THE DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH AORTIC VALVE DISEASE

MEDICAL GRAND ROUNDS

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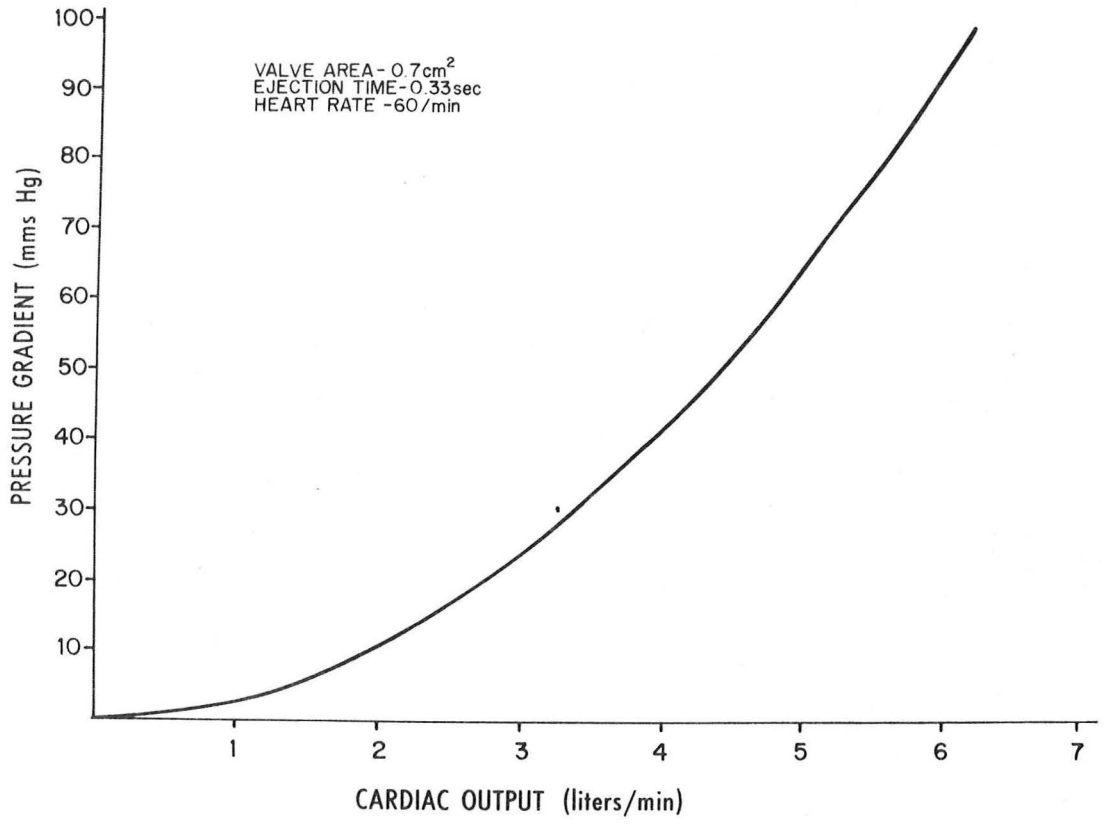
INTRODUCTION

The proper way to care for a patient with aortic valve disease is frequently being modified due to new developments in diagnostic and therapeutic techniques. The new developments are exciting because of the better care they make possible, but these new developments also demand a frequent reassessment of established patterns of care. Today, I am going to review the current knowledge of the pathophysiology, diagnosis, and treatment of aortic stenosis and aortic insufficiency. I will concentrate on those areas which are problems in patient management.

AORTIC STENOSIS

Pathophysiology

The basic problem in aortic stenosis is simply that the stenotic valve obstructs the flow of blood out of the left ventricle. The cardiac output and stroke volume are usually normal, but this output is maintained only because the left ventricle generates a higher than normal systolic pressure to overcome the pressure lost as blood flows through the stenotic valve. The difference between the pressures in the ventricle and aorta is usually called the pressure gradient. A representative relationship between the pressure gradient and the flow through the valve is shown below.



The formula for this relationship is (1):

$$\text{VALVE AREA} = \frac{\text{FLOW}}{\sqrt{\text{PRESSURE GRADIENT}}} \times \text{CONSTANT}$$

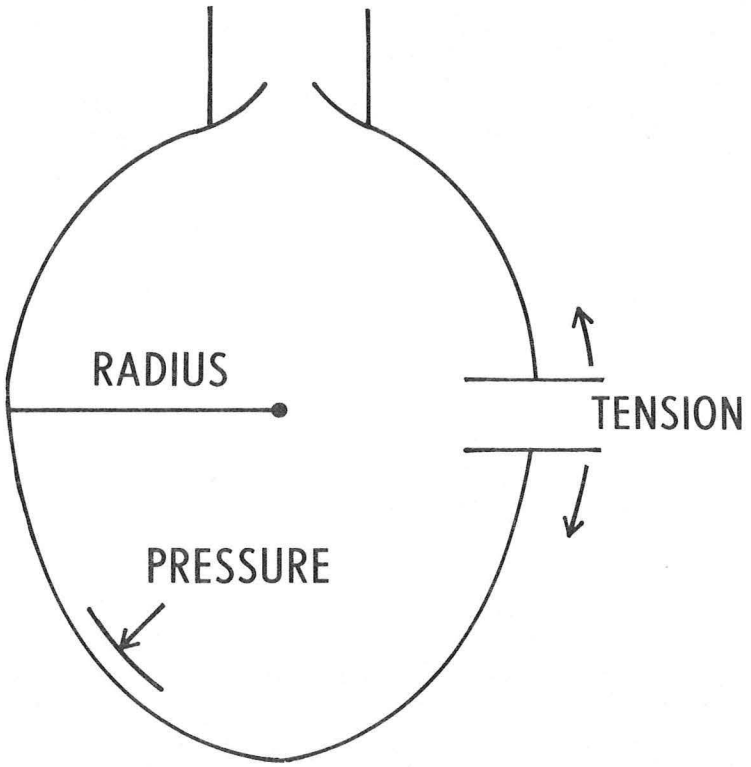
Note that for a given valve area, the pressure gradient changes as flow changes, and furthermore, that the pressure gradient is proportional to flow squared. In other words, if flow doubles, the pressure gradient quadruples. If flow triples, the pressure gradient increases 9 times. From a physiologic point of view, the "valve area" is the numerical relationship between pressure gradient and flow. As the valve area gets smaller, the relationship between pressure gradient and flow gets steeper. When the proper constant is used, the "physiologic" valve area approximates the anatomic valve area. It is academically stimulating to see how close the "physiologic" valve area obtained from catheterization data matches the surgeon's estimate of the anatomic valve area, however, the most important measurement is the steepness of the pressure gradient-flow curve, or the "physiologic" valve area. A valve area of 1.0 cm^2 is moderately severe aortic stenosis.

The fact that the pressure gradient varies with flow is the reason that catheterization reports express the severity of aortic stenosis by giving both the pressure gradient and the valve area. The pressure gradient is the actual extra load imposed on the ventricle. However, if flow is abnormally low, the pressure gradient will not reflect the true severity of stenosis. The most dramatic example of this phenomenon occurs when aortic stenosis and mitral stenosis are both present. Aortic stenosis usually does not cause a decreased cardiac output, but mitral stenosis usually does and may decrease the output to half of normal. At catheterization of a patient with stenotic aortic and mitral valves, the gradient across the aortic valve may be only 20 mm Hg, well below the 40-50 mm Hg usually considered the borderline significant gradient. If the mitral valve only were then replaced, cardiac output may double back to the normal level. This would cause a gradient of 80 mm Hg across the aortic valve. Calculation of valve area circumvents this problem.

The obstruction to flow by the stenotic aortic valve, either directly or indirectly, leads to the 3 symptoms patients with aortic stenosis experience - congestive heart failure, angina, and syncope.

The stenotic valve causes an increase in the left ventricular systolic pressure. The Law of La Place states that this increase in pressure must be met by an increase in wall tension, assuming that the

radius of the ventricle stays constant. (2) This relationship is shown below.



TENSION=PRESSURE×RADIUS

Tension is best described as the force necessary to keep a cut in the wall closed. The increase in systolic pressure is a slow process in aortic stenosis, and clinical studies have now shown that the left ventricle routinely compensates for the increase in wall tension by laying down more contractile elements in parallel, thus increasing wall thickness without changing the ventricular volume. (3-6) This hypertrophy then brings the tension on each contractile element back to normal. The left ventricular mass in patients with aortic stenosis is variable, but on the average, usually doubles. (3-5, 7-10)

Parenthetically, echocardiographers have used the Law of La Place in a novel way to study patients with aortic stenosis. A limitation of the echo technique is that it measures only geometric variables, and cannot

directly measure pressure. However, since wall thickness usually increases in direct proportion to tension, echocardiographers have revised the La Place formula to:

$$\text{PRESSURE} = \frac{\text{WALL THICKNESS}}{\text{RADIUS}} \times \text{CONSTANT}$$

Using this formulation and the appropriate constants, they have predicted intraventricular pressure. (11-13) The actual value of this approach needs further clinical testing.

Congestive Heart Failure

Many patients with aortic stenosis present with congestive heart failure, reflecting an increase in left ventricular diastolic filling pressure. Most of these patients show no impairment of systolic contraction, thus the elevation of their filling pressure is a diastolic or compliance problem, rather than a systolic or contraction problem. (6,7, 14-16) The mechanism of this increased filling pressure can best be seen and explained by again referring to the La Place formula. Recall that the high *systolic* pressure leads to an increase in wall tension which is met by a thickened wall. The ventricle is left with this thickened wall during diastole. Therefore, to get the proper diastolic distending force on each fiber, an increase in wall tension during diastole is necessary, which is met by an increase in *diastolic* pressure. In other words, the ventricle has to suffer during diastole for its compensatory mechanism during systole.

However, in addition to the compliance problem, some patients with aortic stenosis progress to the point where they also have a failure of contraction. (6, 7, 14) When they do progress to this stage, they are at a disadvantage over patients with other types of contractile problems because their noncompliant ventricles prevent them from using the Starling mechanism without raising their diastolic pressures to intolerable levels. (6, 14, 17) The cause of the contractile abnormality in patients with ventricular hypertrophy is unknown. (5, 18-25)

During exercise in healthy persons, the stroke volume increases slightly with a concomitant slight increase in diastolic filling pressure. (26-28) During exercise in patients with aortic stenosis, the stroke volume usually increases appropriately, but the diastolic filling pressure goes much higher than normal. In severely ill patients, the stroke volume may actually drop. (29-32)

Angina

The compensatory increase in left ventricular mass is at least partly responsible for another symptom found in aortic stenosis - angina pectoris. The increased mass is generally perfused by a proportionate increase in coronary blood flow at rest, such that the coronary flow/gram of myocardium is normal. (5, 9, 10) However, during exercise or pacing, ischemia can be shown in a significant percentage of patients by EKG changes, lactate production, and isotope imaging. (9, 33, 34) The exact mechanism of this stress induced ischemia is unknown, (5, 9, 34) but it is commonly thought to be related in some way to the path the arteries must take through the thickened myocardium to the subendocardium. The presence of coronary artery disease must play a role in the genesis of angina in some patients since approximately half of the patients with aortic stenosis and angina have coronary artery disease. (35-39) The other side of this coin is the clinically important question of how many patients with aortic stenosis, but no angina, have coronary disease. This question is important because the answer may dictate whether coronary angiography, a procedure with some risk, should be done during cardiac catheterization. The question is not settled since studies show the incidence of coronary disease to range between 0 - 33% in patients with aortic stenosis who are free of angina. (35-39)

Syncope

The third symptom that occurs in aortic stenosis is syncope. Heart block does occur in aortic stenosis but the majority of syncopal attacks are not initiated by heart block or other arrhythmia. Observation and hemodynamic measurements during syncope show that for the first 20-40 seconds of an attack, the patient is in normal sinus rhythm and has a fall in blood pressure along with a marked decrease in cardiac output. (40, 41) If the attack lasts longer, then arrhythmias may ensue as a secondary phenomenon. Evidence suggests that the mechanism responsible for the syncope is an activation of left ventricular baroreceptors by the high left ventricular pressure. The reflex from these baroreceptors then causes a peripheral vasodilation resulting in a decreased systemic vascular resistance and a diminished venous return. (42, 43)

When complete heart block does occur in patients with aortic stenosis, the etiology is usually impingement on the conducting system by the calcium deposited around the valve. (44) The hemodynamic compensation for the slow heart rate in complete heart block is an increase in stroke volume, which tends to keep the cardiac output normal. This compensatory mechanism works well in patients without valve disease, however, in patients with aortic stenosis, the increased stroke volume results in a marked increase in the gradient across the valve. Hence, slow heart rates are especially detrimental

to the hemodynamic status of patients with aortic stenosis. (32)

Diagnosis

The proper evaluation of a patient suspected of having aortic stenosis is a challenge to the clinician. Most clinicians can remember at least one experience in which they were humbled by mistakenly diagnosing a patient with aortic stenosis as just having a flow murmur. Probably, the most common diagnostic problem concerning murmurs in adults is differentiating an innocent "flow murmur" from significant aortic stenosis. This difficulty is easy to understand since most flow murmurs in adults originate in the aortic outflow tract. (45)

The well-known triad of symptoms in aortic stenosis are angina, congestive heart failure, and syncope. Symptoms usually begin about age 50. (46, 47) The frequency of angina ranges from 30 - 70%; the frequency of congestive heart failure ranges from 45 - 90%; and the frequency of syncope ranges from 20 - 30%. (47-49) Another manifestation of aortic stenosis is sudden death. Death is sudden in about 20% of patients. It is interesting that syncope and sudden death are poorly correlated. In one study, only 2 of 12 patients dying suddenly had a history of syncope. (40) In another study, none of 51 patients experiencing syncope who were followed to death died suddenly. (47) The symptoms of angina and congestive heart failure are relatively nonspecific. Bonafide syncope, on the other hand, occurs in only a limited number of conditions and should alert the clinician to the possibility of aortic stenosis.

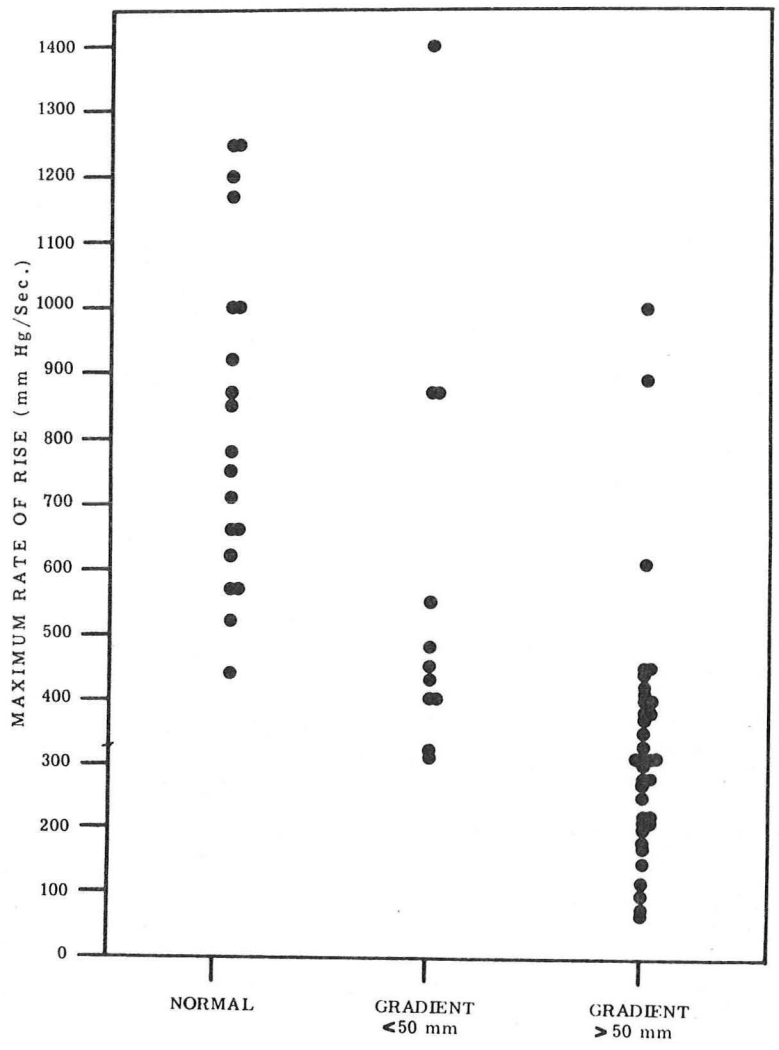
There are 4 commonly recognized auscultatory findings in aortic stenosis: 1) systolic murmur, 2) ejection click, 3) paradoxically split or single S_2, and 4) diastolic murmur. (48) While the ejection click and abnormal S_2 may occasionally be helpful to the true connoiseurs of auscultation, in my opinion, the only consistently useful finding is the systolic ejection murmur. The diastolic murmur of aortic insufficiency is helpful when heard, as it is strong evidence that the aortic valve is indeed diseased. There is usually no diastolic murmur, however. The systolic ejection murmur is usually loudest at the base and radiates to the neck and apex, however, it is occasionally loudest at the apex. The murmur frequently sounds higher pitched at the apex, raising the question of concomitant mitral regurgitation. The murmur of aortic stenosis is frequently well heard over the carotid and may be confused with carotid disease. However, bruits from carotid stenosis are usually not heard at the base of the heart. (50)

After the history and physical, the physician has usually elicited the history of congestive heart failure, angina, and/or syncope; and then has heard a systolic murmur suggestive of aortic stenosis. Simple so far. Next comes

the more difficult step of deciding what the probability is that the patient has aortic stenosis and hence that further workup is appropriate. *The above symptom - murmur complex should not be taken lightly. It is true that many of these patients will not have significant stenosis, but a casual attitude will almost certainly result in missing patients with significant stenosis.*

The two most helpful findings are the carotid pulse and the presence or absence of calcium in the aortic valve. Less helpful are the EKG and echocardiogram.

Palpation of the carotid pulse characteristically reveals a diminution in the rate of rise of the pulse in patients with significant aortic stenosis. As shown in the figure below, a markedly diminished rate of rise means significant stenosis is almost certainly present. However, the converse is not true. *A normal rate of rise in the pulse does not rule out significant stenosis.* (51-53)



If the contour of the carotid pulse is recorded graphically in conjunction with a simultaneous phonocardiogram, a number of characteristics of the pulse and murmur can be quantitiated. The most common of these are the corrected and uncorrected ejection time, QRS to peak of murmur time, maximum rate of rise of the carotid pressure, upstroke time, and "t" time. In the table below, the sensitivity and specificity of these tests are given at the cutoff values commonly recommended. Either a 50 mm Hg gradient or .75 cm^2 valve area is considered significant stenosis. (51-53) Remember that the predictive valve of a test is dependent on the sensitivity and specificity of the test, and the probability that the patient has the disease before he has the test (prevalence is synonymous with probability before the test). In this table, I have assumed that the probability of significant aortic stenosis is 50% before the test in order to calculate the predictive values. The predictive value of a positive test is the probability that the patient will have disease if he has a positive test. The predictive value of a negative test is the probability that the patient will not have disease if he has a negative test. (54, 55) The predictive value of a negative test tells you how good a negative test value is in ruling out stenosis. *Note that none of the measurements of the carotid pulse can absolutely rule out significant stenosis.*

				Prevalence .50	
Study	Measurement	Sensitivity	Specificity	Predictive Value + Test	Predictive Value - Test
Epstein, 1964	Uncorrected ejection time				
	>.34 secs	.78	.47	.60	.68
	>.36 secs	.56	.80	.74	.65
Bonner, 1973	Corrected ejection time				
	>.43 secs	.50	.82	.74	.62
Bonner, 1973	Q-peak murmur				
	≥.20 secs	.61	.82	.77	.68
	≥.24 secs	.19	1.00	1.00	.55
Bonner, 1973	Max. rate of rise carotid				
	>500 mmHg	.92	.36	.59	.82
	≤400 mmHg	.81	.64	.69	.77
Epstein, 1964	Upstroke (u) time				
	>.12 secs	.91	.27	.55	.75
	>.17 secs	.62	.47	.54	.55
Epstein, 1964	"t" time				
	>.046 secs	.81	.53	.63	.74
	>.055 secs	.69	.73	.72	.70
Bonner, 1973	Ejection time >.42 Max. rate rise <500 Q-peak M >.19	.75	.91	.89	.78

The radiographic presence of calcium in the aortic valve is probably the best noninvasive test for determining the presence of significant stenosis. The sensitivity, specificity, and predictive value of a positive and negative test are given in the table below. (56, 57)

Study	Ca ++ in Aortic Valve	Sensitivity	Specificity	Prevalence .50 Predictive Value + Test	Prevalence .50 Predictive Value - Test
Glancy, 1969	1+ (fluoro only)	1.00	.46	.65	1.00
Eddleman, 1973	1+	.95	.40	.62	.89
Glancy, 1969	2+ (specks on CXR)	.85	.54	.65	.78
Glancy, 1969	3+ (heavy)	.63	1.00	1.00	.73

Calcium in the valve which can be seen on a plain chest x-ray is called 3+. Calcium which can be seen only by fluoroscopic examination is called 1+. If calcium is visible on a plain chest x-ray, the probability that the patient has significant stenosis is quite high. On the other hand, if calcium is absent on fluoroscopic exam, the probability that significant stenosis is absent is very high. These studies are valid for patients over 35 years of age and probably are not as helpful when patients have associated mitral valve disease, a finding that implies a rheumatic process. The studies also assume competent interpretation of the fluoroscopic exam. One of the advantages of fluoroscopy is that it can be done in virtually any hospital radiology unit, a situation that makes this test more readily available than some of the other tests that require more specialized or less readily available equipment. In my opinion, the technique of fluoroscopic examination of the heart for calcium is a skill

that can easily be learned by physicians who care for cardiac patients. The best way to learn is probably to befriend a cardiology fellow.

The electrocardiogram usually shows left ventricular hypertrophy or left bundle branch block. However, about 5% of patients with significant stenosis will have a normal EKG. (46-49, 58) The echocardiographic demonstration of left ventricular hypertrophy and thickened aortic valves suggest aortic stenosis, however, the overall value of echocardiography in the diagnosis of significant aortic stenosis has been disappointing. (11-13, 59-61) Aortic stenosis is generally considered a contraindication to exercise testing. (62) However, if a patient is felt not to have significant stenosis, an exercise test may be helpful in assuring the patient and doctor of the safety of exercise.

The most frequent problem in diagnosis is the symptomatic patient with an aortic outflow murmur. The best tests are skilled palpation or graphic recording of the carotid pulse, and fluoroscopic exam for aortic valve calcium. If both of these tests are negative, then significant aortic stenosis can probably be excluded. This recommendation is not absolute, however, and must be used in proper perspective.

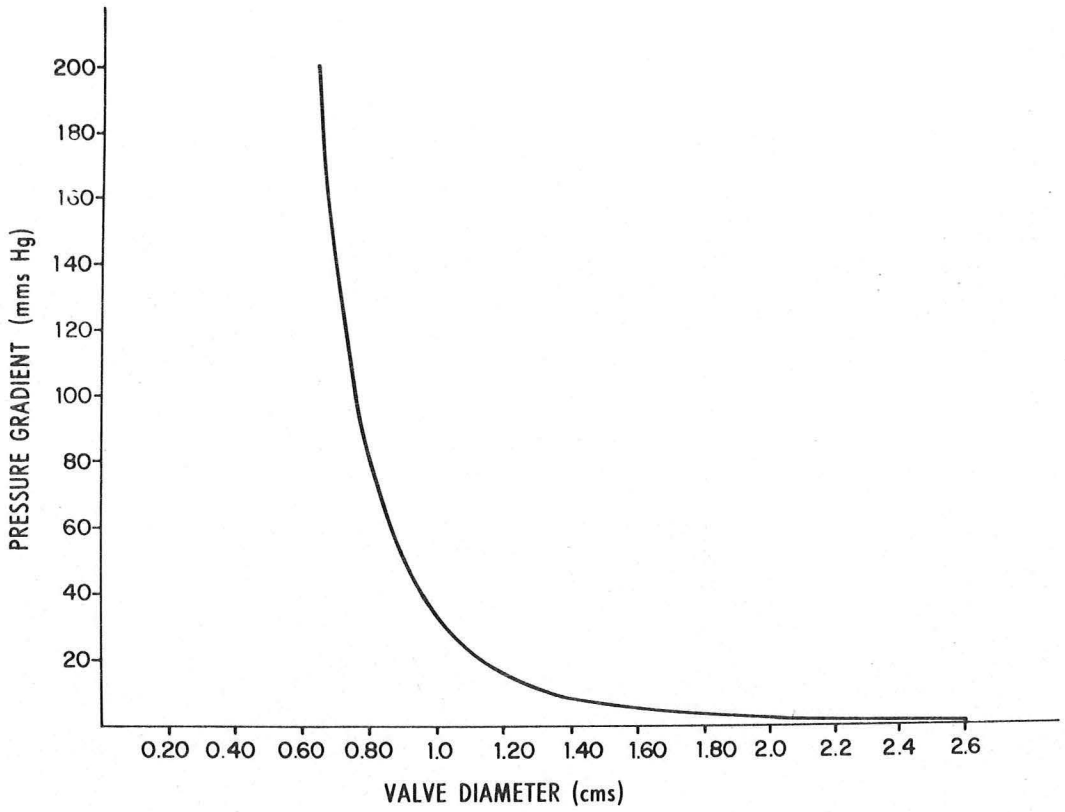
Medical Treatment

The definitive therapy of aortic stenosis is aortic valve replacement. However, medical therapy prior to surgery and in patients in whom surgery is not planned may occasionally be indicated. The proper use of digitalis is unclear. (63) It would seem that digitalis would be of little help in the patient with only hypertrophy before contraction began to fail. The clinical corollary of this would be to digitalize patients only in the advanced stages of failure. Diuretics should be used as necessary with due caution in regard to hypovolemia. If significant bradycardia develops, pacing should be strongly considered as patients with aortic stenosis tolerate bradycardia poorly. (32) However, caution should be used in pacing as the loss of the timed atrial contraction may be detrimental in light of the non-compliant ventricle. This loss of atrial kick is also the reason patients who develop atrial fibrillation often deteriorate, and is the rationale for an aggressive approach to cardioversion. Fortunately, atrial fibrillation is uncommon in aortic stenosis. (47, 48) Vasodilator therapy for the treatment of heart failure is not recommended. (64) The role of nitroglycerin in the treatment of angina is unclear, partly because the mechanism of the cause of angina is unclear. Nitroglycerin should probably be used with caution, if it is effective. Endocarditis prophylaxis should be given for dental procedures, or surgery or instrumentation of the upper respiratory tract, genitourinary tract, or lower gastrointestinal tract. (65) Paradoxically, however, once the valve is heavily calcified, infective endocarditis is rare. (66) *It is good practice to check and have all necessary dental work done on the first encounter with the patient with valve disease.* If this is not done, there is a tendency to forget about

it until the final checklist the day before surgery. Surgeons will cancel surgery for this oversight to the embarrassment of all.

Natural History

Patients with symptomatic aortic stenosis have a poor prognosis without surgery. This poor prognosis is understandable when it is realized that stenosis is a progressive process, and by the time a significant gradient develops, the stenotic process is far advanced. This relationship is illustrated in the graph below where the diameter of the stenotic orifice is compared to the pressure gradient, at a constant flow rate. Note that at the pressure gradient range of about 50-100, which is where clinical symptoms usually develop, only a small decrease in valve diameter will produce an intolerable gradient.



Clinical studies of the natural survival are limited because the techniques to definitively diagnose the disorder were developed about the time that the surgical techniques to correct it were developed. (67) However, the studies that are available indicate that the 3 year survival is about 65%, the 5 year survival is about 50%, and the 10 year survival is about 10%. (67-70) There is probably little difference in prognosis depending on symptom, but possibly the worse prognosis is found in advanced heart failure. (67) Death is sudden in about 20% of patients, all of whom have severe hemodynamic obstruction. (40, 46, 47, 68) Approximately 3-5% of deaths in aortic stenosis occur suddenly in patients without prior symptomatology. (46, 68)

Surgery

The outlook for the patient who has his stenotic aortic valve replaced is dependent on many factors including the operative mortality, function of the artificial valve, improvement in cardiac function, and improvement in survival. I will discuss each of these factors separately.

Operative Mortality

An average operative mortality for surgery to replace the stenotic aortic valve is difficult to give because most of the reported figures come from several years ago in a field that is less than 20 years old, the skill of the surgeons differ, the patient populations differ, and the methods of reporting vary widely. However, a crude overall estimate is around 10% in good centers. (9, 69, 71-87) Surprisingly, little good data is available on predictors of this risk, but in general it seems that the risk is most dependent on functional class, ventricular function, presence of coronary disease, and extent of hypertrophy. The risk does not seem to be dependent on the degree of obstruction per se. (72, 76, 78, 84, 85) The actual cause of death in the perioperative period is divided among many factors, including technical operative complications and noncardiac causes. Hence, the general feeling that the operative mortality in valve surgery is highly dependent on both the technical and general medical ability of the surgeon is probably true. Fortunately, in this institution we are blessed with excellent surgeons.

Artificial Aortic Valves

The first successful use of an artificial heart valve in humans was in 1960. Since that time approximately 50 types of artificial valves have been tried and most discarded. (88) The three types of valves now commonly used

for replacement of the aortic valve are the 1) ball in cage, 2) tilting disc, and 3) tissue valve. The most common brand in use of each type are the Starr-Edwards (ball in cage), Bjork-Shiley (tilting disc), and Hancock (tissue valve). I will discuss the relative merits of these three specific valves since the principles generally hold for the other valves of the same type. Our surgeons here at Parkland and the VA generally use either the Bjork-Shiley or Carpentier-Edwards valve for aortic valve replacement. The Carpentier-Edwards valve is a tissue valve competitive with the Hancock valve, and is quite similar. However, it is newer and there is little data yet reported. The Starr-Edwards valve was first used in 1960, (88) the Bjork-Shiley valve was introduced in 1969, (89) and the Hancock valve was introduced in 1970. (90) The three valves are similar in many ways, but differ in 3 important aspects - durability, hemodynamic function, and frequency of thromboembolic complications. The relative importance attached to each of these aspects determines the choice of valve. Obviously, no one valve is clearly superior overall since they all remain in common use. However, it is important to tailor the valve to the patient, and not just use one valve because of an institutional tradition. (88) I am going to review the relative merits of these valves with regard to durability, hemodynamic function and thromboembolism. More detailed reviews are available from a surgeon's, (87, 91) pathologist's, (88) and internist's (92) point of view.

Durability. The Starr-Edwards caged ball prosthetic valve has the longest proven record of durability of any artificial valve. (91, 93) The original valve developed in 1960 (Model 1000) had a Silastic ball which soon developed swelling, grooving and cracking; a condition known as "ball variance". The Silastic ball was improved in 1965 (Model 1200-1260), and valves that were inserted in 1965 have continued to present without primary failure of the valve. Because of this record of durability, some surgeons still consider the 1260 valve as their first choice. (93) This valve had considerable thromboembolic complications, however, which led to a new model of Starr-Edwards caged ball valve in 1968 in which the struts were covered with cloth (Model 2300-2320). The hope behind the cloth covering was that the cloth would become endothelialized and thereby decrease thromboembolism. The initial model had too small a clearance between the cage and the ball, however, and tissue buildup on the struts led to the ball sticking in some valves. (94) In addition, the ball striking the cloth covered struts caused a tearing of the cloth in some valves. These problems have hopefully been resolved by increasing the ball clearance and the addition of thin metal tracks on the inside of the struts to keep the ball from contacting the cloth (Model 2400). (93) This last modification was made in 1972. There has been no primary valve failure since that time. In summary, the Starr-Edwards ball valve has had some complications along the way, but it is clearly the valve with the most proven durability.

The Bjork-Shiley tilting disc valve, introduced in 1969, initially had a plastic disc which had excellent structural characteristics. However, if the

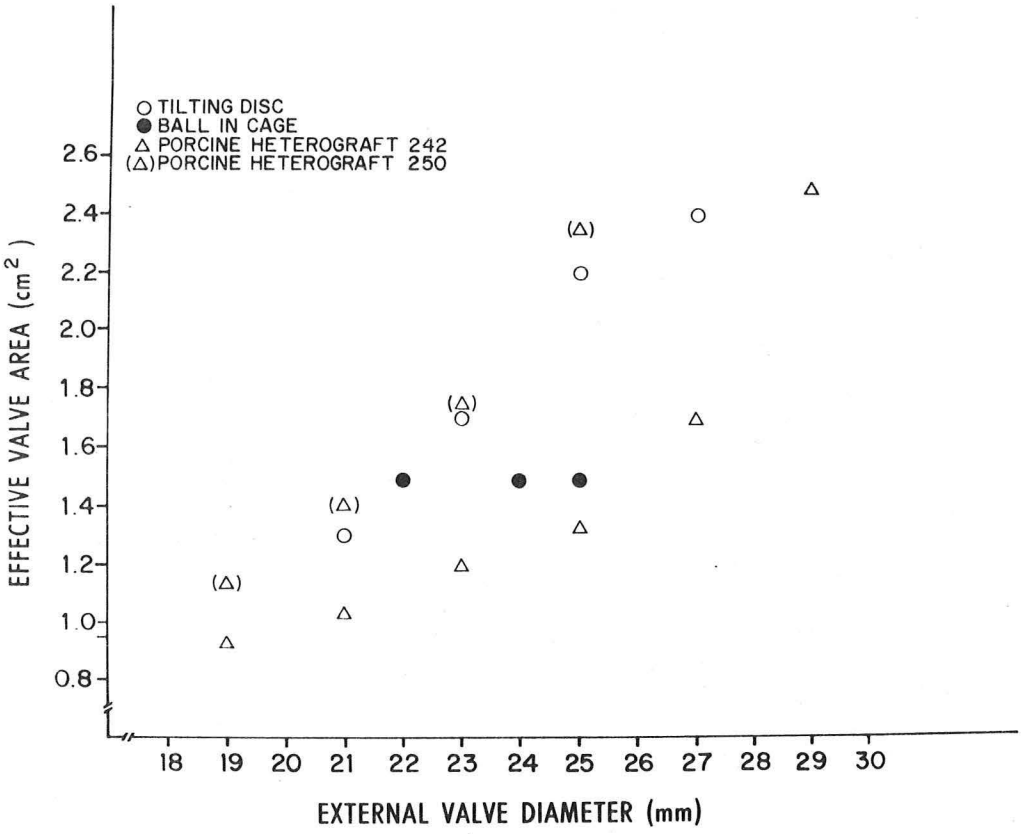
sterilization process was not followed exactly, the disc could swell and stick in a closed position. Therefore, pyrolytic carbon was substituted for the disc material. No structural failure of the Bjork-Shiley valve has occurred clinically, (95-97) and post mortem examination of the valve has shown either minimal or no structural deterioration. (88, 98, 99) Thus, the Bjork-Shiley valve has excellent durability to date, but the followup period is shorter than that of the Starr-Edwards valve.

The Hancock valve is a tissue valve made from the aortic valve of pigs. The valve is mounted on a stent so that it can be sewn in place similar to the method used to insert a caged ball or tilting disc valve. The valve is placed in a glutaraldehyde solution to "fix" the tissue and render it non-antigenic. The hope is that the collagen will retain its structural characteristics and not deteriorate with time. There is no hope that the valve tissue will remain alive. The biggest factor in favor of the tissue valve is its greatly decreased potential for thrombus formation. Compared to the nontissue valves, the biggest question concerning the tissue valve is its durability. Everyone dealing with tissue valves is skeptical because of the history of failure of previous types of tissue valves, usually after initial reports of success. (100) Tissue valves originally were sterilized and preserved with a variety of agents. The breakdown rate of the cusps was high with these different methods, approaching 50% at 5 years. (100) The glutaraldehyde method of preservation has proven to yield the most durable valve and is the current method of preserving the Hancock valve. The valve was introduced in 1970, and to date reports of durability are good. Clinical reports at 2-5 years followup show the structural failure rate to be approximately 0-2%. (90, 101-104) Carpentier, one of the principal developers of the valve, estimates the 10 year structural failure rate to be around 20%. (80) However, microscopic inspection of recovered valves which have been implanted over 2 years show marked deterioration of the collagen fibers and endothelial surface, some bacterial colonization (in the absence of clinical infection), and small areas of calcification. (105, 106) These changes, coupled with the relatively poor structural history of previous tissue valves, properly temper the enthusiasm with which the Hancock valve has been received.

In summary, durability has been best proven with the ball in cage valve. The tilting disc valve appears just as durable, but this has not been proven by as long a followup period. The porcine heterograft tissue valve is promising, but deserves the least confidence in its durability.

Hemodynamic function. The best way to determine the hemodynamic characteristics of an artificial valve is to determine the effective area of the valve in vivo by measuring its pressure gradient and flow the same way that the valve area of naturally stenotic valves is determined. (1)

This effective valve area is usually smaller than the measured orifice of the valve. In general, as the external diameter of the valve increases, the physical size of the valve orifice increases, and consequently the effective valve area increases. Therefore, the size of the tissue annulus into which the valve will be inserted must be considered in conjunction with the characteristics of the valve when the final effective valve area for any given patient is estimated. The tissue annulus in patients undergoing valve surgery generally ranges down to about 20 mm diameter. (108) In the figure below, the reported effective valve areas at different external diameters for the Bjork-Shiley, (89) Starr-Edwards, (107, 109) and Hancock (102, 110-112) valves are shown. It should be clear from this graph that the insertion of an artificial aortic valve usually gives the patient mild to moderate aortic stenosis. This fact should be taken into account when surgery is considered for mild aortic stenosis.



From this graph, it is apparent that the Bjork-Shiley valve has the best hemodynamic function for any given external diameter (Hancock 250 in vitro, (X), will be clarified later). For this reason, it is the preferred valve by many surgeons when they encounter a small root.

On the other hand, the Hancock tissue valve Model 242, the most common model implanted, has the worst hemodynamic function. Notice that in a patient with a small tissue annulus who has a Hancock valve implanted, the patient may end up with an effective valve area that is consistent with significant aortic stenosis. One reason for the small effective valve area was thought to be the fact that one of the cusps had a stiff ridge of muscle on it. Therefore, the valve was recently modified to the Model 250 in which the muscle was removed. An in vitro method to test the effective valve area showed the function of this new valve to be as good as the Bjork-Shiley. (113) However, this improved function has not yet been shown in vivo. Our surgeons here at Parkland and the VA have recently switched to the Carpentier-Edwards porcine heterograft valve. The hemodynamic function of this valve is also supposed to be better than the older Hancock valve. However, this improved function has not yet been demonstrated.

The Starr-Edwards valve is intermediate in terms of its hemodynamic function. In contrast to the central flow valves, the effective valve area of the Starr-Edwards valve does not vary with its external diameter and remains constant at about 1.5 cm^2. This is apparently because the flow is obstructed not only at the orifice, but also between the ball and ring, and possibly also between the ball and aortic wall. Too small a space between the ball and aortic wall is a common cause of early postoperative death. (98)

Thromboembolism. Thromboembolism has been a significant problem in the development of artificial heart valves. This problem has arisen not only from the thrombi and emboli produced by the valve but also by the complications of the anticoagulants used to combat the clotting process. The risk of serious hemorrhage due to anticoagulants is about 1-3% per year, and the risk of death due to hemorrhage is about .1 - .5% per year. (80, 93, 114) In addition, taking anticoagulants and controlling the dosage is inconvenient. Although attempts have been made to the contrary, it is now generally recommended that all artificial valves except tissue valves be anticoagulated.

The freedom from thromboembolism and the consequent necessity for anticoagulation is the chief advantage of tissue valves. The embolism rate of Hancock valves, without anticoagulation, is very low - well under 1% - after several years of followup. (90, 101-104, 110) Most of the few cases of embolism were in patients who had reason to have emboli arising in the left atrium. Although rare, thrombus formation and tissue overgrowth arising from the valve-heart interface do occur and can cause valve malfunction.

The Bjork-Shiley valve is thrombogenic enough that it is recommended that all patients with these valves be anticoagulated. However, the rate of embolism is less than 1% per year. (80, 89, 95, 96) Probably more dangerous than the embolism from this valve is its tendency to clot and abruptly malfunction. Fortunately, the incidence of this complication is less than 1%. (95, 96) Both embolism and valve thrombosis are inversely related to the adequacy of anticoagulation. (96, 97)

The Starr-Edwards valve is the most thrombogenic of the three valve types. The modification in which the struts were covered with cloth decreased the rate of thromboembolism, however, the problem is still significant. The actual rate of embolism varies in different studies, probably depending on the adequacy of anticoagulation and the definition of a significant thromboembolic episode. However, an average rate of significant embolism for anticoagulated patients is about 3% per year. (80, 93, 114-116) The rate is considerably higher when anticoagulation is inadequate. (114-116) One study found the rate of embolism to be much higher in patients who initially received anticoagulation which was later stopped. (115) the rate of embolism is highest in the first 4 years after surgery. (114) Thrombosis leading to valve malfunction does occur, but is rare. When it does occur, it generally causes a relatively slow progression of malfunction compared to the catastrophic thrombosis of a Bjork-Shiley valve. (93) This slow progression of thrombosis on a Starr-Edwards valve is only relative, however. Any suspected thrombosis should be treated as an emergency.

Hemolytic anemia. Significant mechanical hemolytic anemia does not occur with the Hancock heterograft valve or Bjork Shiley tilting disc valve. Significant anemia sometimes occurs with the Starr-Edwards valve, especially if there is tearing of the strut cloth or increased flow due to paraprosthetic regurgitation. (88, 117, 118) Anemia severe enough to require replacement of the valve occurs in about 1% of Starr-Edwards valves. (115)

In summary, the choice of an artificial aortic valve is a compromise between the durability, hemodynamic function, and thromboembolic potential of the various types of valves. The Starr-Edwards ball in cage valve has the best record of proven durability. The Bjork-Shiley tilting disc valve has the best hemodynamic function, especially in small aortic roots. The Hancock tissue valve is the least thrombogenic and is the only valve type not requiring anticoagulation.

	Durability	Hemodynamics	Thromboembolism
Starr-Edwards (ball in cage)	+++	++	+
Bjork-Shiley (tilting disc)	++	+++	++
Hancock (tissue)	+	+	+++
	+ Worst	+++ Best	

Endocarditis. Endocarditis occurs with all types of artificial valves. This complication occurs in about 4% of valve replacements and has a mortality of about 50%. (117, 119-121) The clinical features are similar to endocarditis of a natural valve with fever, regurgitant murmur, systemic emboli, and splenomegaly being the most prominent findings. (117) The onset of symptoms is usually over 25 days after surgery, but can occur earlier. (117, 120, 122) When the onset of the illness is less than 60 days after surgery, infection is probably the result of contamination during surgery. In these early (< 60 days post-surgery) infections, the organism is Staph aureus or Staph epidermis in about half of the cases, and the remaining half have a relatively high percentage of gram negative organisms and Candida. (119-121) When the onset of illness is over 60 days after surgery, infection is usually the result of bacterial blood stream invasion and localization on the valve. In many of these cases, infected teeth, urine, or wounds have been the portal of entry, a fact which emphasizes the necessity of curing chronic infections prior to valve replacement and promptly treating infections after valve replacement. In addition, anti-bacterial prophylaxis should be given for dental procedures, or surgery or instrumentation of the upper respiratory tract, genitourinary tract, or lower gastrointestinal tract. (65) In these late (> 60 days post-surgery) infections, the frequency of responsible organisms parallels that of endocarditis of natural valves, with the streptococcus species being the most common. (117, 119-121) In both early and late endocarditis, blood cultures are usually positive. When they are not, Candida should be suspected. (119) Treatment is recommended if the clinical picture is typical, but cultures are negative. (117) Sandes et al suggests that blood cultures positive with gram negative organisms sooner than 25 days after surgery probably do not represent endocarditis. (122) However, others do not agree and feel that a patient with an artificial valve and positive blood cultures should be presumed to have endocarditis. (117, 120, 121) The post perfusion and post pericardiotomy syndromes are two benign causes of fever which occur in the postoperative period and need to be differentiated from endocarditis. The most helpful findings are atypical lymphocytes and lymphocytosis in the post perfusion syndrome, and pericardial pain and good response to anti-inflammatory therapy in the post pericardiotomy syndrome. Further information on these syndromes is available elsewhere. (117, 118, 123) The treatment of artificial valve endocarditis is begun with antibiotics. An antibiotic regimen has been suggested by Slaughter et al. (121) Antibiotics alone cure about 1/3 of cases. (120, 121) In those patients who do not respond well to antibiotics, deterioration results from uncontrolled infection, large or multiple emboli, refractory heart failure, and/or valvular dysfunction. The valvular dysfunction may either be a regurgitant leak or thrombotic obstruction of the valve. (119) In those cases where the response to antibiotics is poor, surgical removal of the infected valve should be attempted. This results in cure in about 1/2 of the operated cases. (120, 121) In some instances of continued infection, multiple valve replacements have been done, however with little success. (120) The overall mortality in patients with endocarditis occurring less than 60 days after surgery is about 75%, while the mortality with endocarditis occurring over 60 days after surgery is about 40%. (120, 121)

General remarks about complications. A patient who is suspected of having malfunction, thrombosis, or infection of his artificial heart valve is a true emergency. The cardiac surgeons and cardiologists should be consulted immediately. Decisions regarding therapy in these patients is highly judgemental and often difficult. Noninvasive diagnostic techniques such as auscultation, phonocardiography, echocardiography, and fluoroscopy are imperfect tests which must be used in context with other data. *A single "normal" report from any of these studies should never be used as confirmation of the lack of valve complications.* Cardiac catheterization is the most definitive diagnostic procedure, but it too is imperfect. *When valve complications are present, deterioration can occur very rapidly.* When deterioration occurs, surgery is either of no help or has a much higher risk. *For all these reasons admission to a coronary care unit followed by immediate consultation with the surgeons and cardiologists is essential for optimal care.*

Ventricular Function After Valve Replacement

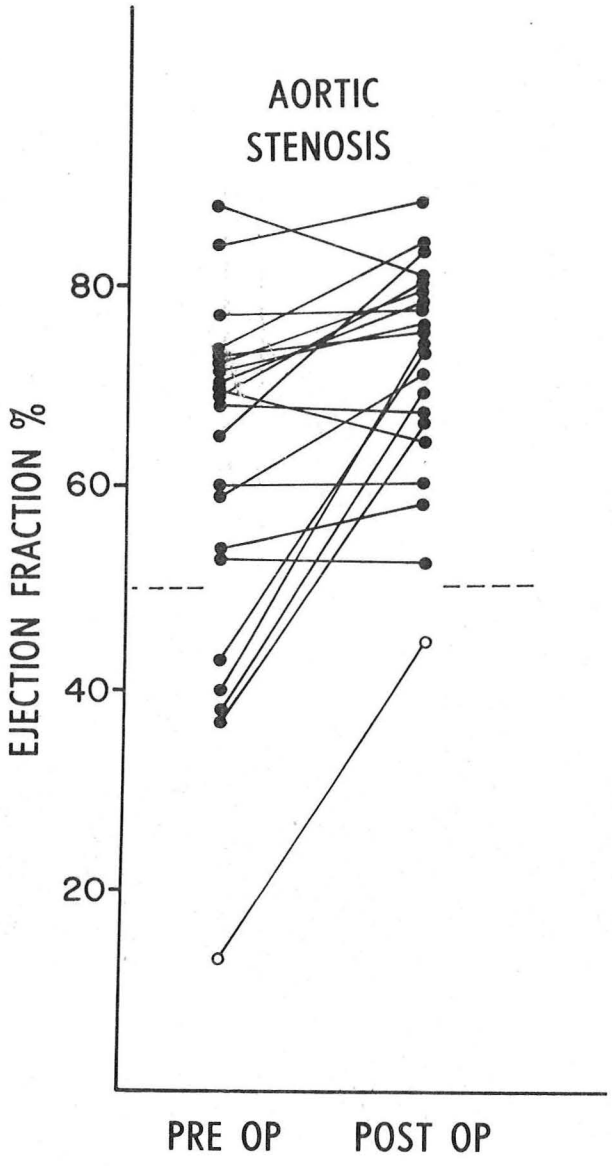
Improvement in abnormal left ventricular measurements are marked after successful aortic valve replacement. The normal left ventricular mass is 100 gm/meter^2 of body surface area. In aortic stenosis, the mass in increased to about 220 gm/m^2. By one year after successful surgery, the mass decreases to about 125 gm/m^2. (79,124) Possibly the small residual elevation of mass is due to the mild aortic stenosis usually present with an artificial valve. As shown in the graph on the next page, myocardial function is improved after surgery, especially in those patients whose preoperative myocardial function was depressed. Myocardial function on this graph is measured by the ejection fraction, of which the lower limit of normal is 50%. This graph is a composite of 4 studies. (15, 79, 86, 124) Each solid circle is a single patient. The open circles are the mean of a group of 7 patients. (86)

The study represented by the open circles showed that in a series of 7 patients with an ejection fraction below 20% (average 13%), successful surgery caused the ejection fraction to increase to an average of 45%. (86) The findings of this study are so dramatic that they need verification by further studies. Another measure of myocardial function, the end diastolic pressure, tends to improve markedly when it was elevated preoperatively. (79)

Overall Functional Improvement

Surgery also causes an improvement in the function of the cardiovascular system during exercise. A series of catheterized patients studied at a constant level of supine exercise increased their stroke volume 30% while decreasing their average wedge pressure from 30 mm Hg to 16 mm Hg. (125) During bicycle exercise, patients are able to pedal against almost twice the resistance after surgery. (89) On the treadmill the postoperative patients are able to walk an average of 80% of the speed and grade which normal persons can walk, (86, 124) even in those patients whose ventricular function was markedly depressed before surgery. (86)

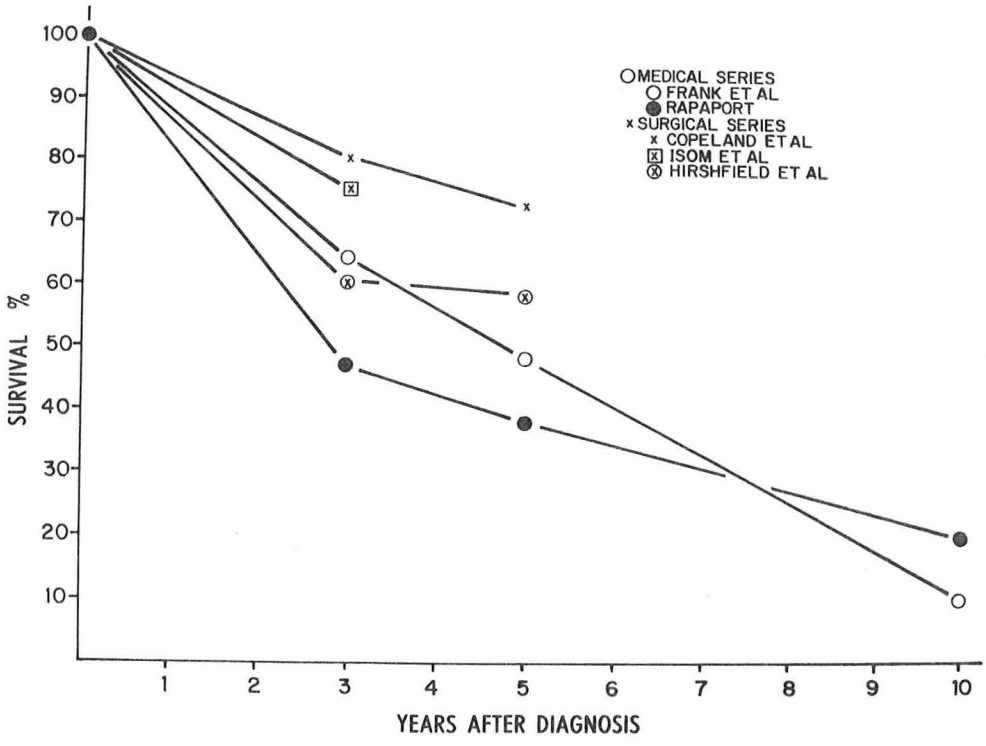
Overall, patients have a marked improvement in function. Approximately 50-75% of successfully operated patients are free of symptoms, and most of the rest are improved. (69, 79, 85, 89, 124, 125) Angina occurring in patients without coronary disease is completely relieved by valve surgery in almost all patients. (85) It is not clear whether valve surgery alone would relieve angina in patients with coronary disease since the practice of coronary angiography during catheterization for aortic stenosis, and the practice of combining bypass grafting with valve surgery began at the same time. However, the high rate of angina relief in earlier studies of patients who probably had coronary disease, but just had valve surgery, suggests that valve surgery alone probably improves or relieves angina in a high percentage of patients. (69, 125)



Survival After Surgery

Many studies address the question of survival after medical (47, 48, 67, 68) or surgical (69, 73, 77, 84, 85, 87, 88, 93, 103, 115, 116, 126) treatment of aortic stenosis, yet relatively few studies are done in a manner that allows meaningful interpretation of how long a patient with aortic stenosis can be expected to live. (46, 70, 75, 76, 80) There are several reasons for this lack of meaningful studies. One reason is that good techniques to diagnose aortic stenosis were developed about the time that surgical techniques to replace the valve were developed. Soon thereafter, it became accepted practice to treat aortic stenosis surgically. Consequently, there are very few studies of patients with well diagnosed aortic stenosis who were followed medically. Another reason for a lack of meaningful studies is that in articles on the followup of surgical patients, it is common to combine patients with aortic regurgitation and stenosis together. This is like combining apples and oranges. Studies which subdivide the patients into stenosis or regurgitation show that they indeed do act differently. (76, 80) In the figure below, two medical and three surgical studies of survival are compared. One medical series is a catheterized group of 15 patients who for variable reasons did not have surgery. (46) The other medical series is a group of 42 patients in whom neither the method of diagnosis nor why they were not operated upon is made clear. (70). The three surgical series were reported between 1974 and 1977. (75, 76, 80) Operative mortality is included.

The survival figures shown in this graph must be interpreted with the



reservations that the patients were not randomized, surgical techniques have improved since the studies were done, and diagnosis has become more sophisticated. The curves do indicate an improvement in survival with surgery, however, the difference is not as great as is generally believed. The causes of late death after surgery are variable with definite cardiac causes accounting for about half of the deaths. (76, 80)

Few factors seem to influence long term survival after surgery. Radiographic heart size, EKG pattern, and symptom complex have little influence. The most influential factor is preoperative functional class with Class I-II patients having a 70-85% 5 year survival and Class III-IV patients having a 50-70% 5 year survival. (76, 80) Associated coronary artery disease adversely affects survival. (80, 84)

Timing of Surgery

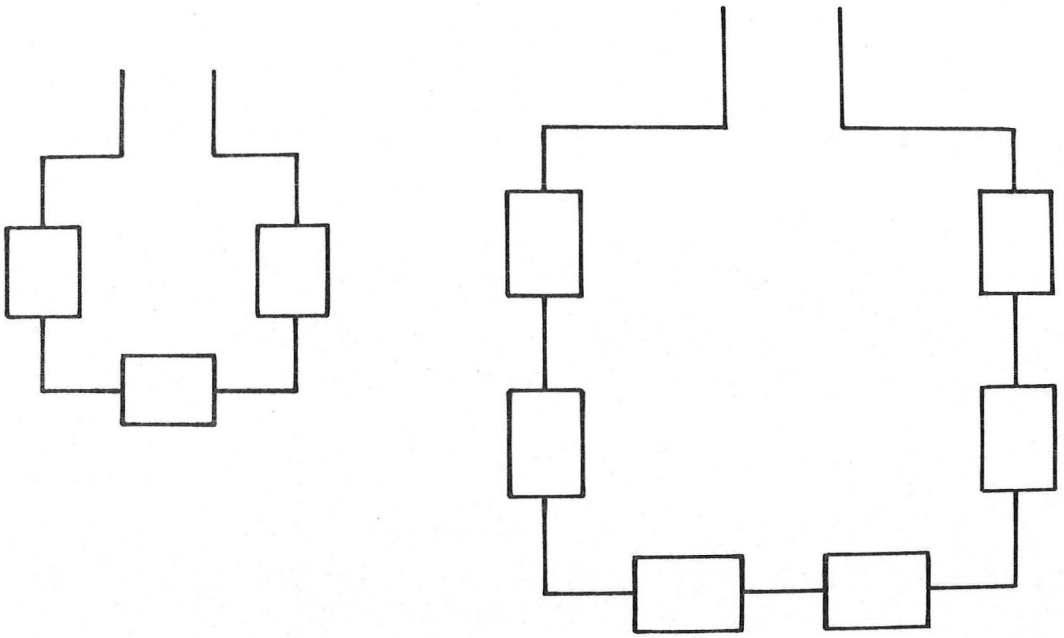
The time to operate on the symptomatic patient with aortic stenosis is almost universally accepted as the time when the diagnosis is established. The rationale for this is that the time from the onset of symptoms to death is short and sudden death may occur, therefore, there is no benign stage of the disease where hesitation is warranted. In addition, a decrease in the patient's functional status worsens the surgical prognosis. Most centers operate on symptomatic patients with aortic stenosis semiurgently. A more difficult question is whether to operate on asymptomatic patients who have hemodynamically significant stenosis. The fact that 3-5% of the deaths in aortic stenosis occur suddenly in patients without symptoms (68) suggests that operation in these patients may be indicated. I know of no further data to help in this decision. I personally would recommend surgery for all patients with significant aortic stenosis who do not have extenuating circumstances.

AORTIC INSUFFICIENCY

Pathophysiology

The basic problem in aortic insufficiency is that blood leaks back into the left ventricle from the aorta during diastole. If the leak occurs acutely, the ventricle responds by using the Starling principle in which the increased volume load caused by the regurgitation stretches the ventricle. This increased diastolic stretch causes an increased stroke volume which is equal to the sum of the normal stroke volume plus the regurgitant volume. However, the amount of aortic insufficiency which can be managed by this acute compensatory mechanism is quite limited, (24) and is far less than the regurgitation frequently seen in chronic insufficiency.

The response of the left ventricle to chronic aortic insufficiency is to generate additional contractile fibers in series, (19, 24) as shown in the figure below. This hypertrophy frequently results in a tripling of the diastolic chamber volume and ventricular mass, (7-9, 79, 124) while the diastolic length of each sarcomere remains constant. (24) Since the individual sarcomeres are not stretched, diastolic pressures are normal in patients who are compensated, even in the presence of marked insufficiency. (7, 17)



Patients may do well for years in this compensated state. However, many patients will eventually develop heart failure. This failure may either be due to a sudden increase in the regurgitant volume for which the ventricle has insufficient time to compensate, or due to the development of myocardial failure. Failure due to a sudden increase in regurgitant volume is essentially acute aortic insufficiency, a subject not covered in this discussion. The more common cause of failure is depression of myocardial contraction, the cause of which is unknown. (9, 15, 18-20, 22, 23) The ejection fraction is the most common measurement used to judge the degree of myocardial contraction. The ejection fraction is the ratio of stroke volume to end diastolic volume and is the cubic

equivalent of the relative amount of shortening of each sarcomere. Since it is a ratio, the ejection fraction reflects the relative amount of sarcomere contraction regardless of the absolute volume of the ventricle. From a clinical standpoint, a depression of the ejection fraction below the lower limit of normal of 50% is generally felt to represent myocardial failure. The point in the course of aortic insufficiency when myocardial failure begins is only generally related to the amount of volume overload, ventricular volume, and ventricular mass. (7, 15, 124) This lack of good correlation is unfortunate since it means that these gradually progressive values of volume and mass are probably not very helpful in predicting when failure is imminent.

As myocardial failure occurs, two compensatory mechanisms occur. The first mechanism is that the ventricle generates even more contractile fibers in series so that stroke volume is maintained, i.e. two fibers in series, each of which only contracts half the normal amount, together contract as much as one fiber normally does. The second mechanism is the Starling mechanism, wherein the end diastolic pressure and consequently the end diastolic fiber length is increased. This increased fiber length tends to maintain stroke volume in a failing ventricle. Both of these mechanisms result in further cardiac enlargement over that due to the volume overload alone.

Patients with aortic insufficiency frequently report a surprisingly small degree of dyspnea on exertion at a point in their course when they are having significant nocturnal symptoms. (127) This discrepancy is due to the slow heart rate at rest which gives a long period of diastole between each beat, the time when aortic insufficiency occurs. In one series of patients, increasing the heart rate from a mean of 70 to 104 by atrial pacing decreased the mean end diastolic pressure from 19 to 8 mm Hg. (128) The most important clinical point from this aspect of the pathophysiology is that *the severity of aortic insufficiency and the degree of myocardial failure cannot be judged accurately from the patient's exercise capacity*. (7, 14) As will be discussed later, myocardial failure that develops as the result of aortic insufficiency is not reversible. In an attempt to predict the phase of the progression of AI where myocardial function is still normal, but is about to deteriorate, angiotensin has been used to increase the blood pressure and thereby stress the ventricle. (129) Under this stress, the ejection fraction of some patients was maintained while the ejection fractions of other patients dropped. Further study needs to be done to see if the patients who dropped their ejection fraction are on the verge of myocardial failure.

Diagnosis

The diagnosis of chronic aortic insufficiency is usually easy. The most significant symptom is congestive heart failure, with nocturnal symptoms frequently more severe than the exertional symptoms. Some patients have angina, even in the absence of coronary disease, (38) however the angina is frequently atypical and is usually not the presenting symptom. Some patients may have dizziness, but frank syncope is uncommon. The diagnostic physical finding is the high pitched blowing murmur heard best along the left or right sternal border. Usually this murmur is not difficult to hear and most mistakes in diagnosis are made when the examiner does not specifically listen for the presence or absence of the murmur. A wide pulse pressure and the physical findings of hyperdynamic arterial pulses are also present and described in standard texts. (130, 131) The real challenge to the modern clinician is not to just make the diagnosis of aortic insufficiency, but to also determine the response of the circulation and myocardium to the insufficiency, and then to use this information to determine the optimal time for surgical replacement of the valve. I will return to this subject later.

Medical Treatment

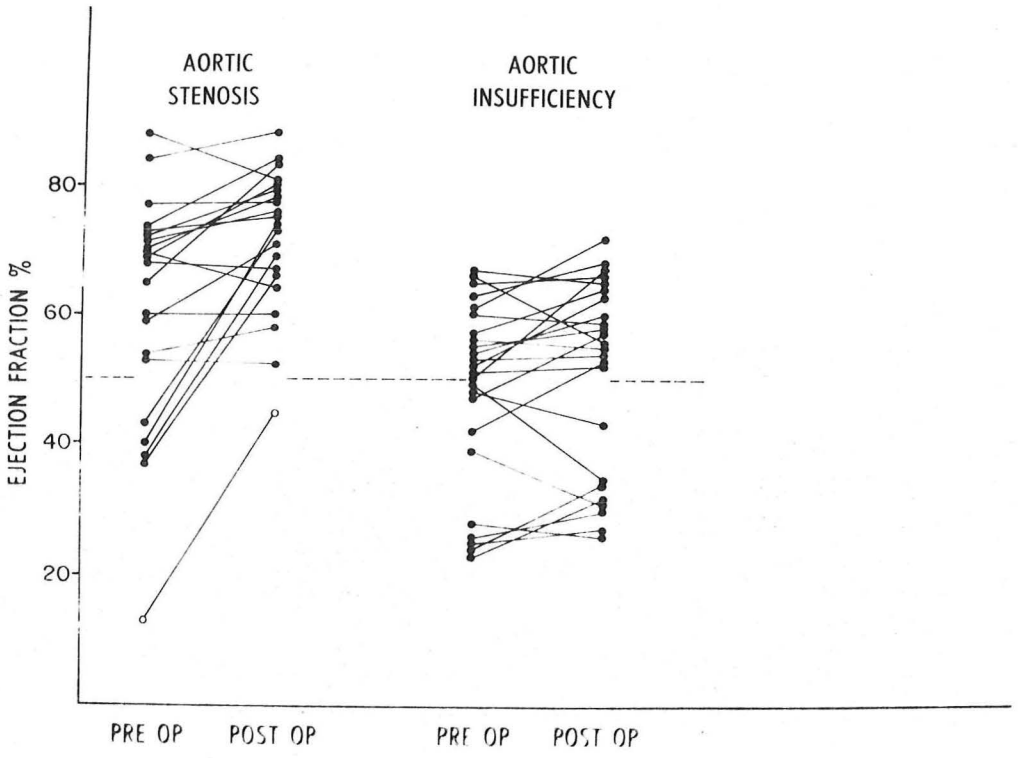
The medical treatment of the patient with symptomatic aortic insufficiency is first begun with digitalis and diuretics. This treatment is time proven to be effective, but there is little data on the specific hemodynamic effect. (63) Vasodilator therapy with nitroprusside has been shown to improve the hemodynamic status of patients with moderately severe insufficiency, (64, 132, 133) although the improvement appears to be marginal. The improvement is due to a reduction in systolic blood pressure with a consequent increase in stroke volume, and a small decrease in aortic diastolic pressure with a consequent decrease in the amount of regurgitation. The end result is a decrease in diastolic ventricular volume and pressure. (132, 133) The combination of slow heart rate and aortic insufficiency is particularly bad, therefore patients with complete heart block benefit from pacing particularly well. (128) Two patients with AI and heart block with a mean ventricular rate of 42 were paced to a heart rate of 77. The mean wedge pressure dropped from 27 to 11 mm Hg. (32) Patients should have endocarditis prophylaxis as detailed in the section on treatment of aortic stenosis. (65)

Surgery

In addition to medical therapy, most patients with aortic insufficiency should have their aortic valve surgically replaced at some point in their course. The time when this surgery should be done is the most important decision facing the clinician caring for the patient with AI. In order to develop an approach to making this decision, I will first discuss the physiologic and functional improvements that can be expected from successful surgery. Then I will compare the medical course of patients with chronic AI, especially in terms of survival, to the course expected after surgery. Finally, I will try to combine the available information into a comprehensible approach.

Hemodynamic Improvement

The hemodynamic defect in patients with aortic insufficiency is two fold--first the volume overload caused by the leaking valve followed at some later point by a depression of myocardial function. The depression of myocardial function is best measured clinically by a decrease in the ejection fraction. Successful surgery obviously repairs the problem due to regurgitation, and thereby lowers the diastolic pressure. However, an important point which has only recently been clarified is that surgery does not improve the depressed myocardial function which is present before surgery. In the figure below I have compiled the results of 4 studies on the effect of surgery on the ejection



fraction. (15, 79, 124, 134) For consistency, I have converted a slightly different type of measurement in one study (134) to ejection fraction by a regression equation. (135) For contrast, I have included the previously presented similar data on aortic stenosis. *Notice that the patient is left after surgery with the same ejection fraction he had before surgery. In other words, if surgery is done after myocardial depression has occurred, the patient is essentially left with a cardiomyopathy.* Throughout the rest of the discussion, this point will be important. I am assuming that these studies done about a year after surgery indicate that if the regurgitant leak is repaired before myocardial depression has occurred, myocardial depression will not occur later. Other catheterization measurements suggest that this is the case but it has not been directly shown.

Functional Improvement

After successful valve replacement, patients as a group improve their overall functional status from significant limitation (NYHA FC 3) to a less symptomatic, but not normal state (NYHA FC 1.5-2). (14, 15, 79, 124) However, the exercise capacity may show little improvement, since exercise capacity is usually well preserved before surgery relative to a patient's view of his overall functional status. In one study, the patients' view of their overall function improved significantly, yet their exercise tolerance on the treadmill only changed from 71% of normal to 75% of normal. (124) As expected, the ejection fraction is an important predictor of whether patients will have a good or poor result after surgery. (14)

Natural History

The natural history of patients with aortic insufficiency is not well known with respect to current standards of hemodynamic assessment. The reason is that aortic valve surgery was introduced just prior to the development of good techniques for assessing myocardial function. Since it is now unusual for a patient to die of aortic insufficiency without valve surgery, the natural history will probably never be known better than it is now. Consequently, we are left having to piece together what is probably the natural history of the disease based on our knowledge of the pathophysiology, studies using nonspecific clinical assessment done before the days of cardiac catheterization, and scant investigation done after the development of catheterization. *The evidence indicates that the course of patients with significant AI is to live a variable length of time, up to many years, while the amount of insufficiency is either stable or progressive. The ventricle compensates by hypertrophy of well functioning myocardium. At some point in time, depression of myocardial function occurs for unknown reasons. This depression of function is progressive until the death of the patient.* I will now try to support this contention.

Several long term studies have shown that patients may survive many years after the diagnosis of AI is made. (70, 136-138) Clinical signs of AI which relate to the hyperdynamic arterial pulse, such as the ratio of pulse pressure to systolic pressure, generally do not correlate well with prognosis. (138-140) This is apparently because these signs estimate the amount of regurgitation and a healthy ventricle can support a large volume overload for some time. Radiographic heart size is a better predictor of prognosis, but is still nonspecific, (139-141) apparently because cardiomegaly can be due to just volume overload, or volume overload and myocardial failure. EKG evidence of left ventricular hypertrophy and arrhythmias also correlate with prognosis, (140, 141) probably because they are generally related to myocardial function, but again the relationship is poor. The clinical status of patients is well known to be related to their prognosis. In fact, this relationship is the basis of the most widely practiced dictum of when to do surgery--that is, when the patient changes from Class II to Class III, or in other words, when he becomes more than minimally disabled. However, the basis of the relationship between clinical status and prognosis is probably based on the relationship between clinical status and myocardial function. This latter relationship is well known to be imperfect. (14)

Direct study of the relationship between myocardial function and natural survival is virtually nonexistent. However, there is one unpublished study of a series of patients who had either aortic insufficiency or aortic stenosis, and who, for undefined reasons, did not undergo surgery. In this study, the 5 year survival was 68% with an ejection fraction above 50%, 42% with an ejection fraction between 31-50%, and 0% with an ejection fraction below 30%. (142)

Operative Mortality

Operative mortality is highly variable, but an approximate overall risk is 10%. (69, 76, 80, 84, 91) The risk depends on both the technical ability of the operating team and patient characteristics. The three patient characteristics which most influence the risk are the structural characteristics of the aortic root, (69, 73) the presence of coronary disease, (80, 84) and myocardial function. (14, 91, 141)

Survival After Surgery

Long term survival after surgery depends on operative mortality, artificial valve function, myocardial function, and a significantly large group of miscellaneous factors. About 2/3 of late postoperative deaths are due to heart failure or arrhythmias, and about 1/2 of all late deaths are sudden. (76) When the indication for surgery is progression of symptoms from minimal to moderate disability (Class II to Class III), 5 year survival is about 50%. (76, 80)

The principles related to the choice, longevity, and complications of artificial valves have already been discussed in the section on aortic stenosis. The principles are the same when the valves are used to treat aortic insufficiency, except that small aortic roots are not a common problem.

The relationship between myocardial function and survival after surgery has been suggested and shown in different ways. Several studies have shown that preoperative x-ray cardiomegaly correlates with a decreased long term survival. (73, 80, 141) However, if the large and small hearts are subdivided as to the diastolic ventricular pressure (a measure of myocardial function), it is apparent that the diastolic pressure and not the heart size per se determines the prognosis. (76) The higher percentage of patients with high diastolic pressures among the patients with large hearts is what gives the broad correlation between heart size and prognosis. Patient disability has been shown to both affect and not affect surgical survival, (76, 80) which is understandable in view of the poor correlation between overall disability and myocardial function. (14) Data comparing preoperative ejection fraction and surgical survival are scant. One unpublished study, which unfortunately combined together patients with either stenosis or insufficiency, shows a 68% survival with an ejection fraction above 50%, 48% survival with an ejection fraction between 31-50%, and a 30% survival with an ejection fraction below 30%. (142) After surgery, diminution in radiographic heart size suggests good myocardial function. In one study, the presence or absence of decreasing heart size (.03 % change in CT ratio over 6 months) divided the patients into groups with 85% and 43% 6 year survival. (76)

Timing of Surgery

We will never know for certain the effect of surgery on the patient with aortic insufficiency. Control patients are no longer available since almost all physicians now consider surgery the treatment of choice. Randomized studies were never done and unfortunately the natural history was never determined in terms of the pathophysiology as we now understand it. However, surgery probably does improve function, relieve suffering, and improve longevity. If we accept this, then the important question becomes when to do the surgery.

The lack of systematic studies has hampered our understanding of when to operate. However, we know these facts. Many patients go years before they deteriorate. It seems unwise to do surgery at this early stage. After myocardial function is depressed, surgical results are worse. It seems unreasonable to wait this late. The point in the progression of the disease at which the expected survival starts to decrease is the point at which myocardial function begins to deteriorate. Surgery preserves myocardial function at the state it was in prior to surgery.

In summary, the evidence indicates that the time to operate is just prior to the point in time when function begins to deteriorate. Symptomatic, radiographic, and electrocardiographic indices are helpful but only approximate measures of this function. The optimal care of the patient with AI should probably be done by repetitive noninvasive evaluation of myocardial function by echo or radionuclide techniques. In my opinion, a reasonable approach is to follow the patient until any symptoms, rapid increase in radiographic heart size, marked cardiomegaly, or an EKG pattern of left ventricular hypertrophy with strain appears. At this point, periodic measurement of myocardial function by echo (16, 59, 60, 143, 144) or isotope (60, 145-149) at approximately 4 month intervals should begin. At the first indication of depression of myocardial function, catheterization should be done. Ideally, the imminent depression of function could be detected before it actually occurs. Possibly, the angiotensin stress test (129) or the measurement of myocardial function during exercise, (150) two techniques which have had only preliminary evaluation, will prove to be helpful in this regard.

SUMMARY

Aortic stenosis is a bad lesion. The patient with aortic stenosis should have surgery as soon as significant stenosis is documented. The chief problem relevant to aortic stenosis is how to pick patients who are likely to have stenosis from those who have flow murmurs. The carotid pulse contour and fluoroscopic examination for calcium are the most helpful noninvasive tests to help make this determination. The chief clinical problem in caring for the patient with aortic insufficiency is when to replace the valve. The time to do this is when myocardial function begins to deteriorate. Noninvasive methods should be repetitively used in this determination. Artificial valves have significant complications. Evaluation of these complications should be done rapidly with as expert advice as can be obtained.

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