Clinical and hemodynamic effects of transcatheter aortic valve implantation
Yong, Z.Y.

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Chapter 4.2

More pronounced diastolic left ventricular dysfunction in patients with accelerated idioventricular rhythm after reperfusion by primary percutaneous coronary intervention

Maurice Remmelink
Ronak Delewi
Ze Yie Yong
Jan J. Piek
Jan Baan, Jr

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ABSTRACT

Objective  Reperfusion-induced accelerated idioventricular rhythm (AIVR) during primary percutaneous coronary intervention (pPCI) may be a sign of left ventricular (LV) dysfunction. We compared LV dynamic effects of reperfusion between patients with and without reperfusion-induced AIVR during pPCI for ST-elevation myocardial infarction (STEMI).

Methods  We studied 15 consecutive patients, who presented with their first acute anterior STEMI within 6 hours after onset of symptoms, and in whom LV pressure-volume (PV) loops were directly obtained during pPCI. Immediate effects of pPCI on LV function were compared between patients with (n = 5) and without (n = 10) occurrence of AIVR after reperfusion, as well as the direct effects of AIVR on LV function compared to sinus rhythm.

Results  Patients with reperfusion-induced AIVR showed more pronounced diastolic LV dysfunction before the onset of the arrhythmia, i.e., a delayed active relaxation expressed by Tau (53 ± 15 vs. 39 ± 6 ms; p = 0.03), a worse compliance curve (p = 0.01), and a higher enddiastolic stiffness (p = 0.07). At the end of the procedure, AIVR patients showed less improvement in diastolic LV function, indicated by a downward shift of the compliance curve (-3.1 ± 2.3 vs. -7.5 ± 1.4 mmHg; p = 0.001), a decrease in end-diastolic stiffness (13 ± 18 vs. 34 ± 15%; p = 0.03) and end-diastolic pressure (12 ± 8 vs. 29 ± 19%; p = 0.07).

Conclusion  STEMI patients with reperfusion-induced AIVR after pPCI showed more pronounced diastolic LV dysfunction before and after AIVR than patients without AIVR, which suggests that diastolic LV dysfunction contributes to the occurrence of AIVR and that AIVR is a sign of diastolic LV dysfunction.
Introduction

Accelerated idioventricular rhythm (AIVR) as a reperfusion arrhythmia\(^1\) is often observed immediately after primary percutaneous coronary intervention (pPCI) for ST-elevation myocardial infarction (STEMI).\(^2\) In general, AIVR is considered to be a relatively benign form of ventricular tachycardia.\(^3\) While some authors suggest that AIVR may be a manifestation of cellular injury,\(^4\) others state that the occurrence of AIVR immediately following pPCI is associated with better clinical outcome, as it is associated with reperfusion at myocardial tissue level.\(^5\) However, there is conflicting evidence of the clinical relevance of reperfusion-related AIVR in pPCI. Whereas, Illia et al found that the presence of AIVR was associated with ST-segment resolution,\(^6\) Bonnemeier et al found no difference in the incidence of AIVR among patients with optimal versus suboptimal TIMI flow grade.\(^2\) Furthermore, the acute effect of AIVR on left ventricular (LV) function during reperfusion by pPCI is unknown. Therefore, we assessed the acute effects of AIVR on LV dynamics, and compared systolic and diastolic LV function between patients with and without reperfusion-induced AIVR among STEMI patients treated by pPCI, in order to investigate whether AIVR implicates LV dysfunction.

Methods

Patients

The study population consisted of 15 consecutive patients who presented with their first acute anterior ST-segment elevation myocardial infarction within 6 hours after onset of symptoms, and in whom LV pressure-volume (PV) loops were directly obtained during pPCI. Recurrent episodes of reperfusion-induced AIVR were observed in 5 patients. 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

An extensive description of the instrumentation and LV dynamic measurements was previously reported.\(^7\) Briefly, patients were treated with aspirin, clopidogrel and heparin before PCI. Heart rate and surface 12-lead electrocardiograms were monitored and aortic pressure was measured via the guiding catheter. Blood samples for hematology and chemistry, including cardiac markers, were drawn.
Before performing pPCI, a 7 French (Fr), pigtail-equipped, combined pressure-conductance catheter (CD Leycom, Zoetermeer, The Netherlands) was placed in the LV through the contralateral femoral artery. PV-loops were continuously assessed during the procedure.

**Analysis of left ventricular function**

LV function effects were assessed during sinus rhythm and compared between patients with (n = 5) and without (n = 10) the occurrence of AIVR after reperfusion. AIVR was defined as a ventricular ectopic rhythm with more than 3 consecutive beats and a rate between 60 and 110 bpm. The initial baseline (pre-PCI) recordings were compared to the recordings at 30 seconds after reperfusion and/or before the onset of AIVR, and at 25 minutes after achievement of an angiographically satisfactory PCI result. 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 taken into account that selected recordings were obtained during stable hemodynamic conditions, without interference of pharmaceuticals (e.g., nitroglycerin).

The active diastolic function was studied by measuring the relaxation time constant Tau, as defined by that time required for LV pressure at the peak negative derivative of LV pressure (dP/dt\textsubscript{min}) to be reduced by half. Diastolic function was further studied by measuring peak filling rate (PFR), end-diastolic volume (EDV), pressure (EDP), and stiffness (E\textsubscript{ED}) as the slope on the EDPVR was estimated by EDP/EDV. The shift of the passive diastolic LV compliance curve was expressed by the mean pressure value over which the overlapping portion of the PV-loop had moved (P\textsubscript{m}), as previously described. Systolic function was studied by measuring stroke volume, ejection fraction, stroke work, cardiac output, end-systolic volume (ESV), pressure (ESP), and elastance as the slope on the ESPVR was estimated by ESP/ESV.

**Statistical analysis**

Data are expressed as mean ± standard deviations (SD) or n (%). The Fisher’s exact test was used to compare dichotomous variables. The 2-tailed paired t-test was used to compare LV dynamic data obtained before and after reperfusion. SPSS release 15.0.1 statistical software package for Windows (SPSS Inc. 2006, Chicago, Illinois) was used for analyses. A p-value < 0.05 was considered statistically significant.
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Results

Patient characteristics. The patient characteristics are shown in Table 1. Markers of cardiac necrosis were higher in the patients with reperfusion-induced AIVR than in the patients without AIVR, while the clinical, hemodynamic and angiographic characteristics were not different. At baseline, just before pPCI, there were no significant differences in diastolic or systolic LV function between the patient groups.

### Table 1. Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>AIVR (n=5)</th>
<th>Non-AIVR (n=10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>65 ± 11</td>
<td>57 ± 12</td>
<td>0.2</td>
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<tr>
<td><strong>Male</strong></td>
<td>3 (60)</td>
<td>7 (70)</td>
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</tr>
<tr>
<td><strong>Body mass index (kg/m²)</strong></td>
<td>24 ± 2</td>
<td>28 ± 4</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>0 (0)</td>
<td>2 (20)</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>0 (0)</td>
<td>5 (50)</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Hypercholesterolemia</strong></td>
<td>1 (20)</td>
<td>2 (20)</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Family history of coronary artery disease</strong></td>
<td>1 (20)</td>
<td>4 (40)</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>Current smoking</strong></td>
<td>3 (60)</td>
<td>6 (60)</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Previous acute myocardial infarction</strong></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Ischemic time (minutes)</strong></td>
<td>241 ± 171</td>
<td>271 ± 187</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Heart rate (beats per minute)</strong></td>
<td>71 ± 7</td>
<td>87 ± 20</td>
<td>0.1</td>
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<tr>
<td><strong>Systolic blood pressure (mmHg)</strong></td>
<td>130 ± 15</td>
<td>127 ± 24</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Diastolic blood pressure (mmHg)</strong></td>
<td>78 ± 13</td>
<td>72 ± 10</td>
<td>0.4</td>
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<tr>
<td><strong>LAD, culprit lesion</strong></td>
<td>5 (100)</td>
<td>10 (100)</td>
<td>1.0</td>
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<tr>
<td><strong>2-vessel disease</strong></td>
<td>2 (40)</td>
<td>2 (20)</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>3-vessel disease</strong></td>
<td>2 (40)</td>
<td>2 (20)</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>Duke's jeopardy score (0-12 points)</strong></td>
<td>7.2 ± 3.3</td>
<td>4.6 ± 2.7</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>TIMI 0-1 flow before primary PCI</strong></td>
<td>5 (100)</td>
<td>10 (100)</td>
<td>1.0</td>
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<tr>
<td><strong>TIMI 2 flow after primary PCI</strong></td>
<td>1 (20)</td>
<td>2 (20)</td>
<td>1.0</td>
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<tr>
<td><strong>STR at 60 minutes (%)</strong></td>
<td>50 ± 27</td>
<td>54 ± 24</td>
<td>0.7</td>
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<tr>
<td><strong>CKMB (µg/L)</strong></td>
<td>354 ± 73</td>
<td>159 ± 118</td>
<td>0.005</td>
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<tr>
<td><strong>Troponin T (µg/L)</strong></td>
<td>14.7 ± 11.1</td>
<td>6.6 ± 4.6</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>NT-proBNP (ng/L)</strong></td>
<td>2343 ± 1029</td>
<td>2765 ± 4764</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Values are n (%) or mean ± standard deviation. AIVR = accelerated idioventricular rhythm; LAD = left anterior descending coronary artery; Duke's jeopardy score = the angiographic extent of coronary artery disease; TIMI = thrombolysis in myocardial infarction; PCI = percutaneous coronary intervention; STR = the summed 12-lead ST-segment resolution as determined at 80 ms after the J-point; CK = creatine kinase; NT-proBNP = N-terminal part of the pro-B-type natriuretic peptide.
**Effects of PCI**

Immediately after reperfusion by pPCI, the active diastolic LV function as indicated by Tau (Figure 1A), was more delayed in patients who developed AIVR (53 ± 15 ms vs. 39 ± 6 ms; p = 0.03). At the end of the procedure, at 25 minutes after reperfusion, Tau remained more delayed in the patients who had AIVR (51 ± 12 ms versus 38 ± 5 ms; p = 0.01). Compared to baseline, the AIVR patients showed a worsening in Tau, while the non-AIVR patients showed a slight improvement (8 ± 10% versus -1 ± 16%; p = NS).

Similar findings were observed in the passive diastolic LV function. Figure 1B shows that immediately after reperfusion, there was a difference in $P_m$ between patients developing AIVR versus the other patients (4.1 ± 4.2 mmHg vs. -3.7 ± 4.9 mmHg; p = 0.01). This shift in the compliance curve remained different at the end of the procedure (-3.1 ± 2.3 mmHg vs. -7.5 ± 1.4 mmHg; p = 0.001). Also, $E_{Ed}$ (Figure 1C) and EDP (Figure 1D) tended to be different at these time points. Compared to baseline, the AIVR patients had shown less improvement at the end of the procedure in $E_{Ed}$ (13 ± 18% versus 34 ± 15%; p = 0.03) and EDP (12 ± 8 versus 29 ± 19%; p = 0.07).

The effect of pPCI on systolic LV indices showed no difference between the patient groups, as illustrated by stroke volume and ejection fraction in Figures 1E and 1F.

**AIVR versus sinus rhythm**

During an episode of AIVR (Figure 2), diastolic LV function decreased as indicated by a decreased LV pressure decay, i.e., $dP/dt_{min}$ decreased by 403 ± 145 mmHg/s (p = 0.003) and Tau delayed by 5 ± 6 ms (p = NS). Furthermore, there was a decrease in PFR of 165 ± 54 mL/s (p = 0.002), in EDP of 11 ± 5 mmHg (p = 0.01), in EDV of 30 ± 18 mL (p = 0.02) and $E_{Ed}$ of 0.045 ± 0.015 mmHg/mL (p = 0.002).

LV contraction decreased as indicated by a decrease in $dP/dt_{max}$ of 303 ± 125 mmHg/s (p = 0.006) and ESP of 33 ± 8 mmHg (p = 0.001). Heart rate, stroke volume, ejection fraction and cardiac output remained unchanged. The beat to beat effects at the onset of AIVR on the LV volume and pressure tracings are illustrated in Figure 3. After return of sinus rhythm, diastolic and systolic LV function showed an immediate restoration.
LV diastolic dysfunction in AIVR after pPCI for STEMI

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Figure 1. Comparison of diastolic and systolic left ventricular (LV) function between patients with the occurrence of accelerated idioventricular rhythm (AIVR) and without the occurrence of AIVR (non-AIVR) during primary percutaneous coronary intervention (pPCI). (A) Active LV relaxation as expressed by the relaxation time constant (Tau), was worse in the AIVR patients at baseline (pre-PCI), immediately after reperfusion and/or before onset of AIVR (reperfusion + 30 seconds), and at 25 minutes after reperfusion (reperfusion + 25 minutes). (B) The shift of the diastolic LV compliance curve, as expressed by the mean pressure value ($P_m$), was downward and more pronounced in the non-AIVR patients. Note that immediately after reperfusion, the shift was in the opposite direction. (C) End-diastolic stiffness ($E_{ED}$) tended to be higher in the AIVR patients after reperfusion (p-values on top). Note that the improvement in $E_{ED}$ was more pronounced in the non-AIVR patients (p-values at bottom). Similarly, in (D), the decrease in end-diastolic pressure (EDP) seems more pronounced in the non-AIVR patients. Stroke volume in (E) and ejection fraction in (F) show no difference between the two patient groups.
Figure 2. Illustration of a changed pressure-volume loop (PV-loop) by accelerated idioventricular rhythm (AIVR). (A) A PV-loop during sinus rhythm. (B) A PV-loop during AIVR, 6 heartbeats later. Note that AIVR substantially decreases left ventricular function as indicated by a decrease in diastolic filling and endsystolic pressure, and a limited decrease in stroke volume. $P_{LV}$ = left ventricular pressure; $V_{LV}$ = left ventricular volume.

Figure 3. Illustration of the beat to beat effects at the onset of accelerated idioventricular rhythm (AIVR). Note that immediately after the onset of AIVR, there is an absence of atrial contribution to diastolic filling in the pressure and volume recordings. At the moment that the QRS complex is not being preceded by the p-top, the reflection of the atrial kick disappears, both at the start of the ascending limb of the pressure curve and by completely dissolving the peak of the volume curve. Also, maximal pressure is markedly decreased. $P_{LV}$ = left ventricular pressure; $V_{LV}$ = left ventricular volume.
Discussion

With this study, we are the first to demonstrate that STEMI patients who experienced AIVR after reperfusion by pPCI are characterized by more pronounced diastolic LV dysfunction before the occurrence of AIVR and show less diastolic LV function improvement.

Primary PCI and LV function

AIVR often occurs after reperfusion in patients with an acute myocardial infarction and is usually considered to be a beneficial sign of successful reperfusion and thus to be a benign form of ventricular arrhythmia. Our study, however, shows that in acute myocardial infarction, patients have more pronounced diastolic LV dysfunction before the occurrence of the arrhythmia. Also, the reperfusion-induced improvement in the passive diastolic LV properties compared to baseline was less in patients with AIVR. Our data therefore suggest that AIVR is not simply a beneficial sign of reperfusion, but is rather a sign of more pronounced LV dysfunction, and is thus indicative of a more strained myocardium when compared to patients without AIVR.

The more pronounced LV dysfunction may be caused by reperfusion injury, since it has been suggested that the abnormal automaticity of subendocardial tissue in AIVR patients may be a sign of additional injury due to the reperfusion process (arrhythmias, stunning, endothelial dysfunction and cell death) or a sign of poor quality of reperfusion. Our findings of a larger infarct size in AIVR patients may also partly explain the differences in LV function, although differences in infarct size were previously reported in two other studies, but not in other reports.

Our findings of a more pronounced diastolic LV dysfunction in AIVR patients may be related to a difference in microvascular reperfusion, resulting in larger infarct size and less improvement in diastolic LV function by pPCI. The abnormal automaticity of subendocardial tissue in AIVR patients may be triggered by increased diastolic LV stretch on cardiac cells. It is known that diastolic LV stretch can cause ectopic excitation of myocytes, potentially triggering arrhythmias.

We recently reported improvement in the passive diastolic LV properties by pPCI in anterior STEMI patients, but there are no reports on LV function in AIVR patients immediately before and after pPCI. Studies that obtained data after reperfusion are in line with our hemodynamic findings. One study showed more severe LV dysfunction in AIVR patients compared to patients without reperfusion arrhythmias, as assessed by echocardiography within 3 days after pPCI. Remarkably, these patients also had a better prognosis, in contrast to earlier studies showing no prognostic benefit during 12-month follow up or worsening of systolic LV function within 2 months after STEMI.
In AIVR patients, we found that reperfusion-induced AIVR caused an immediate decrease in diastolic and systolic LV function as compared to sinus rhythm. There was a decrease in LV pressure decay during isovolumetric LV relaxation and a concomitant decrease in force generation by the LV as indicated by a marked decrease in $\frac{dP}{dt_{\text{max}}}$ and ESP, as illustrated by an altered PV-loop during AIVR in Figure 2. This suggests that “elastic recoil,” i.e., the stored elastic energy during cardiac contraction, which is released in the next diastolic period, is diminished in AIVR patients. Furthermore, there was a decreased diastolic LV filling, which is caused by the absence in the contribution of the atrial contraction, as illustrated in Figure 3. Although AIVR is usually hemodynamically well tolerated and self-limiting, our data suggest that recurrent episodes of AIVR or sustained AIVR may worsen the hemodynamics of STEMI patients.

**Study limitations**

Myocardial (un)-loading interventions to determine the ESPVR and EDPVR were not performed, since we considered these unethical (i.e., delay of reperfusion and possible hemodynamic consequences) for the patients under these circumstances. $E_{\text{ED}}$ estimated from steady-state PV-loops by EDP/EDV underestimates the real slope of the EDPVR at higher filling pressures, because of its nonlinearity. This study was not designed to assess mediators of reperfusion injury. Atrioventricular sequential pacing in patients having atrial fibrillation and concomitant AIVR would be the ideal setting to study the mechanism of the hemodynamic consequences of AIVR and the influence of atrial contraction. Finally, the data are limited to the acute phase of pPCI. Final infarct size was not assessed during follow up. Further studies are needed to confirm our suggested trigger for AIVR, or possibly to find other substrates for AIVR.

**Clinical implications**

AIVR is a phenomenon that is frequently seen and part of daily practice in the catheterization laboratory after reperfusion therapy by pPCI for STEMI. It is conventionally considered to be a nonspecific and benign reperfusion arrhythmia, and therefore of limited clinical importance. However, our study shows larger infarcts and more diastolic LV dysfunction in AIVR patients, which may result in impaired clinical outcome. Our acute findings of the hemodynamic consequences in patients with the occurrence of AIVR during pPCI, and the suggested mechanistic trigger for AIVR as provided by the direct LV dynamic measurements, may encourage larger studies to assess its prognostic value.
Conclusion

Online PV-loop assessment during pPCI show immediate AIVR-related systolic and diastolic LV dysfunction. STEMI patients with AIVR have more pronounced diastolic LV dysfunction before the occurrence of the AIVR and less diastolic LV function improvement than patients without AIVR, implicating that AIVR may be considered as a sign of diastolic LV dysfunction.

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References


