Cardiac hemodynamics in PCI : effects of ischemia, reperfusion and mechanical support
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Improved long-term LV hemodynamics after primary percutaneous coronary intervention for anterior ST-elevation myocardial infarction

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Abstract

Objectives. ST-elevation myocardial infarction (STEMI) causes left ventricular (LV) remodeling, which influences LV function. Therefore, we studied long-term LV dynamic changes after successful primary percutaneous coronary intervention (PCI) in patients with anterior STEMI by invasively obtained pressure-volume (PV) loops.

Methods. We studied 11 consecutive patients (8 males, mean age 58 ± 9 years), who presented with their first anterior STEMI within 6 hours after onset of symptoms, and in whom coronary angiography revealed an occluded left anterior descending coronary artery. Continuous PV-loops were obtained three days and four months after primary PCI by inserting a pressure-conductance catheter in the LV.

Results. Four months after successful reperfusion, a significant increase was observed in LV end-diastolic volume index (EDVI) from 72 ± 17 to 89 ± 15 mL/m² (p = 0.001), as a result of LV remodeling after STEMI. The increase in EDVI was accompanied by significant improvements in diastolic LV function, as indicated by an increased end-diastolic compliance with a 3.7 ± 4.9 mm Hg (p = 0.04) downward shift of the compliance curve. There was also a decrease in end-diastolic elastance from 0.13 ± 0.03 to 0.08 ± 0.03 mm Hg/mL (p = 0.007). Systolic LV function showed an improvement in stroke volume (SV) from 62 ± 20 to 86 ± 25 mL (p = 0.005) and a preserved ejection fraction at increased LV end-diastolic volumes.

Conclusions. Invasive assessment of LV pressure and volume performed after primary PCI in anterior STEMI patients show signs of LV remodeling, which is however accompanied by improvement in both diastolic and systolic LV function.
LV hemodynamics after STEMI

Introduction

Primary percutaneous coronary intervention (PCI) is currently the cornerstone treatment modality for early restoration of epicardial coronary blood flow in ST elevation myocardial infarction (STEMI). Early and successful reperfusion of myocardial tissue is crucial for reduction of infarct size which is an important determinant for post-infarction left ventricular (LV) healing and remodeling. LV remodeling and residual systolic function are important markers of outcome, which have been the focus of research for several decades. Several studies showed that LV remodeling, defined as at least 20% increase in LV end-diastolic volume from baseline up to one year, is still frequently observed after STEMI, despite successful coronary reperfusion. Systolic as well as diastolic LV function after STEMI have shown to be strongly related to LV remodeling and prognosis. However, the LV function parameters assessed in these studies have only been obtained non-invasively by means of echocardiography or cardiac magnetic resonance imaging (CMR). Recently, we reported immediate improvements in LV function during reperfusion by invasively measured LV hemodynamics obtained directly before and after primary PCI in anterior STEMI patients. Invasive assessment of LV hemodynamics is a direct and accurate method to examine changes in LV function that accompany LV remodeling after STEMI. Therefore, we performed online simultaneous LV pressure and volume measurements in primary PCI patients three days and four months after their STEMI.

Methods

Patients

The study population consisted of 11 consecutive patients (8 males, mean age 58 ± 9 years), who presented with their first anterior STEMI within 6 hours after onset of symptoms. Patients were included when coronary angiography revealed an occluded left anterior descending artery prior to primary PCI (see Table 1). Exclusion criteria were cardiogenic shock, refractory ventricular arrhythmias, congestive heart failure, previous myocardial infarction, significant valvular disease, and left ventricular thrombus. The study complied with the Declaration of Helsinki and was approved by the institutional research and ethics committee. All patients gave written informed consent.

Study protocol

Patients were treated with aspirin, clopidogrel, and heparin before PCI. Heart rate and surface 12-lead ECGs were monitored and aortic pressure was measured via the guiding
catheter. Blood samples for hematology and chemistry including cardiac markers were drawn. Adequate medical treatment including statins, ACE inhibitors, β-blockers, aspirin and clopidogrel was started as soon as possible after the primary PCI and continued thereafter.

Three days and four months after primary PCI, LV pressure and volume loop assessments were performed in all patients by placing a 7F pigtail equipped combined pressure-conductance catheter (CD Leycom, Zoetermeer, The Netherlands). A more extensive description of the instrumentation and LV hemodynamic measurements have been reported previously (Remmelink et al. JACC 2009).

LV hemodynamic measurements and analysis

LV hemodynamics were recorded continuously and were analyzed off-line. Per-beat averages of the recorded variables were calculated as the mean of all beats during a steady state of at least 12 seconds and covering two respiratory cycles. It was accounted for that selected recording were obtained during stable hemodynamic conditions, without interference of pharmaceuticals (e.g. nitroglycerin). The following indices were obtained: heart rate (HR), cardiac output (CO), ejection fraction (EF), stroke volume (SV), stroke work as the area of the pressure-volume loop (SW), end-systolic volume (ESV), index (ESVI), end-diastolic volume index (EDV, EDVI), end-systolic and end-diastolic

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**Table 1. Baseline characteristics (n=11)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, y</strong></td>
<td>58 ± 9</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>8 ± 73</td>
</tr>
<tr>
<td><strong>Body mass index</strong></td>
<td>26 ± 5</td>
</tr>
<tr>
<td><strong>Coronary risk factors</strong></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 ± 27</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 ± 27</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>3 ± 27</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>4 ± 36</td>
</tr>
<tr>
<td>Current smoking</td>
<td>8 ± 73</td>
</tr>
<tr>
<td>Previous STEMI</td>
<td>0 ± 0</td>
</tr>
<tr>
<td><strong>Angiographic features</strong></td>
<td></td>
</tr>
<tr>
<td>LAD, culprit lesion</td>
<td>11 ± 100</td>
</tr>
<tr>
<td>2-vessel disease</td>
<td>2 ± 18</td>
</tr>
<tr>
<td>3-vessel disease</td>
<td>4 ± 36</td>
</tr>
<tr>
<td>TIMI 0-1 flow</td>
<td>11 ± 100</td>
</tr>
<tr>
<td><strong>Cardiac markers, peak</strong></td>
<td></td>
</tr>
<tr>
<td>CKMB, μg/L</td>
<td>192 ± 142</td>
</tr>
<tr>
<td>Troponin T, μg/L</td>
<td>8.3 ± 9.6</td>
</tr>
<tr>
<td>NT-proBNP, ng/L</td>
<td>1914 ± 1280</td>
</tr>
</tbody>
</table>

Values are n (%) or mean ± SD. CAD, coronary artery disease; STEMI, ST elevation myocardial infarction; LAD, left anterior descending; TIMI, Thrombolysis in Myocardial Infarction; CK, Creatine Kinase; NT-proBNP, N-terminal part of the pro-B-type natriuretic peptide.
LV hemodynamics after STEMI

The relaxation time constant Tau, as an index for the active diastolic LV properties during isovolumetric relaxation, was defined as that time required for the cavity pressure at \(\frac{dP}{dt_{\text{min}}}\) to be reduced by half \(14\). The end-diastolic elastance \(E_{\text{ED}}\), as the slope on the EDPVR was estimated by \(\frac{\text{EDP}}{\text{EDV}}\) \(^{15}\). The change in the passive diastolic LV properties indicated by the shift of the compliance curve, was expressed by the mean pressure value over which the overlapping portion of the PV-loop had moved \(\left(P_{\text{m}}\right)\), as previously described (see figure 2) \(^{12}\).

Statistical analysis

Data are expressed as mean ± SD or n (%). The 2-tailed paired t-test was used to compare LV hemodynamic data obtained at the different time points after the PCI. SPSS release 16.0.1 statistical software package for windows (SPSS Inc. 2007, Chicago, Illinois) was used for analyses. A p-value of less than 0.05 was considered statistically significant.

Results

Patient characteristics

The baseline characteristics of all 11 patients are shown in table 1. Coronary angiography revealed a right dominant system in 5 (45%) patients. In 5 (45%) patients the culprit lesion was located...
in the proximal LAD (segment 6) and in 6 (55%) patients in the mid part of the LAD (segment 7).

LV hemodynamics at 4 months compared with 3 days after reperfusion
Changes in LV hemodynamics between 3 days and 4 months post-PCI are shown in table 2.

**Table 2. Changes in LV hemodynamics between 3 days and 4 months after primary PCI in 11 STEMI patients**

<table>
<thead>
<tr>
<th></th>
<th>3 days after reperfusion</th>
<th>4 months after reperfusion</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HR, bpm</strong></td>
<td>81 ± 11</td>
<td>67 ± 15</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Diastolic function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDV, mL</td>
<td>143 ± 35</td>
<td>175 ± 27</td>
<td>0.001</td>
</tr>
<tr>
<td>EDVI, mL/m²</td>
<td>72 ± 17</td>
<td>89 ± 15</td>
<td>0.001</td>
</tr>
<tr>
<td>EDP, mm Hg</td>
<td>18 ± 6</td>
<td>15 ± 6</td>
<td>0.1</td>
</tr>
<tr>
<td>EED, mm Hg/mL</td>
<td>0.125 ± 0.034</td>
<td>0.080 ± 0.025</td>
<td>0.007</td>
</tr>
<tr>
<td>Tau, ms</td>
<td>38 ± 5</td>
<td>39 ± 8</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Systolic function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESV, mL</td>
<td>81 ± 23</td>
<td>89 ± 25</td>
<td>0.3</td>
</tr>
<tr>
<td>ESVI, mL/m²</td>
<td>41 ± 12</td>
<td>46 ± 14</td>
<td>0.2</td>
</tr>
<tr>
<td>EF, %</td>
<td>44 ± 9</td>
<td>49 ± 12</td>
<td>0.2</td>
</tr>
<tr>
<td>dP/dt_max, mm Hg/s</td>
<td>1424 ± 320</td>
<td>1459 ± 333</td>
<td>0.7</td>
</tr>
<tr>
<td>SV, mL</td>
<td>62 ± 20</td>
<td>86 ± 25</td>
<td>0.005</td>
</tr>
<tr>
<td>CO, L/min</td>
<td>5.0 ± 1.5</td>
<td>5.7 ± 1.7</td>
<td>0.2</td>
</tr>
<tr>
<td>SW, mm Hg/L</td>
<td>6.02 ± 2.66</td>
<td>9.67 ± 4.15</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Values are mean ± SD. HR, heart rate; EDV, end-diastolic volume; EDVI, end-diastolic volume index; EDP, end-diastolic pressure; EED, end-diastolic stiffness; Tau, relaxation time constant; ESV, end-systolic volume; ESVI, end-systolic volume index; EF, ejection fraction; dP/dt_max, peak positive derivative of LV pressure; SV, stroke volume; CO, cardiac output; SW, stroke work.

Diastolic function. Pronounced changes were seen in diastolic LV function. There was an increase in EDVI from 72 ± 17 to 89 ± 15 mL/m² (p = 0.001, figure 1A), with only a small but not significant change in EDP (p = 0.1). The end-diastolic elastance decreased from 0.125 ± 0.034 to 0.080 ± 0.025 mmHg/mL (p = 0.007, figure 1B), while Tau remained unchanged. The intrinsic diastolic LV properties improved, indicated by a downward shift of the compliance curve (figure 2), and quantified by a $P_m$ of -3.7 ± 4.9 mmHg (p = 0.04).

Systolic function. Small but non significant increases were seen in ESVI and in EF, (both p = 0.2). Improvement in systolic LV function after 4 months was expressed by an increase in SV from 62 ± 20 to 86 ± 25 mL (p = 0.005, figure 1C) and SW from 6.02 ± 2.66 to 9.67 ± 4.15 mmHg·L (p = 0.009).
Clinical outcomes at 4 months after reperfusion

All 11 patients had NYHA class II or less at 4 months follow-up after primary PCI. Coronary angiography at 4 months showed TIMI 3 flow of the LAD (infarct-related artery) in all patients.

Discussion

The present study is the first to describe the improvement in diastolic and systolic LV function by invasively measured LV hemodynamics between 3 days and 4 months follow-up after primary PCI in patients with anterior wall STEMI.

Improvement in LV hemodynamics

Recently, we have shown an immediate improvement of the intrinsic passive LV diastolic properties during primary PCI (Remmelink et al. JACC 2009). The present data show a further improvement in the passive diastolic LV function after the acute phase. End-diastolic elastance decreased and the compliance curve improved during 4 months follow-up. Active myocardial relaxation however, remained prolonged. Systolic LV function also improved, as indicated by the marked increase in stroke volume and stroke work, despite the large increase in EDV due to LV remodeling.
The increase in LV end-diastolic volume is the result of post-STEMI LV remodeling, which is still frequently observed despite successful reperfusion 4-6. Our invasively measured LV volumes show relatively higher values when compared with those estimated previously by means echocardiography in patients after STEMI 4, 5, 16, whereas our measured LV volumes are lower when compared with those assessed by CMR 9. Although in two of the echocardiographic studies only about 50% of the patients had an LAD as the infarct-related artery 4, 16, the mean EDVI at baseline and at follow-up did not differ much from that of the patients in one echocardiographic study which only included patients with anterior wall STEMI 5.

Conductance catheter-derived volumes have shown to correlate strongly with those estimated by CMR 17. Averaging the values obtained by echocardiography and CMR gives an approximation of those acquired by invasive PV loop measurements. The mean relative increase in EDV as part of LV remodeling after STEMI in this study was 24%, which is in the same range as that described in previous echocardiographic and CMR studies 4, 5, 9, 16.

Previous reports on LV diastolic changes in LV remodeling after STEMI were based on echocardiographic parameters 5,7,8,10,16. These parameters were derived from transmitral flow velocity patterns, and therefore influenced by diastolic LV function in various ways. Parameters such as E/A ratio, mitral deceleration time and E/E’ ratio are an indirect reflection of true LV diastolic function, since they depend on left atrial (LA) pressures, pulmonary vein properties and mitral orifice area. For their optimal interpretation other parameters need to be taken into account. By obtaining LV PV-loops, active LV relaxation and passive diastolic stiffness of the myocardium can be assessed independently and in a direct and a quantitative way.

Another advantage of hemodynamic assessment by PV-loops is the possibility to directly relate LV dynamic parameters to each other. This is best described by our finding that PV-loops obtained 4 months after STEMI not only show a rightward shift with regard to those from 4 months earlier, but also a downward shift. So, not only did EDV increase as part of LV remodeling, this was accompanied by a decrease in end-diastolic elastance and an improvement in the compliance curve.

Our study shows a small but no significant increase in LV ejection fraction at 4 months after primary PCI. This finding is in line with previous echocardiographic and CMR studies, showing only small increases in EF up to one year after successful PCI in STEMI patients 4, 5, 9, 16. However, taking into account, the marked increase in EDV due to LV remodeling, ejection fraction gives an underestimation of the true systolic LV improvement, as supported by the large improvement in stroke volume and stroke work. Interestingly, cardiac output remained more or less the same, which is explained by a “compensatory” decrease of heart rate, and partially by betablocking therapy. Our description of improvement in systolic LV function as part of LV remodeling after STEMI, is another example of how different LV hemodynamic parameters can simply be related to each other by means of PV-loops. As far as we know, this is the first study that shows
invasively measured LV dynamic changes accompanying LV remodeling after successful reperfusion in STEMI patients.

Limitations
Myocardial (un)-loading interventions to determine the EDPVR were not performed. However, we believe that interpretation of our data would have remained the same. 18 No significant correlations could be found between hemodynamic or clinical parameters and the extent of LV remodeling. In order to investigate these relations a larger sample size is required.

Clinical implications
Our study is the first to show improvement in both systolic and diastolic LV function 4 months after successfully reperfused anterior wall STEMI, assessed by means of invasively measured load-independent PV-loops. The prognostic and clinical value of systolic LV function on short- and long-term after STEMI have been described extensively 3, 19, 20. More recent studies have shown diastolic LV function to be a strong predictor for clinical outcome after STEMI as well 7, 8, 10. The main finding in these studies is that diastolic LV dysfunction early after reperfused STEMI is predictive for late LV remodeling and unfavorable clinical outcome. The present study shows at long-term after reperfused STEMI that LV remodeling is accompanied by an overall improvement in diastolic LV function. The clinical importance of this finding still remains unclear and may encourage further investigations.

Conclusion
Invasive assessments of LV pressure and volume performed after primary PCI in anterior STEMI patients show evidence of LV remodeling, which however is accompanied by marked improvement in both diastolic and systolic LV function.

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Chapter 11

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