Feasibility of Real-Time Magnetic Resonance Imaging for Catheter Guidance in Electrophysiology Studies

Electrophysiology procedures provide a cure for many atrial and ventricular arrhythmias but remain associated with failures and complications, much of which likely derive from lack of soft-tissue visualization with fluoroscopy. As an alternative imaging modality, magnetic resonance imaging offers 3-dimensional imaging with excellent soft-tissue resolution without the ionizing radiation inherent to fluoroscopy. However, potential interactions of static and gradient magnetic fields and radiofrequency energy from the magnetic resonance scanner with the electrophysiology system must be addressed for safe performance of real-time magnetic resonance–guided electrophysiology procedures. In the present study, we report the feasibility of performing electrophysiology studies with a custom electrophysiology system compatible with real-time magnetic resonance guidance. Successful anatomic targeting of catheters was demonstrated, and comprehensive electrophysiology studies with recording of intracardiac electrograms and pacing were performed. The capabilities of magnetic resonance guidance for superior real-time resolution of anatomic soft tissues, identification of scar arrhythmia substrates, and monitoring of lesion formation within linear sets and with respect to surrounding structures may improve the safety and efficacy of complex electrophysiology procedures. See p 223.

Dietary Patterns and Risk of Mortality From Cardiovascular Disease, Cancer, and All Causes in a Prospective Cohort of Women

Overall dietary patterns can be defined as combinations of characteristic food groups that reflect existing eating habits of a specific study population. The association between such overall dietary patterns and mortality due to cardiovascular disease and other chronic diseases is largely unknown. We followed a population of >70 000 apparently healthy US women over the course of 18 years, assessing dietary intake repeatedly. By applying factor analysis, we identified 2 major dietary patterns. A greater adherence to the pattern labeled as prudent (characterized by a high consumption of plant foods such as vegetables, fruit, legumes, and whole grains as well as fish and poultry) was related to a 28% reduced risk of cardiovascular disease mortality and a 17% reduced risk of premature all-cause mortality. By contrast, a greater adherence to the pattern labeled as western (characterized by a high consumption of red and processed meat, refined grains, french fries, and sweets) was associated with a 22% increased risk of cardiovascular disease mortality, a 16% increased risk of cancer mortality, and a 21% increased risk of premature all-cause mortality. The observed associations were independent of known risk factors including age, smoking, physical inactivity, body mass index, and total caloric intake. Nutritional recommendations to prevent chronic diseases and promote longevity may need to focus on overall dietary patterns rather than individual nutrients. See p 230.

Transcriptomic Biomarkers for Individual Risk Assessment in New-Onset Heart Failure

New technologies that measure expression levels of the entire complement of messenger RNAs in a cell or tissue have become highly useful for clinical prediction of disease origin, prognosis, and therapeutic response. Because they are highly comprehensive, they have the potential to be highly accurate. The present study shows that this approach could be very important to fulfill an unmet need in the field of heart failure: accurate prediction of the long-term clinical course of a patient. New-onset heart failure is very common and has a highly variable outcome; thus, the ability to accurately assess individual patient risk is of major significance. Using endomyocardial biopsy tissue obtained at the time of clinical presentation, we developed a molecular signature comprising 45 genes that predicted long-term clinical outcome in patients with new-onset heart failure. This transcriptomic biomarker distinguished patients who survived at least 5 years after first diagnosis from those who did poorly and required left ventricular mechanical assistance or cardiac transplantation or who died. These findings may provide the physician with important prognostic information about individual patients and could provide tools for personalized treatment or monitoring. Importantly, the biomarker can be obtained from a single endomyocardial biopsy and therefore is clinically practical. The biomarker contained biologically relevant genes, including those involved in regeneration and angiopoiesis, which suggests possible novel therapeutic targets. See p 238.

Heritability and Genome-Wide Linkage in US and Australian Twins Identify Novel Genomic Regions Controlling Chromogranin A: Implications for Secretion and Blood Pressure

Chromogranin A (CHGA) plays a necessary role in the formation of catecholamine secretory granules, where it is cleaved to catestatin, an inhibitor of catecholamine release. Catestatin circulates in human plasma and may be an intermediate phenotype in analysis of genetic risk for cardiovascular disease. In the present investigation, we first observed that CHGA is elevated and its processing to catestatin is diminished in hypertonics. To approach genetic control of catestatin in the population, we used a human twin pair design. Studies of monzygotic and dizygotic twins allow estimation of the contribution of genetic variation to any trait (as heritability, or h²), and dizygotic or sibling pairs allow genome-wide approaches such as microsatellite linkage scanning to identify previously unsuspected loci influencing traits of interest. Our results indicate that the circulating catestatin concentration has substantial heritability and that novel genetic loci on chromosomes 4p, 4q, and 17q contribute significantly to common interindividual variation in expression, secretion, or enzymatic formation of this biologically active peptide. At the ATP6V1N (H-ATPase alpha subunit) positional candidate locus on chromosome 17q, a common 3′-UTR variant predicted plasma CHGA, CHGA-to-catestatin processing, and finally systolic blood pressure in the population. Thus, ATP6V1N represents a novel trans-UTR for sympathochromaffin activity and ultimately blood pressure. See p 247.

Magnetic Resonance Imaging Contrast Agent Targeted Toward Activated Platelets Allows In Vivo Detection of Thrombosis and Monitoring of Thrombolysis

Platelets play a pivotal role in thrombus formation and in the development of atherosclerotic plaques from the very beginning of atherosclerotic disease and particularly in the final stages of plaque rupture and thrombotic vessel occlusion. Imaging of platelets prom-
izes the sensitive detection of thrombi/emboli and the identification of the role of platelets in the development of atherosclerotic plaques. Detection of thrombi (eg, in coronary and carotid arteries) and characterization of plaque stages and the associated risk of vessel closure are of great clinical interest. Recent magnetic resonance imaging (MRI) studies have used microparticles of iron oxide (MPIOs), which cause intense negative contrast effects in T2*-weighted MRI. Here, we describe the generation and application of a targeted MRI contrast agent consisting of MPIOs and a single-chain antibody that selectively binds to ligand-induced binding sites (LIBS) on the activated platelet integrin glycoprotein IIb/IIIa. We show the utility of this contrast agent in the rapid identification of mural platelet-containing thrombi in vivo using a mouse model of carotid thrombosis. Pharmacological thrombolysis was used to demonstrate that LIBS MPIO-induced signal void intensity reports reliably on thrombus size, in particular on thrombus size reduction. Furthermore, we applied LIBS MPIOs in symptomatic human carotid endarterectomy specimens to show the detection of clinically relevant platelet adhesion/aggregation in humans. In conclusion, the described targeted MRI contrast agent represents a novel and unique noninvasive imaging approach that allows the detection and quantification of thrombi and can be used to monitor the success or failure of thrombolytic therapy. See p 258.

**Comparison of Thrombolysis Followed by Broad Use of Percutaneous Coronary Intervention With Primary Percutaneous Coronary Intervention for ST-Segment–Elevation Acute Myocardial Infarction: Data From the French Registry on Acute ST-Elevation Myocardial Infarction (FAST-MI)**

Primary percutaneous coronary intervention (PCI) is the best reperfusion method in patients with ST-elevation myocardial infarction, provided it can be performed in a timely manner. Because it remains difficult to implement on a large scale, however, intravenous thrombolysis is still used in many patients. This report presents data from a nationwide French registry collecting consecutive patients over a 1-month period at the end of 2005 and describes in-hospital and 1-year outcomes in patients treated with primary PCI or intravenous thrombolysis followed by routine coronary angiography in most patients (96%) and a very high rate of secondary PCI (84%). As expected, intravenous thrombolysis could be administered much more rapidly than primary PCI, particularly because two thirds of the patients received thrombolysis in the prehospital setting. There was no difference in early and late mortality between patients with primary PCI and those with a pharmacoinvasive strategy. One-year survival was similar among 2 cohorts of patients matched on a propensity score for receiving thrombolysis or primary PCI (93.8% and 93.3%). Overall, this study shows that the combination of intravenous thrombolysis with early PCI in patients seen in the first hours after symptom onset yields clinical results that compare with those of primary PCI. These findings may have important implications for healthcare organizations. See p 268.

**Cardiovascular Risk Factors and the Metabolic Syndrome in Pediatric Nonalcoholic Fatty Liver Disease**

There are >10 million obese children in the United States. Obese children differ in their risk for cardiovascular disease, which may be underappreciated in part because specific comorbidities are typically the focus of different disciplines such as cardiology, endocrinology, gastroenterology, or nephrology. When working with an obese child, one should consider how any single abnormality may interact with another. Metabolic syndrome is a clustering of risk factors for the development of cardiovascular disease and type 2 diabetes mellitus. Nonalcoholic fatty liver disease (NAFLD) is a common cause of chronic liver disease in children. Both metabolic syndrome and NAFLD are associated with obesity. We performed a case-control study in a large clinical sample of overweight and obese children and adolescents with and without NAFLD. NAFLD was strongly associated with metabolic syndrome. The association was independent of both body mass index and hyperinsulinemia. Thus, when one detects features of metabolic syndrome in an obese child, one must be aware of the risk for NAFLD. Similarly, the presence of NAFLD may serve to stratify risk. The identification of NAFLD in a child should prompt consideration of cardiovascular health. Global counseling should address nutrition, physical activity, and avoidance of smoking. In an integrated model of disease management, therapeutic goals for NAFLD should include not only the prevention of end-stage liver disease but also the prevention of cardiovascular disease and diabetes. See p 277.

**Abrupt Shift of the Pattern of Diurnal Variation in Stroke Onset With Daylight Saving Time Transitions**

In the present study, we analyzed the influence of Daylight Saving Time transitions on the circadian pattern of stroke onset and identified abrupt shifts of stroke onset time points in reference to the time effective before the transitions. Simply put, after the transition into Daylight Saving Time, patients appeared to have their strokes roughly 1 hour earlier than in the weeks before, whereas the transition back from Daylight Saving Time into standard time delayed stroke onset for ~1 hour. Our investigation suggests that the circadian profile of stroke onset is coupled with the actual time of day. In modern civilizations, the sleep-wake cycle is firmly synchronized with the actual time of day, and clock change is likely to abruptly shift the sleep-wake cycle of most individuals. Thus, the sleep-wake cycle and factors associated with awakening (eg, the identification of as yet unrecognized nighttime strokes) appear to be the most important determinants of the diurnal pattern of stroke onset. Conversely, it is well known that physiological parameters such as blood pressure, platelet function, serum concentrations of circulating hormones, and coagulation factors reveal a pattern of diurnal rhythmicity that is governed by the molecular clock and clock genes. However, the rapid shift of stroke onset time points after Daylight Saving Time transitions does not support the hypothesis that these endogenous factors play a major role in determining the circadian profile of stroke onset, because an entrainment of the human circadian clock within hours is unlikely. See p 284.