Multimodality imaging of coronary artery bypass grafts

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CHAPTER 4

Blood flow in coronary artery bypass vein grafts: volume versus velocity at cardiovascular MR imaging

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Radiology 2004; 232, 3, 915-920

Abstract
Forty-nine patients with previous bypass surgery underwent coronary angiography and cardiovascular magnetic resonance (MR) imaging of single vein bypass grafts. Volume flow and velocity analyses were performed and compared on MR velocity maps. Bland-Altman analysis showed close agreement between the two types of analysis. Comparison of areas under the receiver operating characteristic curve revealed no significant differences between the analyses for detection of stenoses of 70% or greater. Diagnostic accuracy for volume flow and velocity parameters was 92% and 93%, respectively. Velocity analysis appears to be the preferred method, because it is less time-consuming and has a similar diagnostic accuracy to volume flow analysis.

Introduction

Volume flow and peak velocity measurements have been used as physiologic markers of stenosis severity in coronary arteries. Volume flow is of direct clinical value, since the quantity of blood flowing through a vessel within 1 minute is measured, and coronary flow reserve (CFR) is correlated with stenosis severity (1); however, direct invasive measurement is restricted to "open chest" procedures. Peak velocity measured by using a Doppler guidewire has been proven to correlate well with volume flow both in vitro and in vivo (2) and has evolved into a well-established method to evaluate stenoses in coronary arteries and bypass grafts in the catheterization laboratory (3,4). Cardiovascular magnetic resonance (MR) velocity mapping is a noninvasive technique used to measure coronary flow and velocity in native coronary arteries (5-8) and bypass grafts (9-12). Both volume flow and velocity can be analyzed on a MR velocity map. MR volume flow analysis has been validated as being an accurate noninvasive method of measuring volume flow (13-15). With this approach, the mean velocity for the whole luminal area of the vessel is multiplied by the luminal area. All pixels are included in the analysis; however, partial volume effects may occur at the edges of the lumen (16). Moreover, this analytical approach is time-consuming. In velocity analysis, the velocity in the center of the vessel is measured. This approach is less time-consuming and has been used successfully in several clinical studies (6,7,17,18). The present study was performed to evaluate whether MR volume flow analysis and MR velocity analysis have comparable diagnostic accuracies for the detection of significant (≥70%) stenosis in single vein coronary artery bypass grafts.

Materials and methods

Patients

A total of 49 patients, who had previously undergone bypass graft surgery, underwent coronary angiography because of recurrent chest pain and, in addition, underwent MR imaging according to the study protocol. Approval of the local medical ethics committee was obtained, and all patients gave informed consent. This study was prospective and was performed in a university hospital (Leiden University Medical Center). MR-related exclusion criteria included implanted metallic devices, unstable angina, irregular heart rhythm, claustrophobia, and the inability to lie flat. Adenosine-related exclusion criteria included chronic obstructive pulmonary disease and second- or third-degree atrioventricular block. Mean age (± standard deviation) in patients was 66.4 years ± 8.7 (range 43-79 years). There were 40 men and 9 women, with mean ages of 65.7 years ± 9.1 (range 43-79 years) and 69.7 years ± 6.3 (range 60-77 years), respectively. Table 4.1 gives pertinent information regarding the 49 patients.

Imaging and Analysis

Coronary Angiography

Coronary angiography was performed according to a standard protocol by using the Seldinger technique. Single vein grafts and recipient vessels (n = 80) were studied in 49 patients. To objectively determine the severity of stenosis, quantitative coronary arteriography was performed by members of an independent core laboratory (Heart Core,

Number of patients (n)	49
Male/female	40/9
Age (years)	66.4 ± 8.7
Time after bypass surgery (years)	13.5 ± 5.3
Number of grafts studied	80
Hypercholesterolemia	40 (82%)
Hypertension	24 (49%)
Current smokers	6 (12%)
Diabetes mellitus	8 (16%)
Family history for cardiovascular disease	28 (57%)

Table 4.1
Patient Characteristics

Leiden, the Netherlands). An experienced analyst from Heart Core, who was blinded to the results of the MR imaging, performed the quantitative coronary arteriography analyses. Quantitative coronary arteriography enabled digital measurement of the diameter of the stenosis (in millimeters) and of a nonstenotic segment of the same vessel (reference diameter). The percentage of stenosis was calculated as the ratio between the diameter of the stenosed segment and the reference diameter. This method of quantitative coronary arteriography was standardized and extensively validated by Reiber et al (19,20). A reduction in vessel diameter of 70% or greater was considered a significant stenosis.

MR Imaging
For MR imaging, a 1.5-T imager (Gyroscan ACS-NT; Philips Medical Systems, Best, the Netherlands) equipped with Powertrak 6000 gradient system, a cardiac research software patch, and a 5-element cardiac synergy coil was used. The investigator (S.E.L.) who performed the MR imaging was blinded to the results of coronary angiography. Information regarding the coronary artery bypass procedure was used as a reference for the course of the grafts. First, gross cardiac anatomy was visualized by means of a scout image. Then, transverse electrocardiographically gated 2-dimensional gradient-echo survey MR images were obtained at the level of the ascending aorta to localize the grafts. A plane perpendicular to the proximal section of the graft was planned on two differently angled survey images, and, for MR velocity mapping, a fast breath-hold turbo-field echo-planar imaging sequence was used at rest and during stress (140 µg of adenosine per kilogram of body weight per minute administered intravenously). The turbo-field echo-planar imaging sequence included the following parameters: 11.0/4.6 (repetition time msec/echo time msec), flip angle of 20°, temporal resolution of 23 msec, field of view of 200x100 mm, data acquisition matrix of 128x60, in-plane spatial resolution of 1.6x1.6 mm reconstructed to 0.8x0.8 mm by means of zero filling of k-space, section thickness of 6 mm, image duration of 20 heartbeats, velocity encoding of 75 cm/sec, and prospective electrocardiographic triggering (9,10).
Volume flow analysis and velocity analysis were performed with an analytic software

package (FLOW; Medis, Leiden, the Netherlands) by the same investigator (S.E.L.), and the flow and velocity analyses of the same velocity map were separated by a minimum of 4 weeks to avoid bias. The duration (in minutes) of the volume flow and velocity analyses per patient was registered from the start of the image analysis to report generation.

For the volume flow analysis, the luminal area was traced manually on the modulus image and transferred to the phase image (Figure 4.1). The position and size of each contour were adjusted according to the cardiac phase. The flow rate (in milliliters per second) was calculated by multiplying the average velocity over the luminal area with the luminal area for each cardiac phase. Flow rate-versus-time curves were reconstructed, and the volume flow rate (in milliliters per minute) was obtained by multiplying the integrated volumetric flow rate per heartbeat with the heart rate (Figure 4.2). Systolic peak flow rate and diastolic peak flow rate were defined as maximal flow rate during systole and diastole, respectively, both measured in milliliters per second. CFR was calculated as the ratio of volume flow during adenosine-induced stress and volume flow at rest. The ratio between diastolic and systolic peak flow rates was regarded as the diastolic-to-systolic flow ratio.

Velocity images consisted of paired modulus and phase images. For the velocity analysis, a region of interest of 2 x 2 pixels was placed in the center of the vessel in each phase image (Figure 4.1). The mean velocity of the 4 pixels was defined as the central velocity for that cardiac phase. Velocity-versus-time curves were drawn (Figure 4.2), which were similar to flow rate curves. Systolic peak velocity and diastolic peak velocity were defined as the maximal central velocity during systole and diastole, respectively, measured in centimeters per second. The mean central velocity was regarded as the average peak velocity. Coronary flow velocity reserve (CFVR) was calculated as the ratio between average peak velocities during adenosine-induced stress and at rest. Diastolic-to-systolic velocity ratio was the ratio between diastolic and systolic peak velocities.

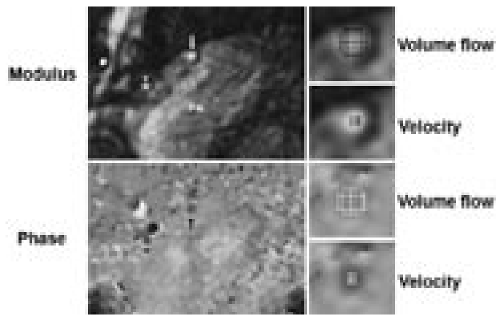

Figure 4.1

Sagittal oblique images from a typical phase-contrast MR examination. Modulus (top) and phase (bottom) images, obtained with a breath-hold turbo-field echo-planar (11.0/4.6) sequence, show the cross section of a vein graft (arrow) to the left anterior descending coronary artery and an arterial bypass graft (arrowhead) to the first diagonal branch during late diastole. Enlargements of the vein graft cross section (right) are shown to illustrate the volume flow and velocity analyses. PA = pulmonary artery; # = artefact derived from sternal wires on the chest wall

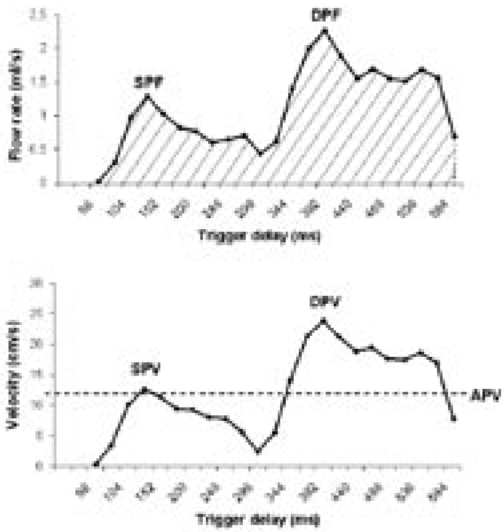

Figure 4.2

Top: Flow rate-versus-time curve. The integral of the curve (hatched area) indicates the volume flow per heartbeat. The volume flow per heartbeat multiplied with the heart rate results in the volume flow per minute. Bottom: Velocity-versus-time curve from the same bypass graft displays the velocity parameters that were distracted from the curve. Flow rate- and velocity-versus-time curves were used to quantify volume flow and velocity parameters. SPF = systolic peak flow; DPF = diastolic peak flow; SPV = systolic peak velocity; DPV = diastolic peak velocity; APV = average peak velocity

Statistical Analysis

Paired correlations of the flow and velocity parameters were determined by calculating the Pearson correlation coefficient. Limits of agreement between the volume flow and velocity analyses were evaluated by means of Bland-Altman analysis (21). Receiver operating characteristic (ROC) curve analysis was employed to determine the diagnostic performance of each flow and velocity parameter for demonstrating a significant stenosis using the Simpson rule (univariate analysis).

Significant parameters from the univariate analysis were subsequently used to perform stepwise multivariate logistic regression and ROC curve analyses to determine the diagnostic performance of the combined set of flow or velocity parameters, respectively, in the detection of a significant stenosis (multivariate analysis). Multiple single vein grafts in the same patient were possibly correlated (22), for instance, because they share the same risk of stenosis due to systemic factors. This correlation was investigated for the calculation of the correlations between the flow and velocity parameters, and for the logistic regression analysis by using a robust estimator of the standard errors and by the subsequent calculation of the p values. Results indicated no correlation between multiple grafts within a patient. Therefore, all grafts were treated independently for calculating correlations and areas under the curve in ROC analysis and for comparing ROC curves. The optimal cutoff values for flow and velocity parameters needed to predict stenosis were defined as those providing the maximal sum of sensitivity and specificity. Sensitivity, specificity, and diagnostic accuracy were based on their standard definitions and are presented with 95% confidence intervals.

For all tests, $p<0.05$ was considered to indicate a statistically significant difference.

Results

A total of 80 single vein grafts were analyzed. Sixteen grafts supplied the left anterior descending artery territory; 25 grafts, the left circumflex artery territory; and 39 grafts, the right coronary artery territory. By means of quantitative coronary arteriography, severity of stenosis was determined to range from 0% to 100% with a mean of 50% ± 39. Stenosis of 70% or greater was detected in 25 grafts (31%).

At MR imaging, 22 of 80 grafts were not visible in their expected course, and these grafts were regarded as occluded. MR velocity mapping was performed in the remaining 58 grafts. Baseline velocity mapping was unsuccessful in 1 graft because of artifacts. Adenosine-induced stress velocity mapping was not possible in 8 grafts because of side effects from adenosine.

Correlations for the volume flow and velocity parameters are shown in Table 4.2. Highly significant correlations were found for all paired parameters both at rest and during stress ($p<0.01$ for all correlations).

Agreement between CFR and CFVR and between diastolic-to-systolic flow ratio and diastolic-to-systolic velocity ratio was quantified by means of Bland-Altman analysis. Figure 4.3 displays the Bland-Altman plot for the CFR and CFVR. There was a close agreement between the two methods of analysis. The mean difference between the CFVR and CFR was not significant. Similar results were found for diastolic-to-systolic flow ratio and diastolic-to-systolic velocity ratio by using baseline and stress parameters. Direct comparison of the remaining parameters was not possible because units of measure were not equivalent; volume flow parameters were measured in milliliters per second, while velocity parameters were measured in centimeters per second.

At univariate analysis, all parameters for both volume flow and velocity methods were significantly different between grafts with and those without stenoses (≥70% stenosis; $p<0.001$). At multivariate analysis, the diagnostic value of all significant univariate flow parameters (volume flow; systolic and diastolic peak flow rates; diastolic-to-systolic flow ratio at baseline and during stress; CFR) were compared with all significant univariate velocity parameters (average, systolic, and diastolic peak velocities; diastolic-to-systolic velocity ratio at baseline and during stress; CFVR) in the detection of a graft stenosis of 70% or more. The estimated regression parameters, selected in the model, are given in Table 4.3. The area under the ROC curve was 0.93 (95% confidence interval: 0.87, 0.99) for the flow parameters and 0.96 (95% confidence interval: 0.92, 1.00) for the velocity parameters. Both ROC areas were significantly larger than 0.50 ($p<0.001$). When the ROC areas were compared, the results showed no significant difference ($p = 0.41$). Optimal cut-off points for the ROC curves are displayed in Figure 4.4. The optimal sensitivity, specificity and accuracy for the volume flow parameters were 90% (95% confidence interval: 83%, 97%), 92% (95% confidence interval: 86%, 98%), and 92% (95% confidence interval: 86%, 98%), respectively. The optimal sensitivity, specificity and accuracy for the

velocity parameters were 95% (95% confidence interval: 90%, 100%), 92% (95% confidence interval: 86%, 98%), and 93% (95% confidence interval: 87%, 99%), respectively. No significant differences in sensitivity, specificity, or accuracy were found between the methods of analysis for demonstrating a bypass graft stenosis of 70% or greater.
The mean duration for performing a volume flow analysis was 25.9 minutes ± 4.3, whereas a velocity analysis was performed in 11.1 minutes ± 2.2 ($p<0.05$).

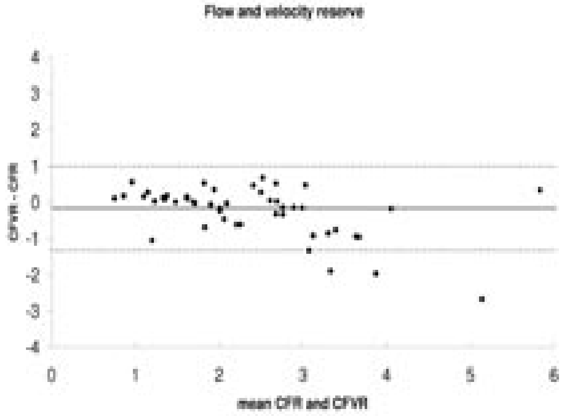

Figure 4.3
Bland-Altman plot of CFR and CFVR derived from the volume flow and velocity analysis, respectively. Solid horizontal line shows the mean difference between CFR and CFVR, and dashed lines are ± 2 standard deviations. The plot shows a close agreement between the two analysis methods. The mean difference between CFVR and CFR was not significant.

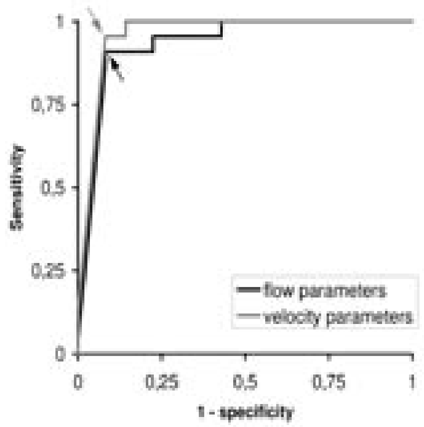

Figure 4.4
Graph shows ROC curves of single vein grafts with luminal stenosis 70% or greater derived from flow and velocity parameters. When the area under the ROC curve for flow parameters was compared with that for velocity parameters, no significant differences were found. Optimal cutoff points are indicated by arrows.

Paired parameters	Correlation coefficient
CFR and CFVR	0.85
Baseline	
Volume flow and average peak velocity	0.85
Systolic peak flow and velocity	0.84
Diastolic peak flow and velocity	0.86
Diastolic-to-systolic flow and velocity ratios	0.90
Adenosine-induced stress	
Volume flow and average peak velocity	0.95
Systolic peak flow and velocity	0.90
Diastolic peak flow and velocity	0.90
Diastolic-to-systolic flow and velocity ratios	0.83

Table 4.2
*Correlations for paired flow and velocity parameters**
** For all correlations p<0.01. Flow and velocity parameters are derived from the volume flow and velocity analysis of the MR velocity maps of 58 single vein bypass grafts.*

	Volume flow		Velocity	
Parameter	b	SEE	b	SEE
Average peak				
Baseline	0.054	0.036	1.72	0.55
Stress	-	-	-	-
Reserve *	-	-	3.12	1.01
Systolic peak				
Baseline	-	-	-0.82	0.28
Stress	-2.15	0.81	-0.28	0.12
Diastolic peak				
Baseline	-	-	-	-
Stress	-	-	-	-
Diastolic-to-systolic ratio	-	-	-	-
Baseline	-	-	-	-
Stress	-1.32	0.37	-7.74	2.14
Constant	1.50	0.58	1.51	0.60

Table 4.3
Estimated regression parameters of the forward stepwise multivariate logistic regression model
** Refers to the CFR or CFVR. b = regression coefficient; SEE = standard error of the estimate*

Discussion

In the present study, two approaches used to analyze MR velocity maps, MR volume flow analysis and MR velocity analysis, were compared in a head-to-head fashion in single vein bypass grafts. Close agreement was shown between the volume flow and velocity methods when comparing CFR, CFVR, diastolic-to-systolic flow ratio, and diastolic-to-systolic velocity ratio. Fair sensitivity, specificity, and diagnostic accuracy were shown for both approaches in depicting significant (≥70%) stenosis. Therefore, a single approach would be sufficient when analyzing MR velocity maps.

The concept of CFR was proposed by Gould et al (1) in the early 1970s, when the necessity arose for a hemodynamic assessment of coronary stenoses visualized on the coronary angiogram. Absolute coronary blood flow could be measured only by using perivascular flow transducers in "open chest" procedures. CFR was therefore validated in animal models or in patients undergoing bypass graft surgery (1,23,24); however, extensive use in the clinical setting was not possible. When the diameter of intravascular catheter-based Doppler ultrasonographic devices could be reduced to an 0.018-inch diameter, it became feasible to measure absolute velocity of blood flow and calculate CFVR in coronary arteries in patients during catheterization. Absolute blood flow correlated well with Doppler-derived absolute velocity and volume flow both in vitro and in vivo (2,25,26). Doppler-derived velocity and CFVR proved their potential in numerous clinical applications, such as in identification of hemodynamically significant stenoses in native coronary arteries and vein grafts (3,4), in the functional assessment of stenoses of intermediate severity (27), in the determination of the need for and the outcome after coronary intervention (28-30), and in the prediction of restenosis (31).

With MR imaging and a velocity mapping sequence, both CFR and CFVR can be calculated, as was described in Materials and Methods. In clinical studies, both the volume flow analysis (8,5,12) and the velocity analysis (7,17,18) have been used successfully. In our study, the accuracies of volume flow and velocity analyses were not significantly different when evaluating MR velocity maps. Other factors, such as errors in phase-contrast MR imaging and the time necessary to analyze the MR velocity maps, become important in choosing a method for analysis.

When obtaining flow measurements at phase-contrast MR imaging, several errors might occur (32). Some errors are dependent on the prescription of the MR velocity mapping sequence (eg. inadequate spatial and temporal resolution, mismatched encoding velocity, deviation of the perpendicular imaging plane from the flow direction). In the present study, an effort was made to keep the effects of errors minimal. Encoding velocity was adequately matched to avoid aliasing, and two survey images obtained at different angles were used to plan the imaging plane perpendicular to the graft. Phase-offset errors are dependent on local magnetic-field inhomogeneities and are usually small. In the analysis of MR velocity maps, all of these errors affect both volume flow and velocity analyses.

In volume flow analysis, all pixels in the cross-sectional area of the graft lumen are included. Pixels on the vessel edge may average signals both from the vessel lumen and from surrounding tissue. This type of error, known as partial volume effect, could either increase or decrease apparent flow (13,33). The extent of partial volume effect depends predominantly on spatial resolution and relative signal intensity of stationary tissue (16).

With the current MR imaging techniques, spatial resolution for flow measurements in small vessels is limited and, due to background noise velocity, is not zero in stationary tissue, enhancing partial volume effects. However, velocities at the vessel edge are expected to be low, as there is a pulsatile laminar flow pattern in bypass grafts with the highest velocity in the center of the vessel (34). Since diagnostic accuracy of the volume flow and velocity analyses did not differ significantly in our study, this might indicate that this type of error has a relatively minor role when MR imaging is used to measure flow in single vein bypass grafts.

In our study, a volume flow analysis required 25.9 minutes ± 4.3 to complete, whereas a velocity analysis required only 11.1 minutes ± 2.2. If clinical acceptance of a diagnostic test is to be achieved, performance and analysis of the test should be fast and straightforward. Since the diagnostic accuracy from both analyses was similar, velocity analysis appears to be the preferable method.

Our study had limitations in that other issues associated with MR velocity mapping, such as reference values of the MR flow and velocity parameters, spatial and temporal resolution of the acquired MR images, and proximal location of the imaging plane in the vessel were not addressed; this is because our purpose was to compare volume flow and velocity analyses of MR velocity maps. In addition, the sample size of our study was small. The study was not designed to test equivalence of the analysis methods. To demonstrate equivalence, a larger data set would be necessary.

Conclusion

In the evaluation of MR velocity maps of single vein coronary artery bypass grafts, there is close agreement between volume flow and velocity analyses. For detection of a stenosis 70% or greater, velocity analysis has a diagnostic accuracy similar to that of volume flow analysis, and is less time-consuming. Therefore, velocity analysis appears to be the method of preference in the analysis of MR velocity maps of bypass grafts.

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