Effect of revascularizing viable myocardium on left ventricular diastolic function in patients with ischaemic cardiomyopathy

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Aims
In patients with ischaemic left ventricular (LV) dysfunction and viable myocardium, revascularization improves systolic function. Diastolic dysfunction is also present in such patients; however, whether revascularization improves diastolic function also is largely unknown.

Methods
Twenty-six patients with chronic ischaemic cardiomyopathy [ejection fraction (EF) 32 ± 6%, wall motion score index (WMSI) 2.45 ± 0.33] and viable myocardium (low-dose dobutamine echocardiography) were examined at baseline and 4 months after revascularization. Diastolic function was assessed by transmitral pulsed-wave Doppler and tissue Doppler imaging (TDI) at the mitral annulus.

Results
At baseline, 62% of patients showed non-restrictive filling (non-RF) pattern, and 38% restrictive filling (RF) pattern. After revascularization, along with improvement in systolic function (EF 43 ± 10%, WMSI 1.78 ± 0.47, P = 0.0002 for both), diastolic filling improved in most patients, with only three patients still exhibiting RF pattern (P = 0.016); furthermore, E’ velocity increased (32 ± 42%, P = 0.0028) and E/E’ decreased (–19 ± 31%, P = 0.0378) compared with baseline. Left ventricular filling pressure also decreased, from 17.5 ± 6.8 to 13.1 ± 6.5 mmHg (P = 0.005). Improvement of diastolic function by TDI was related to the extent of viability at baseline (P = 0.0098) and to LV reverse remodelling after revascularization (P = 0.0092).

Conclusion
In patients with ischaemic cardiomyopathy, LV diastolic filling may largely improve after revascularization. Improvement of diastolic dysfunction is related to the amount of viable tissue and it may represent an additional advantage of revascularizing dyssinergic but viable myocardium.

Keywords
Myocardial viability • Diastolic function • Doppler echocardiography • Heart failure • Hibernating myocardium

Introduction
Patients with severe coronary artery disease and depressed systolic function often show areas of left ventricle (LV) which, while chronically dysfunctioning, may nonetheless remain viable and amenable to recovery.1–3 This observation has spurred much interest, and many studies have demonstrated that revascularization may improve LV ejection fraction (EF) and prognosis if viable myocardium is present.4–8 Assessment of myocardial viability has therefore become an important step in the diagnostic and prognostic work-up of patients with ischaemic cardiomyopathy. However, although in these patients the beneficial effects of revascularization are well established in terms of recovery of regional and global systolic function, little attention has been paid...
to its effects on diastolic function. This may be of particular relevance, as diastolic dysfunction is typically present in patients with ischaemic cardiomyopathy, and is associated with worse haemodynamics, clinical status, and prognosis.

Measurement of early diastolic annular (E) velocity by tissue Doppler imaging (TDI) has been established as a relatively load-independent parameter of LV relaxation, and the ratio of mitral E-wave to E’ velocity (E/E’) has been shown to accurately reflect LV filling pressures. Recently, the availability of these methods has allowed diastolic function to be investigated accurately. Thus, it may be interesting to employ them in patients with hibernating myocardium undergoing myocardial revascularization.

The present study was designed to evaluate, in patients with ischaemic cardiomyopathy and evidence of viable myocardium, the effects of revascularization on LV diastolic behaviour, as assessed by measurements of TDI-derived load-independent parameters, and its relation to improved LV systolic function at follow-up.

Methods

Patient selection

From August 2006 to September 2007, patients scheduled to undergo elective coronary artery revascularization were screened. Inclusion criteria were: (i) coronary artery disease (≥70% stenosis in at least one major coronary artery); (ii) LV dysfunction (EF ≤40%); (iii) adequate thoracic acoustic window; (iv) evidence of myocardial viability; (v) sinus rhythm; (vi) stable clinical and haemodynamic conditions. Patients were excluded if they had acute coronary events ≤3 months prior to the study, valvular stenosis and/or regurgitation greater than mild, left-bundle-branch block, AV conduction delay.

Study protocol

After obtaining written informed consent, eligible patients underwent baseline echocardiography examination for the evaluation of LV global and regional systolic function and diastolic function. Viability of dysynergic segments was then assessed by contractile response to low-dose dobutamine (see below). Patients were referred to undergo revascularization within a month. Stability of clinical and haemodynamic conditions and persistence of wall motion abnormalities were confirmed at pre-operative evaluation. Follow-up evaluation (≥4 months after revascularization) included repeat assessment of LV global and regional contractile function and of diastolic function. The last follow-up assessment was planned in March 2008.

Baseline echocardiography

Two-dimensional echocardiography was performed using SONOS 5500 machine (Philips Technologies, Andover, MA, USA), or GE Vivid 7 ultrasound system (General Electric) equipped with a transducer employing harmonic imaging. Patients were studied in left lateral decubitus, in parasternal short- and long-axis and apical four- and two-chamber views. Left ventricular EF was calculated according to the modified Simpson’s rule. Three cardiac cycles were averaged for each measurement.

Regional wall motion was assessed using a 16-segment model of the LV and a four-point grade scale: 1, normal contractility; 2, hypokinesia; 3, akinesia; and 4, dyskinesia. Wall motion score index (WMSI) was calculated as the sum of the score of each segment divided by the number of segments scored. Patients with mitral regurgitation greater than mild (regurgitant jet area ≤4 cm²) were excluded. Echocardiograms were stored in digital format for subsequent off-line analysis performed by two investigators unaware of clinical and angiographic data; disagreements in interpretation were resolved by consensus.

Diastolic function analysis

Pulsed-wave Doppler interrogation of LV inflow tract was performed from the apical four-chamber view, with the patient in held-expiration. Sample volume was placed at the tips of mitral valve leaflets. Peak early diastolic flow velocity (E), peak flow velocity of atrial contraction (A), and their ratio (E/A) were measured at the maximum amplitude of E velocity. Deceleration time (DT) was measured from peak E velocity to the point when E-wave descent intercepted the zero line. After recording stable transmural flow velocities, the cursor was moved towards the LV outflow tract in the apical five-chamber view to record both mitral and aortic signals. Iso-volume relaxation time (IVRT) was calculated from the onset of aortic flow to the onset of mitral flow. Three cycles were averaged for each measurement. Restrictive filling (RF) pattern was defined when E/A was >1.5 and DT was <150 ms; non-restrictive filling (non-RF) pattern when E/A was ≤1 or E/A was >1 and DT was >150.

After completing transmural flow assessment, pulsed-wave TDI was performed. A 3 mm sample volume was placed at the septal and lateral mitral annulus to obtain early diastolic annular velocity (E’). E/E’ was obtained by averaging septal and lateral E’ velocities, as recommended in patients with wall motion abnormalities. Left ventricular filling pressure (LVFP) was estimated from E/E’ according to the formula: LVFP = 1.9 + 1.24 × E/E’.

Reproducibility of transmural flow parameters was assessed on 15 randomly chosen patients. Two independent investigators performed echo-Doppler evaluation on two separate days. Inter-observer and intra-observer variabilities (variation coefficient) were E-wave velocity, 1.5 and 1.2%; A-wave velocity, 1.1 and 0.8%; DT, 6.2 and 4.5%; IVRT, 5.5 and 2.9%.

Dobutamine stress echocardiography

To assess LV contractile reserve, after 48 h washout of beta-blockers dobutamine was infused intravenously at 5 mcg/kg for 5 min and increased to 10 mcg/kg per min for an additional 5 min; in case of lack of contractile response, an additional 15 mcg/kg were infused for a further 5 min. Parasternal long- and short-axis and apical four- and two-chamber views were monitored during the study. Wall motion score index was calculated at baseline and at the end of dobutamine infusion. Improvement of contractility of ≥1 grade from baseline in two or more adjacent segments indicated viability. Intra- and inter-observer reproducibilities of stress-echo readings in our laboratory were reported elsewhere.

At follow-up, LV systolic and diastolic functions were re-evaluated. When performing follow-up echocardiography, attention was paid to patient angulation, respiratory phases, and transducer position, in order to obtain the same echocardiographic views selected during baseline evaluation. A ≥5% increase in EF was considered as significant improvement of global systolic function. Significant LV reverse remodelling was defined by a ≥20% decrease in ESVI.

Statistical analysis

Data are expressed as mean ± standard deviation for continuous variables or percentage for categorical variables. Differences between groups were compared by Student’s t-test for parametric data, and
Mann–Whitney U test for non-parametric data. Categorical variables were compared by χ² test (with Yates correction when appropriate). Within each group, baseline and follow-up data were compared by paired t-test or Wilcoxon rank test, respectively, for parametric or non-parametric data, and by McNemar test for comparison of proportion. For changes from baseline of post-revascularization variables, we performed an analysis of covariance (ANCOVA) to account for possible baseline differences. To reduce the overall type I error rate, we calculated multiplicity-adjusted P-values, using a method based on bootstrap and resampling (SAS PROC MULTTEST) that incorporates correlations between variables, whenever two or more tests were performed on the same data set.

Correlations between Doppler parameters and echocardiographic indices of viability were performed by computing Pearson’s correlation coefficient, controlling for age and heart rate. Multiple linear regression analysis was performed to identify independent predictors of diastolic dysfunction improvement at follow-up. The per cent changes in E and in E/E′ at follow-up were used, alternatively, as dependent variables in the model. Using an epidemiological approach, only factors known to be important predictors of the outcome (age, previous myocardial infarction, therapy with angiotensin-converting enzyme-inhibitors and beta-blockers, viability indices, kind of revascularization, and changes in EF, EDVI, and ESVI at follow-up) were used in a ‘best-subset’ regression analysis. The best-subset of predictors was identified using both Mallows’s CP and R² criteria using SAS PROC REG. A two-sided value of P < 0.05 was considered significant.

Results

Patients

Thirty-one eligible patients underwent myocardial revascularization. Angioplasty was performed in 7 patients and coronary artery by-pass graft in 24 patients. The modality of revascularization was chosen by the attending physicians, based on coronary anatomy and clinical status. There were no peri-procedural myocardial infarctions. Of 31 revascularized patients, 1 died before follow-up, and 3 were lost at follow-up. One patient was excluded because of acute coronary syndrome prior to follow-up. The remaining 26 patients constituted the final study group. Table 1 summarizes clinical and demographic characteristics of the study population.

Baseline parameters

Left ventricular function at rest

At baseline, in the whole population, the LV was enlarged, and global and regional systolic functions were depressed (EF = 32 ± 6%; WMSI = 2.45 ± 0.33). Mitral regurgitation was absent in 43%, or mild in 57% of patients. Non-RF pattern was found in 16 (62%) patients, and RF pattern in 10 (38%) patients. In 22 patients (85%), relaxation of the LV was impaired, as indicated by E′ velocity <8 cm/s. The E/E′ ratio was <8 in only 2 (8%) patients, between 8 and 15 in 14 (54%) patients, and >15 (indicative of elevated LV filling pressures) in 10 (39%) patients. Table 2 summarizes echocardiographic data of patients divided according to transmitral flow pattern before revascularization; of note, no differences were found between non-RF and RF patients regarding parameters of LV volumes and systolic function. By definition, the two groups significantly differed in transmitral flow parameters by PW-Doppler (Table 2). At TDI analysis, E′ velocity was similar between non-RF and RF patients, although since transmitral E velocity was higher, RF patients tended to show higher E/E′ ratio (adjusted P = 0.2554). When patients were grouped according to baseline values of E/E′ ratio (Table 3), patients with E/E′ ratio at baseline >15 showed lower contractile reserve (P = 0.0328) and lower EF (P = 0.0392) than patients with a baseline E/E′ ratio <15, while LV volumes tended to be larger.

Response to dobutamine

In the whole cohort, low-dose dobutamine infusion elicited a substantial improvement of both EF (from 32 ± 7 to 41 ± 8%, P = 0.0002) and WMSI (from 2.45 ± 0.33 to 1.85 ± 0.36, P = 0.0002), with an average of 5.4 ± 1.7 segments/patient showing contractile recovery upon dobutamine infusion. However, an inverse relationship was observed between severity of diastolic dysfunction and contractile reserve, since: (i) the number of viable segments by dobutamine challenge was significantly lower in patients with baseline RF pattern than in patients with non-RF filling (Table 2), as well as in patients with baseline E/E′ ratio >15 (Table 3); (ii) after controlling for age and heart rate, the extent of viability was positively correlated to baseline DT (r = 0.59, P = 0.002), and to IVRT (r = 0.49, P = 0.014), and inversely related to E/E′ ratio (r = −0.65, P = 0.001) (Figure 1). There was no correlation between number of viable segments and E′ velocity at baseline (r = 0.19, P = 0.358).

Systolic function after revascularization

Follow-up evaluation was performed 8 ± 3 months after revascularization. Patients were in stable clinical and haemodynamic...
Table 2  Echocardiographic data of patients divided according to transmitral flow pattern before revascularization

<table>
<thead>
<tr>
<th></th>
<th>Non-RF (n = 16)</th>
<th>RF (n = 10)</th>
<th>P-value</th>
<th>Multiplicity-adjusted P-value</th>
</tr>
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<tbody>
<tr>
<td><strong>Systolic function</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic volume index (mL/m²)</td>
<td>115 ± 37</td>
<td>136 ± 35</td>
<td>0.155</td>
<td>0.3609</td>
</tr>
<tr>
<td>End-systolic volume index (mL/m²)</td>
<td>79 ± 35</td>
<td>94 ± 10</td>
<td>0.279</td>
<td>0.5765</td>
</tr>
<tr>
<td>EF (%)</td>
<td>32 ± 7</td>
<td>31 ± 7</td>
<td>0.731</td>
<td>0.9752</td>
</tr>
<tr>
<td>Number of viable segments</td>
<td>6.1 ± 1.1</td>
<td>4.2 ± 2.2</td>
<td>0.018</td>
<td>0.0496</td>
</tr>
<tr>
<td><strong>Diastolic function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E velocity (cm/s)</td>
<td>0.57 ± 0.13</td>
<td>0.94 ± 0.11</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>A velocity (cm/s)</td>
<td>0.85 ± 0.19</td>
<td>0.33 ± 0.12</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>0.73 ± 0.34</td>
<td>3.25 ± 1.28</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DT (ms)</td>
<td>262 ± 37</td>
<td>125 ± 21</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IVRT (ms)</td>
<td>115 ± 18</td>
<td>67 ± 9</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>E’ velocity (cm/s)</td>
<td>5.3 ± 1.9</td>
<td>6.5 ± 1.7</td>
<td>0.129</td>
<td>0.5260</td>
</tr>
<tr>
<td>E/E’ velocity ratio</td>
<td>11.5 ± 3.8</td>
<td>15.1 ± 4.6</td>
<td>0.04</td>
<td>0.2554</td>
</tr>
</tbody>
</table>

Table 3  Echocardiographic data of patients divided according to E/E’ ratio before revascularization

<table>
<thead>
<tr>
<th></th>
<th>Before revascularization</th>
<th>Adjusted P-value</th>
<th>After revascularization</th>
<th>Adjusted P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E/E’ &lt; 15 (n = 16)</td>
<td>E/E’ ≥ 15 (n = 10)</td>
<td>E/E’ &lt; 15 (n = 22)</td>
<td>E/E’ ≥ 15 (n = 4)</td>
</tr>
<tr>
<td><strong>Systolic function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic volume index (mL/m²)</td>
<td>114 ± 69</td>
<td>138 ± 47</td>
<td>0.3794</td>
<td>97 ± 4</td>
</tr>
<tr>
<td>End-systolic volume index (mL/m²)</td>
<td>74 ± 25</td>
<td>101 ± 41</td>
<td>0.1662</td>
<td>56 ± 4</td>
</tr>
<tr>
<td>EF (%)</td>
<td>34 ± 6</td>
<td>28 ± 6</td>
<td>0.0392</td>
<td>44 ± 2</td>
</tr>
<tr>
<td>WMSI</td>
<td>2.36 ± 0.29</td>
<td>2.60 ± 0.34</td>
<td>0.2085</td>
<td>1.70 ± 0.07</td>
</tr>
<tr>
<td>Number of viable segments</td>
<td>6 ± 1.2</td>
<td>4 ± 2</td>
<td>0.0328</td>
<td>——</td>
</tr>
<tr>
<td><strong>Diastolic function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E velocity (cm/s)</td>
<td>0.65 ± 0.19</td>
<td>0.81 ± 0.23</td>
<td>0.1536</td>
<td>0.62 ± 0.03</td>
</tr>
<tr>
<td>A velocity (cm/s)</td>
<td>0.70 ± 0.25</td>
<td>0.55 ± 0.37</td>
<td>0.4631</td>
<td>0.80 ± 0.05</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.27 ± 1.26</td>
<td>2.39 ± 1.63</td>
<td>0.1512</td>
<td>0.84 ± 0.11</td>
</tr>
<tr>
<td>DT (ms)</td>
<td>238 ± 69</td>
<td>163 ± 62</td>
<td>0.0283</td>
<td>244 ± 12</td>
</tr>
<tr>
<td>IVRT (ms)</td>
<td>104 ± 28</td>
<td>82 ± 22</td>
<td>0.1216</td>
<td>113 ± 5</td>
</tr>
<tr>
<td>Non-RF (%)</td>
<td>12 (75)</td>
<td>4 (40)</td>
<td>0.074</td>
<td>21 (95)</td>
</tr>
<tr>
<td>RF (%)</td>
<td>4 (25)</td>
<td>6 (60)</td>
<td>1 (5)</td>
<td>2 (50)</td>
</tr>
</tbody>
</table>

*Data are reported as adjusted means by ANCOVA, controlling for baseline values.

conditions, and there had been no major changes in medications since enrolment (Table 4). In the whole population, EF, WMSI, and LV volume indices all significantly improved at follow-up (Table 5), with an average of 5.2 ± 3.0 segments/patient showing ≥1 grade of improvement, consistent with dobutamine response observed at baseline. Ejection fraction increased ≥5% in 21 (81%) patients, and significant LV reverse remodelling was found in 18 (69%) patients. When patients were grouped according to values of E/E’ ratio at follow-up (Table 3), those with E/E’ ratio >15 showed significantly lower EF, worse WMSI, and larger LV volumes than patients in whom E/E’ ratio was <15.

**Diastolic function after revascularization**

After revascularization, a non-RF pattern was found in 23 patients, and only 3 patients still exhibited an RF pattern (Figure 2). Most PW-Doppler-derived parameters of diastolic function significantly improved after revascularization (Table 5). In particular, A-wave velocity significantly increased with a significant decrease in E/A ratio and prolongation of both DT and IVRT (Table 5).

In the whole population, TDI parameters of diastolic function significantly improved at follow-up after revascularization (Table 5). On an average, global E’ velocity increased by 32 ± 42% (P = 0.0028) and E/E’ ratio decreased by 19 ± 31% (P = 0.0378); this was
associated with a significant decrease in estimated LV filling pressure (from $18 \pm 5$ to $14 \pm 7$ mmHg, $P = 0.005$). However, substantial differences were detected among patients at the individual level (Figure 3). In fact, whereas $E/E$’ ratio significantly decreased in 18 (69%) patients, it remained unchanged, or even increased, in 8 (31%) patients. Of note, changes in $E$’ velocity and in $E/E$’ ratio were related to the number of viable segments during low-dose dobutamine echocardiography ($r = 0.49, P = 0.0098$, and $r = 0.44, P = 0.0212$), and to the number of segments that actually recovered function at follow-up ($r = 0.52, P = 0.0060$, and $r = 0.57, P = 0.0020$). Figure 4 shows that $E$’ velocity and $E/E$’ ratio improved at follow-up as the number of recovered segments increased. Furthermore, there was a direct relationship between improvement in load-independent parameters of diastolic function and reduction at follow-up in both EDVI and ESVI (Figure 5). By linear regression analysis, after controlling for confounding factors, independent predictors of improvement in $E$’ velocity after revascularization were the per cent reduction in ESVI at follow-up ($B = -0.76, P = 0.0042$), beta-blocker therapy ($B = 0.25, P = 0.0162$), and, although not significant, age ($B = -1.28, P = 0.079$). Moreover, the only independent predictor of improvement in $E/E$’ ratio after revascularization was the per cent reduction in ESVI at follow-up ($B = 0.72, P = 0.0003$). Changes in DT or IVRT after revascularization were not correlated to myocardial viability indices ($r = 0.08, P = 0.7014; r = 0.10, P = 0.5984$, respectively), nor to the improvement in LV volumes ($r = -0.15, P = 0.4387; r = -0.25, P = 0.2024$, respectively).

### Clinical outcome

Consistent with improvement in systolic and diastolic functions, after revascularization patients also showed improvement of their clinical status, as NYHA functional class decreased from $2.9 \pm 0.7$ to $1.7 \pm 0.9$ ($P = 0.0002$). Improvement in NYHA class was related to the extent of contractile reserve during dobutamine infusion ($r = 0.55, P = 0.0038$), and to the number of myocardial segments that actually recovered function after revasculization ($r = 0.53, P = 0.0050$). Clinical evolution was related to reduction in $E/E$’ ratio ($r = 0.42, P = 0.0328$) after revascularization, but not to improvement in $E$’ velocity ($P = 0.2023$).

Prevalence of NYHA class improvement at follow-up (reduction ≥1 grade from baseline) was of 63% if there was improvement of either EF (>5%) or $E/E$’ ratio (reduction of $E/E$’ ratio from >15 at baseline to 8–15, or to <8 at follow-up, or from 8–15 to <8 at follow-up); improvement in functional status increased at 92% in patients in whom both EF and $E/E$’ ratio improved after revascularization.

### Discussion

In the present study, diastolic dysfunction—characteristically present in patients with ischaemic cardiomyopathy—significantly improved after coronary revascularization, as assessed by parameters of LV filling. A substantial amount of non-contracting yet viable myocardium was initially present in our patients. Consistent with this finding, revascularization also brought about significant improvement of regional and global systolic functions: recovery of diastolic function was associated with the amount of contractile reserve prior to revascularization, and with the extent of recovery of systolic function at follow up. Together, these results support the tenet that in ischaemic heart disease, systolic and diastolic functions go hand-in-glove, and directly demonstrate that revascularizing chronically viable, dysynergic myocardium may also beneficially impact on diastolic function.
Diastolic dysfunction is present in virtually all patients with heart failure,9–11 and it can be traced to abnormal distensibility, filling, or relaxation of the LV.12 On the basis of Doppler evaluation of trans-mitral flow, distinct filling patterns have been described representing various degrees of diastolic impairment.15,19 At the end of the spectrum, ‘restrictive pattern’ reflects high LV filling pressure11–13 and has been associated with worse clinical and haemodynamic status and increased mortality compared with non-RF pattern.13,14 The more benign non-RF pattern is generally associated with delayed relaxation in the presence of normal or modestly increased LV filling pressure.15

In our patients with ischaemic cardiomyopathy, prior to revascularization we invariably observed impairment of diastolic filling and increased LV filling pressures, with a clear relationship between the severity of diastolic impairment and contractile reserve. In this setting, for the first time, we document that, after revascularization, there is an improvement of diastolic filling, as indicated by decreased \( E \) velocity, significant increase in late diastolic velocity (with consequent reduction in \( E/A \) ratio), and prolongation of DT and IVRT. Furthermore, by assessing diastolic function by relatively load-independent TDI measurements, we were able to document improvement of global and regional LV relaxation (\( E_0 \)) after revascularization. Interestingly, the improvement in LV relaxation was associated with the amount of dysfunctioning myocardium that recovered function after revascularization (Figure 4), and with the extent of reverse LV remodelling (Figure 5). These results are consistent with the observation that improvements in LV systolic performance are coupled with improved LV relaxation in patients with heart failure.23

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nonetheless remain viable and amenable to recovery,\textsuperscript{1,2,4,5,27,28} and therefore this condition of 'dormant' myocardium may be an ideal test ground to investigate whether revascularization improves diastolic function, and the relationship with pre-existing viability and subsequent recovery of contractility. Indeed, although it is still debated whether viable-but-dysynergic myocardium is the

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure4}
\caption{Changes in $E^\prime$ (A) and $E/E^\prime$ (B) from baseline to follow-up after revascularization according to the extent of dysfunctioning myocardium that actually recovered function at follow-up.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure5}
\caption{Correlation between per cent of changes in $E^\prime$ (A) and in $E/E^\prime$ ratio (B) and changes in left ventricular volume indices after revascularization.}
\end{figure}
direct result of severe underperfusion (i.e. hibernation) or a consequence of repetitive stunning.\textsuperscript{2,30–31} There is consensus over the obligatory requirement for severe stenosis in the coronary artery perfusing the dysfunctional territory. Therefore, it is conceivable that removing this stenosis would also impact on diastolic function. However, although scores of studies have focused on the effects of revascularization with respect to regional and global systolic function [for review, see references 2–4,8], there is paucity of information concerning possible effects on diastolic function. Studies investigating this issue have typically been performed early after revascularization, and in patients in whom LV systolic function was largely preserved;\textsuperscript{32–36} furthermore, the presence and extent of viable myocardium were not established. Thus, those investigations provide no insights with respect to long-term recovery of diastolic function after revascularization in the setting of ischaemic cardiomyopathy. More recently, Yong et al.\textsuperscript{36} assessed the relationship between LV filling pattern (by PW transmural Doppler) and viability in patients with ischaemic cardiomyopathy. They reported that RF pattern (defined by DT < 150 ms) was negatively associated with myocardial viability at baseline, and with poor recovery of systolic function after revascularization, whereas patients with DT > 150 ms showed substantial viability at baseline and good recovery of LV function at follow-up. Our study confirms these findings; in addition, we extend the observation with regard to other potentially important mechanisms, such as improved LV relaxation observed after revascularization, by analysis of TDI parameters. Furthermore, for the first time, we specifically assessed the consequences of revascularization on diastolic properties of LV and of its relationship with regained contractility of viable segments. Interestingly, the reduction in E/E’ ratio at follow-up was associated with improvement in NYHA functional class after revascularization; this is in agreement with recent observations by Skaluba and Litwin,\textsuperscript{37} who showed that exercise capacity is primarily affected by elevated filling pressures, rather than by impaired LV relaxation.

Finally, in addition to reduction and/or prevention of ischaemia, it is possible that the improvement in diastolic function seen after revascularization is also being driven by improved restoring forces related to smaller LV end-systolic volume, as suggested by the correlation between improvement of both E’ and E/E’ values and the extent of LV reverse remodelling at follow-up (Figure 5), as this mechanism may lead to restoration of diastolic function.\textsuperscript{38}

Limitations

In the present study, we did not attempt to dissect out the various components of diastole: however, analysis of precise mechanisms of diastolic impairment/recovery in ischaemic cardiomyopathy was beyond the scope of this study. Absence of invasive measurement of atrial and ventricular pressures is another limitation, since LV filling is sensitive to loading conditions.\textsuperscript{15} In this respect, however, we took care in investigating only patients in stable conditions and in whom medical therapy had already been adjusted prior to revascularization and had remained unchanged. Use of relatively load-independent TDI parameters further indicates that improved diastolic filling was unlikely to be due to changes in loading conditions.

Another limitation is that we did not randomize patients to revascularization or not. This could not be possibly done for obvious ethical and clinical reasons. Owing to the lack of any control group and of randomization, this study cannot unambiguously assess the effect of interest. However, several considerations concur to indicate that the benefits observed after revascularization on diastolic function were due to recovery of dyssynergetic function, and not to other non-specific mechanisms: (i) in the absence of revascularization, patients’ conditions remained stable, as checked on two occasions 1 month apart; (ii) therapy remained largely unchanged at follow-up; (iii) improvement of diastolic function was mostly confined to patients in whom there was also a substantial recovery of viable segments, not just to all revascularized patients.

Conclusions

In patients with chronic ischaemic cardiomyopathy, the degree of alteration of diastolic function is strictly linked to the extent of contractile impairment and to the amount of chronically dyssynergic myocardium. The present study indicates that improved diastolic function may be an additional salutary effect of revascularization in these patients. As such, it lends further support to the concept that a thorough search for viability (and, hence, for possible revascularization) should be part of diagnostic work-up of patients with ischaemic cardiomyopathy.\textsuperscript{8,39–41}

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