Survival After Open Versus Endovascular Thoracic Aortic Aneurysm Repair in an Observational Study of the Medicare Population

Summary: Using Medicare claims from 1998 to 2007, we examined short and long-term survival of patients with descending thoracic aortic aneurysms (TAA) following open surgical repair and endovascular repair (TEVAR). Overall, we studied 12,573 patients who underwent open repair, and 2,732 patients who underwent TEVAR. Perioperative mortality was lower in patients undergoing TEVAR compared with open repair for both intact (6.1% versus 7.1%, P = 0.07) and ruptured TAA (28% versus 46%, P = 0.0001). However, patients with intact TAA selected for TEVAR had significantly worse survival than open patients at one year (87% open, 82% TEVAR, P = 0.001) and five years (72% open, 62% TEVAR, P = 0.001), and analyses adjusting for patient-level comorbidities produced similar results. Therefore, although perioperative mortality is lower with TEVAR, patients selected for TEVAR have worse long-term survival than patients selected for open repair in our observational analysis of Medicare patients. Future work is needed to determine if these deaths are due to the selection of high-risk patients for TEVAR, or due to late device-related complications from the TEVAR itself.

Conclusions: Although perioperative mortality is lower with TEVAR, Medicare patients selected for TEVAR have worse long-term survival than patients selected for open repair. The results of this observational study suggest that higher-risk patients are being offered TEVAR and that some do not benefit on the basis of long-term survival. Future work is needed to identify TEVAR candidates unlikely to benefit from repair.

Lack of Tissue Inhibitor of Metalloproteinas 2 Leads to Exacerbated Left Ventricular Dysfunction and Adverse Extracellular Matrix Remodeling in Response to Biomechanical Stress

Summary: Tissue inhibitor of metalloproteinas 2 (TIMP2) is one of the TIMPs that is required for regulating the structural remodeling of the cardiac extracellular matrix. Tissue inhibitor of metalloproteinas 2 is the only TIMP with the unique property of activating matrix metalloproteinas 2 (MMP2) in addition to inhibiting a number of MMPs. Tissue inhibitor of metalloproteinas 2 levels are increased in the hearts of patients with aortic valvular stenosis and patients with pressure-overloaded cardiomyopathy. However, whether this increase in TIMP2 is beneficial (through inhibiting MMPs) to the diseased heart is not clear. Our study demonstrates that lack of TIMP2 severely compromises cardiac response to biomechanical stress through adverse structural remodeling and impaired myocyte–extracellular matrix interaction, leading to worsening of left ventricular dilation and dysfunction. On the basis of our study, the rise in TIMP2 in the hearts of patients with pressure-overloaded cardiomyopathy is a compensatory response to overcome the elevated proteolytic activities in these diseased hearts, although it may not reach a sufficiently high level to prevent the disease progression. For this reason, overexpression of TIMP2 could serve as a potential therapy in pressure-overloaded cardiomyopathy.

Conclusions: Lack of TIMP2 leads to exacerbated cardiac dysfunction and remodeling after pressure overload because of excess activity of membrane type MMP and loss of integrin β1D, leading to nonuniform extracellular matrix (ECM) remodeling and impaired myocyte–ECM interaction.

Health-Related Quality of Life After Transcatheter Aortic Valve Replacement in Inoperable Patients With Severe Aortic Stenosis

Summary: Many patients with severe aortic stenosis do not undergo surgical valve replacement because of prohibitive operative risk. In a cohort of such patients, the Placement of Aortic Transcatheter Valves (PARTNER) trial recently showed that transcatheter aortic valve replacement increased 12-month survival by an absolute margin of 20% but was associated with increased risks of vascular complications and stroke compared with standard therapy, which included balloon aortic valvuloplasty in the majority of subjects. In this trial, quality of life was assessed prospectively with the Kansas City Cardiomyopathy Questionnaire and the Short Form-12 General Health Survey. We found that the overall summary score of the Kansas City Cardiomyopathy Questionnaire, the primary quality-of-life end point, improved 20 to 30 points on a 100-point scale 1, 6, and 12 months after transcatheter aortic valve replacement (TAVR), whereas the improvement in the control group was 10 to 12 points at 1 and 6 months and only 4 points at 12 months. Similar patterns were observed for the other quality-of-life measures. Thus, during the first year after intervention, quality of life was substantially better in the transcatheter aortic valve replacement group than in the control group in this clinical trial population.

Conclusions: Among inoperable patients with severe aortic stenosis, compared with standard care, TAVR resulted in significant improvements in health-related quality of life that were maintained for at least 1 year.
Correlates of Delayed Recognition and Treatment of Acute Type A Aortic Dissection: The International Registry of Acute Aortic Dissection (IRAD)

Summary: An acute aortic dissection is a surgical emergency with a high mortality if left untreated. Given the varied presentations, including similarity to the far more common acute coronary syndromes, diagnosis and appropriate treatment are often delayed. This report evaluates the reasons for delay in the diagnosis of 894 patients in the International Registry of Acute Aortic Dissection Registry. Patients with the most typical presenting signs and symptoms, including abrupt onset of severe chest pain, and those with pulse deficits or hypotension, were diagnosed more quickly. In contrast, patients transferred from referral hospitals had significantly longer times to diagnosis and ultimately to surgery, perhaps related to the physician’s experience with dissection at these hospitals. Delays from diagnosis to surgery also occurred in nonwhites, those with prior cardiac surgery, and those without ongoing shock or hypoten- sion. Education directed at recognition of both typical and atypical presentations of aortic dissection, particularly to those centers with low exposure to aortic emergencies, may be of benefit. The fact that the median times from presentation to diagnosis and from diagnosis to surgery exceeded 4 hours suggests that there is substantial room for improvement. The development of systematic care pathways for diagnosis and management of aortic dissection, similar to those in place for acute myocardial infarction, may be of benefit. The focus of these pathways should include recognition of both typical and atypical presentations, with rapid diagnostic imaging in appropriate candidates and prompt transfer and surgery.

Conclusions: Improved physician awareness of atypical presenta- tions and prompt transport of acute aortic dissection patients could reduce crucial time variables.

Arterial Pulse Wave Dynamics After Percutaneous Aortic Valve Replacement: Fall in Coronary Diastolic Suction With Increasing Heart Rate as a Basis for Angina Symptoms in Aortic Stenosis

Summary: Using the new technique of percutaneous aortic valve replacement (PAVR) in combination with wave intensity analysis, we have identified abnormalities in coronary physiology that are rapidly restored to normal after valve implantation. In addition to being of mechanistic interest, quantification of coronary physiological reserve and in particular its paradoxical reversal may offer a potential way of assessing the severity of aortic stenosis in the presence of comorbidities that may mimic or obscure anginal symptoms. Although currently it is possible to do this analysis only with offline analysis tools, the computational processing requirements are minimal and easily automatable, making online analysis a realistic vision for the future.

Conclusions: In aortic stenosis, the coronary physiological reserve is impaired. Instead of increasing when heart rate rises, the coronary diastolic suction wave decreases. Immediately after PAVR, physiological reserve returns to a normal positive pattern. This may explain how aortic stenosis can induce anginal symptoms and their prompt relief after PAVR.

Mortality and Neurological Injury After Surgical Repair With Hypothermic Circulatory Arrest in Acute and Chronic Proximal Thoracic Aortic Pathology: Effect of Age on Outcome

Summary: The aim of this study was to determine whether advanced age affects mortality and incidence of neurological injury in patients undergoing surgical repair with hypothermic circulatory arrest in acute and chronic thoracic aortic pathology. Between 2005 and 2010, 523 patients underwent surgical repair with hypothermic circulatory arrest for repair of acute and chronic proximal thoracic aortic pathology at our institution. Our results show that age is not associated with increased risk for mortality and neurological injury in patients undergoing surgical repair for acute and chronic thoracic aortic pathology with hypothermic circulatory arrest. Extended hypothermic circulatory arrest times, reflecting the extent of disease, and redo surgery predict mortality; emergency surgery and extracardiac arteriopathy predict neurological injury. These data should encourage clinicians to refer elderly patients with acute and chronic thoracic aortic pathology for surgical therapy because the risk for mortality and neurological injury is consistently low even in patients with advanced age.

Conclusions: Age is not associated with increased risk for mortality and neurological injury in patients undergoing surgical repair for acute and chronic thoracic aortic pathology with hypothermic circulatory arrest. Extended hypothermic circulatory arrest times, reflecting the extent of disease, and redo surgery predict mortality, whereas emergency surgery and extracardiac arteriopathy predict neurological injury.

Long-Term Outcome of Patients With Isolated Thin Discrete Subaortic Stenosis Treated by Balloon Dilation: A 25-Year Study

Summary: This study presents the longest follow-up analysis of a series of patients with isolated thin discrete subaortic stenosis treated by transluminal balloon tearing of the membrane. Selection of appropriate candidates for percutaneous treatment was an important issue, and only patients with a thin membrane at the outflow tract without a fibromuscular component were included. After a mean follow-up time of 16±6 years, 11 patients (15%) developed restenosis, 3 patients (4%) progressed to muscular obstructive disease, 1 patient (1.3%) developed a new distant obstructive membrane, and 4 patients (5%) underwent surgery at a mean of 3±2 years after their first treatment. Fifty-eight patients (77%) remained alive and free of redirection or surgery at follow-up. Larger annulus diameter and thinner membranes were independent factors associated with better long-term results. These findings, together with current improvements in image techniques for better delineation of the outflow tract, could help in the selection of patients who can benefit from an interventional procedure as a first-choice treatment. The recurrence rate in this selected group of patients may be similar to that observed in surgical patients, and both are probably influenced by the progressive nature of the disease. If restenosis of the membrane develops, balloon dilation can be repeated successfully in most patients. With this strategy, surgery for a thin membrane may be delayed or even avoided.

Conclusions: Most patients (77%) with isolated thin discrete subaortic stenosis treated with transluminal balloon tearing of the mem- brane had sustained relief at subsequent follow-ups without resteno- sis, the need for surgery, progression to muscular obstructive disease, or an increase in the degree of aortic regurgitation.

Low Prevalence of Abdominal Aortic Aneurysm Among 65-Year-Old Swedish Men Indicates a Change in the Epidemiology of the Disease

Summary: On the basis of results from 4 randomized controlled trials, screening elderly men with ultrasound for abdominal aortic aneurysm (AAA) has emerged as an evidence-based way of reducing mortality from ruptured AAA. Although no trial has assessed the optimum age for AAA screening, current recommendations generally consist of a 1-time ultrasound examination at 65 years of age. In this contemporary population-based AAA screening study of a large cohort of 65-year-old Swedish men, a lower-than-expected AAA
prevalence was found. This was attributed mainly to a changed exposure to known risk factors over the past decades, particularly a significant decline in smoking. At the same time, the life expectancy of the target population has increased significantly while the surgical caseload of AAA has remained unchanged. These observed changes in the epidemiology of AAA disease highlight the need to reevaluate different screening strategies on the basis of modern epidemiological data, which may influence the design of future screening programs.

Conclusions: On the basis of the observed reduced exposure to risk factors, lower-than-expected prevalence of AAA among 65-year-old men, unchanged AAA repair rate, and significantly improved longevity of the elderly population, the current generally agreed-on AAA screening model can be questioned. Important issues to address are the threshold diameter for follow-up, the possible need for rescreening at a higher age, and selective screening among smokers.8

Diabetes Mellitus Worsens Diastolic Left Ventricular Dysfunction in Aortic Stenosis Through Altered Myocardial Structure and Cardiomyocyte Stiffness

Summary: In aging populations, diabetes mellitus (DM) and aortic stenosis (AS) are becoming frequent comorbidities. Studies looking at the interaction between DM and AS investigated mainly the progression of sclerocalcific valvular dysfunction. In heart failure (HF), DM raises diastolic left ventricular (LV) stiffness, which adversely affects morbidity and mortality. The DM-related rise in diastolic LV stiffness was observed both in HF with reduced ejection fraction and in HF with normal ejection fraction. In HF with reduced ejection fraction, DM affected myocardial stiffness through excessive fibrosis and arteriolar or capillary deposition of advanced glycation end products, whereas in HF with normal ejection fraction, the DM-related rise in diastolic LV stiffness was shown to result from all 3 mechanisms, namely, excessive fibrosis, intramyocardial vascular advanced glycation end product deposition, and elevated cardiomyocyte F\textsubscript{passive}. The latter could be attributed to hypophosphorylation of the stiff isoform of the cytoskeletal protein titin, which is largely responsible for cardiomyocyte F\textsubscript{passive}. The observed increase in diastolic LV stiffness in patients suffering from both AS and DM. This increase was evident from higher LV end-diastolic pressure at comparable LV end-diastolic volume index. Furthermore, the increase in diastolic LV stiffness was shown to result from all 3 aforementioned mechanisms, namely excessive fibrosis, intramyocardial vascular advanced glycation end product deposition, and elevated cardiomyocyte F\textsubscript{passive}. The latter could be attributed to hypophosphorylation of the stiff isoform of the cytoskeletal protein titin, which is largely responsible for cardiomyocyte F\textsubscript{passive}. The observed increase in diastolic LV stiffness in patients suffering from both AS and DM could predispose them to earlier development of heart failure symptoms and an earlier need for aortic valve replacement.

Conclusions: Worse diastolic LV dysfunction in AS-DM predisposes to heart failure and results from more myocardial fibrosis, more intramyocardial vascular advanced glycation end product deposition, and higher cardiomyocyte F\textsubscript{passive}, which was related to hypophosphorylation of the N2B titin isoform.9

Aortic Valve Replacement in the Elderly: Determinants of Late Outcome

Summary: To identify patient factors related to increased longevity and to assess the potential impact of valve type on overall survival, we analyzed late outcomes of 2890 consecutive patients aged ≥70 years who had aortic valve replacement (AVR). Our findings may help clinicians in 2 ways. First, we found that several comorbid conditions (eg, renal failure, immunosuppression, concomitant coronary artery disease, history of myocardial infarction, or stroke) were associated with reduced late survival after AVR. These factors, in general, are not modifiable. But the finding that advanced New York Heart Association class predicted poorer late survival emphasizes the importance of not delaying operation unnecessarily in elderly pa-
tients. Delaying surgical referral until symptoms progress will not only result in a higher early mortality but will also decrease the likelihood of a satisfactory long-term survival. Second, our data show no important difference in outcome of patients by type of prosthesis. Our data are reassuring in that there is no survival penalty for use of bioprostheses in elderly patients. In addition, our findings demonstrate that the structural deterioration of aortic bioprostheses is a rare event in elderly patients and that redo AVR is rarely necessary.

Conclusions: Survival of elderly patients after aortic valve replacement is influenced by age and preoperative comorbidities; 33% at lowest risk had overall survival similar to that of an age- and sex-matched general population. There was no sufficient evidence that valve type affected survival. Structural deterioration of aortic bioprostheses was rare.10

Cerebral Protection During Surgery for Acute Aortic Dissection Type A: Results of the German Registry for Acute Aortic Dissection Type A (GERAADA)

Summary: Surgery for acute aortic dissection type A (AADA) requires cerebral protection strategies for aortic arch intervention: Hypothermic circulatory arrest (HCA) alone or with adjunct cerebral perfusion. The optimal strategy is unclear. Through the German Registry for Valve Aortic Dissection Type A (GERAADA), we surveyed the current practice and outcome of cerebral protection during AADA surgery in Central Europe. This is the largest series on this topic published so far. We compared the different cerebral protection strategies: HCA alone, unilateral antegrade cerebral perfusion, and bilateral antegrade cerebral perfusion. Furthermore, we evaluated several technical parameters, eg, perfusion pressures and temperatures within the different strategies. Study end points were mortality and neurological morbidity. The duration of arch intervention turned out to be the major factor influencing the outcome. HCA only appears to be safe for under 30 minutes, whereas antegrade cerebral perfusion doubles the safe time period. Thus, surgery with HCA appears justified only for limited arch interventions. If a more extensive arch reconstruction is required, cerebral perfusion should be initiated immediately. Unilateral and bilateral antegrade cerebral perfusion resulted in equivalent outcomes. We describe parameters that allow the time required for arch reconstruction to be estimated. Referring to our data, we discuss the different cerebral protection strategies and make detailed recommendations on the use of perfusion pressure and other items of clinical importance. This enables the readers to critically reflect and optimize their own practice.

Conclusions: This study reflects current surgical practice for acute aortic dissection type A in Central Europe. For arrest times less than 30 minutes, hypothermic circulatory arrest and antegrade cerebral perfusion (ACP) lead to similar results. For longer arrest periods, ACP with sufficient pressure is advisable. Outcomes with unilateral and bilateral ACP were equivalent.11

One-Year Outcomes of Cohort 1 in the Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry: The European Registry of Transcatheter Aortic Valve Implantation Using the Edwards SAPIEN Valve

Summary: Cohort 1 of the Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry describes the outcomes at 30 days and 1 year of >1000 consecutive patients undergoing transcatheter aortic valve implantation using the Edwards SAPIEN valve. The 30-day results have previously been published and have established the procedural results of the technique in a large group of patients in a multicenter registry. The 1-year data describe the outcomes in the largest group of transcatheter aortic valve implantation patients at this time point. This combined data will allow the
interventional community to adequately consent transcatheter aortic valve implantation patients on the basis of robust data and will also be a benchmark against which future patient groups and any new devices may be measured.

**Conclusions:** The SOURCE Registry is the largest consecutively enrolled registry for transcatheter aortic valve implantation procedures. It demonstrates that with new transcatheter aortic techniques excellent 1-year survival in high-risk and inoperable patients is achievable and provides a benchmark against which future transcatheter aortic valve implantation cohorts and devices can be measured.\(^1\)\(^2\)

**Late Outcomes of a Single-Center Experience of 400 Consecutive Thoracic Endovascular Aortic Repairs**

**Summary:** Operative repair of thoracic aortic pathologies is accompanied by significant morbidity and mortality. Thoracic endovascular aortic repair has become a minimally invasive alternative to open repair in anatomically suitable patients. Although the therapy remains indicated primarily for aneurysms and penetrating ulcers, other pathologies, such as traumatic transections and dissections, have been treated successfully after commercial availability of devices and increasing collective experience of endovascular operators. Early outcomes after thoracic endovascular aortic repair have been promising, but to date most published reports involve limited numbers of patients and are restricted to perioperative outcomes with relatively short-term follow-up. This study represents one of the largest single-center, real-world thoracic endovascular aortic repair experiences, spanning nearly a decade of practice. Our results showed an overall 30-day/hospital mortality of 6.5%, an elective mortality of 2.6%, a stroke rate of 3.0%, and a rate of permanent paraparesis/paraplegia of 4.5%. Survival at 3 years was 60%. The risk of intraoperative surgical conversion was extremely low. The importance of careful case planning and a core multidisciplinary approach cannot be overemphasized. The high rate of late mortality suggests that patients with thoracic aortic diseases may represent a subset whose underlying comorbidities may pose a greater threat to their lives than the aortic disease itself. Perhaps the greatest challenge is not the search for a better widget, but improved patient selection to identify those who will truly benefit from this therapy and those for whom the therapy may represent a futility of care.

**Conclusions:** Thoracic endovascular aortic repair may be used to treat a variety of thoracic aortic pathologies with a very low risk of intraoperative conversion. Overall rates of mortality and neurological complications were relatively low but significantly increased in emergent repairs. There appeared to be a substantial number of late deaths, which may represent a combination of poor patient selection and treatment failures.\(^1\)\(^3\)

**Predictors of Abdominal Aortic Aneurysm Sac Enlargement After Endovascular Repair**

**Summary:** Two recently published randomized trials comparing the effectiveness of open surgical and endovascular repair (EVAR) for the treatment of abdominal aortic aneurysms have demonstrated a significantly lower mortality rate for patients undergoing EVAR. However, the initial short-term survival advantage for patients undergoing EVAR was lost after long-term follow-up. A significant proportion of the late deaths of patients undergoing EVAR were due to aneurysm rupture. These concerning findings raise significant concerns about the long-term risk of aneurysm rupture in patients undergoing EVAR in the United States. Furthermore, over the decade of study, liberalization of the anatomic characteristics deemed suitable for EVAR by device manufacturers has occurred, and several of these liberalized anatomic characteristics independently predict aortic aneurysm sac enlargement.

**Conclusion:** In this multicenter observational study, compliance with EVAR device guidelines was low and post-EVAR aneurysm sac enlargement was high, raising concern for long-term risk of aneurysm rupture.\(^1\)\(^4\)

**Total Arch Repair for Acute Type A Aortic Dissection With 2 Modified Techniques: Open Single-Branched Stent Graft Placement and Reinforcement of the Dissected Arch Vessel Stump With Stent Graft**

**Summary:** In total arch replacement for patients with acute type A aortic dissection, anastomoses of the graft to the left subclavian artery and descending aorta are often difficult, and the arch vessel anastomosis is frequently performed at the dissected site. To reduce such problems, we performed total arch repair for acute type A aortic dissection with 2 modified techniques: open single-branched stent graft placement into the left subclavian artery and the descending aorta and reinforcement of the dissected arch vessel stump with a stent graft neoanastomosis. The initial clinical results show that open single-branched stent graft placement is a simple and effective technique for total arch repair that avoids left subclavian artery anastomosis and distal anastomosis at the descending aorta, and reinforcement of the dissected arch vessel stump with stent graft neoanastomosis is a feasible and effective technique to provide a strong dissected arch vessel stump. Therefore, with these 2 new techniques, total arch repair may become easier and safer for acute type A aortic dissection. Rigorous long-term follow-up and further extensive clinical trials are necessary before these 2 techniques can become a recommendable alternative to conventional total arch repair for acute type A aortic dissection.

**Conclusions:** Open single-branched stent graft placement into the left subclavian artery and the descending aorta and reinforcement of the dissected arch vessel stump with a stent graft neoanastomosis are 2 simple and effective techniques that should make total arch repair an easier and safer procedure for acute type A aortic dissection.\(^1\)\(^5\)

**Sensitivity of the Aortic Dissection Detection Risk Score, a Novel Guideline-Based Tool for Identification of Acute Aortic Dissection at Initial Presentation: Results From the International Registry of Acute Aortic Dissection**

**Summary:** Acute aortic dissection is known to be an underrecognized condition at presentation, yet the mortality associated with delayed or missed diagnosis is substantial. The American Heart Association, American College of Cardiology, and other professional societies recently published the 2010 thoracic aortic disease guidelines, which include recommendations for the initial bedside screening of at-risk patients. The goal of these recommendations is to improve physician recognition and facilitate prompt diagnostic testing in those at risk. In our study, we modified this guideline-based screening tool to define the aortic dissection detection risk score, which divides patients into low-, intermediate-, and high-risk groups on the basis of historical and examination features. We then tested the aortic dissection detection risk score for sensitivity among 2538 patients enrolled in the International Registry of Acute Aortic Dissection. Our results indicate that the aortic dissection detection risk score is 95.7% sensitive for the detection of acute aortic dissection and may help to facilitate prompt evaluation if applied at
the bedside. Additional studies are needed to determine the specificity of the aortic dissection detection risk score and provide prospective validation.

Conclusions: The clinical risk markers proposed in the 2010 thoracic aortic dissection guidelines and their application as part of the acute aortic dissection (ADD) risk score comprise a highly sensitive clinical tool for the detection of acute aortic dissection.

Preoperative Factors Associated With Adverse Outcome After Tricuspid Valve Replacement

Summary: Patients with severe tricuspid regurgitation (TR) may develop progressive biventricular dysfunction and have increased mortality. Referral for surgical correction is often delayed until patients develop significant heart failure. Appropriate patient selection and optimal timing for tricuspid valve replacement are crucial for optimal outcome, but there is a lack of objective criteria to guide clinicians. In the present study, we retrospectively analyzed preoperative clinical and echocardiographic parameters associated with operative and long-term mortality after tricuspid valve replacement surgery. A third of our patients had preoperative NYHA functional class IV, which suggests that surgical timing was late in many patients. Our main finding is that good outcomes for tricuspid valve replacement are achievable in properly selected patients. Operative mortality is reduced to around 6% when patients are operated on in an earlier symptomatic state (NYHA-I/IV), or when hemodynamically stable (no need for IABP). Furthermore, if operated on before echocardiographic evidence of increased RV filling pressure, survival may be improved even further. Therefore, establishment of guidelines using clinical and echocardiographic parameters is critically important. On the basis of our observations, we propose that surgical correction of severe TR should be considered before the development of advanced heart failure (NYHA functional class IV) or evidence of increased RV filling pressure as shown by pseudonormalization of RIMP ratio.

Conclusions: Tricuspid valve replacement for severe tricuspid regurgitation can be performed with an acceptable operative mortality if patients undergo surgery before the onset of advanced heart failure symptoms. Late mortality is associated with a high preoperative Charlson index, short right index of myocardial performance ratio, and advanced New York Heart Association class.

Incremental Prognostic Significance of Combined Cardiac Magnetic Resonance Imaging, Adenosine Stress Perfusion, Delayed Enhancement, and Left Ventricular Function Over Preimaging Information for the Prediction of Adverse Events

Summary: Cardiac MRI (CMR) is unique in its ability to provide assessment of hemodynamics, ventricular structure and function, valvular structure and function, myocardial viability, and stress perfusion. Various CMR-derived data are known to provide prognostic information. However, the relative incremental prognostic value of 4 CMR components (vasodilator stress perfusion, myocardial delayed enhancement, aortic blood flow, and left ventricular volumes) is unclear. We followed up 908 patients for a mean of 2.6±1.2 years after they underwent combined 4-component CMR for suspicion of coronary stenosis and/or ischemia. In total, 101 cardiac events were observed, including 30 cardiac deaths, 36 noncardiac deaths, 5 nonfatal myocardial infarctions, and 19 late revascularizations. Normal 4-component CMR was followed by a 2.4% annual cardiac event rate (<0.4% for cardiac death) whereas abnormal CMR had an event rate of 5.6% to 7.0%. The risk of cardiac events increased significantly with increasing number of abnormal CMR components. After we adjusted for pre-CMR data, the addition of left ventricular ejection fraction, aortic flow, delayed enhancement, and stress perfusion data all added incremental prognostic power. CMR components were additive, not redundant, in predicting risk. Future studies may define how each CMR component is best applied in clinical practice.

Conclusions: CMR analysis of ventricular volume, aortic flow, myocardial viability, and stress perfusion all add incremental value for prediction of adverse events over pre-CMR data and can be combined to further enhance prognostication. Normal combined CMR confers a low risk of subsequent cardiac events.

Upregulation of the 5-Lipoygenase Pathway in Human Aortic Valves Correlates With Severity of Stenosis and Leads to Leukotriene-Induced Effects on Valvular Myofibroblasts

Summary: Aortic valve stenosis is a complex potentially modifiable inflammatory process with a spectrum of disease ranging from aortic sclerosis to severe destroyed valvular architecture, akin to atherosclerosis, and has become the most common indication for surgical valve replacement. The diseased valve is characterized by pathological remodeling and pronounced calcification leading to obstruction of the left ventricle outflow tract. Factors predicting the transition from early potentially modifiable stages of the valvular disease to manifest stenosis have not yet been fully elucidated. Echocardiography is the key tool for assessment of stenosis severity, and clinical decision making is based on its results. The inflammatory environment within the affected aortic valve stimulates the 5-lipoygenase pathway leading to production of potent inflammatory mediators, leukotrienes. In the present study, a unique macroscopic dissection technique was used to model in vivo disease development, representing the entire disease spectrum from early signs to more advanced morphological changes. In addition, correlation analyses between echocardiographic parameters quantifying the stenosis severity and the quantitative gene expression data obtained from the thickened part revealed significant influence of several downstream components of the leukotriene pathway on stenosis severity in an early potentially modifiable stage of the valve disease. The translational implication of our data are that pharmacological intervention using leukotriene receptor antagonists could potentially retard the hemodynamic progression.

Conclusions: The upregulation of the LT pathway in human aortic valve stenosis and its correlation with clinical stenosis severity, taken together with the potentially detrimental LT-induced effects on valvular myofibroblasts, suggests one possible role of inflammation in the development of aortic stenosis.

Cardiac Raptor Ablation Impairs Adaptive Hypertrophy, Alters Metabolic Expression, and Causes Heart Failure in Mice

Summary: Mammalian target of rapamycin (mTOR) is an evolutionarily conserved kinase that regulates cell growth. Rapamycin is clinically used as an immunosuppressant and as potent antiproliferative agents; several rapalogs are in trials for cancer therapy. Rapamycin inhibits, at least in part, the activities of mTOR in mTOR complex (mTORC) 1, 1 of the 2 distinct multiprotein complexes in which mTOR is found. The recently developed active-site mTOR inhibitors inhibit mTORC1 and mTORC2. In the present study, we established that mTORC1 is essential for normal cardiac function and that its activity becomes even more important with increased cardiac work. Thus, deletion of raptor, an essential component of mTORC1, from cardiomyocytes in adult mice caused dilated cardiomyopathy within 6 weeks. Moreover, increased load by dynamic exercise or aortic constriction accelerated progression into heart failure without a prior phase of adaptive hypertrophy. This strengthens the perception that appropriate growth responses with intact signaling via the insulin/insulinlike growth factor/Akt/mTOR pathway are important when the heart has to generate more work, which applies to various clinical conditions such as hypertension, postin-
Permanent Pacemaker Insertion After CoreValve Transcatheter Aortic Valve Implantation: Incidence and Contributing Factors (the UK CoreValve Collaborative)

Summary: Transcatheter aortic valve implantation has entered mainstream interventional cardiology as a treatment for aortic stenosis in patients with prohibitively high operative risk. This is a growing cohort of patients globally, given the increased longevity and prevalence of significant comorbidities. The CoreValve Revalving system (CoreValve Medtronic, Luxembourg) is 1 of the 2 prostheses currently in use, and it has been noted to be associated with an increased need for permanent pacemaker implantation. This study represents the largest analysis of the rates of permanent pacemaker implantation in patients receiving a CoreValve implant and uses clinical ECG data to create an electroanatomic model to explain the phenomenon. Consideration of these factors as addressed in this study has not only implications for the future designs of transcatheter aortic valve implantation devices but also immediate clinical impact on the standard of care of this increasingly numerous patient group.

Conclusions: Patients with low-gradient “severe” aortic stenosis and normal ejection fraction have an outcome similar to that in patients with moderate stenosis.

Comparison of the Structure of the Aortic Valve and Ascending Aorta in Adults Having Aortic Valve Replacement for Aortic Stenosis Versus for Pure Aortic Regurgitation and Resection of the Ascending Aorta for Aneurysm

Summary: There is debate whether an aeurysmal ascending aorta should be replaced when associated with a dysfunctioning aortic valve that is to be replaced. We examined this issue by dividing the patients by type of aortic valve dysfunction—either aortic stenosis (AS) or pure aortic regurgitation (AR)—something not done previously. Of the 59 AS patients, 58 (98%) had a congenitally malformed valve and 53 (90%) had only a zero or 1+ aortic medial elastic fiber loss (graded 0–4+). In contrast, of the 63 pure AR patients, 38 had a bicuspid valve and 20 of them had zero or 1+ EFL and 18 had 2+ to 4+ EFL; of the 25 with pure AR and tricuspid aortic valves, all 13 with the Marfan syndrome had severe (3+ or 4+) EFL and the 12 without this syndrome had either zero or 1+ EFL. These data strongly suggest that when ascending aortic aneurysm is associated with aortic valve disease, the type of valve dysfunction—AS or pure AR—is very helpful in predicting aortic medial elastic fiber loss.

Conclusions: These data strongly suggest that the type of aortic valve dysfunction—AS versus pure AR—is very helpful in predicting loss of aortic medial elastic fibers in patients with ascending aortic aneurysms and aortic valve disease.

Outcome of Patients With Low-Gradient “Severe” Aortic Stenosis and Preserved Ejection Fraction

Summary: This is the first prospective study to determine the outcome of patients with low-gradient “severe” aortic valve stenosis, defined as a severe stenosis based on aortic valve area (<1.0 cm²) and a noneverse stenosis based on mean pressure gradient (≤40 mm Hg). In an analysis of 1525 patients with preserved ejection fraction from the Ezitimibe/Simvastatin in Aortic Stenosis (SEAS) trial, we confirm that this clinically challenging finding is also present in 29% of asymptomatic patients, similar to the percentage observed in unselected patients evaluated for aortic stenosis. The associated echocardiographic characteristics (eg, left ventricular mass) denote no more than moderate aortic valve disease. Comparison to patients with moderate stenosis (aortic valve area 1.0 to 1.5 cm²/mean pressure gradient 25–40 mm Hg) shows a similar progression rate to truly severe stenosis (aortic valve area <1.0 cm²/mean pressure gradient >40 mm Hg) and overall outcome during 46 months of follow-up (aortic valve events 48.5% versus 44.6%; P=0.37). These results indicate a markedly better prognosis in patients with low-gradient “severe” aortic stenosis than suggested in recent retrospective studies. According to our results, patients with low-gradient “severe” aortic stenosis can be managed with serial clinical and echocardiographic evaluations. Surgery is recommended only when symptoms can clearly be attributed to aortic stenosis or other indications according to prevailing guidelines.

Conclusions: Patients with low-gradient “severe” aortic stenosis and normal ejection fraction have an outcome similar to that in patients with moderate stenosis.
Remote Ischemic Preconditioning Protects the Brain Against Injury After Hypothermic Circulatory Arrest

**Summary:** In the repair of complex congenital heart defects or in surgery of the aortic arch, normal circulation may be temporarily halted to ensure a clean bloodless operation field. The brain is the organ most vulnerable to ischemic injury during this period of hypothermic circulatory arrest (HCA), and the mortality and morbidity of these procedures today consists largely of neurological complications. Ischemic preconditioning, a plausible neuroprotective strategy, describes a concept whereby brief exposure to ischemia, in a dose below the threshold for tissue injury, provides robust protection against the injurious effects of a subsequent more severe insult. In remote ischemic preconditioning, intermittent ischemia is induced in a nontarget tissue such as the limb, and the signal is thought to spread systemically by a mechanism that includes activation of the autonomic nervous system and as yet unidentified humoral mediators. Our study demonstrates that the neuroprotective effect after a series of blood pressure cuff inflations of the hind leg before HCA in a surviving porcine model was associated with a significant reduction in some important markers of neurological injury, accelerated neurological recovery and mitigated cerebral histopathologic findings. Remote ischemic preconditioning might be neuroprotective in patients undergoing surgery with HCA and improve long-term outcomes. If intermittent limb occlusions are shown consistently to reduce neurological injury during complex cardiac surgery with HCA, clinical implications can be very important. The intervention is practical, cost effective, and noninvasive. Clinical trials to further investigate its applications are warranted.

**Conclusions:** These data demonstrate that remote ischemic preconditioning (RIPC) protects the brain against HCA-induced injury, resulting in accelerated recovery of neurological function. RIPC might be neuroprotective in patients undergoing surgery with HCA and improve long-term outcomes. Clinical trials to test this hypothesis are warranted.

**Blocking the NOTCH Pathway Inhibits Vascular Inflammation in Large-Vessel Vasculitis**

**Summary:** Giant cell arteritis (formerly called temporal arteritis) is an inflammatory vasculopathy that causes aortic wall damage and lumen-stenosing lesions in medium-sized arteries. Giant cell arteritis preferentially targets extracranial branches of the aorta, resulting in ischemic optic neuropathy, stroke, pulsatility, and aortic aneurysm/dissection. If diagnosed and treated promptly, ischemic organ damage such as blindness can be prevented. The standard of care is anti-inflammatory and immunosuppressive therapy. If disease activity is high, treatment with steroids or azathioprine is indicated. Although advances in surgical and myocardial preservation techniques have substantially reduced the operative risks associated with cardiac surgery, aortic valve replacement surgery is increasingly being performed in elderly high-risk patients who are at high risk of hemodynamic insults such as low cardiac output syndrome. In this single-center, randomized, double-blind, placebo-controlled trial in patients undergoing aortic valve replacement, glucose-insulin-potassium improved the hemodynamic status of treated patients compared with those on placebo. The mechanisms contributing to this beneficial effect of glucose-insulin-potassium are complex and include metabolic enhancement. We demonstrate for the first time in humans that glucose-insulin-potassium augments myocardial signaling by increasing protein O-linked β-N-acetylglucosamination and cardioprotection during ischemia/reperfusion in humans.

**Conclusions:** Although advances in surgical and myocardial preservation techniques have substantially reduced the operative risks associated with cardiac surgery, aortic valve replacement surgery is increasingly being performed in elderly high-risk patients who are at high risk of hemodynamic insults such as low cardiac output syndrome. In this single-center, randomized, double-blind, placebo-controlled trial in patients undergoing aortic valve replacement, glucose-insulin-potassium improved the hemodynamic status of treated patients compared with those on placebo. The mechanisms contributing to this beneficial effect of glucose-insulin-potassium are complex and include metabolic enhancement. We demonstrate for the first time in humans that glucose-insulin-potassium augments myocardial signaling by increasing protein O-linked β-N-acetylglucosamination of selective proteins and Akt/S6-AMP-activated protein kinase phosphorylation. Although requiring replication, this study provides a rationale for the instigation of glucose-insulin-potassium during cardiac surgery and mandates a more detailed assessment of the link between O-linked β-N-acetylglucosamination and cardioprotection during ischemia/reperfusion in humans.

**Glucose-Insulin-Potassium Reduces the Incidence of Low Cardiac Output Episodes After Aortic Valve Replacement for Aortic Stenosis in Patients With Left Ventricular Hypertrophy: Results From the Hypertrophy, Insulin, Glucose, and Electrolytes (HINGE) Trial**

**Summary:** Glucose-insulin-potassium is an effective treatment to prevent low cardiac output in patients undergoing aortic valve replacement. The HINGE trial was designed to test the hypothesis that glucose-insulin-potassium reduces the incidence of low cardiac output episodes after aortic valve replacement. The results of this trial demonstrate that glucose-insulin-potassium reduces the incidence of low cardiac output episodes after aortic valve replacement.

**Conclusions:** Perioperative treatment with glucose-insulin-potassium (GIK) was associated with a significant reduction in the incidence of low cardiac output state and the need for inotropic support. This benefit was associated with increased signaling protein phosphorylation and GlcNAcylation. Multicenter studies and late follow-up will determine whether routine use of GIK improves patient prognosis.

**Incidence and Predictors of Early and Late Mortality After Transcatheter Aortic Valve Implantation in 663 Patients With Severe Aortic Stenosis**

**Summary:** Transcatheter aortic valve implantation using the self-expandable CoreValve prosthesis was performed in 663 patients with severe aortic stenosis and high surgical risk in 14 Italian centers. Procedural success was 98% and in-hospital mortality was 0.98%. The mortality rates at 30 days and 1 year were 5.4% and 15.0%, respectively. Early mortality was acceptably low compared with the anticipated risk calculated by means of the EuroSCORE and was strongly associated with the occurrence of procedural complications. Late mortality continued to occur from 30 days to 1 year after TAVI, primarily as the effect of postprocedural paravalvular aortic regurgitation ≥2+ and nonvalve related comorbidities such as cerebrovascular disease, chronic kidney disease and heart failure. Clinical and hemodynamic benefits observed acutely after TAVI were sustained at 1 year.

**Conclusions:** Benefit of TAVI with the CoreValve Revalving System is maintained over time up to 1 year, with acceptable mortality rates at various time points. Although procedural complications are strongly associated with early mortality at 30 days, comorbidities and postprocedural paravalvular aortic regurgitation ≥2+ mainly impact late outcomes between 30 days and 1 year.
Valve Configuration Determines Long-Term Results After Repair of the Bicuspid Aortic Valve

Summary: Valve replacement has been a reliable therapy for bicuspid aortic valve dysfunction for decades. To minimize valve-related complications, repair techniques have been developed in the last 2 decades. Repair of the bicuspid valve has been less challenging geometrically because only 1 coaptation line has to be corrected. Different publications, however, have given a puzzling view of the functional results of reconstruction with generally excellent early results and a worrisome rate of midterm failures. In the present study, we found that repair, and new questions is that reconstruction of bicuspid aortic valves is worthwhile for the low prevalence of valve-related complications. Repair works well with excellent durability in certain anatomical situations but should be avoided, at least with current reconstructive techniques, in others. A strong influence of anatomical characteristics on long-term durability of repair was found, with commissural orientation and degree of annular dilatation as the 2 most important predictors. Repair also had to normalize cusp configuration to achieve a good long-term result. On the other hand, the findings also emphasize the fact that bicuspid anatomy is not constant but rather includes a wide spectrum of anatomical variations. It is unclear whether annular dilatation is determined by anatomy or the duration of regurgitation. Thus, we need to define whether it can be neutralized by earlier repair. Surgeons will have to develop new strategies to ultimately allow durable reconstructive surgery in a larger proportion of patients with this anomaly.

Conclusions: Reconstruction of bicuspid aortic valve can be performed reproducibly with good early results. Recurrence and progression of regurgitation, however, may occur, depending primarily on anatomical features of the valve.29

Survival Comparison of the Ross Procedure and Mechanical Valve Replacement With Optimal Self-Management Anticoagulation Therapy: Propensity-Matched Cohort Study

Summary: Survival in young adult patients after mechanical aortic valve replacement is reported to be significantly reduced compared with the general age- and gender-matched population, whereas survival after the Ross procedure is excellent and comparable to that in the general population. There is ongoing debate about whether the excellent survival rates observed in Ross patients are a consequence of a hemodynamically superior valve and low valve-related complications, small aortic root, and/or lack of myocardial contractile reserve on dobutamine stress test.

Conclusions: In patients with severe aortic stenosis and depressed left ventricular systolic function considered at high or prohibitive surgical risk, which includes patients with severe comorbidities, small aortic root, and/or lack of myocardial contractile reserve on dobutamine stress test.

Comparison Between Transcatheter and Surgical Prosthetic Valve Implantation in Patients With Severe Aortic Stenosis and Reduced Left Ventricular Ejection Fraction

Summary: Patients with severe aortic stenosis and reduced left ventricular ejection fraction have a poor prognosis with medical treatment but a high operative mortality when treated surgically. These patients pose an important challenge with regard to therapeutic management because they require a valve replacement procedure that ensures optimal valve hemodynamics with complete relief of left ventricular outflow obstruction while minimizing the operative risk. The results of the present study suggest that transcatheter aortic valve implantation may achieve both of these goals. The most important finding of this study is that, despite a much worse risk profile at baseline, transcatheter aortic valve implantation was associated with faster and better recovery of left ventricular ejection fraction compared to surgical aortic valve replacement. This benefit may be due, at least in part, to better periprocedural myocardial protection and superior prosthetic valve hemodynamics. Hence, transcatheter aortic valve implantation may provide a good alternative to surgical aortic valve replacement in patients with severe aortic stenosis and depressed left ventricular systolic function considered at high or prohibitive surgical risk, which includes patients with severe comorbidities, small aortic root, and/or lack of myocardial contractile reserve on dobutamine stress test.

Conclusion: In patients with severe aortic stenosis and depressed left ventricular (LV) systolic function, transcatheter aortic valve implantation (TAVI) is associated with better left ventricular ejection fraction (LVEF) recovery compared with surgical aortic valve replacement (SAVR). TAVI may provide an interesting alternative to SAVR in patients with depressed LV systolic function considered at high surgical risk.31

Volume-Outcome Relationships and Abdominal Aortic Aneurysm Repair

Summary: There is a well-established literature relating procedure volume to outcomes of care, but incorporating such information into clinical decision making is problematic when there is >1 treatment option for a particular condition. In the case of abdominal aortic aneurysm repair, surgeons may choose traditional open or endovascular repair. Because the approach is decided by the surgeon after referral, it is not clear whether the referring physician should consider overall abdominal aortic aneurysm repair volume or specific volumes for open and endovascular repair in their referral decisions. In this study, we used comprehensive data from the Medicare program over the years 2001 to 2006 to investigate the relationship between institutional volume and outcomes of abdominal aortic aneurysm repair. We found that whereas there is a relatively constant relationship between open repair and perioperative mortality, for endovascular repair there is a significant improvement in mortality from the lowest quintile of volume to the second lowest, but improvements beyond that volume are small. Because virtually all high-volume open repair facilities have at least modest endovascular volume, referral decisions should be made on the basis of open repair volume rather than total or endovascular repair volume. Our data also suggest the possibility that as endovascular repair increasingly replaces open repair, fewer hospitals will have adequate open repair volume to maintain the experience needed to achieve optimal outcomes.

Conclusions: We found a steady increase in survival with increasing volume of open repair but relatively little improvement after reaching a relatively low threshold for endovascular repair. Because hospital experience with one repair method does not translate into improved outcomes for the alternative method, referring clinicians must consider both treatment options when making referral decisions.32
Extensive Primary Repair of the Thoracic Aorta in Acute Type A Aortic Dissection by Means of Ascending Aorta Replacement Combined With Open Placement of Triple-Branched Stent Graft: Early Results

**Summary:** In surgical extensive primary repair of the thoracic aorta for acute type A aortic dissection, careful manipulation of the arch and elaborate anastomoses to the distal arch and 3 arch vessels are time-consuming and could induce phrenic and recurrent laryngeal nerve injury. Our results suggest that extensive primary repair of the thoracic aorta for acute type A aortic dissection can be performed simply by both open placement of the triple-branched stent graft into the proximal descending aorta, arch, and 3 arch vessels and graft replacement of the ascending aorta, which can reduce the risk and technical difficulties of extensive thoracic aorta repair to close to those of the conventional ascending graft replacement with open distal anastomosis. Therefore, with open placement of triple-branched stent graft, extensive primary repair of the thoracic aorta may become easier and safer for acute type A aortic dissection. Careful long-term follow-up and further extensive clinical use are necessary to completely evaluate the efficacy of this new technique.

**Conclusions:** Open triple-branched stent graft placement is an effective technique with satisfactory early results. With this technique, extensive primary repair of the thoracic aorta may become easier and safer for acute type A aortic dissection.

Transcatheter Aortic Valve Implantation: Durability of Clinical and Hemodynamic Outcomes Beyond 3 Years in a Large Patient Cohort

**Summary:** Transcatheter aortic valve implantation is rapidly gaining acceptance as a viable therapy for high-risk patients with severe symptomatic aortic stenosis. Thus far, short-term outcomes have been encouraging, with limited data beyond 1 year. The present study evaluated the medium- to long-term outcomes of an early cohort undergoing transcatheter aortic valve implantation, with all patients evaluated by follow-up at a minimum of 3 years from the procedure. The study demonstrated excellent durability, no evidence of structural valvular failure, and preserved hemodynamics. Small changes in valve area and transvalvular gradients were documented for the first time, which were generally similar to those in previously published surgical series that reported on bioprosthetic valves in the aortic position. Patients showed significant improvement in functional state, generally similar to those in previously published surgical series. Postprocedural aortic regurgitation was generally mild and did not appear to worsen over time. Detailed computed tomographic imaging demonstrated no evidence of valve fracture, deformation, or valve migration. At a median of 3.7 years, patients surviving more than 30 days after a successful procedure had a survival rate of 57%. The bulk of late mortality in this high-risk cohort was due to significant comorbidities and was generally unrelated to aortic valve disease. Overall, when used in patients who are deemed to be poor surgical candidates, transcatheter aortic valve implantation appears to offer an adequate and lasting resolution of symptomatic aortic stenosis.

**Conclusions:** Transcatheter aortic valve implantation demonstrates good medium- to long-term durability and preserved hemodynamic function, with no evidence of structural failure. The procedure appears to offer an adequate and lasting resolution of aortic stenosis in selected patients.

Importance of Refractory Pain and Hypertension in Acute Type B Aortic Dissection: Insights From the International Registry of Acute Aortic Dissection (IRAD)

**Summary:** Medical management is generally recommended for patients with uncomplicated acute type B aortic dissection (ABAD), whereas invasive treatment such as surgical or endovascular approaches is typically recommended for ABAD patients with complications such as malperfusion syndromes, extending dissection, or aortic rupture, who are defined as high risk. The optimal approach for uncomplicated ABAD patients who develop refractory/refractory pain or refractory hypertension is still being debated. We used data from the International Registry of Acute Aortic Dissection to better define the importance of refractory pain and/or refractory hypertension in ABAD. We found that in uncomplicated ABAD patients, medical therapy was associated with excellent outcomes, whereas the in-hospital mortality was considerably increased in those ABAD patients with refractory pain and/or refractory hypertension, especially when these patients underwent medical management. These observations suggest that ABAD patients presenting with refractory hypertension and/or pain symptoms in the absence of other complications are at intermediate risk for an adverse in-hospital outcome but still have a better outcome than the high-risk group. More invasive treatment, such as an endovascular approach, may be indicated in this intermediate-risk group.

**Conclusions:** Refractory pain and refractory hypertension appeared as clinical signs associated with increased in-hospital mortality, particularly when managed medically. These observations suggest that aortic intervention, such as via an endovascular approach, may be indicated in this intermediate-risk group.

Spectrum and Outcome of Reoperations After the Ross Procedure

**Summary:** Although this manuscript deals with a topic that is surgical in nature, it also provides valuable information to cardiologists, because they are involved in the preoperative consultation and the long-term follow-up of patients being considered for the Ross procedure. The Ross procedure is performed for aortic valve disease and is offered to patients in all age groups: infants, children, and adults. The operation is palliative, and the need for reintervention (percutaneous or surgical) over a lifetime is inevitable for the majority of patients. This study represents the largest reported series of patients undergoing reoperation after the Ross procedure to date. Although literature is available that quantifies the incidence of reoperation after the Ross procedure, there are no published reports that address the qualitative nature and risks associated with reoperation when it is required. This manuscript provides that “missing” information so the clinician can properly counsel patients not only about the potential need for reoperation but also about the nature of the reoperation when it is necessary.

**Conclusions:** A broad spectrum of complex reoperations may be required after the Ross procedure. Patients and family members considering the procedure should be informed of the potential for associated morbidity should reoperation be necessary.

Maladaptive Aortic Properties in Children After Palliation of Hypoplastic Left Heart Syndrome Assessed by Cardiovascular Magnetic Resonance Imaging

**Summary:** In children with hypoplastic left heart syndrome, the status of the reconstructed aorta after the Norwood operation is of potential prognostic importance. Dilatation and an impaired distensibility of the neoaorta have already been reported in previous echocardiographic and angiocardiographic studies. However, com-
prehensive data on the anatomic and functional properties of the reconstructed aorta and their potential influence on right ventricular function in hypoplastic left heart syndrome are still lacking. The present study used cardiovascular MRI to evaluate the anatomy, bioelastic properties, viability of the aorta and right ventricular ejection fraction in 40 patients with hypoplastic left heart syndrome. Compared with control subjects, patients with hypoplastic left heart syndrome had an increased aortic size and reduced aortic bioelasticity (distensibility and pulse-wave velocity). Fibrosis was detected with cardiovascular MRI in the proximal aorta using the well-proven late gadolinium enhancement technique. Aortic late gadolinium enhancement correlated inversely with reduced right ventricular ejection fraction and distensibility in the ascending aorta. These findings suggest unfavorable aortic-ventricular coupling, which may contribute to a higher risk for later right ventricular failure. This study may help improve our understanding of aortic biophysical properties after extensive surgical reconstruction of the aorta. The results may serve as baseline data for further longitudinal studies in children with hypoplastic left heart syndrome to establish the prognostic value of anatomic and bioelastic aortic properties measured by cardiovascular MRI.

Conclusions: Adverse aortic properties post palliation of hypoplastic left heart syndrome manifest themselves by aortic dilatation, decreased distensibility, and increased volume of nonviable aortic wall tissue. The negative association between aortic late gadolinium enhancement and right ventricular ejection fraction suggests unfavorable aortic-ventricular coupling. The potential impact of these findings on long-term right ventricular function should be evaluated in future studies.37

Differential Cardiac Remodeling in Preload Versus Afterload

Summary: Hemodynamic load regulates myocardial function and gene expression. Increased load triggers molecular, structural, and functional remodeling and eventually heart failure. Increased left ventricular load acts either as preload because of left to right shunt or aortic or mitral regurgitation or as increased afterload because of aortic stenosis or arterial hypertension. In the present study, different cardiac gene expression, signaling, and remodeling with preload or afterload were studied in mice with aortocaval shunt (preload) or aortic stenosis or arterial hypertension. In the present study, different gene expression. Increased preload results in a more favorable type of diastolic dysfunction, suggesting an interaction between excess mineralocorticoid and aldosterone, which may promote the transition from hypertensive heart disease to overt heart failure with preserved ejection fraction, is controversial. In this study, we show that oxidative stress is induced in the hypertensive heart and sensitizes the heart to exogenous mineralocorticoids. In normal mice, exogenous mineralocorticoid had little effect on cardiac structure or function. Mice with pressure-overload hypertrophy had increased myocardial oxidative stress, and in these mice, exogenous mineralocorticoid accentuated hypertrophy, fibrosis, and diastolic dysfunction, suggesting an interaction between excess mineralocorticoid (inappropriate for salt status) and oxidative stress. Interestingly, this effect was observed without evidence of classic mineralocorticoid receptor–mediated gene transcription in the heart (“nongenomic” effects) and independently of changes in the magnitude of pressure overload. These results suggest that aldosterone excess may promote the transition from compensated hypertensive heart disease to heart failure with preserved ejection fraction via nongenomic effects or alternatively through effects on noncardiac cells. Because the nongenomic effects of aldosterone are exerted both via the mineralocorticoid receptor and independent from the mineralocorticoid receptor, development of novel antagonists that...
Relationship of Intraoperative Cerebral Oxygen Saturation to Neurodevelopmental Outcome and Brain Magnetic Resonance Imaging at 1 Year of Age in Infants Undergoing Biventricular Repair

Summary: This study explored whether intraoperative cerebral oxygen saturation (rSO2) measured by near-infrared spectroscopy was associated with neurodevelopmental outcomes at age 1 year among infants undergoing biventricular repair without aortic arch reconstruction. Lower Psychomotor Development Index of the Bayley Scales was modestly associated with lower rSO2 during the 60-minute period after cardiopulmonary bypass and at the time points of 10 minutes of cooling, off-cardiopulmonary bypass, and 60 minutes after cardiopulmonary bypass. Lower rSO2 from postinduction to 60 minutes after cardiopulmonary bypass was associated with hemosiderin foci on qualitative MRI analysis. No relationship could be demonstrated between rSO2 and the Mental Development Index of the Bayley Scales, neurological examination, or head circumference. The relationship of lower rSO2 with lower Psychomotor Development Index score and greater risk of hemosiderin on brain MRI, even after adjustment for age ≤30 days or diagnosis group, suggests that periods of intraoperative and early postoperative decreased cerebral oxygen delivery are associated with adverse longer-term neurodevelopmental outcomes.

Conclusions: Perioperative periods of diminished cerebral oxygen delivery, as indicated by rSO2, are associated with 1-year Psychomotor Development Index and brain MRI abnormalities among infants undergoing reparative heart surgery.

Equilibrium Contrast Cardiovascular Magnetic Resonance for the Measurement of Diffuse Myocardial Fibrosis: Preliminary Validation in Humans

Summary: Diffuse myocardial fibrosis is a final common end point in cardiovascular disease and is associated with symptoms, impaired ventricular function, and adverse prognosis. Even though it is thought to be a key “missing parameter” in clinical cardiology, and it is a target for many therapies (eg, angiotensin-converting enzyme inhibitors, aldosterone antagonists), it can only be quantified by histology on biopsy, with inherent risk and sampling error. As a result, it is not well understood in the clinical arena. Echocardiographic surrogates such as markers of diastolic dysfunction are unsatisfactory because they are influenced by multiple other factors. We developed and performed initial validation for a new technique, equilibrium contrast cardiovascular magnetic resonance (EQ–CMR), as a method to quantify diffuse myocardial fibrosis. We designed it to be easy to implement on any scanner. EQ–CMR involves standard MRI technology and contrast agent and can be integrated into a standard CMR protocol. We have shown that EQ–CMR correlates with histological fibrosis in 2 conditions, aortic stenosis and hypertrophic cardiomyopathy. This work is at an early stage, but it appears that, for the first time, it is possible to measure the diffuse myocardial fibrosis burden noninvasively. With further work, this technique could have widespread implications in disease characterization, monitoring, outcome prediction, and therapeutics.

Conclusions: We have developed and validated a new technique, EQ–CMR, to measure diffuse myocardial fibrosis as an add-on to a standard CMR scan, which allows for the noninvasive quantification of the diffuse fibrosis burden in myocardial diseases.

Thirty-Day Results of the SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry: A European Registry of Transcatheter Aortic Valve Implantation Using the Edwards SAPIEN Valve

Summary: The 30-day SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry results represent the most contemporary results that can be expected with the Edwards SAPIEN valve. These data give the interventional community a benchmark from which they can assess future patient cohorts and results. In addition, they allow physicians performing this procedure to accurately refer these high-risk aortic valve patients for the transcatheter aortic valve implantation procedure. Thirty-day mortality was 8.5% overall, 6.3% for the transfemoral approach, and 10.3% for the transapical approach. The transapical patients were a higher-risk cohort; the logistic EuroSCORE was 29.1% in the transapical group and 25.7% in the transfemoral group. The stroke rate was 2.5%. The requirement for permanent pacemaker was 7%. The major vascular complication rate was 10.6% for the transfemoral approach, but unlike previous studies, this was not associated with an increased mortality. However, a major vascular complication of the transapical approach did result in increased mortality. Any future change in the technology or procedure will be able to be assessed against these results of a consecutive group of patients undergoing the procedure in centers with surgeons experienced in or new to the procedure.

Conclusions: Technical proficiency can be learned and adapted readily as demonstrated by the short-term procedural success rate and low 30-day mortality rates reported in the SOURCE Registry. Specific complication management and refinement of patient selection are needed to further improve outcomes.

Survival of Kidney Transplantation Patients in the United States After Cardiac Valve Replacement

Summary: Valvular heart disease is common in patients with end-stage renal disease. In hemodialysis patients, use of bioprosthetic heart valves was prescribed in past American College of Cardiology/American Heart Association guidelines, reflecting a widely held (but poorly substantiated) perception that bioprosthetic valve failure mandated mechanical prosthetic valves in these patients. In 2006, revised practice guidelines rescinded the prescription. Estimated 2-year mortality of dialysis patients is 60% after heart valve replacement surgery, with no difference in survival for tissue versus nontissue valves. Data on long-term survival of kidney transplantation patients after cardiac valve replacement are few. In this study, we identified 1335 kidney transplantation patients receiving left-sided cardiac valve replacement from 1991 to 2004. Use of tissue valves increased over time (28% overall, 38% in 2000–2004). Mortality risk associated with use of tissue (versus nontissue) valves was minimally reduced. In-hospital mortality was 14.0% overall, 11.4% for tissue-valve patients, and 15.0% for nontissue-valve patients (P = 0.09), and estimated 2-year survival was 61.5% for tissue-valve and 59.5% for nontissue-valve patients (P = NS). The adjusted hazard ratio of death for tissue-valve versus nontissue-valve patients was 0.83 (95% confidence interval, 0.70–0.99). Hospitalizations for endocarditis and gastrointestinal hemorrhage were common (~5%/yr) but not related to valve type. Regardless of the prosthetic valve type, overall 2-year mortality of renal transplantation patients after left-sided cardiac valvular replacement is 40%. The additional requirement for long-term anticoagulation with nontissue valves might support the preferential use of tissue valves by clinicians and their patients who wish to avoid warfarin therapy.

Conclusions: Renal transplantation patients requiring valve replacement have high mortality rates (~20%/yr). These data suggest
Outcomes of Endovascular Repair of Ruptured Descending Thoracic Aortic Aneurysms

Summary: Thoracic endovascular aortic repair has recently offered a less invasive approach, compared with traditional open surgical repair, for the management of ruptured descending thoracic aortic aneurysms. Due to the low incidence, the exact outcome of endovascular management of this emergency is not well known. In the present multicenter study, we found that endovascular repair of ruptured descending thoracic aortic aneurysms was associated with encouraging results, which appeared to be superior to the historic results of open repair. An increased mortality was observed after endovascular management of patients with hypovolemic shock and/or hemothorax at presentation. During follow-up, the incidence of endograft-related complications such as endoleak was considerable, and several patients died as a result of an infected endograft. The findings of the current study suggest that a preferential endovascular approach for the management of ruptured descending thoracic aortic aneurysms may be appropriate; however, it emphasizes the need for continued surveillance during follow-up and perhaps improvement of current endovascular devices.

Conclusion: Endovascular repair of ruptured descending thoracic aortic aneurysms is associated with encouraging results. The endovascular approach was associated with considerable rates of neurological complications and procedure-related complications such as endoleak.

Prosthesis-Patient Mismatch Predicts Structural Valve Degeneration in Bioprosthetic Heart Valves

Summary: Prosthesis-patient mismatch can be predicted at the time of operation. On the basis of this information, the surgical technique and/or the selection of the prosthesis can be modified to prevent prosthesis-patient mismatch or reduce its severity. By avoiding prosthesis-patient mismatch, the incidence of structural valve deterioration should be reduced by ≥50%, which in turn can influence the choice for a bioprosthetic valve instead of a mechanical one. Furthermore, because intrinsically stentless bioprostheses are less prone to prosthesis-patient mismatch, this type of bioprosthesis should then be preferred over stented valves.

Conclusions: These data suggest that stenosis-type structural valve degeneration (SVD) is an early, prosthesis-patient mismatch (P-PtM)-related, and thus preventable phenomenon. Incompetence-type SVD is a time-dependent, nonspecific wear damage to bioprosthetic valves, which is not related to P-PtM.

Transcatheter Valve-in-Valve Implantation for Failed Bioprosthetic Heart Valves

Summary: The majority of prosthetic heart valves currently implanted are tissue valves that can be expected to degenerate with time and eventually fail. Repeat cardiac surgery to replace these valves is associated with significant morbidity and mortality. Transcatheter heart valve implantation within a failed bioprosthesis, a “valve-in-valve” procedure, may offer a less invasive alternative. Valve-in-valve implantations were performed in 24 high-risk patients. Failed valves were aortic (n=10), mitral (n=7), pulmonary (n=6), or tricuspid (n=1) bioprostheses. Implantation was successful with immediate restoration of satisfactory valve function in all but 1 patient. No patient had more than mild regurgitation after implantation. No patients died during the procedure. Thirty-day mortality was 4.2%. Mortality was related primarily to learning-curve issues early in this high-risk experience. New York Heart Association functional class improved in most patients. At a median follow-up of 135 days and a maximum follow-up of 1045 days, 91.7% of patients remained alive with satisfactory valve function. Transcatheter valve-in-valve implantation is a reproducible option for the management of bioprothetic valve failure. Aortic, pulmonary, mitral, and tricuspid tissue valves were amenable to this approach. This finding may have important implications with regard to valve replacement in high-risk patients.

Conclusion: Transcatheter valve-in-valve implantation is a reproducible option for the management of bioprosthetic valve failure. Aortic, pulmonary, mitral, and tricuspid tissue valves were amenable to this approach. This finding may have important implications with regard to valve replacement in high-risk patients.

Early Surgery Versus Conventional Treatment in Asymptomatic Very Severe Aortic Stenosis

Summary: Management of asymptomatic patients with very severe aortic stenosis remains controversial, and the combined risks of aortic valve surgery and late complications of aortic valve prosthesis need to be balanced against the possibility of preventing sudden death and lowering cardiac mortality. We prospectively evaluated 197 consecutive asymptomatic patients with very severe aortic stenosis to compare clinical outcomes of early surgery with those of the conventional treatment strategy. Very severe aortic stenosis was defined as a critical stenosis in the aortic valve area ≤0.75 cm² accompanied by a peak aortic jet velocity ≥4.5 m/s or a mean transaortic pressure gradient ≥50 mm Hg on Doppler echocardiography. Early surgery was performed on 102 patients, and a conventional treatment strategy was used for 95 patients. There were no operative deaths and no cardiac deaths in the early surgery group compared with 18 cardiac deaths in the conventional treatment group, and the risk of all-cause mortality was significantly lower in the early surgery group than in the conventional treatment group (hazard ratio, 0.135; 95% confidence interval, 0.030–0.597; P=0.008). Compared with the conventional treatment strategy, early surgery is associated with improved long-term survival by effectively decreasing cardiac mortality and sudden cardiac death. This result suggests that early surgery can be a therapeutic option to further improve clinical outcomes in asymptomatic patients with very severe aortic stenosis and low operative risk. A prospective randomized trial is required to confirm the efficacy of early surgery.

Conclusions: Compared with the conventional treatment strategy, early surgery in patients with very severe aortic stenosis is associated with an improved long-term survival by decreasing cardiac mortality. Early surgery is therefore a therapeutic option to further improve clinical outcomes in asymptomatic patients with very severe aortic stenosis and low operative risk.

Complement Regulator CD59 Protects Against Angiotensin II–Induced Abdominal Aortic Aneurysms in Mice

Summary: Aneurysm, including abdominal aortic aneurysm (AAA), is considered an immune and inflammatory disease. Complement is a main effector of the immune response and inflammation. However, the role of complement in the aneurysm pathogenesis has not been extensively investigated. The complement system is activated by 3 activation cascades, which lead to formation of the membrane attack complex (MAC). MAC, a macromolecular pore capable of inserting itself into cell membranes and lysing heterologous cells and bacteria, is an important mediator of cellular signals, including nuclear factor-κB and activator protein-1, which trigger mitogenic effects. To protect autologous cells from MAC, an array of complement regulators, including CD59, have evolved to restrict complement activation. CD59 strongly restricts MAC formation. Here, we demonstrated that in the angiotensin-induced abdominal aortic aneurysm model, deficiency of CD59 in ApoE-null mice accelerated the abdominal aortic aneurysm development, whereas transgenic overexpression of CD59 attenuated the abdominal aortic aneurysm progression. The severity of aneurysm positively correlates with C9
deposition, the activities of matrix metalloproteinase-2 and -9, and the levels of phosphorylated c-Jun, c-Fos, IKK-α/β, and p65. Furthermore, we demonstrated that MAC directly induced gene expression of matrix metalloproteinase-2 and -9 in vitro, which depended on the activation of the activator protein-1 and nuclear factor-κB signaling pathways. Together, these results shed light on the important pathogenic role of MAC in aneurysm, point toward the molecular mechanism of MAC-activated signaling pathways in aneurysm, and suggest that inhibition of MAC may provide a novel approach for the treatment/prevention of aneurysm.

**Conclusion:** Together, these results defined the protective role of CD59 and shed light on the important pathogenic role of the membrane attack complex in abdominal aortic aneurysm.

**Regular Exercise Training Prevents Aortic Valve Disease in Low-Density Lipoprotein–Receptor–Deficient Mice**

**Summary:** Calcified aortic valve (AV) stenosis is a large and growing health problem with no alternatives to costly invasive treatment in Western countries. Thus, the optimum timing of novel therapy for the prevention of calcified AV disease is an active area of investigation. AV sclerosis can develop into AV stenosis in many patients. In addition, severe valve calcification indicates a rapid disease progression and poor prognosis in patients with AV stenosis. Thus, an effective intervention at an earlier stage of disease before the development of severe valve calcification (eg, AV sclerosis) would have major clinical benefits. The present study demonstrated that regular exercise training but not occasional exercise training prevented AV sclerosis in mice via numerous favorable mechanisms, including preservation of valvular endothelial integrity and a subsequent decrease in recruitment of inflammatory cells, oxidative stress, and the osteogenic process. These novel findings indicate that regular physical activity may be recommended for prevention of the early stage of calcified AV disease. Accumulated evidence suggests that several cardiovascular risk factors are associated with AV sclerosis/stenosis and that the metabolic syndrome is associated with an increased prevalence of AV calcium or progression of AV stenosis. The metabolic syndrome is a potentially preventable and treatable condition that results primarily from a sedentary lifestyle. Many of the features of the metabolic syndrome are not reversed by the pharmacological treatment of traditional risk factors (eg, statins). Therefore, regular exercise training is warranted and may represent a promising intervention to reduce the incidence and mortality of calcified AV stenosis, particularly at an early stage of disease.

**Conclusions:** In the low-density lipoprotein–receptor–deficient mouse, regular exercise training prevents aortic valve sclerosis by numerous mechanisms, including preservation of endothelial integrity, reduction in inflammation and oxidative stress, and inhibition of the osteogenic pathway.

**Arterial Stiffness and Cardiovascular Events: The Framingham Heart Study**

**Summary:** Various measures of arterial stiffness and wave reflection have been proposed as cardiovascular risk markers; however, no community-based study has compared prognostic utility of pulse wave velocity (PWV), central pulse pressure, and augmentation index. In our study of 2232 Framingham Heart Study participants, after adjustment for risk factors (age, sex, systolic blood pressure, use of antihypertensive therapy, total and high-density lipoprotein cholesterol concentrations, smoking, and presence of diabetes mellitus), a SD increase in carotid-femoral (aortic) PWV was associated with a 48% increase in risk for a first major cardiovascular disease event. Measurement of PWV is noninvasive, safe, and readily implemented in an office setting with inexpensive equipment and a modest amount of training. Aortic PWV is strongly associated with risk, is abnormal in a substantial proportion of middle-aged and older people, and is only modestly correlated with standard risk factors, suggesting that attention should be focused on aortic PWV as a biomarker of cardiovascular risk. The combination of aging of the world population, increasing aortic PWV with age, and increased risk with higher aortic PWV portends a major increase in the burden of disease potentially attributable to abnormal aortic stiffness. These observations suggest a need to identify and implement interventions that limit or reverse arterial stiffening.

**Conclusions:** Higher aortic stiffness assessed by PWV is associated with increased risk for a first cardiovascular event. Aortic PWV improves risk prediction when added to standard risk factors and may represent a valuable biomarker of cardiovascular disease risk in the community.

**Nox Activator 1: A Potential Target for Modulation of Vascular Reactive Oxygen Species in Atherosclerotic Arteries**

**Summary:** After decades of investigation, there remains a need for preventive strategies that can reduce atherosclerosis and atherothrombosis, which are the most common causes of death and disability in the United States. Despite many important advances in the treatment of cardiovascular diseases, elucidation of specific therapies that target vascular wall cells has been elusive. An important limitation of targeting intracellular signaling pathways in dysfunctional vascular cells is that most of them are present ubiquitously and are necessary for normal cellular function. Many investigators have studied the hypothesis that regulated production of reactive oxygen species and oxidative stress in vascular cells are important in atherogenesis and that it may be possible to specifically inhibit upregulation of reactive oxygen species production in vascular cells, and in doing so, limit atherogenesis and atherothrombosis. The pathways that produce reactive oxygen species—NADPH oxidase, xanthine oxidase, cyclooxygenase, lipogenase, and others—are necessary, however, for normal cellular function. The experiments described here were designed to test the strategy of targeting a specific component of NADPH oxidase, arguably the most important regulated system for reactive oxygen species production in vascular cells. To do so, we examined modulation of Nox1, an NADPH oxidase component necessary for upregulation of superoxide production in vascular smooth muscle cells. Our studies indicate that Nox1 is critically important in the NADPH oxidase–mediated overexpression of reactive oxygen species characteristic of vascular diseases. Although specific inhibitors of Nox1 are not known, this work suggests that the strategy of cell-specific modulation of NADPH oxidase function is a therapeutic approach worthy of further investigation.

**Conclusions:** Nox1 is the functional homolog of p67phox in vascular smooth muscle cells (VSMCs) that regulates redox signaling and VSMC phenotype. These findings support the potential for modulation of Nox1 expression as a viable approach for the treatment of vascular diseases.

**Effect of Lipid Lowering With Rosuvastatin on Progression of Aortic Stenosis: Results of the Aortic Stenosis Progression Observation: Measuring Effects of Rosuvastatin (ASTRONOMER) Trial**

**Summary:** Aortic stenosis is an active process with many similarities to atherosclerosis. Animal studies and retrospective clinical studies have shown statins to be effective in reducing the progression of aortic stenosis. In a randomized, double-blind, placebo-controlled trial of 269 patients with a median follow-up of 3.5 years, we assessed the effect of rosvastatin 40 mg daily on the progression of aortic stenosis in asymptomatic patients with mild to moderate aortic stenosis and no
indication for lipid-lowering therapy. We showed that intensive lipid lowering with rosuvastatin was no better than placebo in reducing the progression of aortic stenosis. The lack of benefit was observed in predefined subgroups, including younger patients, patients with milder aortic stenosis, patients with bicuspid aortic valve, and patients with little or no aortic valve calcification. Our findings are consistent with the results of the Scottish Aortic Stenosis and Lipid Lowering Trial, Impact on Regression (SALTIRE) and Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) trials, showing that lipid lowering does not affect the progression of aortic stenosis in patients with no clinical indications for lipid lowering.

Conclusion: Cholesterol lowering with rosuvastatin 40 mg did not reduce the progression of aortic stenosis (AS) in patients with mild to moderate AS; thus, statins should not be used for the sole purpose to reduce the progression of AS.53

Natural History of Very Severe Aortic Stenosis

Summary: This is the first study to assess the outcome of a large series of asymptomatic patients with very severe aortic stenosis managed according to current guidelines. One hundred sixteen consecutive asymptomatic patients with isolated very severe aortic stenosis defined by a peak aortic jet velocity ≥5.0 m/s were prospectively followed up for a median of 61 months. Event-free survival rate (indication for surgery, 90; cardiac death, 6) was poor for patients with a peak aortic jet velocity between 5.0 and 5.5 m/s (n=72), with 76%±5% at 1 year, 43±6% at 2 years, 33±6% at 3 years, and 17±5% at 4 years; it was even worse for patients with a peak aortic jet velocity ≥5.5 m/s (n=44), with 42±8% at 1 year, 25±7% at 2 years, 11±5% at 3 years, and 4±4% at 4 years (P<0.0001). In comparison, event-free survival rate for a series of 82 patients with severe aortic stenosis defined by a peak aortic jet velocity between 4.0 and 5.0 m/s was 82±4% at 1 year, 70±5% at 2 years, 49±6% at 3 years, and 39±16% at 4 years. Furthermore, 6 cardiac deaths occurred in previously asymptomatic patients with very severe aortic stenosis, and symptom onset was more severe for patients with higher peak aortic jet velocities. Peak aortic jet velocity thus yields important prognostic information in the group of patients with severe aortic stenosis. Because of the high event rate and the possibility of rapid deterioration, considering early elective surgery might be worthwhile in patients with very severe aortic stenosis even when they are still asymptomatic.

Conclusions: Despite being asymptomatic, patients with very severe aortic stenosis have a poor prognosis with a high event rate and a risk of rapid functional deterioration. Early elective valve replacement surgery should therefore be considered in these patients.54

References
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The Editors

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