PSEUDO ECG MYOCARDIAL INFARCTION IN YOUNG MAN WITH SEVERE CHORNIC CHAGASIC CARDIOMYOPATHY

PSEUDO ECG DE INFARTO DO MIOCÁRDIO EM HOMEM JOVEM PORTADOR DE CARDIOMIOPATIA CHAGÁSICA CRÔNICA

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Young man (29yo), mulatto agriculture worker, coming from rural Chagasic-endemic area of Minas Gerais State, Brazil (San Francisco River). The patient himself informs clearly that his rural house was infested by triatomine bugs "bichos-barbeiros" or "chupança" at that time and that many times he was bitten by them during the night. Concerning weight gain the last Month (6Kg)

Physical

Head: Normocephalic. Eyes edematous, ears, and throat normal.

Neck: veins distended, increased jugular venous pressure to 12cm. Positive hepatojugular reflux. Carotids without bruits.

Chest: Scattered rhonchi throughout, rales bilateral one third lower bases.

Heart: The apex beat is about 6cm in diameter, or a little more than 2.5 fingertips. It is located in the seventh intercostal space in the anterior axilary line. A palpable pulmonary component of the second heart sound (P2).

Tachycardial pulses (106bpm), and regular. Wide splitting of the second heart sound with an accentuated second component (P2), Third S3 diastolic gallop and fourth heart sounds was noted. Mitral systolic murmur Grade 3/6 irradiate to axila and left sternum border.

Abdomen: Distended abdomen. Liver sensitive and palpable fourth centimeters below right costal margin (hepatomegaly).

Genitalia: swelling scrotum.

Extremities: Swelling of feet and ankles, no clubbing. Pulses intact.

Neurologic:. No localized or sensory deficits. Normal profound reflexes. Mental status intact. Normal profound reflex.

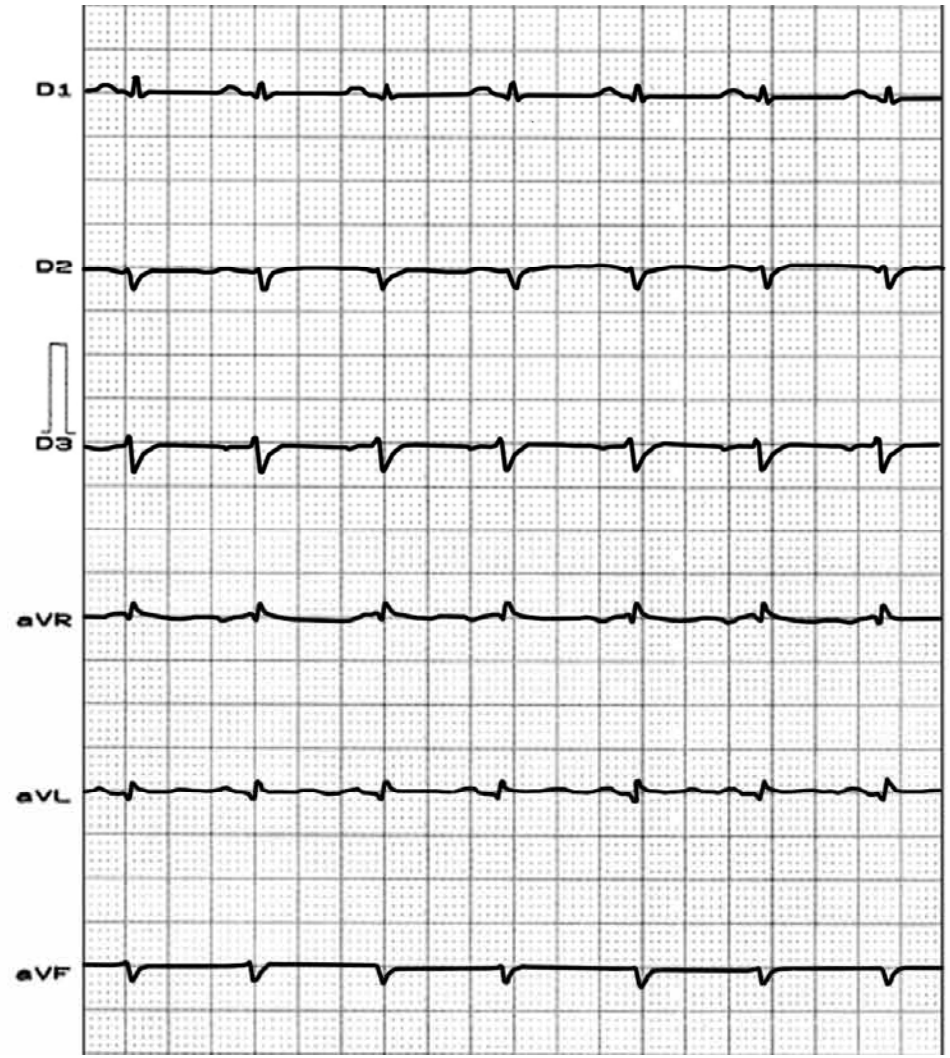
Clear predominant manifestations of right-sided failure: increased jugular venous pressure, peripheral edema, ascites, and hepatomegaly.

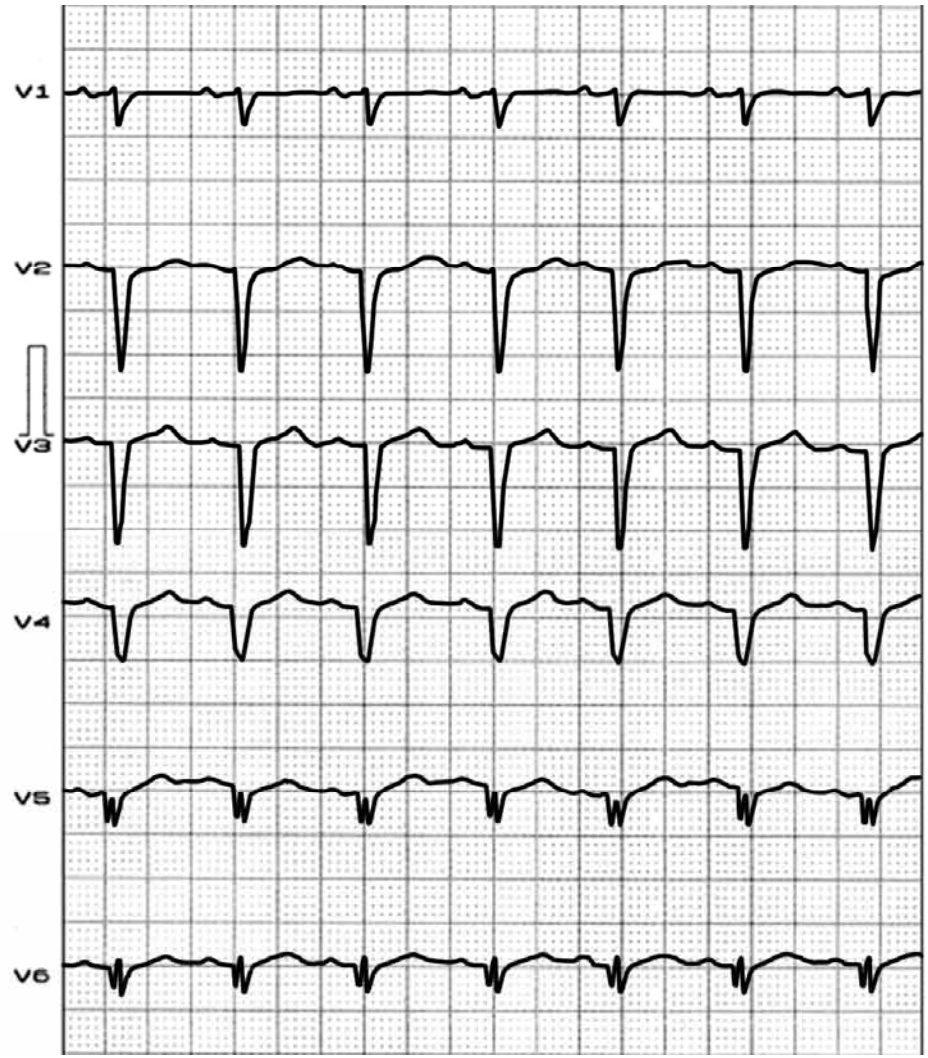
Chest x-ray: marked cardiomegaly (++++) with absence of pulmonary congestion.

Homem Jovem, (29 anos) trabalhador agrícola, procedente de área de endémica rural para Chagas (Interior de Minas Gerais- Rio São Francisco) Brasil. O próprio paciente informa claramente que a sua casa de pau a pique estava infestada por "bichos-barbeiros" ou “chupanças” e que muitas vezes ele fora picado por eles durante a noite.
Refere significativo ganho ponderal no último mês. (6 Kg).

Exame Físico:
Cabeça: olhos edemaciados, ouvidos e garganta normal.
Pescoço: ostensível distensão das veias do pescoço, aumento da pressão venosa jugular com 12cm, refluxo hepato-jugular positivo. Carótidas sem sopros.
Tórax: roncus esparços, estertores bilaterais no terço inferior de ambas as bases pulmonares.
CV: Ápex se observa e apalpa no sétimo espaço intercostal na linha axilar anterior.
Possui aproximadamente 6 centímetros de diâmetro e se cobre com mais de 2,5 dedos.
Segunda bulha (P2) palpável em foco pulmonar.
Pulso regular taquicárdico (106bpm), segunda bulha desdobrada com o componente P2 acentuado, S3 diastólico com cadência de galope e quarta bulha.
Sopro sistólico regurgitante em foco mitral, +++/¨6 irradiado a axila e borda esternal esquerda.
Abdômen: distendido e globulosos. Fígado palpável e sensível a quatro centímetros abaixo da margem costal direita (hepatomegalia).
Genitália: inchaço escrotal.
Extremidades: Edema ambos os pés e tornozelos. Pulsos presentes.
Neurológicas: Sem déficits sensoriais e normoreflexia profunda. Estado mental intacto.
Nítidas manifestações de falencia ventricular direita: aumento da pressão venosa jugular, edema periférico, ascite e hepatomegalia.

Radiografia de Tórax: cardiomegalia acentuada (++++) e pulmões limpos: ausência de congestão pulmonar


D1
D2
D3
aVR
aVL
aVF


V1
V2
V3
V4
V5
V6

Colleagues opinions

Hola Andrés y colegas del foro,
El ECG se parece mucho al que observé hace 15 años en una paciente tambien joven con síncope.
El ECG basal era casi igual: complejos QRS de bajo voltaje en PF y complejos en el PH que remedaban un area de necrosis extensa. Esta paciente presentaba un enorme aneurisma apical (mas grande que el resto del "ventriculo sano").
Es probablemente que sea lo que tenga este paciente.

Saludo a todos
Enrique Retyk MD

Hi Andrés and forum´s colleagues

The ECG is very similar to that for 15 year ago in a young woman with syncope. The baseline ECG was almost the same: low-voltage QRS complexes in FP and HP complexes in that mimicked an extensive area of necrosis. This patient had a large apical aneurysm (bigger than the rest of the "healthy left ventricle”). It's probably what has this patient.

I greet all
Enrique Retyk MD

FINAL DIAGNOSIS

ECG DIAGNOSIS

Sinus rhythm, HR: 100bpm, QRS axis with extreme superior axis deviation (-90º), initial q wave in I and aVL (counter clock wise rotation) sIII>sII: Left Anterior Fascicular block. Low QRS voltage exclusively on limb leads (Voltage of entire QRS complex in all limb leads ≤5mm).Low voltage on the surface ECG is defined as QRS voltage less than 5 mm in all limb leads and less than 10 mm in all precordial leads. An increase in the distance between the heart and the ECG leads, or intrinsic factors such as infiltration of the heart muscle itself and metabolic abnormalities are all associated with low voltage.

CAUSES OF QRS LOW VOLTAGE

I) Extrinsic factors: Increased electrode distance: Obesity, COPD with hyperinflation

II) Influences of the passive body volume conductor (extracardiac).

- Pleural effusion(cardiac tamponade)
- Constrictive pericarditis
- **Anasarca (The present case)**

III) Intrinsic factors due to the heart's generated potentials (cardiac)

- **Cardiomyopathies(the present case)**
- Infiltrative cardiovascular diseases[1]
  - Amyloidosis
  - Sarcoidosis
  - Scleroderma
  - Hemachromatosis
- Metabolic Abnormality
  - Myxedema

1. **Seward JB, Casaclang-Verzosa G. Infiltrative cardiovascular diseases: cardiomyopathies that look alike. J Am Coll Cardiol. 2010 Apr 27;55(17):1769-79.**

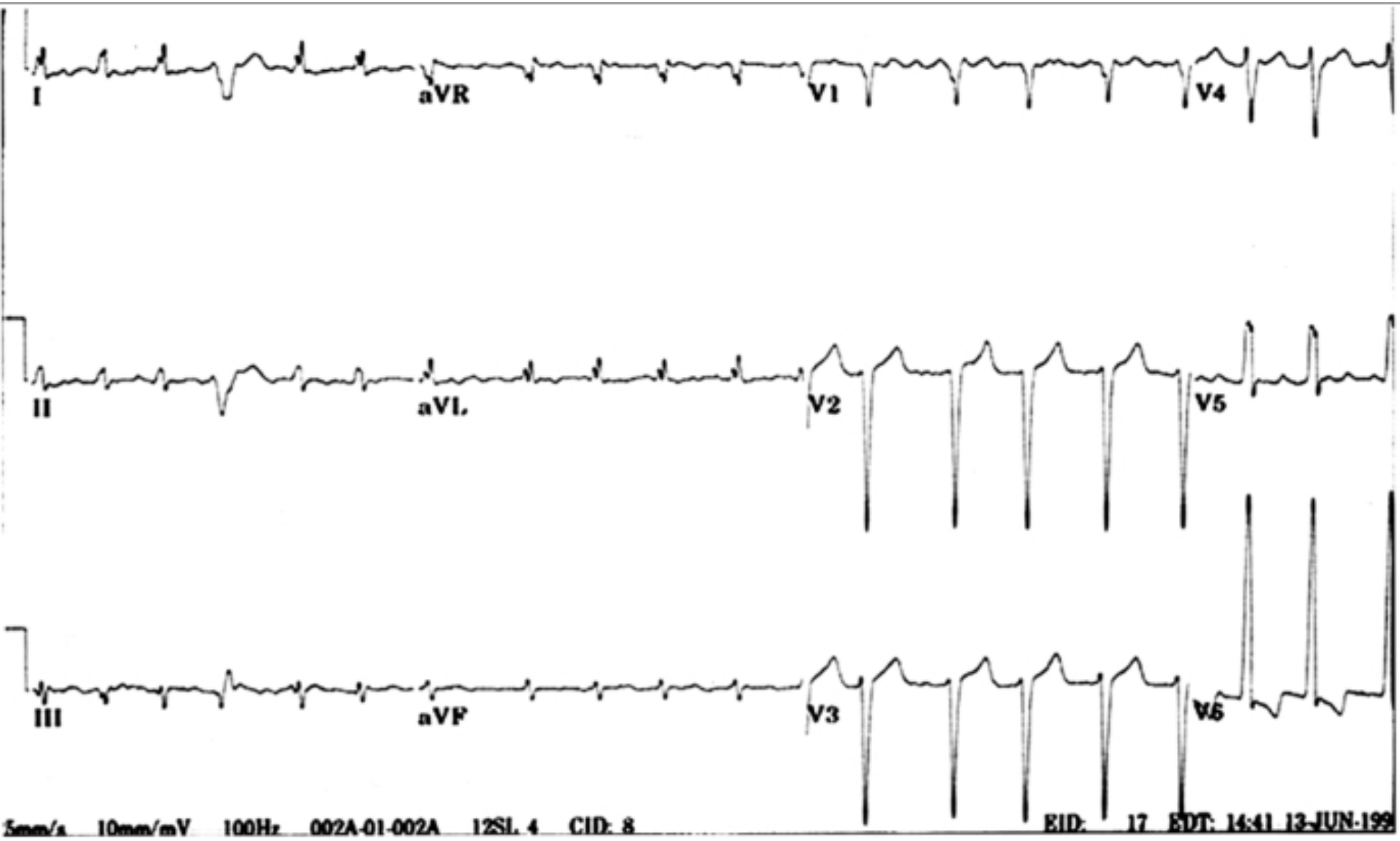
Peripheral edema of any etiology induces reversible low QRS voltage and its causes, reduces the amplitude of the P waves and T waves, decreases the duration of P waves, QRS complexes, and QT intervals, and alters in turn the measurements of the signal-averaged electrocardiogram and T wave alternans, all with enormous clinical implications[1].

The clinical correlate of an ECG with low voltage in the limb leads but normal precordial QRS amplitudes such as the present case was studied by Chinitz e al[1]. 12-lead ECGs with QRS voltage > 5 mm in all limb leads and < 10 mm in at least 2 contiguous precordial leads were collected.

Presence of clinical conditions associated with low voltage was determined from clinical data and chest imaging. 51 of 100 patients had voltage discordant ECGs that correlated with conditions known to cause diffuse low voltage. Among those without associated conditions, 63% had dilated ventricles, with an average ejection fraction of 33%. Low voltage isolated to the limb leads is associated with the same conditions that cause diffuse low voltage in only half of patients. In the remainder, more than 60% have dilated cardiomyopathies[1].(as the present case).

1. **Madias JE. Low QRS voltage and its causes. J Electrocardiol. 2008 Nov-Dec;41:498-500..**
2. **Chinitz JS, Cooper JM, Verdino RJ. Electrocardiogram voltage discordance: interpretation of low QRS voltage only in the limb leads. J Electrocardiol. 2008 Jul-Aug;41:281-286.**

Glancy et al [1]presented a ECG with QRS low voltage in the limb leads and high in the precordial leads associated with atrial fibrillation.



1. **Glancy DL, Newman WP. Atrial fibrillation with QRS voltage low in the limb leads and high in the precordial leads. Proc (Bayl Univ Med Cent). 2008 Oct;21:437-438.**

Extensive anterior transmural electrically inactive area:

Barreto et al[1] studied the ECG of 1004 patients with Chagas' disease. The correlation between the ECG alterations with the cardiac compromise, which was clinically analyzed, by thorax X-ray, echocardiogram and stress test.

The results show that increased cardiothoracic index, and decreased EF, decreased difference between systolic blood pressure before the exercise and at the final of the stress test at maximal weight were associated with greater incidence of PVCs, intraventricular conduction defects, electrically inactive area, ST-T alteration. chi 2 test shows that these association was singnificative. ***The presence of PVCs and electrically inactive area on the ECG study seems to determine worse prognosis to the patients since these alterations were more frequent on the patients that died due to Chagas' disease***.

Symptoms of myocardial ischemia, such as chest pain (sometimes with anginal features), acute myocardial infarction, and segmental wall motion abnormalities (including left ventricular apical aneurysm), frequently occur in patients with CCC. Because these clinical findings occur in the presence of normal coronary arteries, it is possible that an abnormality of the coronary vascular reactivity could be present in these patients. Patients with CCC have an abnormality of the coronary endothelium-dependent vasodilation, and this abnormality may play a role in their chest pain syndrome and in the development of segmental wall motion abnormalities.

Active endothelin-1 (ET-1) contributes to CCC and the mechanism of the increased expression of ET-1 is a result of the activation of the p42/44-mitogen activated protein kinase (MAPK)-AP-1 pathway (that regulates the expression of ET-1.) by T. cruzi infection[2].

1. **Barretto AC, Bellotti G, Deperon SD, Arteaga-Fernández E, Mady C, Ianni BM, et al. The value of the electrocardiogram in evaluating myocardial function in patients with Chagas' disease.Arq Bras Cardiol. 1989 Feb;52:69-73.**
2. **Huang H, Petkova SB, Pestell RG, Bouzahzah B, Chan J, Magazine H, et al.Trypanosoma cruzi infection (Chagas' disease) of mice causes activation of the mitogen-activated protein kinase cascade and expression of endothelin-1 in the myocardium. J Cardiovasc Pharmacol. 2000 Nov;36(5 Suppl 1):S148-150**

Infection with Trypanosoma cruzi causes a generalized vasculitis of several vascular beds. This vasculopathy is manifested by vasospasm, reduced blood flow, focal ischaemia, platelet thrombi, increased platelet aggregation and elevated plasma levels of thromboxane A(2) and endothelin-1.

The assessment and stratification of patients with chest pain in the emergency unit may indicate the appropriate therapy for each patient based on the probability of the presence of acute coronary syndrome disease and on the risk of its major cardiac events. That assessment is based on the triplet:

1. Clinical setting,
2. ECG findings,
3. Biomarkers of myocardial lesion.

Machado et al[1], report the case of a 58-year-old male chagasic chronic cardiomyopathy (CCC) patient admitted to the emergency unit due to chest pain and palpitations, with an ECG showing sustained VT and positive troponin measurement.

The patient underwent cine coronary angiography, which evidenced no obstructive CAD.

In CCC VT may arise from various regions in both ventricles, but LV inferolateral scar is the main source of S-VT reentrant circuits.

There is good topographic correlation between myocardial perfusion, wall motion abnormalities and areas that originate S-VT.

Although to a lesser extent, wall motion and perfusion defects also occur in a relevant proportion of CCC with NS-VT[2].

1. **Machado MN, Suzuki FA, Mouco OC, Hernandes ME, Lemos MA, Maia LN.Positive troponin T in a chagasic patient with sustained ventricular tachycardia and no obstructive lesions on cine coronary angiography. Arq Bras Cardiol. 2005 Feb;84:182-184.**
2. **Sarabanda AV, Sosa E, Simões MV, Figueiredo GL, Pintya AO, Marin-Neto JA. Ventricular tachycardia in Chagas' disease: a comparison of clinical, angiographic, electrophysiologic and myocardial perfusion disturbances between patients presenting with either sustained or nonsustained forms. Int J Cardiol. 2005 Jun 22;102:9-19.**

In patients with Chronic Chagasic Cardiomyopathy (CCC) and normal global ejection fraction there is an early cardiac denervation, when compared to coronary artery disease (CAD) patients. A significant difference was demonstrated between norepinephrine concentrations in CCC patients with normal LVEF and those with CAD with normal LVEF but no difference was found in patients with decreased LVEF[1].

Studies support the microvascular hypothesis to further explain the pathological features and clinical course of CCC. It is our belief that knowledge of this particular and remarkable cardiomyopathy will shed light not only on the microvascular involvement of its pathogenesis, but also on the pathogenetic processes of other cardiomyopathies, which will hopefully provide a better understanding of the various changes that may lead to an end-stage heart disease with similar features[2].

In CCC patients, the progression of left ventricular systolic dysfunction is associated with both the presence of reversible perfusion defects and the increase in perfusion defects at rest. These observations support the notion that myocardial perfusion disturbances participate in the pathogenesis of myocardial injury in CCC[3;4].

1. **Nastari L, Ramires FJ, Salemi VM, Ianni BM, Fernandes F, Strunz CM, et al. Intramyocardial adrenergic activation in chagasic cardiomyopathy and coronary artery disease. Arq Bras Cardiol. 2010 Dec 22. pii: S0066-782X2010005000163.**
2. **Rossi MA, Tanowitz HB, Malvestio LM, Celes MR, Campos EC, Blefari V, et al; Coronary microvascular disease in chronic Chagas cardiomyopathy including an overview on history, pathology, and other proposed pathogenic mechanisms. PLoS Negl Trop Dis. 2010 Aug 31;4(8). pii: e674.**
3. **Hiss FC, Lascala TF, Maciel BC, Marin-Neto JA, Simões MV. Changes in myocardial perfusion correlate with deterioration of left ventricular systolic function in chronic Chagas' cardiomyopathy. JACC Cardiovasc Imaging. 2009 Feb;2:164-172.**
4. **Schwartz RG, Wexler O. Early identification and monitoring progression of Chagas' cardiomyopathy with SPECT myocardial perfusion imaging. JACC Cardiovasc Imaging. 2009 Feb;2:173-175.**

Endothelium may be damaged, especially at the coronary microcirculation, in animal models of CCC by several mechanisms.

Endothelial dysfunction has been reported in CCC patients with HF.

Peripheral endothelial function has never been studied in patients with CCC without HF and other conditions that could per se alter the endothelial function. Consolim-Colombo et al[1] evaluated the endothelial function in 9 patients with CCC, LVEF ≥ 60% and 10 healthy matched controls. Forearm blood flow was measured at baseline and during intra-brachial artery infusion of crescent doses of acetylcholine and nitroprusside, an endothelium-dependent and an endothelium-independent vasoactive drug, respectively.

At baseline, blood pressure and HR and the forearm blood flow were similar in both groups. Acetylcholine and sodium nitroprusside caused significant and similar dose-dependent increases in forearm blood flow of all subjects. No significant systemic hemodynamic changes were observed during the intra-arterial infusion of the drugs.

The authors conclude that the peripheral endothelial function is preserved in CCC patients without HF.

In the chagasic chronic phase, around 70% of infected people are asymptomatic (latent form). The remainder develop CCC and/or digestive syndromes. There is evidence for aggravation of the CCC by endothelin-mediated vasoconstriction. Endothelin ET(A) receptors contribute to the initial mechanisms of parasite control. Impairment of the endothelium-dependent vasodilatation favors hazardous effects. However, blocking endothelin ET(A) receptors can prevent the latter[2].

1. **Consolim-Colombo FM, Lopes HF, Rosetto EA, Rubira MC, Barreto-Filho JA, Baruzzi AC, et al. Endothelial function is preserved in Chagas' heart disease patients without heart failure.Endothelium. 2004 Sep-Dec;11(5-6):241-6.**
2. **Camargos ER, Rocha LL, Rachid MA, Almeida AP, Ferreira AJ, Teixeira A Jr, et al. Protective role of ETA endothelin receptors during the acute phase of Trypanosoma cruzi infection in rats. Microbes Infect. 2004 Jun;6:650-656.**

In the myocardium of infected mice, myonecrosis and a vasculitis of the aorta, coronary artery, smaller myocardial vessels and the endocardial endothelium are observed.
Immunohistochemistry studies employing anti-endothelin-1 antibody revealed increased expression of endothelin-1, most intense in the endocardial and vascular endothelium. Elevated levels of mRNA for prepro endothelin-1, endothelin converting enzyme and endothelin-1 were observed in the infected myocardium. When T. cruzi-infected mice were treated with phosphoramidon, an inhibitor of endothelin converting enzyme, there was a decrease in heart size and severity of pathology. Mitogen-activated protein kinases and the transcription factor activator-protein-1 regulate the expression of endothelin-1. Therefore, Petkova et al [1] examined the activation of mitogen-activated protein kinases in the myocardium by T. cruzi. studies strongly suggests that T. cruzi infection is linked to functional changes in the activity of two potent vasoactive peptidergic mediators, endothelin-1, a vasoconstrictor, and kinins, a group of vasodilator and pro-inflammatory peptides related to bradykinin. Western blot demonstrated an extracellular signal regulated kinase. In addition, the activator-protein-1 DNA binding activity, as determined by electrophoretic mobility shift assay, was increased. Increased expression of cyclins A and cyclin D1 was observed in the myocardium, and immunohistochemistry studies revealed that interstitial cells and vascular and endocardial endothelial cells stained intensely with antibodies to these cyclins.
These data demonstrate that T. cruzi infection of the myocardium activates extracellular signal regulated kinase, activator-protein-1, endothelin-1, and cyclins. The activation of these pathways is likely to contribute to the pathogenesis of CCC. These experimental observations suggest that the vasculature plays a role in the pathogenesis of CCC.
The identification of these pathways provides possible targets for therapeutic interventions to ameliorate or prevent the development of CCC during T. cruzi infection.

1. Petkova SB, Huang H, Factor SM, Pestell RG, Bouzahzah B, Jelicks LA, et al. The role of endothelin in the pathogenesis of Chagas' disease. Int J Parasitol. 2001 May 1;31:499-511.