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VELOCITY MAPPING

Accurate and Reproducible Mitral Valvular Blood Flow Measurement with Three-Directional Velocity-Encoded Magnetic Resonance Imaging

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ABSTRACT

A new method for quantifying the transvalvular flow through the mitral valve (MV) based on three-directional velocity-encoded magnetic resonance imaging (MRI) is presented. For thirty time phases during one cardiac cycle, the three-dimensional (3D) velocity vector field of the blood flow is reconstructed from the MRI measurement. Retrospectively, for each time phase, the MV-plane is indicated manually in the velocity data and the flow through this plane is determined, representing the MV flow. Measurements are performed in 10 healthy volunteers. The new method is compared to the conventional, one-directional velocity-encoded MRI method for which an acquisition plane is positioned at the mitral valve at end-systole and remains fixed during the acquisition. The flow measurements with the new method correlate very well with the flow measured in the aorta (r_P=0.92, p<0.01), whereas the conventional method shows no statistically significant correlation (r_P=0.15, p=0.68). The low differences between the flow measured at the MV and the flow in the aorta proves high accuracy of the new method. Also, the new method shows very low intra- and interobserver variation, proving the high reproducibility. Three-directional

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velocity-encoded MRI is a patient-friendly and easy-to-use method suitable for quantifying accurately and reproducibly the transvalvular MV flow.

Key Words: Magnetic resonance imaging; Mitral valve; Flow quantification; Image processing.

INTRODUCTION

Accurate measurement of the transvalvular blood flow is invaluable for diagnosing patients with valvular disease. Currently, the assessment of mitral valve (MV) regurgitation or stenosis is based on echocardiography. Both two-dimensional transthoracic echocardiography (TTE) (Ascah et al., 1985; Goldman et al., 1987) as well as mono- and multiplane transesophageal echocardiography (TEE) with color Doppler (Caldarera et al., 1995; Helmcke et al., 1987; Shah et al., 1999; Spain et al., 1989) provide the information needed to plan surgical strategy (Hellemans et al., 1997; Miyatake et al., 1986). Quantification of transvalvular flow velocities based on Doppler measurements has to cope with two sources of error: the alignment of the ultrasound beam to the flow direction and the fixed location of the sample volume (Fyrenius et al., 1999; Sahn, 1988). Besides measurement restrictions, the interpretation of echo Doppler measurements to physiological parameters is achieved with the application of geometrical models, which do not apply to all individual subjects. Measurements in multiple planes are necessary, which can yield a summation of errors. Furthermore, imaging the region of interest in TTE can be difficult or even impossible because of acoustic attenuation from structures inside the thorax (lungs, subcutaneous tissues, and ribs) and the heart (prosthetic valve construction materials and calcification). TEE is less limited by attenuation of thoracic structures, but this technique is semiinvasive and patients may experience discomfort during this investigation.

Magnetic resonance imaging (MRI) is a noninvasive technique, which is readily applied for the determination of global and regional left ventricular anatomy and function (Van der Geest and Reiber, 1999). As a three-dimensional (3D) imaging technique, volumetric measurements do not rely on the application of geometrical models. Velocity-encoded cine MRI provides quantitative information on moving spins and can be applied to determine intra–ventricular blood flow (Mohiaddin, 1995; Van Dijk, 1984; Wigström et al., 1999). These promising qualities make MRI a very suitable modality for quantifying transvalvular blood flow. Previous attempts have all encountered the motion of the heart during contraction and relaxation as the main obstacle toward direct acquisition of the transvalvular flow. The mitral annulus moves 12–16 mm toward the apex during contraction (Komoda et al., 1994).

Kayser et al. (1997) showed that for tricuspid flow quantification, correction for through-plane motion is indispensable. This must also be considered for mitral flow. Their method corrects for through-plane motion of the right ventricular annulus in a retrospective manner. Since the acquisition plane has a fixed position during the complete cardiac cycle, the location of the data acquisition is not identical to the plane of the MV for the whole cardiac cycle. This implies that flow quantification does not represent the true transvalvular flow.

Kozerke et al. (1999) introduced a single-slice acquisition for transvalvular aortic and MV-flow quantification adapted to the heart motion, the so-called ''STrack'' technique. With this technique, accurate positioning of the acquisition plane enables measurement of the true valvular flow for all phases. Besides the fact that using this technique requires dedicated scanning software not widely available on all commercial MR scanners, this technique uses prospective triggering. This implies that the final part of the RR-interval will not be acquired and diastolic flow quantification, especially important at the MV, will not be accurate.

Using velocity-encoded MRI, a new acquisition method is introduced in this study to obtain the velocity vector field of the intraventricular blood flow in three directions during the complete cardiac cycle. In this velocity vector field, the MV plane is indicated retrospectively. The velocity values of the vector components going through the MV plane will be reconstructed. For the MV area, this will result in an accurate MV flow measurement.

MATERIAL AND METHODS

MRI Acquisition

Ten volunteers (9 males, 1 female, aged 33–67 years, mean age 54±10 years) were recruited for MR examination, all without cardiac valvular disease as confirmed by TTE and TEE. The Medical Ethical Committee of our hospital approved all examinations. All volunteers gave informed consent. The MRI was performed on a 1.5 T scanner (ACS-NT15 Gyroscan

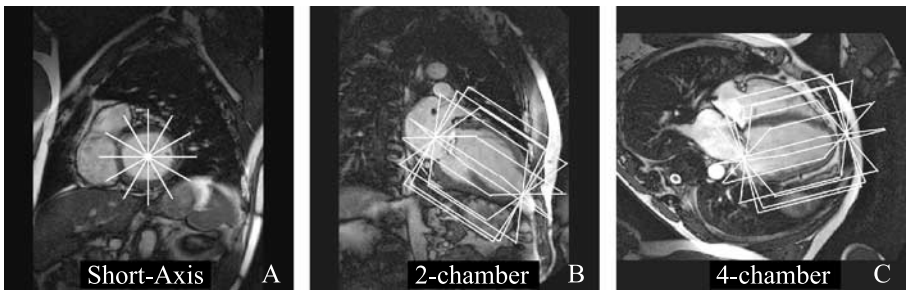

Figure 1. Planning of the 3-dir MV flow acquisition. A radial stack of 6 acquisition planes, with interslice angulation of 30°, is placed on the LV. The long axis of the LV, from MV annulus to apex, coincides with the radial axis of the stack. On a short-axis view (A), a 2-chamber (B), and a 4-chamber (C) view, the position of the stack is planned as illustrated.

with the Powertrack 6000 gradient system; Philips Medical Systems, Best, the Netherlands), using the body coil for transmission and a five-element cardiac phased-array coil placed on the chest for signal reception. First, scout images and two- and four-chamber acquisitions as well as a complete short-axis acquisition were performed [conforming to standard cardiac MR protocols (Van Rossum et al., 1987), using balanced-FFE (Steenbeck and Pruessmann, 2001)], needed for planning the velocity-encoded MR scans. To obtain the velocity vector field of the intraventricular blood flow, a multislice spoiled gradient-echo (phase-contrast) sequence with velocity encoding in all three directions (Pelc et al., 1991) was acquired as follows. A radial stack of six imaging planes was positioned on the left ventricle (LV), with an interplane angulation of 30° and the radial axis of the stack going through the MV annulus and the apex (both found in a short-axis view), coinciding with the long axis of the LV (Fig. 1). In each consecutive imaging plane, velocity values were acquired in three directions, with a maximum velocity sensitivity value of 100 cm/s in each direction. The reconstructed velocity values in three directions represent the velocity vector components. Slice thickness of the imaging planes was 8 mm, field-of-view = 370 mm (60% rectangular), scan matrix = 128×102, with voxels of $2.89 \times 2.89 \times 8.0$ mm. The flip angle $\alpha = 10°$, $TR/TE = 5.8/3.5$; two signal averages were used to increase the signal-to-noise ratio. Retrospective cardiac synchronization was used, 30 phase images were reconstructed for one cardiac cycle. Typical examination time was 9–12 mins, depending on the heart rate.

Image Processing

In the modulus images, the myocardial wall is segmented from the LV blood pool by manual contour drawing. This is performed for each of the 30 phases and each of the 6 slices and copied to the velocity-encoded images, resulting in the velocity vector field of the intraventricular blood flow. The velocity vectors inside the LV were constructed from the three components of the velocity values measured inside these contours.

Also, in the modulus images of each of the phases and each of the slices, the position of the MV was indicated manually by positioning a line on the valve leaflets during systole and on the annulus during diastole, perpendicular to the inflow direction. The center of the MV line was placed on the center of the annulus (where the radial axis of the six acquisition planes intersects the MV annulus). For each time phase, the velocity components perpendicular to each of the six MV lines were projected onto a single two-dimensional (2D) plane, representing the MV plane. The center of each of the six lines is positioned in the center of this MV plane. Triangular interpolation between the sample points on the six lines was used to obtain velocities for the complete 2D MV plane (Fig. 2A).

To obtain the transvalvular velocity of the blood flow, the velocities measured perpendicularly to the reconstructed MV plane have to be corrected for the motion of the myocardium in basal/apical direction. Information needed to perform this correction was obtained from the two- and four-chamber acquisitions. On these images, the annulus of the MV was indicated manually. From the position of the MV annulus at each phase, the displacement of the valve between the phases of the cardiac cycle was determined. Its through-plane velocity was obtained by dividing the displacement of the annulus over the time step between the phases (i.e., the temporal resolution of the two- and four-chamber acquisitions). This velocity value was subtracted from the through-plane velocities measured at the reconstructed plane, resulting in velocity values with respect to the MV annulus. Finally, the transvalvular volume flow is obtained after manually drawing a contour in the reconstructed velocity image of each phase, containing the transvalvular velocities

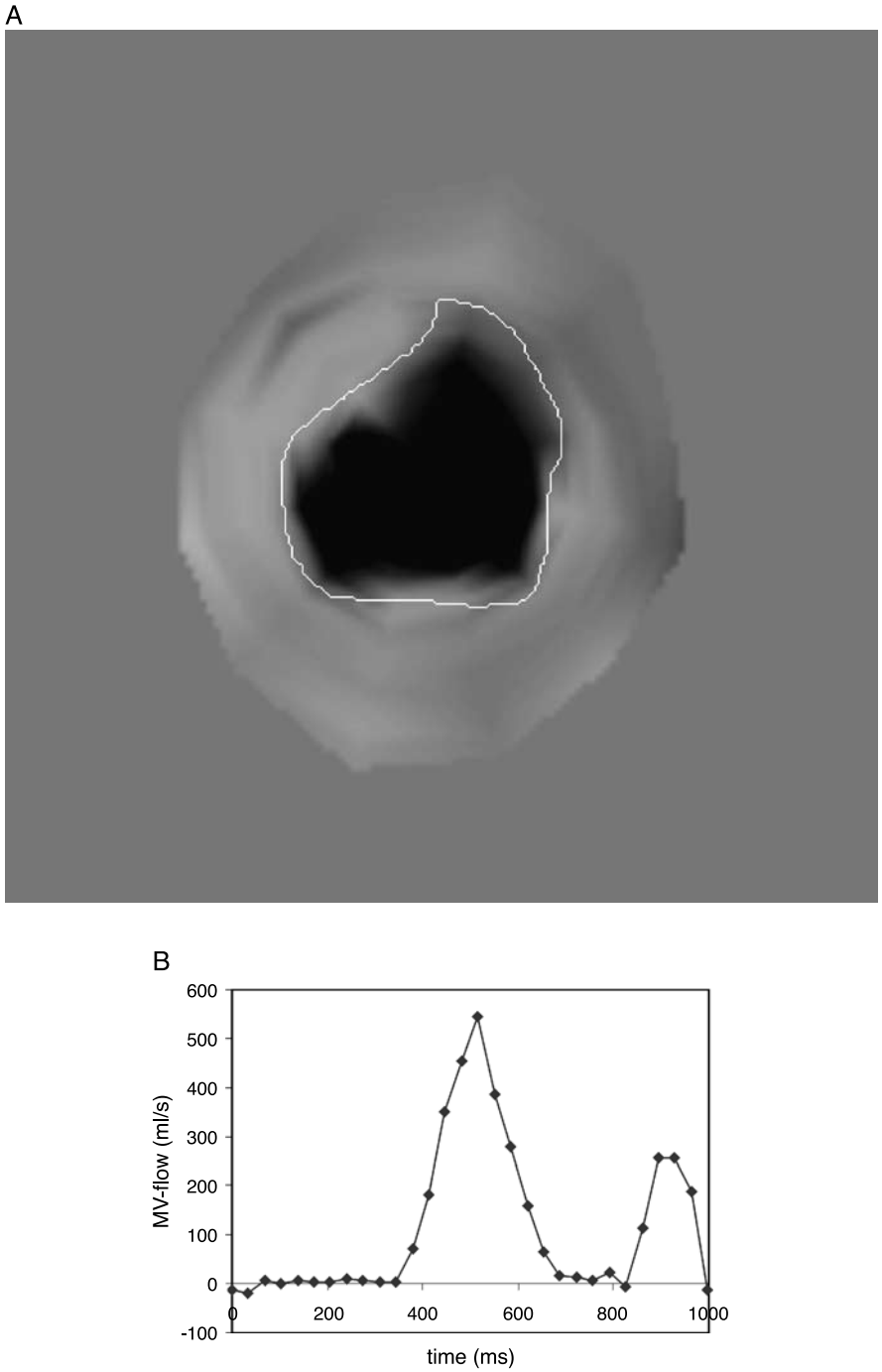

Figure 2. A moment of early diastole (A). By drawing a region of interest, the velocity through the MV can be determined. The flow is calculated by integration. The flow graph is obtained by performing flow measurement in all time phases (B).

and then integrating these velocities over the area. A flow graph of the transvalvular flow during one cardiac cycle can be plotted (Fig. 2B). Finally, the MV-flow volume can be obtained by calculating the Riemann sum of the flow graph (i.e., discretized approximation of calculating the area under the flow graph).

Validation

For each volunteer, the MV-flow volume determined with the new method described above (from hereon noted as the ''3-dir MV flow'') was validated by comparing it with the flow volume measured with

MRI at the ascending aorta [described by Van der Geest et al., 1998], referred to as the AO-flow volume. The same MRI acquisition protocol was used as described above, but now with a single imaging plane positioned perpendicular to the ascending aorta. Also, only the velocity values in through-plane direction, perpendicular to the acquisition plane, were considered. The aortic flow was determined using the FLOW software (Medis, Leiden, the Netherlands) (Van der Geest et al., 1998).

Also, for each volunteer, the 3-dir MV-flow volume was compared with the conventional through-plane MR flow volume measurement described by (Kayser et al., 1997). The same imaging protocol was used as described above, with the single imaging plane positioned at the MV during end-systole. Only the velocity values in through-plane direction were considered. Again, for measuring the MV flow, the FLOW software was used, under condition that correction for through-plane motion was performed (Kayser et al., 1997). The through-plane velocity of the myocardium is assessed in a region of interest, drawn inside the myocardium for each of the phases, by measuring the mean velocity inside this region of interest. The velocity of the myocardium in basal/apical direction was subtracted from the velocity measured at the opening of the MV. Again, the flow can be determined by integrating the velocities over an area, indicated by an observer. The MVflow volume is obtained from the Riemann sum of the flow graph during one cardiac cycle. The MV-flow volume measured with this method, is referred to as the ''1-dir MV-flow volume.''

Statistical Analysis

Correlations between the AO-flow volume measurement and both the conventional 1-dir MV-flow volume and the new 3-dir MV-flow volume were tested by calculating the Pearson correlation coefficient, r_P, under the assumption that the parameters were distributed normally. This assumption was tested with Kolmogorov–Smirnov tests. The approach described by Bland and Altman (1986) was followed to study the differences between both MV-flow volume measurements and the AO-flow volume. The mean differences were determined and the statistical significance of these differences was tested by a paired-samples *t*-test.

The reproducibility of the interpretation of the velocity images, acquired with the new 3-dir MV-flow method, was tested by inter- and intraobserver studies. Two observers (JW, MD) analyzed the 3-directional MR velocity-encoded images to study interobserver variation; one observer (JW) analyzed the images twice, with an interanalysis time of more than one week, to study intraobserver variation. Accuracy and reproducibility were investigated by performing paired samples *t*-test and determining the Pearson correlation coefficient r_P for the repeated measurements.

Clinical Example

The clinical applicability is illustrated by presenting data of two patients with MV regurgitation (one female, 35 years; one male, 43 years). Regurgitation was proven from TEE. The same MR examination was performed as used for the volunteers. The MV regurgitation was determined from the 3-dir MV-flow measurement. The AO-flow volume was used for comparison.

RESULTS

In ten volunteers without cardiac valvular disease (confirmed by TTE and TEE), the transvalvular MV-flow volume was measured with MRI. This was done with the conventional 1-directional, through-plane velocity-encoded MRI (1-dir MV flow), as well as with the new method, 3-directional velocity-encoded MRI (3-dir MV flow). Both flow volume measurements were compared to the flow volume measured with 1-directional through-plane velocity-encoded MRI measured at the aorta (AO flow). The results are presented in Fig. 3. Kolmogorov–Smirnov tests prove that the data of each of the parameters is distributed normally ($p=0.84$ for 1-dir MV flow, $p=0.99$ for 3-dir MV flow, $p=0.89$ for AO flow). The correlation between the MV-flow volumes acquired with both

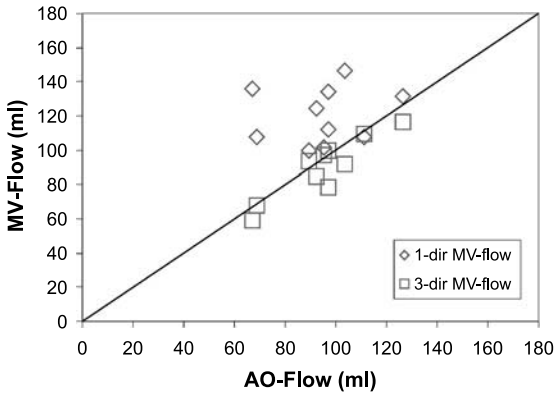

Figure 3. MV-flow volume measurement with the conventional 1-dir MV-flow method and the new 3-dir MV flow method, respectively. The MV-flow is compared with the flow measured at the aorta.

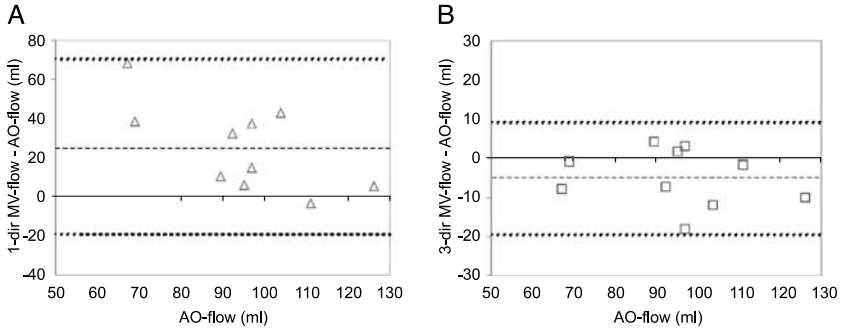

Figure 4. Bland-Altman analysis for studying the differences between the MV-flow volume [determined with the 1-dir MV-flow method (A) and the 3-dir MV-flow method (B), respectively] and the AO flow. The 1-dir MV flow shows a statistically significant overestimation compared to the AO flow. The 3-dir MV flow is not statistically significantly different. The dashed lines represent the mean differences, the dotted line determines the 95% confidence intervals.

methods and the AO-flow volume is tested with Pearson correlation coefficients. The correlation between the 1-dir MV-flow volume and the AO-flow volume is not statistically significant ($r_P=0.15$, $p=0.68$), whereas the correlation between the 3-dir MV-flow volume and the AO-flow volume is statistically significant: ($r_P=0.92$, $p<0.01$).

Differences between the MV-flow volume and the AO-flow volume were studied and conform to the theory of Bland and Altman (1986). The results are presented in Figs. 4A and 4B, respectively. From Fig. 4A, it is clear that the 1-dir MV-flow volume shows an overestimation compared to the AO-flow volume. The mean difference ± standard deviation = 25 ± 22 ml, and this difference is statistically significant ($p<0.01$). From Fig. 4B, no systematic difference between the 3-dir MV-flow volume and the AO-flow volume was found. The mean difference ± standard deviation = −5 ± 7 ml ($p=0.06$).

For studying the reproducibility of the results obtained from analysis of images from the new 3-dir MV-flow method, an intra- and interobserver study was performed. For the intraobserver study, one observer studied the images twice, with an interanalysis time >1 week. The results are presented in Table 1. There is very good correlation between the flow volumes from both analyses, ($r_P=0.97$, $p<0.01$). The differences between both analyses were studied conform Bland and Altman (1986), and are also presented Table 1. There is no statistically significant difference between both analyses ($p=0.61$). The mean difference ± standard deviation is 0.9 ± 5.1 ml.

For the interobserver study, also a second observer performed the image analysis, and the results were compared with the results of the first analysis of the first observer (also Table 1). There is an excellent correlation between the flow measurements from both observers, ($r_P=0.96$, $p<0.01$). The differences are compared to the mean 3-dir MV-flow volume of both analyses. There is no statistically significant difference between the results from both observers ($p=0.49$). The mean difference ± standard deviation is 1.3 ± 5.6 ml.

Table 1. Statistical analysis of the intra- and inter-observer study.

	Observer 1 2nd	↔	Observer 1 1st	↔	Observer 2
Kolmogorov–Smirnov	$p=0.98$		$p=0.99$		$p=0.43$
Pearson correlation		$r_P=0.97$ ($p<0.01$)		$r_P=0.96$ ($p<0.01$)	
Paired t test		$p=0.61$		$p=0.49$	
Mean difference		0.9 ml		1.3 ml	
Standard deviation		5.1 ml		5.6 ml	

Observer 1 performed the analysis twice. The results of both analysis are compared. The results of the first analysis by observer 1 are compared with the results from the analysis of observer 2. To study differences, a paired t test is performed. Correlation is investigated by Pearson's correlation coefficient.

Clinical Example

Two patients with proven MV-regurgitation (confirmed on TEE) were investigated with the same MR examination as was used for the volunteers. In Fig. 5A, a four-chamber MR image of a female patient (35 years) is shown, representing a systolic phase. The arrow indicates the regurgitant jet, flowing from the MV into the left atrium. In Fig. 5B, the reconstructed velocities through the MV are represented for the same phase. The area with regurgitant flow is clearly discriminated. The flow through the MV is measured for each time phase and presented in Fig. 5C. The regurgitant flow volume (i.e., negative flow value in the graph during systole) amounts to 9 ml. The diastolic forward flow volume for this patient amounts to 86 ml, yielding a regurgitant fraction of 10%. Comparing the effective forward flow volume through the MV with the flow volume measured at the aorta (i.e., 81 ml), good agreement is found for this patient. A second case (male, 43 years) also shows good agreement: regurgitant flow volume = 23 ml, diastolic MV flow volume = 101 ml (regurgitant fraction of 23%) and aortic flow volume = 79 ml.

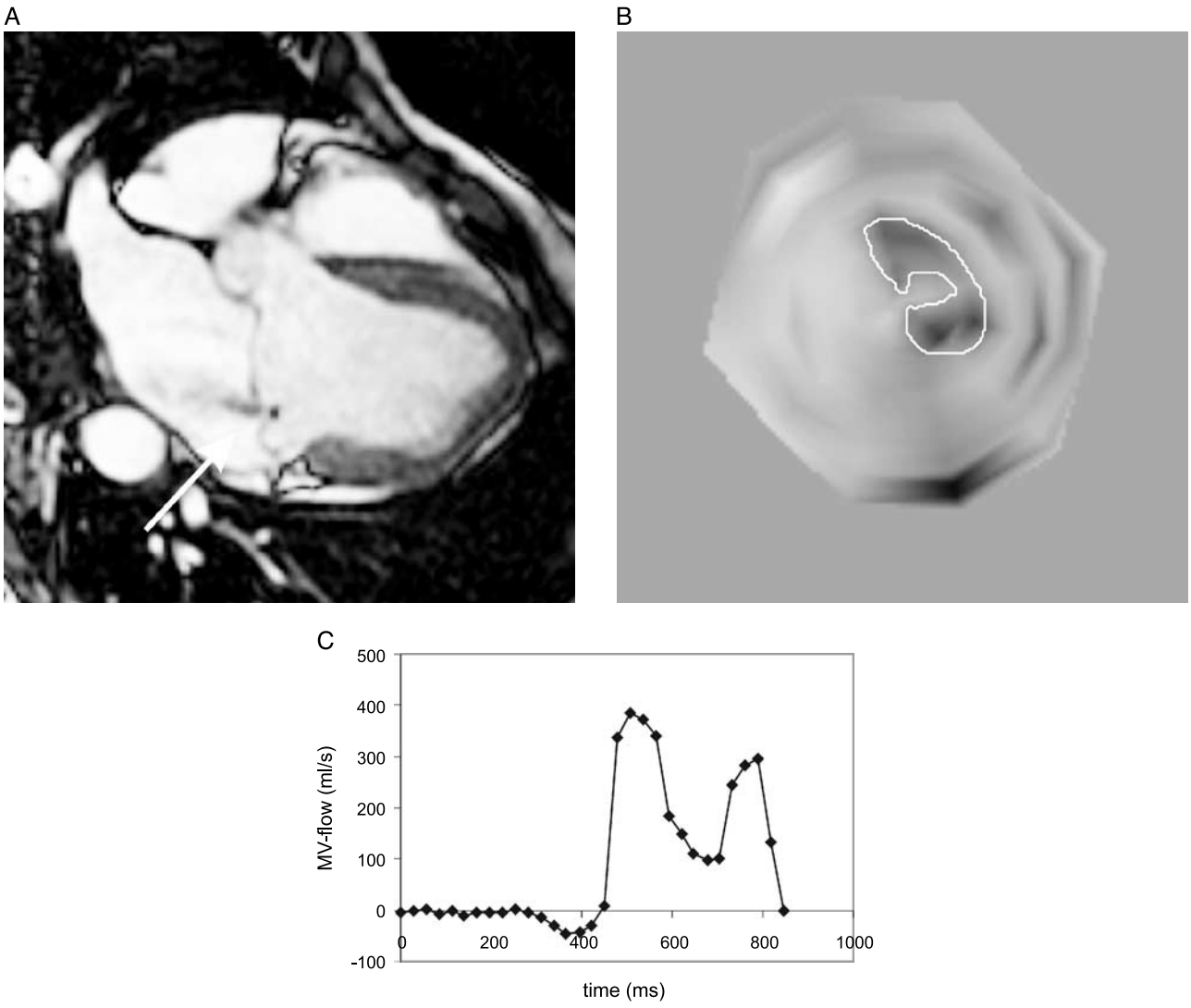

Figure 5. Clinical applicability. A four-chamber MR image of a female patient (35 years), representing a systolic phase (A). The arrow indicates the regurgitant jet, flowing from the MV into the left atrium. The reconstructed velocities through the MV are represented for the same phase (B). The area with regurgitant flow is clearly discriminated. The flow through the MV is measured for each time phase (C).

DISCUSSION

Kayser et al. (1997) demonstrated that myocardial motion correction is mandatory for obtaining accurate transvalvular flow values with single-slice 1-directional velocity-encoded MRI. The motion of the myocardium due to the contraction and relaxation in the same direction of the flow through the MV (i.e., the through-plane motion for 1-dir MV flow) will result in an offset in the velocities measured at the location of the MV annulus. By measuring the through-plane velocity of the myocardium in a region of interest, positioned inside the myocardial wall and subtracting this velocity from the velocities measured at the MV-annulus, motion correction is performed. This motion correction is not sufficient to guarantee that the acquired flow equals the transvalvular flow, though. The single acquisition plane is positioned at the location of the MV at end-systole. Because this plane has a fixed position and is not adapted to the cardiac motion, the acquisition is performed inside the LV during most part of the cardiac cycle. In this study, the MV-flow volume measured conform the method of Kayser et al. (i.e., 1-dir MV-flow volume) was compared to the flow volume measured at the aorta. No statistically significant correlation was found. The 1-dir MV-flow volume showed a statistically significant overestimation compared to the AO-flow volume. This illustrates that the 1-dir MV-flow method, although readily applied in clinical studies (Kroft and de Roos, 1999; Rebergen et al., 1996), is not recommended for accurate transvalvular MV-flow measurement.

Kozerke et al. (1999) introduced a new acquisition method for a single-slice flow measurement at the aortic valve, with the acquisition plane adapted to the heart motion (STrack). The acquisition plane follows the basal level during the cardiac cycle, and after myocardial through-plane motion correction, this results in an accurate transvalvular flow measurement. A disadvantage of their method is the necessity of prospective triggering, resulting in an incomplete acquisition of the cardiac cycle. The final part of the RR-interval cannot be acquired and is ignored. For MV-flow measurement, acquisition of the complete diastole is mandatory. For regurgitation studies, the complete systole and diastole need to be acquired. When studying transvalvular MV flow, the use of retrospective gating is preferred over prospective triggering. Another disadvantage of the method proposed by Kozerke et al. (1999) is that the acquisition software is not available on all commercially available MRI scanners.

In our study, a new method was introduced to assess the true transvalvular MV-flow. No dedicated scanning software is required to apply this protocol. The complete velocity vector field of the blood flow inside the LV, acquired with 3-directional velocity-encoded MRI using retrospective gating, was obtained and reconstructed to 30 time phases covering one average complete cardiac cycle. Retrospectively, the position of the MV in this velocity vector field was indicated manually for each time phase, and from this, the flow through the MV was acquired. The velocities in the MV-plane were corrected for the through-plane motion of the myocardium in the apical-basal direction, perpendicular to the MV-plane itself. Integrating the velocities over the area of the MV annulus (indicated manually) resulted in the MV flow.

Because of time limitations, it is impossible to acquire the complete transvalvular flow with slices oriented parallel to the long axis. Therefore, the flow is acquired with a radial stack of six acquisition planes. The axis of the radial stack is positioned in the center of the mitral annulus. This means that in the blood flow in the center of the mitral annulus will be densely sampled. In the outer part of the mitral annulus, the flow is not sampled in all the parts of the mitral annulus. The acquisition voxels in the plane of the mitral annulus have dimensions of 2.89 mm $\times$ 8 mm. For a circular-shaped mitral annulus with a 40-mm diameter, 62% of the area of the annulus will be covered with acquisition voxels. In reality, the area of the annulus will not be circular shaped and therefore, smaller. The nonsampled parts of flow through the annulus will be reconstructed by triangular interpolation.

This method was applied to obtain the MV-flow volume in 10 healthy volunteers. The 3-dir MV flow showed very good correlation with the AO flow. The differences between the flow volumes from both methods were very small and not statistically significant.

When comparing the MV-flow volume to the AO flow volume, the flow to the coronaries has to be taken into account. The AO flow was acquired at a level distal to the branches of the coronaries. This implies that the AO-flow volume measured at this location will be smaller than the MV-flow volume. In our study, this small systematic difference was not detectable. The contribution of the flow to the coronaries, only 0.5% of the cardiac output (Mymin and Sharma, 1974), was too low to be detected by this method.

A high reproducibility for flow quantification with 3-dir MV flow was found. The manual interaction during image analysis was performed twice by one observer with an interanalysis time >1 week. Excellent correlation between both analyses was found and the differences between the analyses were small and not statistically significant. The interobserver study showed similar results, i.e., very high correlation between observers and small, not statistically significant differences.

Limitations

The new 3-dir MV-flow method enables accurate and reproducible quantification of the true transvalvular MV-flow in a patient-friendly and easy-to-use manner. This method can be applied on most commercially available MRI scanners. Data of two patients with MV regurgitation illustrate the clinical applicability of this method. The acquisition of the radial stack of six imaging planes takes 9–12 min and depends on the patient's heart rate. Scout images, standard two- and four-chamber views, and a set of short-axis images are needed to plan the radial stack of slices. This process takes approximately 15–20 min of examination time. The manual postprocessing is currently the most laborious and needs to be automated before this method can be introduced in daily clinical practice. The reconstruction of the velocity vector field and the manual contour drawing, all needed for the flow analysis, can take up to 1 h per patient. The manual interaction does not result in large intra-or interobserver variations. Automating the manual processing (i.e., indicating the mitral valve in the long-axis images as well as the contour drawing in the reconstructed transvalvular velocity images) will result in a clinically applicable method.

Another limitation of the technique is the incomplete data acquisition of the transvalvular flow. The new 3-dir MV-flow method uses a radial stack of six acquisition planes, positioned on the LV parallel to the long axis, with the radial axis of the stack going through the MV annulus and the apex. This results in a dense sampling in the center of the annulus but sparse sampling at the edges. The velocities going through the MV plane are reconstructed from the sampled data and triangular interpolation is used for the area where no sampling has occurred. Because of this sampling strategy, small eccentric regurgitant jets can be overlooked when they occur in the region where no sampling is performed. The sampling strategy used is a trade-off with available examination time. Also, this is inherent to the limits of MRI flow quantification. It is difficult or impossible to quantify small flow jets with voxels of 2.89×2.89 mm. The two presented clinical cases show that it is very possible to quantify regurgitant MV flow accurately. Future studies investigating MV regurgitation are needed to give more insight on the limits of the new method.

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