Calcification of the Mitral Valve

Results of Valvotomy in 100 Cases

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This paper is concerned with the significance of calcification of the mitral valve in relation to surgical treatment. Wide differences of opinion are still held by physicians and surgeons on the advisability of operation in patients with heavy calcification, and we are aware that many patients have been rejected for valvotomy on account of this complication.

It may be that with the application of open-heart surgery to the mitral valve all patients with heavy calcification will in future come to be treated by this technique and probably in most cases have a prosthesis inserted. However, such treatment is still in the experimental stage in that the fate of the prosthesis and long-term results (including the incidence of systemic embolism) are unknown. There is at present a greater operative risk than with the closed method which in our experience gives worthwhile results for several years in the majority of cases. It is present practice to advise replacement of the valve in such cases only when a previous closed transventricular valvotomy has failed to achieve adequate improvement or if symptoms attributable to valvular obstruction recur. This has been necessary 35 times in the past two years.

Our surgical experience of the closed technique now includes 118 patients with heavy calcification of the valve, and this is a satisfactory number to discuss and is adequate for statistical analysis. In order to include a follow-up period of more than two years, the first 100 patients with heavy calcification have been analysed. They came from a consecutive series of 547 patients treated by valvotomy for severe mitral stenosis between 1950 and 1962.

It should be emphasized that we have rarely rejected for valvotomy any patient in whom severe stenosis was present.

INCIDENCE

The over-all incidence of calcification of the valve of all degrees detected by pre-operative radiography or by palpation at the time of valvotomy was 35 per cent, a figure that is in conformity with other published series, and the incidence of heavy calcification was 18 per cent. There was an increased incidence with age, from 16 per cent in those under 30 years to 51 per cent in those over 50 years of age, and there was a higher incidence in men (70%) than in women (25%): the reason for this is not known (Fig. 1). Nearly all men over 50 with severe mitral stenosis can be expected to have a calcified valve and in half of them it is likely to be heavy.

It is not possible to make an accurate comparison between the incidence of calcification in patients with dominant mitral stenosis and in those with dominant incompetence, because the numbers available with the latter condition are relatively small. We have, however, analysed 81 patients in whom dominant incompetence was proved either at operation for repair or replacement, or in whom dominant incompetence was found when dominant stenosis had been expected.

Although calcification is not infrequently found when moderate stenosis and incompetence are associated, i.e. when there is a regurgitant jet through a valve orifice which accepts no more than the terminal phalanx of the index finger, heavy calcification was found in only 2 and light calcification in only 1 of the 81 patients with severe or dominant incompetence.

CALCIFICATION AND OTHER ADVERSE FACTORS

It is important to appreciate that patients with heavy calcification of the mitral valve have a higher incidence of other potentially adverse factors, including atrial fibrillation, age over 50, a cardiothoracic ratio over 60 per cent, and associated aortic

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TABLE I
HEAVY CALCIFICATION OF MITRAL VALVE: INCIDENCE OF ASSOCIATED ADVERSE FACTORS

Calcification	No. in group	Atrial fibrillation		Age > 50 yr.		Cardiothoracic ratio > 60%		Aortic valve disease	
		No.	%	No.	%	No.	%	No.	%
Heavy calcification... ..	100	57	57	25	25	36	36	57	57
No heavy calcification ..	447	166	37	43	10	88	20	182	41
All cases	547	223	41	68	12	124	23	239	44

valvular disease, than those who do not have heavy calcification (Table I).

Clearly such factors must contribute to the operative risk and to long-term results.

DIAGNOSIS

Calcification of the mitral valve may be suspected from clinical signs, as mentioned below, but can only be established before operation by radiography, at operation by palpation, or at necropsy. The surgeon can only be certain of calcification that impinges on the surface of the cusps, and a hard nodule within may be due to exceptionally dense fibrous tissue and yet have the consistency of calcification. In addition, it is certain that heavy calcification may be present without the surgeon being able to make a confident diagnosis by palpation.

Initially calcification was divided arbitrarily into light, moderate, and heavy grades, but it was not always easy to distinguish between moderate and heavy calcification, and it was found that there was no significant difference between their effects. Consequently they have been grouped together. It was also found that there was no significant difference between the effects of no and light calcification, and in most analyses these two grades have been grouped together.

Physical Signs. Calcification modifies physical signs, as previously described (Turner and Fraser, 1956), and in many patients with severe mitral stenosis may be suspected at the bed side. However, there are no diagnostic signs.

The first heart sound and opening snap tend to be faint or absent. There is usually an apical systolic murmur which is not only loud but tends to be high-pitched and musical in quality rather than harsh. These qualities are doubtless associated with the fact that calcification impedes the normal closure of the mitral valve and the billowing of the anterior cusp when the valve opens. Inevitably irregular cusp margins are unable to come into perfect apposition so that an apical systolic murmur will be present in most cases, and the calcified surface of the cusps modifies the usual pitch associated with a regurgitant jet. Nevertheless, heavy calcification may be present, despite the absence of a systolic murmur and with quite a good first sound and opening snap.

The incidence and intensity of mitral systolic murmurs in patients with heavy, light, and no calcification of the valve is shown in Table IIA, and the incidence of different degrees of calcification in patients with systolic murmurs in Table IIB. Table IIA shows that of 100 patients with heavy calcifica-

FIG. 1.—Incidence of heavy and light calcification in cases of mitral stenosis classified by age and sex.

TABLE IIA
CALCIFICATION AND ASSOCIATED MITRAL SYSTOLIC MURMURS

Grading of murmur	Degree of calcification						Total	
	Heavy		Light		None			
	No.	%	No.	%	No.	%	No.	%
0	23	23	49	55	226	63	298	55
1-2	43	43	29	33	100	28	172	31
3-4	34	34	11	12	32	9	77	14
Total	100	100	89	100	358	100	547	100

TABLE IIB

Degree of calcification			Grading of systolic murmurs						Total	
			0		1-2		3-4			
			No.	%	No.	%	No.	%	No.	%
Heavy	..	..	23	8	43	25	34	44	100	18
Light	..	..	49	16	29	17	11	14	89	16
None	..	..	226	76	100	58	32	42	358	66
Total	..	..	298	100	172	100	77	100	547	100

tion 77 per cent had a systolic murmur which in 34 per cent was loud, whereas of 447 without heavy calcification a murmur was present in only 172 (39%), and it was loud in only 43 (10%). Table IIB shows that of 77 patients with a loud murmur 58 per cent had calcification which was heavy in 44 per cent, whereas of 298 patients without a murmur only 24 per cent had calcification and only 8 per cent had heavy calcification.

Table III shows the greatly increased incidence of a palpable regurgitant jet detected at operation in cases of severe mitral stenosis with heavy calcification.

In summary, a patient with heavy calcification of the valve is much more likely to have a loud apical systolic murmur than if he had no calcification, and if a patient with tight stenosis has a loud mitral systolic murmur he is much more likely to have heavy calcification than if he had no systolic murmur.

It is concluded that in heavy calcification of the valve the presence of a loud apical systolic murmur from associated mitral incompetence may be of relatively little significance. Presumably the rough margins of the valve orifice and imperfect apposition of the cusps, despite severe stenosis, are the factors responsible for the intensity of the murmur.

Calcification of the mitral valve may be detected on a plain radiograph, by radioscopy, by cine-angiography, or by tomography.

Radiography. Heavy calcification may sometimes be seen on a plain postero-anterior or oblique film, and when it is clearly apparent other techniques are unnecessary.

Tomography. Calcification may be readily shown by tomography, and this technique has the advantage of a permanent record. It is useful for purposes of illustration and in teaching and is therefore indicated in some cases on this account. However, recording multiple films is time-consuming and costly. In our opinion it is not only unnecessary for diagnosis but is a less certain method for the detection of relatively minor degrees of calcification, because the characteristic movement of the cusps can only be observed by radioscopy or cine-angiography.

TABLE III
CALCIFICATION OF MITRAL VALVE
PALPABLE REGURGITANT JET

Degree of calcification	No. in group	No. with jet	%
Heavy	100	51	51
Light	89	17	19
None	358	62	18
All cases	547	130	24

Since it is advisable to determine the presence or absence of calcification in every case, routine tomography will entail taking a large number of films for no particular purpose in the majority of cases.

Radioscopy. Radioscopy ("screening"), preferably using an image intensifier, has the advantage of simplicity, speed, and economy. Calcification can be detected with certainty within a few seconds if the observer "cones down" over the appropriate area. It is usually best seen in the right oblique view. Even light calcification of the cusps can usually be picked up in this way because in such instances the dancing movement is often particularly lively. The characteristic movement

is from south-east to north-west, in an anti-clockwise direction and with a relatively rapid downstroke. In moderate calcification this dancing movement of the valve is also seen, but in heavy calcification there is relatively little movement. Light calcification may not be detected by radioscopy, especially in relatively obese patients, but, as will be shown, this degree of calcification is not significant from the point of view of valvotomy and long-term results up to 10 years.

Calcification of the aortic valve can usually be distinguished from that of the mitral valve by its different location and by the different movement of the cusps. The aortic cusp of the mitral valve and the mitral cusp of the aortic valve are contiguous, and calcification of both valves may be present, in which case differentiation may be difficult or impossible.

Comparison between Pre-operative and Operative Findings. Heavy and moderately heavy calcification of the mitral valve can always be observed by careful radioscopy, using an image intensifier. However, it is not always possible to be certain of light calcification, and the surgeon can sometimes feel spicules of superficial calcification which have not previously been observed. On the other hand, he can only be certain of calcification which impinges on the surface, and heavy calcification has sometimes been observed before operation when the surgeon could say no more than that a hard mass was palpable in the substance of the valve. In the great majority of cases the surgeon has confirmed pre-operative findings, but for the above reasons it has not been possible to make an exact comparison. However, all those cases in which calcification was certain have been included. It has never been possible to predict from the radiographic appearances of the calcified valve whether the surgeon would be able to obtain a satisfactory valvotomy.

VALVOTOMY

What is achieved at operation may be expressed in different ways so that there are difficulties in comparing the records of one surgeon with another. Relevant factors include the size of the valve orifice before and after valvotomy, the degree of anterior and posterior separation of previously adherent cusp margins ("commissurotomy"), the extent to which fused chordæ can be separated, and the degree of mobility restored to the cusps.

The extent of valvotomy is sometimes expressed on the basis of a comparison between the initial size of the orifice, as judged by the exploring finger, and that present after the operation, and sometimes on the degree of anterior or posterior separation of the cusps ("splitting"). In the first instance the size of the orifice is judged by palpation, and this necessitates in most cases forceful separation of adherent and sclerotic cusp margins with a vigour which is not comparable with that of the blood stream: consequently an accurate comparison cannot be made. Often the shape of the mitral orifice,

particularly when the cusps are rigid, is very different from that of the exploring finger, so that only an approximate estimate of the two opposite diameters can be made. Splitting of the commissures ("commissurotomy" or separation of the adherent cusp margins towards the anatomical commissure) can be described as complete or incomplete. However, though complete separation of the cusps, i.e. as far as the anatomical commissures, can be recognized by an experienced observer, degrees of completeness cannot be accurately expressed: in some cases there is no anterior or no posterior fusion.

Obviously a complete anterior and posterior valvotomy is the ideal, but in many cases it is impossible to achieve or not attempted for fear of producing a significant degree of traumatic mitral incompetence. Much will depend on the experience and skill of the surgeon. It will also be appreciated that partial anterior and partial posterior valvotomy may produce a better anatomical and functional result than a complete valvotomy in one direction and none in the other.

Another important factor to be taken into consideration is that in the early days surgeons tended to exaggerate what had been achieved by comparison with the greater insight that came with increased experience. Most thoracic surgeons would probably agree that it took many cases and perhaps several years before a full appreciation of the pathological anatomy of the valve was realized in relation to what constituted a complete valvotomy. In addition, the introduction of a new technique, such as a knife or a mechanical dilator, or of a new method of approach to the valve, such as the transventricular route in comparison with the transatrial route, did not necessarily bring a sudden improvement in what could be achieved. In most cases with increasing experience improvement was progressive.

Unquestionably in the present series a higher and increasingly large proportion of "good splits" was obtained following the introduction of the transventricular dilator. On the other hand, a reasonably satisfactory valvotomy was thereafter achieved with cusps that were previously difficult to separate. In other words, better splits were obtained in poorer valves. In the present series the result has been noted as complete or incomplete anterior and posterior separation of the cusps, because this was recorded in all cases.

Accepting all these difficulties and the lack of strict statistical comparability between the relatively small number of patients who had heavy calcification compared with the larger number who had not, the extent of valvotomy has been compared in the three groups of those with heavy calcification, light calcification, and without detectable calcification. Findings are summarized in Table IV.

A great degree of precision is obviously not possible in judging the result of valvotomy at the time of operation. A "good" valvotomy, however, has been recorded when both anterior and posterior commissures have been completely divided (A + P), or one completely and the other partially divided

TABLE IV
EXTENT OF VALVOTOMY AND HEAVY CALCIFICATION

Extent of valvotomy	Grading	Heavy calcification (%)	No heavy calcification (%)
A + P } ..	Good	41	52
Ap + aP } ..	Fair	48	41
A or P } ..	Poor	7	6
a + p } ..		4	1
a or p } ..			
Doubtful } ..			

(Ap or aP). A "fair" result indicates either complete division of one commissure alone (A or P) or partial division of both (a + p).

When this standard was not achieved the result has been judged as "poor".

In our experience the presence of light calcification of the valve has little influence on the extent of valvotomy which the surgeon is able to achieve, and heavy sclerosis is often of greater significance than calcification.

Heavy calcification, on the other hand, does have some effect, both increasing the proportion of "fair" valvotomies (from 41 to 48%) and decreasing the number of "good" valvotomies (from 52 to 41%). This difference is not significant, however.

That heavy calcification should adversely affect the extent of valvotomy is only to be expected. What is surprising is that a "reasonably good" (good or fair) valvotomy should be achieved in as many as 89 per cent of patients with this condition. Unfortunately the functional result is not necessarily commensurate with the degree of "splitting" obtained. There is greater force behind the surgeon's exploring finger or the diverging blades of a dilator than that produced by blood flow from atrium to ventricle.

OPERATIVE MORTALITY

Calcification of the mitral valve might reasonably be expected to increase the operative risk of mitral valvotomy particularly as regards traumatic mitral incompetence and systemic embolism (Table V).

TABLE V
OPERATIVE MORTALITY

	No. in group	Operative deaths
Heavy calcification ..	100	17 (17%)
No heavy calcification ..	447	19 (4%)

However, calcification is often associated with other adverse factors and comparisons are only valid if the groups with and without calcification are comparable in other respects. The other potentially

adverse factors are the age of the patient, the presence of atrial fibrillation, cardiac enlargement, associated aortic valvular disease, and pulmonary hypertension.

We have previously shown that associated aortic valvular disease has little effect on operative mortality (Lowther and Turner, 1962), and this has been confirmed in the present series (Table VI).

TABLE VI
ASSOCIATED AORTIC VALVULAR DISEASE:
OPERATIVE MORTALITY (547 CASES)

	No. in group	Operative mortality (%)
No aortic murmurs	262	5.7
Aortic murmurs present	285	7.4
Stenosis	114	7.9
Incompetence only	171	7.0

As regards pulmonary hypertension (assessed sometimes by catheterization, and sometimes on a presumptive basis from the presence of right ventricular hypertrophy on electrocardiogram, and pulmonary arterial enlargement on radiograph), the operative mortality in the first 195 cases of the series is shown in Table VII. There is no significant difference in the incidence of calcification in the groups with and without moderate or severe pulmonary hypertension, neither is there a significant difference in operative mortality between those with and those without hypertension.

Early in the series most patients were investigated by cardiac catheterization, but subsequently this was done only when there was a particular indica-

TABLE VII
ASSOCIATED PULMONARY HYPERTENSION
(FIRST 195 CASES)

Pulmonary hypertension	Operative deaths		Total
	Heavy calcification	No heavy calcification	
Moderate or severe	3/24	6/107	9/131
Mild or none ..	3/9	2/55	5/64
Total	6/33	8/162	14/195

tion. We have previously shown that there is a good correlation between pulmonary hypertension and electrocardiographic patterns of right ventricular hypertrophy, and also shown, as have others (Davies *et al.*, 1953; Aber, Campbell, and Meecham, 1963), that there is a good correlation with enlargement of the pulmonary artery. The patients were divided arbitrarily into three grades of severity of pulmonary hypertension.

TABLE VIII
OPERATIVE MORTALITY, CALCIFICATION, AND OTHER ADVERSE FACTORS

Calcification	Without other adverse factors			With other adverse factors		
	No. of cases	Operative deaths	%	No. of cases	Operative deaths	%
Heavy.. ..	30	0	—	70	17	24
No heavy calcification	235	2	1	212	19	8

Table VIII shows the operative mortality in the 100 patients with heavy calcification and the 447 without calcification, each group being subdivided into patients without other adverse factors (age > 50, atrial fibrillation, or CTR > 60%), and those having one or more of these features.

In the "good risk" group mortality is low whether heavy calcification is present or not. It is an important finding that when heavy calcification of the valve occurs apart from the other adverse factors analysed, it seems to produce no great increase in operative mortality, but the proviso must be made that as the number of patients at risk in this category is small (30) the conclusion must be a tentative one.

In the group without heavy calcification but with one or more of the adverse factors mentioned above, the mortality increases to 8 per cent (Table VIII). In the group with heavy calcification and one or more of the other adverse factors the mortality may be as high as 24 per cent. It must be emphasized that the incidence of other adverse factors is considerably higher in the calcified than in the non-calcified group (Table I), so that the heavy calcification group includes a higher proportion of the worst cases in the series.

Table IX shows the operative deaths related to various factors. Because there are only 100 cases with heavy calcification and 17 deaths, subdivision into groups makes each too small for percentages to

have much significance, but the absolute numbers are given and may be of interest to those concerned with the problem of surgical treatment. In order to show the effect of calcification on mortality, the operative mortality in heavily calcified and non-heavily calcified groups, matched as regards other adverse factors, viz. age, rhythm, and heart size, is also given. In the majority of the groups mortality is 2-3 times higher in the heavily calcified cases.

It will be noted that the operative deaths in all patients with sinus rhythm amounted to 7 in 324 cases (2.2%), but where heavy calcification was present there were 2 deaths in 43 cases. On the other hand, the mortality in all patients with atrial fibrillation (223) was 13 per cent. Of these there were 14 deaths in 166 cases without heavy calcification (8%) but 15 deaths in 57 cases with heavy calcification. Atrial fibrillation is an adverse factor in all groups mainly because of the higher incidence of clot and systemic embolism. Table X summarizes the operative deaths in various groups of patients having only single adverse factors.

The presence of heavy calcification alone in patients who would otherwise be considered good operative risks should not be thought to add materially to this risk, but when the other adverse factors are present, and in particular atrial fibrillation, the risk is considerably raised.

When the cause of operative death in the two

TABLE IX
OPERATIVE MORTALITY

	No. in group	Operative deaths		No heavy calcification			Heavy calcification		
		No.	%	Sinus rhythm	Atrial fibrillation	Total	Sinus rhythm	Atrial fibrillation	Total
Age > 50 years	68	12	18	1/14	4/29	5/43	0/4	7/21	7/25
Age < 50 years	479	24	5	4/267	10/137	14/404	2/39	8/36	10/75
CTR > 60 per cent ..	124	17	14	2/34	5/54	7/88	2/9	8/27	10/36
CTR < 60 per cent ..	423	19	4.5	3/247	9/112	12/359	0/34	7/30	7/64
Age > 50 years } ..	19	6	3.1	0/2	2/8	2/10	0/0	4/9	4/9
CTR > 60 per cent }									
Age > 50 years } ..	49	6	12.0	1/12	2/21	3/33	0/4	3/12	3/16
CTR < 60 per cent }									
Age > 50 years } ..	105	11	10.0	2/32	3/46	5/78	2/9	4/18	6/27
CTR > 60 per cent }									
Age < 50 years } ..	374	13	3.5	2/235	7/91	9/326	0/30	4/18	4/48
CTR < 60 per cent }									
Sinus rhythm	324	7	2.2	5/281 (1.8%)			2/43 (4.7%)		
Atrial fibrillation ..	223	29	13.0	14/166 (8.4%)			15/57 (26%)		
Whole series	547	36	6.6	19/447 (4.2%)			17/100 (17%)		

TABLE X

MITRAL VALVOTOMY: OPERATIVE MORTALITY
IN CASES WITH SINGLE ADVERSE FACTORS

	No. in group	Operative deaths	Mortality (%)
Sinus rhythm (SR)	235	2	0.9
Age < 50			
No heavy calcification (HC)			
Cardiothoracic ratio (CTR)			
< 60%			
Heavy calcification	30	0	0
SR: age < 50; CTR < 60%			
Atrial fibrillation	91	7	7.7
Age < 50; no HC; CTR			
< 60%			
Age > 50	12	1	—
SR: no HC; CTR < 60%			
Cardiothoracic ratio > 60%	32	2	—
SR: age < 50; no HC			

groups is compared (Table XI) it is clear that absolute numbers are too small for conclusions to be drawn.

There is no doubt that the incidence of each cause is higher in those with heavy calcification, but cardiac arrest, circulatory failure, and hæmorrhage mainly occurred in the early days when experience was limited. Now the principal causes of death in all groups are traumatic mitral incompetence and systemic embolism, but even those occurrences are rare. It may perhaps be emphasized that, using the technique employed in Edinburgh, the incidence of significant traumatic mitral incompetence is low and has not increased since the introduction of the transventricular dilator. In fact there have been only 7 deaths attributable to this cause in a total number of 850 first and second valvotomies from the Western General Hospital since 1950, when the first operation was carried out. The incidence of systemic embolism has steadily fallen over the years as discussed below, and in the past five years there have only been five instances of operative embolism in 335 cases with one death. This is attributable to increasing experience and attention to a number of details rather than to any one cause; it is certainly not attributable to the use of anticoagulants before the operation.

TABLE XI

CAUSES OF OPERATIVE DEATHS

	Heavy calcification	No heavy calcification	Total
No. of cases ..	100	447	547
Cardiac arrest ..	2	2	4
Circulatory failure ..	5	2	7
Systemic embolism ..	7	6	13
Traumatic mitral incompetence ..	3	4	7
Hæmorrhage ..	0	4	4
Pneumonia ..	0	1	1
Total deaths ..	17	19	36

LONG-TERM RESULTS

With a few exceptions, all patients were seen at yearly intervals or more frequently in a special follow-up clinic. Their clinical state was assessed on the basis of symptoms, signs, a radiograph of the heart, and an electrocardiogram. The shortest period of follow-up was two years and the longest 12 years, though for the purpose of this paper the analysis has been stopped at 10 years. The number of patients followed at each year of follow-up is shown as "number at risk" in the histograms: this number includes deaths during the period of follow-up.

In the analysis the 36 operative deaths have been excluded. Many of the patients underwent a second valvotomy as discussed below, but the result for each year has been graded irrespective of whether they were operated on again or not. The reason for this is that this paper is concerned not with the treatment of mitral stenosis in general but with the significance of calcification of the valve.

The results are shown in histogram form (Fig. 2-13), expressed as percentages of those at risk in each year of the follow-up. The column for each year consists of four parts adding to 100 per cent and comprising, from top to bottom, the percentages with good (white), fair and poor (shaded) results, and finally the proportion who have died (black). The number of dead is thus a cumulative one, showing for each year the proportion of the original cohort followed up for that period of years, who have died during that period.

The great majority of deaths was obviously connected with rheumatic heart disease, but a small number was due to other causes. No attempt has been made to eliminate these, and their presence does not affect the comparison of calcified and non-calcified groups.

As in previous reports on this series, the post-operative results have been classified as "good", "fair", and "poor". "Good" implies great functional improvement with ability to carry out normal housework or a previous occupation. "Fair" implies considerable improvement but with some dyspnoea on moderate exercise and usually the necessity for some home help or an occupation involving little physical exertion. "Poor" implies slight or no improvement or actual deterioration due to the operation, caused for example by traumatic mitral incompetence or systemic embolism.

The factors analysed as regards their influence on the long-term results are calcification, age, sex, cardiac rhythm, cardiac enlargement, and mitral incompetence. In order to provide a numerical comparison of the relative influence of these factors,

TABLE XII

LONG-TERM RESULTS—COMPARISON OF HEAVILY CALCIFIED AND NON-HEAVILY CALCIFIED GROUPS

	Deaths								Good results							
	5 years				10 years				5 years				10 years			
		Ratio	χ^2	Signifi- cance		Ratio	χ^2	Signifi- cance		Ratio	χ^2	Signifi- cance		Ratio	χ^2	Signifi- cance
Whole group	$\left\{ \begin{array}{l} 18/64 \\ 24/323 \end{array} \right.$	3.6	19.4	+++	$\left\{ \begin{array}{l} 16/24 \\ 23/147 \end{array} \right.$	3.8	23.2	+++	$\left\{ \begin{array}{l} 30/64 \\ 236/323 \end{array} \right.$	0.61	20.6	+++	$\left\{ \begin{array}{l} 2/24 \\ 73/147 \end{array} \right.$	0.15	15.7	+++
Men	$\left\{ \begin{array}{l} 5/27 \\ 4/46 \end{array} \right.$	2.3	1.0	0	$\left\{ \begin{array}{l} 5/9 \\ 2/14 \end{array} \right.$	4.3	3.5	0	$\left\{ \begin{array}{l} 12/27 \\ 31/46 \end{array} \right.$	0.71	2.0	0	$\left\{ \begin{array}{l} 0/9 \\ 7/14 \end{array} \right.$	—	4.1	0
Women ..	$\left\{ \begin{array}{l} 8/36 \\ 20/178 \end{array} \right.$	3.3	7.9	+++	$\left\{ \begin{array}{l} 7/15 \\ 21/133 \end{array} \right.$	3.5	9.3	+++	$\left\{ \begin{array}{l} 14/36 \\ 206/278 \end{array} \right.$	0.44	14.5	+++	$\left\{ \begin{array}{l} 1/15 \\ 67/133 \end{array} \right.$	0.16	7.1	++
Sinus rhythm	$\left\{ \begin{array}{l} 8/35 \\ 13/215 \end{array} \right.$	3.8	9.0	+++	$\left\{ \begin{array}{l} 6/11 \\ 9/101 \end{array} \right.$	6.1	13.2	+++	$\left\{ \begin{array}{l} 16/35 \\ 176/215 \end{array} \right.$	0.56	19.7	+++	$\left\{ \begin{array}{l} 2/11 \\ 66/101 \end{array} \right.$	0.28	7.2	++
Atrial fibrillation	$\left\{ \begin{array}{l} 6/29 \\ 10/108 \end{array} \right.$	2.2	1.8	0	$\left\{ \begin{array}{l} 9/13 \\ 14/46 \end{array} \right.$	2.3	4.6	0	$\left\{ \begin{array}{l} 15/29 \\ 66/108 \end{array} \right.$	0.85	0.5	0	$\left\{ \begin{array}{l} 0/13 \\ 19/46 \end{array} \right.$	—	5.8	+
Age < 50 years	$\left\{ \begin{array}{l} 13/50 \\ 20/268 \end{array} \right.$	3.7	14.8	+++	$\left\{ \begin{array}{l} 13/19 \\ 19/139 \end{array} \right.$	4.6	24.8	+++	$\left\{ \begin{array}{l} 25/50 \\ 220/268 \end{array} \right.$	0.64	14.4	+++	$\left\{ \begin{array}{l} 2/19 \\ 70/137 \end{array} \right.$	0.19	11.2	+++
Age < 50 years; CTR < 60 per cent	$\left\{ \begin{array}{l} 7/35 \\ 11/245 \end{array} \right.$	4.5	9.8	+++	$\left\{ \begin{array}{l} 7/11 \\ 12/114 \end{array} \right.$	6.0	18.1	+++	$\left\{ \begin{array}{l} 19/35 \\ 194/245 \end{array} \right.$	0.69	9.1	+++	$\left\{ \begin{array}{l} 2/11 \\ 72/114 \end{array} \right.$	0.29	6.6	++
Sinus rhythm Age < 50 years; CTR < 60 per cent	$\left\{ \begin{array}{l} 8/184 \\ 5/26 \end{array} \right.$	4.4	6.3	+	$\left\{ \begin{array}{l} 5/87 \\ 4/8 \end{array} \right.$	8.7	11.9	+++	$\left\{ \begin{array}{l} 150/184 \\ 13/26 \end{array} \right.$	0.61	11.3	+++	$\left\{ \begin{array}{l} 58/87 \\ 2/8 \end{array} \right.$	0.37	3.8	0

In each group the upper fraction refers to cases with heavy calcification, the lower to those with light or no calcification.

and to apply statistical tests of significance, long-term results at 5 and 10 years have been extracted and shown separately in Tables XII and XIII. As a further simplification, figures for the proportion dead at these time intervals after valvotomy and the proportion maintaining a good result are shown alone in these Tables.

Table XII shows in the first line the mortality and the proportion maintaining a good result at 5 and 10 years in the heavily calcified group and in the non-heavily calcified group. The subsequent lines show the same comparison in various subgroups of the total number of patients, for example, men and women, those with and without fibrillation, the younger patients, and those with small hearts. In every case the comparison is between those with heavy calcification and those with light or no calcification. The columns headed "ratio" express the quotient of the preceding column, i.e. the rate for the calcified group divided by that of the non-calcified group. For example, in the first line the mortality at 5 years is 3.6 times as great in the calcified as in the non-heavily calcified group, and good results are maintained only 0.61 times as frequently.

The remaining columns, headed χ^2 and significance, indicate to what extent the difference between the heavily calcified and non-heavily calcified groups can be regarded as statistically significant; +++ indicates a probability of less than one in a thousand of the ob-

served difference being due to chance only. Because of small numbers in some of the groups, apparently large differences may not reach the level of statistical significance. The fact that any particular difference is not statistically significant does not of course prove that it is unimportant, only that it has not been proved to be important.

In Table XIII factors other than calcification have been evaluated in the same way, first (A) ignoring the presence or absence of calcification, and secondly (B) removing the effect of calcification, where numbers permit, by excluding the 100 heavily calcified cases.

In these two Tables the ratios quoted give some numerical comparison of the relative importance of the various factors. It can be seen, for example, that calcification, with mortality ratios of 3.6 and 3.8 and good result ratios of 0.61 and 0.15, is more adverse than atrial fibrillation, where the corresponding figures are 1.4 and 2.9, and 0.77 and 0.53.

Whole Series. Fig. 2 shows the long-term results in all patients in whom a satisfactory follow-up was available. A good result was maintained in 69 per cent at 5 years and 46 per cent at 10 years, though

TABLE XIII

LONG-TERM RESULTS—COMPARISON OF FACTORS OTHER THAN CALCIFICATION

	Deaths								Good results							
	5 years				10 years				5 years				10 years			
		Ratio	χ^2	Significance		Ratio	χ^2	Significance		Ratio	χ^2	Significance		Ratio	χ^2	Significance
<i>A: Whole Series</i>																
Atrial fibrillation	16/137	1.4	0.8	0	23/59	2.9	13.2	+++	81/137	0.77	12.5	+++	19/59	0.53	11.5	+++
Sinus rhythm	21/250				15/112				192/250				68/112			
Age > 50 years	9/41	2.3	4.6	0	7/16	2.1	3.4	0	21/41	0.72	5.8	+	3/16	0.41	3.5	0
Age < 50 years	33/346				32/155				245/346				72/155			
CTR > 60 per cent	13/73	1.9	3.6	0	13/34	1.8	3.3	0	42/73	0.80	4.8	0	11/34	0.62	3.2	0
CTR < 60 per cent	29/314				26/137				224/314				64/137			
MSM + ..	11/122	2.4	3.8	0	17/57	2.1	3.8	0	80/122	0.82	3.1	0	23/57	0.64	5.8	+
MSM - ..	7/187				10/71				149/187				45/71			
Palpable jet ..	11/78	1.4	0.4	0	12/27	2.4	7.0	++	42/78	0.74	5.9	+	6/27	0.46	5.1	+
No palpable jet	31/309				27/144				224/309				69/144			
<i>B: Excluding heavily calcified cases</i>																
Atrial fibrillation	10/108	1.5	0.4	0	14/46	3.4	9.5	+++	66/108	0.75	15.5	+++	19/46	0.63	6.5	+
Sinus rhythm	13/215				9/101				176/215				66/101			
Age > 50 years	4/27	2.2	1.4	0	4/10	3.0	3.6	0	16/27	0.82	0.4	0	3/10	0.61	0.8	0
Age < 50 years	20/268				19/137				220/268				70/137			
CTR > 60 per cent	9/49	2.7	5.2	+	8/29	2.2	2.9	0	37/49	0.84	3.2	0	11/29	0.72	1.5	0
CTR < 60 per cent	15/263				15/118				199/263				62/118			
MSM + ..	4/85	1.6	0.1	0	7/43	1.3	0.1	0	61/85	0.87	3.3	0	22/43	0.77	2.0	0
MSM - ..	5/171				8/66				141/171				44/66			
Palpable jet ..	4/46	1.3	0.1	0	6/19	2.1	2.2	0	28/46	0.80	4.1	0	6/19	0.56	3.0	0
No palpable jet	19/277				19/128				211/277				72/128			

MSM = mitral systolic murmur

40 per cent had had a second mitral valvotomy within the period, as shown in Fig. 14 in the section on re-operation. Worth-while results, that is, good and fair results combined, were maintained in 72 per cent at 10 years: these patients were all still appreciably improved compared with their pre-operative state.

Calcification. The whole group of 511 patients who survived operation was divided into 428 with light or no calcification (Fig. 3A) and 83 with heavy calcification (Fig. 3B). It is apparent from the histograms that at every stage the long-term follow-up results were worse in the heavily calcified group. Good results at 5 and 10 years were maintained in 74 and 53 per cent, respectively, of those without heavy calcification, but in only 45 and 8 per cent of those with heavy calcification. The difference at 5 and 10 years is highly significant statistically (Table XII).

FIG. 2.—Long-term results in 511 survivors of mitral valvotomy followed up for periods up to 10 years. Includes all cases.

FIG. 3.—Long-term results in 511 cases divided into 428 without and 83 with heavy calcification.

FIG. 4.—Long-term results in patients under and over 50 years at time of operation, divided into heavily calcified and non-heavily calcified groups.

FIG. 5.—Long-term results in patients with cardiothoracic ratio under and over 60 per cent, divided into heavily calcified and non-heavily calcified groups.

Since the patients with heavy calcification have a higher incidence of associated adverse factors, further subgroups were compared, matched as far as possible as regards the potentially adverse factors referred to above.

Age. The incidence of heavy calcification increases with age (see Fig. 1). In order to minimize the possible effect of a different age distribution in the heavily calcified and non-heavily calcified groups, comparisons of the effect of calcification were made separately in patients under 50 years (Fig. 4A and B) and those over 50 (Fig. 4C and D). Age did not influence the difference between the two groups. As expected, the over-all results are less good in the older than in the younger age-group, with twice the mortality and two-thirds or less of the good results,

though using the χ^2 test the difference at 5 and 10 years is barely significant (Table XIII).

Cardiac Enlargement. A similar analysis was made between those with a cardiothoracic ratio > 60 per cent (Fig. 5A and B) and those < 60 per cent (Fig. 5C and D). The difference between the calcified and non-calcified groups was again apparent. The over-all adverse effect of cardiac enlargement appeared to be similar or slightly less in degree to that of age (see Table XIII).

Age and Cardiac Enlargement. When the effects of age and cardiac enlargement are eliminated by excluding those over 50 and also those with a cardiothoracic ratio over 60 per cent (Fig. 6A and B) the adverse effect of calcification is even more

FIG. 6.—Long-term results in a group of 359 survivors of operation who were under 50 years of age and had a cardiothoracic ratio under 60 per cent; they are divided into heavily calcified and non-heavily calcified groups.

apparent. As is to be expected, the exclusion of these groups results in an improvement of the long-term results compared with the whole series (compare Fig. 3A and B), though the improvement is less striking in the heavily calcified groups where numbers are small.

The adverse effect of calcification is, therefore, not due to associated age or cardiac enlargement.

Rhythm. The adverse effect of atrial fibrillation in the whole group without regard to calcification is shown in Fig. 7A and B. The difference is highly significant (Table XIII). When the comparison between heavy calcification and light or no calcification is confined to those patients in sinus rhythm (Fig. 8A and B), the unfavourable effect of calcification is obvious. It is equally present in those in atrial fibrillation (Fig. 8C and D). That

atrial fibrillation itself has an unfavourable effect was shown by comparing Fig. 8A with Fig. 8C, and Fig. 8B with Fig. 8D. Tables XII and XIII show that the adverse effect of fibrillation, though highly significant, is less than that due to calcification.

Age, Cardiac Enlargement, and Rhythm. Further subdivision of the groups in Fig. 6A and B according to rhythm (sinus rhythm only, Fig. 9A and B, and atrial fibrillation only, Fig. 9C and D) again confirms the unfavourable effect of calcification of the mitral valve. Although numbers in these groups are relatively small in the longest period of follow-up, they are closely matched as regards other potentially adverse factors in addition to calcification, so that the contrast is correspondingly more significant.

FIG. 7.—Long-term results in 511 survivors of operation divided into 320 with sinus rhythm and 191 with atrial fibrillation. Includes all calcification groups.

FIG. 8.—Long-term results, as in Fig. 7, with further subdivision into heavily calcified and non-heavily calcified groups.

Pulmonary Hypertension. An analysis has been made of 181 cases followed for six years (27 heavily calcified, 154 not heavily calcified) and subdivided into those with radiographic or electrocardiographic evidence of pulmonary arterial hypertension (121) and those without such evidence (60). Table XIV

TABLE XIV

PULMONARY HYPERTENSION AND HEAVY CALCIFICATION (181 CASES FOLLOWED FOR 6 YEARS)

Pulmonary hypertension	Good result after 6 years		
	Heavy calcification	No heavy calcification	Total
Moderate or severe	6/21 (29%)	78/100 (78%)	84/121 (69%)
None or mild ..	3/6 (50%)	34/54 (63%)	37/60 (62%)
Total ..	9/27 (33%)	112/154 (73%)	121/181 (67%)

shows the proportions in each category maintaining a good result at 6 years.

There is a striking difference as regards calcification, but little or no difference as regards the pulmonary hypertension (χ^2 0.50). The incidence of pulmonary hypertension is not different in the presence of calcification, as already shown, and it is concluded that the long-term results up to 6 years are unaffected by its presence.

Pre-existing Mitral Incompetence. The adverse effects of calcification might be attributable to valvular incompetence, since the incidence of mitral systolic murmurs recorded before operation and the finding of a regurgitant jet at operation are more frequent in the calcified group (Tables II and III). However, all patients in the present series had tight

FIG. 9.—Long-term results, as in Fig. 8, but confined to patients under 50 years of age and with cardio-thoracic ratio under 60 per cent.

mitral stenosis, as judged by the surgeon's finger at operation, and free or dominant incompetence was not, therefore, in question.

Fig. 10 shows the results in heavily calcified and non-heavily calcified groups classified according to the presence and intensity of pre-operative systolic murmurs. With increasing loudness of the murmur the results are somewhat less good in both groups, but the predominant difference in each case is between those with and those without heavy calcification.

Fig. 11A and B deal with those patients found at operation to have a regurgitant jet, with and without heavy calcification: the results are again worse in those with heavy calcification.

Table XIII A shows that in the whole series, the long-term results are significantly worse if a regurgitant jet is present than if it is not. This may

partly be due to the relatively greater incidence of heavy calcification in the group with a regurgitant jet (43% as opposed to 16%). However, when this factor is allowed for by considering only those without heavy calcification (Table XIII) the presence of a jet is still seen to have an unfavourable effect, though in this case the difference does not reach the level of statistical significance.

Obviously any degree of associated mitral incompetence is an adverse factor, but in the present context this is not commensurate with the benefit derived from the relief of mitral stenosis.

Ellis, Harken, and Black (1959) analysed their figures, using a statistical technique designed to offset the effect of one of these factors when assessing the importance of the other, and concluded that the presence of mitral regurgitation had an important adverse effect on the results of valvotomy, and

Calcification of Mitral Valve: Results of Valvotomy

FIG. 10.—Long-term results in heavily calcified and non-heavily calcified groups subdivided according to presence and intensity of mitral systolic murmur. All cases had severe mitral stenosis at operation.

TABLE XV
PROPORTION MAINTAINING GOOD RESULT
AT 5 YEARS

	No or light calcification	Heavy calcification	Total
No systolic murmur..	140/171	8/16	148/187
Systolic murmur grade 1-2	46/66	12/20	58/86
Systolic murmur grade 3-4	15/19	7/17	22/36
Total	201/256	27/53	228/309

FIG. 11.—Long-term results in 103 survivors of operation who had a palpable regurgitant jet at operation. They are divided into those with and those without heavy calcification.

was one of the two most important determinants, with calcification, of the outcome of the operation.

In the present series, evidence of mitral regurgitation in the form of a mitral systolic murmur, or a palpable jet at operation, though affecting the long-term results to some extent, does so to a much lesser degree than in the series of Ellis *et al.* The difference between the groups with and without evidence of regurgitation does not reach significance employing the same statistical technique as used by these authors (1965, personal communication).

Table XV shows the proportions of good results at 5 years in those with and those without systolic murmurs in the heavily calcified and non-heavily calcified groups.

If we make the assumption that the presence of a murmur of mitral incompetence does not affect the result, the over-all proportion improved will apply to every grade of murmur and the number in each group expected to be improved can be calculated accordingly. For example, the total 201/256 gives a proportion of 0.785, and this applied to 171, 66, and 19, gives 134, 52, and 15, respectively. The total 27/53 is similarly redistributed. These expected values are shown in Table XVI.

TABLE XVI

EXPECTED PROPORTION MAINTAINING GOOD RESULT AT 5 YEARS

	No or light calcification	Heavy calcification	Total
No systolic murmur . .	134/171	8/16	142/187
Systolic murmur grade 1-2	52/66	10/20	62/86
Systolic murmur grade 3-4	15/19	9/17	24/36

The totals in the last columns of Tables XV and XVI are then compared, representing the actual as opposed to the expected proportions improved. The deviations from the expected totals are thus +6 with no murmur, -4 with grade 1-2, and -2 with grade 3-4 (χ^2 0.67, $p > 0.5$). The adverse effect of the presence of a mitral systolic murmur thus does not reach the level of statistical significance and might have arisen by chance. The result at 10 years, when treated similarly, again shows no significant difference.

Likewise in the case of regurgitation assessed by the presence of a jet at operation, the actual and expected values for good results at 5 years are shown in Table XVII.

The χ^2 value for this difference is 0.82 and $p > 0.5$.

Our results thus differ from those of Ellis *et al.* in that mitral incompetence has an insignificant effect on the long-term result. The difference may be due to the fact that their series included a considerable number of patients without tight mitral stenosis and in whom dominant incompetence was found at operation. In the present series 15 were found to have dominant incompetence at operation, but they have been excluded from consideration

TABLE XVII

PROPORTION MAINTAINING GOOD RESULT AT 5 YEARS

	No or light calcification	Heavy calcification	Actual total	Expected total
No jet	211/277	13/32	224/309	217.5/309
Jet	28/46	14/32	42/78	47.5/78
Total	239/323	27/64	266/387	—

FIG. 12.—Long-term results, as in Fig. 2, subdivided into 100 cases who had post-operative increase in mitral systolic murmur and 411 cases who had no evidence of traumatic incompetence.

because this paper is concerned with dominant mitral stenosis.

The conclusion is that in patients with tight mitral stenosis a loud systolic murmur may be present, or a palpable jet may be due to an insignificant degree of incompetence which does not materially affect the long-term result of operation.

Traumatic Mitral Incompetence. The above analysis considers only pre-operative mitral incompetence. As discussed below there were among those who survived operation, 100 patients in whom a systolic murmur was produced or increased by operation, and there is, therefore, the possibility that traumatic mitral incompetence adversely affects the long-term results (Fig. 12). Table XVIII shows the 5- and 10-year results in the two groups.

Taking the whole group of those with possible evidence of significant traumatic incompetence, it is evident that they had as good an outcome as the others at 5 years but not at 10 years, when the result was significantly worse (χ^2 4.25; $p < 0.05$). The conclusion to be drawn from these figures is not of course that traumatic incompetence is relatively unimportant. It can be a fatal or serious complication of operation. What is suggested is that, in the relatively large group of patients who develop a systolic murmur or have their murmur increased following valvotomy, the incompetence is generally

of minor degree and only affects the long-term results marginally. A fuller discussion of the problem of traumatic incompetence is given below.

Sex. For reasons which are unknown, there is a far higher incidence of calcification in men than in women, and the long-term results are correspondingly poorer. In order to find out whether there were any features other than calcification that might affect the prognosis, the heavily calcified and non-heavily calcified groups were analysed separately according to sex (Fig. 13). It is apparent that when allowance is made for calcification there is no significant difference between the two groups.

Conclusion. The analysis of the long-term results of mitral valvotomy shows that the presence of heavy calcification of the valve is the most important factor which affects the prognosis. At each year of follow-up the influence of this factor at least doubles the mortality and halves the proportion of good results in comparison with those who have light or no calcification of the valve. It outweighs in importance the presence of atrial fibrillation which is the next most significant adverse factor of those considered. The prognosis is poorer in men than in women, owing to a higher incidence of calcification. Age and cardiac enlargement are both

TABLE XVIII

LONG-TERM RESULTS—COMPARISON OF CASES WITH AND WITHOUT EVIDENCE OF TRAUMATIC INCOMPETENCE

Traumatic mitral incompetence	Deaths				Good results			
	5 years	Ratio	10 years	Ratio	5 years	Ratio	10 years	Ratio
Present	6/71	0.74	5/20	1.1	46/71	0.93	4/20	0.43
Absent	36/316		34/151		220/316		71/151

FIG. 13.—Long-term results in heavily calcified and non-heavily calcified groups subdivided by sex. Because of the higher incidence of calcification in men, the over-all results of valvotomy are worse in men.

unfavourable features, but the influence of each is much less than either calcification or atrial fibrillation. In patients with tight mitral stenosis the presence of associated mitral incompetence is of relatively little importance unless associated with a heavily calcified valve.

Nevertheless it is clear, taking the over-all picture which must be representative of any large series of patients, that in patients with heavy calcification the results of closed valvotomy are certainly worth while and no patient should be rejected on the grounds of calcification alone.

Statistics from a large heterogeneous group of patients cannot be applied to the individual case, and each patient must be considered on his or her merits.

Unsatisfactory Results. We have made a special analysis of all patients with heavy calcification of the valve in whom the long-term results were less than good after five or more years. It is clear that

in the majority of such cases deterioration was essentially due to progress in the natural history of severe rheumatic heart disease, with atrial fibrillation, cardiac enlargement, involvement of more than one valve, pulmonary congestion, myocardial damage, and cardiac failure. Congestive failure is of course essentially due to myocardial failure. Deterioration in fact was often multifactorial. A few died from systemic or pulmonary embolism, and a few died from unassociated disease, such as cancer.

It is clear that heavy calcification of the valve is usually associated with hearts severely damaged in other ways by the rheumatic process. Nevertheless, in due course it will be most interesting to compare the results in a similar group of patients treated by valve replacement. In such cases re-stenosis cannot occur neither can traumatic mitral incompetence or further pulmonary damage from unrelieved stenosis, but it may be that in some cases myocardial damage will be progressive or at least irreversible.

TRAUMATIC MITRAL INCOMPETENCE

The term traumatic mitral incompetence signifies incompetence which is produced or increased by valvotomy. The effect of this may be catastrophic, leading to immediate or early death; insignificant, i.e. of no apparent hæmodynamic importance; or anything between these extremes.

Often it is not possible at operation to estimate with the gloved finger the amount of reflux present, owing to the variable influence of valve size and shape and the force of left ventricular contraction, the latter being usually reduced as a result of anæsthesia and the surgical manipulations.

A regurgitant jet of some degree through a severely stenosed orifice is a frequent finding at operation, and in these cases the valve cusps are often rigid or calcified. Such a jet is of no dynamic significance in comparison with the effects of severe stenosis. Nevertheless, since forward flow through the mitral valve is increased, what might be termed "effective mitral stenosis" is increased. Likewise, the degree of mitral incompetence produced by an adequate valvotomy may not prove to be serious.

It is not usually possible after operation to assess the immediate significance of regurgitation by auscultation. If a systolic murmur has developed and is loud, harsh, and well heard towards the left axilla or lung base, it is likely to be important. However, a regurgitant jet through roughened margins can certainly produce a loud murmur which is not of dynamic significance. Severity may be indicated by failure to improve after operation or by progressive deterioration thereafter. In such cases there may be obvious evidence of left ventricular failure with pulmonary oedema or peripheral signs of congestive failure, but in other cases, at least in patients deteriorating during the first few days or weeks, such signs may not be so definite, and breathlessness and fatigue without other obvious causes are the indications. In addition to a mitral systolic murmur there may be a third heart sound, clinical and radiographic evidence of left ventricular dilatation, and, if the patient survives long enough, subsequent electrocardiographic evidence of left ventricular hypertrophy.

By far the most frequent situation has been that a regurgitant jet of variable force was felt at the time of operation, that following valvotomy an apical systolic murmur was heard, which was not present before or had increased, and, in the majority of cases during the 2-10 years for which patients have so far been followed, there has been no clinical, radiographic, or electrocardiographic evidence that regurgitation is of clinical significance in comparison with the degree of post-operative im-

provement. In most other cases, subsequent deterioration is explicable on some other basis.

The rigid irregular cusp margins of a heavily calcified valve make it inevitable that perfect apposition of their surfaces in ventricular systole is rarely possible, and as a result some degree of regurgitation is usually present and may be demonstrated by a palpable jet or an apical systolic murmur. We have compared these two manifestations of incompetence in patients with heavy, light, or no detectable calcification, respectively, and the results of this analysis are shown in Tables II and III. It is apparent that the incidence and intensity of associated apical systolic murmurs increase with the degree of calcification, as does the incidence of a palpable regurgitant jet.

Since for a number of reasons observations made by the surgeon at the time of valvotomy may be misleading, incompetence has been assessed only by a comparison between pre- and post-operative clinical features. All findings were graded independently by at least two to three experienced observers.

Symptoms. Failure to improve after mitral valvotomy raises the possibility of significant mitral incompetence. In some cases death during or shortly after operation is due unequivocally to the production of traumatic mitral incompetence. Some survivors are worse as a result of the procedure and in others there is no material improvement. In some, despite relief of severe stenosis, the effect is disappointing and the post-operative result can only be graded as "fair".

In some patients there is an immediate good result which persists for a variable number of years and is then followed by deterioration. This may be mainly or in part due to the late development of secondary effects from traumatic mitral incompetence, but may also be due to other adverse factors attributable to severe rheumatic heart disease. When several factors are involved it is difficult to determine the precise significance of each.

In a few patients in whom the initial result has been only fair or poor on account of traumatic mitral incompetence, compensation by the left ventricle subsequently occurs, with corresponding subjective improvement.

Systolic Murmur. The production of, or increase in, the intensity of a mitral systolic murmur is the most obvious sign of incompetence, and where a murmur was increased by 2 grades (out of 5) it has been regarded as potentially significant. A murmur of only grade 1 intensity has been ignored, because it may well have been missed before operation, and in no such instance has there been any

evidence to indicate hæmodynamic significance. A murmur that apparently increased from grade 1 to grade 2 has been noted, and these patients were kept under observation, but there are obvious difficulties in being certain about such a slight change and again there has been no evidence that incompetence was clinically significant in such a case.

On the other hand, if a murmur of grade 2 or 3 intensity is increased to grade 3 or 4, respectively, it might well be important, because particular attention will have been paid to pre-operative grading. In three such patients the surgeon had observed that the force of the jet immediately before valvotomy was apparently increased by the operation, and in two there was other evidence to suggest that incompetence might be of clinical significance.

In the great majority of cases in which there has been the production of or an increase in the loudness of a mitral systolic murmur, this is clearly of no clinical significance commensurate with the relief of tight mitral stenosis at least for the follow-up period which has so far been possible.

Third Heart Sound. In none of the survivors was a third heart sound produced.

Thrill. The development after operation of an apical systolic thrill always signifies important incompetence.

Left Ventricular Enlargement. Radiographic evidence of left ventricular enlargement may be apparent, but often there are difficulties in being certain of relatively minor degrees, because films are not always comparable as regards the precise timing of the exposure in the cardiac cycle, the phase of respiration, and the degree of rotation in oblique and lateral views.

Left Ventricular Hypertrophy. In the present context the development of electrocardiographic signs of left ventricular hypertrophy, in the absence of other relevant factors such as aortic valvular disease or systemic hypertension, is usually but not necessarily evidence of important mitral incompetence. In our experience, this has rarely developed in the years following operation. Presumably either the patient succumbs to severe incompetence in the early days or weeks or, with lesser degree of incompetence, it may take many years to develop.

With all these points in mind we have classified our patients into four groups. (1) Definite severe incompetence; (2) probable important incompetence but other relevant factors present; (3) possible incompetence with no supporting evidence for

dynamic significance; (4) no traumatic incompetence.

¶ *Results.* In the whole group of 547 patients from which come the 100 with heavy calcification who were treated by valvotomy for severe stenosis and followed thereafter for more than two years, there are 100 with some degree of traumatic mitral incompetence, as judged by an apical systolic murmur which was produced or increased at operation.

The incidence of palpable reflux immediately after valvotomy did not always correspond with the post-operative clinical signs, probably because in some cases it was caused by temporary distortion of the valve and in others because the heart beat might have been relatively weak at the time of palpation. Post-operative auscultation was, therefore, accepted as the criterion for incompetence.

Of these 100 patients, 78 have maintained a good result so far, that is for 2-10 years, and there is nothing to suggest that the systolic murmur reflects mitral incompetence of clinical significance or at least commensurate with the relief of symptoms obtained by reduction of stenosis.

In 22 patients (Table XIX) there has been some evidence that traumatic mitral incompetence may be a contributory factor in explaining why post-operative improvement has been less than good. These 22 patients have been divided into two groups. In Group 1 (definite), there were 16 in whom there was no doubt that the incompetence was responsible for post-operative death or later deterioration. In Group 2 (probable or possible), there were six in whom some degree of incompetence had been produced, but other adverse factors were present which could have been responsible for most or all of the deterioration or failure to improve.

TABLE XIX
CALCIFICATION AND TRAUMATIC MITRAL
INCOMPETENCE

Severity of mitral incompetence	Calcification			
	Heavy (100)	Light (89)	None (358)	Total (547)
Fatal	3	2	2	7
Severe	1	1	7	9
Probable ..	0	0	2	2
Possible ..	1	1	2	4
	5	4	13	22

Group 1: 16 Definite Cases. Seven patients died, four within a few days and three within two months of the operation at which incompetence was produced. Three of these had heavy calcification of the valve, two had light calcification, and two had none.

In nine patients there was evidence that traumatic incompetence was at least a contributory factor in explaining why post-operative improvement was less good or maintained for a shorter time than might otherwise have been the case: five of these were subsequently treated by repair or replacement of the valve.

One patient had a poor result from the beginning and died after three years and two others deteriorated after some initial improvement and died two and four years later, respectively. Only one of these nine patients had heavy calcification, one had light calcification, and seven had none.

Group 2: 6 Probable or Possible Cases. Six patients had other features that were certainly contributory and possibly accounted for all the disability. These included myocardial damage, as reflected in considerable cardiac enlargement before operation, severe pulmonary hypertension, a rigid or calcified valve with relatively poor function, aortic valvular disease, and systemic hypertension. Each of these might be responsible for dyspnoea or congestive failure. Aortic valvular disease and systemic hypertension might be responsible for left ventricular hypertrophy and enlargement. In addition, in two patients it was reasonably certain that active carditis was present. Only one of these six patients had heavy calcification, one had light calcification, and four had none.

The incidence of mild traumatic incompetence in the 78 patients, in whom there is no evidence that it has influenced the post-operative result so far, is 18 of 100 patients with heavy calcification (18%) and 46 of 358 without heavy calcification (11%).

In summary, traumatic mitral incompetence in a series of 547 patients accounted for seven operative deaths, in three of whom there was heavy calcification; nine poor results, in one of whom there was heavy calcification; and possibly contributed to six other relatively poor results, in one of whom there was heavy calcification.

It is concluded that heavy calcification is of little importance in the production of traumatic mitral incompetence.

CLOT AND SYSTEMIC EMBOLISM

Systemic embolism continues to be one of the chief unpredictable hazards of mitral valvotomy, though with increasing experience the incidence has fallen to a low level.

The over-all incidence of *clot* detected in auricle or atrium at operation for mitral valvotomy in the consecutive series of 547 patients on which this paper is based was 18 per cent, a figure in agreement

TABLE XX
CALCIFICATION OF THE MITRAL VALVE
INCIDENCE OF CLOT AND SYSTEMIC EMBOLISM
AT OPERATION

Calcification	No. in group	Clot		Embolism		Fatal embolism	
		No.	%	No.	%	No.	%
Heavy ..	100	33	33	14	14	5	5
Light ..	89	22	25	2	2.3	0	0
None ..	358	45	13	14	3.9	3	1
All cases ..	547	100	18	30	5.5	8	1.5

with that from other centres. In the individual patient the probability of clot is dependent on a number of factors. The incidence of clot was higher in those with heavy calcification (33%) than in those with light calcification (25%), and considerably lower in those without calcification (13%) (Table XX). However, in attempting to analyse the importance of calcification itself other relevant factors must be taken into consideration.

The incidence of clot was considerably higher in those with atrial fibrillation (48%) than in those with sinus rhythm (2%), and in those with a past history of systemic embolism (59%) than in those without such a history (16%). The incidence increased with age and was higher in those with relatively large hearts. Whereas the incidence of clot was lower in those with dominant mitral incompetence than in those with dominant mitral stenosis, in patients with severe stenosis there was no difference between those who had and those who had not a relatively unimportant regurgitant jet.

In patients with heavily calcified valves *embolism* may result from the displacement of calcific material or of clot, but usually it is not possible to be certain which is responsible. Undoubtedly calcareous embolism can occur and has occasionally been demonstrated at necropsy or, as in one of our patients, by radiography of a peripheral artery.

Clot was found in 100 of the 547 patients at the time of operation. Systemic embolism occurred in 30 patients and in 8 of them it was fatal. Over-all, there was a much higher incidence of operative embolism in the heavily calcified group (14%) than in those not heavily calcified (3.6%)—a difference that is highly significant (χ^2 17.8; $p < 0.005$). With increasing experience the operative incidence of embolism has fallen. In the years 1950–1957, there were 24 incidents of embolism in 367 cases (6.5%), and in the years 1958–1962 6 incidents in 180 cases (3.3%). In the earlier period, 10 incidents, and in the later, 4 incidents, were in patients with heavily calcified valves. Thus, in both periods the incidence in the calcified group was 3 to 6 times

TABLE XXI
CALCIFICATION OF THE MITRAL VALVE
INCIDENCE OF SUBSEQUENT EMBOLISM

Calcification	No. of cases	Length of follow-up (patient years)	Emboli	Rate of embolization (patient years)
Heavy	100	710	14	1 per 50.7
Light or none	447	3105	33	1 per 94.0
All cases	547	3815	47	1 per 81.2

higher than in the others, the difference being statistically significant (1950-57: χ^2 7.8; $p < 0.01$; 1958-62: χ^2 6.7; $p < 0.01$).

The conclusion is that while the incidence of operative embolism is now low ($< 1.5\%$) calcification is a predisposing factor.

The incidence of subsequent embolism is also nearly twice as high in the heavily calcified group (Table XXI). This difference, which is barely significant statistically (χ^2 2.25; $p < 0.25$), cannot be accounted for by a higher incidence of atrial fibrillation in the calcified group.

HEAVY CALCIFICATION AND RE-STENOSIS

Figure 14 shows, in histogram form, the cumulative proportion of the total number followed up at each year who had been operated on for the second time. The difference between the two calcification groups does not appear striking, except in the 4- to 6-year period. When, however, account is taken of the number each year who were at risk as regards re-operation a somewhat different picture emerges.

For this purpose those at risk comprise the survivors in each year, less those who had already been re-operated on, since they were clearly not to be included in this category.

Table XXII shows the numbers at risk in each year in the two groups, together with the number who underwent re-operation during that year. From this can be calculated the percentage rate of re-operation, and these rates applied successively to an initial group of 100 patients. From the Table it is apparent that the rate of re-operation is considerably higher in the heavily calcified group. Of 100 patients operated on with heavy calcification 50 per cent will have re-stenosis after a lapse of 8 years, compared with only 30 per cent in the non-heavily calcified group.

It is concluded that patients with heavily calcified valves are more likely to require re-operation than those without. There are several possible reasons for this. Although it is possible that the rheumatic process which led to calcification in the first place may be accelerated in these cases, we have no evidence to suggest that this in fact took place. The initial valvotomy tended to be less good as shown in Table IV; but more important probably is the tendency for functional stenosis, owing to the rigidity of the cusps, to persist in some degree whatever the extent of valvotomy. It is also likely that rigidity of the cusps, consequent upon calcification, predisposes to more rapid organic re-stenosis which is believed to be initiated by platelet deposition in the narrow angle between the cusps.

FIG. 14.—Cumulative incidence of re-stenosis in survivors of mitral valvotomy, divided into heavily calcified and non-heavily calcified groups.

TABLE XXII
CALCIFICATION AND RE-VALVOTOMY

Years	Light or no calcification				Heavy calcification			
	No. at risk	Re-valvotomy	Re-valvotomy per cent per annum	Cumulative per cent with re-valvotomy	No. at risk	Re-valvotomy	Re-valvotomy per cent per annum	Cumulative per cent with re-valvotomy
1	415	0	0	0	82	0	0	0
2	411	2	0.5	0.5	78	1	1.3	1.3
3	380	7	1.8	2.3	69	2	2.9	4.2
4	327	4	1.2	3.5	57	4	7.0	10.9
5	282	7	2.5	5.9	44	2	4.6	15.0
6	235	18	7.7	13.1	34	3	8.8	22.5
7	180	20	11.1	22.7	24	5	21.0	38.8
8	124	13	10.5	30.8	13	3	23.0	52.9
9	77	11	14.3	40.7	6	3	—	—
10	55	7	12.7	48.2	3	0	—	—

SURGERY FOR RE-STENOSIS

In many patients with mitral re-stenosis, there is still a place for a second closed valvotomy, though the numbers of patients are likely to decrease. It has yet to be shown that the results of open valvotomy are better than those with the closed technique, with its lower operative risk and less traumatic procedure. It is known that, even with heavily calcified valves, over half of those undergoing transventricular valvotomy maintain a good result for five years, and a further 20 per cent maintain a fair result (Logan, Lowther, and Turner, 1962).

An encouraging factor is that the operative mortality for re-stenosis is low. Inevitably post-operative improvement tends, in many patients, to be relatively less satisfactory and short-lived if only because so often there has been progressive sclerosis and calcification of the valve, though of course there may be other causative factors.

At present it seems that a second operation cannot be avoided in a considerable proportion of patients 5–10 years after the first procedure, and it may be that some time in the future the first operation in patients with heavy calcification should be that of valve replacement. However, at present the operative risk is relatively high and there is no proof that the prosthesis will continue to function adequately over a long period; in addition, the incidence of subsequent embolism is relatively higher. Nevertheless, if it is known, from the first operation, that the valve is heavily calcified or that more than mild associated mitral incompetence is present, then operation under direct vision should be advised with a view to valve replacement.

It is only to be expected that the technique of open-heart surgery with cardiopulmonary bypass will improve and become safer and simplified, and that post-operative management will likewise become better understood.

A second operation should not be deferred after

symptoms have returned, especially if they are progressive and cannot be attributed to some other cause, and if it is certain from haemodynamic studies that re-stenosis is the principal factor.

DISCUSSION

There is a large group of patients with a severe and progressive disability from tight mitral stenosis and a hopeless outlook without surgical treatment, in which the operative risk is relatively high on account of associated adverse factors.

The results of this analysis show that the most important of them is heavy calcification of the valve. Its effect on the survival rate is shown in Fig. 15. However, many in this group do surprisingly well with surgical treatment and maintain their post-operative improvement for a reasonable number of years. Although sometimes disappointed at subsequent deterioration, they consider the operation to have been well worth while. Inevitably too, there are some in this group who die as a result of the operation and who might have continued to live a restricted life for a limited time without it. The difficulty is that even from a multifactorial analysis in a large group of patients it cannot be foretold in the individual case what the outcome of operation will be.

In our experience, with the proper use of the transventricular dilator, traumatic mitral incompetence is uncommon, and with increasing experience the incidence of operative embolism is lower.

Heavy calcification of the valve should never itself be a contraindication to valvotomy, and the problem of advising surgical treatment in this group mainly arises in those patients who have a number of associated potentially adverse factors.

It is a serious fact that "medical" deaths in patients with valvular disease in whom operation has not been advised are rarely criticized. In striking contrast to this attitude any operative death

FIG. 15.—Calculated survival rates, based on operative and subsequent yearly mortality rates, in groups with and without heavy calcification of the mitral valve.

is considered to warrant a special inquiry, though in our experience it is the decision not to operate which is much more often questionable.

In the individual case, of course, many factors must be taken into consideration, and this is one of the relatively few instances in which the patient and relatives must take a major part in the decision, knowing that the operative risk is somewhat above average and the chances of a persistently good post-operative result relatively low. What must be decided in the individual case is whether existence at the present level of activity and of restrictions is worth while, or whether it will be preferable to accept the operative risk and the possibility of a relatively disappointing result. It must of course be explained that the doctors not only expect survival but also a worth-while degree of improvement, at least for a considerable time, though this cannot be predicted with certainty. This situation is a good example of the importance of the physician knowing his patients well and consulting with the family and with the general practitioner.

At present the risks of open-heart surgery are still greater than those of closed operations, and it is for this reason that we continue to advise transventricular valvotomy in the relatively "bad risk" group. If the result is not satisfactory, a new valve can often be inserted subsequently.

SUMMARY

In a consecutive series of 547 patients treated by valvotomy for severe mitral stenosis between 1951 and 1962, there were 100 with heavy calcification of the valve who have been followed for 2–10 years.

The over-all incidence of calcification was 35 per cent and of heavy calcification 18 per cent.

The incidence increased with age and was considerably higher in men than in women. Nearly all men over 50 years of age had a calcified valve.

The incidence of other potentially adverse factors, including atrial fibrillation, age over 50, cardiothoracic ratio over 60 per cent, associated aortic valvular disease, and pulmonary hypertension, was higher in those with heavy calcification than in those without, and probably in part accounted for a higher operative mortality and relatively poor long-term results. There was a low incidence of heavy calcification in a parallel series of patients with dominant mitral incompetence. As would be expected, a higher proportion of good valvotomies was achieved in patients without heavy calcification of the valve, but the difference was not striking and a good valvotomy was achieved in the majority. However, it is thought that a relatively high degree of functional stenosis remained in those with a heavily calcified valve.

The operative mortality was higher in those with heavy calcification than in those without, but this was largely related to the higher incidence of other adverse factors. Heavy calcification alone in patients otherwise considered to be good operative risks should not be considered as adding materially to this risk.

With the proper use of the transventricular dilator the incidence of significant traumatic mitral incompetence is low in all groups, so that it is difficult to analyse the importance of calcification in this respect.

The incidence of operative systemic embolism was

higher in the presence of heavy calcification, but it has become low in both groups.

Long-term results were analysed with regard to a number of factors, in addition to calcification. In the whole series, a good result was maintained at five years in 69 per cent of those who survived the operation, and in 46 per cent at ten years, though over 70 per cent of the latter group had had a second valvotomy within the period. Worth-while results, that is, good and fair combined, were maintained in 72 per cent of all patients at ten years.

In those with heavy as opposed to light calcification of the valve, results were poorer at every stage. Results were good in only 47 per cent at five years and 8 per cent at ten years, and "worth while" in 36 per cent at ten years. Since those with heavy calcification had a higher incidence of associated adverse factors, subgroups were compared, matched as far as possible as regards these factors. Age and cardiac enlargement both adversely affected long-term results, but did not account for the major difference in prognosis between the groups with and without heavy calcification. Atrial fibrillation was by far the most adverse of the other factors but, though highly significant, its effect was less than that due to calcification. Pulmonary hypertension did not influence results materially. In the present context of patients with severe stenosis, associated mitral incompetence whether pre-existing or produced by the valvotomy had, except in a few cases, only a slight adverse effect which was mainly due to a higher incidence of heavy calcification in this

group. The incidence of clot at operation, subsequent systemic embolism, re-stenosis, and re-operation were all higher in those with heavy calcification.

It is concluded that heavy calcification of the mitral valve is the most important of adverse factors affecting prognosis after valvotomy. Its presence, however, should not itself be a contra-indication to valvotomy either on grounds of operative mortality or of long-term results. Until further experience has been gained with valve replacement it seems that closed transventricular valvotomy should be advised in the first instance, and valve replacement should be carried out at a later date if the post-operative result is unsatisfactory.

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