In Utero Diagnosis of Long QT Syndrome by Magnetocardiography

Long QT syndrome (LQTS) is among the most common causes of sudden cardiac death in the young. Although its role in sudden infant death syndrome has been known for more than a decade, a very recent study by Crotti and colleagues suggests that LQTS may also be responsible for >10% of unexplained fetal death. This finding implies that many lives might be saved if LQTS could be accurately diagnosed and effectively treated in utero. Our study demonstrates that both are possible. Using fetal magnetocardiography (fMCG), the magnetic analog of ECG, we show that fetal QTc has diagnostic value for identification of fetuses with LQTS and prognostic value for prediction of a severe phenotype. In addition, fMCG was invaluable for definitive detection of the signature lethal rhythm of LQTS, Torsades de Pointes. The fMCG findings not only prompted successful in utero pharmacological treatment to restore sinus rhythm and postpone the delivery of a premature fetus, but also guided anticipatory neonatal care. Because of the known association between LQTS and low heart rate, some fetuses with an isolated finding of low-for-gestational-age heart rate (<3%) were referred for fMCG testing and were found to have LQTS. This led to the identification of LQTS in several unsuspecting first-degree relatives. Currently, fMCG is not readily accessible to clinicians because of the cost and complexity of the instrumentation; however, a new technology, based on atomic magnetometers, has the potential to rectify this situation. See p 2183.

Causes of Death and Influencing Factors in Patients With Atrial Fibrillation: A Competing-Risk Analysis From the Randomized Evaluation of Long-Term Anticoagulant Therapy Study

Atrial fibrillation (AF) increases overall mortality. A better understanding of the mechanisms of death in AF patients is required to further refine approaches to reducing the mortality associated with AF. The Randomized Evaluation of Long-Term Anticoagulant Therapy (RE-LY) study (which compared dabigatran etexilate to warfarin), with a mean follow-up of 2 years, provided the opportunity to study causes of deaths and their predictors among a representative set of >18,000 AF patients undergoing anticoagulation. Deaths (1371 deaths), their causes, and major events during follow-up were prospectively collected and blindly adjudicated, and predictors of cause of death were evaluated with competing-risk analysis. Dabigatran significantly reduced vascular-related mortality compared with warfarin but had no effect on other causes of death, which constituted the vast majority (up to 90%) of deaths in this study. This implies that future improvements in antithrombotic treatments may lead to few additional reductions in overall mortality among patients with AF. In contrast, intervening in other mechanisms such as mitigating ventricular remodeling and comprehensive management of cardiovascular risk factors and comorbidities may be more effective in eventually decreasing the 2 most common causes of death in AF patients: sudden cardiac death and death from progressive heart failure. Our results also emphasize the prognostic importance of nonfatal stroke and bleeding events. See p 2192.

Placental Vascular Dysfunction, Fetal and Childhood Growth, and Cardiovascular Development: The Generation R Study

Low birth weight is associated with cardiovascular disease in adulthood. These associations may be explained by developmental adaptations in early life in response to suboptimal fetal nutrition. Suboptimal placental growth and function may lead to fetal undernutrition and persistently influence growth and cardiovascular function in later life. Placental vascular function can be assessed by ultrasound assessment of the feto-placental vascular resistance and utero-placental vascular resistance. Increased vascular resistance in the umbilical and uterine arteries, which may occur as a result of impaired placentation or suboptimal fetal vascular development, is associated with increased risks of adverse maternal and fetal pregnancy outcomes. We observed, in a large population-based prospective cohort study among 6716 mothers and their children, that higher third trimester feto-placental and utero-placental vascular resistance were associated with lower third trimester fetal length and weight growth with persistent growth effects until the age of 6 years. Higher third trimester feto-placental vascular resistance, but not utero-placental vascular resistance, was also associated with an adverse cardiovascular profile in childhood. These associations were only partly explained by birth weight, and tended to be stronger among girls than among boys. Our study provides novel insight in the long-term growth and cardiovascular consequences of placental vascular dysfunction, and is important from a cardiovascular developmental perspective. Further studies are needed to explore whether interventions to improve placental vascular function will lead to better cardiovascular health in later life. See p 2202.

Age-Associated Defects in EphA2 Signaling Impair the Migration of Human Cardiac Progenitor Cells

Human cardiac progenitor cells (hCPCs) have recently been introduced in the experimental treatment of ischemic cardiomyopathy in humans. One of the critical variables of hCPC function is dictated by their motile state that conditions the translocation of cells to the damaged myocardium. Cardiac aging is coupled with alterations in the migratory capacity of hCPCs, although the mechanisms involved are largely unknown. We have found that the inadequate activation of the EphA2 receptor in old hCPCs affects their movement in vitro and in the injured myocardium in vivo. Cellular aging does not change the protein level of EphA2 receptors in hCPCs nor the early events involved in receptor binding to the ephrin A1 ligand, pointing to abnormalities in the activity of this receptor tyrosine kinase in senescent cells. Our findings support the
view that oxidative stress is a crucial determinant of hCPC aging. The accumulation of reactive oxygen species in old hCPCs induces post-translational modifications of the EphA2 protein interfering with the receptor tyrosine kinase function. Although the specific residues affected by oxidative stress were not identified, oxidation is known to abrogate receptor activity. The age-dependent consequences of EphA2 receptor oxidation were reversed by exogenously expressed functionally-competent EphA2 receptors in old hCPCs. Importantly, protocols have been defined for the preferential isolation of young efficient hCPCs, a strategy that may have significant implications in the future management of chronic heart failure. See p 2211.

Automated External Defibrillators Inaccessible to More Than Half of Nearby Cardiac Arrests in Public Locations During Evening, Nighttime, and Weekends

Out-of-hospital cardiac arrest is a major public health concern and is associated with a poor prognosis. Automated external defibrillators (AEDs) can increase survival markedly after out-of-hospital cardiac arrest and can be used safely and effectively by laypersons. During the past years, there has been increasing focus on community-based AED deployment to establish grounds for public-access defibrillation. To increase survival, AEDs need to be used within minutes and thus must be close to the victim, locatable, and accessible to bystanders. Despite widespread AED dissemination, AED use and effect on survival in community settings have remained limited, and the reasons for this are not completely understood. So far, efforts to increase AED use have focused on widespread AED dissemination, optimizing AED placement and establishing linkage to emergency dispatch centers. Our study shows that AEDs were highly accessible during the daytime on weekdays but considerably inaccessible during the evening, nighttime, and weekends, when most cardiac arrests occurred. Thus, limited AED accessibility greatly reduced the potential for the AED to be used. The results provide insight into how AED accessibility affects AED coverage of cardiac arrests in public locations and serve as guidance for other communities seeking to optimize AED use. These findings underline that not only strategic placement but also uninterrupted AED accessibility warrant attention if public-access defibrillation is to improve survival after out-of-hospital cardiac arrest. See p 2224.