Hotline Editorial

Natural history of mitral regurgitation due to flail leaflets

Mitral regurgitation is now a common valvular disease because of the increasing age of the population and the frequency of degenerative disease with ruptured chords and flail leaflets.

Rationale for analysing the natural history of mitral regurgitation

Mitral regurgitation can be treated successfully by valve replacement or repair with excellent relief of symptoms. Therefore, the presence of marked symptoms is a widely accepted indication for surgery. However, with this traditional approach, left ventricular dysfunction is a frequent postoperative complication, which carries a poor long-term prognosis. The frequency and severity of this complication have led to the suggestion that surgery should be performed early in the course of the disease before severe symptoms occur. Low operative mortality, excellent long-term survival and feasibility of valve repairs have made this approach clinically possible. Valve repair tends to preserve left ventricular function better than valve replacement, but it has not eliminated left ventricular dysfunction and consequently is not a justification for delaying surgery but rather should be considered as an incentive for early surgery. However, early surgery is controversial, mainly because solid data on the natural course of medically treated mitral regurgitation are lacking.

Previous studies on the natural history of mitral regurgitation

The natural history of mitral regurgitation has not been defined satisfactorily. The reported survival rates after diagnosis have varied widely, ranging from 95% at 20 years, to 70% at 10 years, and to 46% and 50% at 5 years. These differences are probably due to small study populations, associated co-morbid conditions, and considerable selection bias. An important source of variability is the poorly defined and probably variable degrees of regurgitation. The predominance of rheumatic lesions also makes these series less relevant to current practice. Finally, cardiac complications such as heart failure have been reported rarely and inconsistently. Therefore, these data are not helpful for making clinical decisions.

Rationale for analysing mitral regurgitation due to flail leaflets

Mitral regurgitation due to flail leaflets represents a unique opportunity for analysing the natural history of mitral regurgitation. This lesion produces uniformly severe regurgitation, and it has been reliably diagnosed non-invasively with echocardiography for many years, which allows the analysis of long-term outcome. In western countries, flail leaflets are the most frequent cause of surgical correction of mitral regurgitation. Nevertheless, its natural history is poorly known and contradictory assertions implying either a poor or good prognosis in patients treated medically have led to diametrically opposed recommendations regarding surgery.

Mitral regurgitation due to flail leaflets: excess mortality and high morbidity

We recently analysed the Mayo clinic experience during the decade of 1980 to 1989 with 229 patients in whom mitral regurgitation due to flail leaflet was diagnosed with echocardiography. Follow-up began at diagnosis and continued as long as the patients were medically followed. As expected, the left ventricle was enlarged (diameter: 34±5 and 19±4 mm m⁻² at end-diastole and end-systole, respectively). Remarkably, the main reason for consultation generally was not related to cardiac symptoms and 71% of the patients were in New York Heart Association class I or II at diagnosis. Nevertheless, these patients exhibited an excess mortality (Table 1), in comparison with the general population of the same age and sex (mortality 43%±7% at 10 years, or 6.3%/year, P=0.016) (Fig. 1). The cause of death was cardiac in 70% of the cases resulting in a cardiac mortality of 33%±7% at 10 years, and although this is not testable, it appears in excess to expected (45% and 12% respectively for the general population of similar age). Morbidity was high, with
Table 1 Occurrence of events after diagnosis of mitral regurgitation due to flail leaflets

<table>
<thead>
<tr>
<th>Event</th>
<th>Overall 5-year rate (mean ± SE)</th>
<th>Overall 10-year rate (mean ± SE)</th>
<th>Overall linearized yearly rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>28 ± 4</td>
<td>43 ± 7</td>
<td>6.3</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>21 ± 4</td>
<td>33 ± 7</td>
<td>4.3</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>30 ± 4</td>
<td>63 ± 8</td>
<td>8.2</td>
</tr>
<tr>
<td>Chronic atrial fibrillation</td>
<td>8 ± 3</td>
<td>30 ± 12</td>
<td>2.2</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td>12 ± 3</td>
<td>12 ± 3</td>
<td>1.9</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>1 ± 1</td>
<td>3 ± 2</td>
<td>0.4</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>5 ± 2</td>
<td>8 ± 3</td>
<td>1.5</td>
</tr>
<tr>
<td>Mitral surgery</td>
<td>57 ± 3</td>
<td>82 ± 4</td>
<td>2.0</td>
</tr>
<tr>
<td>Mitral surgery or death</td>
<td>69 ± 3</td>
<td>90 ± 3</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Excess mortality, high morbidity and surgery almost unavoidable within 10 years of the diagnosis in spite of the low co-morbidity and rarity of symptoms at baseline.

Mitral regurgitation due to flail leaflets: can low- and high-risk groups be defined?

In addition to age, the baseline predictors of survival were ejection fraction and symptoms. Patients with an echocardiographic ejection fraction <60% had an excess mortality (11.3% yearly). Patients with class III or IV symptoms, even transient, also had considerable mortality if treated medically (34% yearly). Therefore, high-risk groups can be defined that evidently require immediate surgery, unless contraindicated by overwhelming co-morbidity. Conversely, no group at very low risk could be defined. A notable mortality is observed in patients with an ejection fraction ≥60% (5.3% yearly) or in those in class I or II (4.3% yearly) or both. Although patients in class II had more heart failure and surgery during follow-up than those in class I, survival with medical therapy was not different between the two classes. In our opinion, the persistent risk in these groups should lead to the consideration of surgery in all patients with mitral regurgitation due to flail leaflets when the diagnosis is made. In support of this approach is the improved prognosis associated with surgery whenever it is performed (adjusted risk ratio 0.29, 95% confidence interval, 0.15-0.56).

However, early surgery is not necessarily indicated in all patients. Several factors should be considered. An important factor is operative risk, which is determined mainly by the age of the patient. The repairability of the valve is another important aspect to consider, as is the quality of results achieved in the institution where the surgery is contemplated. Nevertheless, these data should lead to the consideration of early surgery in mitral regurgitation due to flail leaflets even in patients with no or minimal symptoms.

Mitrail regurgitation: future directions

Management of mitral regurgitation is at a crossroads. The conservative approach, i.e. waiting for signs of left ventricular dysfunction to proceed with surgery has shown its major weaknesses. The difficulties in measuring left ventricular function in mitral regurgitation are demonstrated by the lack of wide agreement on what indices should be monitored and
by the postoperative occurrence of ‘unexpected’ left ventricular dysfunction. We hypothesize that a strategy of early surgery in patients with severe mitral regurgitation even with no or minimal symptoms may well provide an improved outcome\textsuperscript{[13]} in view of the current risk and high feasibility of valve repair. This view is not yet shared by all\textsuperscript{[14]} and much work remains to be accomplished. First, the prerequisite for the new paradigm of early surgery should be emphasized. (a) A firm diagnosis of severe mitral regurgitation is required. This can now be reliably determined (regurgitant volume $\geq 60$ ml, fraction $\geq 50\%$, effective regurgitant orifice $\geq 40$ mm\textsuperscript{2}) by the new non-invasive quantitative methods using Doppler echocardiographic imaging\textsuperscript{[15]}, (b) Accurate anatomical delineation of the aetiology of mitral regurgitation is necessary. Early surgery is recommended for degenerative diseases such as flail leaflets but not currently for rheumatic or ischaemic mitral regurgitation. The results of valve repair in these lesions need to be carefully analysed to modify this position. (c) Early surgery is defensible only in medical centres that achieve low risk ($<2\%$) and high success ($>90\%$) with valve repair. Second, more studies need to be done. The outcome of patients with 60 ml of regurgitant volume may not be the same as in those with 100 ml of regurgitant volume, although severe regurgitation is present in both groups. It is essential that future studies analyse the natural history of mitral regurgitation on the basis of prospectively collected quantitative data. Finally, the magnitude of the effect of early surgery should be critically analysed, preferably by a controlled trial, in relatively low-risk groups such as patients with severe mitral regurgitation, class I or II symptoms and ejection fraction $\geq 60\%$. Currently, we believe that the facts should be discussed with the patients and that early surgery should be considered after the diagnosis is made of mitral regurgitation due to flail leaflets.

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References