Coronary Artery Injury Due to Catheter Ablation in Adults: Presentations and Outcomes

Coronary artery injury is a rare but important complication after catheter ablation. In this study we report 4 patients (0.09%) who sustained a coronary injury of a cohort of patients undergoing 4655 ablation procedures. Coronary injury occurred in 3 patients after radiofrequency ablation, and a moderate asymptomatic stenosis occurred after cryoablation in the other patient. Branches of the right coronary artery were involved in all cases. There is a spectrum of presentations of coronary injury after ablation procedures. Acute occlusion of the artery was seen in 2 patients. Coronary stenting appears to be required for acute occlusion that does not respond to nitroglycerin but may be complicated by the phenomenon of coronary no-reflow. Although the majority of coronary injuries present acutely, delayed presentations of up to 2 weeks may also occur. Coronary arteries appear to be particularly susceptible to injury from ablation in the epicardium and the middle cardiac vein. Unanticipated anatomic variation may also predispose to coronary injury. Awareness of these features should help with the risk/benefit assessment for ablation in locations where coronary arteries are at risk. Coronary injury must be considered in patients who develop persistent chest discomfort, especially if ablation occurs in areas adjacent to the coronary circulation. See p 1465.

Predictors of Improvement of Unrepaired Moderate Ischemic Mitral Regurgitation in Patients Undergoing Elective Isolated Coronary Artery Bypass Graft Surgery

In this study, we sought to investigate preoperative predictors of moderate ischemic mitral regurgitation (IMR) improvement after elective isolated coronary artery bypass graft (CABG) surgery. The persistence of moderate IMR after isolated CABG surgery is an important independent predictor of long-term mortality. However, mitral valve repair at the time of CABG surgery does not appear to improve survival. In contrast, concomitant mitral valve repair is associated with increased perioperative risks compared with CABG alone. Hence, the optimal surgical management of patients with moderate IMR undergoing CABG surgery is unclear. In the present study, the presence of significant myocardial viability and the absence of dysynchronous between papillary muscles were major independent predictors of long-term IMR improvement after isolated CABG surgery. Moreover, patients with IMR improvement also showed improved survival compared with patients who failed to improve. IMR is caused by disease of the left ventricle with a secondary distortion of mitral valve geometry. This suggests that recovery of left ventricular function by revascularization of viable myocardium or resynchronization of contractions between the papillary muscles through biventricular pacing may be the optimal therapy addressing the underlying IMR mechanism, i.e., disease of the left ventricle. Thus, assessment of myocardial viability and dyssynchrony may provide a basis for clinical decision making as to whether to perform mitral valve repair at the time of surgical revascularization in patients with moderate IMR referred for elective CABG surgery. See p 1474.

Predictors of Technical Success and Postnatal Biventricular Outcome After In Utero Aortic Valvuloplasty for Aortic Stenosis With Evolving Hypoplastic Left Heart Syndrome

In fetuses with aortic stenosis and evolving hypoplastic left heart syndrome, technically successful prenatal aortic valvuloplasty alters the growth and function of some left heart structures. In fetuses with a large left ventricle before intervention, aortic valvuloplasty increased the probability of a biventricular outcome after birth. A multivariable threshold scoring system that takes into account the size of the aortic valve, mitral valve, and left ventricle, as well as left ventricular pressure, allows highly sensitive and moderately specific identification of fetuses able to survive postnatally with a biventricular circulation. See p 1482.

Cardiovascular Benefit of Magnitude of Low-Density Lipoprotein Cholesterol Reduction: A Comparison of Subgroups by Age

Recent studies have demonstrated that intense cholesterol-modifying therapy is more effective than moderate cholesterol-modifying therapy in older patients; however, no researchers to date have quantified the cardiovascular benefit of the magnitude of low-density lipoprotein (LDL) cholesterol reduction in subjects of various ages. In the present analysis, we examined the effect of an LDL cholesterol reduction of varying magnitude in a cohort of veterans at high risk for adverse cardiovascular events. We found that in all age quartiles and in a subgroup of veterans 80 years of age or older, the magnitude of cardiovascular risk reduction was proportional to the magnitude of LDL cholesterol reduction. Quantitatively, we found that veterans in all age quartiles who achieved a large LDL cholesterol reduction of 70 mg/dL or greater experienced an approximately 70% reduction in risk for acute myocardial infarction or revascularization. The implications for the practicing clinician who manages subjects at high risk for adverse cardiovascular events are 2-fold. First, these findings support aggressive lipid lowering in older patients with high cardiac risk, as in younger high-risk subjects. Second, these findings support treating the patient to achieve the largest LDL cholesterol change that is feasible and safe. See p 1491.

Final 5-Year Results of the TAXUS II Trial: A Randomized Study to Assess the Effectiveness of Slow- and Moderate-Release Polymer-Based Paclitaxel-Eluting Stents for De Novo Coronary Artery Lesions

TAXUS II was the first randomized, double-blind, controlled trial specifically designed to assess the long-term safety and efficacy of the TAXUS paclitaxel-eluting stent for the treatment of de novo coronary artery lesions. It is also the first large TAXUS trial to reach 5-year follow-up and the first trial designed to compare the performance of the slow-release and an investigational moderate-release formulation of the TAXUS stent with an otherwise identical bare-metal stent. Through 5 years, both the slow- and moderate-release stents significantly lowered the rates of target-vessel and target-lesion revascularization without increasing the rates of death, myocardial infarction, or stent thrombosis compared with bare-metal stents. The absence of stent thrombosis beyond 2 years in the slow-
and moderate-release stents with 2 events in the bare-metal stent arm provides reassurance that there is no excessive long-term risk of stent thrombosis with paclitaxel-eluting stents compared with bare-metal stents. Furthermore, the sustained reduction in revascularization rates up to 5 years with both the slow- and moderate-release stents provides evidence that there is no late catch-up phenomenon. Finally, the moderate-release formulation, which delivers a 3-fold greater amount of paclitaxel than the slow-release formulation, demonstrated equivalent safety through 5 years, thereby establishing a clear safety margin for the slow-release formulation, which has been implanted in more than 4 million patients worldwide. See p 1498.

**Long-Term Clinical Outcome After Fractional Flow Reserve–Guided Treatment in Patients With Angiographically Equivocal Left Main Coronary Artery Stenosis**

Significant left main coronary artery stenosis is an accepted indication for surgical revascularization. Angiography alone has limited accuracy in assessing actual stenosis severity, and there is great interobserver variability in lesions of the left main coronary artery. Consequently, ambiguous left main coronary artery disease sometimes results in considerable uncertainty as to which therapeutic strategy may be best for the patient. Fractional flow reserve (FFR) can be measured at the time of coronary angiography and identifies coronary lesions responsible for ischemia. Because FFR-guided revascularization strategies are associated with favorable clinical outcomes in patients with single-vessel or multivessel disease, the main goal of this retrospective study was to evaluate the long-term clinical outcome of an FFR-guided revascularization strategy in patients with angiographically equivocal left main coronary artery stenosis. Patients with FFR ≥0.80 were treated medically or percutaneously, and patients with FFR <0.80 were treated surgically. The 5-year survival and 5-year event-free survival estimates were similar in the 2 groups. Angiographic assessment of the lesions, either by quantitative coronary angiography or by visual estimation, failed to identify the stenosis significance in almost one third of the total patient population. Angiography alone does not allow appropriate individual decision making about the need for revascularization in patients with equivocal left main coronary artery lesions and often underestimates their functional significance. FFR should be assessed in such patients before a decision is made “blindly” about the need for revascularization. See p 1505.

**Cardiomyocyte Differentiation of Human Induced Pluripotent Stem Cells**

Cell-replacement therapy is emerging as a novel experimental therapeutic paradigm for myocardial repair/regeneration but is hampered by the limited sources of autologous cardiomyocytes. The breakthrough technology, allowing the reprogramming of adult human fibroblasts with a set of transcription factor into pluripotent stem cell lines (induced pluripotent stem [iPS] cells), may provide a possible solution to the aforementioned cell-sourcing problem. In the present study, we describe the in vitro differentiation of human iPS (hiPS) cells into the cardiac lineage and demonstrate that the molecular events characterizing this differentiation process parallel previously reported in vitro and in vivo cardiomyogenic models. The generated hiPS-derived myocytes displayed molecular, structural, and functional properties of early-stage human cardiomyocytes and responded appropriately to adrenergic and cholinergic signaling. In addition, the hiPS differentiating system was not limited to the generation of isolated cardiomyocytes; rather, a functional cardiomyocyte syncytium was established with stable pacemaker activity and action potential propagation. Finally, proof-of-concept pharmacological studies demonstrated the potential of the hiPS cell–derived cardiac tissue to serve as a unique platform for individualized drug testing and specifically for “QT screening.” In conclusion, the ability to generate a reproducible hiPS-cardiomyocyte differentiation system may bring unique value to the emerging field of personalized medicine: for the establishment of patient/disease-specific disease models, for drug screening and target validation, and for the establishment of future autologous myocardial cell-replacement therapies. See p 1513.

**MicroRNA 217 Modulates Endothelial Cell Senescence via Silent Information Regulator 1**

Cellular senescence of endothelial cells has been involved in causes of atherosclerosis, although the mechanisms underlying the aging-induced attenuation of endothelial functions are unknown. On the basis of recent evidence, we hypothesized that microRNAs, a class of endogenous, small, noncoding, single-stranded RNAs of approximately 22 nucleotides that are known to negatively regulate gene expression, may be a cause of endothelial dysfunction. In the present study, we used a model of endothelial senescence to identify microRNAs associated with the aging process and to recognize their potential targets. We found that a particular microRNA, miR-217, is progressively expressed in endothelial cells during senescence. In silico analysis indicated that silent information regulator 1 (SirT1) is a potential target of miR-217. SirT1 is an NAD+–dependent deacetylase that regulates gene expression and exerts protective effects against endothelial dysfunction and metabolic syndrome. SirT1 action is lost during aging, but the cause of the age-related decline of SirT1 is unknown. Thus, in the present studies, we sought to address whether endothelial senescence is determined by a miR-217–dependent SirT1 loss of function. We observed that miR-217 inhibits SirT1 function in endothelial cells, specifically by reducing its ability to modulate the function of a transcription factor called FoxO1 that is involved in angiogenesis, apoptosis, and stress resistance. The inhibition of miR-217 rescues the phenotype of senescent endothelial cells. The evidence for such a miR-217–SirT1–FoxO1 pathway in atherosclerotic plaque from human donors has clear clinical implications for the possibility of interfering with miR-217 by use of treatments to antagonize its function in the endothelium of patients. See p 1524.