

## A STUDY CORRELATING PREDICTION AND OUTCOME OF CARDIAC VALVE DISORDER

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### ABSTRACT

The Objective of study was Correlating prediction and outcome of cardiac valve disorders. A retrospective cohort study using population-based administrative databases in CIMS hospital, Ahmedabad. Each individual was observed before treatment and after 1 year of treatment. Total 144 Cardiac valve disorder patients were selected according to inclusion criteria. Echocardiography was used for evaluation of disease and parameters of chamber dimension and doppler findings were considered for correlation of prediction and outcome of valvular disease. Total 144 Patients were treated either surgically or medically. There was a significance difference between surgically or medically treated patients. In this study there were MS, MR, MS-MR, AS and AR found in total 144 patients. Prevalence of MS was higher than other valvular diseases. MS was highest in female patients. The prevalence of valvular disease was higher in 31-50 years of patients. PAH was found in patients with valve disease and there was a significant improvement in patients with severe PAH after treatment whether patients were treated either surgically or medically. There was statistically significant ( $p < 0.05$ ) difference in the parameters of chamber dimensions and doppler findings. It indicates the given treatment was effective. In conclusion, Left ejection indices (Left ventricular ejection fraction, left ventricular shortening fraction), Left atrium (LA) length were predictor before treatment in MS, MR, MS-MR, AS, AR. It showed statically significant difference after treatment. The pressure gradient from doppler findings was the predictor only in MS. Velocity from doppler findings was not predictor of any of the valvular disease. Left ejection indices, LA length, pressure gradient decreases after treatment and showed good clinical outcome.

**Keywords:** Cardiac valve disorder, Echocardiography, Doppler findings.

### INTRODUCTION

People with valvular heart disease are living longer, with less morbidity, than ever before. Advances in surgical techniques and a better understanding of timing for surgical intervention account for increased rates of survival. Echocardiography remains the gold standard for diagnosis and periodic

assessment of patients with valvular heart disease. Generally, patients with stenotic valvular lesions can be monitored clinically until symptoms appear. In contrast, patients with regurgitant valvular lesions require careful echocardiographic monitoring for left ventricular function and may require surgery even if no symptoms are present.<sup>1,2</sup>

Doppler echo cardiography can be used to reproduce the hemodynamic severity of aortic stenosis. The rate of change of transaortic pressure gradient varies among patients and the gradient may not increase even when stenosis severity worsens. Although stenosis severity progresses more rapidly in patients who develop symptoms requiring valve replacement, these patients cannot be identified at the initial study<sup>3</sup>.

The ability of physical examination to predict valvular aortic stenosis severity and clinical outcome in 123 initially asymptomatic subjects is limited. Researchers found that along with physical examination, echocardiography still is needed to exclude severe obstruction reliably when this diagnosis is suspected<sup>4</sup>.

Little data are available on the natural history of young adults with congenital valvular aortic stenosis (AS). The study was done to determine the progression rate of AS in young adults, and to identify predictors of stenosis progression and outcome. Older age was the predictor and associated with more rapid progression<sup>5</sup>.

Cardiac valve disorder remains leading cause of the death. However determination of the predictors can improve the clinical outcome. There is a lack of data of early predictors of valvular heart disease in Indian population. Recent study will determine the predictors based on the parameters of echocardiogram and correlate with clinical outcome of the disease using statistical plan. This study is keen to add knowledge to field of cardiac valve disorder prediction and relation to clinical outcome.

## METHODS

### Study population

Patients with cardiac valve disorder were retrieved from the echocardiographic digitally archived database of 144 in and out patients studies performed between January 2009 to December 2010 at Care Institute of Medical Science, Ahmedabad. Patients who had recent history of kidney or liver dysfunction, Contraindication to oral anti coagulation treatment or transesophageal echocardiography, Female subject who is pregnant or breastfeeding, Severe locomotion disability were not included. Patients with isolated valvular heart disease were included in this study.

### Echocardiography parameters

Echocardiographic data were obtained with the use of commercially available ultrasound systems. All patients underwent a comprehensive examination, including M-mode echocardiography, two-dimensional echocardiography, and conventional and color Doppler ultrasonography, conducted by an experienced echocardiographer. For all patients for whom at least two echocardiographic studies, separated by at least six months, were available. There were mainly two parameters measured i.e. chamber dimensions and Doppler findings (Table-2). In chamber dimensions, Left ventricular diastole dimensions (LvdD), Left ventricular systole dimensions (LvsD), Left ventricular ejection fraction (LVEF), Left ventricular shortening fraction (LVFS), Aortic root (AO), Left atrium length (LA). In doppler findings, flow velocity and pressure gradient were measured.

### Statistical analysis

Continuous baseline and outcome variables were given as mean value  $\pm$  SD (standard deviation) while discrete variables were given as absolute values and percentages. Comparison between continuous variables was performed using paired student's t-Test while discrete variables were compared using a conventional chi-square test. All  $p$  value  $<$  0.05 was indicative of significance. All analyses were performed utilizing Graphpad prism version 5.04.

## RESULTS

In this study of Cardiac valve disorder total 144 patients were taken according inclusion criteria. In cardiac valve disorder there were five types of disease are found from 144 patients. There were Mitral Stenosis (MS), Mitral regurgitation (MR), Mixed valvular disease (MS-MR), Aortic stenosis (AS), Aortic regurgitation (AR). These patients were treated either surgically or medically. Table-1 shows the distribution of patients by Diagnosis, Therapy, and sex. Table-1 shows no. of patients of cardiac valve disorder there are 50 (34.72%), 40 (27.78), 22 (14.58), 20 (13.89%), 12 (8.33%) patients of MS, MR, MS-MR, AS, AR respectively. As shown in table, there was statistically significance between surgically treated patients and medically treated patients in MS ( $p=0.0001$ ), MR ( $p=0.0003$ ), AS ( $p=0.0001$ ). There was no significant  $p$  value in sex distribution. As per

figure-1 which shows prevalence of cardiac valve disorder there are 50 (34.72%), 40 (27.78), 22 (14.58), 20 (13.89%), 12 (8.33%) patients of MS, MR, MS-MR, AS, AR respectively. The prevalence of MS is highest and AR is less prevalent among the patients of the study.

The echocardiography parameters were measured in this study shown in table-2. There were mainly two parameters were measured i.e. chamber dimensions and Doppler findings. In chamber dimensions LvdD (mm), LvdS (mm), LVEF (%), LVFS(%), AO (mm) and LA (mm) length were measured. In doppler findings velocity (m/sec) and pressure gradient (mmhg) are measured. Data are shown as a Mean  $\pm$  SD.

It is observed that total female patients were more than male patients. As shown in figure-2 68(47%) were male patients and 76 (53%) were female patients. Table-3 and figure-3 shows gender based prevalence and distribution in various cardiac valve disorders. Figure-3 shows that female gender was more prevalent in MS as the MS was highest prevalent disease among all cardiac valve disorder as per figure-1. Whereas female was less prevalent in AR and male was highest prevalent in AR and less prevalent in MS-MR. As shown earlier in table-1, there were 50 patients in MS. There was statistically significant difference in male and female patients in MS ( $p=0.0164$ ). About 19 patients were male with mean age of same patients is  $36.94 \pm 12.14$  and no. of female patients were 31 with mean age of  $46.77 \pm 12.73$ . There was no significant difference in patients of MR ( $p=0.1797$ ). In MS-MR, about 7 patients were male with mean age of  $42.29 \pm 12.64$  and 14 patients are female with mean age of  $42.5 \pm 11.43$ . There is a statistically significant difference between male and female patients in MS-MR ( $p=0.0308$ ). In AS ( $p=0.0114$ ) and AR ( $p<0.0001$ ) also there was a statistically significant difference between male and female patients. There were 14 and 11 patients were male in AS and AR respectively and 6 and 1 patients were female in AS and AR respectively. The mean age of male and female in AS was  $54.79 \pm 9.47$  and  $59.17 \pm 9.46$  respectively.

Table-4 shows prevalence of cardiac valve disorder in each age group. Cardiac valve disorder began to appear in subjects above 18 or more years. However, AS was not appeared at early age of life. As the age advances, AS increases progressively. MS, MR and mixed mitral valve disease (MS-MR) began to appear

at the age  $\leq 30$  and was common in 31-50 years, 50%, 55 % and 12 % respectively and was rare in subjects 60 years or old in MS and MR and mixed mitral valve disease (MS-MR). AR is not appeared at late stage of the age.

Table-5 and figure-4 shows severity of PAH in cardiac valve disease before and after treatment. These patients were treated either surgically or medically. As per table-5 there was a improvement in patients with PAH after treatment but only patients with severe PAH shows statistically significant value ( $p<0.05$ ). There were 20 (13.89 %) Patients with severe PAH before treatment and after treatment only 8 (5.56 %) patients were remained severe. There was also decrease in patients with moderate PAH from 17 (11.81%) to 15 (10.42%) but it didn't show statistically significance. No. of Patients with No PAH and Mild PAH shows improvement after treatment but same as moderate PAH patients, It didn't show any statistically significance.

Table-6 list the  $p$  value derived from Statistical analysis for echocardiographic variables. These parameters were analyzed by paired student's t-test method. Total eight parameters were analyzed. Only statistically significant ( $p<0.05$ ) parameters were listed in table for cardiac valve disease patients who were either treated surgically or medically. As per table-6 left ventricular ejection fraction (LVEF) was predictor ( $p<0.05$ ) for aortic stenosis and mitral regurgitation. Before treatment, LVEF was  $54.53 \pm 7.04$  and after treatment, it was  $49.75 \pm 8.18$  in aortic stenosis. In mitral regurgitation LVEF was  $55.62 \pm 7.13$  and after treatment it was  $53.88 \pm 7.51$ . Left ventricular shortening fraction (LVFS) is predictor of aortic regurgitation (AR) and mitral regurgitation (MR) and mitral stenosis (MS). There was improvement of after treatment in LVFS in AR, MR and MS. Left atrium length was a predictor in both mixed mitral valve disease and MR. In MS and MS-MR pressure gradient was improved after treatment. It was predictor of MS and MS-MR. None of these diseases showed improvement in chamber dimension parameters like LvdD, LvdS and AO and in Doppler findings like velocity.

## DISCUSSION

In this study of cardiac valve disorder, we have identified five types of diseases namely Mitral stenosis (MS), Mitral regurgitation (MR), mixed mitral valve disease (MS-MR),

Aortic stenosis (AS), and Aortic regurgitation (AR) by 2D echocardiography and Doppler echocardiography. These patients were treated either surgically or medically. Out of 144 patients 108 were treated surgically and 36 patients were treated medically. Mitral stenosis (34.72%) was the highest and Aortic regurgitation (8.33%) was lowest among all valvular disease in this study. Mitral stenosis was found highest in female patients and Aortic regurgitation was found highest in male patients. Mostly all valvular disease occurs in age group of 31 -50 years (Table-4). There were 4 types of interventions performed on total 108 patients. Mitral valve replacement and percutaneous balloon mitral Valvotomy were performed on patients with mitral valve disease. Double valve replacement was performed on patients with mix valvular stenosis. This study showed improvement in pulmonary arterial hypertension (Figure-4) after treatment, whether patients were treated either surgically or medically. We analyzed total eight parameters by student's t-test. Table-6 listed statistically significant value. In mitral stenosis LVFS and pressure gradient showed significance ( $p < 0.05$ ). In mixed mitral disease LA length and pressure gradient are predictors. Pressure gradient is common predictor in both MS and MS-MR. In AS, LVEF only showed significant  $p$  value ( $p < 0.05$ ). LVEF had significance in AS and MR out of all disease group. LVFS had shown statistically significance ( $p < 0.05$ ) in AR and MR. LVFS and LA length is predictor of MR. Only four parameters out of eight are predictor for cardiac valve disease patients whether they treated either surgically or medically. In patients undergoing aortic valve replacement, preoperative ejection phase measures of left ventricular systolic performance and indexes of left ventricular end-systolic volume are predictive of both short term and long-term survival and left ventricular function after operation<sup>6-18</sup>. In our study, Patients undergoing aortic valve replacement or medical treatment, pretreatment LVFS and LVEF are predictor of survival. In earlier study, they had taken left ventricular diastolic dimension (LvD), left ventricular systolic dimension (LvS), Left ventricular shorting fraction (LVFS) and left ventricular wall thickness were measured for assessment of aortic regurgitation<sup>19</sup>. We measured same parameters except left ventricular thickness. We also measured

Doppler findings like pressure gradient and flow velocity. In our study, valvular stenosis and valvular regurgitation were studied. Valvular stenosis and valvular regurgitation was common in aged (51-60 years) patients. The high prevalence of valvular regurgitation in aged might be related to myxomatous degeneration of valves and their supporting structures. Grossly, the atrioventricular valves become thicker and more opaque with advancing age<sup>20</sup>. In previous study of valvular regurgitation, disease increases progressively with the age, In our study results were not matched with that study. In this study It is observed that, left sided heart valve (mitral and aortic valve) diseases were found only. There were no right sided heart valve (tricuspid and pulmonary) diseases in our study. Left- sided valves are of course, exposed to high pressures or long standing mechanical stress and may therefore undergo degenerative changes earlier than right-sided valves. Many physicians are reluctant to refer patients with severe aortic stenosis for valve replacement as long as they remain asymptomatic. However, there remains concern about the risk of irreversible myocardial damage or sudden death among such patients who do not undergo surgery. In this study left ventricular diastole dimensions, left ventricular systole dimensions, left ventricular ejection fraction and left ventricular shortening fraction were measured to quantify the cardiac compensation or myocardial damage. However there was no death in study and only LVEF shows significant improvement after surgery in AS.

**Table 1: Distribution of patients by Diagnosis, Therapy, and Sex**

| Diagnosis        | Surgically treated- no.(%) | Medically treated- no.(%) | p value |
|------------------|----------------------------|---------------------------|---------|
| MS               | 42(84)                     | 8(16)                     | <0.0001 |
| MR               | 28(70)                     | 12(30)                    | 0.0003  |
| MS-MR            | 13(61.91)                  | 9(38.09)                  | 0.12    |
| AS               | 17(85)                     | 3(15)                     | <0.0001 |
| AR               | 8(66.67)                   | 4(33.33)                  | 0.1025  |
| Sex Distribution | 51- M<br>57-F              | 17-M<br>19-F              | 1       |

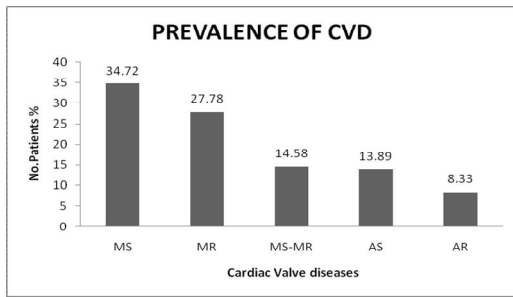


Fig. 1: Prevalence of Cardiac valve diseases

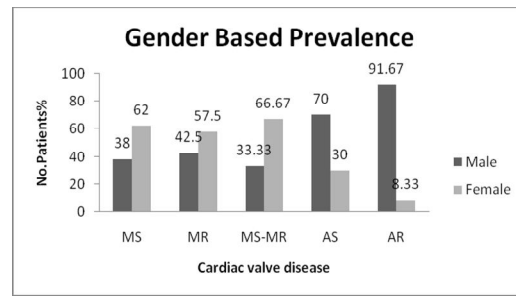


Fig. 3: Gender Based Prevalence

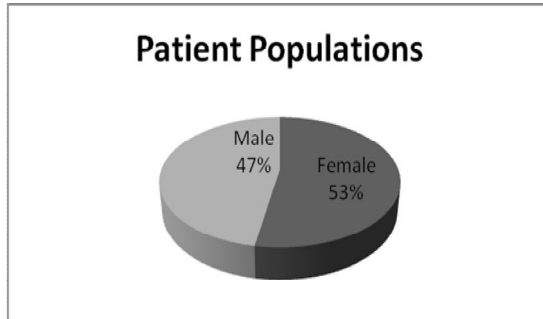


Fig. 2: Patient Population in Cardiac valve disorder

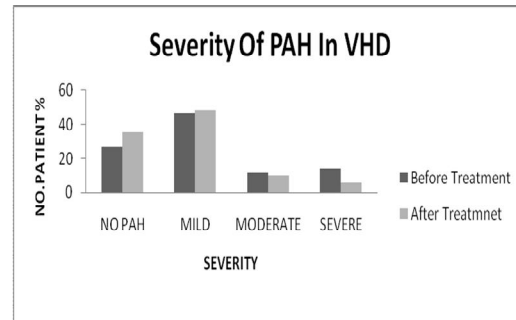


Fig. 4: Severity Of PAH

Table 2: Echocardiographic Measurement

| Disease       | Types Of Treatment |    | Chamber Dimensions |           |          |          |                  | Doppler Findings |                  |                 |
|---------------|--------------------|----|--------------------|-----------|----------|----------|------------------|------------------|------------------|-----------------|
|               |                    |    | LvdD (mm)          | LvdS (mm) | LVEF (%) | LVFS (%) | Aortic-Root (mm) | LA-length (mm)   | Velocity (m/sec) | Gradient (mmhg) |
| MS (N=50)     | Surgical N=42      | M  | 45.36              | 28.79     | 54.19    | 34.1     | 28.24            | 48.2             | 2.04             | 18.86           |
|               |                    | Sd | 6.64               | 7.03      | 7.53     | 8.05     | 3.24             | 10.1             | 0.56             | 9.77            |
|               | Medical N= 9       | M  | 44.13              | 28.13     | 58.75    | 38.13    | 28.5             | 48.8             | 1.89             | 16.38           |
|               |                    | Sd | 7.16               | 5.6       | 4.22     | 8.99     | 4.97             | 10.1             | 0.68             | 10.61           |
| MR (N=40)     | Surgical N=28      | M  | 48.57              | 32.11     | 55.73    | 33.32    | 28.89            | 49.5             | 1.87             | 16.38           |
|               |                    | Sd | 6.93               | 7.17      | 7.49     | 7.98     | 3.42             | 11.1             | 0.68             | 10.61           |
|               | Medical N= 12      | M  | 48.78              | 31.5      | 59.17    | 42       | 26.5             | 50               | 1.88             | 16.81           |
|               |                    | Sd | 7.9                | 5.92      | 4.23     | 9.3      | 5.5              | 11.3             | 0.64             | 9.4             |
| MS-MR (N= 21) | Surgical N=13      | M  | 45.92              | 28.38     | 56.54    | 34.15    | 28.31            | 52.2             | 2.2              | 24.23           |
|               |                    | Sd | 6.33               | 6.54      | 6.95     | 7.53     | 3.32             | 11.1             | 0.59             | 10.73           |
|               | Medical N= 8       | M  | 48.13              | 31.38     | 57.5     | 34       | 29.25            | 46.5             | 1.9              | 21.63           |
|               |                    | Sd | 7.45               | 5.67      | 4.56     | 8.98     | 5.31             | 10.3             | 0.97             | 19.88           |
| AS (N= 20)    | Surgical N=17      | M  | 45.47              | 29.29     | 53.56    | 34.47    | 31               | 39.4             | 2.87             | 42.49           |
|               |                    | Sd | 7.32               | 7.09      | 8.58     | 8.03     | 3.46             | 14.5             | 1.32             | 34.49           |
|               | Medical N= 3       | M  | 48                 | 30.67     | 60       | 35       | 33.67            | 40.7             | 2.8              | 43.33           |
|               |                    | Sd | 8.04               | 6.3       | 4.25     | 5.59     | 5.45             | 10.5             | 0.83             | 16.4            |
| AR (N= 12)    | Surgical N=8       | M  | 53.88              | 36.38     | 53.75    | 33.38    | 30.75            | 43.3             | 2.91             | 37.57           |
|               |                    | Sd | 6.75               | 7.36      | 6.89     | 8.49     | 3.55             | 7.4              | 1.5              | 19.15           |
|               | Medical N= 4       | M  | 54.5               | 34.5      | 57.5     | 47       | 29.25            | 44               | 2.96             | 37.54           |
|               |                    | Sd | 7.58               | 5.98      | 4.36     | 10.28    | 5.23             | 10.6             | 0.89             | 16.16           |

**Table 3: Gender distributions in Various Cardiac valve disorder**

| Cardiac valve disorder | Male           |          |       | Female          |          |       | P value |
|------------------------|----------------|----------|-------|-----------------|----------|-------|---------|
|                        | N0.Of patients | Mean Age | SD    | N0. Of Patients | Mean Age | SD    |         |
| MS(50)                 | 19             | 36.94    | 12.14 | 31              | 46.77    | 12.73 | 0.0164  |
| MR(40)                 | 17             | 43.47    | 14.16 | 23              | 36.35    | 13.85 | 0.1797  |
| MS-MR(21)              | 7              | 42.29    | 12.64 | 14              | 42.5     | 11.43 | 0.0308  |
| AS(20)                 | 14             | 54.79    | 9.47  | 6               | 59.17    | 9.46  | 0.0114  |
| AR(12)                 | 11             | 37.45    | 14.16 | 1               |          |       | <0.0001 |

**Table 4: Prevalence of cardiac valve diseases in each age group**

| Age (years) | Cardiac valve disorder |          |           |       |          |
|-------------|------------------------|----------|-----------|-------|----------|
|             | MS                     | MR       | MS-MR     | AS    | AR       |
| ≤ 30        | 10(20)                 | 11(27.5) | 5(23.81)  | 0     | 5(41.67) |
| 31-50       | 25(50)                 | 22(55)   | 12(57.14) | 6(30) | 4(33.33) |
| 51-60       | 12(24)                 | 4(10)    | 3(14.29)  | 5(25) | 3(25)    |
| ≥ 61        | 3(6)                   | 3(7.5)   | 1(4.76)   | 9(45) | 0        |

**Table 5: Severity of Pulmonary arterial hypertension (PAH)**

| Severity Of PAH | Before Treatment-no.(%) | After Treatment-no.(%) | p value |
|-----------------|-------------------------|------------------------|---------|
| No PAH          | 40(27.08)               | 52(35.42)              | Ns      |
| Mild            | 67(46.53)               | 69(47.92)              | Ns      |
| Moderate        | 17(11.81)               | 15(10.42)              | Ns      |
| Severe          | 20(13.89)               | 8(5.56)                | <0.05   |

Ns=not significant

**Table 6: Statistical significance (Expressed as a p value) of echocardiographic variables for the prediction of surgically or medically treated cardiac valve diseases patients**

| Valvular Diseases | Echocardiographic Variables | Before treatment Mean ± SD | After treatment Mean ± SD | P value |
|-------------------|-----------------------------|----------------------------|---------------------------|---------|
| MS                | LVFS                        | 34.74±8.72                 | 24±5.69                   | 0.0156  |
|                   | Pressure gradient           | 18.77±10.98                | 14.63±7.81                | 0.015   |
| MR                | LVEF                        | 55.62±7.13                 | 53.88±7.51                | 0.011   |
|                   | LVFS                        | 35.14±8.91                 | 31.6±5.83                 | 0.0019  |
|                   | LA length                   | 47.05±10.94                | 43.9±10.66                | 0.0218  |
| MS-MR             | LA length                   | 50.05±10.79                | 45.9±10.03                | 0.0166  |
| AS                | LVEF                        | 54.53±7.04                 | 49.75±8.18                | 0.0444  |
| AR                | LVFS                        | 39.09±13.47                | 28.45±5.97                | 0.015   |

**CONCLUSION**

In this study of cardiac valve disorder we concluded that there was highest prevalence of mitral stenosis among MR, MS-MR, AS, AR valve disease and it was highest in age group of 31-50 years. The statistic values showed that given treatments were effective. Echocardiography provides the better understanding of predictor and outcome of cardiac valve disorder. Left ejection indices (Left ventricular ejection fraction, left ventricular shortening fraction), Left atrium (LA) length were predictor before treatment in MS, MR, MS-MR, AS, AR. It showed statically

significant difference after treatment. The pressure gradient from doppler findings was the predictor only in MS. Velocity from doppler findings was not predictor of any of the valvular disease. Left ejection indices, LA length, pressure gradient decreases after treatment and showed good clinical outcome.

**REFERENCES**

1. Shipton B and Wahba H. Valvular heart disease: review and update. Am Fam Physician. 2001;63:2201-8.
2. Otto CM, Pearlman AS and Gardner CL. Hemodynamic progression of aortic



- stenosis in adults assessed by doppler echocardiography. *J Am Coll Cardiol.* 1989;13:545-50.
3. Yap SC, Kouwenhoven GC, Takkenberg Johanna JM, Galema TW, Meijboom FJ and Ron van Domburg. Congenital aortic stenosis in adults: Rate of progression and Predictors of clinical outcome. *Int J Cardiol.* 2007;122:224-31.
  4. Munt B, Legget ME, Kraft CD, Miyake-Hull CY, Fujioka M and Otto CM. Physical examination in valvular aortic stenosis: Correlation with stenosis severity and prediction of clinical outcome, valvular and congenital heart disease. *Am Heart J.* 1999;137:298-306.
  5. Cohn PF, Gorlin R, Cohn LH and Collins JJ. Left ventricular ejection fraction as a prognostic guide in surgical treatment of coronary and valvular heart disease. *Am J Cardiol.* 1974;34:136-141.
  6. Fischl SJ, Gorlin R and Herman MV. Cardiac shape and function in aortic valve disease: Physiologic and clinical implications. *Am J Cardiol.* 1977;39:170-176.
  7. Copeland JG, Griep RB, Stinson EB and Shumway NE. Long term follow-up after isolated aortic valve replacement. *J Thorac Cardiovasc Surg.* 1977;74:875-889.
  8. Herreman F, Ameer A, deVernejoul F, Bourgin JH, Gueret P, Guerin F and Degorges M. Pre- and postoperative hemodynamic and cineangiographic assessment of left ventricular functions in patients with aortic regurgitation. *Am Heart J.* 1979;98:63-72.
  9. Henry WL, Bonow RO, Borer JS, Ware JH, Kent KM, Redwood DR, McIntosh CL, Morrow AG and Epstein SE. Observations on the optimum time for operative intervention for aortic regurgitation. I. Evaluation of the results of aortic valve replacement in symptomatic patients. *Circulation.* 1980;61:471-483.
  10. Borow KM, Green LH, Mann T, Sloss LJ, Braunwald E, Collins JJ, Cohn L and Grossman W. End-systolic volume as a predictor of postoperative left ventricular performance in volume overload from valvular regurgitation. *Am J Med.* 1980;68:655-663.
  11. Forman R, Firth BF and Barnard MS. Prognostic significance of preoperative left ventricular ejection fraction and valve lesion in patients with aortic valve replacement. *Am J Cardiol.* 1980;45:1120-1125.
  12. Cunha CLP, Giuliani ER, Fuster V, Seward JB, Brandenburg RO and McGoon DC. Preoperative M-mode echocardiography as a predictor of surgical results in chronic aortic insufficiency. *J Thorac Cardiovasc Surg.* 1980;79:256-265.
  13. Greves J, Rahimtoola SH, McAnulty JH, DeMots H, Clark DG, Greenberg B and Starr A. Preoperative criteria predictive of late survival following valve replacement for severe aortic regurgitation. *Am Heart J.* 1981;101:300-308.
  14. Gaasch WH, Carroll JD, Levine HJ and Criscitiello MG. Chronic aortic regurgitation: Prognostic value of left ventricular endsystolic dimension and end-diastolic radius/thickness ratio. *J Am Coll Cardiol.* 1983;1:775-782.
  15. Bonow RO, Picone AL, McIntosh CL, Jones M, Rosing DR, Maron BJ, Lakatos E, Clark RE and Epstein SE. Survival and functional results after valve replacement for aortic regurgitation from 1976 to 1983: Impact of preoperative left ventricular function. *Circulation.* 1985;72:1244-1256.
  16. Taniguichi K, Nakano S, Hirose H, Matsuda H, Shirakura R, Sakai K, Kawamoto T, Sakaki S and Kawashima Y. Preoperative left ventricular function: Minimal requirement for successful late results of valve replacement for aortic regurgitation. *J Am Coll Cardiol.* 1987;10:510-518.
  17. Bonow RO, Dodd JT, Maron BJ, O'Gara PT, White GG, McIntosh CL, Clark RE and Epstein SE. Long-term changes in left ventricular function and reversal of ventricular dilatation after valve replacement for chronic aortic regurgitation. *Circulation.* 1988;78:1108-1120.
  18. Bonow RO, Lakatos E, Maron BJ and Epstein SE. Serial long-term assessment of the natural history of asymptomatic patients with chronic aortic regurgitation and normal left ventricular systolic function. *Circulation.* 1991;84:1625-1635.
  19. David MJ, Moore BP, Brainbridge MV. The floppy mitral valve: study of incidence, pathology, and complication in surgical, necropsy, and forensic material. *Br Heart J.* 1978;40:468.

20. Akasaka T, Yoshikawa J, Yoshida K, Okumachi F, Koizumi K and Shiratori K. Age-related valvular regurgitation: A study by pulsed Doppler echocardiography. *Circulation*. 1987;76:262-265.