This review covers the period from July 2010 to June 2011 with one exception.

**Aortic Stenosis (AS)**

Aortic valve and arterial calcification inversely correlate with osteoporotic bone remodeling. Using near-infrared fluorescence molecular imaging agents targeting macrophages and osteogenesis, investigators were able to visualize arterial, valvular, and bone metabolism (1). In apolipoprotein E−/− mice with or without renal disease, significant arterial and aortic valve (AV) calcification was shown to correlate with the severity of atherosclerosis. Additional sophisticated studies were performed. The authors concluded: “This study provides direct in vivo evidence that in arteries and aortic valves, macrophage burden and calcification associate with each other, whereas inflammation inversely correlates with bone mineralization. Thus, understanding inflammatory signaling mechanisms may offer insight into selective abrogation of divergent calcific phenomena.”

Inflammation is increased in mild and moderately calcified AV with mild/moderate AS but not in severely calcified valves with severe AS. Inflammation was assessed with fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging in 42 patients with AS and 42 controls (2). The AV PET signal (target-to-background [TBR]) was increased compared to controls. Further, TBR was increased in mildly and moderately calcified AV valves (and in mild and moderately severe AS), but not in severely calcified valves (and in severe AS) (Fig. 1). Thus, inflammation may reduce in “late” stage AS. These findings, note the authors, may have implications in the design of future studies assessing the effects of agents attempting to modify the progression of AS.

Abnormal multidirectional myocardial functions in patients with AS and preserved left ventricular (LV) function. A total of 420 patients with mild, moderate, and severe AS (mean age 66.1 ± 14.5 years) had multidirectional strain and strain rate imaging by 2-dimensional (2D) speckle tracking (3) function. Patients were more likely to be older and at a worse New York Heart Association (NYHA) functional class (for both, p < 0.001) with increasing AS severity. The investigators found a progressive stepwise impairment in longitudinal, circumferential, and radial strain and strain rate with increasing severity of AS (all p < 0.001). The abnormal strain started in the subendocardium in mild AS, progressed to mid-wall with moderate AS, and to transmural dysfunction with severe AS.

Inappropriately high LV mass is associated with worse outcomes in asymptomatic patients with severe AS. Inappropriately high LV mass (LV mass exceeding 10% of expected value from height, sex, and stroke work) was present in 121 patients with asymptomatic severe AS. Their outcomes were compared to 88 patients with asymptomatic severe AS but appropriate LV mass (4). Mean age in the study was 75 ± 10 years. At the end of follow-up (22 ± 13 months), a clinical event (all-cause death, aortic valve replacement, or hospital admission for nonfatal myocardial infarction and/or heart failure) occurred in 67% of those with inappropriately high LV mass versus 30% in those with appropriate LV mass (p < 0.001). Subjects with inappropriate LV mass were older and had lower blood pressure than those with appropriate LV mass. At 1, 3, and 5 years, event-free survival was significantly higher in patients with appropriate LV mass compared to those with inappropriate LV mass (all p < 0.01). Left ventricular hypertrophy (LVH) was detected in 75% of the sample. In patients with high LV mass and LVH, the risk of adverse events was 69% versus 24% in those with LVH but normal LV mass (Fig. 2).

**COMMENT.** In 1988, Carroll et al. (5) described the phenomenon of “excessive hypertrophy,” which also occurred more commonly in women. Only changes in severity of AS are predictors of symptomatic deterioration in asymptomatic patients with moderate or severe AS and normal left ventricular ejection fraction. A total of 183 patients with moderate or severe AS (aortic valve area [AVA], mean 0.96 cm², age median 70 years, and LVEF median 0.74) were followed for a median of 31 months (6). Patients were followed with clinical...
evaluation at 6-month intervals and had echocardiograms every 12 months for first 24 to 36 months. During follow-up, 58% suffered symptomatic deterioration (including 3 sudden cardiac deaths and 1 resuscitated cardiac arrest) and higher peak aortic valve velocities. AVA decrease (0.1 cm²/m²; hazard ratio [HR]: 1.23; 95% confidence interval [CI]: 1.12 to 1.35; \( p < 0.004 \)) and aortic velocity increase (0.5 m/s; HR: 1.43; 95% CI: 1.25 to 1.64; \( p < 0.0001 \)) were predictors of symptomatic deterioration.

**COMMENT.** Although these “older” patients were followed carefully at 6-month intervals, there were 3 sudden deaths and 1 cardiac arrest. There are no data on coronary arteriography; incidence of diabetes, lipid abnormalities, and renal dysfunction were not presented.

**Fewer women with severe AS are referred for aortic valve replacement (AVR).** From 2004 through 2005, 362 adult patients with severe AS and class I indication for AVR were identified at a single institution (7). Of these, 52% were women. Overall, 72% underwent AVR; in patients who underwent AVR, Kaplan-Meier survival rates were similar in women and men. AVR was performed in 64% of women compared to 81% of men (\( p < 0.001 \)). After adjusting for multiple covariates, women had 2.1-fold lower odds of undergoing AVR compared to men (\( p = 0.02 \)). After matching for age and Society of Thoracic Surgeons (STS) risk score, women underwent AVR at a 19% lower relative rate compared to men (\( p = 0.03 \)). Importantly, of patients with Class I indication for AVR, 83% of men versus 68% of women (\( p = 0.001 \)) were referred for evaluation by a cardiac surgeon. Of those referred for cardiac surgical evaluation, 98% of men and 93% of women underwent AVR (\( p = 0.07 \)).

**COMMENT.** This is an important paper. Hartzell et al. (7) have presented an excellent study that is comprehensive, with superior analysis and presentation of the data.

**Percutaneous balloon aortic valvuloplasty (PBAP) was still being performed as a clinical procedure for patients with severe AS...why?** From December 2004 to December 2008, 111 patients (mean age 82 ± 8 years, 56% female) had...
PBAP for severe AS. Compared to patients <80 years of age, patients ≥80 years of age had lower left ventricular ejection fractions (43.5% vs. 1%; p < 0.01) and smaller aortic valve areas (0.59 vs. 0.73 cm²; p < 0.01). About 90% were in NYHA functional class III or IV, 5% were asymptomatic, and 6% were in class II. The majority of patients (77%) were considered not to be surgical candidates. The procedure was elective in 22% and emergent in 5%. In the 2 subgroups, the AVA increased to 0.89 ± 0.31 cm² in the older group and 1.02 ± 0.37 cm² in the younger group (p < 0.05). Complication rates: 1) composite of vascular complications at access site was 10.8%; 2) composite of intraoperative complications of intubation, pressor therapy, cardiopulmonary resuscitation (CPR) and death was 32.4%; 3) composite of in-hospital complications (death, cardiac arrest, myocardial infarction, tamponade) was 20.7%. In-hospital mortality was 8.1%.

**COMMENT.** In 1991, this procedure was shown in a large National Heart, Lung, and Blood Institute registry to be ineffective with regard to clinical status and outcome (9). Other registries also showed it was ineffective and percutaneous balloon aortic valvuloplasty was abandoned. The 1998 and 2006 American College of Cardiology/American Heart Association guidelines for the management of valvular heart disease gave it a Class III grade for calcified valves. Data on the indications, clinical benefits of the procedure, on patient follow-up, and frequency of subsequent AVR were not presented.

Refusal or denial of AVR in octogenarians with severe AS results in 2-fold excess mortality in up to 5 years of follow-up. A total of 163 octogenarians (mean age 84 ± 3 years) with severe AS and an indication for AVR were entered in an echocardiographic registry (10). The 5-year survival for the 97 patients who had AVR versus the 66 patients who were treated conservatively was 66% and 31%, respectively (p < 0.001). After adjustment for propensity score, patients undergoing AVR had a better outcome than those treated conservatively (HR: 0.56, 95% CI: 0.29 to 0.91, p = 0.022).

**Aortic Regurgitation (AR)**

Good results of aortic valve repair (AVrepair) for AR due to aortic valve-cusp prolapse (AV-CP). A total of 111 patients with trileaflet valves had AVrepair for AV-CP: 50 of these patients had AR due to AV-CP (“isolated group”) and 61 also had aortic dilation (“associated group”) (11). On pre-operative echocardiography, the presence of an eccentric aortic insufficiency jet (of any severity) had 92% sensitivity, 96% specificity for the detection of single AV-CP. A transverse fibrous band on the prolapsing cusp correctly localized the AV-CP (sensitivity 57%; specificity 92%). At 8 years of follow-up, AV reoperation was needed in 0% in the isolated group versus 7 ± 5% in the “associated” group (p = 0.33). At 5 years, AR (2+) was present in 10 ± 5% in the isolated group versus 15 ± 8% in the associated group (p = 0.54).

**Bicuspid Aortic Valve (BAV)**

Greater loss of aortic medial elastic fibers in ascending aortic aneurysm with AR than with AS. Of 122 patients with ascending aortic aneurysm without aortitis or acute dissection, the AV was congenitally malformed (unicuspid or bicuspid) in 58 of 59 (98%) of patients with AS and in 38 of 63 (60%) with AR (12). Loss of medial elastic fiber in the ascending aortic aneurysm was 0 to 1+ (grading scale 0 to 4+) in 90% of patients with AS and bicuspid valves. In those with “pure” AR, medial elastic fiber loss of 2+ to 4+ was present in 47% of those with bicuspid valves and in all 13 patients with tricuspid–Marfan syndrome. In an unadjusted analysis in 96 patients with congenitally malformed valves, the 38 patients with AR had a higher likelihood of 2+ to 4+ loss of medial elastic fiber (odds ratio [OR]: 8.78; 95% CI: 2.95 to 28.13).

**Low risk of aortic events in patients with BAV following AVR.** Among 1,286 patients age 58 ± 14 years, the indications for AVR were AS (83%), AR (5%), and AS/AR (12%) in patients with ascending aorta of ≥40 mm. At a median of 12 years after AVR (13), the incidence of aortic dissection, ascending aortic aneurysm replacement, and of progressive aortic enlargement were 1%, 0.9%, and 9.9%, respectively.

**COMMENT.** Does this study provide the clinical implications for the study of Roberts et al. (12)?

**Mitral Regurgitation (MR)**

Real-time 3-dimensional transesophageal echocardiography (RT3D-TEE) provides more accurate mapping of mitral valve prolapse (MVP) than do 2D imaging and RT3D transthoracic echocardiography (TTE). In 222 consecutive patients undergoing MV repair for MVP, RT3D-TEE identified MVP in 204 patients more accurately (92%) than 2D-TEE (78%), RT3D-TTE (80%), and 2D-TTE (54%) (14). In 60 patients with complex MVP (>1 segment localization or commissural lesions), RT3D-TTEE were correctly identified 58 patients (96.5%), compared to 70%, 52%, and 35% detected by 2D-TEE, RT3D-TTE, and 2D-TTE, respectively (p < 0.0001) (Fig. 3). Multiplanar reconstruction enabled RT3D-TTEE to differentiate dominant (>5 mm) displacement and secondary (2- to <5-mm displacement) in agreement with surgically recognized dominant lesions 100% of the time. RT3D-TTEE also correctly identified clefts and subclefts in the MV.

**COMMENT.** This is an important and valuable study. It provides a major step in the more accurate, and hopefully more reproducible, assessment of MVP.

**Increased left atrial (LA) volume index is associated with worse outcome?** Patients with LA volume ≥60 ml/m² determined echocardiographically had a worse outcome with “medical therapy” than those with smaller LA volumes (15). Those with regurgitant volume ≥60 ml/m² and LA
index ≥60 ml/m² had worse outcome with medical therapy than with surgery.

**COMMENT.** The accompanying excellent editorial (16) emphasized that there are many causes and mechanisms of increased LA size. It is also well known that increased LA size in many disorders other than MR, increased LA size is associated with worse outcomes. In this study, the authors did not provide the cause(s) or mechanism(s) for increase of LA size (volume). It also has similar generic problems to other previous studies of MR from this group (17).

**Studies of pulmonary hypertension (PHTN) in MR.**

**FREQUENCY AND SIGNIFICANCE OF PHTN IN PATIENTS WITH MR DUE TO FLAIL LEAFLETS.** MIDA (Mitral Regurgitation International Database) is a registry of these patients in 1 U.S. and 4 European centers (18). It included 437 patients seen between 1987 and 2004, of whom 102 (23.8%) had PHTN (defined as pulmonary arterial systolic pressure [PASP] >50 mm Hg at rest) determined by Doppler echocardiography at baseline. Of 427 patients, 153 (35%) were NYHA functional classes III to IV; the remainder had “no or minimal symptoms.” History of coronary artery disease was 8.2%. The aim was to determine the role of PHTN; the main endpoint of the study was “overall survival” (i.e., all-cause death), and one of several endpoints was death due to cardiovascular disease. Follow-up was 4.79 ± 2.8 years; 1-year and 5-year survival was 96 ± 0.1% and 81 ± 2%, respectively. There were 101 (23%) deaths, of which only 72 of 101 (71%) were cardiovascular deaths. MV surgery was performed in 325 (74.4%) patients at a median time of 1.8 months (IQR: 0.5 to 6.4 months). Independent predictors of PHTN were age and left atrial size (p < 0.001). PHTN was associated with a higher mortality under “medical management” and with surgical treatment (HR: 2.09, 95% CI: 1.39 to 3.13, p < 0.001); the cutoff value of 50 mm Hg was best associated with outcome and had a very low sensitivity of 41% and specificity of 82%. Following diagnosis, 104 of 437 (24%) patients presented with heart failure.

**COMMENT.** This study provides data on a large number of patients with flail leaflets. However, there are areas of concern. 1) The PASP could not be determined in 44% of patients screened for this study. Thus, 437 patients included in MIDA represent a select population out of 780 patients with flail leaflets, and extrapolation of these data to all patients with flail leaflets should be done with great care. 2) The study focused on PHTN, and there are a large number of statistical analyses of PHTN including 40 HRs, but the clinical value of many of these analyses are not apparent. 3) There were 13 sudden deaths, 38.5% of which occurred in those who had undergone surgery. Of 101 deaths, 72 were cardiovascular deaths, but were they due to the MR or to associated disease such as coronary artery disease (CAD)? The age of these patients was 67.5 ± 11.4 years. There is no data on the incidence of hypertension, diabetes, lipid abnormalities, or of smoking status or about their “medical management.” The percentage of patients who had coronary arteriography is not stated. The baseline data did not provide incidence of angina, of previous myocardial infarction, and of myocardial revascularization; the statement of “history of CAD” should be defined. 4) They did not separate the incidence of NYHA functional class II from class I that is mildly symptomatic from the asymptomatic patient. The indications for surgery and the percentage of patients who had MV repair versus
mitral valve replacement (MVR) were not presented. Also, it is not clear what is meant by patient presented with HF “following diagnosis.”

**PHTN is a predictor of outcome in organic MR.** A total of 256 patients age 63 ± 12 years were referred for MV surgery, 80.3% of whom had “degenerative” MVP. PASP was ≥50 mm Hg in 82 patients (32%) (19). PASP ≥50 mm Hg was “an independent predictor of overall and cardiovascular mortality after surgery in organic MR.” LA volume correlated with PASP (r = 0.31, p < 0.001); receiver-operating characteristic (ROC) of LA volume of 50 ml/m² for predicting PASP ≥50 mm Hg had an area under the curve of 0.68. ROC for PASP to predict long-term survival after surgery had an area under the curve of 0.7; threshold of 50 mm Hg had a sensitivity of 61% and specificity of 72%. The indications for surgery were not presented.

**COMMENT.** Studies of mitral stenosis and MR from the 1950s to the 1980s indicated that PHTN and LA hypertension determined with invasive techniques were associated with poorer outcomes, which were improved with surgical therapy. Those who improved and had reduced but persistent PHTN after surgery also had a poorer outcome. Thus, the importance of PHTN has been recognized for a long time.

The first method to diagnose PHTN is by physical examination of the patient; in the early stages, by the increased intensity of the pulmonary component of the second heart sound (P₂) at rest and, if necessary, by exercising the patient at the bedside; in the later stages, by its effects on the right ventricle (RV). Currently, the issue is the limits of measurement of PHTN by echocardiography-Doppler. These include the following. 1) In a significant percent of patients, PASP cannot be estimated. This was so in 43.9% of patients in MIDA (18) and 40% in the Mayo Study (20). This potentially would affect the assessment of the clinical applicability of the observed findings. 2) In the study of Le Tourneau et al. (19) where PASP was measured in 38 patients by noninvasive and invasive methods within 48 h of each other, the r value was 0.74 (Fig. 4), and difference was 7.6 ± 9.6 mm Hg (mean ± 2 SD); the Bland-Altman analysis showed a difference of ±15 mm Hg for estimated PASP that ranged from 20 to 80 mm Hg and particularly in the PASP range of 40 to 60 mm Hg. 3) A meta-analysis of 29 published studies (21) and 429 patients showed a modest correlation with invasively measured PASP even in those with a PASP threshold of 40 mm Hg. Eight of 29 studies included only cardiac cases. These authors concluded: 1) echocardiography is a useful noninvasive modality for measuring pulmonary pressure; and 2) considering the limitations, “the diagnosis of pulmonary hypertension and the assessment of response to therapy requires right heart catheterization.” The authors of MIDA acknowledged the “reproducibility of estimation of PASP is more limited than is achievable by other techniques (specifically right heart catheterization)” (18). Right heart catheterization with measurement of mean PA, mean PA wedge pressures (indirect LA pressure), and cardiac output by invasive techniques also allows for determining the mechanism of PHTN.

**Exercise echocardiography.** There were 2 publications in “consecutive” patients by the same group: Study A was published in the *Journal* on July 20, 2010 (22), and Study B was published in *Circulation* on July 6, 2010 (23) (Table 1).

**Tricuspid Regurgitation (TR)**

Wide range of mechanical prosthetic heart valve (PHV) areas “early” after PHV implantation. Prostheses developed by St. Jude Medical (St. Paul, Minnesota) (n = 51), Cardiomedics (Irvine, California) (n = 17), and Starr-Edwards (n = 10) mechanical prosthetic valves were studied (24). PHV area and index in each valve size overlapped with those of other valve sizes for each brand of PHV. The authors stated: “Hemodynamic variables were considerably less favorable in patients with Starr-Edwards prosthesis.”

**COMMENT.** This is an interesting and valuable study. Note: Starr-Edwards PHV sizes 30, 32, and 34 mm were studied but had data from only 1, 3, and 6 patients, respectively.

**Infective Endocarditis (IE)**

**Point system for predicting mortality/complications of IE surgery.** Using the STS database of 19,543 patients undergoing IE surgery from 2002 through 2008, a risk scoring system was developed (25). Overall unadjusted mortality was 8.2%. The individual points in the system ranged from 1 to 17. The greater number of points predicted a higher incidence of complications, which occurred in 53% of patients.

**Women have less surgery and worse prognosis than men.** From 2000 through 2008, 271 new cases with IE were identified at a large university hospital in Barcelona: 183 were men and 88 were women (26). Women were older than men were (63 ± 16 years vs. 58 ± 18 years, p = 0.006) but had similar comorbidities. When surgery was indicated, women were less likely to undergo the procedure than were men (26% vs. 47%, p = 0.001) and had higher in-hospital mortality (32% vs. 23%, p = 0.05) and 1-year mortality (38% vs. 26%, p = 0.04). Surgery was a protective factor for both values of mortality.

**Transcatheter Valve Therapy (TVT)**

The Valve Academic Research Consortium report presents standardized endpoint definitions for transcatheter aortic valve implantation clinical trials (27).

**Aortic**

Randomized trial: TVT with Sapien valve (Edwards Lifesciences, Irvine, California) is not inferior to surgical AVR at 1 year in high-risk patients with severe AS. In 699 high-risk patients, overall mean score of 11.8% on
the risk model of STS, the rates of death from any cause in the TVT group versus the surgical group at 30 days were 3.4% versus 6.5% (p = 0.07), respectively, and at 1 year were 24.2% versus 26.8% (p = 0.44) (Fig. 5). The statistically significant differences at 30 days and at 1 year are shown in Table 2. The expected 30-day mortality from the STS score (11.8%) was much higher than the mortality in patients who actually had the surgery (8.0%). In the TVT group, at 30 days, the symptomatic status and 6-min walking distance was greater; at 1 year, there was no significant difference between the 2 groups. In the TVT group, the mean AV gradient was lower (10.2 ± 4.3 mm Hg vs. 11.5 ± 5.4 mm Hg, p = 0.008) and AVA was greater (1.59 ± 0.48 cm² vs. 1.44 ± 0.47 cm², p = 0.002); 16 patients in the TVT group had surgical AVR. The valve sizes of the PHV that were inserted in the 2 groups were not provided.

COMMENT. This is another landmark important randomized trial. However, there are several areas of concern. 1) It was recommended that the patients entered into the study should have a score of at least 10% on the STS risk model. However, the determination of operative risk was made by the surgeons at each of 25 medical centers, which is a major problem for a randomized trial. The surgeons estimated the risk was 15%, but the actual risk was 6.5%. Thus, the surgeons’ estimates were overestimated by about 150%. The overall mean score was 11.8%; any measure of variability and the range of scores were not provided. In the PARTNER B (Placement of Aortic Transcatheter Valves [Cohort B]: Transfemoral TAVI vs. Medical Management) trial, the variability was 5.8%. Is it likely that some patients had a risk score of much <10%, which may account partly for the observed lower mortality, and that not all patients may have been at high risk? 2) The incidence of major stroke at 1 year was more

<table>
<thead>
<tr>
<th>Study A*</th>
<th>Study B*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Goals/aim</strong></td>
<td>1. Determine exercise-induced changes in MR and in PHTN (PASP) 2. Evaluate their impact on symptom-free survival</td>
</tr>
<tr>
<td><strong>Patient entry/study entry</strong></td>
<td>74 consecutive asymptomatic patients/NP: 13 excluded, 61 included</td>
</tr>
<tr>
<td><strong>Patient characteristics</strong></td>
<td>Degenerative MR (flail MV leaflet in 5) Age 62 ± 14 yrs; men 51%</td>
</tr>
<tr>
<td><strong>Exercise duration, min</strong></td>
<td>8.9 ± 2.3 min</td>
</tr>
<tr>
<td><strong>Induced PHTN, n</strong></td>
<td>Yes (<em>n</em> NP)</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Months, mean ± SD</strong></td>
<td>22 ± 13</td>
</tr>
<tr>
<td><strong>Developed symptoms</strong></td>
<td>30 (49%)</td>
</tr>
<tr>
<td><strong>Conclusions</strong></td>
<td>Exercise-induced increases in MR and in PASP are associated with reduced symptom-free survival up to 30 months (at 24 months, was 26 ± 11% vs. 67 ± 8%)</td>
</tr>
<tr>
<td><strong>Study not cited</strong></td>
<td>B</td>
</tr>
</tbody>
</table>

*Table was developed from data in Study A (22) and Study B (23).  Degenerative = mitral valve prolapse; MR = mitral regurgitation; MV = mitral valve; NP = not presented; PASP = pulmonary artery systolic pressure; PHTN = pulmonary hypertension.
than twice as high in the TVT group than in the surgical group, which is of serious concern (29). In the author’s clinical experience, patients and their spouses/nearest relatives/caregivers are fearful of the patient experiencing a major stroke. 3) Thirty-eight patients (10.8%) in the surgical group did not have surgery versus only 4 (1.1%) in the TVT group, who did not have TVT, and 16 (13%) in the TVT group, who had surgical AVR. This may bias the trial. 4) In the STS registry, only 5% of patients with AS had a risk score >10%. Does this mean that the findings of this trial may apply to 5% of patients with AS? 

TVT is in its early stages. Improvements in the devices, procedures, and patient selection will occur in the coming years. Particular attention should be directed to eliminating, or at least markedly reducing, the incidence of stroke.

**Myocardial injury is common after TVT and has deleterious effects.** In this study, 101 patients had successful TVT; evidence for myocardial injury was present in 97% transfemoral and 100% with transapical procedures as evidenced by a rise in cardiac troponin T and by creatine kinase-myocardial band elevation in transfemoral (47%) and transapical (77%) patients (30). A transapical approach and baseline renal dysfunction were associated with greater increases in biomarkers (p < 0.01 in both). The relationship of changes in LVEF to biomarker showed that increases in the 2 biomarkers was associated with reductions of LVEF (creatine kinase-myocardial band: r = -0.41, p = 0.009; cardiac troponin T: r = -0.46, p = 0.003). The increase of cardiac troponin T was an independent predictor of mortality at 9 ± 10 months of follow-up.

**AR grade ≥2+ in 40% of patients who had TVT with CoreValve bioprosthesis.** A total of 50 patients with severe AS age 80.5 ± 7.9 years had TVT using the Medtronic CoreValve prosthesis (Medtronic, Minneapolis, Minnesota) (31). The predictions of ≥2+ AR were increased with the increasing angle of the LV outflow tract to the ascending aorta (OR: 1.24, p < 0.001); chance of “significant AR” was

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**Figure 5 Time-to-Event Curves for Transcatheter and Surgical Aortic Valve Replacement**

Kaplan-Meier analysis for various events after aortic valve replacement by surgery (blue) and transcatheter (red). The p values were obtained by log-rank test. Reprinted, with permission, from Smith et al. (28).
Table 2  AVR: TVT Versus Surgical at 30 Days and at 1 Year

<table>
<thead>
<tr>
<th></th>
<th>TVT</th>
<th>Surgical</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>5.5</td>
<td>2.4</td>
<td>0.04</td>
</tr>
<tr>
<td>Major stroke</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Vascular complication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>17.8</td>
<td>3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Major</td>
<td>11.0</td>
<td>3.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>9.3</td>
<td>19.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>New onset AF</td>
<td>8.6</td>
<td>16.0</td>
<td>0.006</td>
</tr>
<tr>
<td>Paravalvular AR</td>
<td>12.2</td>
<td>0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>8.3</td>
<td>4.3</td>
<td>0.04</td>
</tr>
<tr>
<td>Major stroke</td>
<td>5.1</td>
<td>2.4</td>
<td>0.07</td>
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<tr>
<td>Vascular complication</td>
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<tr>
<td>Any</td>
<td>18.0</td>
<td>4.8</td>
<td>&lt;0.001</td>
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<tr>
<td>Major</td>
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<td>&lt;0.001</td>
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<td>Major bleeding</td>
<td>14.7</td>
<td>25.7</td>
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<tr>
<td>New onset AF</td>
<td>12.1</td>
<td>17.1</td>
<td>0.07</td>
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<tr>
<td>Paravalvular AR</td>
<td>6.8</td>
<td>1.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are %. Adapted from data in Table 2 of Smith et al. (28).

Mitral

Randomized trial: TVT with MitraClip (MVmc) is less effective than surgical MV repair at reducing MR but had superior safety and similar clinical outcomes. Of 279 patients, ages 67 ± 13 years, with grade 3+ or 4+ MR, 184 were assigned to percutaneous MV repair and 95 to surgical MV repair or replacement (32). At 30 days, the incidence of major adverse events in the percutaneous arm was 15%, compared to 48% for the surgical arm (p < 0.001), indicating percutaneous repair had superior safety. At 12 months, the rates of primary endpoint for efficacy were 55% for MVmc versus 73% for surgical intervention, respectively (p = 0.007). The respective components of primary endpoints were: death: 6% and 6%; surgery for MV dysfunction: 20% versus 2%; and grade 3+ or 4+ MR: 21% and 20%. At 12 months, both groups had improved LV size, NYHA functional class, and quality-of-life measures as compared to baseline.

COMMENT. This is a landmark and important randomized trial.

Beneficial hemodynamics immediately after MV repair with the MitraClip. Immediately after successful MitraClip implantation, hemodynamics were determined, with use of a Swan-Ganz balloon-flotation catheter (Edwards Lifesciences), while the patients were still under general anesthesia (33). TTE was performed before and 24 h after MitraClip implantation (Table 3).

Healing response of explanted MitraClip devices. Investigators evaluation 67 explanted devices from 50 patients; implant duration was 1 to 1,878 days (34). Explants were analyzed in 4 post-implantation intervals. The authors concluded: “In all patients, device mechanical integrity was maintained up to time of explantation. Four phases of physiological healing were observed: platelet and fibrin deposition, inflammation, granulation tissue, and finally fibrous encapsulation. Long-term device fibrous encapsulation with extension over adjacent mitral leaflets and tissue bridge formation adds structural stability.”

Tricuspid

Melody pulmonary TVT for tricuspid valve implantation. Fourteen patients had off-label use of the pulmonary TVT in the tricuspid position (35). All had prior surgery and had persistent hemodynamic compromise. Median age was 31.5 years (range 8 to 64 years). The valves were competent, and TR was eliminated as evaluated by RV angiography (Fig. 6) and by echocardiography/Doppler. One patient developed heart block. Follow-up was up to 9 months (median 4 months).

COMMENT. This is an important step (TVT for TR) that was much needed.

Pulmonary

Pulmonary valve TVT for RV outflow tract dysfunction in “adults.” A total of 102 patients, median age 21.5 years (range 16.2 to 30.1 years) had pulmonary TVT with Melody valves (Medtronic) for right ventricular outflow tract dysfunction (36). The patients had undergone previous cardiovascular surgery. In 96 of 102 patients, pre-stenting was performed. The systolic gradient between RV and PA was reduced from a median of 37 to 14 mm Hg. The ratio of systolic RV to systolic aortic pressure was reduced from 62% to 36% (p < 0.0001). Pulmonary regurgitation, assessed by magnetic resonance imaging, was reduced from a median of 16% to 1% (p < 0.0001). Complications included severe compression of the left coronary artery in 1 patient, who died 2 weeks later; transient complete AV block (n = 1); a single fracture of stent without loss of stent integrity (n = 2); and endocarditis (n = 1). The incidence of stent fractures was 5

Table 3 Beneficial Hemodynamics With MVmc

<table>
<thead>
<tr>
<th>Data From</th>
<th>Pre-MVmc</th>
<th>Post-MVmc</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac catheterization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac output, l/min</td>
<td>5.0 ± 2.0</td>
<td>5.7 ± 1.9</td>
<td>0.003</td>
</tr>
<tr>
<td>Cardiac index, l/min/m²</td>
<td>2.7 ± 1.0</td>
<td>3.0 ± 1.0</td>
<td>0.0025</td>
</tr>
<tr>
<td>Forward stroke volume, ml</td>
<td>57 ± 17</td>
<td>65 ± 18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SVR, dyn·s/cm²</td>
<td>1,226 ± 481</td>
<td>1,004 ± 442</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDP, mm Hg</td>
<td>11.0 ± 8.6</td>
<td>8.8 ± 6.0</td>
<td>0.016</td>
</tr>
<tr>
<td>TTE†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MR grade</td>
<td>3.3 ± 0.7</td>
<td>1.7 ± 0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regurgitant volume, ml</td>
<td>51.5 ± 20.4</td>
<td>29.8 ± 20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDV, ml</td>
<td>172 ± 37</td>
<td>158 ± 38</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean ± SD. *Obtained immediately after procedure. †Obtained 24 h later and analyzed in core laboratory at University of California, San Francisco under the skilled and expert direction of Elyse Foster, MD. Adapted from Siegal et al. (33).

LVEDP = left ventricular end-diastolic pressure; LVEDV = left ventricular end-diastolic volume; MR = mitral regurgitation; MVmc = mitral valve MitraClip; SVR = systemic vascular resistance; TTE = transthoracic echocardiography.
of 102 (5%). The median follow-up was 352 days (range 99 to 390 days).

**Prosthetic Heart Valve (PHV)**

Randomized trial: larger PHV index with Edwards Perimount Magna than with Medtronic Mosaic. A total of 108 patients undergoing AVR for AS, AR, or AS/AR were randomized to the Edwards Perimount Magna bovine pericardial valve versus Medtronic Mosaic porcine bioprosthesis (37). There were fewer patients in the labeled valve sizes 19 and 27. PHV index at 1 (median 12/11006 1.5 months) and 5 years (median 4.9/11006 0.8 years) are shown in Table 4. LV mass regression was greater with Perimount Magna than with the Mosaic at 5 years by 47.4/11006 35 g/m² versus 44/11006 36.1 g/m², respectively (p < 0.0001).

** Excellent results of AVR in octogenarians.** Investigators studied 249 patients, age 84 ± 3 years (range 80 to 95 years), who underwent minimally invasive AVR, 21% of whom had previous cardiac surgery (38). The STS-PROM (STS Predicted Risk of Mortality) score was 10.5% (IQR: 7% to 17%), C-index = 0.67, p = 0.18, and the modified EuroSCORE (European System for Cardiac Operative Risk Evaluation) was 11% (IQR: 6% to 14%), C-index = 0.527, p = 0.74. The observed operative mortality was 3%. Stroke rate was 4%. The 1-, 5-, and 10-year survival was 93%, 77%, and 56%, respectively, which was not significantly different from that of U.S. age- and sex-matched populations.

**COMMENT.** The C-index is the area under the ROC curve and quantifies discriminatory ability, with a value of 0.5 indicating random chance and 1.0 indicating perfect discrimination (39). A measure of variability of the values for survival was not provided. The accompanying commentary by Moon (40) is superior.

**Mechanical prosthesis (MP) versus bioprosthesis (BP).** A total of 5,433 patients undergoing AVR coronary artery bypass graft (CABG) from a review of published studies were studied; a large number of brands of PHV were included (41). Patient survival at 1, 5, and 10 years was 90%, 78%, and 57%, respectively. Multivariate predictors of mortality were age in 10-year increments (OR: 1.53, 95% CI: 1.27 to 1.86, p < 0.001), concomitant CABG (OR: 1.35, 95% CI: 1.01 to 1.82, p = 0.05), and creatinine in 10-U increments (mmol/l) (OR: 1.05, 95% CI: 1.03 to 1.06, p < 0.001). The crossover point at which life expectancy with MP and BP was similar was 59 years for both men (range 56 and 69 years) and women (range 58 and 63 years). Long-term survival was independently influenced by age, male sex, and associated CABG. For men ages 50, 55, 60, 65, 70, and 75 years at initial operation, the lifetime incidence of structural valve disease was 58%, 50%, 40%, 30%, 20%, and 13%, respectively.

**COMMENT.** This is an important study.

### Table 4

<table>
<thead>
<tr>
<th>Valve Size *</th>
<th>PHV Area Index (cm²/m²)</th>
<th>Medtronic Mosaic</th>
<th>Perimount Magna</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 mm, n = 34</td>
<td>1 year</td>
<td>0.83 ± 0.14</td>
<td>0.99 ± 0.21</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>5 years</td>
<td>0.67 ± 0.15</td>
<td>0.90 ± 0.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>23 mm, n = 41</td>
<td>1 year</td>
<td>0.98 ± 0.17</td>
<td>1.16 ± 0.21</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td></td>
<td>5 years</td>
<td>0.77 ± 0.14</td>
<td>1.12 ± 0.28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>25 mm, n = 17</td>
<td>1 year</td>
<td>1.00 ± 0.24</td>
<td>1.22 ± 0.18</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td></td>
<td>5 years</td>
<td>0.77 ± 0.20</td>
<td>1.18 ± 0.23</td>
<td>&lt;0.007</td>
</tr>
</tbody>
</table>

Values are mean ± SD. *Valve sizes are the labeled valve sizes. Adapted from data of Dalmau et al. (37).

PHV = prosthetic heart valve.
Survival after valve replacement (AVR/MVR) in patients with kidney transplantation. Of 1,698,706 patients in the Renal Data System database, the investigators indentified 1,335 patients with kidney transplantation patients who had valve replacement between 1991 to 2004 (42). In-hospital mortality was 14.0% overall, 11.4% for tissue-valve patients, and 15% for nontissue-valve patients patients (p = 0.09). Two-year survival rates for BP and MP were 61.5% and 59.5%, respectively (p = 0.30). Annual mortality was about 20%; 8-year mortality was about 80%. The most powerful predictors of death were age >75 years (HR: 3.76%, 95% CI: 2.62 to 5.39), age 65 to 74 years (HR: 2.11, 95% CI: 1.65 to 2.68), AVR + MVR (HR: 1.71, 95% CI: 1.35 to 2.16), and end-stage renal disease caused by diabetes (HR: 1.59, 95% CI: 1.28 to 1.98). Of patients undergoing AVR, the causes of death with tissue valves versus nontissue valves were cardiovascular (32.1% vs. 28.1%), infection (11.6% vs. 14.8%), and other/unknown (56.3% vs. 57.1%), p = 0.62.

AVR: Increasing pre-operative renal dysfunction is associated with increasing operative mortality and reduced survival up to 10 years of follow-up. In this retrospective review, 1,512 patients had AVR, and 896 had AVR + CABG (43). Patients were classified as normal or with mild, moderate, or severe renal dysfunction based on glomerular filtration rate estimated using the Modification of Diet in Renal Diseases (MDRD) formula. In-hospital mortality was increased with renal dysfunction, from 2.9% for patients with no renal dysfunction to 15.8% for those with severe dysfunction (p < 0.001). In patients requiring dialysis, in-hospital mortality was 17.3%. Compared to the normal group, the OR in the severe renal dysfunction group for new dialysis was 15.29 (p < 0.001). For worsening renal dysfunction in the moderate group, the OR was 2.51 (p = 0.01); and for the severe renal dysfunction group, the OR was 8.82 (p < 0.002).

Same-day coronary arteriography in selected patients undergoing elective AVR is safe. A total of 1,413 patients who underwent AVR with or without CABG were separated into 2 propensity-matched groups: 321 with coronary arteriography on the same day as AVR (group 1) and 321 who did not have coronary arteriography on the same day as AVR (group 2) (44). Patients who were believed to be at higher risk for acute kidney injury (AKI) were excluded. AKI was defined by the criteria of the AKI Network. Six views of the coronary arteries were obtained using a hand injection technique. Severity of renal dysfunction was defined by creatinine clearance obtained by the Cockcroft-Gault formula. Patients were not routinely given sodium bicarbonate or n-acetylcysteine. AKI occurred in 23.4% in group 1 and in 22.3% in group 2.

COMMENT. The most common definitions of contrast-induced AKI is a rise of serum creatinine by 0.5 mg/dl or a 25% relative rise of serum creatinine at 48 h of contrast exposure (45). A large number of factors have been identified as risk factors for AKI. Major risk factors that are common include moderate or severe RD, “nothing by mouth” status, “excessive” diuresis especially in the previous 24 to 48 h, diabetes, reduced LV function, low cardiac output, amount of contrast medium injected, and use of even therapeutic doses of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and of nonsteroidal anti-inflammatory drugs in those with severe abnormalities of the above listed risk factors.

Valve Prosthesis-Patient Mismatch (VP-PM): Mitral

Severe VP-PM in patients >65 years of age with bioprosthesis is associated with worse survival. From 1992 to 2008, 765 patients underwent bioprothetic (42%) or mechanical (58%) mitral valve replacement; 48% were older than 65 years of age (46). VP-PM was classified as severe (PHV area <0.9 cm²/m²) in 107 patients, moderate (PHV area 0.9 to 1.2 cm²/m²) in 286 patients, and absent (PHV area >1.2 cm²/m²) in 372 patients. More severe VP-PM was 1 of 9 risk factors that were predictive of late death on multivariate analysis (p < 0.05). For bioprosthetic recipients older than 65 years of age, survival of those with severe VP-PM versus moderate or “absent” at 5 years, was 30 ± 7% versus 43 ± 4%, and at 10 years was 0 versus 21 ± 5%, respectively (p = 0.05). For patients with mechanical prostheses, survival with severe or moderate versus absent VP-PM at 5 years was 77 ± 4% versus 82 ± 3%, and at 10 years, it was 62 ± 6% versus 66 ± 4%, respectively (p = 0.08).

COMMENT. This valuable study documents that even in patients with severe VP-PM, associated comorbid conditions are important factors for late all-cause mortality.

REFERENCES


Key Words: aortic regurgitation • aortic stenosis • bicuspid aortic valve • valvular heart disease.