Learning Minimally Invasive Mitral Valve Surgery: A Cumulative Sum Sequential Probability Analysis of 3895 Operations From a Single High-Volume Center

Minimally invasive operations have gained wider acceptance in the field of cardiac surgery during the last decade. Despite the obvious advantages, these operations have been challenged for delivering the same results as conventional surgery. Particular concerns have been raised because an additional learning phase is required. However, the often cited learning curves have barely been examined methodically. The purpose of this study was to assess the learning process involved in the performance of minimally invasive surgery of the mitral valve. It comprises a frank analysis of the past and delivers insight in the current training program and its monitoring. It also shows the usefulness of the sequential probability cumulative sum failure analysis as an easy tool for early detection of systemic problems. We found that a true learning curve exists for minimally invasive surgery of the mitral valve operations. Although the number of operations required to overcome the minimally invasive surgery of the mitral valve learning curve is substantial, marked variation exists between individual surgeons. For some surgeons, the analysis even resulted in retraining under supervision. Such information could be very helpful in structuring future training and maintenance of competence programs for this kind of surgery. See p 483.

Acute Rheumatic Fever and Rheumatic Heart Disease: Incidence and Progression in the Northern Territory of Australia, 1997 to 2010

This is the first time that longitudinal data from a registry have been analyzed on the presentation and progression of acute rheumatic fever and rheumatic heart disease, conditions that continue to cause a large burden of morbidity and mortality in developing populations. This article analyzes data collected over a 13-year period in an area of high prevalence of acute rheumatic fever/rheumatic heart disease (the Northern Territory of Australia) and provides insights into trends in incidence, recurrence, and presentation over time. To the best of our knowledge, this is the only in-depth analysis in the last half-century of the progression of disease. The findings inform disease prevention and control efforts in the Northern Territory but also provide insights into pathogenesis and disease burden that may be useful in other populations. This is of particular importance given that developing countries, where the main disease burden continues to lie, do not currently have the resources or capacity to establish registers on a large scale and to maintain quality surveillance of individual cases over the long term. The data presented in this article will be important references for international guidelines and controversies in diagnosis and public health policy. See p 492.

Riociguat for Patients With Pulmonary Hypertension Caused by Systolic Left Ventricular Dysfunction: A Phase IIb Double-Blind, Randomized, Placebo-Controlled, Dose-Ranging Hemodynamic Study

Pulmonary hypertension caused by systolic left ventricular dysfunction is one of the most common forms of pulmonary hypertension and is associated with considerable morbidity and mortality in patients with heart failure. Currently, no approved heart failure therapies target the pulmonary vasculature of heart failure patients with pulmonary hypertension caused by systolic left ventricular dysfunction, highlighting an urgent unmet medical need in this population. Riociguat is a novel soluble guanylate cyclase stimulator and pulmonary vasodilator currently under investigation as a therapy for pulmonary arterial hypertension. Building on a pilot study, which showed hemodynamic improvements in patients with pulmonary hypertension caused by systolic left ventricular dysfunction after a single dose of the soluble guanylate cyclase stimulator BAY 60-4552, the present study investigated the chronic hemodynamic effects and safety of riociguat in heart failure patients with pulmonary hypertension caused by systolic left ventricular dysfunction. Patients were randomized to double-blind treatment with oral placebo or riociguat (0.5, 1, or 2 mg 3 times daily) for 16 weeks in 4 parallel arms. Despite the primary end point, placebo-corrected change from baseline to week 16 in mean pulmonary artery pressure, not being met, riociguat was well tolerated and improved cardiac index, stroke volume index, and both pulmonary and systemic vascular resistance without significantly changing systemic arterial pressure or heart rate. These hemodynamic changes were accompanied by favorable exploratory clinical outcomes, including an improvement in quality of life as measured by the Minnesota Living With Heart Failure score. Future studies are required to validate the mechanism of the increase in cardiac index seen with riociguat and its clinical implications. See p 502.

Therapeutic Efficacy of AAV1.SERCA2a in Monocrotaline-Induced Pulmonary Arterial Hypertension

Pulmonary arterial hypertension (PAH) is characterized by dysregulated pulmonary vascular remodeling that leads to increased pulmonary vascular resistance, right ventricular hypertrophy, and, ultimately, uncompensated right heart failure and death. In the systemic circulation, vascular injury is associated with downregulation of the cardiac isoform of the sarcoplasmic reticulum Ca\(^{2+}\)-ATPase (SERCA2a), which, in turn, stimulates vascular smooth muscle cell proliferation and vessel remodeling. In the present study, we examined the role of SERCA2a in vascular remodeling in PAH and the therapeutic potential of selective pulmonary SERCA2a gene transfer. We found that SERCA2a expression was decreased in hypertrophied pulmonary arterioles from patients with PAH and in the rat monocrotaline model of PAH. In pulmonary vascular smooth muscle cells, we showed that gene transfer of SERCA2a decreased proliferation by regulating nuclear factor of
activated T cells and signal transducer and activator of transcription-3 signaling. We also found that selective pulmonary SERCA2a gene transfer with the use of aerosolized adenovirus serotype 1 (AAV1.SERCA2a) reversed established pulmonary hypertension by improving pulmonary vascular remodeling, lowering pulmonary artery pressures, and decreasing right ventricular hypertrophy. Pulmonary SERCA2a gene transfer also prevented the development of PAH in the rat monocrotaline model. The present study suggests that selective pulmonary gene transfer of SERCA2a with the use of AAV1.SERCA2a, which is already in clinical trials for the treatment of congestive heart failure, may be a novel therapeutic approach to limit adverse pulmonary vascular and right ventricular remodeling associated with PAH. The use of aerosolized AAV1.SERCA2a represents a novel strategy for the treatment of a disease state that has few therapeutic options. See p 512.

Blood Pressure and Left Ventricular Hypertrophy During American-Style Football Participation

Emerging data indicate that increased blood pressure in early adulthood is associated with cardiovascular disease risk in later life. Identification of populations at risk for early adult hypertension is therefore of critical importance. Prior cross-sectional studies document a high prevalence of hypertension and premature cardiovascular mortality in professional American-style football players. To what degree these findings apply to the large population of younger men who participate in competitive high school or collegiate American-style football in the United States is not known. We conducted a prospective, longitudinal study as part of the Harvard Athlete Initiative to examine blood pressure trends, left ventricular remodeling, and the incidence of hypertension among competitive collegiate American-style football participants. We observed that American-style football participation was associated with significant increases in systolic (116±8 versus 125±13 mm Hg; P<0.001) and diastolic (64±8 versus 66±10 mm Hg; P<0.001) blood pressures. At the postseason assessment, the majority of athletes met criteria for stage 1 hypertension (53 of 113, 47%) or stage 1 hypertension (16 of 113, 14%). Several readily available clinical factors, including lineman field position, intraseason weight gain, and a family history of hypertension, identify athletes at greatest risk. Further analyses suggest that the concentric left ventricular hypertrophy in this population is driven by increases in resting blood pressure and not simply the transient isometric stress that occurs during training and competition. Enhanced surveillance and timely, carefully selected intervention may represent an important opportunity to improve later-life cardiovascular health outcomes in this sizable population. See p 524.

Thrombolytic Therapy for the Treatment of Prosthetic Heart Valve Thrombosis in Pregnancy With Low-Dose, Slow Infusion of Tissue-Type Plasminogen Activator

Prosthetic heart valve thrombosis (PVT) is an uncommon but very serious complication of heart valve replacement procedures. Normal pregnancy is accompanied by changes in hemostasis that produce a hypercoagulable state. Most clotting factors usually increase in pregnancy, together with a decrease in several anticoagulants and fibrinolytic activity. Because of these alterations, pregnancy in women with mechanical heart valves carries a high rate of PVT and thromboembolic complications, a double jeopardy to mother and fetus. This single-center, prospective, nonrandomized, observational study included 24 consecutive pregnant women (25 pregnancies with 28 PVT episodes over an 8-year period) with left-sided PVT (all mitral; n=27). Patients with obstructive and nonobstructive PVT with recent systemic thromboembolic and thrombus diameter of >5 mm and patients with asymptomatic mobile nonobstructive PVT with thrombus diameter of at least 10 mm were included in this study. A specific thrombolytic protocol (25 mg tissue-type plasminogen activator infusion in 6 hours for each thrombolytic session, repeated once after 24 hours up to 6 times with a maximum total dose of 150 mg). We found a 100% thrombolytic success rate without any maternal mortality. Despite the limitations of this study, our protocol seems to be an effective therapy with an excellent success rate for the treatment of PVT in pregnant women. This protocol also seems to be safer than cardiac surgery or alternative medical strategies published to date. We suggest that low-dose, slow-infusion tissue-type plasminogen activator should be considered first-line therapy in pregnant patients with PVT. See p 532.

Integrin α₆β₁ Is the Main Receptor for Vascular Laminins and Plays a Role in Platelet Adhesion, Activation, and Arterial Thrombosis

The central role of platelets in arterial thrombosis renders them attractive targets for antithrombotic drugs. Current antiplatelet agents such as P2Y₁₂ receptor antagonists and integrin α₅β₃ blockers target platelet activation and aggregation, thereby considerably reducing the morbidity and mortality associated with ischemic events, especially myocardial infarction. However, this strategy results in an increased risk of hemorrhagic complications, particularly in stroke patients and in those undergoing coronary bypass grafting, endarterectomy, or neurosurgery. Experimental and clinical evidence has suggested that the inhibition of platelet adhesion to glycoproteins of the arterial wall such as von Willebrand factor and collagen could pave the way to safer therapies causing minimal perturbation of hemostasis. In the present study, we investigated the relevance of targeting the interaction of platelets with subendothelial laminins. Using an in vitro blood perfusion assay, we showed that integrin α₅β₃ plays a critical role in platelet adhesion to laminins with an α₅ or α₃ chain, which are the major isoforms expressed in arteries. Compared with wild-type mice, those with a platelet-specific deletion of integrin α₅ presented a marked decrease in thrombosis in 3 models of mechanically- or laser-induced injury of the carotid artery, aorta, and mesenteric arterioles. In contrast, the tail bleeding time and volume of blood lost remained unchanged in α₅-deficient mice, suggesting normal hemostasis. In conclusion, this study provides the first evidence that inhibiting platelet integrin α₅β₃ could represent an alternative antithrombotic strategy with a potentially low bleeding risk. See p 541.