

# Hypoperfusion of the Left Ventricle in the Absence of Changes in Segmental Contractility as Observed through Echocardiography by Using Microbubbles During Dobutamine Infusion

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Male patient with chest pain and dislipidemia, an ex-smoker with a family history of coronary artery disease (CAD), whose electrocardiogram and ergometric test were both negative for CAD. Due to persistent symptoms, he was submitted to a dobutamine-atropine stress echocardiogram with contrast agent for study of myocardial perfusion, which showed a hyperdynamic response of the left ventricle at peak stress, but clear perfusion defects of the anterior, lateral and apical walls. Cineangiography revealed multivessel coronary lesions.

Echocardiography with the use of microbubbles is a recent diagnostic advance in cardiology that allows better evaluation of left ventricular function (ventriculography with microbubbles) and myocardial perfusion, since the microbubbles reach coronary microcirculation. One of the most important potential applications of this method is the investigation of coronary artery disease (CAD) through echocardiographic studies based on induction of ischemia. Temporary changes in the segmental contractility of the left ventricle (LV) are signs of myocardial ischemia easily detected by echocardiography. Dobutamine stress echocardiography is one of the most frequently used methods in medical practice and has shown good accuracy for the diagnosis of significant coronary obstructions<sup>1</sup>. The association of contrast echocardiography with microbubbles allows evaluation of contractility and perfusion in a single test in real time, in an only slightly invasive manner.

The form of contrast echocardiography used in this case consisted of a stable solution containing microbubbles from 3 to 5  $\mu$  in size, which are able to pass through the pulmonary capillary barrier and reach the left ventricular cavity. However, due to the elevated number of high energy ultrasound pulses, the microbubbles burst rapidly, making it difficult to evaluate myocardial perfusion in real

time. With the recent development of intermittent harmonic imaging, it is possible to emit an ultrasound pulse every 1, 3, 5, 7 or more heartbeats, greatly decreasing the destruction of microbubbles and thus allowing evaluation of perfusion<sup>2-4</sup>.

## Case Report

This is the report of a 46-year-old businessman with a 3-month history of short term precordial burning at rest and occasionally at moderate exertion, without irradiation, and no other accompanying symptoms. He had a history of dislipidemia, had stopped smoking seven years prior, and had a brother who had died of acute myocardial infarct one month before the exam.

He had a normal physical examination; his total serum cholesterol level was 295mg/dl, with an LDL of 198mg/dl, HDL of 38mg/dl and triglycerides of 293mg/dl. His resting electrocardiogram showed an upper left anterior divisional block (fig. 1). Left ventricular function was normal at rest, and his treadmill test was negative for myocardial ischemia.

Due to the persistence of his symptoms, the patient underwent a dobutamine-atropine stress echocardiogram associated with the use of PESDA (*perfluorocarbon-exposed sonicated dextrose and albumin*) contrast echocardiography, after having signed an informed consent. This examination is included in a multi-center trial approved by UNIFESP's commission on medical ethics in research and CONEP (the National Ethics and Research Commission).

The PESDA contrast agent was continuously administered intravenously with an infusion pump at rest and at peak dobutamine infusion, at which point, real-time and intermittent harmonic images were obtained in five different acoustic windows<sup>3</sup>. Complete left ventricular filling was obtained with a dose of 4ml/min (0.05ml PESDA/kg diluted in 90ml of 0.9% saline solution) during continuous infusion of the contrast agent.

Total doses of 40 $\mu$ g/kg/min of dobutamine and 0.5mg of atropine were infused, and a peak heart rate of 150bpm

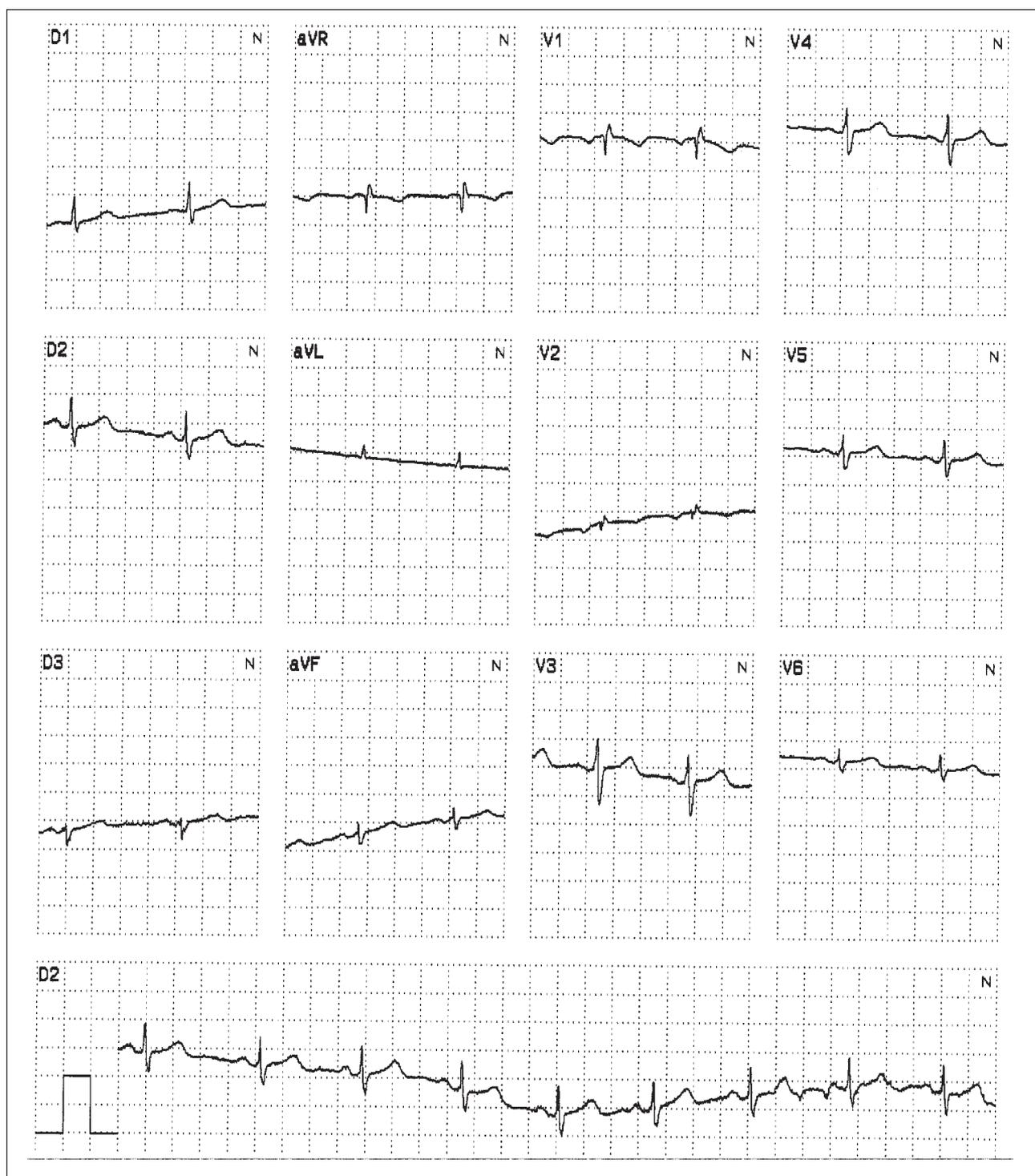


Fig. 1 – Twelve-lead electrocardiogram at rest showing an upper left anterior divisional block

(85% of maximum predicted cardiac frequency) was attained without significant symptoms or side effects. There were no electrocardiographic changes during the examination (fig. 2).

Blood pressure, heart rate, oxygen saturation, respiratory frequency and symptoms were recorded at rest and on a continuous basis during dobutamine and contrast infusion, up to 30 minutes after termination of the exam.

Myocardial contractility was analyzed as normal at peak infusion, and signs of hypoperfusion were observed in the lateral, anterior and apical walls without pericardial pain, electrocardiographic changes or new wall motion abnormality (fig. 3). Cineangiography showed total occlusion of the anterior descending artery, a severe lesion in the 1<sup>st</sup> marginal branch of the circumflex artery and subocclusion of the right coronary artery (fig. 4).

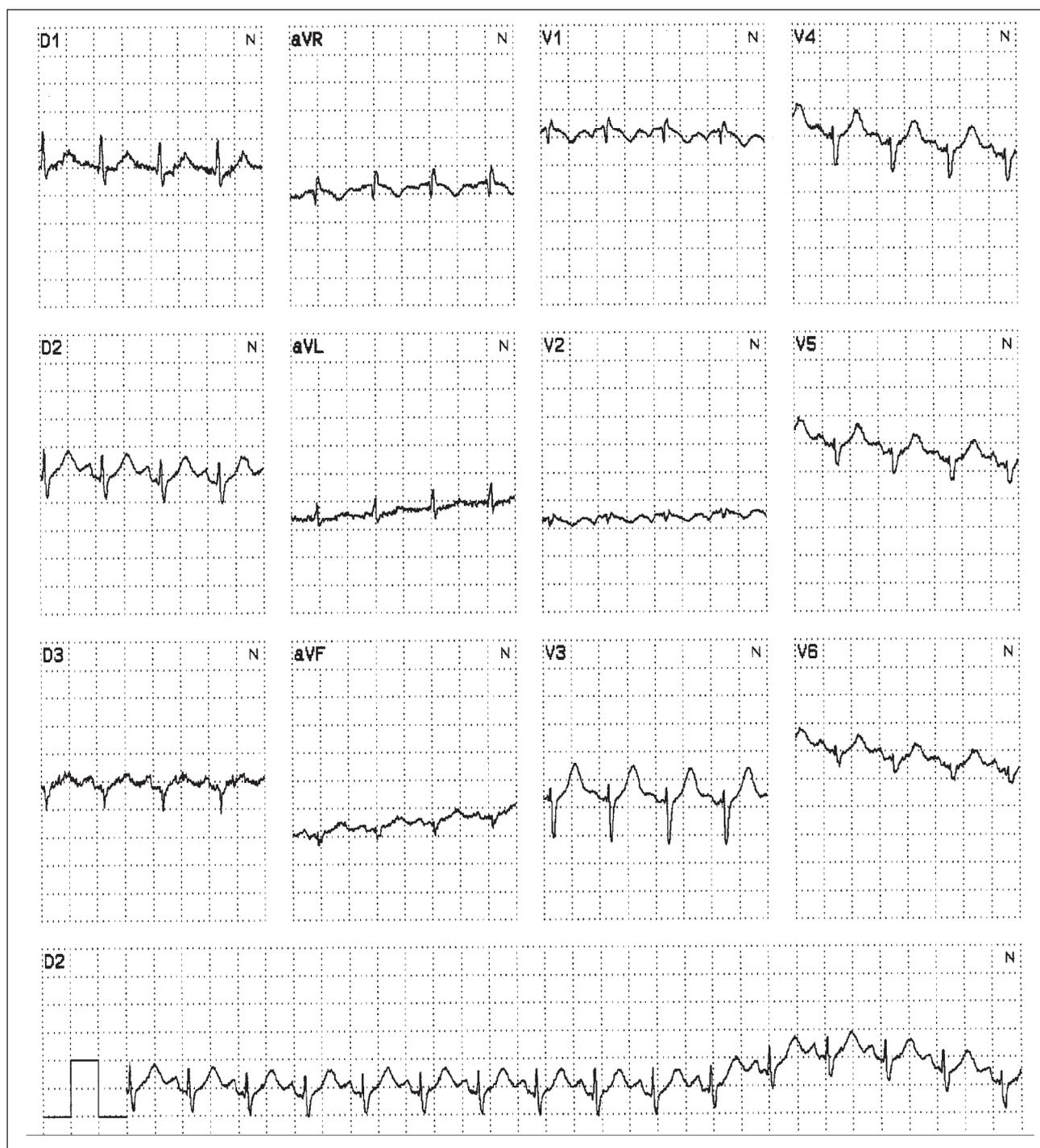


Fig. 2 – Twelve-lead electrocardiogram at peak dobutamine infusion.

## Discussion

Echocardiography with ultrasound contrast has only recently been introduced in clinical practice and is a non-invasive, relatively simple, apparently safe and low cost method for analysis of myocardial perfusion.

Continuous infusion of an echocardiographic contrast agent improves the delineation of endocardial borders and can radically improve the quality of images obtained

during an examination, making it possible to visualize segments of the LV that cannot be seen without the use of contrast, thus improving the evaluation of regional contractility and optimizing diagnostic accuracy<sup>5</sup>. Of all the methods currently in use, none adequately provides for evaluation of myocardial perfusion in real time. The association of microbubbles with echocardiography allows for significant improvement of the signals coming from the LV walls, which are characterized by an increase in the brightness of the

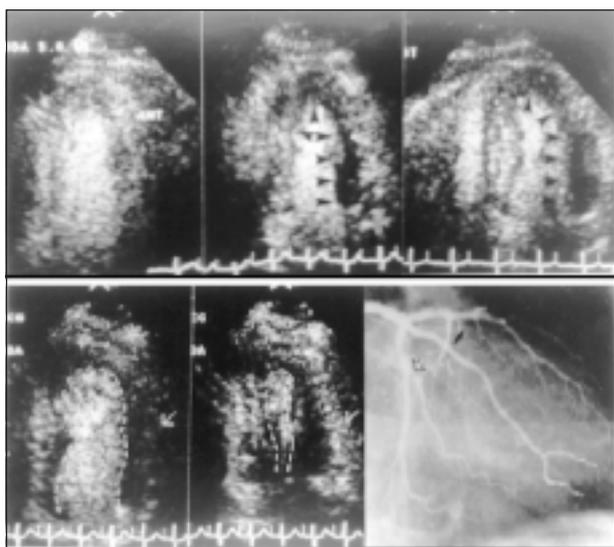


Fig. 3 – In the upper quadrants, from left to right, the two-chamber apical view at rest with normal perfusion (ecodense walls – signal emitted by microbubbles in circulation) and at peak dobutamine infusion during hyperdynamic movement of the left ventricular walls, showing the anterior-apical and lateral areas of hypoperfusion (dark arrows). Note the hyperdynamic response of the anterior wall in the two lower quadrants (white arrows). The lower right quadrant shows right anterior oblique angiography of the left coronary artery with total occlusion (wide arrow) of the anterior descending artery and subocclusion of the 1<sup>st</sup> marginal branch of the circumflex coronary artery (arrow).

myocardium. Perfusion defects can be identified by a lack of increase in the brightness, which is subjectively analyzed by an experienced observer. The study of myocardial perfusion with microbubbles through use of intermittent harmonic imaging during dobutamine stress echocardiograms appears to improve detection of CAD<sup>4</sup>. Intermittent imaging permits better evaluation of myocardial perfusion since it allows for decreased destruction of microbubbles due to the lower number of ultrasound pulses directed at tissues. A number of echocardiographic contrast agents for intravenous use are in the clinical experimental stages. The contrast agent used in this study was PESDA, which is made from decafluorobutane, an inert gas that has been used for many years in ophthalmologic surgery.

Several issues related to the above case are worthy of mention. The changes in myocardial perfusion are apparently not explained by the absence of changes in contractility. We can speculate that at peak infusion, the absence of contractility in the subendocardial region was masked by the hypercontractility of the subepicardial regions. Another possible but less plausible explanation resides in the difference between the time sequence of changes caused by myocardial ischemia, in that alterations in perfusion would occur earlier than alterations in contractility (ischemic cascade). It is therefore possible that in the present case there was not enough time for the changes in contractility to be observed. However, since time differences between changes in perfusion and contraction amount only to a matter of seconds, it is not very likely that this explains what was observed. There is also the possibility that the observed perfusion defect was a weak ultrasound signal, which is common in the lateral, ante-

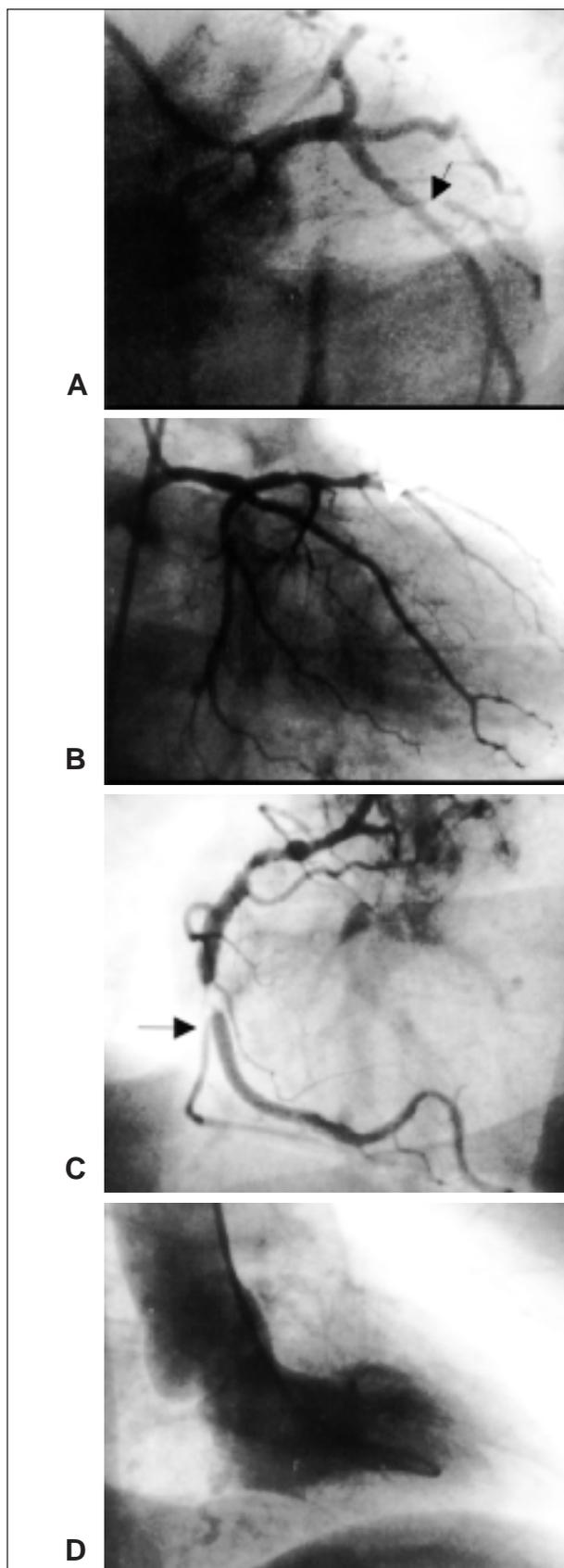


Fig. 4 – Cineangiography – A) Spider of the left coronary artery with a severe lesion (arrow) at the 1<sup>st</sup> marginal branch; B) right anterior oblique view of the left coronary artery with total occlusion (arrow) of the anterior descending artery; C) left anterior oblique view with a severe lesion (arrow) at the third median of the right coronary artery; D) left ventriculography showing normal contractile function.

rior and apical walls. Yet the brightness in these regions was normal at rest and only worsened at peak infusion (fig. 3). It should be noted that the exam, as currently performed, requires adequate training since it is operator-dependent. There is also a need for development of techniques that make it possible to quantify regional coronary flow. Work on such techniques is already in the experimental stage with animals<sup>6</sup>.

We conclude that echocardiography with the use of microbubble contrast agents shows great potential for use during pharmacological stress echocardiography. Not only can it increase diagnostic accuracy, but it can also improve evaluation of the extent and severity of coronary disease in that it better detects endocardial borders and makes it possible to evaluate myocardial perfusion.

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