Characterization of dysfunctional remote myocardium in left ventricular anterior aneurysms and improvements following surgical ventricular restoration using cardiac magnetic resonance imaging: preliminary results

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Abstract

OBJECTIVES: In patients with previous myocardial infarction, the remote uninfarcted regions, although contractile, demonstrate dysfunctional wall kinetics because of increased afterload, which improves after surgical ventricular restoration (SVR). We characterized left ventricular (LV) mean myocardial velocity (MMV) through an analysis of endocardial motion and wall thickening (WT) over the cardiac cycle using standard cardiac magnetic resonance (cMR).

METHODS: LV endocardial motion and WT from cMR data in 7 heart failure (HF) patients with postinfarction antero apical aneurysm were compared against normal controls to establish a baseline for the mean myocardial velocity during phases of the cardiac cycle. The HF patients’ MMV and WT curves were compared with post-SVR data.

RESULTS: Global MMV showed significant postoperative improvements in the ejection phase of systole and the early filling phase of diastole. The aneurysmal wall was dyskinetic in both systole and diastole. The remote myocardium preoperatively had a delayed peak velocity during the ejection phase of systole and diminished velocity during early filling in diastole. After SVR, the remote myocardium had an increased MMV with an earlier peaking during the ejection phase and slightly improved early diastolic velocity. WT increased cumulatively during systole and decreased during diastole with improved end-systolic and end-diastolic wall thickness after SVR. The end-systolic wall thickness showed a significant correlation with left ventricular ejection fraction ($r^2 = 0.89$, $P = 0.001$) and stroke volume ($r^2 = 0.80$, $P = 0.02$). The MMV had a significant correlation with WT over the phases of the cardiac cycle ($r^2 = 0.953$, $P \leq 0.0001$).

CONCLUSIONS: In patients with chronic ischaemic heart disease with LV aneurysms/large areas of scar, improvements in the remote myocardial MMV and WT underline LV systolic function improvements after SVR. The persistence of myocardial WT in early diastole is the likely mechanism for incomplete or absence of relief of LV diastolic dysfunction by SVR.

Keywords: Aneurysm • Cardiac volume • Ventricles • Imaging
examination in patients with ischaemic cardiomyopathy, both pre- and post-SVR, is ‘Grade 2 or ‘abnormal relaxation’ pattern [4], corresponding to a reduced protodiastolic LV filling. Very few researchers have examined myocardial mechanics during this phase of the cardiac cycle. The analysis of LV twist by means of cardiac magnetic resonance (cMR) has shown a reduced diastolic untwisting rate in patients with dilated cardiomyopathy only partially relieved by SVR [5].

SVR mainly comprises surgical decrease in LV end diastolic volume (EDV), with resultant increases in the left ventricular ejection fraction (LVEF), which have been assessed as a surrogate of improved systolic shortening and contractility. However, this might be an erroneous assumption because after an ‘iatrogenic’ EDV reduction, an increase in ejection fraction (EF) cannot be simply attributed to an improved LV contractility. The chronological assessment of myocardial velocities in systole and diastole might give a better quantification of systolic and diastolic function. This can be used to define optimal/suboptimal exclusion of dysfunctional myocardium constituting the infarcted area by determining remote myocardial kinetics after SVR.

Using standard cMR, we characterized MMV through a systematic analysis of 4D (3D + time) endocardial motion and of myocardial wall thickness over the cardiac cycle, to assess the effects of SVR on myocardial performance.

MATERIALS AND METHODS

**Study subjects**

We studied 7 patients diagnosed with ischaemic cardiomyopathy with anterior LV aneurysms. All patients had a past history of ST elevation myocardial infarction and had received pharmacological thrombolytic therapy. Inclusion was based on Q-waves on the surface electrocardiogram (ECG) and regional wall motion evaluation by 2D echocardiography. All patients were subjected to cMR studies detailed in the sections below. The studies were done before and 6 weeks following SVR. The institutional review board approved the study. To establish a baseline for novel shape-derived metrics of endocardial motion, the mean myocardial velocity (MMV) and the myocardial wall thickening (WT) and thickness were compared with seven normal age- and sex-matched controls.

**Surgical technique**

We modified the technique of endoventricular patch plasty by making the patch linear to address the dyskinetic/akinetic area, and adding a Teflon-buttressed linear repair to the ventriculotomy site. The LV cavity was opened by a linear incision parallel to the left anterior descending (LAD) artery. The residual LV cavity was assessed visually. We did not use any residual LV-cavity measuring devices. Instead, we used cMR analysis, which gave an accurate estimate of the residual LV cavity. A 3- to 10-cm linear Hemashield patch was used for infarct exclusion. Demarcation of the infarct zone was not done by any means; we did not plicate the border zone. The linear patch was sutured to the border zone into the LV cavity, which excluded the infarcted areas of the myocardium and had an oblique lie from base to apex (Fig. 1). This patch was not preformed and, hence, was individualized to each ventricular volume and geometry. The ventriculotomy site was closed with a Teflon-buttressed linear repair. Concomitant CABG was performed in 5 patients who received 2 ± 1.2 grafts. Additional mitral valve repair was done in 3 patients by rigid annuloplasty.

**Figure 1:** The rectangular intraventricular patch sutured to the border zone excluding the anterior scarred aneurysmal myocardium.

### Magnetic resonance imaging

Using a 1.5-T cMR, 8-Ch system (Philips-Achieva, Eindhoven, Netherlands) equipped with a 4-channel phased-array body radio-frequency (RF) coil, we performed magnetic resonance imaging (MRI) in standard short-axis and long-axis planes in two orthogonal directions for each plane. The imaging sequences analysed in this study included: ECG-gated 2D steady-state free precession cine cMR images from LV base to apex (8-mm-thick slices, zero spacing), both with and without RF tagging; as well as late Gadolinium enhancement. The extent of scarred regions from late gadolinium extraction images was characterized as a percentage scar extent for each patient, using Otsu’s method of thresholding, available in Medviso Segment. All studies had prospective ECG gating.

**Image analysis**

First, LV endocardial contours were extracted from MRI data using the Medviso Segment (MedvisoAB, Lund, Sweden), at each cardiac phase. Next, to establish a metric of intraventricular dyssynchrony, an in-house plug-in was developed in Paraview (Kitware, Inc., Clifton Park, NY, USA) to compute a signed Hausdorff distance [6, 7] at each endocardial surface point, characterizing phase-to-phase displacement—a velocity metric—that inherently establishes point correspondences between consecutive cardiac phases. Finally, phase-to-phase displacement histories of several uniformly spaced points were established based upon endocardial surface correspondences, thereby defining a metric of myocardial velocity at each cardiac phase. The displacement histories of each point were recorded.

The average and standard deviation (SD) in the endocardium-averaged displacement history characteristic curves for our cohort of HF patients and normal controls were compared over uniform intervals of the cardiac cycle to establish a baseline. The MMV was evaluated at uniformly spaced temporal instants through the
cardiac cycle. The cardiac cycle was defined by 6 standardized periods labelled as atrial contraction/late diastolic filling (AC), isovolumetric contraction (IC), ventricular ejection (VE), isovolumetric relaxation (IR), rapid ventricular filling (RVF) and diastasis. It was also possible to estimate the timing of contraction in milliseconds based on information in the DICOM image headers.

The myocardial WT was assessed by tracing both epicardial and endocardial contours by similar methods. The WT during the cardiac cycle phases was plotted (mm/phase). The cumulative WT, and the instantaneous wall thickness, which is an absolute wall thickness value during the cardiac cycle, were plotted (mm).

Following SVR, the MMV and myocardial WT of these 7 patients were compared with their baseline values at various phases of the cardiac cycle. We used the WT during the cardiac cycle phases and instantaneous wall thickness at end-systole and end-diastole for comparisons because they are more sensitive and specific indicators of dysfunctional myocardium during the cardiac cycle [8].

**Statistical analysis**

All continuous values were expressed as mean ± standard deviation (SD), and categorical variables as numbers (%). The Wilcoxon signed-rank test was used to compare the continuous variables between the baseline preoperative values and the same following SVR. Student’s t-test was used to compare the means and SD of preoperative MMV with MMV following SVR. The Pearson correlation coefficient was used to correlate the commonly used standard quantifications of systolic and diastolic LV function with the phases of MMV and WT. A P-value ≤0.05 was considered significant. SPSS v13 (SPSS, Inc., Chicago, IL, USA) was used for statistical analyses. Root mean square error nearing zero were considered similar to the compared control values and error nearing unity [9] were considered different from control values.

**RESULTS**

**Clinical outcomes**

The study cohort comprised 6 male patients and 1 female patient, with an age range of 45–70 years (mean age: 55.6 ± 12.9 years). All patients had a past history of anterior wall myocardial infarction corresponding to the LAD coronary artery occlusion. The interval from infarction to LV aneurysm diagnosis was 39.3 ± 13.3 months. The interval from the occurrence of myocardial infarction to cMR imaging was 41.8 ± 12.2 months. All patients presented with congestive cardiac failure-NYHA Class 3 ± 1.2. The baseline heart rate was 88 ± 2.5 beats per minute (bpm). There were no mortalities. All patients underwent cMR studies after 6 weeks of SVR. All patients improved clinically to NYHA Class 1.2 ± 0.8. Following SVR, all patients had a heart rate of 72 ± 4.5 bpm.

**Imaging results**

**LV geometry and function.** The mean EDV was 174.8 ± 100.4 ml/m² body surface area. All patients had large anterior LV aneurysms, which were ~30% of the LV volume. The mean

<table>
<thead>
<tr>
<th>Table 1: Mean and standard deviations of the phase-to-phase displacement velocities or mean myocardial velocities of patients with left ventricular aneurysms and controls</th>
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</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
</tr>
<tr>
<td>Systole</td>
</tr>
<tr>
<td>0.2162 ± 0.6268</td>
</tr>
<tr>
<td>0.1659 ± 0.5933</td>
</tr>
<tr>
<td>Diastole</td>
</tr>
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<td>-0.0405 ± 0.3703</td>
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<td>-0.0842 ± 0.4268</td>
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</table>

All values are in millimetres.

aneurysm volume over a cycle for the cohort was 40.1 ± 24.3 ml [i.e. total regional LV volume (RLV) <1 SD below the mean RLV per slice level], mean ESV = 161.8 ± 99.3 ml and mean EF was 18.2 ± 8.8%. The amount of scar was 40 ± 4%. Following SVR, the mean indexed end diastolic volume was 130 ± 35.01 ml and the mean indexed ESV was 42.6 ± 11.2 ml. The stroke volume increased from 27.6 ± 10.6 to 37.4 ± 11 ml (P = 0.06). The EF increased significantly to 29.8 ± 9.47% (P = 0.027).

**Global mean myocardial velocities**

When the global MMV for controls and HF patients were compared, there was a significant difference in the ejection phase velocities (P = 0.002), early filling diastolic phase velocities (P = 0.001) and the end-diastolic phase velocities (P = 0.01) (Table 1). Given that all our patients had similar baseline heart rates, correction for heart rate was not done. The MMV demonstrated positive systolic velocities and negative diastolic velocities in controls. It was noted that the IC phase was prolonged in patients. The ejection phase demonstrated lower myocardial velocities and extended into the IR phase. In diastole, the early filling phase had significantly lesser myocardial velocities as with the late filling phase. At end-diastole, there was a significantly lower myocardial velocity that extended into the beginning of the next cardiac cycle (Fig. 2).

The MMV in the ejection phase correlated significantly with the LVEF, \( r^2 = 0.98, P = 0.001 \). The MMV in the early filling phase of diastole correlated significantly with mitral inflow E-wave velocities by 2D Doppler echocardiography (\( r^2 = 0.86, P = 0.01 \)). MMV correlated significantly with myocardial WT velocities (\( r^2 = 0.953, P < 0.0001 \)). The systolic phase of the MMV correlated with the WT more significantly than the diastolic phase of MMV (\( r^2 = 0.66, P = 0.03 \) vs \( r^2 = 0.58, P = 0.14 \)). The global MMV following SVR was significantly greater than the baseline MMV during the ejection phase of systole (P = 0.04) and the early filling phase of diastole (P = 0.05) (Fig. 3).

**Regional mean myocardial velocity of remote myocardium and aneurysm**

When the regional MMV at the aneurysm and remote myocardial areas were assessed, the areas subtending the aneurysm were truly dyskinetic with the systolic ejection phase being negative and the diastolic phase of early and late filling being positive
The remote myocardium exhibited prolongation of the IC phase with delay to onset of peak ejection and decreased velocities during early rapid filling in diastole. The wall thickness analysis during the phases of the cardiac cycle demonstrated decreased WT in systole and decreased wall thinning in diastole, which was more pronounced in early diastole.

Regional MMV demonstrated that the patch, although akinetic, exhibited passive movements concordant with the remote myocardial movements predominantly in systole during the ejection phase (Fig. 3) (Table 2). The remote myocardium exhibited early onset of peak ejection with increases in myocardial velocities compared with preoperative values, with the MMV during ejection phase correlating positively with the improvements in the LVEF ($r^2 = 0.86$, $P = 0.02$). Improved velocity of early rapid filling during diastole was observed compared with the preoperative remote myocardial MMV (Fig. 3). This had a positive correlation with the amplitude of the E wave of the mitral Doppler ($r^2 = 0.82$, $P = 0.032$).
Wall-thickening analysis during systole

Following SVR, WT over the phases of the cardiac cycle was significantly greater than baseline values (0.649 ± 0.387; 0.877 ± 0.451, \( P < 0.0001 \)). The WT in systole improved following SVR, although was not statistically significant (0.034 ± 0.012; 0.037 ± 0.011, \( P = 0.229 \)).

The instantaneous wall thickness increased significantly from baseline at end-systole (\( P = 0.04 \)) and at end-diastole (\( P = 0.012 \)). The end-systolic wall thickness correlated significantly with the LVEF at baseline and after SVR (\( r^2 = 0.89, P = 0.001 \)).

Diastolic function assessment from wall-thickening analysis

At baseline, the onset of diastolic wall thinning was delayed far beyond mitral valve opening and was prolonged as evidenced by flattening of the diastolic curve (Fig. 4).

<table>
<thead>
<tr>
<th></th>
<th>Preop</th>
<th>Postop</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systole</td>
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<td>0.4495 ± 0.6415</td>
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</tr>
<tr>
<td></td>
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<td>0.4742 ± 0.6926</td>
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<td>0.1699 ± 0.5933</td>
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<td>0.03</td>
</tr>
<tr>
<td>Diastole</td>
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<td>−0.042 ± 0.5362</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>−0.1483 ± 0.6671</td>
<td>−0.064 ± 0.5532</td>
<td>0.04</td>
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<td></td>
<td>−0.1498 ± 0.6987</td>
<td>−0.0847 ± 0.571</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>−0.1246 ± 0.6797</td>
<td>−0.1032 ± 0.5846</td>
<td>0.04</td>
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</table>

All values are in millimetres.

DISCUSSION

The visual assessment of regional wall motion abnormalities, which characterize ischaemic heart disease, is subjective, whereas quantification of regional myocardial velocities both during systole and diastole defines an objective parameter of regional myocardial kinetics [11]. Several imaging methods have been used to quantify regional wall motion abnormalities that correspond to the assessment of MMV [8, 12–14]. Quantification of myocardial WT during the cardiac cycle is a specific objective parameter of dysfunctional myocardium and is additional to the MMV [15–18].

Application of mean myocardial velocity in left ventricular aneurysms

All our patients had predominant dyskinetic anterior LV aneurysms, although all had received pharmacological thrombolysis. The
increases in the LVEF following SVR are not as dramatic, with non-significant changes in the LV stroke volume that are not indicative of improved LV contractility [9]. The demonstration of improvements in LV contractility will need pressure-volume studies that are not feasible in large patient cohorts. We have documented the benefits of MMV assessment as an objective parameter of regional myocardial velocity during the various phases of the cardiac cycle. Regional parameters such as regional LV volumes and regional LVEF have been used to document LV shape distortions and regional LV systolic function [19]. We have correlated MMV with LVEF and E-wave velocity in the Doppler mitral inflows to validate the MMV in accurate delineation of LV systolic and diastolic functions. This analysis, although labor intensive, has distinct benefits in application for patient selection for SVR, and to assess the success of SVR.

Characterization of regional myocardial characteristics by mean myocardial velocity preoperatively and their improvements after surgical ventricular restoration

The preoperative MMV demonstrated a prolonged remote myocardial IC that extended into the peak ejection phase with a reduced velocity of peak ejection, whereas the IR was also prolonged and extended into the peak filling phase. This regional MMV assessment clearly delineates the myocardial velocities in the aneurysm and the subtending remote myocardium, which is critical for SVR, especially in dilated akinetic LVs. The presence of contractile myocardium is essential for the success of SVR and, in patients with predominantly akinetic aneurysms, it is vital to assess the remote myocardial characteristics.

Following SVR in our patients, there was a significant improvement in the systolic phase of the MMV that became more positive, and significant improvements in the early and late diastolic MMV that became more negative. The improvements could be clearly discerned in the early systolic peaking of the MMV and increased peak systolic velocity of the remote myocardium when compared with the baseline and with the early diastolic dip and increased velocities of early and late diastolic filling. The intraventricular patch, although passive, tended to move in consonance with the remote myocardium, especially in systole, which is similar to the tethering effect of the necrotic scar observed in myocardial infarction.

Regional wall thickening in left ventricular aneurysms and characterization of left ventricular systolic and diastolic functions following surgical ventricular restoration

The end-systolic wall thickness and end-diastolic wall thickness improved significantly following SVR, indicating improvements in the remote myocardium, which was dysfunctional at baseline. The WT over the phases of the cardiac cycle demonstrated improvements in systole, although not statistically significant. The WT analysis during diastole delineated the persistence of mild diastolic dysfunction after SVR. The improvement of the echocardiographic diastolic filling pattern despite the unchanged or even increased WT, might be related to the marked decreases in EDV, which shift the pressure/volume relationship to a less steep tract of the curve [20], improving mitral flow velocity in both proto- and end-diastole. Thus, the diastolic WT could be considered a more sensitive marker of LVDD Grade 2, unmasking the normal Doppler mitral inflow pattern following SVR. In patients with more dilated LV and Grade 3 diastolic dysfunction by 2D echocardiographic examination before SVR, the sharp reduction of the EDV likely improves ventricular interdependence [21]. The effects of mitral valve repair on the remote myocardial kinetics are distinct from those of SVR alone, but, in our patient cohort, we were limited by the small sample size (n = 7, of which only 3 patients received additional mitral valve repair) for a meaningful analysis.

Di Donato et al. [22] have documented inferior wall curvature changes after SVR for LV anterior aneurysms by centreline analysis on contrast ventriculography. The disappearance of the negative curvature of the remote myocardium at the inferior wall seen at baseline in dyskinetic anterior aneurysms defined normalization of the LV shape after SVR and normalization of remote myocardial mechanics by improvements in systolic shortening. cMR allows a 3D analysis of myocardial wall mechanics, both in systole and in diastole, taking into account endocardial movements and WT.

The remote myocardial MMV assessment will also help validate optimal/suboptimal infarct exclusion by SVR. This will have application for SVR in predominantly akinetic aneurysms.

Limitations

Given that our sample size was small, we could not establish quantitatively the effects of SVR on diastolic function. We also do not have volume–time data in our patients because of logistic constraints, the inclusion of which would have validated our diastolic MMV and WT findings, contributing to a better understanding of the diastolic function abnormalities. We have also not conducted viability studies and, hence, cannot assess the effects of revascularization separately on remote myocardial functional improvements. The inherent limitations of MMV are that it was not possible to delineate the regional MMV and WT corresponding to the AHA 17 segment LV polar plot. We have studied a small sample size of 7 patients with predominantly dyskinetic aneurysms. Our results demonstrate the remote myocardial kinetics after SVR. This has potential clinical applications in patients with predominantly akinetic LV aneurysms. We will expand our study to a larger cohort that will include patients with akinetic aneurysms to demonstrate the benefits of regional MMV.

CONCLUSIONS

Our preliminary results in patients with predominantly dyskinetic anterior aneurysms are that, following SVR, MMV and WT improved significantly both in systole and in diastole. The beneficial effects of SVR on systolic LV function are evidenced by early onset and increased peak systolic velocities of the remote myocardium. Myocardial WT suggests that an active abnormal myocardial contraction (late and sustained shortening, more than slow relaxation) decreases optimal early LV diastolic filling, reflecting the presence of a subtle diastolic function. These findings will be verified in a larger prospective study.

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REFERENCES


