Early Reperfusion During Acute Myocardial Infarction Affects Ventricular Tachycardia Characteristics and the Chronic Electroanatomic and Histological Substrate

Reperfusion therapy during acute myocardial infarction results in myocardial salvage. The duration of coronary artery occlusion and early reperfusion have been shown to affect the size and geometry of fibrosis after myocardial infarction. The 3-dimensional scar geometry influences reentry circuit location and ventricular tachycardia (VT) characteristics. Current substrate-based catheter ablation strategies for VT after myocardial infarction are based predominantly on studies in patients and animals with a chronically occluded infarct-related artery resulting in large homogeneous scars. In the present study, we demonstrate that early reperfusion influences the characteristics of post–acute myocardial infarction scars assessed by electroanatomic voltage mapping and by histology after myocardial infarction compared with patients without reperfusion therapy. Early reperfusion was associated with less dense and less confluent electroanatomic scars consisting of thicker layers of viable myocardium that appear to give rise to faster spontaneous and inducible VTs. These findings may have important implications for the management of patients in the reperfusion era who present with VTs. Poorly tolerated VT requires a substrate-based ablation approach. However, current substrate-based techniques relying on voltage and pace mapping to target the scar border zone may not be applicable for smaller, less dense, and less confluent scar. Whether these changes in the electroanatomic VT substrate of reperfused patients will pose a challenge in ablation needs further evaluation. Studies in animal models more realistic in the reperfusion era are warranted to reevaluate the relationship of the VT circuit and the architecture of the scar and to reassess substrate-based ablation concepts. See p 1887.

Risk Factors for Venous Thromboembolism: Results From the Copenhagen City Heart Study

Deep vein thrombosis and pulmonary embolism are often viewed as 1 disease denoted venous thromboembolism (VTE), which is the cause of considerable morbidity and mortality. VTE and atherosclerotic disease such as acute myocardial infarction have for many years been considered 2 different disease entities with important differences in their pathways to thrombosis and hence in their preventive measures. Recent studies, however, have disputed this, among these a large clinical trial (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin [JUPITER]) showing an impressive lowering of VTE incidence with statin treatment. In this hitherto largest study, we studied common risk factors for atherosclerotic disease to determine whether these were also associated with VTE but found that only obesity and smoking were important risk factors for VTE, whereas total/high-density lipoprotein/low-density lipoprotein cholesterol levels, triglyceride levels, and diabetes mellitus were not. This would indicate that any beneficial effect of statins on VTE is through pleiotropic mechanisms and that treatment of dyslipidemia in itself may be of low value for preventing VTE. Conversely, management of obesity and smoking cessation are likely to be beneficial for both VTE and atherosclerotic disease. See p 1896.

Excessive Supraventricular Ectopic Activity and Increased Risk of Atrial Fibrillation and Stroke

Supraventricular ectopic complexes are quite common, and ~10% to 15% of middle-aged and elderly subjects with no apparent heart disease may have excessive supraventricular ectopic activity. This study shows that excessive supraventricular ectopic activity in these subjects increases the risk of death, stroke, and atrial fibrillation beyond conventional risk factors or the Framingham risk score for atrial fibrillation. Physicians frequently see patients with excessive supraventricular ectopic activity during routine examinations or in other contexts. The finding that such supraventricular activity leads to a high risk may urge physicians to intensify risk modification, treat comorbidities more aggressively, and perhaps increase patient compliance. Closer follow-up of these subjects is likely to identify subjects with asymptomatic atrial fibrillation and thus promote appropriate preventive treatment as well as antiarrhythmic therapy. Interventional studies to prevent atrial fibrillation and later stroke or death in such patients are welcome. See p 1904.

Cardioprotective and Antiapoptotic Effects of Heme Oxygenase-1 in the Failing Heart

Heme oxygenase-1 (HO-1), which degrades heme to biliverdin, ferrous iron, and carbon monoxide (CO), is rapidly inducible and cardioprotective during acute stress. However, its pathophysiological role in chronic heart failure (HF) is unknown. Using myocyte-restricted HO-1 transgenic mice, we evaluated whether HO-1 up-regulation in the failing heart is a beneficial adaptation that alleviates pathological remodeling. Nontransgenic and HO-1 transgenic mice underwent either sham operation or permanent left coronary ligation to induce HF. After 4 weeks, compared with nontransgenic mice with HF, HO-1 transgenic mice with HF exhibited improved postinfarction survival and significantly less left ventricular dilatation and dysfunction, cardiac hypertrophy, fibrosis, and oxidative stress, together with improved tissue neovascularization and reduced myocardial p53 expression and apoptosis. In isolated mitochondria, mitochondrial permeability transition was inhibited by HO-1 in a CO-dependent manner and was recapitated by the CO donor tricarbonylchloro(glycinato)ruthenium(II) (CORM-3). HO-1–derived CO also prevented H2O2–induced cardiomyocyte apoptosis and cell death. Finally, sustained in vivo treatment with CORM-3 alleviated postinfarction left ventricular remodeling, p53 expression, and apoptosis in wild-type mice. Our results establish that sustained HO-1 upregulation in HF is an important beneficial adaptation that serves to counteract detrimental left ventricular remodeling via antioxidant, antihypertrophic, antiinfectious, and proangiogenic effects. We have also identified an in vivo antipapoptotic action of HO-1 in the failing heart that is related, at least in part, to CO-mediated stabilization of mitochondrial pore opening. Therefore, augmentation of HO-1 or its product, CO, should be explored as a therapeutic approach to limit pathological left ventricular remodeling and myocyte loss in HF. See p 1912.

Impact of ABO-Incompatible Listing on Wait-List Outcomes Among Infants Listed for Heart Transplantation in the United States: A Propensity Analysis

Unlike older children and adults awaiting heart transplantation, infants are unique in their capacity to safely receive a heart transplant from an ABO-incompatible donor. Although the purported advan-
tage of ABO-incompatible (ABO-I) listing is to reduce wait times and secondarily waiting list mortality, limited data are available on actual waiting list outcomes for infants listed for a potential ABO-I HT or recent changes in clinical practice in the willingness of US institutions to list infants for an ABO-I heart transplantation. The present study describes recent trends in the US practice of listing infants for an ABO-I heart transplantation using data from the Organ Procurement and Transplant Network and analyzes the impact of ABO-I listing on organ waiting times after adjustment for patient factors. In short, the clinical practice of listing infants for a potential ABO-I HT has risen dramatically in recent years in the United States but still appears to be used preferentially for sicker infant candidates. Eligible infants listed for a potential ABO-I heart, especially infants with blood type O, can expect a meaningful reduction in waiting time for a donor heart and potentially a higher probability of surviving to transplantation. The ABO-I listing strategy may be currently underused by many US centers and may benefit a broader range of transplant candidates. See p 1926.

**Combined Mitral and Tricuspid Valve Repair in Rheumatic Valve Disease: Fewer Reoperations With Prosthetic Ring Annuloplasty**

This study with very long-term results shows, probably for the first time, that in patients undergoing either mitral or tricuspid valve repair when both lesions have a rheumatic origin, the results obtained are more favorable with the use of a prosthetic ring annuloplasty. Implantation of a prosthetic ring in the mitral or tricuspid position was associated with significantly fewer valve dysfunction–related reoperations and a longer reoperation-free survival. As a result of this finding, mitral valve repair using percutaneous balloon dilatation of the valve might be a suboptimal technique. On the other hand, the historical comparison of patients with double rheumatic valve disease (mitral and tricuspid) treated with prosthetic mitral valve replacement confirms, even at very long-term follow-up, that mitral repair offers a better alternative with longer survival and fewer valve dysfunction reoperations. The present study is the largest experience of surgical treatment of rheumatic mitral/tricuspid valve disease with the longest follow-up. Although rheumatic disease is eradicated in the developed world, rheumatic fever is still the first cause of heart valve disease in 5 million people around the world. See p 1934.

**Composition of Carotid Atherosclerotic Plaque Is Associated With Cardiovascular Outcome: A Prognostic Study**

Postmortem studies have revealed plaque characteristics that are associated with clinical cardiovascular events. However, the prognostic value of the vulnerable plaque characteristics for the development of a cardiovascular event is unknown because prospective studies are lacking. Atherosclerosis is considered a systemic disease. Currently, most research focuses on the local plaque characteristics as a determinant of future plaque thrombosis. In this study, we followed a different concept. We assumed that local atherosclerotic lesions hold cellular and molecular information that reflects the stability of atherosclerotic lesions in all other vascular territories. Therefore, we performed a prospective study investigating whether the morphology of the local atherosclerotic carotid plaque enables identification of patients who are at increased risk to suffer from a cardiovascular event within 3 years after carotid endarterectomy. This innovative approach would facilitate risk stratification for systemic cardiovascular events in patients after carotid endarterectomy. In addition, plaque characteristics may serve as imaging targets for diagnostic applications. In the present study, we show for the first time that plaque hemorrhage and increased vessel density in a local atherosclerotic lesion are associated with increased risk for cardiovascular events. This study shows that local vascular plaque tissue that is dissected during vascular surgery procedures holds prognostic information. In addition, this study supports the concept that plaque revascularization and intraplaque bleeding are a hallmark of the progression of the disease. Following this concept, molecular local plaque studies could be considered that reveal targets for individual risk stratification, imaging applications, and pharmaceutical interventions to prevent acute clinical manifestations of atherosclerotic disease. See p 1941.