Physical Activity and Incidence of Atrial Fibrillation in Older Adults: The Cardiovascular Health Study

Physical activity is often considered to increase the risk of atrial fibrillation (AF), on the basis of anecdotal reports, case series, and retrospective studies evaluating vigorous exertion and endurance training in younger and middle-aged athletes; however, most AF cases do not occur in athletes but in the general population of older adults (≥65 years old), in whom 10-year risk of AF approaches 20%. At these ages, AF risk factors include long-standing hypertension, reduced ventricular compliance, and structural heart disease, all of which are risk factors that might be improved or prevented by habitual light to moderate activity. However, relationships of physical activity with incidence of AF in older adults had not been evaluated. We prospectively investigated associations of habitual light to moderate activity, including leisure-time activities and walking, with AF incidence among 5446 individuals ≥65 years of age over a 12-year period. After adjustment for other risk factors, both leisure-time activity and walking were associated with significantly lower AF incidence, including a 36% lower risk for the highest versus lowest quintile of leisure-time activity and a 50% lower risk for the highest versus lowest category of walking distance/pace. Strenuous exertion was not required: Lower risk was seen with regularly walking 5 to 10 blocks per week and at 2- to 3-mph paces (greater distances and paces were associated with even lower risk). Although these observational findings do not prove causality, the strength and consistency of associations, including among individuals with and without preexisting cardiovascular disease, and the known biological effects of exercise suggest that regular light to moderate activity may reduce AF incidence in older adults. This provides additional strong impetus for clinicians and policy makers to focus on regular physical activity, including leisure-time activities and walking, to maintain cardiovascular health in older adults. See p 800.

Contemporary Analysis of Descending Thoracic and Thoracoabdominal Aneurysm Repair: A Comparison of Endovascular and Open Techniques

Numerous comparisons have been conducted between open and endovascular repair of aortic lesions; however, in nearly all reports, with the exception of the prospective randomized trials involving infrarenal abdominal aortic aneurysm, significant anatomic differences exist between groups. The present contemporary comparison of 724 consecutive patients treated with open surgery (372) or pure endovascular (352) procedures with thoracic and branched technology contrasted outcomes in the context of the anatomic extent of the repair. The results demonstrate similar incidences of paraplegia and 30-day and 12-month mortality irrespective of the repair technique used; however, an inherent treatment bias existed toward the repair of younger healthier patients with conventional treatments, whereas endovascular repair was reserved for less fit patients. Endovascular patients were on average 9 years older and were sicker by nearly every metric considered (cardiac, pulmonary, and renal disease; diabetes mellitus; smoking; and cancer). The highest risk for death and paraplegia occurred with the most extensive aneurysms (isolated thoracic aneurysms), with paraplegia occurring in <1% of these individuals. Prior distal aortolentic operations were associated with a higher incidence of paraplegia in endovascular patients, and chronic dissections also increased the incidence of paraplegia in patients who underwent open surgical repair. On the basis of the observations of this study, it is clear that endovascular repair of extensive aneurysms is feasible and capable of producing results similar to open surgical techniques, even in more physiologically challenged patients. See p 808.

Improvement in Left Ventricular Remodeling by the Endothelial Nitric Oxide Synthase Enhancer AVE9488 After Experimental Myocardial Infarction

Nitric oxide (NO) generated by the endothelial NO synthase (eNOS) plays a key role in vascular tone and cardiomyocyte contractility and protects against hypertrophy and atherosclerosis. Cardiac and vascular NO bioavailability is reduced in heart failure, contributing to contractile dysfunction, ventricular hypertrophy, and remodeling, as well as endothelial dysfunction. Overexpression of the eNOS gene in endothelial cells or cardiomyocytes improved cardiac performance in mice after myocardial infarction. Various established pharmacological interventions in heart failure enhance NO bioavailability. Nitric oxide donors widely used in coronary artery diseases and heart failure. However, nitrate tolerance and the induction of reactive oxygen species formation limit their benefits. In the present study, we tested the concept of directly augmenting eNOS by pharmacological intervention. The novel compound AVE9488, shown to elevate eNOS expression and NO production, improved left ventricular remodeling and contractile dysfunction in rats after coronary artery ligation. Myocardial molecular alterations were prevented by AVE9488; endothelial vasomotor dysfunction and superoxide formation were attenuated; and levels of circulating eNOS uncoupling, which may lead to production of superoxide anions instead of NO, was not observed after treatment with AVE9488. Thus, a pharmacological intervention to increase eNOS expression and subsequent NO formation constitutes a promising therapeutic approach for the amelioration of postinfarction ventricular remodeling and heart failure. See p 818.

Smoothelin-B Deficiency Results in Reduced Arterial Contractility, Hypertension, and Cardiac Hypertrophy in Mice

The causes of essential hypertension remain largely unknown, although it is commonly accepted that vascular smooth muscle dysfunction is a potential culprit. Improved insight into the mechanisms and regulation of smooth muscle contraction may provide additional therapeutic targets to treat pathologies such as hypertension. However, our current understanding of these 2 aspects of smooth muscle function is limited. Here, we introduce smoothelin, a protein specifically expressed in fully differentiated, contractile smooth muscle cells, as a crucial component of the vascular smooth muscle cell contractile apparatus. We demonstrate for the first time that smoothelin is necessary for physiological vascular smooth muscle contraction. Smoothelin deficiency in mice resulted in severely reduced contractile potential, particularly in smaller arteries. Paradoxically, this was accompanied by hypertension and concomitant cardiac hypertrophy. Analyses of differently sized blood vessels indicated that the cause of the hypertension is likely to be downstream of vessels like the saphenous artery and/or mediated by overcompensation of blood pressure regulatory systems like the
renin-angiotensin system. Recently, imatinib, a drug used in clinical practice, was shown to specifically promote smoothelin expression in vascular smooth muscle cells. Considering the currently reported data, such an increase in smoothelin concentration not only may indicate a more contractile phenotype of the vascular smooth muscle cell but also may improve vascular smooth muscle contractile potential. The combination of an increased knowledge of smoothelin function and the availability of pharmacological tools that affect smoothelin expression provides interesting opportunities to treat pathologies originating from vascular smooth muscle cell dysfunction. See p 828.

**Cardiac Magnetic Resonance With T2-Weighted Imaging Improves Detection of Patients With Acute Coronary Syndrome in the Emergency Department**

Cardiac magnetic resonance (CMR) is emerging as an alternative noninvasive diagnostic test for rapid and accurate assessment of patients with acute chest pain who present to the emergency room, particularly for patients with intermediate risk of developing an acute coronary syndrome. We demonstrated that CMR with T2-weighted imaging and left ventricular wall thickness analysis provided not only high diagnostic accuracy for detection of patients with acute coronary syndrome but also allowed the differentiation of patients with acute versus old myocardial infarction. Furthermore, the CMR changes presented before the rise of cardiac enzymes in patients with non–ST-segment myocardial infarction (6±2 hours), and the combination of T2-weighted imaging, a signature of myocardial edema, and delayed hyperenhancement, which represents myocardial necrosis, allowed further characterization as unstable angina or non–ST-segment myocardial infarction. Finally, the CMR data provided significant incremental value over initial clinical assessment and traditional cardiac risk factors (odds ratio 129.4, 95% confidence interval 11.8 to >999.9). These data suggest that a 30-minute CMR protocol is feasible and accurate in the emergency department setting. Future studies will need to determine the impact of CMR in clinical decision making and assess the cost-effectiveness of CMR in the emergency department setting. See p 837.

**Mitral Leaflet Adaptation to Ventricular Remodeling: Occurrence and Adequacy in Patients With Functional Mitral Regurgitation**

Left ventricular remodeling after myocardial infarction or in dilated cardiomyopathy creates mismatch between mitral leaflet and ventricular size, which leads to ischemic mitral regurgitation, a source of increased heart failure and mortality. We explored whether the valve itself adapts to the stresses imposed by the dilating ventricle. Three-dimensional echocardiography, validated against excised valves, measured diastolic leaflet area in 80 patients and control subjects. Leaflet area was an average of 35% greater in patients with left ventricular dysfunction than in control subjects. Leaflet area showed comparable adaptation to annular area in all groups (nearly 2-fold ratio). However, leaflet area was a strong independent predictor of mitral regurgitation, and patients with mitral regurgitation had reduced ratios of total leaflet area to the tented leaflet area required to close the annular orifice in systole. The valve therefore adapts to the increased size of remodeled ventricles, but the degree of adaptation may be insufficient to prevent mitral regurgitation by meeting the geometric demands imposed on the stretched leaflets. Understanding the mechanisms of mitral valve adaptation can potentially provide new therapeutic targets. See p 845.

**Electroanatomic Mapping of the Left Ventricle in a Porcine Model of Chronic Myocardial Infarction With Magnetic Resonance–Based Catheter Tracking**

During catheter ablation of cardiac arrhythmias, the importance of delineating the cardiac anatomy is undisputed. Currently, image integration with either computed tomographic or magnetic resonance (MR) imaging is used both to enhance the acquisition of 3-dimensional electroanatomic mapping and to guide radiofrequency ablation. Typically, the imaging is performed before the procedure and registered to the patient’s anatomy at the time of the procedure using fiducial land marks. However, a more ideal paradigm would be to perform these procedures completely in an MR imaging environment. Both errors in registration and exposure to ionizing radiation could theoretically be eliminated. Superior anatomic visualization could be possible with the generation of vascular roadmaps by MR angiography and visualization of abnormal infracted or ablated myocardium with myocardial delayed enhancement imaging. In this porcine study, MR tracking of microcoils embedded in electrophysiology catheters was used to navigate the catheters to the left ventricle at rates approaching that of x-ray fluoroscopy (13 to 15 frames per second) using MR angiography vascular roadmap guidance. With myocardial delayed enhancement images, it was possible to accurately maneuver the catheter within the chamber, to measure intracardiac electrograms, and to project this spatial and electrogram information onto the MR angiography–generated 3-dimensional left ventricle models. In infracted animals, MR imaging–based voltage maps were compared with standard x-ray–based electroanatomic voltage maps to establish the equivalency of this MR-tracking approach to ventricular mapping. This article demonstrates that it may be possible to use these imaging techniques with active MR tracking to perform electrophysiology procedures in a clinically relevant manner completely in an MR imaging environment. See p 853.