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THE ROLE OF SURGERY AND THE BURDEN AND COST OF VALVE REPLACEMENT

by

Dr. Simón Muñoz

Surgical treatment of rheumatic valvular heart disease by valvulotomy, valve repair or valve replacement is the most widely used and until recently the only form of therapy to relieve the mechanical overload imposed to the heart by the valvular lesion, but it has the disadvantages of being expensive, practicable only in highly specialized centers and of exposing the patient to a variable risk of death.

The following surgical procedures are presently in use for patients with chronic rheumatic valvular disease:

- Mitral Commissurotomy and plastia, for patients with pure, isolated mitral stenosis, without more than trivial mitral regurgitation, severe enough to require surgical relief, but with mobile, not severely scarred or heavily calcified cusps and without serious damage of the subvalvular apparatus.
- Mitral valve repair, for patients with severe mitral regurgitation or mixed stenosis and regurgitation, without severely scarred, deformed and/or calcified valve cusps.
- Mitral valve replacement, for patients with severe mitral stenosis and/or regurgitation, with severely scarred, deformed and/or calcified valve cusps, and/or serious damage of the subvalvular apparatus, altogether not amenable to valve repair.
- Aortic valve replacement, for severe aortic regurgitation.
- Tricuspid valve surgery is almost always carried out as a part of multiple valve surgery, as rheumatic tricuspid valve disease almost never occurs as an isolated lesion, but generally accompanies mitral or mitral-aortic valve disease. Tricuspid commissurotomy, repair, annuloplasty or replacement may be performed, according to the type and severity of valve lesion.
- Multiple valve surgery is not rarely necessary for patients with multiple valve disease. The type of surgery for each diseased valve must be individualized. All of the following procedures have been used: double (mitral and aortic, mitral and tricuspid) valve replacement; triple (mitral, aortic and tricuspid) valve replacement; mitral commissurotomy or repair with aortic valve replacement; mitral and tricuspid commissurotomy and/or repair; mitral commissurotomy or repair with tricuspid annuloplasty; mitral and/or tricuspid commissurotomy or repair with aortic valve replacement.

Influence of Surgery on the Natural History of Rheumatic Valvular Disease.

Surgical therapy decidedly prolongs survival and improves the quality of life of patients with chronic rheumatic heart disease.

In a study of the natural history of chronic rheumatic heart disease (1) we found that in 3 groups of medically treated patients with rheumatic pure isolated mitral stenosis, pure isolated mitral regurgitation and combined mitral stenosis and mitral regurgitation, respectively, the 5 year actuarial survival rate was 45%. In a comparable group of patients with pure isolated mitral stenosis subjected to mitral commissurotomy and plastia, the 5 year actuarial survival rate was substantially better (85%). In patients with more severe mitral valve lesions subjected to mitral valve replacement, an increase of the 5 year actuarial survival rate to 60% was found, of less magnitude than that obtained with mitral commissurotomy, but statistically significant. Thus, the most dramatic beneficial effect of surgery in mitral

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rheumatic valve disease is obtained through mitral commissurotomy, an operation which is feasible only in patients with pure isolated mitral stenosis, severe enough to need surgical relief, with mobile, flexible, non calcified cusps, without more than trivial regurgitation and with absence of serious damage to the subvalvular apparatus. Presently, heart catheterization is required in most centers to recognize with certainty patients that are amenable to mitral commissurotomy. Heart catheterization facilities are critically low in precisely those countries where rheumatic fever and chronic rheumatic heart disease are more prevalent. More recently introduced, less costly and more easily available noninvasive techniques, such as two-dimensional echocardiography and Doppler technique have proved equally reliable to obtain the necessary information for the indication of mitral commissurotomy (2).

Open-Chest commissurotomy is the technique used in most centers, although the closed chest technique continues to be used in some countries, with comparable early and longterm results (3).

A variable number of patients subjected to mitral commissurotomy develop restenosis, and reoperation may be needed 5 to 10 years later. Rheumatic recurrences are an important factor contributing to restenosis. Thus, all patients subjected to mitral commissurotomy must follow a strict programme for prevention of recurrences.

#### Valve Replacement.

Since the introduction of mitral valve replacement by Starr and of aortic valve replacement by Harken in 1960, early results have improved a great deal, with a very low mortality, together with a remarkable functional and symptomatic improvement.

Early mortality has fallen from about 50% at the beginning to about 3-5% presently, in highly specialized centers. Early risks, such as early endocarditis, have been controlled to a great extent. Longterm survival has been significantly increased as compared with medically treated patients (1,4). Yet, late mortality remains a problem, particularly following mitral valve replacement. Late death is mostly due to heart failure or arrhythmia, related to the underlying rheumatic heart disease, in 85-90% of cases. Complications of the prosthetic valve or graft itself accounts for only 10-15% of all late deaths (5). Thus, even if a hypothetical "perfect" prosthesis could be developed, only 10-15% of all late deaths would be prevented. Thrombogenicity of prosthetic valves has not been solved, thromboembolic episodes constitute a frightful complication, and longterm anticoagulation is mandatory in all patients with mechanical prostheses and in some patients with bioprostheses (4,5). The need for long-term anticoagulant treatment adds its own rate of hemorrhagic complications, morbidity and mortality to that related to the underlying rheumatic heart disease and to that related to the prosthesis or graft itself.

The most frequent complications related to the prosthesis or graft are the following: Thromboembolism, thrombosis without embolism, paravalvular leakage, hemolysis, poppet embolism, ball variance, cusp rupture, strut fracture, sutures dehiscence and endocarditis (6).

Table 1 summarizes the materials most frequently used as a valve substitute.

The 3 most important criteria for evaluation and selection of a valve substitute are: durability, hemodynamic performance and incidence of valve-related complications.

Table 2 summarizes the advantages and disadvantages of the different types of valve substitutes.

Structural failure is a common problem with bioprostheses, which undergo degeneration, cusp disintegration, perforation and calcification, leading to valve regurgitation, stenosis or both. Calcification is more frequent and accelerated in children and adolescents, probably related to differences in calcium metabolism.

On the other hand, the rate of thromboembolic episodes is lower in bioprostheses than in mechanical prostheses.

Bioprostheses are not free from thromboembolic complications. A high incidence of thromboembolism occurs early after valve replacement. Anticoagulation is indicated, starting 48-72 hours postoperatively and continued for a period of 3 months after mitral valve replacement and for a period of 10 days after aortic valve replacement. Pretreatment with oral dipyridamol for 3 days before operation reduces the incidence of thromboembolism during the early postoperative days, both with mechanical and tissue valves (7). Longterm anticoagulation with coumarin derivatives is indicated with bioprostheses in the mitral position, when there is atrial fibrillation, a very large left atrium, a history of previous embolism, or when the

presence of atrial thrombi has been found at the moment of surgery.

Longterm anticoagulation is exceptionally needed with bioprostheses in the aortic position (atrial fibrillation, history of previous thromboembolism).

No device will serve for all purposes. Bioprostheses are indicated mainly in the following situations: 1) Contraindication of anticoagulant therapy. 2) Life expectancy (because of advanced age or for whatever reason) shorter than 10 years, that is, shorter than the period of increased incidence of bioprosthetic valve degeneration and failure. 3) Women of child-bearing age who wish to have a family and accept the prospective of a new operation some years later to have the bioprosthesis replaced by a mechanical prosthesis when valve failure occurs. The avoidance of anticoagulation during pregnancy eliminates the risk of warfarin embryopathy and/or fetal loss associated with this type of therapy (4).

Bioprostheses are contraindicated in children and adolescents because of their poor durability and the higher rate of calcification in younger persons. Mechanical prostheses have to be used for valve replacement in these age groups. We are then left with the risks of anticoagulation in an active child or young person. There is no totally satisfactory solution to this problem. Low level anticoagulation (keeping patient-control prothrombin time ratio around 1.5) as opposed to deep level anticoagulation (keeping prothrombin time around 2 to 2.5 times the control value), usually indicated with mechanical prostheses, has been advised (5). Another alternative is the combination of low level anticoagulation with an antiplatelet agent, active on mechanical surfaces, such as dipyridamol. Others recommend the use of antiplatelet agents alone (8,9).

Although the prevalence and severity of chronic rheumatic heart disease is decreasing in many countries, the need for mitral valve replacement is increasing throughout the world, at a rate of about 5-6% per year (10), mainly as a result of the introduction in many developing countries of the technology and medical facilities necessary to treat the accumulated population of patients with severe chronic rheumatic valve disease who have not been operated upon because of previous lack of such facilities. The cost of a valve repair operation varies between U.S.\$ 2,000 and U.S.\$ 3,500; and that of a valve replacement, between U.S.\$ 7,000 and U.S.\$ 20,000, in different countries. A good number of countries with a high prevalence of chronic rheumatic heart disease cannot afford a program aimed at offering surgical treatment to all rheumatic patients who need it. Furthermore, surgically treated patients continue to need permanent, frequent and costly follow-up at specialized centers, which includes clinical examination, ECG, ChestX-ray, echocardiography and Doppler studies, as well as laboratory controls.

In vast regions with a high prevalence of chronic rheumatic heart disease, a correct laboratory control of anticoagulation is not feasible; this is a fact that constitutes an almost unsurmountable obstacle to the use of mechanical prostheses, which are the devices of choice for children, adolescents, young people and middle aged adults, that is, the age groups in whom valve replacement for chronic rheumatic heart disease is most frequently indicated. Bioprostheses, which do not need longterm anticoagulation in most cases, are not a satisfactory alternative for these age groups, because of their increasing rate of valve failure after the first 5 post-operative years, that would lead to repeated reoperations, particularly in younger patients, with the corresponding toll of morbidity, mortality and financial burden.

The very high cost of surgical therapy contrasts with the relatively low cost of preventive programs. In Venezuela, the total cost of a secondary prevention program during 10 years for 100 patients admitted to the program immediately after a first attack of acute rheumatic fever (97% of whom were kept in functional classes I or II, without requiring surgery), equalled the cost of mitral valve replacement for the 3 of them who required such intervention (11,12).

The risk of rheumatic recurrences does not disappear after valve replacement, particularly in young people. The myocardium or other valves may be damaged in each recurrence, thus contributing to deterioration of the patient. Prevention of recurrences must be maintained after valve replacement, particular in young patients.

A good deal of research is being carried out with the purpose of improving presently used valve substitutes. The newest developed mechanical valves offer a more satisfactory hemodynamic performance (8), but the problem of thrombogenicity has not been solved and longterm anticoagulation continues to be mandatory in all mechanical models. Regarding bioprostheses, efforts are mainly aimed at reducing cusp perforation and at preventing calcification. It has

been suggested that cusp perforation is the result of excessive tissue stress; and engineering modifications are being studied to reduce tissue stress and prevent cusp perforation (13,14). A large series of chemicals and processes with the potential of preventing or altering the onset of calcification of bioprostheses are being tested (15).

Selection of patients and timing for valve replacement in order to obtain the best early and longterm results are not totally solved problems for patients with left ventricular volume overload due to mitral or aortic regurgitation. The main single factor that influences the outcome of valve replacement in these patients is the status of left ventricular myocardial function (4,10). Patients with left ventricular dysfunction have a higher early and late mortality both for mitral and aortic valve replacement; symptomatic improvement is frequently not obtained or symptomatic deterioration may occur if replacement is carried out after myocardial dysfunction has developed. If valve replacement is indicated too early, the associated mortality, morbidity and deterioration of the quality of life may be higher than the expected mortality, morbidity and life quality deterioration without surgical treatment.

There is a consensus that, in general, surgery is indicated in symptomatic patients with chronic rheumatic valvular disease when symptoms are due to the hemodynamic overload imposed by the valvular dysfunction (4,10). In asymptomatic patients, the optimal time for valve replacement is more difficult to establish. Several parameters have been used to preoperatively predict the outcome after valve replacement in patients with mitral or aortic regurgitation, such as radiological heart size, echocardiographic left ventricular end diastolic and end systolic dimensions, and ejection fraction calculated by echocardiography or at heart catheterization (16-18). All of them are in a variable degree related to the status of left ventricular myocardial function. But no one has proved to be a reliable predictor of operative mortality or of symptomatic response to surgery. In patients with severe mitral regurgitation it is difficult to assess left ventricular function because a large part of the blood volume ejected by the ventricle regurgitates towards the left atrium, a very low impedance chamber; due to this fact, the total afterload faced by the left ventricle is quite low, which facilitates the handling of the volume overload by the left ventricular chamber. After mitral valve replacement, the left ventricle is faced entirely to the high aortic impedance, and a group of patients with inadequate left ventricular hypertrophy may develop overt left ventricular failure and have a stormy postoperative course, associated with a high early postoperative mortality. A low ratio of left ventricular mass to end diastolic volume has been recently identified as a discriminator of patients who will have early postoperative severe left ventricular dysfunction (19).

The preceding discussion demonstrates that preoperative assessment of rheumatic patients with predominant regurgitant lesions requires a lot of non invasive and invasive explorations, which are not easily available in most countries with a high prevalence of chronic rheumatic heart disease.

#### New Trends: Percutaneous Balloon Mitral Valvotomy.

A new, invasive, non surgical procedure, presently in the stage of clinical research, has been recently introduced for the treatment of rheumatic pure isolated mitral stenosis without severe valve calcification or serious damage of the subvalvular apparatus; that is, for patients amenable to surgical mitral commissurotomy. The procedure consists of performing the valvuloplasty using a balloon placed in the mitral orifice by means of a transvenous catheter, using the transeptal technique (20).

In a cooperative study carried out by the services of cardiology of the Massachusetts General Hospital of Boston and the University Hospital of Caracas, the initial results have been very satisfactory, with definite symptomatic and hemodynamic improvement (21). Successful early results have been reported in 2 cases with calcified mitral stenosis (22,23).

The procedure has to await long-term follow-up before being recommended for general clinical use. If the initial good results are maintained in the longterm, it might become a procedure of choice for selected patients with rheumatic pure isolated mitral stenosis. The patients are discharged 24 to 48 hours after the procedure, surgical morbidity is eliminated and the costs of treatment are substantially reduced.

#### References.

- 1.- Muñoz S, Gallardo J, Díaz-Gorrín JR, Medina O. Influence of surgery on the natural history of rheumatic mitral and aortic valve disease. Am J. Cardiol. 1975; 35: 234-42.

- 2.- Muñoz S, Berti C, Pulido C, Blanco P. Combined use of two-dimensional echocardiography and pulsed Doppler techniques in the evaluation of mitral rheumatic valve disease. In "Pediatric Cardiology", Doyle EE, Engle MA, Gersony WM, Rashkind WJ, Talner NS, editors. Springer-Verlag, New York, Berlin, Heidelberg, Tokyo, 1986, pp. 987-93.
- 3.- John S, Bashi VV, Jairaj PS, Muralidharan S, Ravijumar E, Rajarajeswari T, Krishnaswami S, Sukumar IP, Rao PSS. Closed mitral valvotomy: early results and long-term follow-up of 3724 consecutive patients. Circulation 1983; 68: 891-6.
- 4.- Rahimtoola SH. Valvular heart disease: A perspective. J. Am. Coll. Cardiol. 1983; 1: 119-215.
- 5.- Starr A. The Starr-Eduards valve. J. Am. Coll. Cardiol. 1985; 6: 899-903.
- 6.- Vogel JHK: Seminar on cardiac valve replacement. I. Introduction: Valve replacement: The first quarter century. J. Am. Coll. Cardiol. 1985; 6: 897-8.
- 7.- Chesebro JH. Thromboembolism after biologic prosthetic heart valve replacement. ACCEL. Vol. 17 No 10, 1985.
- 8.- Czer L, Matloff J, Chaux A, De Robertis M, Yoganathan A, Gray RJ. A 6 year experience with the ST. Jude Medical Valve: Hemodynamic performance, surgical results, biocompatibility and follow-up. J. Am. Coll. Cardiol. 1985; 6: 906-12.
- 9.- Pass HI, Sade RM, Crawford FA, Hohn AR. Cardiac valve prostheses in children without anticoagulation. J. Thorac Cardiovas. Surg. 1984; 87: 832-5.
- 10.- Starr A. Status of mitral valve replacement. ACCEL 1986; Vol. 18 No 2.
- 11.- Muñoz S. Medical management to decrease disability in rheumatic and congenital heart disease. III World Congress of Cardiac Rehabilitation. Symposium: Rehabilitation in Pediatric and Adolescent Cardiac Patients. Caracas, October 20-23, 1985.
- 12.- Varnauskas E, Fernández Y, Muñoz S, Hatcher Ch, James F. Rehabilitation of pediatric and adolescent cardiac patients. In: "Rehabilitation of the Cardiac Patients". Advances in Cardiology, Kellerman JJ, Editor. Vol. 33, Basel, 1986.
- 13.- Ferrans VJ, Sparay TL, Billingham ME, Roberts WC. Structural changes in glutaraldehyde-treated porcine heterografts used as substitute cardiac valves. Transmission and scanning electron microscopic observations in 12 patients. Am J. Cardiol. 1978; 41: 1159-65.
- 14.- Thubrikan M, Piepgrass WC, Deck JD, Nolan SP. Stresses of natural versus prosthetic aortic valve leaflets in vivo. Ann Thorac Surg. 1980; 30: 230-5.
- 15.- Lentz DJ, Pollock EM, Olsen DB, Andrews EJ, Murashita J, Hastings WL. Inhibition of mineralization of glutaraldehyde-fixed Hancock bioprosthetic heart valves. In "Cardiac Bioprostheses". Cohn LH, Gallucci V, editors. Yorke Medical Books, New York 1982 - pp. 306-19.
- 16.- Szlachcic J, Massie BM, Greenberg B, Thomas D, Cheitlin M, Bristow JD. Inter-test variability of echocardiographic and chest X-Ray measurements: Implications for decision making in patients with aortic regurgitation. J. Am. Coll. Cardiol. 1986; 7: 1310-7.
- 17.- Henry WL, Bonow RO, Rosing DR, Epstein SE. Observations on the optimum time for operative intervention for aortic regurgitation. II. Serial echocardiographic evaluation of asymptomatic patients. Circulation 1980; 61: 471-83.
- 18.- Bonow KM, Green LH, Mann T. End-systolic volume as a predictor of post-operative performance in volume overload from valvular regurgitation. Am J. Med. 1980; 68: 655-63.
- 19.- Bove A. Prediction of left ventricular dysfunction after mitral valve surgery. ACCEL. Vol. 18 No 8, 1986.
- 20.- Inoue K, Owaki T, Nakamura T, Kitamura F, Miyamoto N. Clinical application of transvenous mitral commissurotomy by a new balloon catheter. J Thorac Cardiovas. Surg. 1984; 87: 394-402.
- 21.- Block PC, Palacios IF, Brandt SC, Blanco P, Casal H, Pulido JI, Muñoz S, D'Empaire G, Ortega MA, Jacobs ML, Vlahakes G. Percutaneous balloon valvotomy for mitral stenosis. X World Congress of Cardiology, Washington, September, 14-19, 1986.
- 22.- Palacios IF, Lock JE, Deane JF, Block PC. Percutaneous transvenous balloon valvotomy in a patient with severe calcific mitral stenosis. J. Am. Coll. Cardiol. 1986; 7: 1416-9.
- 23.- MacKay RG, Lock JE, Keane JF, Safian RD, Aroesty JM, Grossman W. Percutaneous mitral valvuloplasty in an adult patient with calcific rheumatic mitral stenosis. J. Am. Coll. Cardiol. 1986; 7: 1410-5.
- 24.- Zerbini EJ, Puig LB. The dura-mater allograft valve. In: "Tissue Heart Valves" Ionescu MI, editor, Butterworths, London, 1979, pp. 253-301.
- 25.- Walker WE, Duncan JM, Frazier OH Jr, Liversay JJ, Ott DA, Reul GJ, Cooley DA. Early experience with the Ionescu-Shiley pericardial xenograft valve. Accelerated calcification in children. J. Thorac Cardiovasc. Surg. 1983; 86: 570-5.
- 26.- Ross DN, Sommerville J. Correction of Pulmonary atresia with a homograft aortic valve. Lancet 1966; 2: 144-51.
- 27.- Barratt-Boyes B, Roche AHG, Whitlock RML. Six-year review of the results of free hand aortic valve replacement using an antibiotic sterilized homograft valve. Circulation 1977; 55: 353-61.

Table 1

Valve Substitutes Presently in Use for Valve Replacement.

- Mechanical prostheses. (All parts are mechanical)	- Ball valve prostheses (e.g: Starr-Edwards valve, silastic ball valve) - Tilting disc, low profile prostheses (e.g: Björk-Shiley prosthesis) - Bileaflet, low profile, mechanical prostheses (e.g: St. Jude Valve)
- Bioprostheses (compounded of mechanical and biologic components)	- Porcine bioprostheses (e.g: Hancock valve, Carpentier-Edwards porcine valve) - Pericardial bioprostheses (e.g: Carpentier-Edwards pericardial valve, Ionescu-Shiley valve) - Duramater valve
- Grafts (replacement by purely biological materials)	- Aortic homograft. - Pulmonary autograft, combined with aortic homograft to replace the pulmonary valve

Table 2

Advantages and Disadvantages of the Different Types of Valve Substitutes.

<u>Type of Valve Substitute</u>	<u>Advantages</u>	<u>Disadvantages</u>
Ball Valve Prostheses (4,5)	- Proven durability, up to 25 years	- Need for long-term anticoagulation. - Patient-valve mismatch may occur, particularly in children and small patients
Tilting disc, low profile, mechanical prostheses (4,5)	- Proven durability, up to 16 years. Lower incidence of patient-valve mismatch, as compared to ball valve prostheses	- Need for long-term anticoagulation. - High incidence of abrupt valve -- thrombosis (3 to 10 times higher, as compared to ball valve prostheses)
St. Jude Valve (8)	- Expected durability; proven up to 6 years - Most favorable hydrodynamic performance of all valve designs	- Need for long-term anticoagulation
Porcine bioprosthesis (4)	- No need for long-term anticoagulation in most cases - Valve failure usually is not abrupt, thus allowing elective reoperation	- Poor durability. Increasing rate of valve failure after 5 years, with consequent need for reoperation
Duramater valves (24)	- No need for long-term anticoagulation in most cases - Valve failure usually is not abrupt, thus allowing elective reoperation	- Poor durability. Presently, very restricted use
Pericardial bioprosthesis (25)	- No need for long-term anticoagulation in most cases - Valve failure usually is not abrupt	- Durability not proven
Aortic homografts (26,27)	- No need for long-term anticoagulation - Proven durability	- Poor availability - Little experience in patients with rheumatic valve disease. - Logistic problems for harvesting and conservation