Left Ventricular Cine-angiocardiology in the Assessment of Mitral Regurgitation

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Accurate clinical assessment of the severity of mitral regurgitation is often difficult, and left ventricular cine-angiocardiology is probably the most commonly used method of estimating it. It is therefore important to try to determine the accuracy of this method and to identify as far as possible any causes of error. We have attempted to do this in a series of 137 patients submitted to operation.

SUBJECTS AND METHODS

The patients included in this series were all studied in the course of assessment for operation. Those with pure uncomplicated mitral stenosis were normally not investigated, and the series comprises patients with mitral valve disease in whom the relative importance of stenosis and regurgitation was in doubt, those with clinically pure or dominant mitral regurgitation, those with aortic valve lesions and doubtful associated mitral disease, and those with multivalvular disease. Of 255 patients who had left ventricular cine-angiocardigrams up to the end of 1966, 144 were subsequently submitted to operation (open or closed mitral valvotomy, mitral repair or replacement, or open procedures on the aortic valve). Technically satisfactory cine-angiocardigrams were available for review in 137 of these 144 cases.

Right heart catheterization was carried out from an antecubital vein, under light barbiturate sedation. The left ventricle was entered retrogradely in 106 cases using a Teflon, Dacron, or Positrol catheter introduced either by brachial arteriotomy or percutaneously by the Seldinger method from the femoral artery. The trans-septal approach was employed in 31 cases using a Brockenbrough catheter (Brockenbrough, Braunwald, and Ross, 1962). 35 mm. cine-angiocardigrams were obtained in the right anterior or the left posterior oblique projection using a Cinelix image-intensifier and Old Delft camera at a film speed of 30–40 frames per second.

The contrast medium was either Hypaque 85 per cent or Triosil 75 per cent in a dose of approximately 1 ml./kg. body weight injected with a Gidlund pump at a pressure of 7–8 kg./sq.cm. Injection times were commonly between 2 and 3.5 seconds. The injection was signalled on the electrocardiographic record.

Assessment of Mitral Regurgitation. Mitral regurgitation was classed as grade 1 (trivial or mild), grade 2 (moderate), or grade 3 (severe). Grade 0 denotes no regurgitation at all; any reflux, however slight, placed a case into grade 1. The grading of reflux is essentially subjective and, like others, we have found that it is not possible to define exact criteria for each grade. Attention was paid to the width and density of the regurgitant jet, the degree and speed of opacification of the left atrium, and presence or absence of opacification and systolic expansion of the right pulmonary veins; the size of the left atrium was taken into consideration as this influences the rate at which the chamber opacifies. The occurrence of regurgitation during diastole, preceding the onset of visible contraction of the ventricle, and of multiple ventricular ectopic beats during the injection, was also noted.

All the cine-angiocardigrams in this series were independently examined by three observers, all with considerable experience in this field, who, working together in the same department, might be expected to have evolved similar criteria in assessing mitral regurgitation. At this stage, the observers were unaware of the surgical findings. The first observer (A) examined all the films on a second occasion in ignorance of his first assessment, and when his two assessments differed he viewed the films a third time for a final grading. This final grade was then compared with the grades allocated by observers B and C; where there was any disagreement in the grading, all three observers reviewed the films together and decided on an agreed grading.

In the 137 cases suitable for analysis, the angiographic assessment was compared with the surgical findings. In 67 cases the operation note included a clear statement of the estimated severity of mitral regurgitation. Some surgeons employ a five-grade scale (0, 1–4) or intermediate grades such as 1–2, and it was then necessary

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to edit the surgical grade so that all cases fell into one of 4 grades (0, 1-3). In 26 cases, no formal grading of severity was recorded in the operation note, but adequate information was available to allocate a presumptive grading. In the remaining 44 cases, most of which had an open operation, there was insufficient recorded surgical information on which to base a grading of regurgitation.

Finally, in cases where there was disagreement between the angiographic and the surgical assessments an attempt was made to identify the factors responsible.

RESULTS

Consistency of Angiographic Assessment. Table I shows how many cases each observer (observer A on two separate occasions) allocated to each of the four grades (0, 1-3). There was close agreement concerning the small number of cases with no regurgitation. When regurgitation was present, observer C allocated a similar number of cases to each grade; observer B assessed fewer cases as grade 1 and more as grade 2; and observer A, on both his readings, placed fewer cases in grades 1 and 3 and twice as many in grade 2 as in either of the other two grades. Table II shows that observer A allocated the same grade on both readings to four-fifths of all cases. Each observer agreed with one of his colleagues in two-thirds of the cases, but all three observers agreed in only half. Table I suggests that this unexpectedly low level of agreement may be largely due to the impossibility of defining the borderline between adjacent grades.

TABLE I
GRADING OF MITRAL REGURGITATION BY THREE OBSERVERS (137 CASES)

Observer	Grading of regurgitation			
	0	1	2	3
A (i)	15 (11%)	37 (27%)	59 (43%)	26 (19%)
A (ii)	16 (12%)	33 (24%)	66 (48%)	22 (16%)
A	16 (12%)	35 (25%)	63 (46%)	23 (17%)
B	15 (11%)	35 (25%)	49 (36%)	38 (28%)
C	16 (12%)	44 (32%)	39 (28%)	38 (28%)
Final agreed	14 (10%)	37 (27%)	49 (36%)	37 (27%)

TABLE II
INTER- AND INTRA-OBSERVER AGREEMENT IN 137 CASES

Observer A allocated same grade each time	113 (82.5%)
Observer A agreed with Observer B	92 (67%)
Observer A agreed with Observer C	92 (67%)
Observer B agreed with Observer C	88 (64%)
All three observers agreed	68 (49.5%)
In cases in which Observer A allocated different grades on two assessments (24 cases) all three observers agreed	8 (33%)

In support of this interpretation, it was found that in those cases in which observer A gave the same grade on both occasions, all three observers agreed in 53 per cent, whereas in those cases to which observer A allocated a different grading on his two readings the level of agreement between all three observers fell to 33 per cent ($0.1 > p > 0.05$).

TABLE III
COMPARISON OF SURGICAL AND ANGIOGRAPHIC ASSESSMENT (93 CASES)

		Angiographic grade of mitral regurgitation			
		0	1	2	3
Surgical grade of mitral regurgitation	0	9	12	7	0
	1	2	13	7	2
	2	0	2	9	5
	3	0	0	6	19

Comparison Between Surgical and Angiographic Assessment. Table III shows that there was agreement between the angiographic and surgical grading in 50 (54%) of the 93 cases. The level of agreement in those cases to which a presumptive surgical grading was given (61% of 26 cases) does not differ significantly from those with a definite surgical grading (51% of 67 cases), and all cases will therefore be considered together when possible factors leading to disagreement are analysed. In three-quarters of the cases of disagreement the angiographic grade exceeded the surgical, in 9 instances by two grades. Of special interest are 19 cases with no mitral regurgitation recognized at operation, but in which an angiographic estimate of mild (grade 1, 12 cases) or moderate (grade 2, 7 cases) regurgitation had been made.

Possible Causes of Surgical-angiographic Disagreement. (i) *Intramyocardial contrast injection* occurred in 7 cases, in 6 of which a surgical grading was available. This was a highly significant cause of disagreement, and in all 6 cases the surgical and angiographic assessment differed ($p < 0.01$). In 4 of these 6, the degree of regurgitation was underestimated by cine-angiogram, whereas in the whole series of 93 cases with surgical comparison, there were only 10 in which this was the case ($p < 0.02$).

(ii) *The transseptal approach* (Table IV). Though surgical-angiographic disagreement occurred more commonly (15 out of 24 cases, 62.5%) in cases studied by this method than in those studied by

TABLE IV
COMPARISON BETWEEN TRANSEPTAL AND
RETROGRADE ROUTES

	Trans-septal	Retro-grade	
Total	31	106	
With surgical grading	24	69	
Angio-surgical disagreement (% of cases with surgical grading)	15 (62.5%)	28 (40.5%)	0.1 > p > 0.05
Intramyocardial contrast in- jection (% of total)	5 (16%)	2 (2%)	p < 0.001
Intramyocardial contrast in- jection cases with surgical grading	4	2	
Angio-surgical disagreement excluding intramyocardial injection cases (% of cases with surgical grading with- out intramyocardial injection)	11 (55%)	26 (39%)	0.1 > p > 0.05

the retrograde approach (28 out of 69 cases, 40.5%) this difference was not statistically significant ($0.1 > p > 0.05$). Two-grade disagreement also occurred more commonly with the transseptal technique. Of the 19 cases without regurgitation at operation in which angiography had shown grade 1 or 2 regurgitation, 7 had been studied by the transseptal technique (29% of all transseptal), but only 12 by the retrograde route (17.5% of all retrograde). These differences were, however, not significant.

Intramyocardial contrast injection, itself shown to be a cause of error, occurred more frequently (16%) in transseptal cases than in retrograde cases (2%) ($p < 0.001$). After removal of cases of intramyocardial contrast injection from the analysis, there was still a difference (though not a statistically significant one) in the frequency of surgical-angiographic disagreement between transseptal (55%) and retrograde cases (39.5%).

(iii) *Multiple ventricular ectopic beats.* In the great majority of cases, some ectopic beats were seen on the electrocardiogram. A run of ventricular ectopic beats during the contrast injection was apparent on viewing the cine-angiocardigram in 14 cases (10% of the whole series), and scrutiny of the electrocardiogram where available in these cases shows a series of 5 to 14 ectopic beats. The transseptal technique was used in 8 of these 14 cases. In 9 of them, regurgitation was overestimated by the cine-angiocardigram, while, in another, regurgitation was plainly artefactual as there was none visible during a normal cycle. Of the 9 cases in which the angiographic grading exceeded the surgical by two grades, 4 showed an obvious run of ectopic beats. Intramyocardial contrast injection was invariably associated with a rapid discharge of ventricular ectopic beats and surgical-angiographic disagreement.

(iv) *Atrial fibrillation* (Table V) was the basic

TABLE V
INFLUENCE OF ATRIAL FIBRILLATION

Rhythm	All cases	With surgical grading	Angio-surgical	
			Agreement	Disagree-ment
Sinus	45	35	23 (66%)	12 (34%)
Atrial fibrillation	92	58	27 (46.5%)	31 (53.5%)
All	137	93	50	43

rhythm in 92 cases (67% of the whole series), and in 31 out of 43 (72%) where there was surgical-angiographic disagreement. The surgical and angiographic assessment agreed in 23 out of 35 cases (66%) in sinus rhythm, but in only 27 out of 58 cases (46.5%) in atrial fibrillation; this difference, however, is not statistically significant ($0.1 > p > 0.05$).

(v) *Diastolic regurgitation* (Table VI) was observed in 12 cases, in 7 of which a surgical grade was allocated: it was only associated with surgical-angiographic disagreement in 2 of these. Thus, though spurious regurgitation in diastole might cause difficulties in interpretation in individual cases, its occurrence did not usually affect the accuracy of angiographic assessment of reflux.

Analysis of these 12 cases and of 5 others not in the present series, in which spurious diastolic regurgitation was seen, showed that this always occurred in relation to a long diastole. In 13 cases, a simultaneous electrocardiograph showed that it followed a ventricular ectopic beat in 8 of them (6 in sinus rhythm, 2 in atrial fibrillation); the remaining 5 were all in atrial fibrillation. The duration of the diastole in which reflux occurred exceeded 1 second in 9 of the cases, and was never less than 0.84 sec. Exact timing of the reflux was difficult, but this either just preceded the QRS complex terminating the long diastole, or followed within a few milliseconds.

In 15 of the 17 cases, the mitral valve was either normal, or mildly stenosed (with or without regurgitation); in none of those in which it was measured was there an end-diastolic gradient across the valve at the end of a long diastolic filling period. There were 2 cases with mitral stenosis requiring valvotomy (orifice length 1 cm.), but in neither of these was the gradient measured; in one, an extremely long diastole may have permitted equalization of pressures at end-diastole. In 9 of the 17 cases there was important aortic valve disease, and 2 of these had severe aortic regurgitation. Of the 125 cases without spurious diastolic reflux, 32 had important aortic valve disease, 15 of these having severe aortic regurgitation.

TABLE VI
ANALYSIS OF CASES SHOWING SPURIOUS DIASTOLIC REGURGITATION

Cine No.	Catheter technique*	Basic rhythm	QRS complex preceding diastolic reflux	Length of cycle in which reflux occurs (sec.)	Mitral valve lesion (orifice size)	Mitral diastolic gradient†	Other lesions
86	Retro	Atrial fib.	‡	‡	Pure mitral stenosis (1.0 cm.) (op.)	—	Severe tricuspid regurgitation
228	"	Sinus	Ventricular ectopic	1.26	Normal (op. and necropsy)	—	Aortic regurgitation and fistula aorta-rt. ventricle
324	"	"	Ventricular ectopic	1.20	Normal (or minimal mitral regurg.) (op.)	0 (reversed gradient at end of long diastole)	Severe aortic regurgitation
335	T/S	Atrial fib.	Normal conducted	0.84	Mixed mitral stenosis and regurg. (grade 2) (2.0 cm.) (op.)	Mean 12 mm.; end 0-10 mm.	Trivial aortic regurgitation
408	Retro	Sinus	Ventricular ectopic	0.86	Mixed mitral stenosis and regurg. (grade 1) (2.0 × 0.25 cm.) (op.)	Mean 8 mm.; no gradient pre-a	None
451	"	Atrial fib.	Normal conducted	1.06	Pure mitral regurg. (grade 3) (op.)	0	Organic tricuspid disease; trivial aortic regurgitation
483	"	" "	Normal conducted	1.52	Mixed mitral stenosis and regurg. (op.)	Mean 12 mm.; end 0-12 mm.	None
535	T/S	" "	Ventricular ectopic	1.13	Mixed mitral stenosis and regurg. (necropsy)	Mean 10 mm.; end 0-10 mm.	Severe aortic stenosis
547	Retro	" "	Ventricular ectopic	1.10	Mixed mitral stenosis and regurg. (op.) (1.5 × 1.0 cm.)	Mean 8 mm.; end 0-8 mm.	Mild aortic regurgitation
583	"	Sinus	Ventricular ectopic	1.18	Mild mitral regurg. (necropsy)	0	Severe aortic regurgitation
616	Retro	Atrial fib.	‡	‡	Pure mitral regurg. (grade 3) (op.)	End 0-7 mm.	None
723	T/S	Sinus (76/min.)	‡	‡	Normal (op.)	0	Severe aortic valve disease (aortic stenosis and regurgitation)
<i>Additional cases not in main series</i>							
99	T/S	Atrial fib.	‡	‡	Mild mitral stenosis (catheter)	Mean 3 mm.; end 0	Trivial aortic regurgitation
410	Retro	" "	Normal conducted	1.60	Pure mitral stenosis (1.0 × 0.5 cm.) (op.)	—	Moderate aortic valve disease (aortic stenosis and regurgitation)
655	"	" "	Normal conducted	‡	Mild mitral stenosis and regurg. (catheter)	Mean 5 mm.; end 0-8 mm.	Mild aortic valve disease; ? ischaemic heart disease
867	T/S	Sinus	Ventricular ectopic (or fusion beat)	0.90	Normal (op.)	0	Severe aortic stenosis
872	"	"	Ventricular ectopic	1.16	Normal (or minimal mitral regurg.) (op.)	0	Severe aortic stenosis

* Retro, T/S. = retrograde or transeptal approach.

‡ Either no electrocardiogram during injection or no record of injection on electrocardiogram.

† LV-LA, or LV-PA wedge (simultaneous records or in immediate succession).

DISCUSSION

It is clear that cine-angiocardiology is a surprisingly imprecise method of evaluating the degree of mitral regurgitation. Even when the aim is only the modest one of classifying regurgitation as mild, moderate, or severe, there is a remarkably low level of agreement between experienced observers, and between an agreed angiographic assessment and the surgical grading. If the technique is to be usefully applied, it is necessary to be aware of the causes of error in interpretation, and also to relate the angiographic findings to the clinical features of the case and the result of haemodynamic studies.

Causes of Disagreement between Observers. The major cause of disagreement in grading mitral re-

gurgitation is the difficulty of defining criteria for distinguishing one grade from the next; as a result there will always be difficulty in grading borderline cases. Furthermore, the grading of regurgitation is not a simple process depending on the assessment of one variable only, but depends on a complex evaluation of a number of angiographic features; inevitably different observers will attach different importance to these. For example, difficulty may arise in classifying a case in which there is a broad regurgitant jet but relatively slow and incomplete opacification of a rather large left atrium; or in assessing reflux when this appears to be increased by a run of ectopic beats, or during the powerful systole following the long diastolic pause after a series of ectopic beats. Technical factors, such as a slow injection or dilution of the contrast medium in a very large left ventricle, insufficient obliquity,

bad centering, or a badly positioned catheter, may also make interpretation difficult.

Causes of Disagreement between Angiographic and Surgical Grading. (i) *Errors in surgical assessment.* Palpation of the regurgitant jet or stream is a crude method of assessing mitral regurgitation, though no method hitherto used can compare with it in accuracy, provided that certain causes of error are borne in mind. A small but powerful central jet is more easily appreciated than a broader but less intense stream. Mitral regurgitation may vary in degree from time to time, being influenced particularly by the level of left ventricular systolic pressure and the presence of arrhythmias. If it is accepted that the surgical assessment is on the whole likely to be correct, and that technical inadequacy in the angiogram can usually be recognized, then other disturbing factors must be identified.

(ii) *Transseptal catheterization and intramyocardial contrast injection.* In our experience, there are certain disadvantages in using the transseptal approach. Thus, despite all precautions, it was associated with a significantly higher incidence of intramyocardial contrast injection, and this in turn was associated with a significantly higher incidence of surgical-angiographic disagreement. Intramyocardial contrast injection is always associated with multiple ventricular ectopic beats and commonly with an *underestimate* of mitral regurgitation; inadequate ventricular filling and transient depression of ventricular function lead to a succession of ineffective beats which not only fail to open the aortic valve, but also result in a lesser degree of mitral regurgitation than is present under more physiological circumstances. Even in those cases in which intramyocardial contrast injection did not occur, the transseptal technique was more commonly associated with surgical-angiographic disagreement than was the retrograde approach, though this difference was not statistically significant. The suspicion must, therefore, remain that in certain cases the presence of a rigid catheter through the mitral valve may impair its competence.

(iii) *Influence of ventricular ectopic beats and of atrial fibrillation.* Ventricular ectopic beats occur during a majority of left ventricular cine-angiograms in our experience and that of others (Ross and Criley, 1962; Sellers *et al.*, 1964; Rees, Jefferson, and Harris, 1965; Nagle, Walker, and Grainger, 1968), though opinions differ as to their significance. In our series, ventricular ectopic beats appear to be an important cause of angiographic overestimate of mitral regurgitation; it is not disputed that in *some* cases with a competent or almost competent valve, multiple ectopic beats

are *not* associated with significant reflux. Disagreement between the surgical and angiographic assessments was also commoner in cases with atrial fibrillation than in those with sinus rhythm, though this difference was not statistically significant. Atrial fibrillation has been shown experimentally to cause mitral regurgitation in normal dogs (Daley, McMillan, and Gorlin, 1955), though there is no evidence that this is so in patients with normal mitral valves.

During a rapid succession of beats, whether conducted or ventricular ectopic, diastole is short and atrial pressure rises; in the absence of the normal sequence of atrial contraction and relaxation, the mitral valve is wide open at the onset of systole, and delayed closure of a rigid valve may then lead to early systolic regurgitation. The normal pathways of ventricular activation are disturbed when the impulse arises from an ectopic ventricular focus; regurgitation may then be the result of delayed activation of papillary muscles. The first post-ectopic beat follows a long diastolic filling period, and the resulting increased force of ventricular contraction and increased ventricular systolic pressure may then cause increased regurgitation through an incompetent valve.

(iv) *Spurious diastolic regurgitation.* Diastolic reflux could usually be readily recognized as it preceded the onset of visible contraction of the ventricle, and took the form of a puff of dye gently floating into the atrium rather than a jet with force behind it; its occurrence was not associated with an increased likelihood of angiographic overestimate of mitral regurgitation, though it is possible that diastolic reflux may have been overlooked when it occurred during a period of rapid heart action. In our experience, recognizable diastolic reflux occurred at the end of a long diastole, either in atrial fibrillation, or after an ectopic beat in sinus rhythm, at a time when left atrial and ventricular pressures had equalized, i.e. during diastasis. Thus, with only two exceptions, it did not occur when there was more than slight mitral stenosis; however, even with tight mitral stenosis, pressures may equalize at the end of a prolonged diastolic filling period. Aortic regurgitation may have been a factor in some cases, by causing more rapid equalization of atrial and ventricular pressure, or even a reversal of gradient before the end of diastole (Rees *et al.*, 1964; Oliver, Gazetopoulos, and Deuchar, 1967; Lochaya, Igarashi, and Shaffer, 1967).

Other Information Obtained from Left Ventricular Cine-angiogram. We have found that angiography in the right anterior or left posterior oblique projection is of relatively little value in assessing

cuspid mobility. In this view, though the left atrium and ventricle are clearly separated, the long axis of the mitral valve is at right angles to the path of the x-ray beam, and the larger antero-medial cusp overlies the smaller postero-medial cusp (Ross and Criley, 1962). The cusps cannot be seen separately, and though excessive mobility due to chordal rupture, or cusp prolapse (Criley *et al.*, 1966; Stannard *et al.*, 1967) may be recognized, lesser degrees of abnormality are not shown well.

A crude assessment of left ventricular function can be made when there is satisfactory opacification of the left ventricle during normal sinus rhythm or slow atrial fibrillation, without disturbing rapid ectopic rhythms; the degree of systolic emptying of the ventricle may then give a rough measure of ejection fraction, and we are now attempting to quantitate this. More accurate angiographic estimates of left ventricular contractility depend on volume measurements from biplane angiocardigrams (Miller, Kirklin, and Swan, 1965).

Role of Left Ventricular Cine-angiocardiology in Practice. It is clear that cine-angiocardiology cannot be relied on to give an accurate quantitative measure of mitral regurgitation in all cases. For this reason it is essential that the angiogram should always be evaluated in relation to all the clinical and haemodynamic evidence. In uncomplicated mitral valve disease, without significant associated aortic or tricuspid valve disease, the relative importance of stenosis and regurgitation can usually be judged on clinical criteria alone, and cine-angiocardiology adds little to the accuracy of the clinical diagnosis. When the clinical picture is modified by the presence of pulmonary hypertension or disease of other valves, we have found that angiography does provide a useful addition to the available evidence on which to base an accurate diagnosis. This is particularly so when the investigation shows slight or no regurgitation in the presence of equivocal clinical signs. When the angiogram suggests moderate or severe regurgitation, it is important to examine it closely to see whether ventricular ectopic beats may have increased the reflux under the conditions of the investigation, and to note whether the angiographic assessment is consistent with the haemodynamic findings. Left ventricular cine-angiocardiology may be the only way of assessing the relative importance of mitral regurgitation and impaired myocardial function in patients with congestive cardiomyopathy, and in ischaemic and other forms of left ventricular disease with papillary muscle rupture or dysfunction.

SUMMARY

The left ventricular cine-angiocardigrams of 137 operated patients have been reviewed by three observers, both independently and together, and the degree of mitral regurgitation graded. A surgical grading of mitral regurgitation was available in 93 cases.

Two observers agreed on the grading in two-thirds of the cases, and all three in a half. The angiographic and surgical gradings agreed in only 50 of the 93 cases. Disagreement between observers is due to the difficulty of defining a borderline between adjacent grades, in a subjective assessment based on several angiographic features. Disagreement between surgical and angiographic gradings was invariable in the few cases with intramyocardial contrast injection, and was commoner in those cases studied by the transseptal technique, and when there were multiple ventricular ectopic beats during the injection. Spurious diastolic regurgitation was easily recognized and was not a cause of error in interpretation; it occurs at the end of a long diastole in atrial fibrillation or after a ventricular ectopic beat, usually in the absence of significant mitral stenosis.

Left ventricular cine-angiocardiology often provides valuable information about the severity of mitral regurgitation in a difficult case, but this evidence must be related to the clinical and haemodynamic findings, and the causes of error in interpretation must always be remembered.

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