Quantitative Ultrasonic Myocardial Blood Flow Reserve Reproducibility in Men

DF Vitale, A Nicolino, GL Iannuzzi, G Longobardi, G Furgi, F Cacciatore, F Rengo

Fondazione Salvatore Maugeri, Telese Terme, Italy

Abstract

Quantitative assessment of myocardial blood flow (MBF) by contrast echocardiography (CE) has the potential to become a routine procedure with continued methodologic enhancements.

Improved hardware technology, better physical characteristics of the contrast agent (microbubbles), and the development of more advanced algorithms to compute blood flow underlie the advances in this field.

The purpose of this study was to assess the reproducibility of quantitative CE blood flow parameters obtained with the destruction-reperfusion principle.

1. Introduction

MBF reserve can be measured using CE and relates to the coronary stenosis severity [1].

The acceptance into the clinical practice of the ultrasonic MBF evaluation is conditioned by the introduction of an effective and reliable method for the objective quantification of myocardial perfusion.

A method based on continuous infusion of contrast agent during intermittent triggered imaging has been proposed to overcome the limitations encountered with other methods [2,3].

The technique is based on the destruction-reperfusion principle, i.e., given (i) a constant microbubbles blood concentration and (ii) that the microbubbles disrupt when exposed to an acoustic field, the velocity of microbubbles video intensity reappearance in the myocardial region of interest of the echo images (obtained at increasing time from destruction) is related to the blood velocity and can be estimated by fitting time course data with the exponential function $y= A(1-e^{\beta t})$. A is an estimate of the vascular volume, β is related to the perfusion velocity and the product $A\beta$ is related to the myocardial flow.

Echo images at increasing interval from destruction may be obtained with 2 techniques. The first is the intermittent triggered pulsing interval procedure that uses constant high power destructive ultrasonic beams. The second is the real-time approach that makes use of the recently introduced "pulsing inversion" technique that allows selective ultrasonic power levels for destructive (high power) or imaging (low power) frames [4-6].

In our echo laboratory we implemented this method in order to quantify myocardial blood flow parameters from contrast ultrasonic studies using the real-time imaging (RTI) approach.

This study is devoted to assess the variability of the myocardial reserve (MR) obtained from repeated ultrasonic acquisitions.

2. Methods

2.1. Patients

21 Subjects with and without documented coronary artery disease scheduled for standard echocardiographic examination with medium to good ultrasonic image quality where eligible for the study. Patients gave written, informed consent to be included in the study.

Ultrasonic contrast medium (SonoVue®, Bracco) was administered by constant intravenous pump infusion (1-1.5 ml/min).

A separate pump infusion set was used to induce hyperaemia with adenosine at 140 µg/kg/min [7].

2.2. Contrast echocardiography

A S3 transducer coupled to a Sonos 5500 system (Phillips Corp.) was used for RTI (TCE3 with angio).

Ten impulses (flashes) at maximum power where used to destroy microbubbles.

Table 1. Mean ± sd myocardial reserve in patients with and without coronary artery disease (CAD).

	No CAD	CAD	Δ
$A\beta$	3.1±1.2	1.3±0.5	1.8
β	2.3±0.9	1.2±0.4	1.1

RTI after flashes was performed with a frame rate of 18-21 Hz at a mechanical index of 0.1.

Each single study lasted for 9 sec.; patients were asked to hold breath during this period.

Gain was adjusted before contrast administration so

that no noise was detectable over the myocardium and thereafter it was held constant during the study.

Table 2. Myocardial reserve parameters first and second study mean ± sd and their difference ± sd.

Parameter	1st Study	2nd Study	Δ	
			Mean	SD
A	147.0±40.4	145.4±40.7	1.6	15.2
β	1.56±0.74	1.56±0.74	0	0.25
Aβ	248±170	247±169	1.3	40.5
β reserve	1.7±0.73	1.69±0.75	0.01	0.33
Aβ reserve	2.23±1.1	2.16±1.1	0.07	0.43

Imaging was performed using either 2 or 4 chamber view; transducer position was held constant throughout the study .

In each echo examination the 2-3 basal studies were started 2 minutes after contrast infusion beginning in order to allow constant microbubbles blood concentration. The 2-3 hyperaemic studies were started after 1.5 min of adenosine infusion. One study was made before contrast infusion for background correction.

At the end of the examination all studies were transferred to a PC for off line processing.

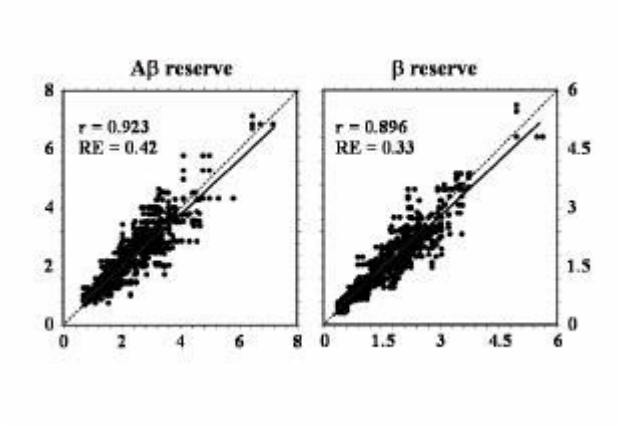

Figure 1. Aβ and β reseve regression analysis.

The analysis was performed using a custom made software package and started drawing a region of interest (ROI) on well defined areas of the myocardium. Multiple ROI were drawn on each study (mean 3±1.1).

Each ROI was registered respect to myocardial wall boundaries along all study frames (150-160 Fr's) in order to compensate for wall displacements.

The ROI's mean video intensity of the frames following the last destructive impulse were interpolated with the exponential function $y= A(1-e^{\beta t})$; A, β an Aβ were recorded.

ECG signal was digitized and RR was computed in real-time, thus allowing the automatic drive of the impulse train start so that the last destructive impulse occurred just on the R wave.

Since myocardial contrast intensity has a cardiac cycle dependent variation, a random impulse train start would lead to changes in the outline of the video intensity curve. In this case, the RR phase in which the impulse train occurred would shape the curve.

Consistent end diastolic triggering abolished this source of error in our studies.

Myocardial reserve was computed as the ratio between the hyperaemic value over the basal value for both β and Aβ parameters.

3. Results

In order to have a measure of the magnitude of the myocardial reserve differences encountered in the clinical settings we divided our study population in patients with (group 1) and without (group 2) coronary artery disease (CAD). Table 1 reports the mean±sd reserve values and the difference between the 2 groups.

Figure 1 shows the linear regression analysis between the repeated acquisition measure of the parameters of primary clinical interest, namely the myocardial reserve of both β and Aβ parameters.

Figure2 shows the relative scatterplots of the inter-study differences.

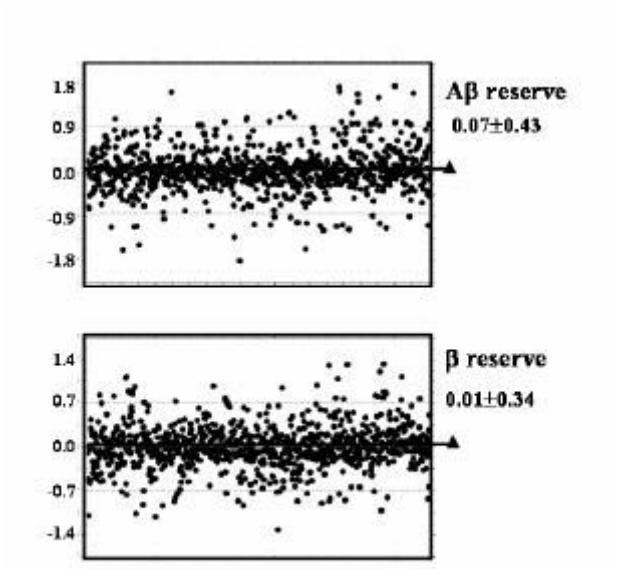

Figure 2. Aβ and β reserve inter-study differences scatterplot.

Table 2 reports the mean and the standard deviation of the difference between the repeated measures of all 5 parameter; A, β , Aβ, β reserve and Aβ reserve.

4. Discussion and conclusion

The knowledge of the reproducibility of a quantitative parameter is mandatory for its use in the clinical settings. Moreover, since the quantification of myocardial blood flow by contrast ultrasonic procedures is an emerging technique not yet fully standardized and is performed with algorithms and software packages developed "in loco" by each laboratory, computation of its own reproducibility is strongly recommended to each laboratory. Measures of inter- and intra- observer variability should be added to the inter-study variability.

We used the inter-study variability of ultrasonic contrast parameters (as measured by the standard deviation of the inter-study difference or, equivalently, by the residual error of the linear regression analysis) to assess the reproducibility of the myocardial reserve as assessed by contrast echocardiography.

The inter-study variations reported in table 2 have a meaning only if compared with the expected differences in the clinical settings.

It has been reported in humans a β reserve difference of 1.7 units between mild and severe stenosis severity [1], while we found a difference of 1.1 units for this index and a value of 1.8 units for the Aβ reserve between subject with and without CAD. Changes in the coronary stenosis severity can account for these variations.

Most importantly, these differences face favourably with the observed variability magnitude of 0.43 and 0.33 units for Aβ and β reserve respectively.

In case a greater accuracy is required or if the method has to be applied in a setting in which smaller differences are expected, repeated measure can help to achieve the required variability reduction, e.g. the variability will be reduced by a factor of 1.7 with a triplicate measurement.

References

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Address for correspondence.

Dino F Vitale.
Via Morghen 187
80129 Napoli, Italy.
E-mail address:dvitale@fsm.it.