Left Atrial Size and Atrial Fibrillation in Mitral Stenosis

Factors Influencing Their Relationship

By Peter Probst, M.D., Nora Goldsclager, M.D., and Arthur Selzer, M.D.

SUMMARY

In a series of 135 patients with mitral valvular stenosis, three groups were identified: those in sinus rhythm, those with intermittent atrial fibrillation, and those with longstanding, established atrial fibrillation. Examination of the relationships between atrial fibrillation, hemodynamic findings and radiologic data in mitral stenosis was undertaken. Analysis of clinical and hemodynamic factors in the three groups revealed that: 1) age is an etiological factor in the production of atrial fibrillation, as suggested by the age distribution among the three groups; 2) left atrial enlargement may be the result, rather than the cause, of atrial fibrillation; and 3) severity of mitral stenosis is not invariably related to the incidence of atrial fibrillation. Hemodynamic measurements were not significantly different among the three groups, with the single exception of lower cardiac outputs found in patients with established atrial fibrillation. Since no single consequence of mitral stenosis always produces atrial fibrillation, it is suggested that several factors in different combinations can initiate the self-perpetuating process of atrial fibrillation and that the classic form of the arrhythmia may lead secondarily to left atrial enlargement.

Additional Indexing Words:
Mitral valve area Mitral insufficiency

Atrial fibrillation occurs in clinically normal individuals1-3 and as a complication of virtually every known form of cardiac disease. It does, however, have a preferential tendency to develop in certain specific cardiac conditions, of which mitral valve disease is the most noteworthy. The incidence of atrial fibrillation in mitral stenosis has been estimated at 40%,3 and in mitral regurgitation at 75%.4 Aside from the obvious fact that the left atrium is the chamber bearing the brunt of the overload in both mitral stenosis and regurgitation, the factors predisposing to the development of atrial fibrillation in mitral valve disease have not been adequately clarified.

The purpose of this investigation was to analyze the relationships among the radiologic evidence and hemodynamic consequences of mitral valve stenosis and the presence of atrial fibrillation. As quantification of severity of the mitral lesion can be achieved with reasonable accuracy only in pure mitral stenosis, patients with mitral incompetence were not considered in the study. Our investigation differs from earlier reports5-7 in that patients with atrial fibrillation were divided into those with intermittent and those with chronic, established atrial fibrillation.

Methods

All patients with pure or predominant mitral stenosis who had undergone complete right heart catheterization including cineangiography performed from the main pulmonary artery were included in the study. Of the 135 patients analyzed, 62 were in stable sinus rhythm (Group 1); 27 had had intermittent episodes of atrial fibrillation (Group 2), terminated periodically by either antiarrhythmic agents or D.C. cardioversion; and 46 had established atrial fibrillation (Group 3). In most patients (52 of 73) with intermittent or chronic atrial fibrillation, the duration of the arrhythmia was known; in the remaining 21, the history was inadequate to assess duration.

Hemodynamic data were obtained at rest and during four minutes of supine exercise performed on a bicycle...
ergometer; the level of exercise was sufficient to double or triple the resting oxygen consumption. The pulmonary artery wedge pressure was considered to reflect left atrial pressure. Cardiac index was calculated from the Fick formula and was considered abnormal if it was less than 2.5 liters/min/m² and/or failed to rise appropriately with exercise. Standard formulae were used in the calculations of total pulmonary and pulmonary vascular resistances. The exercise factor was determined by dividing the amount of increase in cardiac output during exercise by the increase in oxygen consumption; the lower limit of normal in our laboratory is 350. Mitral valve areas were calculated from the formula of Gorlin and Gorlin. Cineangiography of the left atrium and mitral valve was performed in the right anterior oblique projection with the cardiac catheter positioned in the main pulmonary artery. The size of the left atrium was evaluated by four independent observers and was graded as normal or minimally enlarged, or grossly enlarged.

The interrelationships of left atrial size, presence and duration of atrial fibrillation, pulmonary artery wedge pressures, pulmonary resistances, cardiac outputs at rest and during exercise, and mitral valve areas were examined with a view toward clarifying some of the determinants of left atrial size and cardiac rhythm.

**Results**

The average age of the 62 patients in sinus rhythm (Group 1) was 42 (range, 18-66) (table 1). In the majority (36 of 62, 58%), the left atria were of normal size or only slightly enlarged. However, 20 patients (32%) had moderate atrial enlargement and six (10%) marked enlargement (table 1). Atrial size in these patients was unrelated to age (table 2). Of interest was the observation that of six patients with marked left atrial enlargement, four were under 45 years of age.

Group 2 patients (intermittent atrial fibrillation) ranged in age from 28-69 (average 50). The majority of these patients (15 of 27, 55%) had left atria of normal or slightly enlarged size, 11 of 27 (41%) had moderate atrialmegaly, and one (4%) had marked atrial enlargement (table 1). The distribution of atrial sizes of groups 1 and 2 is not statistically significantly different.

The average age of the 46 patients in established atrial fibrillation (Group 3) was 54 (range 30-74, table 1). In this group, normal-sized left atria were present in only about 36%, with essentially equal numbers of the remaining patients having moderately and grossly enlarged atria (table 1).

There was a fairly clearcut relationship between atrial fibrillation and age, and thus, by implication, duration of disease (table 2). Table 3 shows that the duration of the arrhythmia had little definite relationship to left atrial size, suggesting that either left atrial enlargement is not an invariable consequence of chronic atrial fibrillation, or the duration of the disease state plays the predominant role (see

**Table 1**

**Historical, Radiographic, and Hemodynamic Data in 135 Patients with Mitral Stenosis**

![Table 1](https://circ.ahajournals.org/)

**Table 2**

**Left Atrial Size by Decade and by Rhythm**

![Table 2](https://circ.ahajournals.org/)
Table 3

<table>
<thead>
<tr>
<th>Duration of AF (yrs)</th>
<th>Left atrial size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal or mildly enlarged</td>
</tr>
<tr>
<td>&lt;1</td>
<td>IA F</td>
</tr>
<tr>
<td>1-2</td>
<td>7</td>
</tr>
<tr>
<td>3-5</td>
<td>1</td>
</tr>
<tr>
<td>&gt;5</td>
<td>1</td>
</tr>
</tbody>
</table>

Abbreviations: AF = atrial fibrillation; IAF = intermittent atrial fibrillation.

Discussion). Figure 1 illustrates the incidences of the cardiac rhythms for a given left atrial size. Patients in sinus rhythm comprise the greatest percentage of those with small left atria, whereas larger atria are seen mainly in patients with established atrial fibrillation.

Analysis of the hemodynamic data obtained in the three groups of patients (table 4) reveals significant differences between groups 1 (sinus rhythm) and 3 (established atrial fibrillation) only in cardiac indices at rest and during exercise. There are no significant differences in mitral valve area, pulmonary artery wedge pressure, total pulmonary or pulmonary vascular resistances, or exercise factor among the three groups. When all rhythm groups are combined and the relationship of calculated mitral valve area to atrial size is compared, patients with smaller valve areas are, not unexpectedly, usually shown to have larger atria. However, over

Figure 1

Relationship of cardiac rhythm to left atrial size in patients with mitral stenosis. In general, patients in sinus rhythm comprise the largest percentage of normal-sized or minimally enlarged, as well as moderately enlarged, atria, whereas those with chronic established atrial fibrillation comprise most of the atria that are markedly enlarged. Of note, however, are the stable proportions of patients in all three rhythm groups that are present in the normal to moderately enlarged atrial size category.
one third of the patients with valve areas of less than 1.0 cm² have normal or only minimally enlarged atria, and over one fourth of those with moderate mitral stenosis (valve area: 1.0-1.4 cm²) have marked atrial enlargement. When mitral valve area, atrial size, and cardiac rhythm are considered together (table 5), it becomes apparent that valve area is not the prime determinant of left atrial size.

**Discussion**

Earlier studies dealing with possible factors in the development of atrial fibrillation in patients with mitral stenosis have not shown consistent results. Fraser and Turner⁶ concluded from a study of 269 patients with mitral valve disease that atrial fibrillation bears no direct relationship to severity of mitral disease. **Atrial enlargement**, on the other hand, has been found with greater frequency in patients with atrial fibrillation than in those in sinus rhythm. This relationship has been established by both estimation of atrial size by plain chest radiography⁷ and by left atrial volumetric determinations.⁸ Although Loogen and Panayotopoulos⁹ suspected some correlation between severity of mitral stenosis and left atrial size, Pech and Munster¹⁰ could not reach similar conclusions on the basis of atrial volume determinations. Other investigators⁶,⁷,¹² have also been unable to find a consistent relationship between atrial size and various hemodynamic parameters in mitral stenosis.

Thus, beyond the well-known observation that atrial fibrillation and significant left atrial enlargement, and often both, frequently accompany mitral stenosis, we know little about what factors influence the development of atrial fibrillation. There are two points of general agreement: 1) mitral regurgitation is a more powerful stimulus for the development of both atrial fibrillation and gross enlargement of the left atrium, and 2) age, and thus presumably, duration of disease is an important contributory factor in the development of atrial fibrillation.³,¹⁰ As neither atrial fibrillation nor marked atrial enlargement can consistently be related to the severity of mitral stenosis as determined by valve area size or to any other measurable hemodynamic variable affected by mitral valve obstruction, the question of whether left atrial enlargement is the cause or the effect of the arrhythmia remains unresolved. In order to confirm that enlargement causes fibrillation, the assumption that large atria are more susceptible to this arrhythmia would have to be made; on the other hand, any effort to prove that the abnormal rhythm causes enlargement must be based on the presumption that the intrinsically abnormal state of the fibrillating atria leads to distension.

The design of this study differs from earlier investigations in that the size of left atrium was determined angiographically in a sufficiently large number of patients to encompass a broad spectrum of cases of mitral stenosis, and in that patients with atrial fibrillation were assigned to one of two categories: those with intermittent arrhythmias (representing an early stage), and those with established atrial fibrillation (representing the late stage of this arrhythmia). Although left atrial volume determinations were not carried out in this

<table>
<thead>
<tr>
<th>Left atrial size</th>
<th>MVA (cm²)*</th>
<th>0.3-0.9</th>
<th>1.0-1.4</th>
<th>1.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal or</td>
<td></td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Mildly enlarged</td>
<td>Group 1</td>
<td>12</td>
<td>52</td>
<td>13</td>
</tr>
<tr>
<td>N = 68</td>
<td></td>
<td>5</td>
<td>22</td>
<td>1</td>
</tr>
<tr>
<td>Moderately enlarged</td>
<td>N = 47</td>
<td>6</td>
<td>38</td>
<td>8</td>
</tr>
<tr>
<td>Grossly enlarged</td>
<td>N = 20</td>
<td>1</td>
<td>31</td>
<td>2</td>
</tr>
</tbody>
</table>

*Mitral valve area (MVA) calculations not performed in five patients due to technical errors in cardiac output determinations.
†Percentages refer to the distribution of Groups 1, 2, and 3 per category of MVA and left atrial size.
study, the classification of left atrial size by the degree of enlargement is adequate to detect the relationships under consideration.

The three groups of patients under consideration represent three stages in the natural history of mitral stenosis. To elucidate the causal relationships between atrial fibrillation and left atrial size, we propose that any variable showing a stepwise change in incidence among these three groups would suggest a causative contribution to the genesis of atrial fibrillation. If a variable present in both patients in sinus rhythm and in those with intermittent atrial fibrillation (Groups 1 and 2 combined) differs significantly from that variable in Group 3, the implication is that this variable is the effect, rather than the cause, of atrial fibrillation.

Our study shows a stepwise increase in incidence of atrial fibrillation with increasing age, confirming that age (duration of mitral stenosis) is an important contributory factor in the genesis of atrial fibrillation. Patients in Groups 1 and 2 were found to have comparable cardiac outputs, but their outputs were significantly higher than those in Group 3, implying that lower cardiac output is a result of chronic atrial fibrillation. No differences could be demonstrated between incidence of atrial fibrillation and level of left atrial pressure, mean pulmonary arterial pressure, or degree of pulmonary vascular resistance among the three groups. A high incidence of marked left atrial enlargement was seen only in Group 3 patients, confirming the conclusions of others; this finding supports the proposal that gross atriomegaly is an effect rather than a cause of atrial fibrillation in most patients, and conforms to our finding that duration of the arrhythmia has no direct bearing per se on atrial size. Presumably, then, other factors such as atrial muscle properties or duration of the valvular stenosis, are playing a role (see below). Interestingly, although some relationship between severity of mitral stenosis and left atrial size can be shown (fig. 2), no clear relationship between severity of mitral stenosis and incidence of atrial fibrillation is demonstrable (table 1).

On the basis of the information now available, we suggest the following hypothesis for the development of atrial fibrillation in patients with mitral stenosis. The mechanical consequences of mitral stenosis—although not expressed by any single hemodynamic measurement—may be assumed to traumatize the left atrium, providing prerequisites for the electrophysiologic inhomogeneity of atrial conduction times and refractory periods that are demonstrable in experimental atrial fibrillation. Once present, atrial fibrillation leads to a further increase in the degree of left atrial enlargement that was initially the result pari passu of obstruction at the mitral valve. The arrhythmia is self-sustaining, and the vicious cycle is further perpetuated by the advancing age of the patient. The relationship between severity of mitral stenosis and incidence of atrial fibrillation will tend to be obliterated by considering together both older individuals who have mitral stenosis in a mild, nonprogressive form who, because of their age, are more prone to develop atrial fibrillation, and younger patients in whom the traumatic effect of mitral stenosis may be insufficient to initiate the arrhythmia even though the atrium may be quite significantly enlarged. Patients with mitral stenosis who remain in sinus rhythm may be presumed to have noncompliant, hypertrophied atria which usually resist significant dilatation. Whether or not a given patient remains in sinus rhythm or develops atrial fibrillation must depend, at least in part, on the individual properties of cardiac muscle, as well as possibly the speed of development of the mitral valve lesion.

The role of traumatic injury in producing atrial fibrillation finds support in the variety of conditions other than mitral stenosis which may lead to this arrhythmia. Stimulation of the atria produced during cardiac catheterization occasionally initiates a bout of atrial fibrillation. The more severe mechanical myocardial and pericardial trauma sustained during cardiac surgery produces postoperative atrial fibrillation in a large proportion of individuals. It has been shown that manipulation of the left atrium, as in mitral valve repair or replacement, produces postoperative atrial fibril-

![Figure 2](image-url)

**Figure 2**

Calculated mitral valve area in cm² related to left atrial size. All cardiac rhythm groups are combined. When thus considered, it is seen that, on the whole, the smaller the valve area the larger the left atrium. Despite the suggested relationship between these variables, there is considerable overlap in the data, and all degrees of severity of mitral stenosis are seen in left atria of all sizes.

*Circulation, Volume XLVIII, December 1973*
lation six times more commonly than surgical trauma to the aorta or aortic valve. Atrial fibrillation also occurs in conditions in which primary anatomic changes in the atria exist such as pericarditis, atrial infarction, and invasive tumors.

Established atrial fibrillation is associated with structural alterations in the atrium consisting of fibrosis, loss of muscle mass, and disruption of normal architecture. These morphologic changes are presumably consequences of the process by which, in association with chronic atrial fibrillation, atrial enlargement develops. The proposed suggestion that such anatomic abnormalities are related to rheumatic activity is implausible for several reasons: first, atrial fibrillation is exceedingly rare in the early stages of rheumatic fever, when rheumatic activity is highest and when microscopic changes in the myocardium are demonstrated; second, the role of persistent rheumatic activity in the later progression to stages of mitral stenosis has now been seriously questioned; third, nonrheumatic diseases associated with overload of an atrium such as nonrheumatic mitral regurgitation and atrial septal defect are associated with as high an incidence of atrial fibrillation as in cases with a history of rheumatic disease; fourth, rheumatic disease affecting predominantly the aortic valve shows a very low incidence of atrial fibrillation.

References
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Circulation. 1973;48:1282-1287
doi: 10.1161/01.CIR.48.6.1282

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