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Semi-Automated Analysis of Coronary Flow Doppler Images: Validation with Manual Tracings

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***Abstract*—Coronary flow velocity reserve (CFVR) is conventionally obtained by manual tracings of Doppler profiles, as ratio of stress vs baseline diastolic peak velocity. When <1.9, this parameter evidences reduced coronary flow and possible microcirculatory disease. Our goals were: 1) to develop a novel technique for semi-automated detection of Doppler flow velocity profile, allowing the automated computation of CFVR and other parameters; 2) to validate this technique in comparison with conventional measurements obtained by manual tracing; 3) to test for differences between normal (N) subjects and patients with rheumatoid arthritis (RA). Linear correlation and Bland-Altman analyses showed that the proposed method was highly accurate and repeatable compared to the manual measurements. Comparison between N and RA groups evidenced significant differences in some of the automated parameters.**

I. Introduction

CORONARY flow velocity reserve (CFVR) represents an important functional parameter to assess epicardial coronary stenosis and to evaluate the integrity of coronary microcirculation [1], [2]. CFVR can be measured, during adenosine or dipyridamole infusion as the ratio of maximal (pharmacologically stimulated) to baseline (resting) diastolic coronary blood flow velocity peak. Even in absence of stenosis, the CFVR may be decreased when coronary microvascular circulation is compromised by arterial hypertension with or without left ventricular hypertrophy, diabetes mellitus, hypercholesterolemia, syndrome X, hypertrophyc cardiomyopathy and connective tissue disease. Several methods have been established for measuring CFVR: invasive (intracoronary Doppler flow wire), semi-invasive and scarcely feasible (transesophageal Doppler echocardiography) or extremely expensive and scarcely available (PET, SPECT, RMN) methods [3]-[5].

Transthoracic Doppler echocardiographic imaging provides a reliable, non-invasive diagnosis of coronary artery disease by means of evaluation of CFVR in the distal portion of the left anterior descending (LAD) coronary artery, using pulsed wave Doppler echocardiography under the guidance of color Doppler flow mapping [6]-[8].

In spite of the advantages introduced by this direct and noninvasive evaluation, the quantification of CFVR is based on manual identification, often on a single beat, of the Doppler flow velocity peak, introducing subjectivity in the analysis.

As transthoracic Doppler echocardiography is rapidly gaining appreciation as a popular tool to noninvasively evaluate CFVR, the need for a technique that would eliminate some of the limitations inherent to the manual analysis of CFVR becomes essential. Moreover, while a CFVR<1.9 is considered as pathologic, and CFVR>2.5 is associated with normal coronary microvasculature, the clinical meaning of 1.9<CFVR≤2.5 is still not clear. Thus, the computation of other parameters than the CFVR from the coronary flow Doppler profile could provide new indices potentially useful in the diagnostic process.

Accordingly, our goals were: 1) to develop a technique for semi-automated detection of Doppler flow velocity profile, thus allowing the automated computation of CFVR and other parameters; 2) to validate this technique in comparison with conventional measurements obtained by manual tracing; 3) to test for differences in the computed parameters between normal (N) subjects and patients with rheumatoid arthritis (RA).

II. Methods

A. Experimental Protocol

Transthoracic Doppler echocardiography was performed with a Sonos 5500 (Philips Medical Systems, Andover, USA) ultrasound unit equipped with a broad-band, high-frequency (3.5 to 7 MHz) transthoracic transducer (S8) with the patients in the left lateral decubitus position. Coronary flow in the mid-distal portion of the LAD artery was searched under the guidance of color-Doppler flow mapping. Pulsed Doppler was then activated to acquire the coronary flow velocity profile at baseline. Stress echo was performed with dipyridamole infused at 0.56 mg/kg over 4 minutes, and then at 0.28 mg/kg over 2 minutes, acquiring coronary flow velocity profile at peak stress. At the end of the protocol, all patients received 125 to 250 mg of aminophylline to counteract the effect of dipyridamole. Images were stored on the magneto-optical disk for off-line analysis. In total, we studied 17 N subjects (mean age, 58±12) and 41 RA patients (61±12) for CFVR evaluation.

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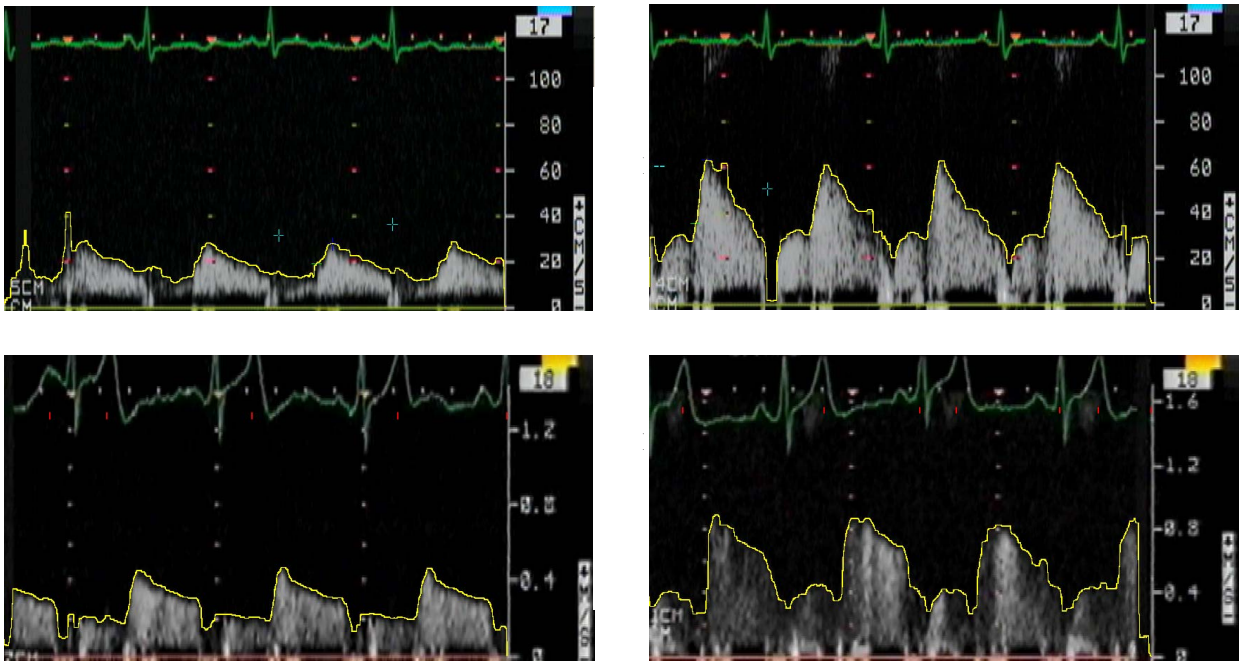

Fig. 1: Doppler flow velocity profile with its contour semi-automatically detected and overimposed for visual assessment. Top panels: RA subject; bottom panels: N subject. Left: baseline; right: stress.

B. *Image Analysis*

We developed a novel custom software using Matlab (The Mathoworks), to detect and analyze the Doppler flow velocity profile. The acquired images were in the RGB format, composed of 1500 lines x 1125 columns x 3 color maps, using an intensity scale of 256 levels.

First, both the region of interest containing the Doppler tracings and the ECG signal were detected from the image. Then, a horizontal Sobel filter was applied to detect the baseline, thus determining the positive velocity subimage. To calibrate the measurements, a vertical Sobel filter was used to detect the scale factor on the velocity axis of the Doppler coronary velocity signal.

As a next step, each pixel column was scanned from the bottom to the top, to search for the first pixel with intensity lower than a predetermined threshold. To automatically obtain the threshold value, the image was divided in three partially overlapped rectangular regions. For each region, its videointensity histogram was computed, and the videointensity L at which the 25% of the pixels had an intensity greater than L, was assumed as a threshold for that region, where the value of 25% was experimentally obtained as the best choice. In the overlapped areas, the mean of the two thresholds was considered.

From the binary image resulting by the thresholding operation, the velocity signal was extracted and filtered with a median filter, to remove outliers; finally, it was overimposed to the original image to allow visual verification of the accuracy of the detected profile (Fig. 1). Subsequently, a cubic spline interpolation was applied to obtain a denser sampling, and the resulting signal was filtered with a low-pass FIR filter.

Basing on the ECG signal detected from the initial image, each beat was automatically identified. Then, for the velocity profile corresponding to each beat, its first derivative was computed and some fiducial points were automatically identified: diastolic (D) peak velocity, as the maximum in an window ranging from ¼ to ¾ of the total beat duration; D maximum first derivative, has the maximum in the 20% of

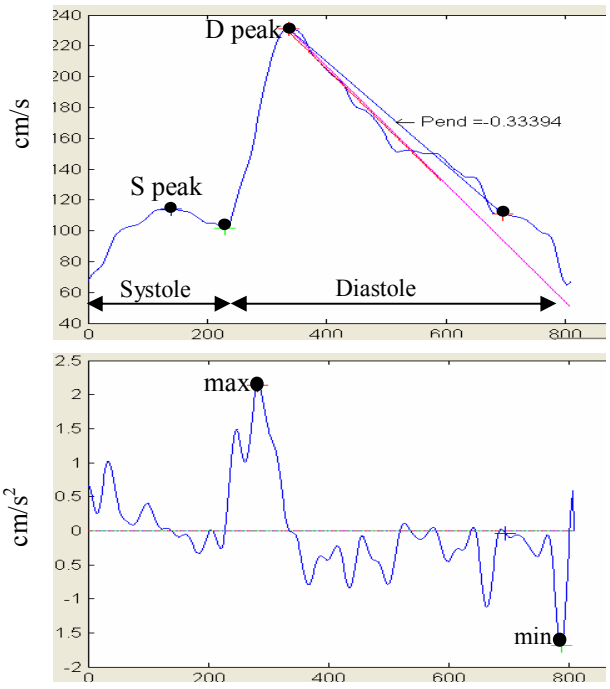

Fig. 2. Detected coronary flow velocity profile (top) and its derivative (bottom) with the identified fiducial points (black dots).

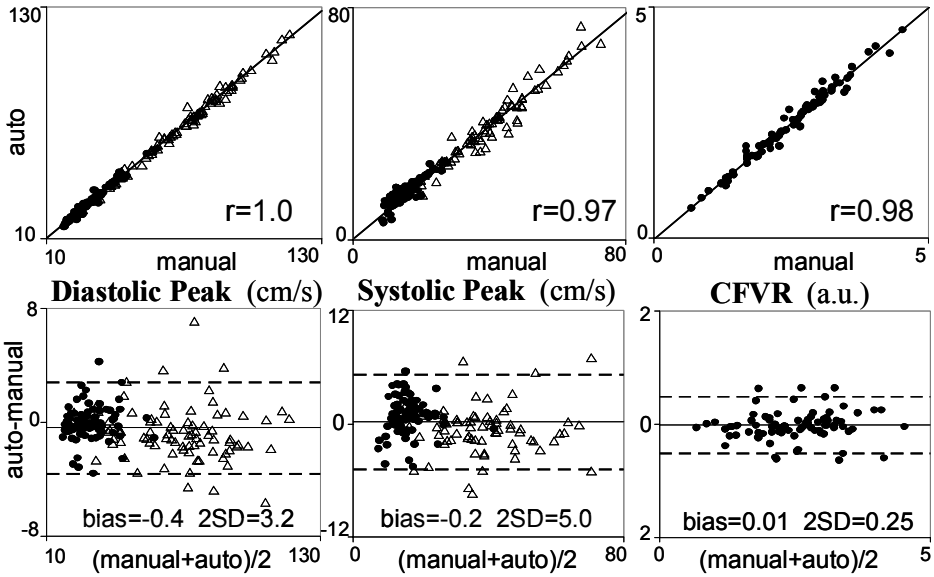

Fig. 3. Linear regression (top panels) and Bland-Altman (bottom panels) analyses between manual measurements, considered as the "gold standard", and the results of the automated analysis. Black dots correspond to baseline measurements, while triangles correspond to peak stress measurements.

the curve before the D peak; the ending point of the systolic (S) phase, as the minimum in a window preceding the D maximum first derivative; S peak velocity, as the maximum in the window ranging from the first point of the profile and the ending point of the systolic phase; the D minimum first derivative was determined as the minimum value in the window starting from the D peak. From these fiducial points, the following measurements were obtained (Fig. 2): S and D mean velocities, CFVR, S and D phase durations (with and without normalization for heart rate), D slope, D to S peak velocity ratio (DSVR). The results obtained from three consecutive beats were automatically averaged to minimize respiratory variations.

C. Validation Protocol

"Gold standard" values of D and S velocity peaks, CFR and DSVR were obtained as the mean of the manual measurements performed by two expert cardiologists, blinded to each other, by using the built-in calculation package of the ultrasound unit. These values were compared by linear regression and Bland-Altman analyses to the mean of the automated measurements obtained by two observers, who independently analyzed the same images with the proposed algorithm. For each technique, manual and automated, the inter-observer variability was computed as the SD of the two measurements obtained by the two readers, and expressed as percentage of their mean.

III. Results

The proposed algorithm was able to correctly detect the Doppler velocity profile in 91% of the analyzed frames without need of manual interaction. In the remaining 9%, manual adjustment of the threshold parameter was needed to correctly identify the profile. The time needed for analysing three beats with the automated analysis ranged between 10-40 sec, while manual analysis required 3-4 min. Comparison with the "gold standard" values by linear regression and Bland-Altman analyses (Fig. 3) showed excellent correlation and not significant bias in each of the examined parameters (not showed in the figure, DSVR: r=0.79, bias:0±0.6). Inter-observer variability with the proposed technique was found to be comparable with that of conventional manual tracings in all computed parameters (range 2% - 7%).

RA patients showed a significant (unpaired t-Test, $p<0.05$) decrease in CFVR (2.5±0.7) compared to N subjects (3.1±0.5). Interestingly, at baseline D and S peak and mean velocities were found already increased in RA compared to N (Table 1). In addition, other of the new parameters (D slope, diastolic phase duration at stress) evidenced significant differences between the two groups (Table I).

IV. Discussion and Conclusions

The proposed method for semi-automated detection of Doppler coronary flow velocity profile resulted in fast, accurate and reproducible measurements, when compared with manual analysis. The criterium used to automatically determine the local pixel threshold to identify the profile showed to be quite robust and reliable, despite the different artifacts and noise which often affect this kind of signal.

The automated extraction of other parameters than CFVR could give the clinician new indices potentially useful in discriminating between normal and abnormal values. At baseline, the increase in S and D peak and mean velocities noticed in the RA subjects, as well as in D slope, could reflect some pathophysiology differences associated with the connective tissue disease affecting the RA patients.

As these differences were evidenced at baseline, they could conduct, if confirmed by further investigations to be performed in large numbers of patients with RA, to limit the evaluation of coronary microcirculation in RA patients to the baseline condition only, thus avoiding the pharmacologically induced stress.

In conclusion, the measurements obtained with the proposed semi-automated detection procedure were found accurate and reproducible compared with manual tracing, with a reduction of the time needed for the analysis. The proposed method allows the computation of additional

TABLE I
RESULTS OBTAINED IN 17 NORMAL SUBJECTS (N) AND 41 PATIENTS WITH RHEUMATHOID ARTRITHIS (RA) FROM THE DOPPLER FLOW VELOCITY ANALYZED WITH THE PROPOSED METHOD

		N		RA	
		Ctrl	Stress	Ctrl	Stress
S peak	(cm/s)	14±3.0	39±14*	17±6.0#	38±14*
D peak	(cm/s)	23±5.0	72±15*	30±8.0#	72±21*
S mean vel.	(cm/s)	11±4.0	31±11*	15±6.0#	29±11*
D mean vel	(cm/s)	19±3.0	46±12*	22±6.0#	45±13*
D slope	(cm/s^2)	-0.09±0.05	-0.62±0.22*	-0.16±0.09#	-0.90±0.55*
S time	(ms)	260±80	250±40*	240±50	250±40
D time	(ms)	490±120	390±90*	450±80	340±70*#
Total time	(ms)	749±151	641±103*	694±105	583±67*#
S time/HR	(%)	35±8	39±8	35±6	42±8*
D time/HR	(%)	65±8	61±8	65±6	58±8*
D max der.	(cm/s^2)	0.21±0.11	0.42±0.18*	0.22±0.12	0.44±0.19*
D min der.	(cm/s^2)	-0.17±0.08	-0.49±0.29*	-0.15±0.12	-0.43±0.26*
DSVR	(a.u.)	1.7±0.22	2.02±0.63*	1.83±0.38	2.03±0.46*
CFR	(a.u.)	3.12±0.48		2.46±0.71#	

*:p<0.05 paired t-test (Ctrl vs Stress); #: p<0.05 unpaired t-test (N vs RA)

indices, which may be useful in the diagnostic phase. Rheumatoid arthritis patients showed alterations in some of the computed indices. Evaluation of these indices in different populations with microcirculatory diseases is required to verify their clinical applicability.

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