Association Between Smoke-Free Legislation and Hospitalizations for Cardiac, Cerebrovascular, and Respiratory Diseases: A Meta-Analysis

Secondhand smoke causes cardiovascular and respiratory disease, and implementation of smoke-free legislation is followed by drops in hospitalizations and deaths from these diseases. This meta-analysis of 45 studies of 33 smoke-free laws found that smoke-free legislation was associated with significantly lower rates of hospital admissions (or deaths) for coronary events, other heart disease, cerebrovascular accidents, and respiratory disease. There was a dose-response relationship between the strength of the law; more comprehensive laws (including workplaces, restaurants, and bars) had the largest health benefits. This study provides strong evidence not only of the health benefits of smoke-free laws, but also of the need to enact comprehensive laws without exceptions. See p 2177.

Sex-Related Trends in Mortality in Hospitalized Men and Women After Myocardial Infarction Between 1985 and 2008: Equal Benefit for Women and Men

During the past decades, medical management and outcomes of acute myocardial infarction have improved substantially. It has been suggested that women with myocardial infarction have benefitted less from these improvements in treatment and outcomes compared with men because they were underrepresented in clinical trials. With the present study, however, we are the first to test this suggestion over a 24-year study period. We demonstrate that adjusted short- and long-term mortality rates were similar and declined markedly and equally in women and men during the 24 years studied. Furthermore, we also present long-term mortality data, up to 20 years after the myocardial infarction, which are sparse. This study is important because it helps to direct both further research and further management, in which women deserve to be treated with the same evidence-based care. In addition, the observed temporal trends are encouraging and suggest that both men and women will benefit from further improvements in care for acute myocardial infarction. See p 2184.

Short- and Long-Term Outcomes of Coronary Stenting in Women Versus Men: Results From the National Cardiovascular Data Registry Centers for Medicare & Medicaid Services Cohort

Coronary stenting has become a standard of care for the treatment of medically refractory coronary artery disease, with approximately one third of percutaneous coronary interventions (PCIs) performed in women in the United States. Although procedural success rates are similar by sex, it remains unclear whether disparate in-hospital and long-term outcomes exist between the sexes. In addition, the long-term safety and effectiveness of drug-eluting stents versus bare metal stents were compared in women and men. In the contemporary PCI era, our study shows that elderly women undergoing index PCI remain at higher risk of in-hospital mortality and other complications compared with men. In contrast, long-term outcomes are similar or better in women than in men. The use of drug-eluting stents is associated with a similar benefit in both men and women. Further studies are needed to understand the causative factors for these findings. See p 2190.

Outcomes of Medicare Beneficiaries Undergoing Catheter Ablation for Atrial Fibrillation

Catheter ablation is increasingly used in older patients with atrial fibrillation for whom medical therapy has failed. However, clinical trials of catheter ablation have enrolled relatively young patients with limited comorbidity. To describe the use of catheter ablation and associated outcomes in older persons with atrial fibrillation, we conducted a retrospective cohort study of 15 423 Medicare beneficiaries who underwent catheter ablation for atrial fibrillation between July 2007 and December 2009. For every 1000 procedures, there were 17 cases of hemopericardium requiring intervention, 8 cases of stroke, and 8 deaths within 30 days. More than 40% of patients required hospitalization within 1 year; however, atrial fibrillation or atrial flutter was the primary discharge diagnosis in only 38.4% of cases. Eleven percent of patients underwent repeat ablation within 1 year. Renal impairment, age ≥80 years, and heart failure were major risk factors for mortality within 1 year after catheter ablation. Whereas major complications after catheter ablation were associated with advanced age, they were fairly infrequent, and few patients underwent repeat ablation. Randomized trials are needed to assess the efficacy of catheter ablation in older adults and to better inform risk-benefit calculations for older patients with drug-refractory, symptomatic atrial fibrillation. See p 2200.

Pathological Role of Serum- and Glucocorticoid-Regulated Kinase 1 in Adverse Ventricular Remodeling

Patients with heart failure have an increased risk of ventricular arrhythmias and sudden cardiac death. Heart failure is associated with changes in the electrical properties of the heart that form the triggers and substrate for ventricular arrhythmias. Available antiarrhythmic drugs have not shown any clinical benefit in patients with heart failure and have significant proarrhythmic side effects. To gain a better understanding of mechanisms that underlie the electrical changes in heart failure, we focused on the serum- and glucocorticoid-regulated kinase-1 (SGK1), a component of the cardiac phosphatidylinositol 3-kinase signaling pathway that is activated in heart failure. Our results demonstrated that activation of SGK1 in the heart increased mortality, cardiac dysfunction, and ventricular arrhythmias. The proarrhythmic effects of SGK1 were linked to biochemical and functional changes in the cardiac sodium channel and could be reversed by treatment with ranolazine, a blocker of the late sodium current. Conversely, inhibition of SGK1 in the heart protected against fibrosis, heart failure, and sodium channel alterations after hemodynamic stress. Our studies highlight the importance of sodium flux in the pathogenesis of arrhythmia in heart failure and raise the possibility that drugs that block the late sodium current could be useful in this setting. Moreover, these results identify SGK1 as a novel kinase target for treatment of both arrhythmia and cardiac dysfunction. The potential clinical importance of this observation is
underscored by the therapeutic success of kinase inhibitors in other disease processes. See p 2208.

Moderate Aortic Enlargement and Bicuspid Aortic Valve Are Associated With Aortic Dissection in Turner Syndrome: Report of the International Turner Syndrome Aortic Dissection Registry

Aortic dissection and rupture occurs in young women with Turner syndrome. Although this observation is reiterated in case reports, the rarity of its occurrence has limited the availability of information about the natural history and the clinical picture of aortic dissection in Turner syndrome. We estimated that it would require 50,000 patient-years in a prospective longitudinal study to accumulate data similar to the data obtained from the 20 cases we describe from the International Turner Syndrome Aortic Dissection registry. We show that aortic dissection can occur in individuals with Turner syndrome who have no other documented cardiovascular problems. Pregnancy was associated with 1 of 19 subjects in the International Turner Syndrome Aortic Dissection registry, which is 10 times more common than in the general TS population. Bicuspid aortic valve occurred in 95% of the subjects, but it also occurs commonly in those without aortic dissection. We found that aortic dissection in Turner syndrome occurs at a significantly smaller aortic size than in other genetically triggered aortopathies. Data from 5 individuals with serial echocardiographic measurements obtained before their aortic dissection indicates that a stable ascending aortic size over time may not be a reassuring finding. We conclude that an ascending aortic size index $>2.5$ cm/m$^2$ is a significant risk factor for aortic dissection in those with Turner syndrome. See p 2220.

Endogenous and Natural Complement Inhibitor Attenuates Myocardial Injury and Arterial Thrombogenesis

Reperfusion of ischemic tissues induces tissue injury that is mediated by complement activation. We have identified a novel, endogenous, natural complement inhibitor that displaces the 3 serine proteases (ie, mannose-binding lectin/ficolin-associated serine protease-1, -2, and -3) from the mannose-binding lectin complex in a dose-dependent manner. Furthermore, at pharmacologic concentrations, mannose-binding lectin-associated protein-1 prevents arterial thrombogenesis, as well as myocardial injury after ischemia and reperfusion in vivo. The mannose-binding lectin complex has been associated with several clinical diseases, and mannose-binding lectin-associated protein-1 may represent a novel molecular mechanism to modulate its activity in vivo. See p 2227.

Rho-Associated Coiled-Coil-Containing Kinase 2 Deficiency in Bone Marrow–Derived Cells Leads to Increased Cholesterol Efflux and Decreased Atherosclerosis

The retention of modified cholesterol by macrophages and their development into foam cells are critical steps in atherogenesis. Cholesterol retention in macrophages is governed by cholesterol uptake and efflux. The precise signaling pathways that regulate cholesterol uptake and efflux are not known. The Rho-associated coiled-coil-containing kinases (ROCK1 and ROCK2) are serine-threonine protein kinases that are involved in the regulation of the actin cytoskeleton. Recent studies suggest that deletion of ROCK1 in bone marrow–derived cells is atheroprotective. However, the role for ROCK2 in the pathogenesis of atherosclerosis has not been determined. In the present article, we show that ROCK2-deficient mice on a genetic atherosclerotic background developed substantially fewer atherosclerotic lesions in the aorta and subaortic sinus after consumption of a high-cholesterol diet. These findings correlated with decreased foam cell formation and increased cholesterol efflux in ROCK2-deficient mice that are mediated, in part, through the peroxisome proliferator-activated receptor-$\gamma$/liver X receptor/ATP-binding cassette transporter A1 pathway in macrophages. In contrast, cholesterol efflux was unchanged in ROCK1-deficient macrophages, indicating a distinct role for ROCK2 in the reverse cholesterol transport system. These findings provide important and novel insights into the signaling mechanism that governs cholesterol efflux, which could lead to the development of selective ROCK inhibitors as therapeutic agents for atherosclerotic vascular disease. See p 2236.
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