

Evaluation of the left anterior descending coronary artery flow velocity by transthoracic echo-Doppler without contrast enhancement

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Key words:
Coronary
microcirculation;
Echocardiography.

Background. The evaluation of the coronary flow velocity and coronary flow reserve (CFR) can provide important information on the functional significance of stenoses and of abnormalities of the coronary microcirculation. To date, the potential of echo-Doppler in the noninvasive evaluation of the coronary flow has been mainly reported for small groups of patients with stenoses of the left anterior descending coronary artery (LAD), eventually treated with percutaneous coronary angioplasty. The great majority of publications report the use of echo-Doppler together with contrast enhancement for an optimal visualization of the LAD. The aim of our study was to evaluate the feasibility of echo-Doppler examination of the LAD with a high-frequency probe and without the use of contrast enhancement.

Methods. We studied, in basal conditions, a group of 116 consecutive patients with a wide range of cardiovascular diseases. CFR was evaluated during infusion of adenosine in a subgroup of patients with a recent coronary artery bypass graft and left ventricular dysfunction (ejection fraction < 40%).

Results. The LAD was visualized in 105 out of 116 patients (90%), with no difference between the various cardiac pathologies. The mean diameter of the LAD was 1.8 ± 0.4 mm. The peak systolic flow velocity was 16.3 ± 6 cm/s and the peak diastolic flow velocity 28.5 ± 10 cm/s. The mean CFR was 1.9 ± 0.8 .

Conclusions. The coronary flow of the LAD can be evaluated at transthoracic Doppler echocardiography without contrast enhancement in a wide range of cardiac pathologies. The noninvasive evaluation of the CFR with transthoracic echo-Doppler should be borne in mind during the clinical and instrumental work-up of cardiac patients.

(Ital Heart J 2002; 3 (9): 520-524)

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Received August 21,
2002; accepted August
30, 2002.

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Introduction

The evaluation of the coronary flow velocity (CFV) and coronary flow reserve (CFR) can provide useful information on the functional significance of stenoses¹ and of abnormalities of the coronary microcirculation. To date, the potential of echo-Doppler in the noninvasive evaluation of the coronary flow has been mainly reported for small groups of patients with stenoses of the left anterior descending coronary artery (LAD), eventually treated with percutaneous coronary angioplasty (PTCA), and the great majority of publications report the use of echo-Doppler together with contrast enhancement for an optimal visualization of the LAD^{2,3}.

The aim of our study was to evaluate the feasibility of echo-Doppler examination of the LAD with a high-frequency probe and without the use of contrast enhancement in basal conditions in a group of patients with a wide range of cardiovascular diseases.

Moreover, the adenosine test was performed in a subgroup of patients with recent coronary artery bypass graft (CABG) and left ventricular dysfunction (ejection fraction < 40%) in order to calculate the CFR.

Methods

Study group. One hundred and sixteen consecutive patients, referred to our laboratory for echocardiographic screening before commencing cardiac rehabilitation, underwent echo color Doppler examination of the LAD, with no exclusion criteria except for atrial fibrillation or clinical instability. Seventy one patients had recently undergone CABG, 15 aortic valve replacement, 10 had a history of recent myocardial infarction, 5 had chronic ischemic heart disease, 10 had dilated cardiomyopathy of nonischemic origin, and 5 had recently undergone cardiac transplantation; 92 of them

were males; the mean age was 68 ± 12 years. Pharmacological therapy was suspended on the day of the examination.

To evaluate the potential of this noninvasive and noncontrast approach in the assessment of the CFR, a subgroup of 16 patients with recent CABG at least of the LAD underwent the adenosine test. The exclusion criteria were a history, electrocardiographic or echocardiographic evidence of myocardial infarction of the anterior wall, severe stenoses of the carotid arteries, hypotension (systolic blood pressure < 100 mmHg), clinical instability, severe or moderate anemia (hemoglobin ≤ 10 mg/dl), a history of moderate to severe obstructive lung disease, sick sinus syndrome and clinically relevant pleural or pericardial effusion.

Transthoracic echocardiography and color Doppler.

The LAD flow was identified as suggested by previous reports¹. The basal echocardiographic examination was performed with a Sonos 5500 ultrasound unit (Philips, Andover, MA, USA), using a broadband transducer (S3). The left ventricle was adequately visualized in all subjects. Once a 2-chamber view was obtained, the S12 probe was superimposed over the same point on the thoracic surface, and a modified foreshortened 2-chamber view was obtained by sliding the transducer superiorly and medially. The epicardial segment of the anterior wall was focalized to find and best visualize the color-coded blood flow in the anterior groove area. In case of scarce visualization from the apical view, a short-axis view of the left ventricular apex and of the anterior groove was obtained, trying to visualize the coronary flow with color Doppler.

Once a good color-coded flow image was obtained, pulsed wave Doppler was attempted using a gate size set at 4.0 mm. Attention was paid to maintain the angle between the color flow and the Doppler beam below 20° ; we never needed to correct the angle using the software package.

We observed a learning curve of about 1 month (with not less than three examinations of the LAD per day); no difference between the two operators was seen, either in terms of the learning time and ability to visualize the LAD or in the quality of echo-Doppler recordings.

Echocardiographic measurements. Color and pulsed wave Doppler signals were classified as visualized or not visualized. The feasibility of coronary imaging and of Doppler recordings was evaluated by consensus of two cardiologists, skilled in cardiac ultrasound examination.

All 116 examinations were recorded on optical disks and then read off-line by two independent observers who were unaware of the results of coronary angiography. Color Doppler recordings of the LAD were reviewed and the coronary diameter was measured. Then, in order to calculate the CFR, the Doppler

recordings were analyzed, both in basal conditions and during adenosine infusion in the subgroup of 16 patients. The CFR was calculated as the ratio between the peak diastolic flow velocities during hyperemia and in basal conditions.

Adenosine test. Sixteen consecutive patients with an ejection fraction $< 40\%$, who had undergone CABG within the previous 10 days, were evaluated by means of myocardial perfusion scintigraphy in basal conditions and during infusion of adenosine. Before starting the infusion the distal LAD was visualized as described above, and then pulsed wave Doppler was recorded in basal conditions and throughout the adenosine infusion time (Fig. 1). Adenosine (Adenoscan, Sanofi-Synthelabo, Milan, Italy) was infused via the antecubital vein, at a rate of 0.14 mg/min/kg for 5 min. All patients had continuous heart rate and electrocardiographic monitoring; the blood pressure was recorded at baseline, at 3 and 5 min during adenosine infusion, and at the end of the study (recovery). The maximal increase in the coronary flow was observed within 60 s of drug infusion, whereas the flow returned to baseline within 30 s of drug discontinuation. There were no major adverse reactions, and the test was well tolerated in all cases; we observed, in the great majority of patients, a very modest hyperventilation that in all cases rapidly resolved at the end of the infusion. No electrical disorders or arrhythmias were detected, nor were any anginal symptoms induced.

Statistical analysis. Data are expressed as mean values \pm SD. To evaluate the intra and interobserver variability, two independent and blinded observers (F.S. and E.E.) analyzed 20 randomly selected Doppler recordings, and one of them (F.S.) repeated the same measurements on the same recordings 15 days apart. The intra and interobserver variability was calculated as the SD of the differences between the two measurements, expressed as a percentage of the average value.

Results

The LAD was visualized in 105 out of 116 patients (90%), with no difference between the various pathologies. In 41 of them the LAD was well visualized from the 2-chamber apical view, whereas in the remaining 64 patients a good visualization of the LAD was only possible from a modified short-axis parasternal view. The LAD was not visualized in 11 patients: 3 patients had a hypoplastic LAD, 1 had complete LAD occlusion, and in the remaining 7 patients poor echocardiographic and Doppler signals were obtained. For these reasons, we decided to consider the LAD as "not visualized".

Basal visualization and examination of the LAD lasted no more than 10 min; both operators were involved in performing the adenosine test, and the global

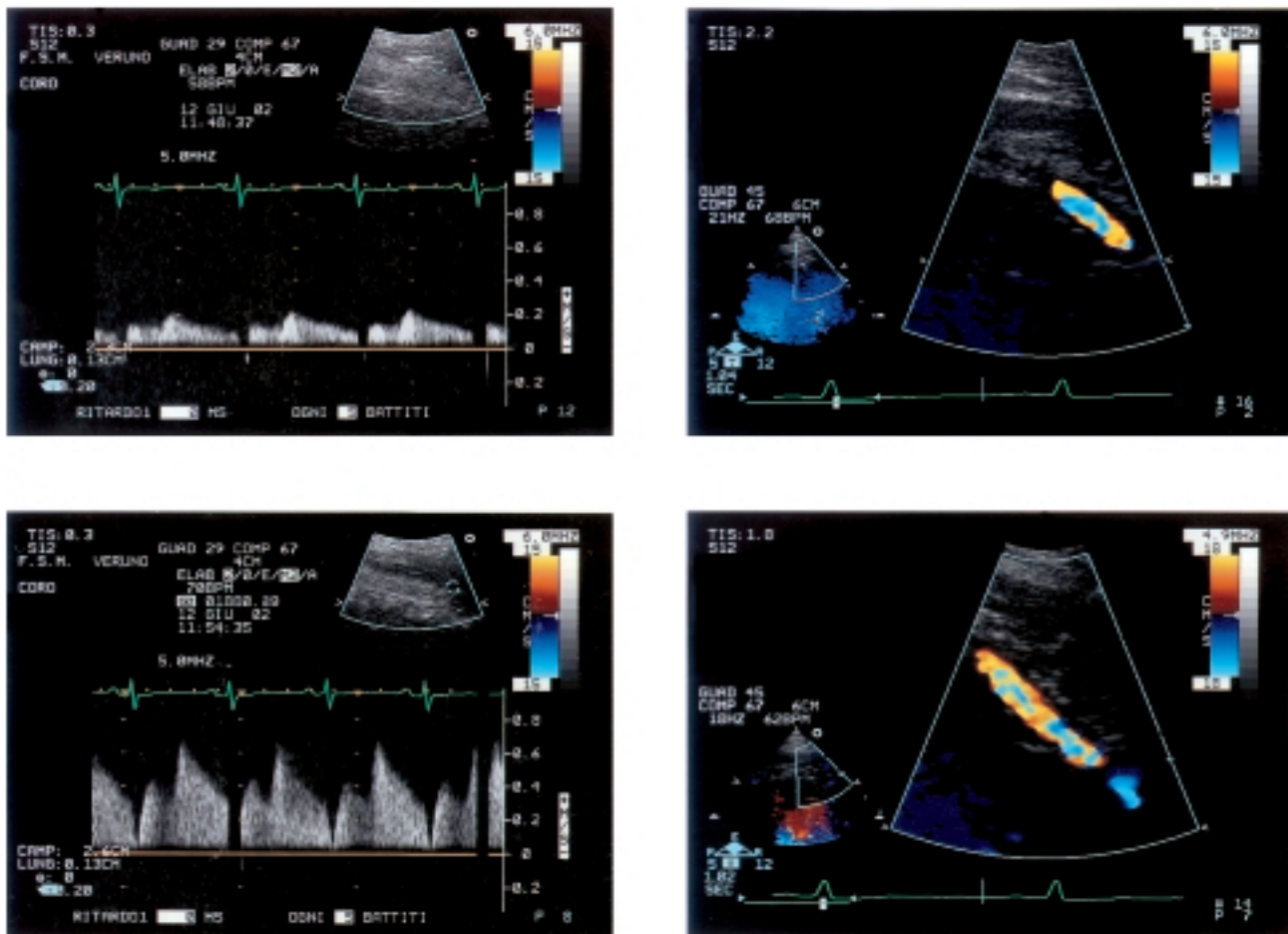


Figure 1. Pulsed wave Doppler flow recording and color flow visualization of the left anterior descending coronary artery in basal conditions (top) and during adenosine infusion (bottom); coronary flow reserve = 3.

examination time (basal + test) was 30 ± 4 min. A slightly longer time was needed to perform the test in patients in whom adequate visualization of the LAD was more problematic, mainly due to high thoracic impedance or to an “unusual” displacement of the LAD (36 ± 4 vs 25 ± 8 min, $p = \text{NS}$). The maximal increase in CFV was observed within 60 s of drug infusion, and the flow returned to baseline within 30 s of drug discontinuation.

The mean diameter of the LAD was 1.8 ± 0.4 mm, with an intra and interobserver variability respectively of 1.9 and 2.1%; the peak systolic flow velocity was 16.3 ± 6 cm/s, the peak diastolic flow velocity was 28.5 ± 10 cm/s (with an intra and interobserver variability respectively of 1.7 and 1.8%, $p = \text{NS}$, 1.9 and 1.8%, $p = \text{NS}$). In spite of moderate tachycardia and tachypnea, the visualization of the LAD and the coronary flow monitoring by pulsed wave Doppler during adenosine infusion were as good as in basal conditions. The mean CFR was 1.9 ± 0.8 . No difference was detected in terms of blood pressure, whereas a mild but significant increase in heart rate was observed during adenosine infusion (from 71 ± 7 to 90 ± 5 b/min, $p = 0.03$).

Discussion

Evaluation of the CFV and of the CFR can provide important information on the functional significance of stenoses and of abnormalities of the coronary microcirculation. In past years, sensor-tipped angioplasty Doppler guide wires were commonly used to measure the CFR in large epicardial vessels; unfortunately, this method is invasive and highly expensive and it is only applicable in the cardiac catheterization laboratory. Alternatively, the CFR can be evaluated by means of transesophageal Doppler echocardiography which however is, in any case, a semi-invasive approach, or with positron emission tomography, which is expensive and not commonly available. Maybe one of the next applications of magnetic resonance imaging could be the measurement of CFR⁴, but studies elaborated with the aim of clearly demonstrating the feasibility of a wide application of this method are still underway. In any case, MRI is more expensive than echo-Doppler.

Contrast enhanced echo-Doppler evaluation of the left anterior descending coronary artery. A few years ago, the introduction of a second harmonic echo-

Doppler modality combined with contrast enhancement resulted in new possibilities for the visualization of the LAD and enabled transthoracic echo measurements of the coronary flow to be made with a high success rate¹. To date, the potential of echo-Doppler in the noninvasive evaluation of the coronary flow has been reported for small groups of patients with coronary artery disease, generally with stenoses of the LAD recently treated with PTCA. The great majority of publications report the use of echo-Doppler together with contrast enhancement for an optimal visualization of the LAD. The clinical utilization of echo-Doppler evaluation of the coronary flow of the LAD consists mainly in the quantification of the CFR, evaluating the diastolic and systolic flows in basal conditions and during vasodilation with adenosine or dipyridamole infusion. A good specificity and sensitivity in the detection of significant LAD stenoses has been demonstrated, together with a close agreement with the CFR as determined at intracoronary flow wire recordings¹. The CFR, as measured by transthoracic echocardiography, has an excellent correlation also with that measured at positron emission tomography³. More recently, Takeuchi et al.⁵ demonstrated the feasibility of measuring the CFV by means of contrast enhanced transthoracic Doppler echocardiography during dobutamine infusion. This, in order to detect stress-induced ischemia in the LAD territory. Stoddard et al.⁶, using transesophageal Doppler echocardiography, had reported similar data a few years before.

Though this method is absolutely noninvasive and reproducible, the use of contrast media may constitute a limitation to the wide application of the transthoracic evaluation of the coronary flow, mainly due to the high costs and to some technical problems (e.g. the need to administer contrast medium by continuous infusion in a peripheral vein with at least 18G catheters; the setting of the machine).

The new chance of ultrasound technology. More recently, the possibility of measuring the coronary flow in the distal LAD at transthoracic Doppler echocardiography without a contrast agent has been reported for a population of 70 patients with coronary artery disease, recently treated with PTCA of the LAD. All these patients underwent the stress test (adenosine infusion) to evaluate the CFR with a noncontrast approach that proved to be feasible and cheaper than the methods previously proposed². Our study brings new data confirming the possibility of visualizing the LAD and of measuring the coronary flow at transthoracic Doppler echocardiography without contrast enhancement in a larger population. The learning curve is relatively short, and the intra and interobserver variability is minimal. A limitation of our works derives from the decision not to evaluate the CFV and CFR with contrast enhancement, neither in patients in whom the LAD was easily visible nor in patients in whom we were not able to determine the LAD flow at conventional color flow mapping. In

1999 Caiati et al.⁷ reported a success rate of 96% in the optimal detection of flow with the contrast enhancement approach, while we found a 90% success rate without contrast enhancement. As stated by Caiati et al., we considered the visualization of the LAD of sufficient quality when we measured a diameter ≥ 1 mm; in all these cases we were able to obtain a good pulsed wave Doppler flow recording both in basal conditions and during adenosine infusion. Moreover, the visualization of the LAD and consequently the coronary flow recording were improved by the infusion of adenosine, in spite of tachycardia and tachypnea induced by the drug. All these findings lead us to believe that contrast enhancement only slightly improves the identification of the LAD and the evaluation of the CFR with respect to basal echo-Doppler performed with a high-frequency and broad band transducer. The present article reports, for the first time, that high-resolution echo-Doppler of the LAD is feasible even in a totally unselected population. A high thoracic impedance, tachycardia, obesity, tachypnea, or recent cardiac coronary or valvular surgery did not constitute a limitation to the study.

In our series, patients with a recent CABG and left ventricular dysfunction who underwent the adenosine test showed a wide range of values of CFR. Some new studies, elaborated with the aim of defining the meaning of the baseline differences and over time variations in the CFR in this population, are underway. In any case, we are convinced that in terms of the feasibility from a technical point of view, our data can be easily extrapolated to a wider population. With regard to the safety of the test, no minor or major complication or side effect was reported: the adenosine test is a good test in terms of tolerability, even though literature data regarding patients recently submitted to cardiac transplantation are scarce.

Future applications. To date, only a few studies have evaluated the coronary microcirculation in hypertrophic cardiomyopathy, and they were performed in a strictly speculative setting. The clinical applications of the evaluation of the CFR have mainly been restricted to the follow-up of PTCA of the LAD with or without stent implantation²; we hypothesized that echo-Doppler examination of the LAD should not be limited to the post-procedural stratification of PTCA, but could be successfully used to investigate and speculate on the significance of the CFR in a wider range of cardiac diseases. Perhaps new information on the mechanisms of left ventricular remodeling in ischemic and idiopathic dilated cardiomyopathy may be derived from the study of the CFR. Even the management of patients with heart transplantation (host rejection, early recognition and prognostic stratification of coronary disease) could be influenced by the evaluation and monitoring of the CFR over time.

The CFR is impaired in young men with familial hypercholesterolemia⁸, while at present little is known

about the influence of hormones on the coronary vascular reactivity, endothelial dysfunction and CFR⁹. Finally, the challenge of a completely noninvasive functional and anatomic evaluation of the coronary circulation seems not to be so far, as even the imaging of the posterior descending coronary artery has been recently reported¹⁰.

In conclusion, we have demonstrated that the LAD flow can be easily evaluated by means of transthoracic Doppler echocardiography without contrast enhancement in patients with different cardiac pathologies. The success rate is high and similar to that reported for contrast enhancement. To date, this technique proved to be useful for the assessment of the indication to PTCA of the LAD, or to evaluate the results of PTCA of the LAD over time. Our data demonstrate that echo-Doppler evaluation of the CFR is feasible and reliable in different cardiac diseases; the evaluation of the CFR could contribute to a further understanding and perhaps a better management of various cardiac pathologies, namely chronic heart failure of ischemic and nonischemic etiology, and to a more accurate monitoring of transplanted hearts.

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