The Syndrome of Severe Mitral Regurgitation with Normal Left Atrial Pressure

By Eugene Braunwald, M.D., and William C. Awe, M.D.

It has been demonstrated repeatedly that when mitral regurgitation is produced in experimental animals, an elevation of left atrial pressure occurs. Similarly, numerous hemodynamic studies in patients with this valvular lesion have shown that the left atrial or pulmonary artery wedge pressures generally exceed the values observed in normal individuals, and the V-wave peaks in these pressure pulses are particularly prominent. These pressure elevations have been attributed to the increased volume of blood that enters the left atrium during ventricular systole. Indeed, elevation of the mean left atrial pressure with particularly tall V waves has become the hemodynamic hallmark of mitral regurgitation, and the diagnosis of this abnormality by cardiac catheterization has been based, in large measure, on these characteristic pressure changes. It is the purpose of this report to focus attention on a group of patients with severe mitral regurgitation in whom these alterations in the left atrial pressure pulse are not evident, and who appear to constitute a distinct segment in the clinical-hemodynamic spectrum of mitral regurgitation.

Description of Patients

Studies on a total of 10 patients constitute the basis of this report. Congenital mitral regurgitation was present in one patient, an 8-year-old girl. The other nine patients (seven women and two men) have acquired rheumatic mitral valvular regurgitation. These nine patients ranged in age from 27 to 49 years, with an average age of 39 years.

History

A history of active rheumatic fever was elicited from all nine patients with rheumatic mitral regurgitation, and multiple attacks occurred in seven of them. All ten patients were severely disabled and were considered, on clinical grounds, to be in functional classes III or IV (New York Heart Association). The patient with congenital mitral regurgitation had symptoms for 1 year, whereas the other patients had symptoms for 4 to 19 years (average of 9.3 years). All patients complained of severe fatigability and various degrees of exertional dyspnea. Symptoms or clinical signs of left ventricular failure had been present for 1 to 8 years (average of 3.2 years). All 10 patients were receiving maintenance digitalis therapy at the time of study and had been receiving this medication for 1 to 33 years (average of 7.4 years). Five patients had experienced paroxysmal nocturnal dyspnea, two of them had had hemoptyses, and five had had ankle edema.

Physical Examination

All 10 patients had prominent left ventricular lifts and in five of them a strong systolic thrill was palpable at the apex. A holosystolic murmur, of at least grade III/VI intensity, was heard at the apex and was transmitted into the axilla in all 10 patients, and nine of them also had the short, low-pitched, mid-diastolic murmur at the apex, which is typically heard in patients with severe mitral regurgitation. Hepatomegaly and edema were present in only three instances. None of the patients had clinical or laboratory evidence suggestive of active rheumatic fever at the time of study.

Electrocardiograms

All 10 patients exhibited atrial fibrillation. Right axis deviation was present in one patient, while in the other nine the electrical axis was normal. The voltage criteria for left ventricular hypertrophy were satisfied in seven patients.

Roentgenograms

Gross cardiac enlargement was evident on the chest roentgenograms of all 10 patients. The left atrium was considered to be moderately enlarged in three patients, and markedly enlarged in the remainder (fig. 1). Although it was difficult to define the presence or absence of left ventricular enlargement, this chamber was considered to be enlarged in eight of the 10 patients.

Hemodynamic Studies

The pulmonary artery or right ventricular sys-
Figure 1
Roentgenograms of patients with severe mitral regurgitation, marked left atrial enlargement, and normal left atrial pressures.

tolic pressures were within normal limits for this laboratory (under 30 mm. Hg) in all, except patient R.F. (table 1). The mean pulmonary artery pressures ranged from 13 to 22 mm. Hg. Left atrial pressures, measured by the transseptal or transbronchial technics, were within the normal range for this laboratory (under 30 mm. Hg) in all, except patient R.F. (table 1).

Pathologic Data
Nine of the 10 patients included in this report are alive, so that pathologic data are available on one patient (S.H.). In this 8-year-old girl the left ventricle was hypertrophied, and the left atrium was markedly dilated. The anterior mitral leaflet was shortened, and the chordae tendineae to both leaflets were markedly shortened, preventing valve closure.

Discussion
The hemodynamic findings in patients with mitral regurgitation have been well documented. In patients in whom this is the predominant valvular lesion, and who exhibit congestive heart failure or symptoms of diminished cardiac reserve, the cardiac output has frequently been noted to be below normal, the mean left atrial pressure elevated, and the ‘‘V’’-wave peaks have been particularly high. In a significant number of such patients, the pulmonary artery pressure is elevated proportionately more than the left atrial pressure due to associated elevations of the pulmonary vascular resistance. In this latter group of patients clinical manifestations of right heart failure are not unusual.

Perusal of the published clinical and hemodynamic data obtained from patients with mitral regurgitation has revealed an occasional exception to this pattern. In each of several series of patients with this valvular abnormality there have been one or two patients who evidently exhibited clinical mani-
festations of reduced cardiac reserve and who had left atrial enlargement but in whom the left atrial (or pulmonary artery wedge) pressures were within normal limits.\textsuperscript{8, 10, 12, 20} The data obtained from the patients described in this report focus attention on the syndrome of severe mitral regurgitation with normal left atrial pressure. On clinical grounds, all 10 of these patients had a markedly reduced cardiac reserve, and several were considered to be approaching the termination of their illness. With the exception of the child with congenital mitral regurgitation, the other nine patients had symptoms for many years. The chronicity of the process was also reflected in the atrial fibrillation in all 10 patients. The clinical findings characteristic of mitral regurgitation were unequivocal, and there was no clinical or hemodynamic evidence of any associated cardiovascular abnormality. Whereas other series of patients with rheumatic mitral regurgitation have had a preponderance of male patients,\textsuperscript{21-23} seven of the nine patients with rheumatic heart disease included in this report were female. Although a history of active rheumatic fever has been reported in 25 to 50 per cent of patients with chronic mitral regurgitation,\textsuperscript{8, 22} it could be elicited in all nine patients with rheumatic mitral regurgitation reported herein. Atrial fibrillation and gross left atrial enlargement were present in all 10 patients. Although absolute measurements of mitral regurgitant flow in man are not feasible, the contour of the arterial indicator-dilution curves following injection into the left side of the heart were suggestive of massive regurgitation (fig. 3).

If the compliance of the left atrium remained constant, enlargement of this chamber could occur only in association with an increase in the transmural pressure. The association of a normal mean left atrial pressure and a normal left atrial V wave, with a markedly enlarged left atrium indicates that the walls of the left atrium and of the pulmonary venous bed are more compliant than

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
Patient & Age, yrs., sex & PA S/d, mm. Hg & LA, mean mm. Hg & LA, \textquoteleft V\textquoteright\ wave peak mm. Hg & LVED grad. mm. Hg & Cardiac index L./min./M.\textsuperscript{2} \\
\hline
L.P. no. 00-82-40 & 43, F & 27/ & 11 & 23 & 6 & 1 & 1.21 \\
\hline
P.K. no. 02-68-76 & 44, F & 25/7 (13) & 5 & 11 & 3 & 0 & 1.73 \\
\hline
H.E. no. 02-55-35 & 45, F & 25/9 (15) & 8 & 11 & 3 & 3 & 1.07 \\
\hline
I.H. no. 03-38-41 & 49, F & 27/5 (18) & 10 & 16 & 7 & 2 & 2.68 \\
\hline
A.P. no. 01-25-02 & 40, F & 28/10 (20) & 7 & 14 & . & . & 2.53 \\
\hline
R.F. no. 03-29-28 & 47, M & 32/14 (22) & 12 & 22 & 4 & 0 & . \\
\hline
E.C. no. 03-75-61 & 38, F & 28/9 (19) & 12 & 22 & 7 & 0 & 1.40 \\
\hline
R.G. no. 02-96-85 & 24, F & 26/10 (20) & 9 & 15 & 13 & 2 & . \\
\hline
B.R. no. 03-88-86 & 27, M & 25/10 (18) & 9 & 12 & 2 & 3 & 3.30 \\
\hline
S.H. no. 03-07-20 & 8, F & 28/12 (20) & 8 & 14 & 7 & 0 & . \\
\hline
\end{tabular}
\caption{Hemodynamic Findings}
\end{table}

PA, pulmonary artery pressure; S/d, mm systolic/diastolic, mean pressures, LA, left atrial pressure; LVED, left ventricular end-diastolic pressure; LA-LV end-diast. grad., left atrial-left ventricular end-diastolic pressure gradient.

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usual in the patients described herein. It is suggested that long-standing mitral regurgitation may, in some instances, alter the length-tension characteristics of the left atrial wall and thereby displace the atrial pressure volume curve to make it more compliant, so that a normal pressure exists in a greatly enlarged atrium.

The possibility that alterations in the pressure-volume relationships of the left atrium may occur is not a new concept. It has been postulated by a number of investigators that differences in atrial compliance occur among different patients with mitral valve disease.\textsuperscript{9, 13, 29, 24-26} Indeed, the difficulties encountered with analyses of the left atrial pressure pulse contour for the separation of patients with mitral stenosis from those with mitral regurgitation have been attributed to variations in the pressure-volume relationships in the left atrium and the pulmonary venous bed.\textsuperscript{9, 25}

Although it is possible that chronic active rheumatic fever played a role in the alterations of the mechanical properties of the left atrium, it is evident that, since one of the patients (S.H.) had congenital rather than rheumatic disease, the presence of rheumatic activity is certainly not essential to the development of the syndrome described. Furthermore, none of the nine patients with rheumatic mitral regurgitation exhibited any clinical or laboratory findings that suggested the presence of rheumatic activity. Since all of the patients had had mitral regurgitation for many years, it is likely that the changes in atrial distensibility that were present at the time of study had not been present earlier, but had developed during the course of the illness. Unfortunately, serial measurements of atrial pressure had not been carried out on any of these patients. Studies on a patient not included in this series,\textsuperscript{27} provide strong suggestive evidence that the increase in atrial compliance may occur as a late development in the course of chronic mitral regurgitation. This 9-year-old boy developed exertional dyspnea at the age of 8 years and examination at this time revealed that he had a regular rhythm and the physical findings characteristic of mitral regurgitation. Right heart catheterization revealed elevation of the pulmonary artery pressure (58/30, mean = 40 mm. Hg), and transseptal left heart catheterization showed the left atrial pressure to be elevated as well (mean = 25 mm. Hg, V peak = 45 mm. Hg). The patient's symptoms of congestive heart failure increased in severity in spite of intensive therapy, and 1 year after these studies his cardiac rhythm changed to atrial fibrillation. There was roentgenographic evidence of further increase in the size of the left atrium, but surprisingly, the left atrial pressure had declined quite strikingly (mean = 15 mm. Hg, V peak = 24 mm. Hg). Thus, in this patient a decline in the mean left atrial pressure and the atrial V-wave peak pressure occurred in the face of an increase in left atrial size. Since he showed striking clinical improvement after operation which was accompanied by a further decline of atrial pressure to a mean of 7 mm. Hg, as well as spontaneous reversion to sinus rhythm, it would appear that the increase in atrial compliance is not necessarily accompanied by irreversible depression of left ventricular function. The presence of atrial fibrillation in the 10 patients described herein, as well as
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the transient period of fibrillation in patient A.J. discussed above, suggests the possibility that the process that changed atrial compliance may also have been related in some fashion to the development of this arrhythmia.

The compliance of the left atrium and pulmonary venous bed appears to be capable of modifying profoundly the clinical and hemodynamic picture exhibited by patients with mitral regurgitation. On the basis of differences in atrial compliance, three major groups of patients with mitral regurgitation can be identified: 1. A group of patients with mild or moderate enlargement of the left atrium, but with quite striking elevation of the mean left atrial pressure, and particularly of the V wave. In many patients in this group, severe mitral regurgitation has developed acutely, as for example those in whom there occurs sudden rupture of chordae tendineae or a tear of a mitral leaflet (fig. 4). Marked elevation of pulmonary vascular resistance occurs with considerable frequency in this group of patients, and therefore right heart failure is not an unusual clinical manifestation. 2. By far the most common group of patients with mitral regurgitation is represented by those with moderate or massive enlargement of the left atrium, associated with significant elevations of the left atrial pressure. 3. The third group of patients in this spectrum is represented by the patients with the syndrome of severe chronic mitral regurgitation and normal left atrial pressure described in detail in the present report. It seems likely that these three groups form a continuum and that numerous gradations exist between them.

Since effective surgical treatment for mitral regurgitation is now becoming a reality some comment is warranted on how the variations of left atrial compliance, and the resultant clinical-hemodynamic findings modify the selection of patients. Since, with any given magnitude of regurgitant flow the atrial pressure varies inversely with the compliance of the atrium, the extent to which the atrial pressure can be expected to decline following successful operation will also vary inversely with atrial compliance. Accordingly, the clinical and hemodynamic benefits of operation may be expected to be greatest in the patients with relatively small left atria and high left atrial pressures. Conversely, the benefit in the patients described in this report would not be expected to be as striking, since their left atrial pressures cannot decline to any significant extent. By diminishing the hemodynamic burden imposed on their left ventricles, however, operation may be expected to elevate the low cardiac outputs in these
patients. Indeed, a number of observations suggest that operative intervention should also be considered in patients with the syndrome of severe mitral regurgitation and normal left atrial pressure. Among these are (1) the favorable effects of operation in patient A.J. described above, (2) the fact that patient S.H. succumbed to chronic congestive heart failure in spite of the finding of a normal atrial pressure at catheterization carried out several months earlier, and (3) the fact that these patients, in spite of normal atrial pressures, were all incapacitated.

Summary

It has been generally thought that significant elevations of the left atrial and pulmonary vascular pressures occur in patients with mitral regurgitation of sufficient severity to produce serious disability and gross enlargement of the left atrium. Ten patients with severe mitral regurgitation have been encountered in whom gross left atrial enlargement was accompanied by normal left atrial and pulmonary artery pressures. These patients ranged in age from 8 to 49 years, all were in functional classes III or IV, and the average duration of symptoms was 7.3 years. Nine patients had rheumatic mitral regurgitation while one had a congenital lesion. Atrial fibrillation and the physical findings of pure mitral regurgitation were present in all patients, as was striking left atrial enlargement on their roentgenograms. Left atrial pressure, determined by left heart catheterization, averaged 9.1 mm. Hg and did not exceed 12 mm. Hg in any patient, and the V wave was not particularly prominent. The cardiac index was markedly depressed and averaged 2.0 L./min./M.² B.S.A.

The observed discrepancy between left atrial size and pressure must reflect a disturbance in the compliance of the left atrial wall. It is suggested that long-standing mitral regurgitation may modify the mechanical characteristics of the atrial wall and that the presence of a normal left atrial pressure must not be assumed to exclude the presence of severe mitral regurgitation. The manner in which variations in left atrial compliance affect the clinical picture of mitral regurgitation and the selection of patients for operative intervention are discussed.

References

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Training the Doctor of Tomorrow

In matters of health and medical care, the doctor no longer stands alone. He continues to be the leader and captain of the team, or teams, but he is assisted by at least 132 groups who have been specially trained in careers of health service. There are in the United States 2,500,000 people engaged in the so-called health professions. Today, doctors do many things. There are thousands of doctors who are never seen at a patient's bedside. Dr. A travels to the hospital administrator's office or to the Dean's office with a brief case; Dr. B spends his working life amid test tubes; Dr. C is a detective who can tell whether a woman was hanged or strangled; and Dr. D tests whether atom scientists have absorbed excessive radiation. Thus, I could go on and on, down the alphabet several times. The doctors who treat patients, however, whether in their offices or at the bedside, are the men responsible for the doctor-patient relationships and are largely responsible for the public attitudes about the profession.—Chester S. Keefer, M.D. Training the Doctor of Tomorrow, Boston, The Boston Medical Quarterly 12: 87, 1961.
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