Guidelines on Valvular Heart Disease

American College of Cardiology/American Heart Association (1).

Comment: A total of 124 pages and 1,066 references. Of the 324 recommendations, 1 (0.3%) and 242 (74.7%) are on the basis of the Level of Evidence A and C, respectively. Level of Evidence “C”: Consensus opinion of experts, case studies, standard of care.

European Society of Cardiology (2).

Comment: A total of 32 pages and 232 references. Of the 64 recommendations, 0 and 58 (90.6%) were on the basis of the Level of Evidence A and C, respectively. Level of Evidence C: Consensus of opinion of the experts, and/or small studies, retrospective studies, registries.

Aortic Stenosis (AS)

Early identification of aortic valve (AV) disease. Molecular imaging with the use of in vivo panel of near-infrared fluorescence imaging agents in AV of hypercholesterolemic apolipoprotein E-deficient mice (3) demonstrated that AV contained macrophages, that the macrophages were thicker than in wild-type mice, and that early dysfunction detected with magnetic resonance imaging in vivo and fluorescence imaging enabled researchers to detect uptake of macrophage-targeted magnetofluorescent nanoparticles. Valvular macrophages showed proteolytic activity. Endothelial activation and active osteogenesis were observed in valve commissures and inflamed valves, respectively (Fig. 1). The aortic wall contained advanced calcification.

Calcific AS in old hypercholesterolemic mice. Twenty-four genetic knockout mice that lack the gene for the low-density lipoprotein (LDL) receptor and express only apoB100/1000 (ApoE100/1000) were fed normal chow until age 20.1 months. Twenty-one age-matched C57 B1/6 mice served as controls. Aortic stenosis with >75% reduction in valve area occurred in 8 of 24 mice and in no control mice (p = 0.01) (4). Hypercholesterolemic mice were prone to develop AV calcification and oxidative stress (Fig. 2). At cardiac catheterization, the mean AV gradient was 57 ± 6 mm Hg, left ventricular (LV) mass was increased by 67%, and left ventricular ejection fraction (LVEF) was decreased by 30%.

Low fetuin-A correlates with calcification. Fetuin-A is a serum-based inhibitor of calcification. In 970 ambulatory persons with coronary heart disease and without severe kidney disease, 20% had mitral annular calcification and 8% had AS (5). There was an inverse relationship between fetuin-A and mitral annular calcification as well as AS.

Comment: An accompanying editorial comment presents a review of fetuin-A (6).

Transforming growth (TGF)-B1 and AV calcification. The use of TGF-B1 caused sheep AV interstitial cells to calcify as the result of an early maximal increase in alkaline phosphatase activity with associated apoptotic events and increased matrix metalloproteinase 9. A similar gene expression pattern changes was observed in calcific AS valves obtained at surgery (7).

Comment: The use of TGF-B1 is known to stimulate collagen development by fibroblasts, which could have distorted the valves irrespective of the calcium.

Lower serum calcium levels and calcific AS. A total of 228 excised valves showed a trend toward greater levels of valve calcification (r = −0.15, p = 0.026) (8), which appeared only in men whose valves contained more hydroxyapatite than in women (26 ± 9% vs. 22 ± 9% of valve mass; p < 0.001).

Comment: This study indicates the importance of calcium independent of calcium metabolism or renal function.

The genetic background of AS and coronary artery disease (CAD) are different. A total of 538 patients with severe AS and 536 controls (no heart disease age >65 years) were studied (9). Apolipoprotein E (ApoE) is an essential structural component of cholesterol and is expressed in diseased valves. There were no significant differences in ApoE e2, e3, and e4 between patients with AS and controls and in AS between those with and without CAD. The authors concluded that “ApoEe4 is not associated with AS
reflecting the different genetic background of AS and CAD.”

Use of rosuvastatin slowed the progression of moderate AS in patients with marked increases of LDL cholesterol. An open-label, prospective study (10) of 121 patients was undertaken, 61 of whom were treated with rosuvastatin for 18 months and 60 of whom were not. Patients had moderate AS, and the mean gradient in the 2 groups was 35.3 ± 13.4 mm Hg and 36.1 ± 13.4 mm Hg. At baseline, many differences existed between the 2 groups, including LDL, which in the treated group was 158.2 ± 31.7 mg/dl and in the nontreated group was 116.5 ± 20.9 mg/dl. Two primary end points were progression of AS and improvement in LDL cholesterol.

Echocardiographic/Doppler data were obtained by 2 investigators who were blinded to the treatments.

There was a significant reduction of LDL cholesterol only in the treated group, from 159.7 ± 33.4% to 93.3 ± 21.1% (p < 0.001). Aortic valve area (AVA) in the treated group changed from 1.22 ± 0.40 to 1.16 ± 0.42 (p = 0.01) and in the untreated group changed from 1.24 ± 0.35 to 1.11 ± 0.35 (p < 0.001). In the treated group the correlation of change in LDL cholesterol to change in mean gradient was very weak: r = 0.224, p = 0.027.

Comment: This was a nonrandomized, open-label, observational, very short-term study that nevertheless is of interest. The areas of concern include: 1) the large difference of LDL cholesterol at baseline between the 2 groups and 2) a small change in AVA in the treated group (mean difference 0.06 cm²). The intraobserver and interobserver coefficients of reproducibility of AVA were 0.22 cm² and 0.18 cm², respectively.

**Aortic Regurgitation (AR)**

“Improved” outcome after aortic valve replacement (AVR) for chronic AR with severe LV dysfunction. A total of 724 patients had AVR from January 1972 to January 1999. With the use of propensity matching, saturating modeling, greedy matching strategy, estimating shaping parameters, and bootstrap bagging, a propensity score for each patient “was then found,” which was then forced into the model to “further adjust for known differences between patients.”

Of 88 patients with severe left ventricular dysfunction (LVD) (i.e., LVEF ≤ 0.30) 53 had AVR before January 1, 1985, with 17% operative mortality and 35 patients who had AVR after that date with 0% operative mortality (11). Of the entire group, those with proximity-matched survival in those with “nonsevere” LVD (n = 71; ? operative survivors) versus those with severe LVD (n = 62; ? operative survivors) was 62% versus 46%, respectively, at 10 years (numbers at risk 27 and 17) and 12% versus 5%, respectively, at 25 years (numbers at risk 2 and 1).

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In propensity-matched patients who underwent surgery in 1985 and beyond, 10-year survival in 35 patients with severe LVD was 51% and in 37 patients with nonsevere LVD was 55% (p > 0.9). The authors' main conclusion was that “Neutralizing risk of severe LVD has improved early and late survival such that aortic valve surgery for chronic AR and cardiomyopathy is no longer a high-risk procedure. . .”

Comment: Can multiple, complex biostatistical analyses accurately correct the problems of a study? The authors' main conclusion is based on a comparison of 35 and 37 patients. Some of the important missing information is as follows: 1) In each of the 2 groups, the number of patients who had coronary arteriography, the percent of them who had significantly obstructive CAD, and the percent of these who had coronary artery bypass graft (CABG). The survival difference at 25 years between patients with nonsevere LVD and severe LVD is largely caused by a high operative mortality in the latter group. Can the high (17%) operative mortality before 1985 be explained by CAD that was not bypassed? 2) In the group of severe LVD, the mean ± SD and range of LVEF and the number of patients with LVEF <0.25 (see below). 3) No data on changes in LV size and function and patients’ functional class were supplied. An earlier study of 17 consecutive patients who underwent surgery from 1973 to 1977 had AVR for severe AR with LVEF (0.25 to 0.49) plus CABG in 3 and ascending aortic aneurysm correction in 2 (12). The operative mortality was 0, and at follow-up 14.5 ± 3 months later, there were statistically significant decreases in LV end-diastolic pressure, LV end-diastolic and LV end-systolic volumes, and LV mass. Left ventricular volumes and LVEF normalized in 20% and 40% of patients, respectively, who were restudied, and almost all of the patients were in New York Heart Association (NYHA) functional classes I and II.

Comment: Additional studies are needed to determine the significance of this finding in an increasingly important clinical condition.

**Mitrail Regurgitation (MR)**

Genetic cause of myxomatous valve disease. X-linked myxomatous valvular dystrophy is a rare form of inherited nonsyndromic valvular dystrophy that was previously mapped to chromosome Xq28. This study identified a P637Q mutation in the filamin A gene in all affected members (16). Clinically, patients present with mitral valve prolapse, MR, and/or AR. Among carriers of FLN mutation, the penetrance of the disease was complete in men and was incomplete in women. Female carriers could be mildly affected, and the severity of the disease was highly variable among mutation carriers.

Comment: Additional studies are needed to determine the significance of this finding in an increasingly important clinical condition.

**Randomized trial of rings with mitral valve repair (MVrep)**. A total of 363 patients underwent MVrep by Carpentier technique plus Carpentier rigid ring (n = 186) or Duran flexible ring (n = 170) (17). Operative mortality was 1.1%. Follow-up was for 3 to 126 months (mean 46.6 months). There was no difference in survival, LV systolic function, and freedom from significant MR between the 2 groups.

Comment: Previous studies have documented the beneficial effects of the addition of a ring to mitral valve repair. This is a useful randomized trial that determined that the type of ring does not influence severity of subsequent MR.

**Euro Heart Survey: symptomatic patients with severe MR but denied surgery.** A total of 396 hospitalized patients were studied, with an age 66 ± 13 years, of whom 10% were >80 years and 35% were age 70 to 80 years. Mitral valve prolapse was present in 53%, and 40% had ≥1 comorbidity. Coronary arteriography was performed in 58%, and CAD was present in 44% of these patients (18). The decision to operate was taken in 203 (67%). In multivariate analysis, the reasons not to operate were lower LVEF, nonischemic etiology, older age, higher Charlson comorbidity index, and grade 3 MR. The 1-year survival was 96 ± 1.4% in those recommended for surgery (only 67% of whom had surgery during the survey period) and in those who did not undergo surgery (“denied surgery”) was 89.5 ± 2.3% (p = 0.02).

Comment: The Euro Heart Survey for valvular heart disease (VHD) is an important study; the concern does not relate to findings but the conclusion “denied surgery.” It seems accusatory. Determining the precise reason(s) for not
recommending surgery is difficult from a survey if specific questions are not included and if the actual medical record is not reviewed. The reasons usually are multifactorial; patients in their 70s and 80s do refuse surgery. Patients were hospitalized and must have had complications of MR or had other problems; their symptoms may not have been due to MR. In patients in whom surgery was not recommended, the incidence of comorbid conditions was greater, for example, of heart failure (HF), previous myocardial infarction, very low LVEF, diabetes, and chronic obstructive pulmonary disease. There is no trial showing improved survival and outcomes with surgery in such a group of patients. The better term might be “surgery was not recommended.”

**Hospital procedural volume on care process for MR surgery.** The Society of Thoracic Surgeons Database has information on 13,614 patients who underwent MV surgery between 2000 and 2003 (19). Hospital annual MV volume for the lowest-volume quartile (LVQ) was 22 cases per year, and the highest-volume (HVQ) was 394. The risk-adjusted ratio for hospital mortality in the HVQ compared with the LVQ was 0.48 (95% confidence interval 0.28 to 0.82). The rate of MV rep in the LVQ was 47.7% and in the HVQ was 77.4% (p < 0.0001). The association between volume and mortality when adjusted for operation type was attenuated from an odds ratio of 0.48 to 0.59 (95% confidence interval 0.35 to 1.01, p = 0.05).

**Comment:** There is a need for considerable caution to extrapolation of these findings to all low-volume centers because: 1) the odds ratio narrowed when adjustments were made for operation type and 2) there might be a chance that all risk factors may not have been accounted for, for example, indications for surgery. Surgeons in hospitals with HVQ may tend to operate on minimally symptomatic or asymptomatic patients; it is possible that the clinical condition of the patients were also different.

**Surgery for MR in the elderly.** Patients age ≥75 years (n = 284), operated for MR in 1980 to 1983, 1984 to 1987, 1988 to 1991, and 1992 to 1995 were compared with younger patients (65 to 74 years, n = 504 and <65 years, n = 556). Preoperative risk characteristics were more severe in elderly patients (all p < 0.002). In the 4 time periods, MV rep was performed in 30%, 46%, 81%, and 84%, respectively (20). The observed 5-year survival in the 3 groups (≥75, 65 to 74, and <65 years) was 57 ± 3%, 73 ± 2%, and 85 ± 2% (p < 0.001), the ratio of observed (after excluding operative mortality) to expected survival in these 3 groups was 83%, 85%, and 88%, respectively. Temporal trends showed that risk of operative mortality, although greater in elderly patients (p < 0.001), declined markedly for all 3 patient groups from 27% to 5% (p < 0.001), 21% to 4% (p < 0.001), and 7% to 2% (p < 0.06), respectively.

**Comment:** These results demonstrate a remarkable advance of surgery. Areas of concern include: 1) The number of patients in each of the NYHA functional classes I and II are not described, which in those age ≥75 years totaled 30%. 2) In the latest era (1992 to 1995) MV rep was performed in 84%. Thus, 16% had MVR, and one should be cautious about extrapolating these data to recommending surgery to patients in NYHA functional class II and particularly to those in class I. 3) The percent of patients seen at their institution during each of the 4 time periods with similar characteristics as in this study but who did not have surgery would be important to know. 4) The entry of patients ended in 1995, and only the 5-year survivals are reported 11 years later in 2006. The 10-year survival data are not reported in the text but only in Figure 1A, after excluding operative mortality, appears to be about 20%, 50%, and 70%. 5) Finally, it would have been important to know whether the “recent” benefit was maintained from 1996 to 2000 and 2001 to 2004.

**Tricuspid Regurgitation (TR)**

**Changes in tricuspid valve annular (TVA) shape with functional TR.** Tricuspid valve annulus was studied with real-time 3-dimensional echocardiography in 35 patients with functional TR and 40 with normal tricuspid valve function. Annular area and mediolateral in addition to anteroposterior and high (superior)-low (inferior) distances were calculated (Fig. 3) (21). The normal TVA has a bimodal pattern (high-low distance = 7.23 ± 1.05 mm). With ≥ moderate TR, TVA become dilated (TR vs. referent, 17.4 ± 4.75 cm² vs. 9.83 ± 2.18 cm², p < 0.0001), more planar with decreased high-low distance (4.14 ± 1.05 mm), and more circular with decreased ratio of mediolateral/anteroposterior (TR vs. referent, 1.11 ± 0.09 vs. 1.32 ± 0.09, p < 0.001).

**Tricuspid valve repair (TV rep) with an annuloplasty ring improves outcomes.** Of 702 patients who underwent TV rep, 493 had predominantly a De Vega procedure (no ring) and 209 also had an annuloplasty (ring) (22). At 15 years, comparison of “ring” versus “no ring” survival was 49 ± 5% versus 36 ± 8%, p = 0.007; event-free survival was 34
Survival was an independent predictor of survival and event-free survival. Multivariate analysis showed use of an annuloplasty ring vs. recurrent TR was 82 ± 5% versus 39 ± 11%, p = 0.03. Multivariate analysis showed use of an annuloplasty ring vs. recurrent TR was 82 ± 5% versus 39 ± 11%, p = 0.03. Multivariate analysis showed use of an annuloplasty ring was an independent predictor of survival and event-free survival.

Comment: Similar to MVrep, annuloplasty is not as effective as ring plus annuloplasty.

**Infective Endocarditis (IE)**

**Outcome of urgent surgery for IE.** A total of 89 of 508 (18%) consecutive episodes of IE needed urgent surgery; 72% of them for HF unresponsive to medication and 31% for persistent infection despite appropriate antibiotic treatment (23). Hospital mortality was 36%; multivariate analysis showed that persistent infection and renal insufficiency were independent predictors of mortality.

**Long-term survival after surgery.** Of 383 consecutive patients who underwent surgery for active IE, native valve was involved in 266 and prosthetic heart valves (PHVs) in 117. Operative mortality was 12%, and late deaths were 23% (24). At 15 years, survival was 44 ± 5%; for native valve IE was 59 ± 5%; and for PVE was 25 ± 7% (p = 0.001) (Fig. 4). At 15 years, freedom from recurrent IE was 86 ± 3% and from reoperation was 70 ± 6%; both events were similar for native valve and prosthetic valve endocarditis (PVE).

**Surgery improves survival.** A prospective study of 203 episodes in 193 patients showed PVE occurred in 34%. A total of 33% of episodes were nosocomial (25), 43% were Staphylococcus aureus, 26% streptococcal, and 17% enterococci. At least 1 complication occurred in 79% of the episodes, and 63% had surgical intervention. Six-month mortality was 22%; 33% for staphylococci, 24% for enterococci, and 8% for streptococci. A total of 74% of those with a contraindication to surgery died. By multivariate logistic regression, predictors of 6 month mortality were age (p = 0.03), the causative microorganism (p = 0.04), and treatment group (p < 0.001).

In 116 consecutive patients with staphylococcal IE, hospital mortality was 26%, and 3-year survival was 57 ± 5% (26). Hospital and 3-year mortality were related to complications and comorbidities; the rate of hospital mortality was lower with early surgery (16% vs. 34%, p = 0.034); 3-year survival was better with early surgery than with medical therapy (77 ± 6% vs. 39 ± 7%, p = 0.001).

A total of 364 consecutive patients had surgery for IE. Survival at hospital discharge and 5 and 10 years for surgical patients was 91%, 69%, and 41% and for medically treated patients was 85%, 60%, and 31%, respectively, p < 0.001 (27).

A total of 69 patients on hemodialysis with IE were identified. Duration of dialysis was 37 ± 32 months (28). S. aureus was the organism in 57.9%, of whom 43.5% were methicillin resistant. Fifteen patients had valve surgery. Hospital mortality was 49.3%. More patients who had surgery survived than patients who did not (odds ratio 5.39, 95% confidence interval 1.3 to 17.6, p = 0.018). Surgery was the only independent factor predicting survival (p = 0.023).

**Surgery does not improve survival in patients with left-sided IE.** A total of 546 patients who had IE between 1980 and 1998 were included (29). There were many statistically significant differences at baseline between the surgical (n = 129) and nonsurgical (n = 417) groups. After multiple statistical analyses, including propensity scoring, adjustments for survivor bias by matching follow-up times, and valve surgery as a time-dependent covariate in different Cox models, all models were adjusted for prognostic variables “known to be predictive of 6-month mortality,” and after adjustment for early (operative) mortality, surgery was not associated with a survival benefit up to 6 months of follow-up (adjusted hazard ratio 0.92, 95% confidence interval 0.48 to 1.76), numbers of patients at-risk not given.

The authors concluded that “Given the disparity between the results of our study and those of other observational studies, well-designed prospective studies are needed to further evaluate the role of valve surgery in endocarditis management.”

**Comment:** Can multiple biostatistical analyses accurately correct the many complex study problems? A few of the many clinical issues include the following: 1) Because follow-up was only 6 months, why did the recruitment of patients end in 1998 when the study is published in 2007? 2) The long delay (30 days) between onset of diagnosis and surgery suggests there was extensive valve destruction/disruption and extension of infection (e.g., abscess) beyond the valve (See MVrep study below and urgent surgery study above). Should the patients have had surgery very much earlier? 3) There are 12 authors but none from the Division of Cardio-Thoracic Surgery and 2 cardiologists, one from Canada and one from Scottsdale, Arizona, but none from Rochester, Minnesota; and 4) When a prospective study is designed, the authors should ensure that a clinical cardiologist is responsible for the care of the patient and that the decision for surgery and its timing is a joint responsibility of the patients’ cardiologist and cardiac surgeon.
Use of $\text{MV}_{\text{rep}}$ results in better outcomes than MVR: a review of 1,194 patients. A systematic review of 24 studies showed 470 patients had $\text{MV}_{\text{rep}}$ and 724 had MVR (30). $\text{MV}_{\text{rep}}$ compared with MVR was associated with a lower 30-day mortality (2.3% vs. 14.4%, $p < 0.0001$) and ≥30-day mortality (7.8% vs. 40.5%, $p < 0.0001$) (Fig. 5). The use of $\text{MV}_{\text{rep}}$ also was associated with significantly lower reoperation rates, recurrent endocarditis, and cerebrovascular events.

Comment: This is an important and useful review. Performance of $\text{MV}_{\text{rep}}$ requires: 1) the necessary surgical skill and experience, and 2) early surgery before extensive valve destruction and extension of the infection beyond the valve leaflets occur.

Time to early-onset PVE is up to 1 year. A total of 172 patients with PVE who were nondrug users were identified from 640 patients with IE. There were no statistically significant differences in microbiological profile in those <2 months and 2 to 12 months after PHV replacement (31). Methicillin-resistant coagulase-negative staphylococci was the most common pathogen.

Data from the International Collaboration on Endocarditis-Prospective Cohort Study in 2000 to 2005 showed PVE occurred in 556 (20.1%) of 2,670 patients with IE (32). The most common organisms were $s. \text{ aureus}$ (23%) and coagulase-negative staphylococci (16.9%). Seventy-one percent of health care-associated organisms occurred within the first year of valve implantation.

Comment: Calderwell et al. (33) showed in 1985 that the time of onset of early PVE was up to 1 year.

American Heart Association Guidelines on the Prevention of Infective Endocarditis (34)

Comment: Very controversial.

Catheter-Based Valvular Intervention

Transapical transcatheter AV implantation. Transapical AV was implanted in 7 patients, age 77 ± 9 years, in whom surgical risk for AVR “was deemed excessive because of comorbidities” (35). Echocardiographic median AVA increased from 0.7 ± 0.1 cm$^2$ to 1.8 ± 0.8 cm$^2$ (interquartile ranges). There were no intraprocedural deaths. At follow-up of 87 ± 56 days, 6 of 7 patients were alive and well.

Comment: This procedure was previously reported by Professor Mohr’s group in Leipzig (36). At the European Society of Cardiology Congress in September 2007, Mohr updated the data (37). The first patients were done in 2004; lessons were learned, and changes were made. The program was restarted in 2006. As of September 2007, 122 valves were implanted, 30-day mortality was 6.5%; by the Society of Thoracic Surgeons database criteria, the predicted mortality would have been 20%. A total of 4.7% needed immediate conversion to open heart surgery. At 1 year, an additional 13.8% had died for an actuarial survival of 74.4 ± 6%. Reoperation rate was 1.6%.

![Figure 5](image-url) Mitral Valve Repair and Replacement in Endocarditis: A Systematic Review of Literature

From Feringa et al. (30).

![Figure 6](image-url) Representation of Valved Stent Repositioning

(A) The valved stent has been voluntarily misplaced too proximally inside the failed bioprosthesis. (B) Recompression of the valved stent. (C) The valved stent has been ultimately placed in an adequate position. (D) Right lateral view of the heart (right atrium and anterior part of right ventricle has been resected showing “excellent” positioning of the valved stent inside the failed bioprosthesis. From Zegdi et al. (38).
Endovascular treatment of deteriorated bioprosthesis; valve in a valve (VinV) procedure. Five sheep underwent, on beating heart, tricuspid VR with a stented bioprosthesis. Prolapse of 1 leaflet was induced by tearing a leaflet, which produced severe TR. After surgical exposure of the intraventricular inferior vena cava, the VinV procedure of repositioning of valved stent (VS) was successful in all 5 sheep (Fig. 6) (38). The use of transthoracic echocardiography showed unrestricted movements of the VS leaflets. There was no TR or periprosthetic regurgitation. Mean transvalvular gradient was 7 mm Hg (range 6 to 8 mm Hg). The explanted hearts showed VS in good position, anchorage of the VS inside the bioprosthesis was firm and the leaflets were “perfectly mobile” without macroscopic injury.

Comment: This study is another exciting development in catheter-based valve implantation. At the European Society of Cardiology Congress in September 2007, Mohr reported on the first human and successful VinV procedure for structural valve deterioration of aortic bioprosthesis (37).

Percutaneous mitral anuloplasty: relationship of coronary sinus (CS) to mitral valve annulus (MV ann). In 61 excised cadaveric human hearts, the maximum distance between CS to MV ann was 19 mm (mean 9.7 ± 3.2 mm) (39). The CS lies behind the left atrial wall not behind the MV ann, the implantation of a percutaneous mitral anuloplasty device into the coronary sinus could theoretically result in compression of the first diagonal artery and/or ramus branch in 16.4% of cases, of the circumflex artery in 63.9% cases, and of the AV nodal artery in 37.7% of cases.

In 105 patients, 64-slice MSCT was used to assess the relationship of CS, MV ann, and circumflex artery. The CS was located along the left atrial wall, rather than along the MV ann, in the majority of patients ranging from 90% at the level of MV ann to 14% at the level of the CS (Fig. 7) (40). The minimal distance was 5.1 ± 2.9 mm; in patients with severe MR, the distance between CS and MV ann was 7.3 ± 3.9 mm, and in those without severe MR it was 4.8 ± 2.5 (p < 0.05). In 68% of patients, the circumflex artery courses between the CS and MV ann.

“Long-term” outcomes after percutaneous mitral valvuloplasty (PMV). Need for surgery. In 380 patients, commissural MR that originated at the site of successful commissurotomy occurred in 27 of 47 (57%). Noncommissural MR occurred in 20 of 47 (43%), of which 12 had subvalvular damage (ruptured chordae, fail leaflet) and 8 had leaflet laceration. The 8-year event-free survival was lower in those with severe MR versus without MR (47 ± 8% vs. 83 ± 3%, p < 0.001) (41). Patients with commissural MR had a lower rate of MVR versus noncommissural MR (15% vs. 70%, p < 0.001). Multivariate analyses showed significant predictors for MVR were atrial fibrillation (Afib), mean MVG after PMV, and noncommissural MR.

Fifty of 243 (21%) patients undergoing PMV needed MVR at a median interval of 6 months (range 0 to 130), 18% of whom had it within 15 days and 82% had it later. Surgery free survival at 5 years was 80% (42).

Rhythm control is better than rate control: a randomized trial. A total of 183 Chinese patients, average age 37 years with Afib of ≤12 months’ duration with a mean duration of 5.5 months were evaluated. A post-PMV LA size ≤45 mm, average size <40 mm, mean left atrial pressure 11 mm Hg, and MVA 1.8 cm² were randomized to rhythm control versus rate control (43). At 1 year, the incidence of sinus rhythm in the 2 groups was 96% and 2%, respectively. Improvement in the primary end point (Afib-related symptoms) was greater in the rhythm group (approximately 80% vs. 30% to 40%, p < 0.001 from Fig. 2), who also had a better walking distance in the 6-min walk test, quality of life, and LA size normalization. In this group of patients, sinus rhythm was restored easily and was safe to achieve and maintain.

Comment: It should be noted that this finding relates to those undergoing PMV for MS. The hemodynamics and atrial size were very favorable for conversion to and maintaining sinus rhythm. It should not be extrapolated to patients without valve disease or to other patients with valve disease without proof from outcome data.

Prosthetic Heart Valves

Randomized trials. Carbomedics versus St. Jude. Up to 10 years, there were no significant differences between the
2 types of PHV with regard to survival (Fig. 8) and freedom from complications (44).

**STENTLESS PHV: CRYOLIFE O’BRIEN VERSUS TORONTO.** A total of 78 patients received valve sizes 21 to 29 mm. At 1 year, AVA of Cryolife O’Brien was larger than the Toronto, 1.81 \( \pm \) 0.50 versus 1.30 \( \pm \) 0.42 cm\(^2\), \( p < 0.0001 \) (45).

**Comment:** It should be noted that small numbers of patients in valves of several different sizes were included. More data are needed.

**Cost-effectiveness and economic value of AVR.** With the use of standard econometric techniques in 4,617 patients operated on from 1961 to 2003 and followed as of 2005, the cost-effectiveness was $13,528 per quality-adjusted life year gained, $19,826 for octogenarians and $27,182 for nonagenarians (46).

The value of life-years proposed by economists was applied to determine the economic value of additional life by AVR. The gross value was $14.6 billion, and expected gain without surgery was estimated at $3.0 billion. The net life-years gained were worth $11.6 billion and $451

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**Table 1 Nineteen Variables That Independently Influenced Operative Mortality (All \( p < 0.01 \)); Society of Thoracic Surgeons Database; 409,904 Valve Procedures**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic root reconstruction</td>
<td>2.78</td>
</tr>
<tr>
<td>Tricuspid valve surgery</td>
<td>2.26</td>
</tr>
<tr>
<td>Nonelective (acute) presentation</td>
<td>2.11</td>
</tr>
<tr>
<td>Multiple valve procedures</td>
<td>2.06</td>
</tr>
<tr>
<td>Advanced age</td>
<td>1.88</td>
</tr>
<tr>
<td>Reoperation</td>
<td>1.61</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>1.59</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.58</td>
</tr>
<tr>
<td>Valve replacement versus valve repair</td>
<td>1.52</td>
</tr>
<tr>
<td>Isolated mitral</td>
<td>1.47</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.37</td>
</tr>
<tr>
<td>Earlier year of operation</td>
<td>1.34</td>
</tr>
<tr>
<td>Reduced ejection fraction</td>
<td>1.34</td>
</tr>
<tr>
<td>Pulmonic</td>
<td>1.29</td>
</tr>
<tr>
<td>Any single other comorbidity</td>
<td>1.19</td>
</tr>
</tbody>
</table>

Renal failure or multiple co-morbidities could be “very significant.” *Aortic operations were the reference operation.

Data from Rankin et al. (49).

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**Table 2 Aortic Root Reconstructions (n = 11,545)**

<table>
<thead>
<tr>
<th>Incidence</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending aortic aneurysms</td>
<td>6,044 (52)</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>435 (4)</td>
</tr>
<tr>
<td>No aortic root pathology</td>
<td>5,066 (44)</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>42.3%</td>
</tr>
<tr>
<td>Aortic stenosis or regurgitation</td>
<td>50.7%</td>
</tr>
</tbody>
</table>

Operative mortality for AVR with aortic root procedures for

- Aortic aneurysm: 10.5%
- Aortic dissection: 23.7%
- No aortic root pathology: 9.5%

*Isolated aortic valve replacement (AVR) without aortic root procedures was associated with an operative mortality rate of 5.7%.

Data from the Society for Thoracic Surgeons Database: 409,904 valve procedures [from Rankin et al (49)].
million was cost of surgery, thus, the net value gained by AVR was $11.2 billion (47). The mean net value decreases according to age at surgery, $600,000 for octogenarians and $200,000 for nonagenarians.

**Comment:** Calculating the value of cardiothoracic procedures to the economy of U.S. is an important and a new direction of study (48).

**Operative (hospital) mortality.** SOCIETY OF THORACIC SURGEONS DATABASE OF 409,904 VALVE PROCEDURES, 1994 TO 2003. Aortic root reconstruction had the highest odds ratio (Table 1) (49). For a single AV procedure (n = 216,245) the unadjusted mortality was 5.7% and for AVR having aortic reconstruction when there was no aortic root pathology was 9.5% (Table 2). One of the main conclusions of the authors was that “Because aortic root reconstruction doubles mortality compared with simple aortic valve procedures, root replacement should be reserved for specific root pathology.”

**Comment:** This study is an important one. Procedures that require root reconstruction without root pathology include use of stentless valves, homografts and pulmonary autografts (Ross principle).

**NEW YORK STATE CARDIAC SURGERY DATA.** Data from 2001 and 2003 showed hospital mortality for isolated valve procedures in 10,702 patients was 4.1%, for valve plus coronary artery bypass graft CABG in 8,823 patients was 8.9%. Risk scores were assigned and predicted mortality related to those scores was presented (50). For isolated valve procedures, the risk of hospital mortality ranged from <1% to >90% for risk scores of ≤3 to ≥34 and valve plus CABG risks ranged from 1.18% to >90% for risk scores of 0 to ≥24.

**Comment:** One has to be cautious about use of these data to determine risks at other centers because: 1) the findings from 2001 and 2003 were different from those in 1998 to 2000 and may be very different in 2004 to 2006; and 2) data from New York may not be applicable to all of the U.S. population.

**Aortic valve replacement in octogenarians.** From 2000 to end of 2004, 442 consecutive patients aged ≥80 years (82.7 ± 2.3 years; 14% ≥85 years) had AVR. These octogenarians represented 16% of 2,760 patients who had AVR. Hospital mortality was 7.5% (51). On multivariate analysis, the predictors of mortality were LVEF (p = 0.003), emergency surgery (p < 0.017), and “redo” surgery (p < 0.002). Without these risk factors, the risks were low (Fig. 9). The actual mortality matched those predicted from EuroScore.

**Comment:** This is a valuable study.

**Engineering living heart valves.** “Prenatal fetal progenitors obtained from routine chorionic villus sampling were successfully used as an exclusive, new cell source for the engineering living heart valve leaflets” (52).

**Valve prosthesis-patient mismatch (VP-PM). IMPACT OF VP-PM WITH MVR.** In 929 consecutive patients, VP-PM was classified on the basis of the projected MVA indexed for body surface area: >1.2 cm²/m² as “not clinically significant” was present in 22%, >0.9 and ≤1.2 cm²/m² as moderate in 69%, and ≤0.9 cm²/m² as severe VP-PM present in 9% (53). Patients with severe VP-PM had lower 6-year and 12-year survival (74 ± 5% and 63 ± 7%) than for patients with moderate VP-PM (84 ± 1% and 76 ± 2%, p = 0.027) or clinically not significant (90 ± 2% and 82 ± 4%, p = 0.002) (Fig. 10). On multivariate analysis, severe VP-PM was associated with a greater mortality (hazard ratio 3.2, 95% confidence interval 1.5 to 6.8, p = 0.003).

**Comment:** This is the first detailed study of VP-PM after MVR that adds to many valuable contributions by Pibarot and Dumesnil.

In 884 patients mitral VP-PM, defined as MVA ≤1.25 cm²/m², was present in 32%. Mitral VP-PM was associated with elevated mean MVG, recurrent HF (p = 0.05). When
compared with “without” VP-PM survival was worse at 5 years (78% vs. 86%) and at 10 years (65% vs. 75%) (54).

**AORTIC VP-PM HAS WORSE OUTCOMES IN PATIENTS WITH LOW-GRADIENT AS (LG-AS).** The authors found that LG-AS, defined as AVA <1.2 cm², mean aortic valve gradient <40 mm Hg, and LVEF <0.50, was present in 79 of 664 (12%) patients (55). In LG-AS patients, VP-PM (defined as AVA index of ≤0.85 cm²/m²) was independently associated with increased rates of HF (hazard ratio 3.6 ± 1.9, p = 0.039), impaired LV mass regression (p = 0.037), and a “trend” toward increased late mortality (hazard ratio 3.0 ± 1.9, p = 0.084).

**BEST METHOD TO PREDICT VP-PM PRIOR TO AVR:** The PHV area was obtained in 383 patients with echocardiography at 6 months after AVR. The preoperative prediction of VP-PM obtained in these patients was tested by 4 methods: 1) PHV areas obtained in “normal” PHV from echocardiography at 6 months after valve replacement in their own laboratory; 2) indexed geometric orifice area calculated from the internal diameter provided by the manufacturer; 3) PHV areas estimated from charts provided by PHV manufacturers (which are based either on in vitro or on echo data); and 4) PHV areas estimated from reference echo data published in the literature to predict VP-PM (56). The sensitivity to predict VP-PM by method 1 (previous medical records based on echo data at 6 months after AVR), method 3, and method 4 were 53%, 80%, and 71%, respectively, and the specificity of these 3 methods was 83%, 53%, and 67%, respectively. The sensitivity of method 2 and of charts based on in vitro data (parts of method 3) to predict VP-PM was 0% to 17%. The incidence of VP-PM could be reduced from 8.7% to 0.8% with the use of method 1 (p = 0.003). Method 1 was the best.

**Miscellaneous**

Drug-induced VHD. Ergot-derived dopamine agonists, pergolide and cabergoline, which were used in the treatment of Parkinson’s disease and the restless leg syndrome, caused cardiac-valve regurgitation (57,58).

**Comment:** This was first described in 2002 (59,60).

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**REFERENCES**


