	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
Nº of pills/day, mean	3.8	3.6	0.421
Nº 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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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.

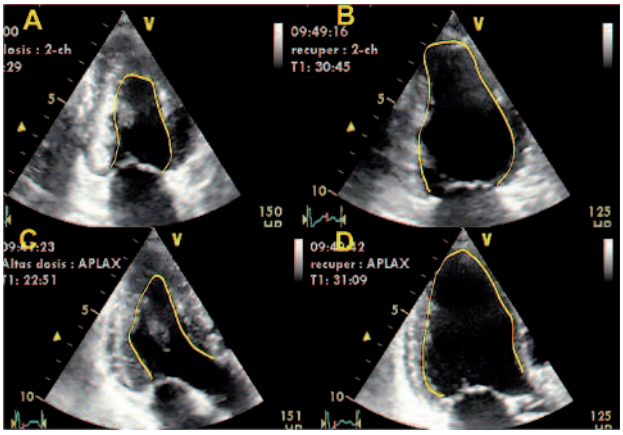

Fig. 1. Images during ventricular systole in two-chamber view (**A** and **B**) and apical long axis view (**C** and **D**). The first column occurs in the maximum dose phase, and the second column occurs after atenolol administration. Akinesia involving the anterior wall and anterior septum is observed.

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 nonselective 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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