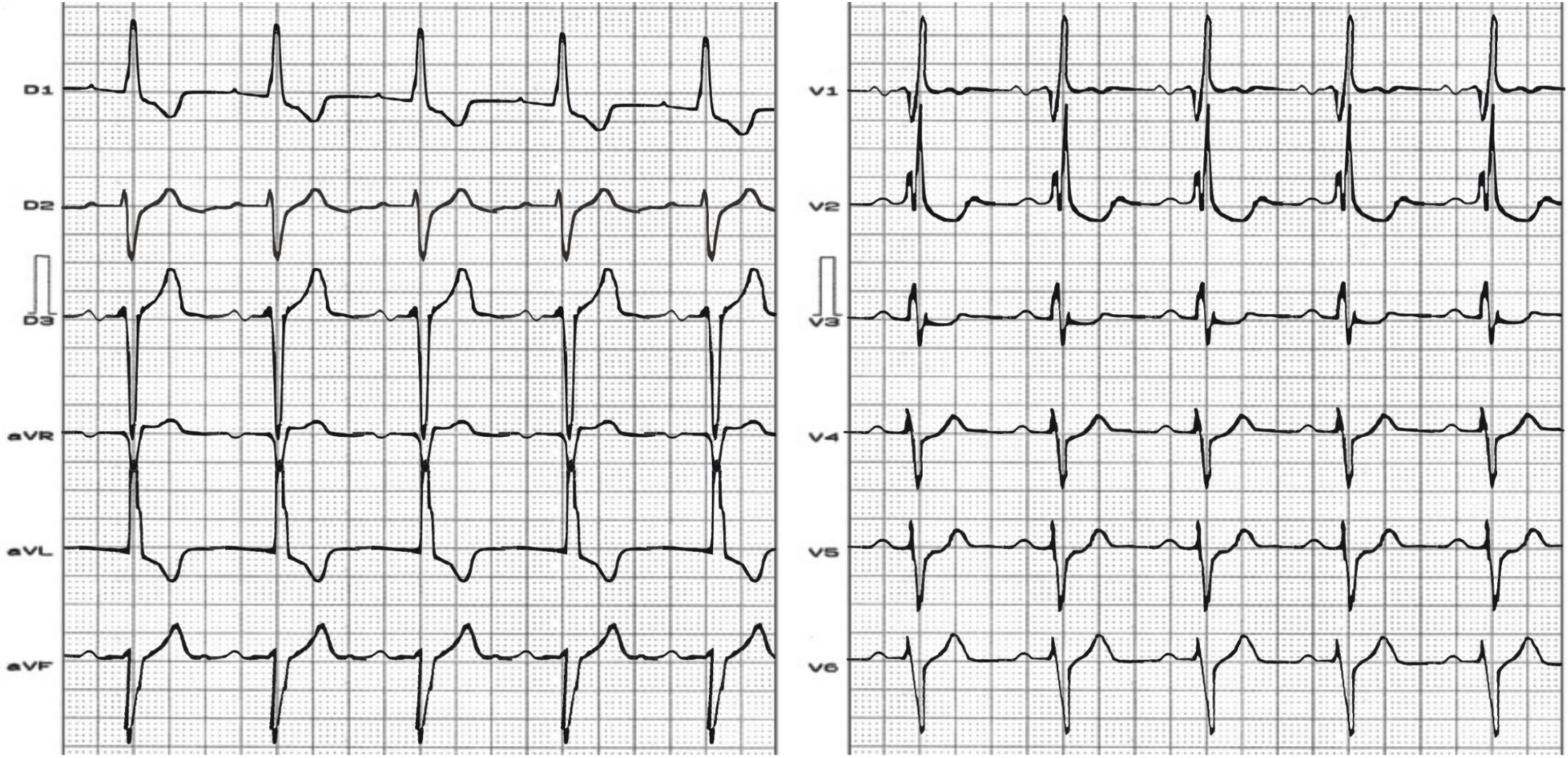
In standard type, in frontal plane there are four main developmental phases that do not necessarily occur in the chronological sequence. Table 1 shows the four main developmental ECG patters of standard type.

The precordial type shows the pattern of CRBBB in the right precordial leads and complete LBBB in the left-side precordial leads. This result from CRBBB associated with severe LVH, 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 that patients with this finding may require permanent pacemaker implantation, especially if they are symptomatic (**Kowey 1989**).

A possible new masquerading variant with severe *chronic* fibrotic form *of chagasic cardiomyopathy* is present c*oncomitant standard and precordial masquerade CRBBB*.(see slide number 40). The standard left limbs I and aVL shows qR pattern with low r voltage and wide QRS duration (pseudo-atypical complicated LBBB pattern) and in the anterior wall from V1 to V4 QS or Qr pattern consequences of severe anterior fibrosis that masquerade the existent CRBBB. Only the left leads V5-V6 they denounce to witnesses of the RBBB. Progression to high degree atrioventricular block is quite common in the presence of masquerading bundle branch block . It is frequently associated to advanced heart failure, so the prognosis is usually poor (**Bayés de Luna 1988; Gómez Barrado 1997**).

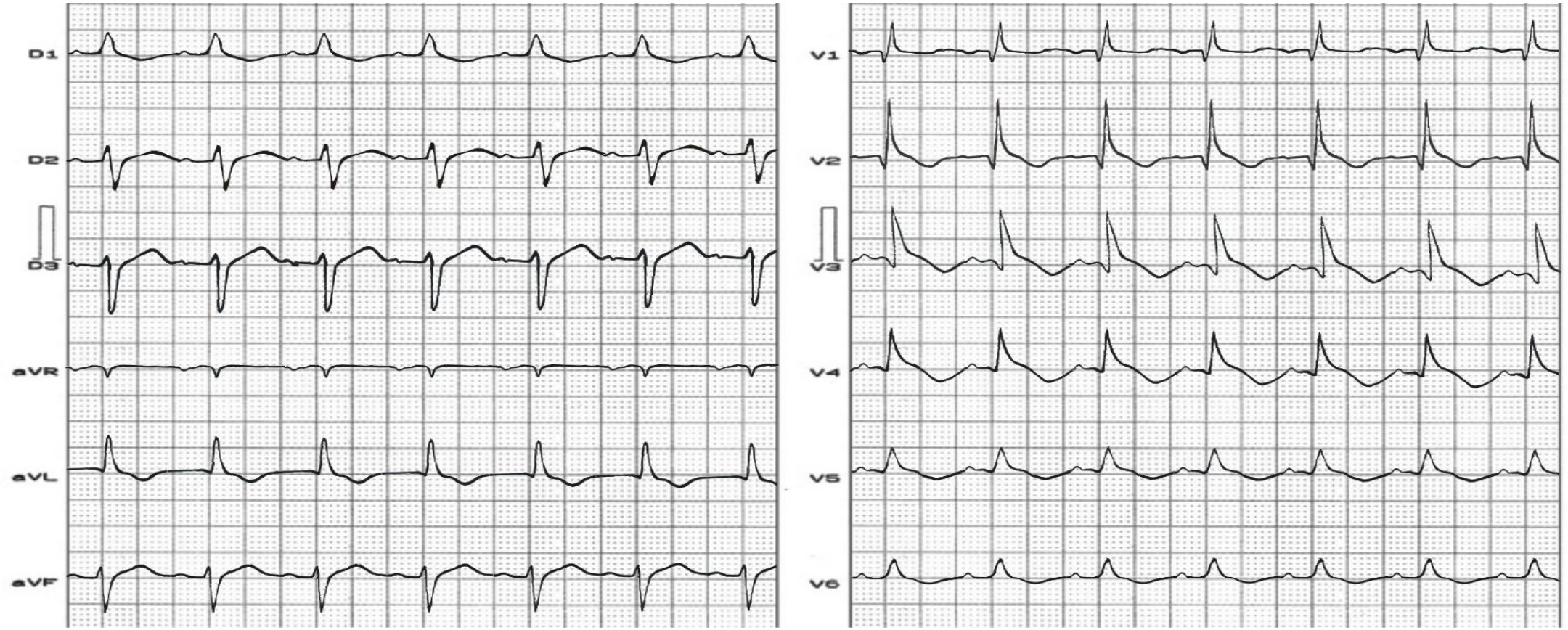
Example of *"Standard Masquerading Right Bundle-branch Block"*



Extreme QRS left axis deviation (SÂQRS -50°), SIII>SII: LAFB. The limb leads show a LBBB-like pattern, but the precordial leads show a RBBB. SIII > 15mm: Type IV Rosembaum LAFB: association of LAFB + LVE or LVH.

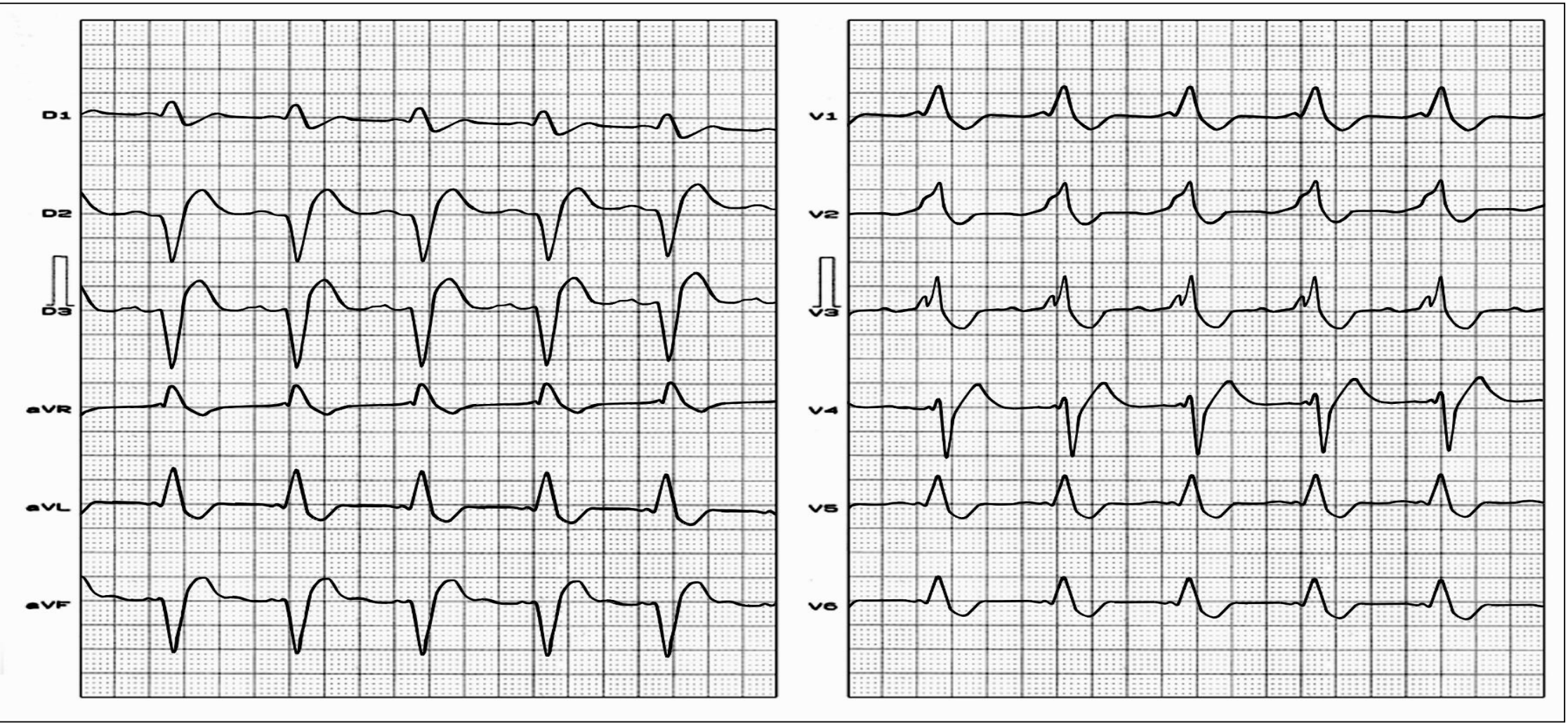
II. Example of the *precordial masquerading right bundle-branch block*

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 that patients with this finding may require permanent pacemaker implantation, especially if they are symptomatic (**Kowey 1989**).



III. Example of *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 manifestations of chronic chagasic myocarditis

The main pathogenetic mechanisms to explain the development of chronic chagasic myocarditis are: autonomic nervous system derangements, parasite-dependent myocardial aggression, immune-mediated myocardial injury, microvascular disturbances.

Microvascular disturbance: A considerable amount of clinical and experimental data gives support to the concept that transitory ischemic events caused by functional disturbances of coronary blood flow regulation is a relevant pathogenetic mechanism in chronic chagasic myocarditis (**Mengel 1992**). In fact, atypical precordial chest pain, usually prolonged and recurrent, but with no clear provocative factors, is a frequent and disabling complaint by chagasic patients (**Marin-Neto 1998**). Sometimes the symptom assumes an acute coronary syndrome presentation, masquerading as acute myocardial infarction or unstable angina, but with normal coronary arteries at angiographic studies (**Hagar 1991**). It's worth to note that investigations of esophagus, an organ often involved in chronic chagasic myocarditis digestive tract manifestation, as a possible alternative source of these angina-like symptoms has produced no conclusive results (**Ejima 1998**). Thus, considering the association between chest pain and laboratory documentation of myocardial ischemia with normal coronary arteries , it's conceivable to suppose the participation of functional alterations of the arterial coronary bed in the genesis of that clinical set. This hypothesis is primarily based on reports of hystopathological studies showing small coronary artery lesions (**Ferrans 1988**), and has been recently reinforced by experimental model observations and some scarce clinical reports (**Torres 1995**).

Chronic Chagasic myocarditis is characterized, fundamentally, by focal mononuclear inflammatory infiltrates associated to reactive interstitial fibrosis and myocitolytic necrosis.

Myocytolysis is a particular form of cell degeneration apparently related to hypoxia secondary to low intensity repetitive ischemic episodes as it has been observed in ischemia and reperfusion experimental models (**Baroldi 1975**). Moreover, the occurrence of flow disturbances at the microcirculatory level is quite conceivable as the tissue lesion is focal, encompassing discrete cellular groups, and the associated reparative interstitial fibrosis seems to be characteristic of chronic hypoxic damage. These hystopathological aspects give support to the participation of myocardial ischemia, depending on microvascular abnormalities, in the pathogenesis of chronic chagasic myocarditis (**Rossi 1996**). Early pathological observations have already documented inflammatory lesions of small coronary vessels in humans, both in heart and digestive tract, and similar findings were also reported in murine experimental models. The topographic distribution of myocardial capillar chagasic vessels, in comparison to normal individuals, has shown areas of reduced vascularization. This named "mesenquimal-reactive decapillarization" seems to be secondary to extra-luminal compression, being responsible for the myocytolysis found in these hearts.

The course of the murine model of acute and chronic chagasic myocarditis reproduces quite closely the main pathological features seen in human disease. Platelet aggregation generating occlusive thrombi has been reported in small epicardial and intra-mural coronary vessels. Further studies in murine model, employing hystochemical methods has shown evidence of myocardial hypoxic alterations related to foci of myocitolitic necrosis. Furthermore, morphological studies of the microcirculation in mice with acute*T. cruzi* infection have demonstrated areas of focal vascular constriction, microaneurysm formation, dilatation, and proliferation of microvessels (**Factor 1985**). In addition, the use of verapamil, a calcium channel blocker (with vasodilatory action in small vessels and anti-platelet activity), achieved significant reduction in mortality and ameliorated myocardial tissue lesions in mice infected with *T. cruzi*. The usage of the scintigraphic method for myocardial blood flow distribution assessment in humans has also yielded results consonant with this hypothesis. Rest Thallium-201 studies has shown marked heterogeneity in radiotracer distribution in the majority of patients, that was significantly improved after prolonged treatment with dypiridamole (**Rotondaro 1979**). These findings were confirmed by myocardial perfusion studies in Chagas' heart disease patients employing rubdium-86 that showed reduced myocardial blood flow at rest and poor increment during stress (**Kuschnir 1974**). More recently, these observations were extended to patients with chronic chronic chagasic myocarditis presenting precordial chest pain and angiographically normal coronary arteries (**Marin-Neto 1995**) by Thallium–201 myocardial perfusion studies at stress and rest. A high frequency of perfusion defects in areas with normal left ventricular wall motion was detected. All patients in that report had at least one segment of left ventricular wall showing perfusion defects. Transient perfusion defects, ischemic or paradoxical (both potentially related to abnormalities in regional blood flow) were predominantly found. The evaluation of myocardial perfusion using scintigraphic images after intracoronary injection of 99mTc-labeled-microespheres in chagasic patients with chest pain also yielded positive results of prominent perfusion disturbances with normal coronary arteries.

Most recently, additional evidence for abnormal coronary blood flow regulation was obtained by assessment of flow responses to pharmacologic stimuli employing intra-coronary doppler studies. Paradoxical responses of flow reduction to acetilcholine, and attenuated vasodilation to adenosine were documented. These results indicate endothelial dysfunction as responsible for abnormal coronary vasodilation capacity.. Furthermore, abnormal vasoconstrictor behavior of epicardial coronary artery vessels was observed in chagasic patients with precordial chest pain submitted to the hyperventilation stimulus. The time course relationship between myocardial ischemia and development of regional myocardial contraction disturbances has been recently addressed[28]. In this study three groups of patients with progressive severity of Chagas' disease myocardial damage were studied with stress-rest Thallium-201 myocardial scintigraphy. A high incidence of perfusion defects was documented even in patients asymptomatic with normal EKG, and global and segmental normal LV function. About 40% of perfusion defects in each group were ischemic and occurred with normal coronary arteries.

Ventricular aneurysms are a common finding in chronic chagasic myocarditis. Pathological and functional data suggest that the microvascular control in chagasic hearts, in comparison with non-chagasic hearts, may be severely impaired, probably due to the presence of abnormal substances induced by the inflammation and/or directly by the parasites. These microvascular disturbances might lead to the existence of regional patterns of abnormal vasodilation or vasoconstriction, especially in the watershed zones of the main epicardial coronary arteries. It has been postulated that the consequent low pressure perfusion and associated ischemia may occur in two border zones between the principal coronary artery branches: one involving the anterior descending and the posterior descending arteries, and resulting in the formation of the apical aneurysm, and the other between the right and the circumflex arteries, resulting in the formation of an aneurysmatic lesion at the basal posterior wall of the left ventricle (**Higuchi 2003**).
Various lines of evidence from pathological, experimental, and clinical grounds suggest that microvascular abnormalities that lead to myocardial ischemia may contribute to the pathogenesis of chronic chagasic myocarditis.

Histopathology Studies in Humans

The first reports on the pathology of the acute phase of chronic chagasic myocarditis implicated vascular disturbances caused by perivascular inflammation as mechanisms for myocardial degeneration (**Vianna 1911**). The concept was revived in necroscopic studies of chronic patients, which described diffuse collapse of intramyocardial arterioles, with lumen constriction attributed to intimal proliferation (**Torres 1960**). These microvascular abnormalities were deemed responsible for the focal diffuse myocytolysis observed in these necroscopic studies and also in biopsy specimens that showed extensive capillary basement membrane thickening (**Ferrans 1988**). Several subsequent investigations reinforced the notion of abnormal vasodilatation and vasoconstriction at the microcirculatory level that cause myocardial damage in patients with chronic chagasic myocarditis (**Higuchi 1998**). Also, on the basis of the focal distribution of cell necrosis and subsequent reparative interstitial fibrosis found in chagasic hearts, which was similar to what is seen in experimental models of ischemia and reperfusion, transient microvascular ischemic disturbances of low intensity and short duration have been postulated to be causative mechanisms of chronic chagasic myocarditis (**Rossi 1990**). Among factors that lead to the development of aneurysms in chagasic patients, coalescent microinfarctions have been postulated to occur in watershed coronary areas because of unopposed sympathetic overstimulation (**Oliveira 1985**). This last notion has been considered a pathophysiological link between the microcirculatory hypothesis and the neurogenic theory of chronic chagasic myocarditis.

Experimental and In Vitro Studies

In experimental murine models of Chagas disease, microcirculatory derangements include the occurrence of occlusive platelet thrombi in small epicardial and intramural coronary arteries, which lead to ischemia detected in vivo by histochemical techniques (**Rossi 1985**). Focal vascular constriction and microvascular proliferation were also prominent structural abnormalities in this experimental model (**Factor 1985**). To elucidate the mechanisms responsible for the occlusive platelet thrombosis and microcirculatory spasm, a direct participation of *T cruzi* infection that causes endothelial cell damage (**Rossi 1997**) and endothelium damage by immune effector cells (**Andrade 1994**) have been reported. Also, in vitro *T cruzi* infection of human umbilical vein demonstrated increased production of endothelin, which mediates arteriolar spasm and inhibits cAMP, with consequent stimulation of platelet adhesion to the vascular wall (**Morris 1992**). Trypomastigote forms of *T cruzi* also produce a neuraminidase that removes the sialic acid from the surface of mammalian myocardial and endothelial cells (**Libby 1986**). The loss of this protective component of the endothelial surface may cause platelet aggregation and microvascular thrombosis. These abnormal findings are corroborated by the demonstration of increased levels of thromboxane-A_2 and enhanced platelet adherence and aggregation in *T cruzi*–infected mice (**Tanowitz 1990**). Local production of cytokines by the inflammatory infiltrate cells may also contribute to microvascular abnormal reactivity in the chagasic heart. This has been shown to be partially reversible by long-term administration of verapamil, a calcium channel blocker with vasodilating and anti-platelet–aggregating effects that lead to attenuation of myocardial lesions and increased survival in a murine model of chronic chagasic myocarditis (**Morris 1989**). This hypothesis was further supported by a study that used in vivo visualization of the murine cremaster vascular bed. In comparison with control animals, animals infected with *T cruzi* had segmental arteriolar spasm and flow velocity reduction; these abnormalities were also reversed by verapamil (**Tanowitz 1996**). Finally, recent data showed that calreticulin, a calcium-binding protein present in *T cruzi* that is quite similar to its human counterpart, may modulate the complement system and inhibit angiogenesis. This could constitute a potential molecular mechanism that leads to microvascular damage and dysfunction (**Ferreira 2005**).

Clinical Studies

Various clinical aspects of chronic chagasic myocarditis suggest the participation of myocardial ischemia in its pathophysiology. A substantial proportion of chagasic patients (20% to 30%) complain of chest pain that resembles angina in location and character, but this pain has no consistent relationship to effort and is not relieved by nitrates. Many patients have concomitant ST-T changes and abnormal Q waves compatible with electrically inactive ventricular areas (**Simões 1993**). Furthermore, similar to coronary artery disease, segmental LV dysfunction is common in chagasic patients, even those with dilated hearts (**Hammermeister 1984**). Despite these findings that suggest the occurrence of myocardial ischemia, coronary angiography in chronic chagasic myocarditis invariably demonstrated the absence of obstructive disease at the epicardial level (**Hagar 1991**). Nevertheless, consistent with the experimental studies, impairment of endothelium-dependent coronary vasodilatation in response

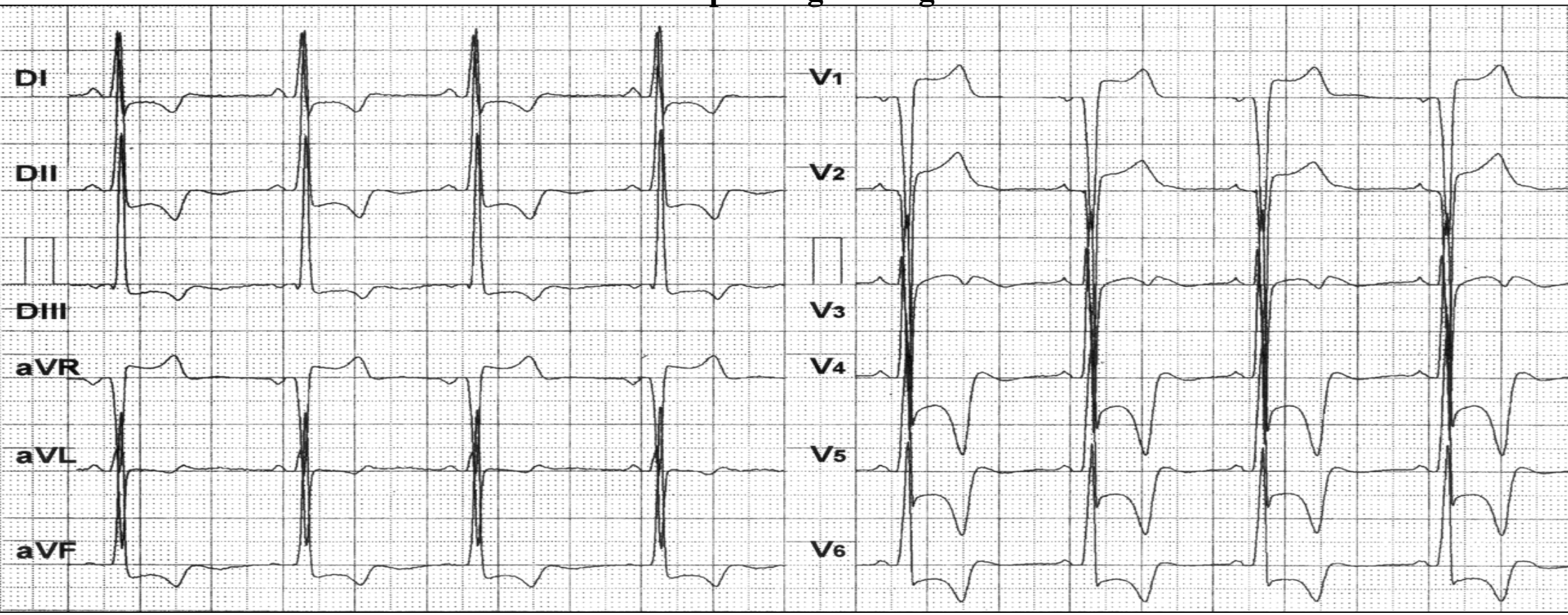
to acetylcholine, with preserved response to adenosine, has been reported in patients with chronic chagasic myocarditis (**Torres 1995**). Also, chagasic patients with atypical angina that was severe enough to warrant coronary angiography were shown to have blunted vasomotor epicardial responses to hyperventilation and dinitrate isosorbide (**Marin-Neto 1995**). Taken together, these findings show abnormal coronary flow regulation related to endothelial and nonendothelium dysfunction in chagasic patients with chest pain and angiographically normal epicardial coronary arteries. Several independent investigations have shown striking myocardial perfusion abnormalities in chagasic patients with angiographically normal coronary arteries, and these studies lend support to the concept of abnormal myocardial flow regulation at the microvascular level (**Marin-Neto 1992**). In one of these investigations that used ^{201}thallium stress-redistribution myocardial perfusion scintigraphy, every type of perfusion defect was seen in all 23 chagasic patients studied; although fixed defects that denoted myocardial fibrosis were found in myocardial segments that exhibited akinesis or dyskinesis, stress-induced reversible myocardial ischemia was detected in LV segments with less severe wall motion impairment in 8 patients (35%) (**Marin-Neto 1992**). Another study that used ^{201}thallium single photon emission computed tomography myocardial scintigraphy focused on the topographical correlation between segmental myocardial perfusion abnormalities and regional LV dysfunction in 37 patients with various stages of Chagas heart disease; again, some kind of perfusion defects (fixed, paradoxical, and reversible) were seen in 78% of patients. Significant topographical correlation occurred between perfusion changes and wall motion abnormalities that predominated in the apical and inferior-posterior LV segments. Reversible stress-induced myocardial perfusion defects were detected in segments that exhibited normal wall motion in 5 of 12 chagasic patients with no other evidence of myocardial disease. Of note, these reversible ischemic defects were seen in the apical and inferior-posterior LV segments (ie, the same regions where regional contractile dysfunction prevails in later stages of chronic chagasic myocarditis) (**Simões 2000**).

The tracer used in the studies quoted above was ^{201}thallium, whose accumulation and retention could be influenced by cardiomyocyte metabolic derangements related to the underlying inflammatory process. Hence, some of the scintigraphic defects described in the previous studies could be independent of real perfusion abnormalities. This alternative possibility is reinforced by the frequent occurrence in those studies of reverse redistribution defects that predominate in LV regions with normal or mildly impaired wall motion. However, myocardial perfusion was also evaluated in 18 chronic chagasic myocarditis patients with recurrent chest pain severe enough to warrant coronary angiography with an exclusive perfusion tracer, ^{99m}technetium-labeled microspheres injected in the LV cavity (**Marin-Neto 1995**). None of the patients had angiographic evidence of apical coronary artery disease. Ten of the 18 patients exhibited extensive perfusion defects in 49 of 126 (39%) LV segments. Nineteen of these segments (40%) with perfusion defects had severely impaired wall motion, which probably corresponded to extensive fibrosis. The remaining 60% of the segments with perfusion defects had normal or mildly reduced wall motion. Thus, this investigation clearly showed marked resting myocardial perfusion abnormalities before the appearance of wall motion impairment.

Pathophysiological Consequences of Microvascular Derangements

On the basis of these clinical investigations and the background information provided by the experimental studies discussed above, it is a reasonable hypothesis that chronic myocardial hypoperfusion would contribute as a pathogenetic mechanism to the development of the characteristic regional LV dysfunction seen in chronic chagasic myocarditis. This would be similar to hibernating myocardium seen in chronic CAD, and this might have relevant clinical implications for the management of chagasic patients. This hypothesis is compatible with the results of studies that show improvement of LV function in chronic chagasic myocarditis patients who received short-term or long-term administration of dipyridamole (**Kuschnir 1983**) and isosorbide dinitrate (**Marin-Neto 1988**). In these studies, however, no clear relationship between the LV function improvement and the relief of myocardial ischemia was demonstrated. Moreover, changes in ventricular loading conditions associated with these modalities of treatment could also have contributed to the improvement in the ventricular performance. Thus, although attractive, the hypothesis of chronic myocardial ischemia in chronic chagasic myocarditis still awaits the conclusive support that should be derived from a prospective cohort study that shows a beneficial effect of long-term vasodilator or antiplatelet therapy on the clinical course of chagasic patients with angina-like symptoms. It should be emphasized that the triad of chest pain, myocardial perfusion disturbances, and normal coronary arteries has also been described in patients with ventricular dysfunction caused by dilated cardiomyopathy of other causes (**Pasternac 1982**). Therefore, this is not a specific feature of chronic chagasic myocarditis. Moreover, no prospective cohort studies have been conducted that correlate the presence and extent of myocardial perfusion disturbances with the temporal development of segmental LV wall motion abnormalities in the same chagasic patients. In summary, despite these limitations, experimental and clinical studies strongly support the notion that functional and structural microvascular abnormalities occur in chronic chagasic myocarditis, possibly as a consequence of the underlying inflammatory process. Thus, it is possible that microvascular ischemia, even if it is not an independent and self-sustained pathogenetic mechanism, could at least constitute an ancillary factor to potentiate and amplify the chronic inflammatory aggression to myocardial tissue.

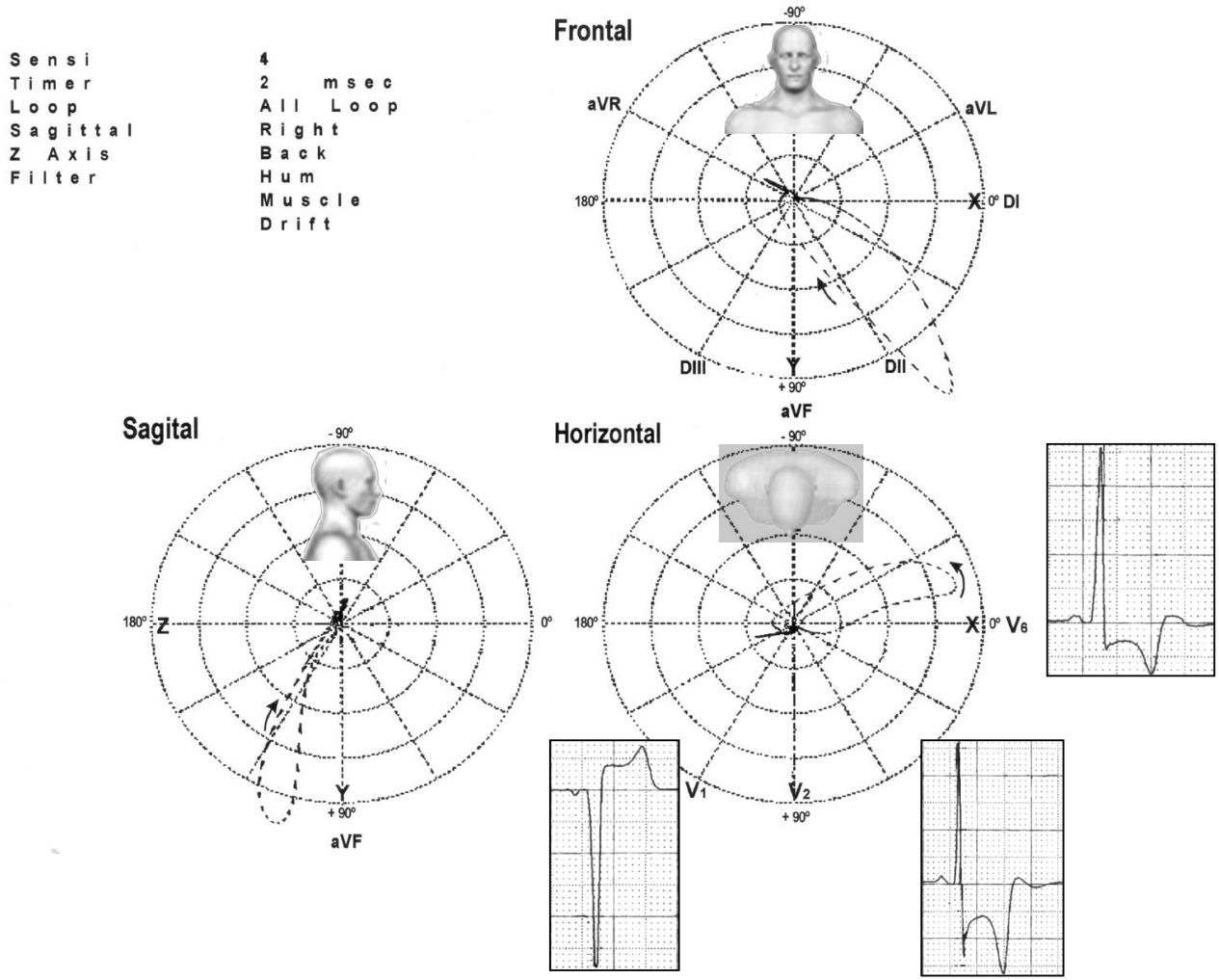
Main clinical examples of giant negative T-waves



Clinical/echocardiographic diagnosis: Non-obstructive hypertrophic cardiomyopathy. Diastolic thickness of interventricular septum in the apical region greatly increased (32 mm): Ap-HCM.

Electrocardiogram diagnosis: sinus rhythm, left atrial enlargement, normal QRS axis on frontal plane (+50º), left ventricular hypertrophy (positive Sokolow-Lyon index: S of V1 + R of V5≥ 35 mm or 3.5 mV in adults older than 30, 40 mm or 4.0 mV between 20 and 30 years (Sokolow-Rapaport) and > 60 mm between 16 and 20 years and > 65 mm between 11 and 16 years), QS pattern in V1-V2 contrasting with abruptly prominent QRS anterior forces in intermediate leads (V3-V4), R wave of V5 or V6 > 26 mm and strain pattern of ventricular repolarization from V4-V6, high lateral (I aVL), and inferior wall (II-III-aVF) leads (wide QRS/ST/T angle: near 180º).

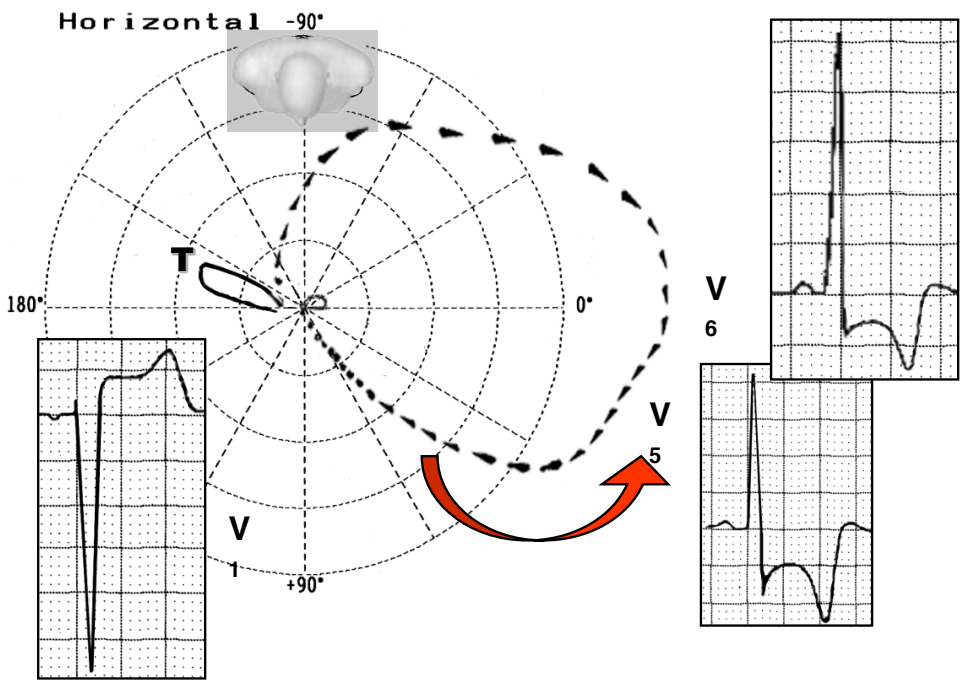
ECG/VCG correlation



Vectorcardiogram diagnosis: The main body of the QRS loop located in the left, inferior, and posterior quadrant and the magnitude of maximal QRS vector clearly augmented (>2.2 mV): LVH.

Vectocardiogram in Ap-HCM: LVH vectocardiographic type IV LVE

Horizontal Plane



1) Initial vectors of QRS loop heading forward and to the left;

2) Anteriorization of QRS loop predominantly located in the left anterior quadrant;

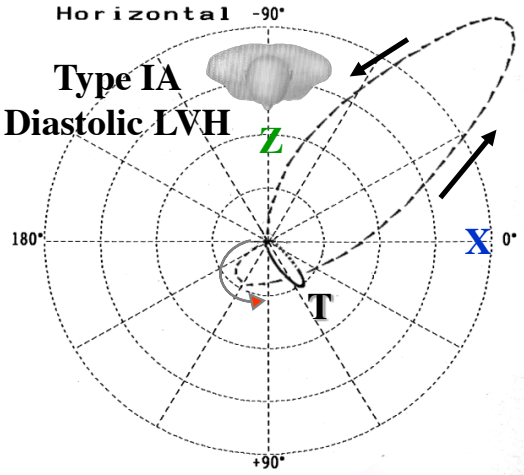
3) Maximal vector that increases voltage;

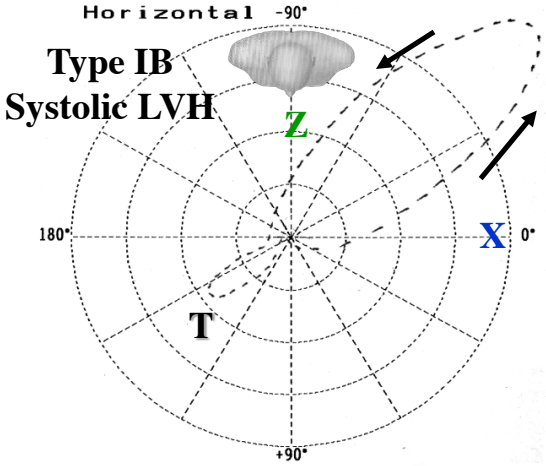
4) Final vectors located to the right and backward with ST/T vector in the right posterior quadrant;

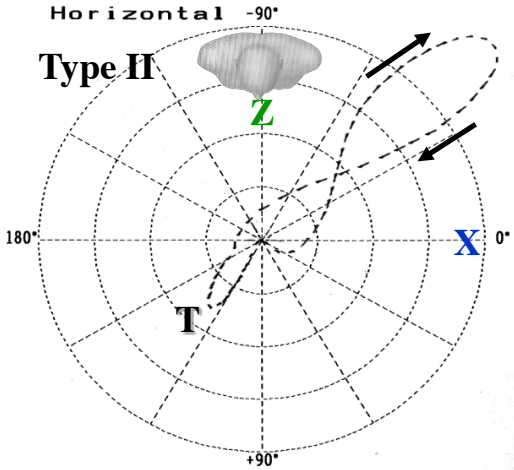
5) E point that does not match the 0 point and is located backward and rightward from the latter.

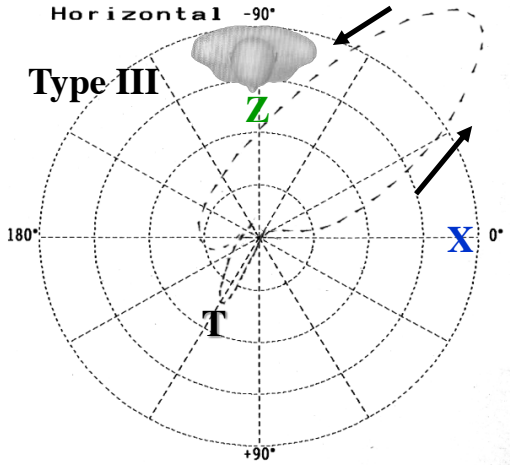
Vectocardiogram features in Apical Hypertrophic Cardiomyopathy.

The five vectorcardiographic types of LVH in the HP: IA, IB, II, III and IV





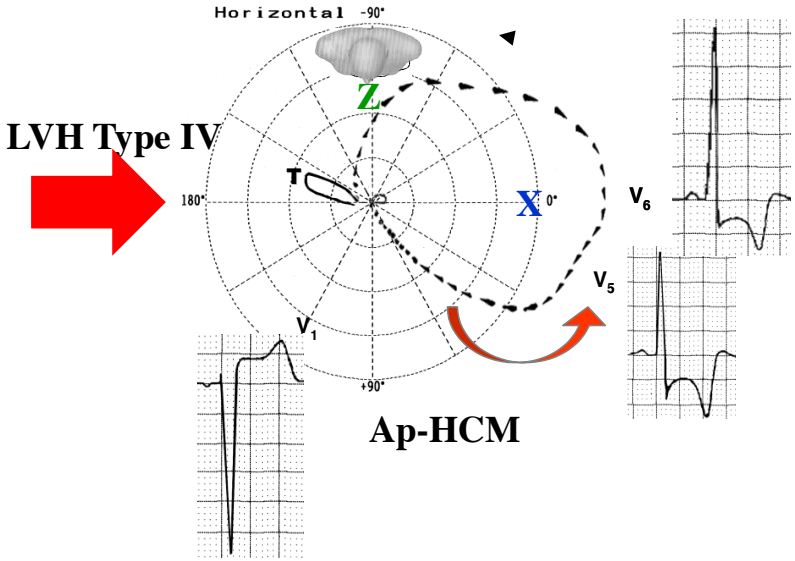




Eccentric LVH

Concentric LVH

LVH Type IV



Ap-HCM

Apical hypertrophic cardiomyopathy electrocardiogram features

Giant negative T waves in the precordial ECG leads: Giant negative T waves negativity ≥ 1.0 mV (10 mm). Giant negative T waves are more common in Japanese patients than American patients: 15% in Japan vs 3% in US (**Kitaoka 2003**). The singnificative posterior and rightward shift of the ST/T vector is responsible for the characteristic giant negative T wave (>10 mm) in the leads of the horizontal plane from V2 to V5. T waves at the onset, may not present a significant voltage and may appear later with the evolution of the disease.(**Bielli 1991**)

The depth of negative T waves is related to craniocaudal asymmetry and apical late-enhancement (**Dumont 2006**)

Stress test may decrease the depth of T waves. (**Tilmant 1980**)

Three hypotheses aroused to explain these negative T waves: 1) apical subendocardial ischemia.; 2) apical cell disorder;3) greater duration of action potential of hypertrophied cells, thus conditioning the area to have a slower repolarization.(**Tilmant 1980**)

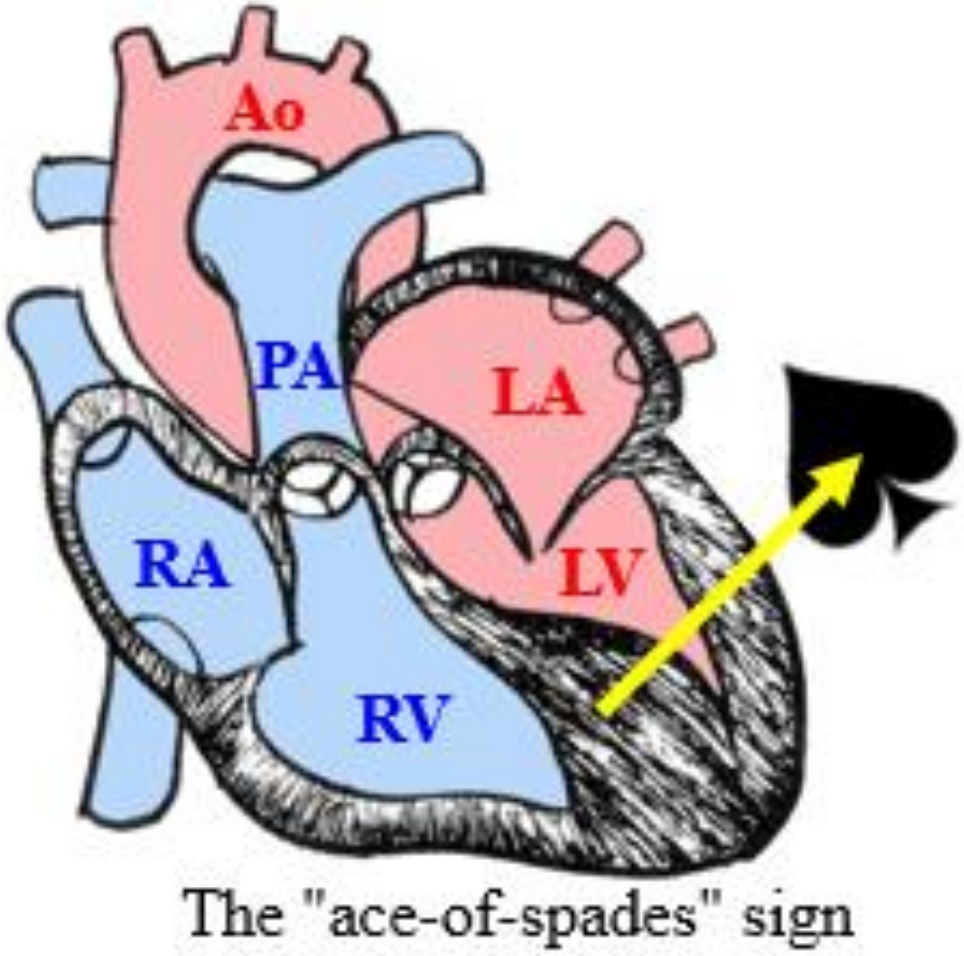
The prevalence in the western world of this form of HCM is approximately 0.02 to 0.2% and it constitutes 8% of the cases of the entity. In Japan, the apical form of HCM constitutes 25% of HCM.(**Maron 1990**) .Sometimes R-wave voltage and T-wave negativity progressively decreased in magnitude at serial ECGs.Non-sustained or sustained VT can be observed in patients that developed apical aneurysm with normal coronary arteries; To clarify the mechanisms of ECG abnormalities in hypertrophic cardiomyopathy, 102 patients were examined with CMR. Distribution and magnitude of hypertrophy and late-enhancement were correlated with ECG abnormalities:

Abnormal Q waves reflect the interrelation between upper anterior septal thickness and other regions of the left and right ventricles, and wider Q waves are associated with late-enhancement;

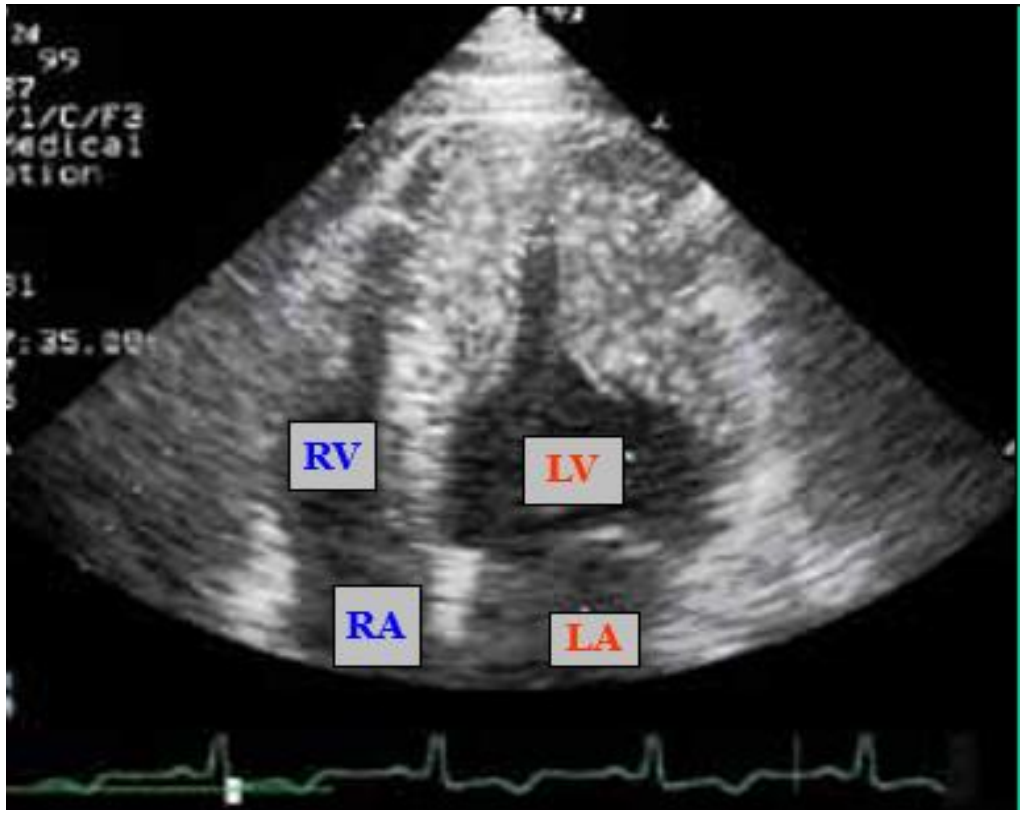
Conduction disturbances and absent septal Q waves are associated with late-enhancement;

The depth of negative T waves is related to craniocaudal asymmetry and apical late-enhancement (**Dumont 2006**).

Apical Hypertrophic Cardiomyopathy (ApHCM)
(Yamaguchi variant of hypertrophic cardiomyopathy)



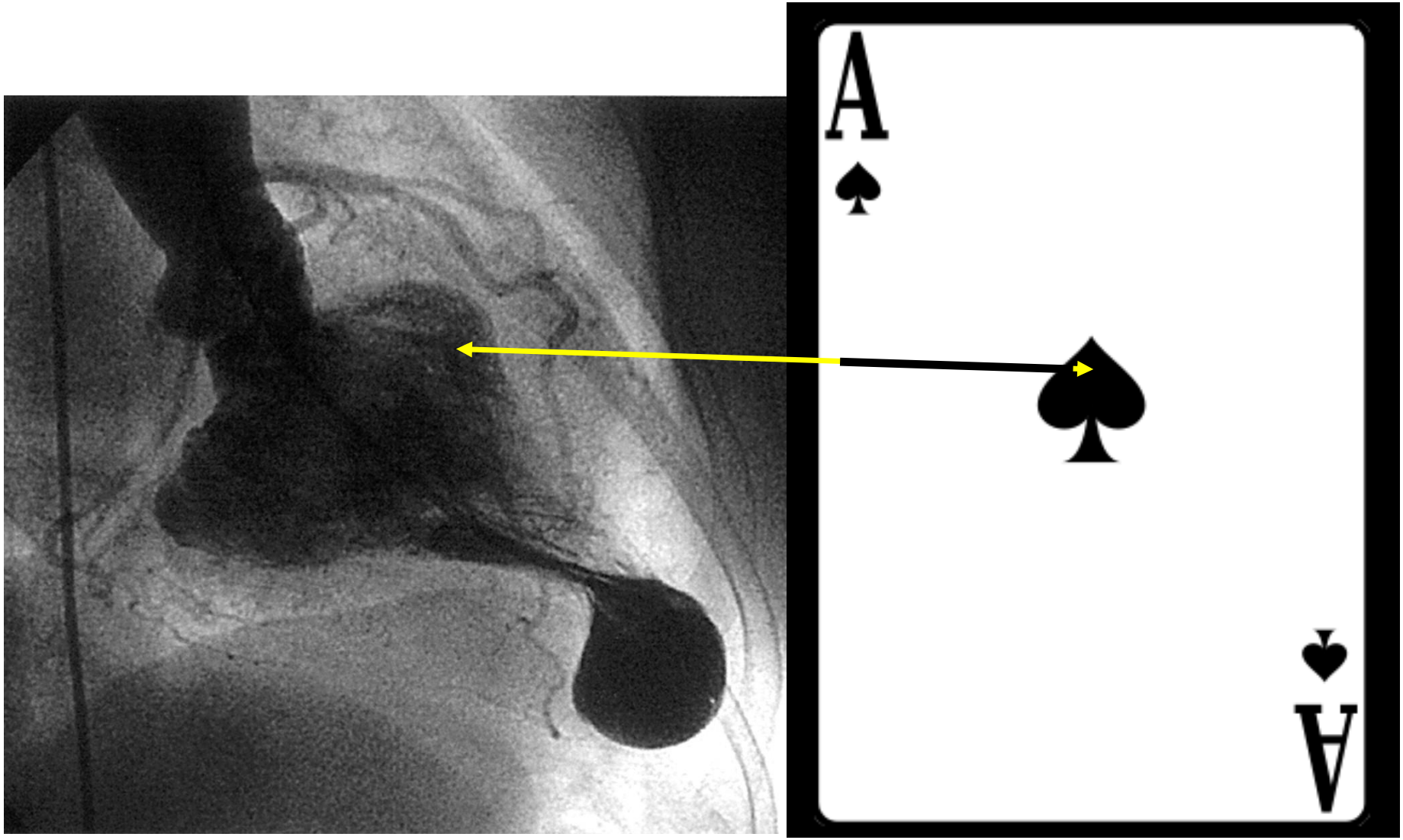
Transtoracic two-dimensional echocardiography



Two dimensional echocardiogram. Apical 4-chamber view shows apical hypertrophy in the apical one third of the ventricle, with apical left ventricle cavity obliteration.
RV = right ventricle **RA** = right atrium **LA** = left atrium **LV**= left ventricular cavity

Left Ventriculography in Ap-HCM

The "ace-of-spades" sign on left ventriculography being pathognomonic (**Olearczyk 2008**).



Prognosis

The prognosis of ApHCM with regard to SCD is believed to be better than that of common HCM. Patients with the Ap-HCM had a benign clinical course. However, the mutation Arg719Trp in the cardiac beta-myosin heavy chain (beta MHC) gene is a high risk factor for sudden death and can be associated with an unusual ApHCM (**Döhlemann 2000**). Current evidence suggests that these patients experience severe symptoms and are at increased risk of ventricular arrhythmias and death, especially in the presence of an apical akinetic chamber.

Morbid sequel, and others extra-cardiac disorders such as:

Atrial fibrillation, diastolic dysfunction, left atrial enlargement, apical thrombi, ventricular aneurysms/ apical akinetic chamber, myocardial infarction, progressive heart failure, high incidence of coronary fistulae and morbid atrial fibrillation (**Chung 2010**).

Neuromuscular disorders ApHCM is only rarely associated with NMDs, such as limb girdle muscular dystrophy, glycogen storage disease, metabolic myopathy, myopathy of unknown significance, or eosinophilia-myalgia syndrome. The rare association of NMDs with ApHC might be due to absence of systematic neurologic investigations of patients with AHC and vice versa (**Finsterer 2009**).

The probability of survival without morbid events at 10 years was 77 ± 4%. Three independent predictors of cardiovascular morbidity were identified: age at diagnosis ≥ 60 years, left atrial diameter ≥ 36 mm, and New York Heart Association class ≥ III at baseline (**Yan 2012**).

Management

1. **Drugs** Medications used to treat symptomatic patients with ApHCM include verapamil, beta-blockers and antiarrhythmic agents such as amiodarone and procainamide.
2. **Ablation:** Monomorphic VT in a ApHCM can be due to endocardial, epicardial or intramural reentry in areas of apical scar. Epicardial ablation or transcoronary alcohol ablation is required in some cases (**Inada 2011**).
3. **Apical myectomy** improves functional status by decreasing left ventricular end-diastolic pressure, improving operative compliance, and increasing stroke volume. This procedure might be of value in other patients with HCM who have severe hypertrophy and small LV end-diastolic volume (**Schaff 2010**).
4. **Heart transplantation:** ApHCM is a morphologic variant in which the hypertrophy is primarily localized to the apex of the LV. A subset of patients have progressive, drug-refractory diastolic heart failure with severely limiting symptoms caused by low cardiac output. Heart transplantation has been the only therapeutic option available for such patients.
5. **Implantable cardioverter defibrillator:** An ICD is recommended for high risk patients. (See next slide)

ICD indications in HCM if one or more of the acknowledged SCD risk factors were present:

1. Family history of premature HCM-related death particularly if sudden, in a close relative, or multiple in occurrence;

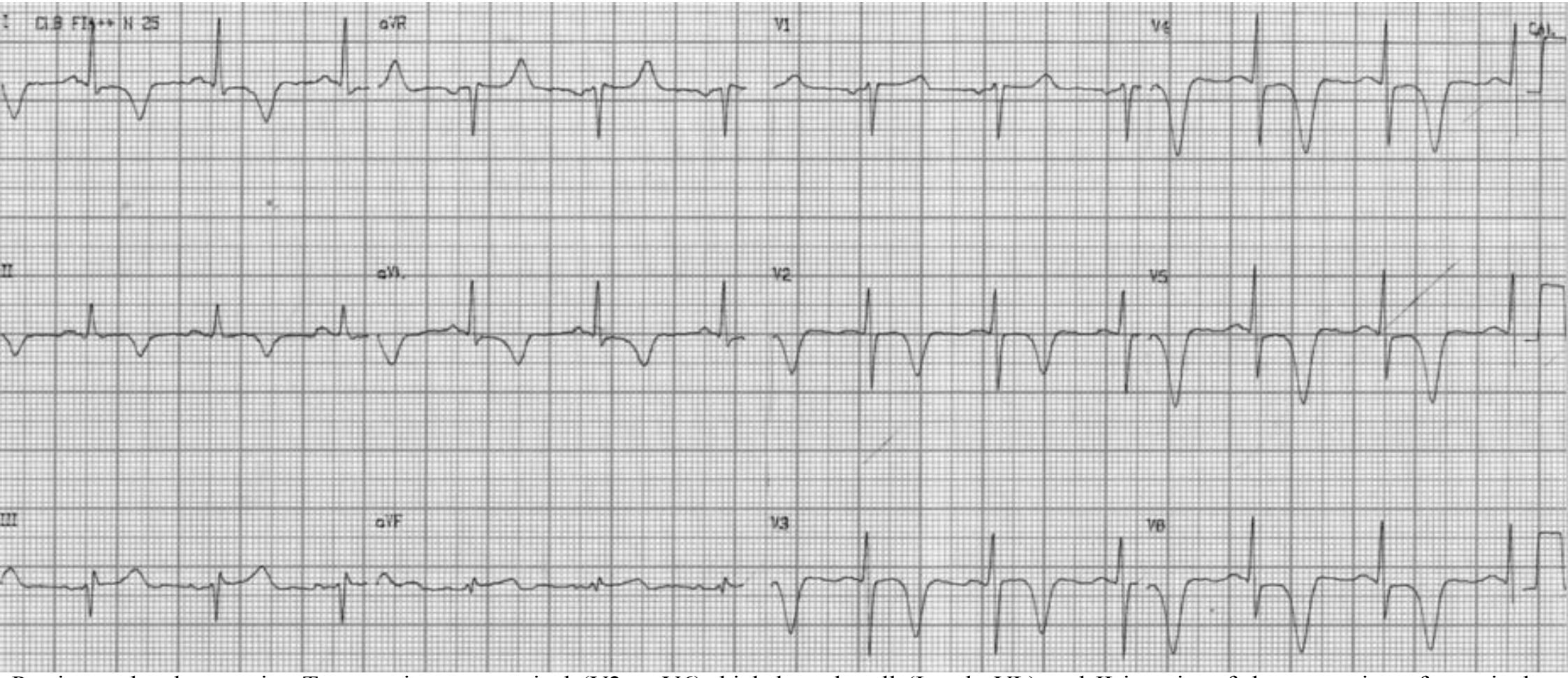
2. Unexplained syncope, particularly in young patients , or if demonstrated to be arrhythmia-based;

3. Frequent, multiple, or prolonged episodes of NSVT documented on serial ambulatory Holter monitoring;

4. Hypotensive or attenuated blood pressure response to exercise;

5. Extreme left ventricular hypertrophy (≥30mm) particularly in young patients.

Typical ECG example of Takotsubo (***in Japanese, describes an octopus trap***) cardiomyopathy (TCM)Stress-induced cardiomyopathy, broken heart syndrome, transient left ventricular apical ballooning or apical ballooning syndrome, adrenergic cardiomyopathy, and with the eponymous name of Gebrochenes-Herz.



Persistent deeply negative T waves in antero-apical (V2 to V6), high lateral wall (I and aVL) and II in spite of the regression of ventricular dysfunction. These ECG findings are very important in differentiating TCM from acute myocardial infarction.

The ECG in TCM is characterized by circumferential subepicardial ischemia. These ECG changes are significantly different from those that occur in acute segmental transmural ischemia characteristic of STEMI. Although some segmental contractile alterations (apical dyskinesis and basal hyperkinesis) occur in TCM, STSE is more diffuse in comparison to STEMI. This paradox can be explained by considering the electrophysiological and molecular alterations. The ECG pattern of TCM has 3 successive stages or phases .

First stage: characterized by discrete STSE, usually in the precordial leads but also sometimes in the lateral and inferior leads. The magnitude of STSE is usually less than ST segment elevation in STEMI. T waves are tall but do not exceed 12-15 mm as is sometimes seen in STEMI where they may exceed 18 mm. The maximal ST segment alteration usually occurs in leads V3-5.

Second stage: seen after 2-3 days; STSE resolves with appearance of diffuse, deep and inverted T waves except in lead aVR where T waves are positive. The presence of positive T waves in aVR is a valuable sign in differentiating TCM from MI. The non-segmental distribution of T wave alterations is a characteristic. The QT and QTc intervals may also be prolonged. Pathological Q waves are rarely seen.

Third stage: T wave inversion and QT prolongation typically resolves after 3-4 months, but in some cases these changes may last up to 1 year. Resolution of changes may sometimes occur earlier after 3-4 weeks. The combination of ST segment depression in aVR along with absent STSE in V1 has 91% sensitivity, 96% specificity and 95% predictive accuracy for TCM. A summary of the significant ECG criteria for diagnosis:

Absence of ST segment elevation in V1,

Absence of reciprocal changes in inferior leads

Presence of ST segment elevation in inferior leads, especially in II

Sum of ST segment elevation in V4-6 ÷ V1-3 ≥1.

ST segment depression in aVR.

Deep negative T waves associated with prolonged QTc.

Another characteristic of the negative T waves is that they remain negative in spite of regression of myocardial contractile dysfunction, unlike what happens in segmental ischemia where T waves became positive with the recovery of myocardial contractility. This evolution of ECG changes is illustrated in another case of TCM shown in Low QRS voltage and shortening of QRS duration are highly prevalent ECG signs in patients with Takotsubo syndrome. This is a reason why these ECG characteristics are useful in differentiating it from ACS during the first contact with the patient in the ED. This sign along with the echocardiogram and coronary angiography could be of great diagnostic importance.

Malignant ventricular arrhythmias, including TdP) associated with QT prolongation, may occur in 8% of the cases, especially when QTc > 500 ms ICD implant should be considered in cases of persistent QTc > 500 ms with a previous history of syncope or cardiac arrest (18). In a systematic review of TCM the incidence of late SCD is 0.5% (25).

Main disorders that may involve the left ventricular apex (Cisneros 2011)

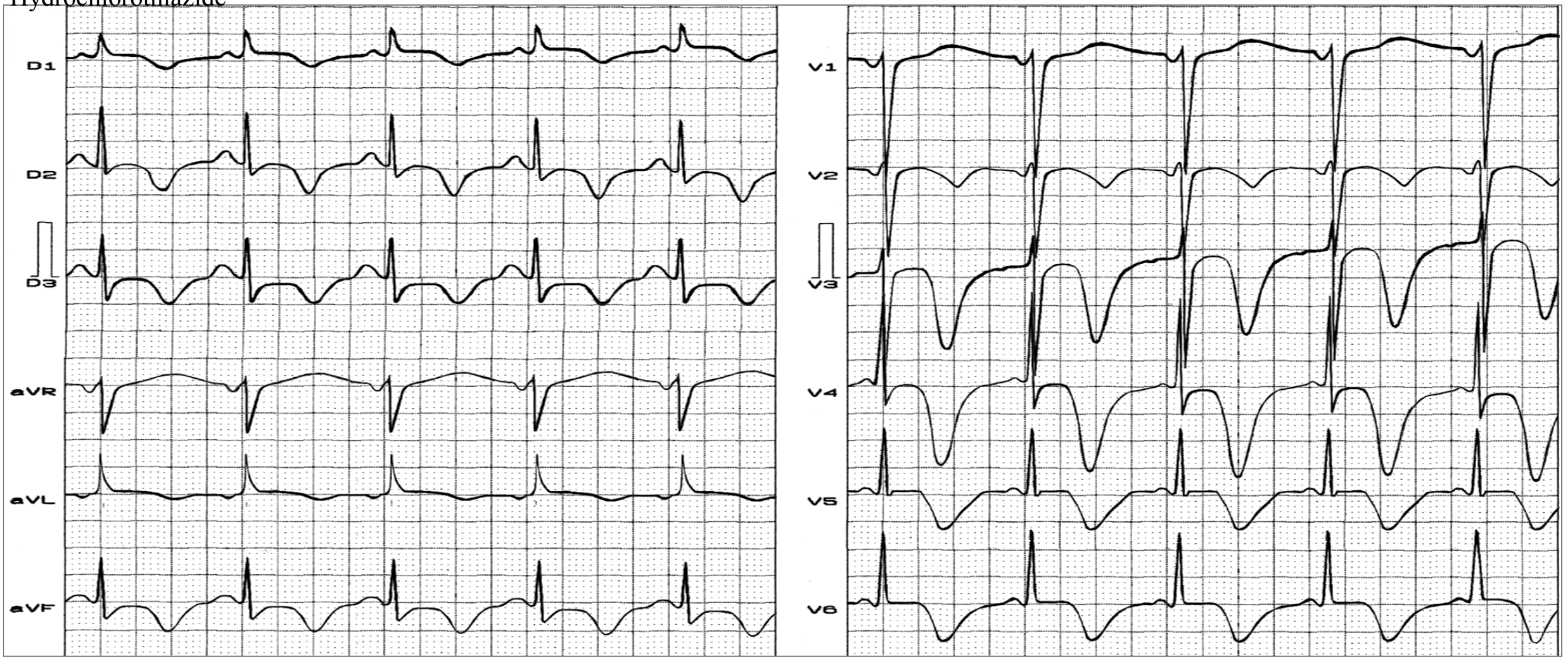
There are many disorders that may involve the left ventricular apex; however, they are sometimes difficult to differentiate. the spectrum of diseases that most frequently affect the apex of the left ventricle including:

1. Takotsubo cardiomyopathy “octopus trap”, transient apical ballooning syndrome, apical ballooning cardiomyopathy, stress-induced cardiomyopathy, Gebrochenes-Herz-Syndrome, broken heart, and simply stress cardiomyopathy a bulging out of the left ventricular apex with a hypercontractile base of the LV is often noted. It is the hallmark bulging out of the apex of the heart with preserved function of the base that earned
2. Left ventricular aneurysms and pseudoaneurysms
3. Apical diverticula
4. Apical ventricular remodeling
5. **Apical hypertrophic cardiomyopathy (ApHCM)**
6. Left ventricular non-compaction
7. Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) with left ventricular involvement
8. Left ventricular false tendons: are fibrous or fibromuscular bands that stretch across the LV from the septum to the free wall. They can also tether to a papillary muscle, but unlike the chordae tendineae, do not connect to the mitral leaflets. They are anatomic variants that should not be mistaken for abnormalities such as tumors, subaortic membranes, thrombus borders, septal hypertrophy.
9. Chronic chagasic myocarditis

With an emphasis on the diagnostic criteria and imaging features. In this setting cardiac imaging methods can provide the clue to obtaining the diagnosis.

Central nervous system diseases and giant negative T-wave

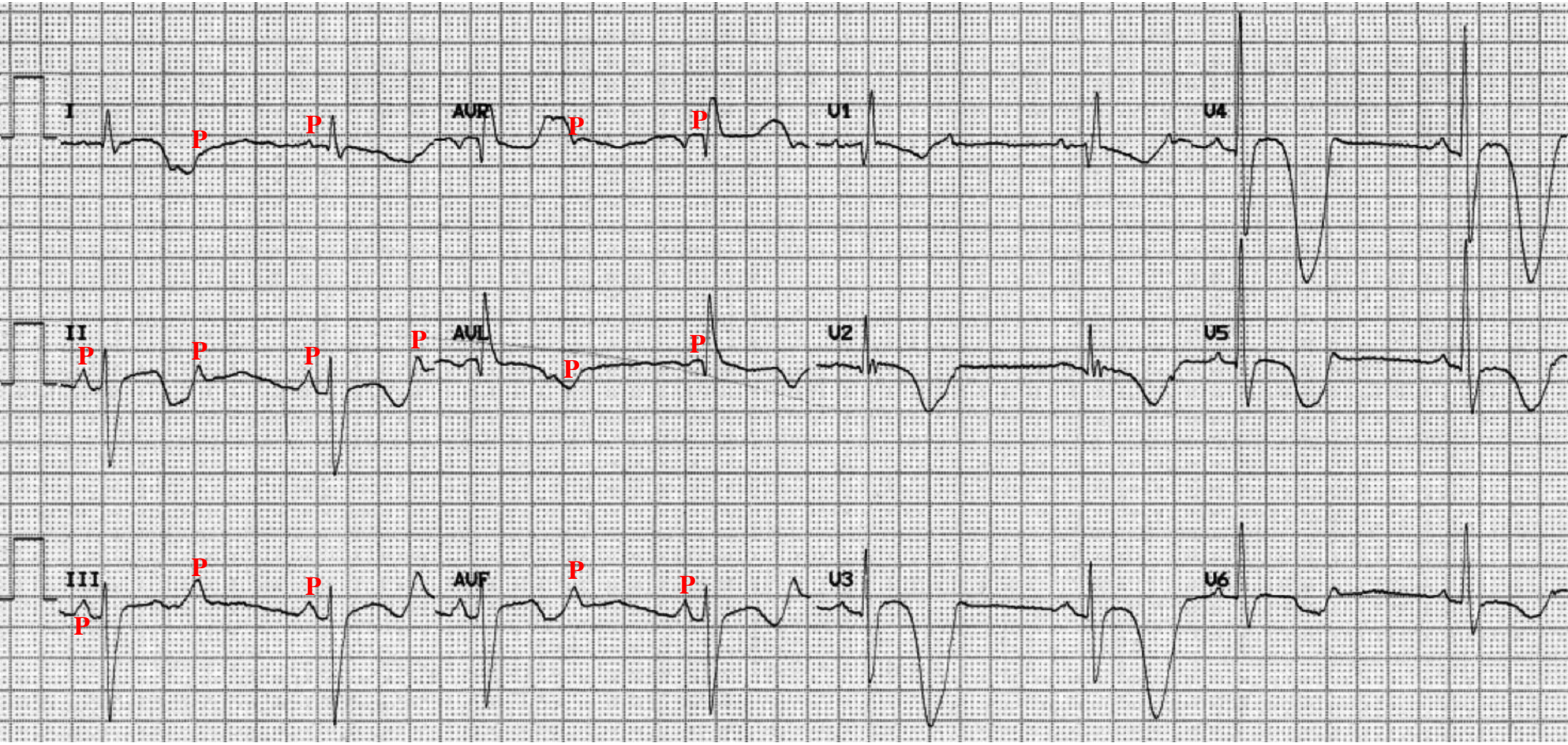
Name: E.A.D; **Age:** 68 y.o. **Sex:** Fem..; **Race:** White.; **Date:** 01/21/1999**Weight:** 65 Kg.;**Height:** 1.65 m**Medication in use:** Enalapril + Hydrochlorothiazide



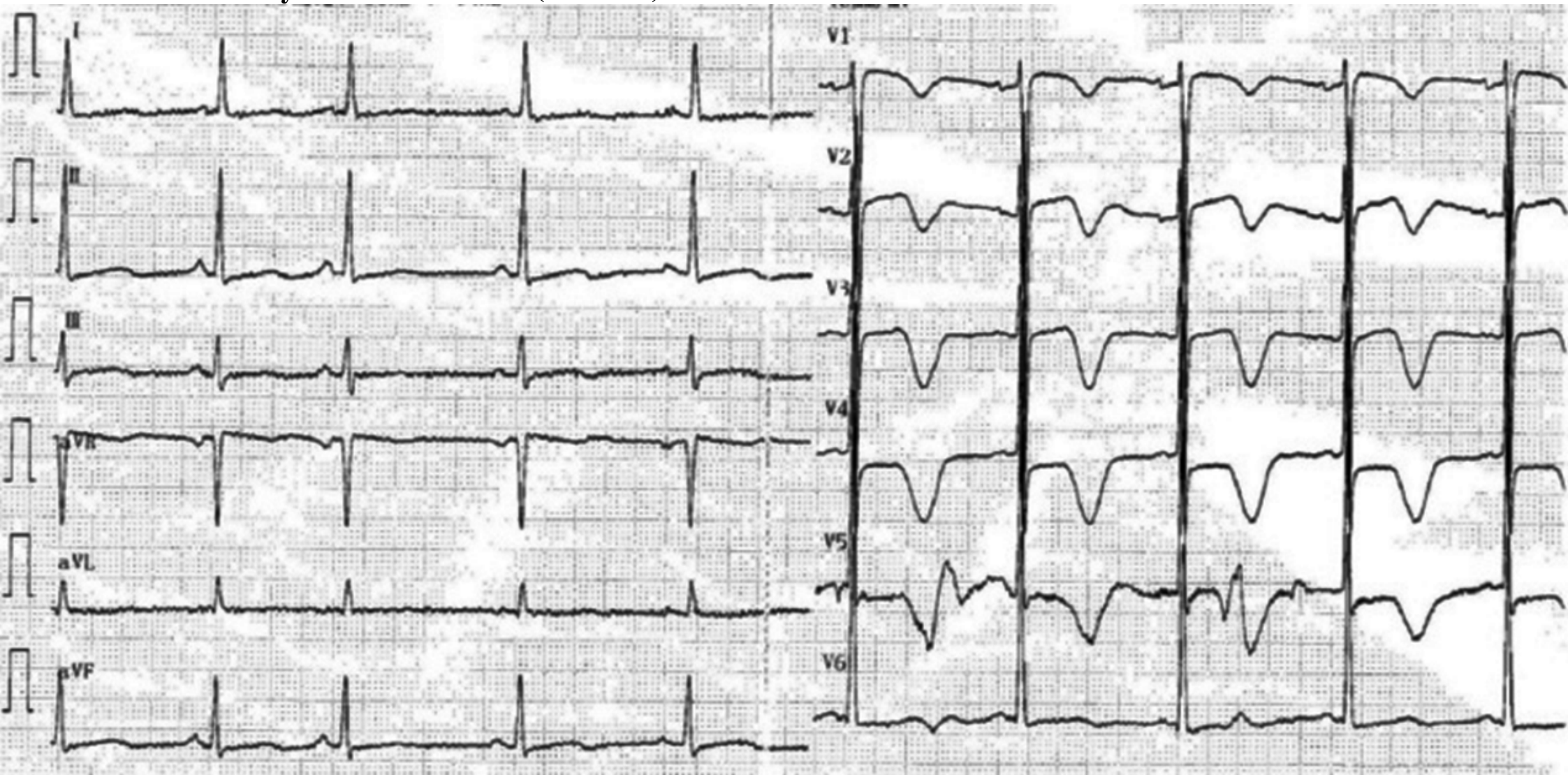
Clinical diagnosis: subarachnoid hemorrhage.

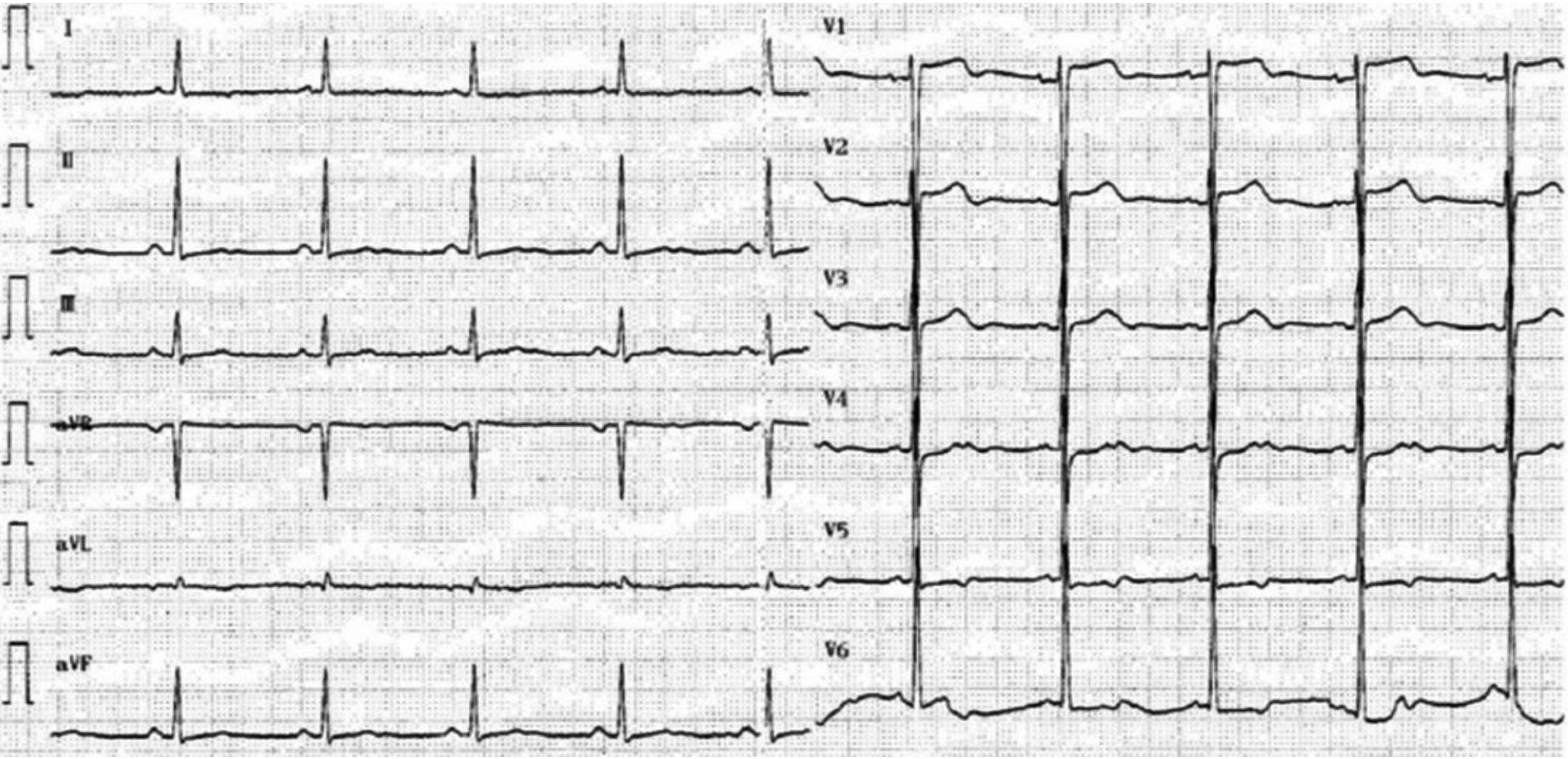
ECG diagnosis: long QT interval, great-width and inverted T waves: giant T waves. Typical ECG of subarachnoid hemorrhage with long QT interval. Deeply inverted T waves.

Complete Heart Block after Morgagni-Adams-Stokes syndrome events and Giant Inverted T-waves and prominent QT interval prolongation



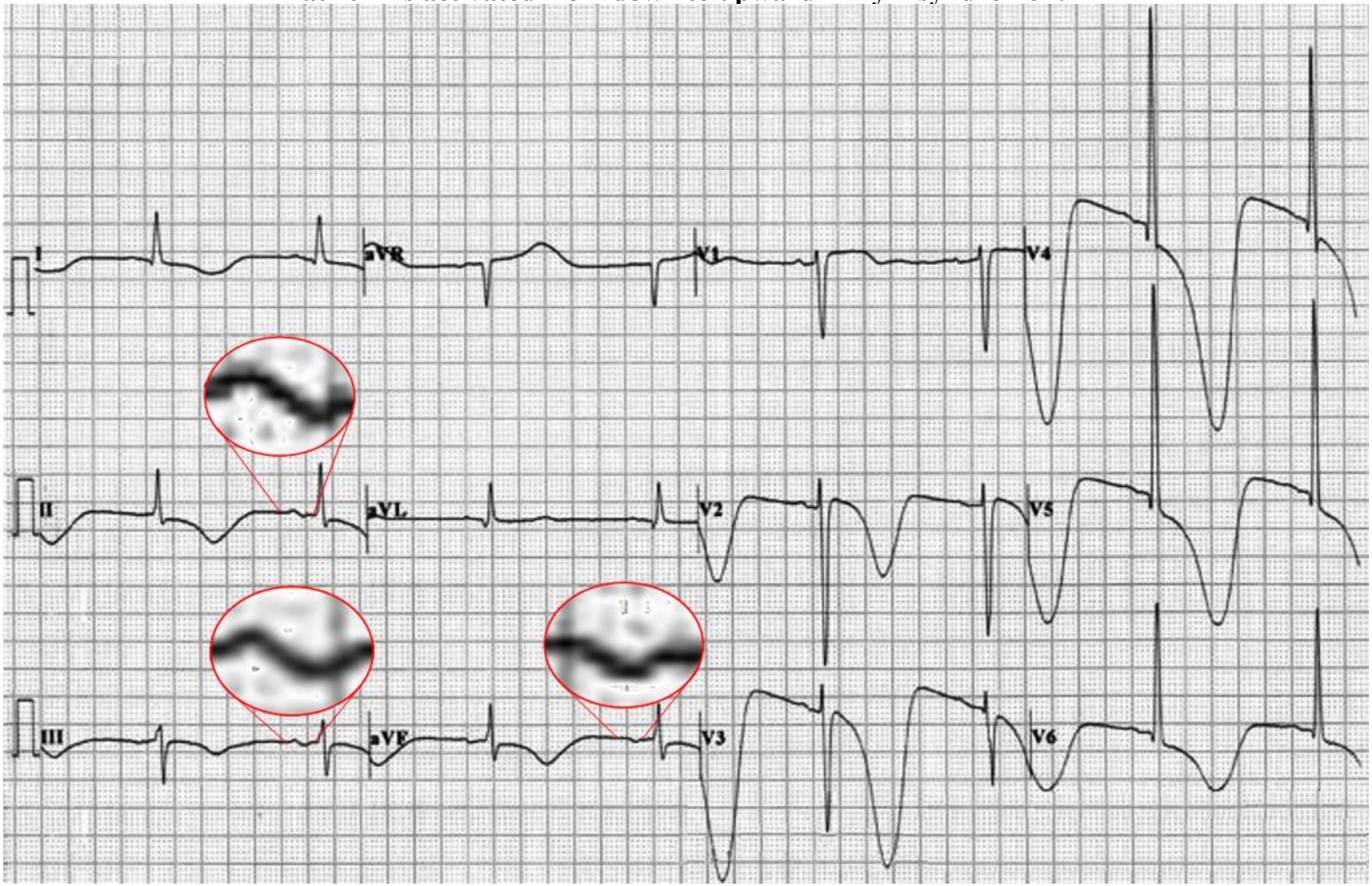
Drugs effects: ECG showing prominent QT interval prolongation (QTc = 618 ms) and giant inverted T waves 2 h after intravenous azithromycin administration (Yu 2014)





48 hours after the discontinuation of azithromycin, the QT interval and QTc were reduced to 440 ms and 443 ms, respectively, and the giant inverted T waves disappeared

Giant T-wave inversions in inferior leads and from V2 to V6 with significant QT/QTc prolongation associated with myocardial stunning without AMI. Additionally, clear complete interatrial block (plus-minus and prolonged P-wave in inferior leads: Bachman block). Left atrium is activated from down to upward "Bayés syndrome"?



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