

Relationship of Adherence to Treatment and Blood Pressure Control in Outpatients. Registry on Hypertension in the Andean Region of the 42nd Parallel (REHTACAP 42)

Cardiovascular disease is the leading cause of death in Argentina, and hypertension (HTN) is one of the most important risk factors given its high prevalence and the difficulties in achieving the goals proposed by national and international guidelines on this entity. Poor adherence to drug therapy is a public health issue that hinders the achievement of those goals, particularly in countries with great social and economic difficulties. The 8-item Morisky Medication Adherence Scale (8-MMAS) is one of the tools used to measure the level of adherence to antihypertensive medications, and has been widely used and validated in different languages around the world. (1) There are reports on the use of the 4-item Morisky-Green-Levine Medication Adherence Scale in Argentina (2), predecessor of the scale used in this work, but no papers of this tool for measuring adherence to treatment of HTN in Argentina have been published. An important contribution to understand the risk factors in Argentina has been the data from the National Survey on Risk Factors carried out by the National Ministry of Health in 2005, 2009, and 2013; however, data published in scientific journals from small towns are sparse, where their inhabitants' characteristics and habits are different from people living in other areas of the country. The purpose of this study is to identify the levels of HTN control and their relationship with the adherence to treatment in outpatient settings of the Andean Region of the 42nd Parallel.

A prospective registry of consecutive hypertensive outpatients under drug therapy for at least 6 months was performed between May 2015 and April 2016. The first consultation was done in two private offices in El Bolsón city (Río Negro), and a private office in Epuypén (Chubut). Patients between 20-80 years of age were enrolled and pregnant women, secondary hypertensive patients, and patients who refused to sign the informed consent form were excluded. Demographic data, blood pressure (BP), drug therapy, and level of adherence were recorded, according to an 8-MMAS scale translated into Spanish. A score of 8 was considered high adherence, 6 and 7 was medium adherence, and a score ≤ 5 and BP ≥ 140 and/or 90 mm Hg was considered low adherence. Participants were asked about their compliance with medication schedules, and whether they had seen their doctor over the past year. Statistical analysis was performed with the chi-square test to measure the association between HTN control and (high or medium versus low) adherence, and with Student's t test or the Mann-Whitney test

depending on the type of sample distribution for systolic and diastolic BP recordings; a p value < 0.05 was considered significant.

A total of 164 patients aged 65.1 (± 10.1) years were enrolled: 62.2% women, 63.4% with incomplete secondary school education, and 1.4% without health coverage. Fifty percent of patients had history of dyslipidemia, 18.9% of diabetes, 13.4% of smoking, 50.0% of obesity, 13.4% of coronary artery disease, 3.7% of heart failure, and 5.5% of atrial fibrillation. Mean years of antihypertensive treatment was 10.2 (± 9.3) years; 89.0% took one or two pills to treat HTN, 90.8% took one or two antihypertensive medications and a total average of 3.7 (± 2.3) pills per patient was taken, adding those prescribed to control BP and the medications prescribed for other conditions. There were differences in the characteristics of the adherent group (A, high or medium adherence) versus the non-adherent group (no A, low adherence): group A had a higher level of instruction and higher percentage of dyslipidemic participants (Table 1). Hypertension was the reason for consultation in 62 patients (37.8%), preoperative evaluation in 45 (27.4%), and other reasons in 57 (34.8%). Median systolic BP was 150.0 mmHg (interquartile range 136-164), and median diastolic BP was 80.0 mm Hg (73-88). Hypertension was present in 70.7% of patients, 36.6% with grade II or III. Mean 8-MMAS score was 6.1 (± 1.9); 38.4% of patients were non-adherents, 28.0% had medium adherence, and 33.5% high adherence. Medication schedules were not complied with in 26.4% of cases and 32.3% had not seen the doctor who managed their HTN over the past year. Forgetfulness was the most common cause of non-adherence (54.0%), followed by feeling better (28.6%), and possible adverse effects (12.7%). There was no difference in HTN as per the level of adherence to medications ($p = 0.117$) or in the values of diastolic BP ($p = 0.072$), but there was a difference in the levels of systolic BP ($p = 0.042$) (Table 2).

In a population of essential hypertensive patients under drug therapy consulting in an outpatient office of the Andean Region of the 42nd Parallel, a low level of BP control at the expense of systolic BP was observed, a finding related to the age group participating in the study. Most participants take one or two pills to treat their HTN, and one or two antihypertensive medications (sometimes combined in only one pill), suggesting a non-intensive treatment for their BP values. The levels of adherence were acceptable compared with similar studies, being higher than those carried out in underdeveloped countries, and lower than those with higher income. (3-6) It was concluded that the studied population had an acceptable level of adherence to antihypertensive treatment with poor control of BP values. An association between adher-

	Adherence (n = 101)	Non-adherence (n = 63)	p
Age, years, mean	65.5	64.5	0.661
Female sex, %	67.3	54.0	0.086
Incomplete secondary school education, %	56.4	74.6	0.018*
Dyslipidemia, %	56.4	39.7	0.036*
Diabetes, %	17.8	20.6	0.650
Smoking, %	10.9	17.5	0.229
Obesity (BMI ≥ 30), %	46.5	53.8	0.700
Ischemic heart disease, %	10.9	17.5	0.229
Heart failure, %	2.0	6.3	0.147
Atrial fibrillation, %	5.9	4.8	0.747
N° of pills/day, mean	3.8	3.6	0.421
N° of antihypertensive pills/day, mean	1.59	1.63	0.88

BMI: Body mass index. *Significant.

Table 1. Characteristics of the population as per level of adherence (medium or high vs. low)

	Adherence	Non-adherence	p
SBP, median (IQR)	147 (135-161)	157 (140-168)	0.0416*
DBP, median (IQR)	79 (72-86)	83 (75-92)	0.0727
No control of BP, %	63.3	77.8	0.1172

IQR: Interquartile range. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. BP: Blood pressure. *Significant.

Table 2. Relationship between level of adherence (medium or high vs. low) to drug therapy and control of blood pressure

ence and systolic BP and tendency in diastolic BP was found but no relationship between adherence and HTN control when analyzed as a qualitative variable. Larger studies could demonstrate such association. Building strategies to improve the levels of patients' adherence and doctors' prescription for more intensive treatments could increase the number of patients achieving BP goals suggested by the guidelines.

Conflicts of interest

None declared.

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César Berenstein, M.D.

Clínica La Merced de El Bolsón (Rio Negro),
Instituto Médico de la Comunidad de El Bolsón (Rio Negro)
and Consultorios Lahuen de Epuyén (Chubut)
Los Notros 4789, Barrio Arrayanes, (8430) El Bolsón, Rio Negro.
e-mail: ceber31@hotmail.com

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Use of Intravenous Beta-Blockers in Dobutamine Stress Echocardiography

Stress echocardiography is a first-line study for the detection of myocardial ischemia, supported by several scientific studies since it was first introduced some four decades ago. While physical exercise is the most widely used stressor, about one third of patients cannot perform it properly due to musculoskeletal issues. For this group of patients, dobutamine and dipyridamole are the most commonly used drugs. (1)

Dobutamine is a short half-life synthetic catecholamine obtained from the molecular structure of isoproterenol, which mainly acts on β -1 receptors (and

to a lesser extent on β -2 and α -1 receptors) of the myocardium, leading to increased heart rate (HR) and inotropism, with the consequent increase of oxygen consumption. Although the sensitivity and specificity of the study –conducted with the highest standards by well-trained staff– are high and comparable to other imaging studies such as nuclear medicine, it is well known that sensitivity is reduced in one vessel lesions compared with multivessel disease. (2)

Even though intravenous (IV) bolus of beta-blockers can be used as antidote at the end of dobutamine infusion, various scientific research studies (including our laboratory) have reported that its use increases the diagnostic sensitivity of the study. Still, we believe that this strategy is underutilized in the current practice. Below is a description of some representative cases from our experience (Table 1).

The first case was a 56-year old male patient whose baseline analysis showed no motility disorders. The patient reached 94% maximum HR with dobutamine 40 γ /kg/min, with increased global contractility. After propranolol administration, extensive severe hypokinesia involving anterior, lateral, anteroseptal, and inferolateral segments was evident, with severe impairment of systolic function, hypotension, angina, and 3 mm ST-segment depression. Coronary angiography (CAG) revealed two severe proximal lesions in the anterior descending (ADA) and circumflex (Cx) arteries.

The second case was a 76-year old man with precordial pain under evaluation. Baseline analysis showed inferolateral and lateral basal hypokinesia [ejection fraction (EF) 63%]. The patient reached 90% maximum HR with dobutamine 20 γ /kg/min, with increased global contractility. A bolus of 1 mg propranolol was administered. After propranolol administration, lateral and inferolateral akinesia with fall of EF

to 55% was observed. Coronary angiography revealed severe lesion in the first diagonal artery (80%), 95% occlusion of the first lateral ventricular branch of the Cx artery, and moderate lesion (60%) of the first posterior ventricular branch of the right coronary artery (RCA).

The third case was a 48-year old woman with history of RCA infarction. Baseline analysis showed severe basal and mid inferior hypokinesia and basal posterior septal akinesia (EF 53%). The study with dobutamine 40 γ /kg/min improved contractility in inferior segments, with hypercontractility in the rest of the segments. After 1 mg atenolol administration, extensive akinesia involving the anterior septum, apical segments, and the anterior wall (ADA territory) was observed (Figure 1; Videos 1 and 2). Coronary angiography showed patent stents and thin-caliber ADA, with no significant lesions.

The fourth case was a 55-year old woman with precordial pain under evaluation. Baseline analysis showed no motility disorders. No new dissynergies to the maximum dose were observed, and coronary flow reserve of the ADA was normal. After atenolol administration, extensive hypokinesia involving the apical and mid lateral and anterior septal segments was observed. Coronary angiography was normal.

In a study of 100 patients in 2003, Mathias et al. reported that the use of IV metoprolol 5 mg injected at peak of dobutamine infusion significantly raised the sensitivity of the study from 84% to 92%, mainly at the expense of the coronary involvement of a single vessel (from 73% to 88%) without significant specificity reduction. (3) Another study including twice the number of patients showed identical results. In this case, sensitivity increased from 88% to 97%, and in 7% of cases (14 patients) the assessment of motility disorders dur-

Table 1. Main aspects of the clinical cases presented

Patient	History	Drug	Symptoms	ECG	Ischemia	CAG
Male, 56 years of age	- Peripheral arthropathy - HIV	Propranolol	Angina	Infra-ST	Anterior, lateral, anteroseptal, inferolateral	Severe proximal lesion in ADA & Cx
Male, 76 years of age	- HTN - Crohn's disease	Propranolol	No	Normal	Lateral and inferolateral	Severe lesion in 1st Dx, 1st lateral ventricular (Cx), and posterior ventricular (RCA)
Woman, 48 years of age	- Inferior AMI - Stent in RCA	Atenolol	Angina	STEMI	Anterior septum, anterior and apical	- Thin-caliber ADA, without lesions
Woman, 55 years of age	- HTN - Diabetes - Dyslipidemia - Pacemaker	Atenolol	Dyspnea	PMK rhythm	Septal, anterior and lateral.	- Patent stents - CAG with no lesions.

ECG: Electrocardiogram. CAG: Coronary angiography. HIV: Human immunodeficiency virus. ADA: Anterior descending artery. Cx: Circumflex artery. HTN: Hypertension. Dx: Diagonal artery. RCA: Right coronary artery. AMI: Acute myocardial infarction. PMK: Pacemaker.

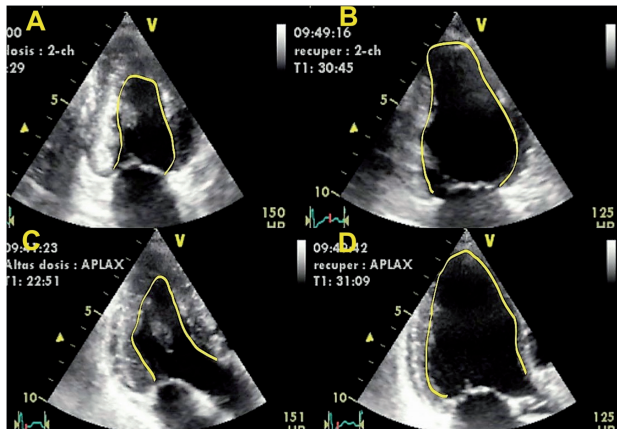


Fig. 1. Images during ventricular systole in two-chamber view (A and B) and apical long axis view (C and D). The first column occurs in the maximum dose phase, and the second column occurs after atenolol administration. Akinesia involving the anterior wall and anterior septum is observed.

See videos on the web.

Video 1. Two-chamber view at baseline (top, left), low dose (top, right), maximum dose (bottom, left), and post-atenolol (bottom, right) phases.

<https://youtu.be/DaOxn7D7jMY>

Video 2. Three-chamber view at baseline (top, left), low dose (top, right), maximum dose (bottom, left), and post-atenolol (bottom, right) phases.

<https://youtu.be/R4g8iXPKPyM>

ing the recovery phase after metoprolol was determinant in the final interpretation of the study. (4)

An analysis from our laboratory showed that 17.7% of the 96 patients studied had further motility disorders (7 patients) or worsening of baseline dissynergies (5 patients) during the recovery phase after atenolol administration. Significant coronary artery disease was confirmed in 10 of the 12 patients undergoing invasive studies. (5)

Among the mechanisms that could play a role in this apparently paradoxical effect of beta-blockers on myocardial contractility, we should consider, in the first place, the dragging effect of the endocardium by the middle and subepicardial layers of the myocardium, whose hypercontractility is blocked by IV beta-blockers, thus revealing the endocardial ischemia (disappearing later). This could have happened with the first two patients we presented. Second, we should bear in mind that the higher the dobutamine dose, the greater the effect on β -2 (vasodilator) and α -1 (vasoconstrictor) receptors. Therefore, when blocking β receptors, an imbalance in favor of vasoconstriction occurs, with greater chances of coronary spasm (which would explain what happened to our last two patients). As expected, the risk is greater when non-selective drugs –such as propranolol– are used. Finally, another mechanism to be considered is that HR reduction per se allows for better visual assessment of myocardial contractility and detection of disorders

that could have gone unnoticed in the previous stages of greater tachycardia. It is clear that one or various mechanisms may occur in the same patient. (6)

From a practical viewpoint, a rapid bolus of beta-blocker is recommended during the recovery phase. Once frequency is reduced to less than 100 beats per minute, myocardial motion is analyzed again. Any new or worsened dissynergies are considered abnormal. Considering the pathophysiological mechanisms involved, beta-blockers should not be used in hypertensive patients during the study, since it could worsen the condition due to vasoconstriction; the use of selective β -1 drugs such as atenolol, metoprolol, or esmolol is recommended given the lower risk of vasospasm. In case of using beta-blockers to counteract significant ischemia, we recommend IV slow injection instead of bolus.

Finally, according to the published evidence and to our experience, we believe that the adequate use of IV beta-blockers after dobutamine infusion is useful to increase the diagnostic precision of the methods, resulting in better understanding of the pathophysiology of patient symptoms; we therefore recommend its routine use.

Conflicts of interest

None declared.

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**Ariel K. Saad, Sergio E. Veloso,
Gustavo F. Zambrana, Carlos S. Porley,
Jorge A. Lowenstein**

Cardiac Diagnostic Section, Investigaciones Médicas
E-mail: arielsaad@gmail.com

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Mini Off-Pump Coronary Artery Bypass Surgery Plus Medical Treatment: An Option for High Risk Coronary Patients

In high-risk patients with multiple vessel disease who are not candidates for conventional surgery with extracorporeal circulation or for percutaneous procedures as a single treatment, the alternative of left mammary artery to left internal descending artery bypass graft surgery without extracorporeal circulation offers advantages over medical treatment. (1) The MIDCAB operation (2) is effective to treat high risk patients with multiple vessel disease. Greater long-term follow-up is necessary to clarify the indications and validate the procedure for this type of patients. (3)

MINI OPCAB surgery (Xiphoid Approach) is a surgical technique in which the left internal mammary artery is bypassed to the anterior descending artery (ADA) by a medial inferior sternotomy approach in the 3rd or 4th intercostal space, leaving intact the sternal manubrium (Figures 1 & 2). Long-term results have already been published, reaching 82% survival at 12 years (Kaplan-Meier). (4) This presentation describes the experience with this surgical technique in our institution.

Fourteen high risk patients with multiple vessel coronary artery disease with mean age of 71.07 years (± 9.051 , 95% CI), 21% women and mean preoperative Logistic EuroSCORE of 10.68 (± 5.407 , 95% CI), were operated-on in the last 7 years and followed up in our institution with strict medical treatment and control of risk factors.

Operative mortality in this series was 0%, the incidence of perioperative infarction was 0%, the average duration of surgery was 2 hours and 20 minutes; 10 (71%) patients were extubated in the operating room and average hospital stay was 2 days and 11 hours. Following the intervention, one patient received a stent in the right coronary artery and another in the circumflex artery for presenting large arteries with severe lesions. In this group of patients, major adverse cardiovascular events were 0% at 80 months. Survival rate was 82% at 7 years (Kaplan-Meier); an 85-year-old woman died 5 years after surgery due to stroke.

The combination of a MINI-OPCAB surgery for bypass of the left internal mammary artery to the left anterior descending artery (5, 6) together with an adequate medical treatment and a hybrid treatment when the right coronary artery or circumflex artery are of high caliber, is a viable option for elderly and high-risk patients. More experience is needed to confirm these initial results.

Conflicts of interest

None declared.

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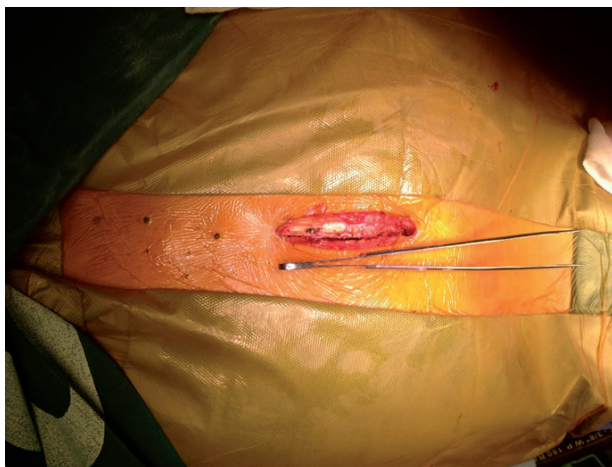


Fig. 1. Medial inferior sternotomy.

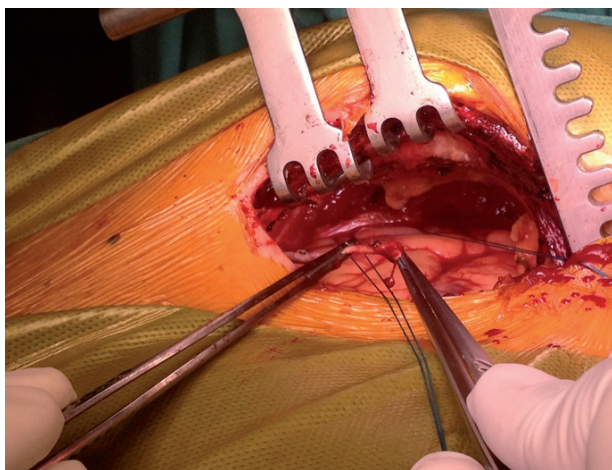


Fig. 2. Left internal mammary artery and anterior descending coronary artery exposed through mini-sternotomy.

Federico Benetti, Natalia Scialacomo,
José Luis Ameriso

Fundación Benetti, Department of Cardiac Surgery
Alem 1846, Rosario, Argentina

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Post-Infarction Lipomatous Metaplasia and Ventricular Arrhythmia

We report the case of a 58-year-old man with the following cardiovascular risk factors: hypertension, dyslipidemia, type 1 diabetes, ex-smoker, and history of myocardial infarction in 2003. Since then, the patient had given up treatment and had undergone few medical controls. The patient was admitted to the Emergency Department (ED) of our clinic for two syncope episodes preceded by trepidation. At the ED, the patient had cardiopulmonary arrest with ventricular fibrillation. Cardiopulmonary resuscitation (CPR) and defibrillation with 300 J was performed, recovering pulse and consciousness. The ECG showed sinus rhythm, left anterior hemiblock, and septal sequelae, without dynamic changes in repolarization.

A Doppler echocardiography revealed mild left ventricular enlargement (LVDD: 62 mm) with severe impairment of systolic function (LVEF: 30%), secondary to anterior akinesia and anterior and septal apical aneurysm, grade-II diastolic dysfunction, mild to moderate left atrial enlargement and no significant valve diseases. During hospitalization, a new coronary angiography (CAG) showed a patent stent in the mid segment of the ADA with mild, diffuse restenosis and good distal bed.

An implantable cardioverter defibrillator (ICD) was used as secondary prevention of sudden death. A cardiac magnetic resonance imaging scan with gadolinium (Magnetom Essenza, Siemens; Erlangen, Germany) was previously performed (See videos 1 and 2) showing severe systolic function impairment (LVEF: 31%), secondary to transmural anteromedial, septal-apical, anterior apical, mid-septal and cardiac apex infarction. It also showed a linear image in the akinetic segments, hyperintense in T1-weighted sequences (Figure 1), and hypointense in those acquired with fat suppressed sequences (Figure 2), consistent with adipose tissue. The cine-sequences showed the so-called india ink artifact (See videos 1 and 2), consistent with adipose tissue and water in that region. (1) These findings were consistent with lipomatous metaplasia.

Adipose metaplasia was first described in 1997 by Baroldi et al. in excised hearts, and it is a common histopathological finding in myocardial scarring tissue observed in ischemic, heart valve and dilated cardiomyopathies (68%, 37% and 26%, respectively). (2) However, in recent years it has also been identified in vivo as a result of the development of new diagnostic

imaging techniques such as computed tomography and, particularly, cardiac magnetic resonance imaging, which can differentiate tissues (myocardium, fat, fibrosis) in the infarcted site. The etiology of lipomatous metaplasia is unknown and its presence is associated with greater infarct age and larger transmural extent. (1) Recent studies have associated lipomatous metaplasia with ventricular arrhythmia and death. (3, 4)

Pharmacological treatment was adjusted and ICD was implanted prior to hospital discharge. The patient has been asymptomatic on the 6-month control and has not presented with further episodes of ventricular arrhythmia.

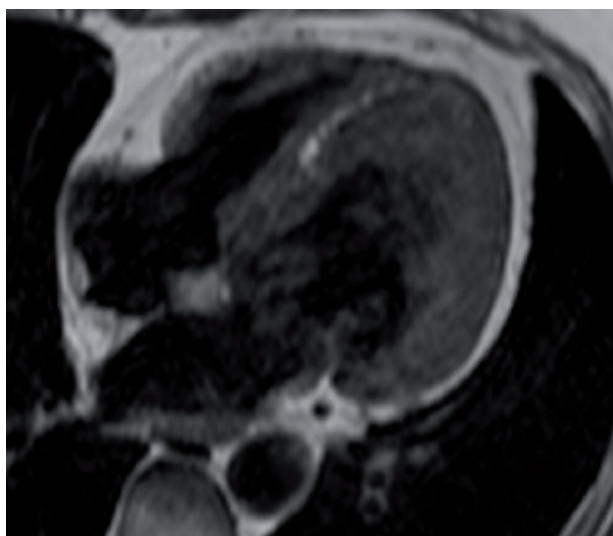


Fig. 1. Cardiac magnetic resonance imaging, T1-weighted sequences. See explanation in the text.

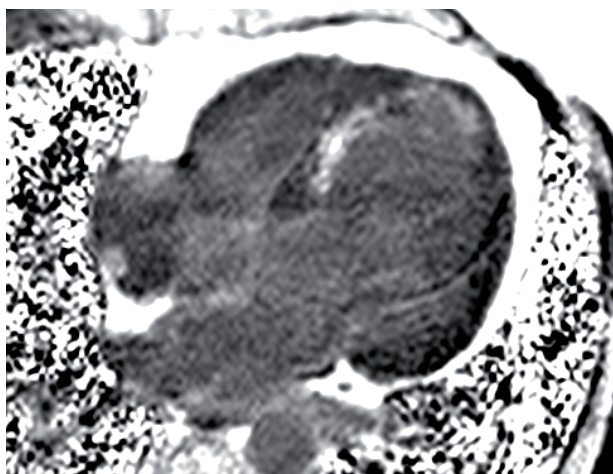


Fig. 2. Cardiac magnetic resonance imaging. Image obtained with fat suppression. See explanation in the text.

See videos 1 and 2 on the website

Conflicts of interest

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Federico Landeta, Marcelo Rodríguez

Clínica 25 de Mayo. Mar del Plata, Provincia de Buenos Aires
Clínica Colón. Mar del Plata, Provincia de Buenos Aires
Instituto Radiológico Mar Del Plata. Mar del Plata,
Provincia de Buenos Aires
e-mail: flandeta01@gmail.com

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