Apixaban in Comparison With Warfarin in Patients With Atrial Fibrillation and Valvular Heart Disease: Findings From the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) Trial

The coexistence of atrial fibrillation and valvular heart disease (VHD) is associated with a higher risk of thromboembolic events and bleeding. There is a lack of available data evaluating new oral anticoagulants in patients with VHD and atrial fibrillation. We compared the effect of apixaban and warfarin on rates of stroke or systemic embolism, major bleeding, and death in 4808 patients with and without moderate or severe VHD, from the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) study. Apixaban, in comparison with warfarin, had similar relative and larger absolute benefits in reducing stroke or systemic embolism, causing less bleeding, and reducing mortality in patients with VHD in comparison with those without VHD. The current analysis provides a reliable evaluation of the efficacy and safety of apixaban in patients with VHD, and the results will potentially improve the cardiovascular burden of atrial fibrillation in VHD. See p 624.

Long-Term Outcome of Mustard/Senning Correction for Transposition of the Great Arteries in Sweden and Denmark

This is, to our knowledge, the largest studied cohort of patients with Mustard and Senning repair of the transposition of the great arteries. Transposition of the great arteries is a common cyanotic heart defect. The Mustard and Senning repair (atrial switch repair) of transposition of the great arteries was used in the 1960s, 1970s, 1980s, and early 1990s. Centers treating adults with congenital heart disease will have a cohort of patients who have had atrial switch repair, and the clinicians will want to identify those patients who have the highest risk of needing reoperation or who are at risk of dying. The atrial switch repair leaves the right ventricle in the systemic position and subjects the right ventricle to systemic afterload. This study finds that the type of repair (Mustard/Senning) is not statistically significantly associated with long-term survival or the risk of reoperation. The risk of reoperation is determined by who did the surgery, and the only factor we could identify that is statistically significantly associated with increased mortality is the implantation of a pacemaker. See p 633.

Estimated Global, Regional, and National Disease Burdens Related to Sugar-Sweetened Beverage Consumption in 2010

Sugar-sweetened beverages (SSBs) increase obesity and type 2 diabetes mellitus and are now consumed worldwide. Yet, the impact of SSBs on global diabetes mellitus—and obesity-related diseases by nation, age, and sex has not been reported. We developed a global model incorporating diverse data sources across 187 countries, by age and sex, on the following: SSB intake patterns from individual-level dietary surveys and national food availability; effects of SSBs on adiposity and diabetes mellitus from meta-analyses of longitudinal cohort studies; impact of adiposity on diabetes mellitus, cardiovascular disease, and cancers from meta-analyses of international pooling projects; and numbers of cause-specific national deaths from the Global Burden of Diseases study. Using a comparative risk assessment model, in 2010, we estimated ~184,000 deaths/y and 8.5 million disability-adjusted life-years per year attributable to SSBs worldwide; 75% of deaths and 85% of disability-adjusted life-years occurred in low- and middle-income countries. Tremendous geographic variation was evident, with the largest burdens in Latin America and the Caribbean, and the smallest burdens in East Asia. Proportional impacts (percentage of disease attributable to SSBs) were highest in young adults, particularly young men. In Mexico, 1 in 3 diabetes mellitus– and obesity-related deaths in men <44 years of age were attributable to SSBs; and in the United States, 1 in 10 such deaths were attributable to SSBs. Given a dramatic inverse gradient between age and SSB intake in most nations, future health burdens could be even higher as younger populations age. Our findings highlight the large global health burdens, and the key geographic and demographic variation, as well, attributable to SSBs, providing the basis for targeted health policy and interventions. See p 639.

Patient-Level Discordance in Population Percentiles of the Total Cholesterol to High-Density Lipoprotein Cholesterol Ratio in Comparison With Low-Density Lipoprotein Cholesterol and Non–High-Density Lipoprotein Cholesterol: The Very Large Database of Lipids Study (VLDL-2B)

The limitations of using a cardiovascular management strategy based on low-density lipoprotein cholesterol (LDL-C) exclusively have been extensively delineated in the literature with some current worldwide guidelines recommending the use of other parameters such as non–high-density lipoprotein cholesterol (non–HDL-C) and apolipoprotein B. However, guidelines do not recommend using total cholesterol to HDL-C ratio (TC/HDL-C) because it remains uncertain what information it may add given that TC and HDL-C are already used in risk estimation scores. Recent literature has also argued against a causal role for HDL-C in cardiovascular disease. Nevertheless, TC/HDL-C, readily available from the standard lipid profile, has been suggested to potentially carry information reflecting atherogenic particle size and concentration not available in LDL-C or non–HDL-C. Therefore, we aimed to assess the extent of patient-level discordance of TC/HDL-C with LDL-C and non–HDL-C, because the fundamental existence of discordance opens the possibility of additional clinical information. In our contemporary, cross-sectional, big data analysis of 1.3 million US adults, 1 in 3 patients had ≥25 percentile units discordance between TC/HDL-C and LDL-C, whereas 1 in 4 had ≥25 percentile units discordance between TC/HDL-C and non–HDL-C. Patients with a disproportionately high TC/HDL-C did not differ in age, but were mostly men and had a more atherogenic lipid phenotype with higher triglycerides and lower HDL-C. From a clinical perspective, the extent of patient-level discordance...
suggests that TC/HDL-C, available at no extra cost, potentially offers additional information to LDL-C and non–HDL-C. The next step is clinical outcomes studies using discordance analyses to further evaluate the potential value of TC/HDL-C discordance in risk assessment and treatment. See p 667.

**Autotaxin Derived From Lipoprotein(a) and Valve Interstitial Cells Promotes Inflammation and Mineralization of the Aortic Valve**

Calcific aortic valve disease (CAVD) is the most prevalent heart valve disorder. Mechanisms that promote CAVD are not fully understood. Lipid-derived products may drive aortic valve inflammation and mineralization. In this work, we identified that autotaxin was overexpressed in both human mineralized aortic valves and in a mouse model of CAVD. We found that autotaxin is possibly transported in the aortic valve by lipoprotein(a) and also is secreted by valve interstitial cells. We show in human valve interstitial cells and in a mouse model that autotaxin by its downstream product, lysophosphatidic acid, promotes inflammation, osteogenic transdifferentiation of valve interstitial cells, and the development of CAVD. Thus, autotaxin and lysophosphatidic acid could represent novel targets in CAVD. See p 677.