Interaction between left ventricular wall motion and intraventricular flow propagation in acute and chronic ischemia

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Edvardsen, Thor, Olaf Rodevand, Knut Endresen, and Halfdan Ihlen. Interaction between left ventricular wall motion and intraventricular flow propagation in acute and chronic ischemia. Am J Physiol Heart Circ Physiol 289: H732–H737, 2005.—Myocardial ischemia has been associated with left ventricular (LV) postsystolic shortening. The combination of tissue Doppler imaging and high frame-rate acquisition of two-dimensional color flow makes it possible to study the interaction between LV wall motion and intraventricular flow propagation. The aim of this study was to examine in a clinical model the impact that acute myocardial ischemia and prior myocardial infarct might have on LV flow patterns and to explain the underlying mechanisms from the tissue Doppler data. LV flow propagation and tissue velocities during early diastole were studied in 18 healthy individuals, 17 patients with prior anterior myocardial infarct, and 16 patients before and during percutaneous coronary intervention (PCI) of the left anterior descending artery. Normal individuals had intraventricular flow propagation toward the apex during isovolumic relaxation. During this early diastolic time phase, myocardial velocities measured at mid- and apical septal segment were directed away from the apex. Before PCI, patients without myocardial infarction had similar findings as in normal individuals. In contrast, each patient with either prior myocardial infarction or PCI-induced acute ischemia had flow propagation opposite to normal individuals, and tissue velocities reversed toward the apex during early diastole. Reversal of early diastolic LV flow propagation in acute and chronic anterior myocardial ischemia reflects postsystolic shortening in the dyskinetic apical and septal myocardial segments.

MATERIALS AND METHODS

Control group. Eighteen healthy individuals were recruited from the hospital staff. None had a prior history of cardiac disease. LV function was normal as evaluated from echocardiography.

Myocardial infarct group. Seventeen patients with prior anterior myocardial infarct were included. All had diameter stenosis of more than 50% in the left anterior descending coronary artery (LAD), except for two patients that did not have significant stenosis. LV dysfunction corresponding to the LAD territory was present at rest as demonstrated by the ventriculogram or echocardiography. Normal myocardial function was found in the other LV regions.

Acute ischemic group. Sixteen patients with stable angina undergoing percutaneous coronary intervention (PCI) were included in this group. All had significant diameter stenosis (>50%) of the LAD without any LV dysfunction at rest. In addition, five patients had significant stenosis of the circumflex artery, and eight had stenosis of the right coronary artery (RCA). The lesion in the LAD was always treated first by angioplasty. Patients with significant collateral arteries were not studied to ensure that PCI created significant myocardial ischemia. No patients had a history or findings of valvular heart disease. All were in regular sinus rhythm. Clinical and hemodynamic characteristics of all study subjects are presented in Table 1. The regional ethical committee on human research approved the study. Written informed consent was given by all individuals.

Cardiac catheterization. Standard left heart catheterization with coronary angiography was performed in all angina patients and in those with prior anterior myocardial infarction. LV ejection fraction was calculated using a single plane ellipsoidal formula. PCI of the LAD stenosis was performed in those with angina pectoris by using the standard approach. The balloon inflations lasted 30–120 s. Coronary stenting was performed in 14 patients.

Echocardiography. Studies were performed with a System Five system (GE Vingmed Ultrasound, Horten, Norway). All echocardiographic images of the left ventricle were obtained from the apical four-chamber view with a visualization of the aortic valve at rest and during the balloon inflation. This scanner enables visualization of low-velocity, 2-D blood flow, and the low-velocity filter was set at 4
cm/s to obtain color flow maps during IVR (6). The duration of IVR was measured by standard pulsed Doppler methods. Color M-mode recordings of LV inflow were performed from the LV base to the apex.

TDI measures were performed in the apical and midslices of the septal and lateral walls. Myocardial longitudinal velocity vectors were displayed as color-coded images superimposed on the 2-D gray scale echocardiographic images in real-time display as previously described (7). The color-coded tissue velocities were decoded to numeric values (Echopac, GE Vingmed). Image acquisitions in the acute ischemia group were performed before, during, and after balloon inflation.

**Data analysis.** The IVR period in the 2-D color flow recordings was defined as the period between the closure of the aortic valve with interrupted outflow and the mitral valve opening associated with the start of inflow velocities. The image frames from the start to the end of IVR were examined for the extent and direction of intraventricular flow. The largest unidirectional flow area was traced from the apical septal and lateral walls. Myocardial longitudinal velocity vectors were analyzed statistically significant if the value was *P* < 0.05 compared with normal individuals; †*P* < 0.001 compared with acute ischemia; ‡*P* < 0.001 compared with normal individuals.

**RESULTS**

All recordings were of technically acceptable quality. Intraventricular flow propagation and TDI measures could be obtained from all individuals at rest and in patients during acute ischemia. The frame rate obtained during flow recordings was 32 ± 6 and 96 ± 10 frames/s during TDI recordings. On average, 3.8 ± 1 frames of flow images were imaged during the IVR period.

There was a strong inverse linear correlation between intraventricular flow velocities and tissue velocities from midseptal segment during IVR (*r* = 0.75, *P* < 0.05) (Fig. 1). This relationship was also found between apical septal velocities and flow (*r* = 0.75, *P* < 0.001).

**Healthy individuals.** During the IVR period, intraventricular flow propagation was directed toward the apex in all individuals (Table 2). Flow was present through most of the period, but the velocities varied in different parts of the ventricle. The mean area of the apical-directed flow was 9.0 ± 4.4 cm². In accordance with the flow propagation, all healthy participants demonstrated a dominant peak myocardial velocity at midseptal level directed away from the apex during IVR (V_{IVR}) −2.0 ± 1.4 cm/s. The corresponding velocity in the lateral midsegment was −1.7 ± 0.8 cm/s [not significant (NS)]. There was no difference between tissue velocities in septum and the lateral wall when measured at the apical LV level (−1.0 ± 0.7 and −1.0 ± 1.0 cm/s, NS).

**Anterior myocardial infarct.** In contrast to the findings in normal individuals, the intraventricular flow was directed away from apex and blue encoded during IVR in patients with prior myocardial infarct. This reversed flow was mostly confined to the apical two-thirds of the left ventricle in all patients with LV dysfunction. The mean area of the flow directed to the LV base was −8.3 ± 4.8 cm². This was in accordance with the TDI findings that demonstrated postsystolic shortening with myocardial velocities directed toward the apex (2.4 ± 1.2 cm/s, *P* < 0.001, midseptal segment compared with healthy individuals). Apical TDI velocities from the LV septum and lateral wall showed in principle the same findings and were reversed (1.5 ± 0.7 and 0.7 ± 1.3 cm/s, respectively, *P* < 0.001 compared with healthy individuals). The midsegment of the lateral wall, however, showed normal tissue velocities during IVR directed away from the apex −1.5 ± 0.8 cm/s (*P* < 0.001 compared with midseptal velocities).

**Table 1. Clinical and hemodynamic characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Normal Individuals</th>
<th>Acute LAD Ischemia</th>
<th>Anterior Myocardial Infarct</th>
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<tbody>
<tr>
<td>n</td>
<td>18</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>Age, yr</td>
<td>47 (SD 11)</td>
<td>58 (SD 11)*</td>
<td>56 (SD 12)</td>
</tr>
<tr>
<td>Women/Men</td>
<td>7/11</td>
<td>4/12</td>
<td>5/12</td>
</tr>
<tr>
<td>LVEDP, mmHg</td>
<td>14 (SD 6)</td>
<td>19 (SD 8)</td>
<td></td>
</tr>
<tr>
<td>LVEF, %</td>
<td>68 (SD 5)</td>
<td>80 (SD 7)</td>
<td>46 (SD 16)*</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>63 (SD 11)</td>
<td>58 (SD 8)</td>
<td>66 (SD 12)</td>
</tr>
<tr>
<td>Duration of IVR, ms</td>
<td>77 (SD 11)</td>
<td>109 (SD 27)*</td>
<td>109 (SD 25)*</td>
</tr>
<tr>
<td>LAD lesion, area stenosis %</td>
<td>83 (SD 8)</td>
<td>82 (SD 33)</td>
<td></td>
</tr>
</tbody>
</table>

Data are means ± SD; *n* = number of individuals. LVEDP, left ventricular end-diastolic pressure; LVEF, left ventricular ejection fraction (in normal individuals by two-dimensional echocardiography, in the other groups by angiography); HR, heart rate; LAD, left anterior descending coronary artery.

**Table 2. Myocardial (LV septum) and intraventricular flow velocities from normal individuals and patients with anterior myocardial infarction**

<table>
<thead>
<tr>
<th></th>
<th>Normal Individuals</th>
<th>Anterior Infarct</th>
</tr>
</thead>
<tbody>
<tr>
<td>V$_m$ midsegment</td>
<td>4.9 (SD 1.1)</td>
<td>1.8 (SD 1.0)*</td>
</tr>
<tr>
<td>V$_m$ apical segment</td>
<td>2.5 (SD 0.9)</td>
<td>1.4 (SD 0.8)*</td>
</tr>
<tr>
<td>V$_{LV}$ midsegment</td>
<td>−2.0 (SD 1.4)</td>
<td>2.4 (SD 1.2)†</td>
</tr>
<tr>
<td>V$_{LV}$ apical segment</td>
<td>−1.0 (SD 0.7)</td>
<td>1.6 (SD 0.7)†</td>
</tr>
<tr>
<td>Flow</td>
<td>25.1 (SD 9.5)</td>
<td>−14.3 (SD 10.7)†</td>
</tr>
</tbody>
</table>

Data are means ± SD (expressed as cm/s); LV, left ventricular; $V_m$, Peak myocardial systolic velocity; $V_{LV}$, Peak myocardial velocity during isovolumic relaxation. *P* < 0.01 compared with normal individuals; †*P* < 0.001 compared with normal individuals.
Acute LAD ischemia. At baseline, flow propagation during IVR was directed toward the apex (Fig. 2 and Table 3) and was similar to the flow pattern found in healthy individuals. As in normal individuals, flow was present through most of the period. TDI before balloon inflation showed a predominant V_{IVR} directed away from the LV apex (Fig. 3) and did not differ from healthy individuals (2.3 ± 1.1 cm/s at the midseptum level, NS).

During the LAD occlusion, all had significant (>0.1 mV) ST segment changes in the precordial electrocardiographic recordings. Heart rate was not significantly changed during LAD occlusion.

Figure 4 shows a representative recording of the reversed intraventricular flow in a patient during balloon inflation. Flow propagation as visualized by 2-D color Doppler and color M-mode Doppler during LAD occlusion was reversed and uniformly directed toward the LV base.

TDI showed reduced systolic velocities of the ischemic myocardial segments, whereas velocities during IVR were reversed and directed toward the apex during balloon inflation (Table 3, Fig. 3). In the lateral apical segment, V_{IVR} was also reversed during ischemia (1.0 ± 2.1 vs. −2.2 ± 1.1 cm/s, \( P < 0.001 \)). The reversed septal and lateral velocities represent a postsystolic shortening that started in late systole, continued through IVR, and into the filling period. There was no change in systolic shortening or V_{IVR} in the nonischemic segment at the midlateral wall even during LAD ischemia.

After ischemia. Ten minutes after balloon deflation the intraventricular flow propagation during IVR was directed toward the apex again, similar to the flow direction at baseline, except in one patient. Consistent with this, tissue velocities during IVR returned back to negative velocities with two exceptions. The patients had neither pain nor ECG changes at that time.

**DISCUSSION**

This study demonstrates that modern echocardiographic technology can document the interaction between myocardial wall motion and intraventricular flow. This refinement may have impact on the ability and accuracy to diagnose ischemic myocardial disease and furthermore to understand the underlying mechanisms of intraventricular flow. Patients with anterior acute myocardial ischemia and prior myocardial infarction were associated with an abnormal reversal of flow propagation during IVR. The reversal of IVR flow was unequivocally associated with abnormal postsystolic shortening of dyskinetic myocardium supplied by the LAD as demonstrated by TDI. This postsystolic shortening or recoiling effect was acting in the long-axis direction of the left ventricle, including the apex, and thus was pushing blood toward the base.

Regional wall motion abnormalities during the earliest diastolic cardiac phase have also been shown by LV angiograms and M-mode echocardiography (10, 14). This may result in altered intraventricular pressure and flow as confirmed by Nikolic et al. (20). Sonomicrometry and LV pressure measurements in a recent experimental study demonstrated that a pressure gradient from the LV outflow tract directed toward the apex is present in the nonischemic ventricle during IVR (36). During LAD occlusion, however, this pressure gradient reversed and was directed toward the LV outflow tract. These studies are in accordance with our findings and suggest that reversal of flow propagation reflects ischemia-induced changes of intraventricular driving pressure.

**Intraventricular flow pattern and regional wall motion abnormalities.** The LV intraventricular flow pattern is very complex due to shifting myocardial contractile and elastic proper-

**Table 3. Myocardial velocities from angina patients**

<table>
<thead>
<tr>
<th></th>
<th>( V_s )</th>
<th>( V_{IVR} )</th>
<th>Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>2.2 (SD 1.5)</td>
<td>2.1 (SD 1.1)</td>
<td>23.0 (SD 12.0)</td>
</tr>
<tr>
<td>Occlusion</td>
<td>2.0 (SD 1.0)†</td>
<td>2.4 (SD 1.0)†</td>
<td>−14.2 (SD 1.6)†</td>
</tr>
<tr>
<td>After</td>
<td>2.3 (SD 0.9)†</td>
<td>0.8 (SD 0.9)†</td>
<td>14.8 (SD 1.0)†</td>
</tr>
</tbody>
</table>

Data are means ± SD (expressed as cm/s). \( V_s \), Peak myocardial velocity during the ejection period; \( V_{IVR} \), Peak myocardial velocity during isovolumic relaxation. Velocities were measured in the midseptal wall segment during ejection and postsystolic period at baseline, during and after LAD occlusion.

Intraventricular flow velocities were measured during IVR from the same time points. *\( P < 0.01 \) compared with baseline; †\( P < 0.001 \) compared with baseline.
ties throughout the cardiac cycle. Current echocardiographic methods cannot depict velocities in real three-dimensional (3-D) mode, but because of high frame rate and the ability of measuring tissue velocities, important information of this complex pattern can be obtained.

Kerber et al. (17) were the first investigators to demonstrate that segmental dysfunction occurred in normally perfused myocardium immediately adjacent to areas of ischemia. The LV apical-lateral segment is perfused by the LAD or the left circumflex coronary artery (LCX) (22). Measurements closer to the midlateral segment will increase the likelihood of measuring an area perfused by the LCX. The reversed myocardial velocities during IVR in the apical-lateral segment found in our study are due to tethering effects from the ischemic part of the apex and the ischemic area itself. The tethering effect of the adjacent segment will augment the LV area affected by LAD ischemia and thus cause further impact on intraventricular flow propagation.

Limited reports of early diastolic flow pattern have been published, and no clinical study relating myocardial properties by TDI to intraventricular flow exists. In a recent 2-D flow study, however, we were able to study flow during IVR in detail (6). Intraventricular flow propagation during IVR is very slow and requires a low-velocity filter setting. Modern ultrasonic technology has increased sensitivity for the detection of intraventricular flow, which can be assessed with relatively high frame rates. Ohte et al. (21) found that the greater magnitude of LV elastic recoil and the faster LV relaxation in patients without LV apical asynchrony produce apically directed flow during IVR. Nonuniform contraction and filling are associated with ineffective shifting of blood volume within the left ventricle. This phenomenon was most pronounced during the isovolumic periods in a study by conductance catheter in patients with coronary artery disease (27).

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Fig. 3. Demonstration of the striking alterations from baseline (A) to acute ischemia (B) in one patient undergoing percutaneous coronary intervention (PCI) of the left anterior descending coronary artery (LAD). Tissue velocities during IVR are prominently negative at baseline, reversing into a marked postsystolic shortening in acute ischemia.

Fig. 4. Reversed intraventricular flow propagation during IVR in a patient during PCI of the LAD. Same reversed flow propagation (arrow) is demonstrated in the color M-mode image.
Regional wall motion abnormalities may also exist in nonischemic related conditions (3). Negative inotropic interventions have been shown to cause a nonhomogenous LV response with greater depression of LV apical contraction compared with the LV base (4). Strum and Pinsky (29, 30) showed in an experimental model that effective regional stroke volume and phase angle analyses by conductance catheter were more sensitive measures of regional wall motion abnormalities than measures of maximal stroke volume. Their analyses of effective stroke volume are comparable to our TDI measures that assess myocardial velocities throughout the cardiac cycle. They found that regional ejection may not be synchronous with global systole. Dysfunctional myocardium often continues to contract after global end systole, and this might be difficult to detect with an ordinary 2-D echocardiographic study. Our findings of delayed systolic velocities that occur after global end ejection in ischemic patients support their notion that the extent of regional dysfunction could be underestimated by the use of wall motion analyses from 2-D echocardiography.

Furthermore, a heterogeneous wall motion pattern can also be found in normal hearts (1, 13, 23). An augmentation of the normal IVR velocities directed toward the apex has been found in patients with hyperdynamic ventricles (25). This was related to a more asynchronous relaxation of the ventricle. In our study no reversed flow pattern was observed in healthy individuals. This suggests that the usual spectrum of wall motion variation in normal persons is not enough to cause reversed flow during IVR.

Severe ischemia leads to paradoxical systolic movement of the ischemic region followed by a recoil or active contraction during end systole, continuing into the early diastolic period. These altered myocardial contraction patterns must have a vital impact on the intraventricular flow pattern as clearly demonstrated in our study. One might also expect that this finding may contribute in part to the decreased mitral-to-apical flow propagation seen by color M-mode Doppler during the succeeding diastolic filling phase (2, 32). In the normal left ventricle, flow propagates rapidly to the apex during the diastolic filling period, and as earlier demonstrated by color M-mode Doppler, there is an almost instant onset of filling velocities along the entire LV inflow tract (24). In patients with reduced LV function, however, the mitral-to-apical flow propagation may be markedly delayed (2, 31, 32). This retarded flow propagation might depend of a decrease of LV relaxation, which causes a decrease in mitral-to-apical driving pressure (28).

Clinical implications. Visual interpretation of 2-D wall motion in ischemia is at best semiquantitative and may be difficult. TDI has been suggested as a helpful and accurate tool in diagnosing ischemic conditions. We have demonstrated that apical-to-mitral directed flow during IVR is closely connected to postsystolic shortening of dysskinetic myocardium and may thus represent an expression of myocardial dysfunction. Combined analyses of intraventricular flow and myocardial tissue velocities may therefore be used for echocardiographic detection of myocardial ischemia. Because the reversal of IVR flow is a distinct qualitative observation, it may be helpful in the diagnosis of ischemia when borderline velocity changes are measured by TDI.

Strain measures versus TDI. The current echocardiographic technology does also allow interpretation of strain Doppler echocardiography (SDE). SDE has earlier demonstrated superiority over TDI concerning location and distribution of regional ischemia (7, 37). SDE measures the intrinsic myocardial deformation, whereas TDI measures the myocardial velocities. Strict regional diagnosis of the ischemic myocardium was, however, not considered as an essential issue in our study because the location of ischemia was predetermined. TDI measures the sum of the actual point of interest plus the tethering effects in the adjacent segments to the ischemic zone. Therefore, TDI velocities from the proximal part of the lateral apical segments include velocities from the apex curve that again most likely represent an important contribution to the flow propagation seen in this study.

Furthermore, the noise problems in measurements with the SDE technique remain high and probably higher than found in measures from TDI (39). Moreover, SDE and TDI from the LV apex might be difficult to interpret due to angle problems inherited in all Doppler modalities (37).

Limitations. Acute and chronic ischemia in the distribution areas of the LCX and the RCA were not studied. An earlier report from a myocardial infarct in the RCA area did not show evidence of reversed flow during IVR, probably due to preserved contraction of the anterior and apical parts of the left ventricle (6).

The changes in LV cavity shape during IVR are complex, and the unidirectional measures used in this study are inadequate for real 3-D knowledge of intracavitary flow. The imaging sequences in our study were limited to the apical four chamber due to the short period time of balloon inflation. All our efforts were therefore made to provide reliable data from the apical four-chamber view.

The duration of the IVR period is short. On average, 3.8 frames of 2-D flow were imaged during IVR. However, postsystolic shortening followed by apical-to-mitral directed flow propagation during IVR was demonstrated in every individual with apical and septal ischemia.

In conclusion, interaction between regional myocardial wall motion and intraventricular flow could be assessed by the use of echocardiographic equipment. In each patient the reversal of intraventricular flow during IVR in acute and chronic LAD ischemia was caused by postsystolic shortening of the apical part of the left ventricle.

GRANTS

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