Weak Concordance Between Wall Motion and Microvasculature Status After Acute Myocardial Infarction: Study with Myocardial Contrast Echocardiography in Real Time with Power Modulation


Aims: The microvasculature damage after myocardial infarction has important implications. The hypothesis of the study was that wall motion abnormalities and microcirculation status do not necessarily match after myocardial infarction, and therefore the study of only myocardial wall motion could offer an incomplete evaluation in these patients.

Methods: Wall motion and myocardial perfusion assessed by contrast echocardiography were evaluated by two different blinded investigators in 29 patients with recent (<1 week) myocardial infarction. Myocardial perfusion was assessed in real-time using power modulation after Optison (1.5–3.0 ml) intravenous administration.

Results: One hundred and ninety-nine segments could be adequately evaluated. Of these, 54 (27%) were akinetic. Regarding contrast opacification, 134 segments (67%) had a normal perfusion, whereas the remaining 65 (33%) had an impaired (n=37, 19%) or absent (n=28, 14.1%) perfusion. Concordance between presence of akinesia and abnormal contrast opacification was only moderate (kappa index 0.42) and agreement only occurred in 116 segments (58%). Fourteen per cent of normoquinetic segments had an impaired perfusion, whereas 35% of akinetic segments had a preserved perfusion. Correlation between the proportion of segments with akinesia and the proportion of segments with impaired perfusion was moderate (r=0.41), and there was no correlation between the proportion of segments with akinesia and the percentage of segments with absent perfusion.

Conclusion: There is a weak association between regional systolic function and myocardial perfusion after myocardial infarction, as assessed by real-time contrast myocardial echocardiography using power modulation.

Key Words: myocardial infarction; microvasculature; echocardiography; contrast; systolic function.

Introduction

In addition to the myocardium, the microcirculation may be also damaged in acute myocardial infarction (AMI). The microvasculature damage that occurs in AMI has important prognostic implications. About one-third of patients with an angiographically successful recanalization of the culprit vessel either with thrombolysis or with primary angioplasty suffer a non-successful myocardial reperfusion, and this is mainly due to microvasculature damage. Additionally, left
ventricular wall motion may suffer some dynamic changes after AMI\(^5,6\), and it has been proposed that the microvasculature status after AMI may be involved in the physiopathology of these changes\(^7-10\). Therefore, the assessment of the extension of AMI by the left ventricular systolic abnormalities early after AMI is of limited value, and the evaluation of myocardial microvasculature could be of interest in this respect.

Recently, myocardial contrast echocardiography (MCE) has made it possible to non-invasively evaluate the status of myocardial microvasculature\(^[11,12]\). The hypothesis of the present study was that the infarct area, when assessed by two-dimensional echocardiography, does not necessarily match the microvasculature status after AMI. The objective, therefore, was to evaluate the extent of microvasculature damage after AMI, and compare it with the size of the infarcted area assessed by two-dimensional echocardiography. For this purpose, we have used a novel MCE technique that allows real-time evaluation of myocardial perfusion using power modulation.

**Patients and Methods**

**Study Population**

The study population is constituted by 29 patients with recent (<1 week) AMI. Mean age was 62 ± 10 years, and eight (27.6%) were female gender. Of them, 18 (62%) had been reperfused with either thrombolysis or primary angioplasty. Echocardiographic studies were not performed after the first 48 h after symptom onset because the microvasculature function may either suffer impairment or improvement. During the first hours, a reversible decrease in vasodilation response, the so-called microvascular 'stunning', has been demonstrated after reversible coronary occlusion in some experimental studies\(^[13,14]\). On the other hand, an impairment of microvasculature function may be observed some hours after coronary reperfusion, due to both the progression of microvascular damage for several hours after reperfusion and to the under-estimation of microvasculature damage secondary to the reactive hyperaemia in the first few hours after reperfusion\(^[15,16]\).

**Echocardiographic Study**

In patients with anterior (n=15) and lateral (n=3) location AMI, the four chamber apical view was used, evaluating the basal, mid and distal segments of the interventricular septum, and the lateral wall (up to six segments per patient). In those with inferior AMI (n=11), the two chamber apical view was also used, thus also evaluating the basal, mid and distal segments of the inferior wall. The anterior wall was not evaluated because in our experience, its evaluation is of suboptimal quality in a high proportion of patients (up to nine segments per patient with inferior AMI).

Studies were performed with Phillips Sonos 5500 equipment and the S3 probe, with the patient in left lateral position. Patients underwent a two-dimensional echocardiography in order to determine the area with abnormal systolic function. A different investigator blinded to the results of the two-dimensional echocardiography evaluated the myocardial perfusion with MCE.

MCE was performed using the technique of power modulation, which combines low (0.1) and high (1.7) mechanical index. The use of a low mechanical index allows a real-time evaluation of myocardial perfusion (a non-destructive technique). Power modulation is based on the different behaviour of the tissue (linear) and the bubbles (non-linear) under low mechanical index, and permits the subtraction of the signal produced by the tissue, and therefore the evaluation of the specific signals produced by the bubbles.

After obtaining an adequate acoustical window, depth was adjusted so only the left ventricle filled the image sector. After selecting the Angio mode, gain was adjusted to the limit where tissue noise was beginning to appear. Pulse repetition frequency was set at 20, and gain at 55%, and increased or decreased subsequently as necessary during the study to optimize the quality of the images. Optison\(^6\) 1.5 ml was given i.v. for 3 min, and an additional bolus of 1.5 ml for 3 min was administered if necessary to obtain a good quality image. During the study, angio gain was readjusted (a lower and a higher gain to reduce blooming and to increase the contrast signal, respectively). When good angio signal was seen in the myocardium, a five-frame high mechanical index impulse (1.7) was given in order to destroy contrast and so ensure signal was not artefact. According to the quality of myocardial opacification with contrast agent, three different degrees of myocardial perfusion were defined: (1) normal: complete or homogeneous opacification; (2) patchy: incomplete or heterogeneous opacification; and (3) absent: absence of myocardial opacification. Thus, patchy or myocardial contrast opacification was considered as abnormal perfusion. Figure 1 illustrates cases showing complete, patchy and absent myocardial perfusion.

**Statistical Analysis**

Quantitative variables are expressed as mean ± SD, and qualitative variables as proportions (percentages). Comparison of proportions were evaluated by the Chi-square test (Fisher’s correction when necessary). The Spearman coefficient correlation was used to study the association between two continuous variables (proportion of segments per patient with abnormal/normal perfusion or motion). Associations were considered to be statistically significant in presence of a P value <0.05.
Results

Out of the 207 segments, 199 (96·1%) could be adequately evaluated by two-dimensional echocardiography and MCE. Out of these 199 segments, 54 (27·1%) were akinetic, whereas the remaining 145 (72·9%) were normoquinetic (n=121, 60·8%) or hypoquinetic (n=24, 12·1%).

As regards the degree of myocardial contrast opacification by MCE, 134 (67·3%) had a normal perfusion, whereas the remaining 65 (32·7%) had an impaired perfusion: 37 (18·6%) patchy and 28 (14·1%) absent.

In order to evaluate intra- and inter-observer variability, 11 patients (65 myocardial segments) were randomly selected and evaluated by two blinded investigators. Intra-observer agreement was 98·5% for absence/presence of perfusion, 96·9% for normal/abnormal perfusion, and 95·4% for absent/incomplete/complete perfusion. Inter-observer agreement was 93·8% for absence/presence of perfusion, 84·6% for normal/abnormal perfusion, and 80·0% for absent/incomplete/complete perfusion.

Table 1. Relationship between systolic wall motion and myocardial perfusion assessed by myocardial contrast echocardiography.

<table>
<thead>
<tr>
<th>Myocardial contrast opacification</th>
<th>Normal</th>
<th>Patchy</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>134</td>
<td>37</td>
<td>28</td>
</tr>
<tr>
<td>Systolic motion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>104</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Hipoquinesia</td>
<td>11</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Akinesia</td>
<td>19</td>
<td>16</td>
<td>19</td>
</tr>
</tbody>
</table>

The proportion of segments with impaired and absent perfusion was 33·6 ± 24·6% and 15·9 ± 20·8% per patient, respectively. Regarding systolic function, it was impaired in 39·1 ± 29·6% segments per patient, whereas 28·0 ± 22·7% were akinetic. Thus, the proportion of segments with impaired myocardial perfusion was lower than the proportion of segments with impaired systolic function. Similarly, the proportion of segments with absent perfusion was lower than the proportion of akinetic segments.

Relationship Between Systolic Function and Myocardial Contrast Opacification

The association between systolic function and myocardial perfusion is shown in Table 1. The frequency of abnormal perfusion was significantly higher in akinetic myocardial segments (65% vs 21%, Chi-square 34·8, P<0·001).

However, concordance between presence of akinesia and abnormal contrast opacification by MCE was only moderate (kappa index 0·42) and agreement only occurred in 116 segments (58%). Most (78%) segments with normal perfusion were normoquinetic, and 67·9% of segments with absent perfusion were akinetic. Nevertheless, 14% of normoquinetic segments had an impaired myocardial perfusion, whereas 35% of akinetic segments had a preserved myocardial perfusion. Regarding hypoquinetic segments, 54% had an impaired or absent perfusion, and the remaining 46% had a preserved contrast opacification.

Correlation between the proportion of segments with akinesia and the proportion of segments with impaired perfusion showed a coefficient of only 0·41. More importantly, there was absence of correlation between the proportion of segments with akinesia and the percentage of segments with absent perfusion at MCE (Figs 2 and 3).

Discussion

Some previous studies have shown the usefulness of MCE in the assessment of microvasculature status after...
AMI\[3,4,7\]. However, most of these studies used intra-coronary contrast agents, limiting their applicability to research studies. We now have the possibility to use new bubbles, able to cross the lung barrier, and with small size that allows myocardial contrast opacification\[17\]. On the other hand, the use of a low mechanical index allows us to easily evaluate myocardial perfusion in a real time. Other real-time MCE techniques using low mechanical index (power pulse inversion, PPI) have been previously evaluated\[18\].

The microvascular damage that occurs in AMI has important prognostic implications. About one-third of patients with an angiographically successful recanalization of the culprit vessel either with thrombolysis or with primary angioplasty suffer a non-successful myocardial reperfusion, and this is mainly due to a microvasculature damage\[2–4\]. On the other hand, left ventricular wall motion may suffer some dynamic changes after AMI. Segments with impaired systolic function due to myocardial stunning may improve over some weeks, and a progressive impairment on systolic function may be observed over the time in some patients due to cardiac remodelling. It has been proposed that the microvasculature status after AMI may be involved in the
physiopathology of these changes\[7–10\]. Therefore, the knowledge of not only wall motion, but also the microvasculature status should be desirable to achieve a complete evaluation of the extent of myocardial damage after AMI.

The results of our study show that there is a weak association between regional systolic function and myocardial perfusion after AMI, as assessed by real-time MCE. In our study, 35% of akinetic segments had a preserved myocardial perfusion, and 21% of no akinetic segments had an incomplete or absent myocardial perfusion.

Thirty-five per cent of akinetic segments (19 out of 54) had a preserved myocardial perfusion. Some data indicate that these segments could have a relatively preserved microvasculature and this could be related to the presence of myocardial viability. In the recently reported experimental study by Ohmori et al., akinetic myocardial segments that showed a preserved myocardial perfusion by MCE had a relatively preserved microvasculature, but not myocardial cells, in the histopathological study\[19\].

Although most normoquinetic segments in our study had a normal myocardial perfusion, 9% and 5% had an incomplete and absent perfusion, respectively. Other studies have also found some myocardial segments with preserved systolic function but with absent myocardial perfusion. Although it is speculative, these segments could be considered to be areas of myocardium at risk of suffering necrosis extension and/or subsequent myocardial remodelling\[19\].

In conclusion, the results of the present study show that the study of only myocardial wall motion may offer an incomplete assessment of the extent of myocardial damage after myocardial infarction. MCE using power modulation allows us a simultaneous evaluation of both myocardial wall motion and microcirculation status, and therefore a more complete evaluation of patients after AMI.

**Study Limitations**

This study has several limitations. First, the study population is relatively small, and thus no prognostic data could be obtained. Second, those segments which represent in particular the perfusion bed of the left anterior descending were not completely evaluated in this study, since anterior wall was not studied. In contrast, the basal segment of the interventricular septum is normally not considered to be perfused by the left anterior descending and is not affected by an occlusion of this vessel resulting in an anterior myocardial infarction.

**References**


**Table 2.** Correlation between perfusion and systolic function.

<table>
<thead>
<tr>
<th>% of segments with impaired perfusion vs.</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>impaired systolic function</td>
<td>0·41</td>
<td>0·029</td>
</tr>
<tr>
<td>% of segments with impaired perfusion vs</td>
<td>0·40</td>
<td>0·030</td>
</tr>
<tr>
<td>segments with akinesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of segments with absent perfusion vs.</td>
<td>−0·24</td>
<td>NS</td>
</tr>
<tr>
<td>impaired systolic function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of segments with absent perfusion vs.</td>
<td>0·01</td>
<td>NS</td>
</tr>
<tr>
<td>segments with akinesia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


