INTRODUCTION: THE CORONARY FLOW RESERVE

The coronary flow reserve (CFR) represents an important functional parameter to assess epicardial coronary stenosis and to evaluate the integrity of coronary microcirculation (Kern, 2000; Sadamatsu, Tashiro, Maehira, & Yamamoto, 2000). CFR can be measured, during adenosine or dipyridamole infusion, as the ratio of maximal (pharmacologically stimulated) to baseline (resting) diastolic coronary blood flow peak. Even in absence of stenosis in epicardial coronary artery, the CFR may be decreased when coronary microvascular circulation is compromised by arterial hypertension with or without left ventricular hypertrophy, diabetes mellitus, hypercholesterolemia, syndrome X, hypertrophic cardiomyopathy, and connective tissue diseases (Dimitrow, 2003; Strauer, Motz, Vogt, & Schwartzkopff, 1997). Several methods have been established for measuring CFR: invasive (intracoronary Doppler flow wire) (Caiati, Montaldo, Zedda, Bina, & Iliceto, 1999b; Lethen, Tries, Brechtken, Kersting, & Lambertz, 2003a; Lethen, Tries, Kersting, & Lambertz, 2003b), semi-invasive and scarcely feasible (transesophageal Doppler echocardiography) (Hirabayashi, Morita, Mizushige, Yamada, Ohmori, & Tanimoto, 1991; Iliceto, Marangelli, Memmola, & Rizzon, 1991; Lethen, Tries, Michel, & Lambertz, 2002; Redberg, Sobol, Chou, Malloy, Kumar, & Botvinick, 1995), or extremely expensive and scarcely available methods (PET, SPECT, MRI) (Caiati, Cioglia, Montaldo, Zedda, Rubini, & Pirisi, 1999a; Daimon, Watanabe, Yamagishi, Muro, Akioka, & Hirata, 2001; Koskenvuo, Saraste, Niemi, Knuuti, Sakuma, & Toikka, 2003; Laubenbacher, Rothley, Sitomer, Beanlands, Sawada, & Sutor, 1993; Picano, Parodi, Lattanzi, Sambuceti, Andrade, & Marzullo, 1994; Saraste, Koskenvuo, Knuuti, Toikka, Laine, & Niemi, 2001; Williams, Mullani, Jansen, & Anderson, 1994), thus their clinical use is limited (Dimitrow, 2003). In addition, PET and intracoronary Doppler flow wire involve radiation exposure, with inherent risk, environmental impact, and biohazard connected with use of ionizing testing (Picano, 2003a).

In the last decade, the development of new ultrasound equipments and probes has made possible the noninvasive evaluation of coronary blood velocity by Doppler echocardiography, using a transthoracic approach. In this way, the peak diastolic coronary flow velocity reserve (CFVR) can be estimated as the ratio of the maximal (pharmacologically stimulated) to baseline (resting) diastolic coronary blood flow velocity peak measured from the Doppler tracings. Several studies have shown that peak diastolic CFVR, computed in the distal portion of the left anterior descending (LAD) coronary artery, correlates with CFR obtained by more invasive techniques. This provided a reliable and non-
invasive tool for the diagnosis of LAD coronary artery disease (Caiati et al., 1999b; Caiati, Montaldo, Zedda, Montisci, Ruscario, & Lai, 1999c; Hozumi, Yoshida, Akasaka, Asami, Ogata, & Takagi, 1998; Koskenvuo et al., 2003; Saraste et al., 2001).

Moreover, this parameter has been shown to be able to detect coronary stenosis (> 90%) in the LAD coronary artery (Voci, Pizzuto, Mariano, Puddu, Chiavari, & Romeo, 2002) with high sensitivity and specificity (90% and 93%, respectively). In particular, a value of peak diastolic $\text{CFVR} < 1.9$ has been associated to severe coronary stenosis (Matsumura, Hozumi, Watanabe, Fujimoto, Sugioka, & Takemoto, 2003), while a peak diastolic $\text{CFVR} \geq 2.5$ is representative of normal coronary epicardial stream (Picano, 2003b).

BACKGROUND: TRANSTHORACIC DOPPLER ECHOCARDIOGRAPHY

Transthoracic Doppler echocardiography is usually performed using an ultrasound unit equipped with a broad-band, high-frequency (3.5 to 7 MHz) transducer, with the patients in the left lateral decubitus position. The conventional imaging approach consists first in obtaining a short axis of the left ventricular apex and anterior groove to search for middistal LAD coronary flow using the Color-Doppler flow modality. When a diastolic circular color-coded blood flow is visualized in the anterior groove area, the transducer is rotated clockwise to obtain the best long axis of color flow, as visualized in Figure 1. Alternatively, a modified foreshortened two-chamber view could be obtained by sliding the transducer superiorly and medially from an apical two-chamber position.

Then, a careful search for color-coded blood flow is made over the epicardial part of the anterior wall with simultaneous attempts to optimize the visualization of the anterior groove area by very slight counterclockwise rotation and medial angling of the probe.

To minimize artifacts due to systolic cardiac contraction, the sample volume is placed in correspondence to the diastolic position of the explored vessel cross-section, and maintained fixed for all the acquisition period. Pulsed-wave Doppler spectral tracings of LAD flow velocity is then recorded by fast Fourier transformation analysis (Caiati et al., 1999a).

Particular care has to be taken in maintaining the pulsed-wave Doppler aligned parallel to the blood flow. The achievement of this task can be confirmed by the fact that the spectral Doppler flow shows the characteristic biphasic flow pattern, with a larger diastolic component, and a smaller systolic one.

Once the image is optimized, multiple still-frame image acquisition is performed to obtain representative images of consecutive beats at baseline, digitally stored for off-line analysis. Then, the maximal stress condition is pharmacologically induced by injecting adenosine or dipyridamole. When dipyridamole is utilized (0.56 mg/kg i.v. in four minutes, and successively 0.28 mg/kg i.v. in two minutes, to induce vasodilation of the microcirculation), image acquisition is performed after two to four additional minutes from the drug subministration, depending on the patient response, with the same ultrasound settings of the baseline acquisition (Lim, Shim, Rhee, Kim, Hwang, & Kim,

Figure 1. Example of a diastolic frame acquired with the color-doppler flow modality activated

Figure 2. Example of the Pulsed-wave Doppler spectral tracings of flow velocity in the LAD coronary artery. The characteristic biphasic flow pattern can be observed.
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