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# Studies explore lifestyle choices and heart risks

***Dark chocolate, nicotine patches examined for impact on heart function***

Genetics and family history play a large role in a person's risk for heart disease, but factors in diet, lifestyle and the environment are also thought to influence susceptibility to the disease. A number of studies presented today at the American College of Cardiology's 56th Annual Scientific Session look at how health-related behaviors can influence a person's risk for cardiovascular disease. ACC.07 is the premier cardiovascular medical meeting, bringing together cardiologists and cardiovascular specialists to further breakthroughs in cardiovascular medicine.

"Because scientific advances are pushing forward at such an incredible pace, our insight into the mechanism and progression of cardiovascular disease is growing exponentially," said Robert S. Rosenson, M.D., of University of Michigan, Preventive Cardiology, in Ann Arbor, Mich. "The research presented here today further demonstrates how researchers are beginning to understand the links between cardiovascular diseases and changes in lifestyle, including quitting smoking, geographic location, diet and weight, and other related factors."

Effects of Sustained Ingestion of Cocoa on Endothelial Function in Adults with BMI between 25-35 kg/m2: A Randomized, Single Blind, Placebo Controlled Trial (Presentation Number: 1026-34)

Flavonoids, a group of antioxidant compounds found in fruits and vegetables, are not generally labeled as essential nutrients, but play an important role in maintaining one's health. In fact, studies indicate that there is a strong inverse correlation between the consumption of foods rich in flavonoids ‹such as wine, green tea, fruits and vegetables ›and cardiovascular disease. Cocoa or dark chocolate products are considered one of the most concentrated sources of flavonoids among commonly consumed foods. Since endothelial function has been used extensively to evaluate the effects of foods and nutrients on cardiac risk, researchers at the Yale

Prevention Research Center in Connecticut conducted a trial to assess whether the consumption of cocoa would provide any sustained benefits on endothelial function.

Specifically, the team measured the function of the brachial artery to relax and expand to accommodate increased blood flow (also know as flow mediated dilation, or FMD) in adults with a body mass index (BMI) between 25 and 35 kg/m2. In the randomized, single-blind, placebo-controlled crossover study, 45 subjects recruited from the general population of southwestern Connecticut were randomly assigned to one of the three consumption groups: eight ounces of either cocoa without sugar, cocoa with sugar or placebo. For six weeks, all participants underwent endothelial function testing, assessing FMD of the brachial artery using high frequency ultrasound before and after the daily cocoa or placebo consumption.

Cocoa was considered a successful vehicle to improve endothelial function in this trial. Of the 39 subjects who completed the trial, FMD improved significantly in the groups consuming cocoa with no sugar (2.4 %) and cocoa with sugar (1.5 %) from baseline values when compared to placebo (-0.8 %).

"In this sample of healthy adults with BMI between 25 and 35 kg/m2, dark chocolate ingestion over a short period of time was shown to significantly improve endothelial function, leading our team to believe that greater benefit may be seen through a long-term, randomized clinical trial," said Valentine Yanchou Njike, M.D., of Yale Prevention Research Center, and co-investigator on this study. "While the findings from this study do not suggest that people should start eating more chocolate as part of their daily routine, it does suggest that we pay more attention to how dark chocolate and other flavonoid-rich foods might offer cardiovascular benefits."

Dr. Njike will present this study on Tuesday, March 27, at 11:00 a.m. in Hall H.

Effects of Diabetes on the Prevalence of Aspirin Resistance During Low Dose Aspirin Therapy (Presentation Number: 1019-179)

Coronary heart disease deaths are often caused by platelets sticking together and forming blood clots (thrombosis) that limit blood flow within heart arteries and result in heart attacks. The use of aspirin has been shown to reduce the risk of heart attack by keeping platelets from sticking together, specifically by blocking an important enzyme, cyclooxygenase-1 (COX-1). However, recent studies suggest that some diabetic patients may be less responsive to these important benefits of aspirin. To date, no prospective analysis of the effects of aspirin dose on platelet inhibition in diabetic versus non-diabetic patients has been conducted.

Researchers from the Sinai Center for Thrombosis Research at Sinai Hospital in Maryland, studied 120 patients (30 patients with diabetes) with stable coronary artery disease, who were randomly assigned to progressively receive 81 mg, 162 mg, or 325 mg of aspirin daily for four weeks each, for a total of 12 weeks. The response to aspirin was measured by methods that directly and indirectly measure inhibition of COX-1, including: adenosine diphosphate (ADP)-induced aggregation and collagen-induced aggregation (important platelet activators playing a role in the development of thrombosis); the VerifyNow aspirin assay test, which determines how well COX-1 is blocked in platelets; and urinary thromboxane, which assesses how well COX-1 is blocked in vivo.

Overall, the prevalence of aspirin resistance was low (less than 5%) during the 81 mg aspirin treatment period using direct measurement of COX-1 inhibition. However, resistance at this dose was markedly higher in diabetic patients as measured by indirect measurements of COX-1 such as the levels of adenosine diphosphate (ADP) (27 vs.14 %), collagen-induced aggregation (27 vs. 4 %), a point-of-care VerifyNow aspirin assay (13 vs. 3 %) and urinary thromboxane levels (37 vs. 17 %).

Despite significant differences at the 81 mg aspirin dose, resistance among diabetics decreased as aspirin dose was increased. At a 325 mg daily dose, collagen-induced platelet aggregation fell significantly, from 54 to 29 percent, as did the prevalence of resistance determined by VerifyNow and urinary thromboxane results. These findings, which are being studied further, suggest that diabetic patients may receive greater benefit from higher aspirin doses.

"Aspirin is a fundamental part of the prevention and treatment of coronary heart disease, but the impact of diabetes and other demographic variables on the responsiveness of platelets to aspirin and accurate dosing remains unclear," said Paul A. Gurbel, M.D., of Sinai Center for Thrombosis Research and lead author on this study.

"Diabetic patients with coronary artery disease exhibited a higher prevalence of resistance than non-diabetics during therapy with low-dose aspirin, indicating a higher risk of thrombosis. However, at a higher aspirin dose we observed better platelet inhibition in the diabetic patient. Our hope is that this will lead to future studies looking at the best aspirin doses for diabetic patients, moving physicians away from the one-size-fits-all approach to aspirin therapy," according to Dr. Gurbel.

Dr. Gurbel will present this study on Monday, March 26, at 2:30 p.m. in Hall H.

Nicotine Patches are Safe to Use in Patients with Coronary Artery Disease and Stress-Induced Myocardial Ischemia (Presentation Number: 1013-70)

The most commonly used nicotine replacement products ,which help relieve some of the withdrawal symptoms of smoking cessation ,are nicotine patches. However, the safety of using these patches for smoking cessation among patients with heart conditions like ischemia (insufficient blood flow to the heart) or coronary artery disease (CAD) is uncertain. Therefore, researchers from the Methodist DeBakey Heart Center in Texas conducted a study to assess the effects of nicotine patches on stress-induced myocardial ischemia using single photon emission computed tomography (SPECT), an imaging technique using gamma rays to show how well blood flows to heart tissue.

In this prospective, multicenter, randomized, placebo-controlled trial, 55 participants ,all of whom had greater than nine percent ischemic perfusion defect size (or PDS, a measure of the amount of ischemic heart muscle) according to SPECT scans and who smoked more than 20 cigarettes per day ,were randomized to receive either 21 mg nicotine patches or placebo patches while continuing to smoke. After one week, a SPECT scan was repeated and patients were then encouraged to stop smoking and continue to use the patches. Patients underwent a third scan at week four. Nicotine and exhaled carbon monoxide (CO) levels were measured prior to each SPECT and researchers compared the results of active patch-using patients to those given a placebo.

After four weeks, when compared to baseline, nicotine patch users showed a greater rate of CO reduction (22 vs. 12 parts per million, or ppm) versus those administered placebo (23 vs. 19 ppm), which paralleled their decreased cigarette use. However, despite a significant increase in nicotine levels in the active patch group over those four weeks, no significant changes in total or ischemic PDS were observed from baseline, when compared to patients receiving the placebo patches (15 vs. 13 %, compared to 12 vs. 11 %).

"Smoking is a major cause for coronary artery disease, and quitting is the best way to reduce the level of cardiac risk. This is the first prospective study looking at the effects of nicotine patches on changes in blood flow to the heart," said Monika J. Leja, M.D., of Methodist DeBakey Heart Center, and lead author on this study. "The results from this study show that nicotine patches do not increase stress-induced myocardial ischemia and therefore appear to be a safe method for aiding smoking cessation, even in patients with coronary artery disease and active ischemia."

Dr. Leja will present this study on Monday, March 26, at 10:00 a.m. in room Hall H.

Evidence Does Not Support Obesity as a Relative Contraindication to Heart Transplantation (Presentation Number: 1016-108)

Recently, guidelines for listing candidates for heart transplant were revised to include obesity (body mass index (BMI) greater than 30 kg/m2) as a potential reason to deny transplantation. However, the evidence supporting this recommendation remains weak. Therefore, using data from the United Network for Organ Sharing (UNOS) Registry, researchers at Columbia University College of Physicians and Surgeons in New York examined the relationship between pre-heart transplant BMI and post-transplant survival.

In this study, investigators looked at 18,622 first-time adult transplant recipients between 1995 and 2005. Using a design developed by the National Heart, Lung, and Blood Institute, recipients were divided into standard BMI categories: underweight (less than 18.5, n=713), normal (18.5-24.99, n=7,539), overweight (25-29.99, n=6,915), obese (30-34.99, n=2,857), severely obese (35-39.99, n=515) and morbidly obese (greater than 40, n=120). Findings from the study demonstrate that while normal weight patients experienced the best survival (10.1 years), survival after transplantation in obese patients (9.6 years) was not statistically different than survival of less severely overweight patients (9.7 years).

"This analysis does not support the latest recommendations, but rather demonstrates that obese patients do not face an increased risk of death after heart transplantation," said Mark J. Russo, M.D., M.S., of Columbia University 痴 International Center for Health Outcomes and Innovation Research and lead author on this study.

"This also reveals important information regarding underweight patients who appear to experience the same increased risk of death as patients in the most extreme weight categories (severely and morbidly obese), especially in the first year following transplantation," according to Dr. Russo.

While the relationship between obesity and cardiac disease receives great attention and the latest recommendations regarding patient selection for heart transplantation focus on the effect of obesity on survival after transplant, it is known that poor nutritional status in patients with end-stage heart failure is a marker for poor prognosis.

"Findings from our current study highlight the risks that malnourished patients face after heart transplantation, which are most comparable to patients with BMIs in most extreme obesity

categories," said Yoshifumi Naka, M.D., Ph.D., of New York-Presbyterian Hospital and Columbia University College of Physicians and Surgeons and senior author on this study. "This emphasizes the need to optimize the nutritional status of patients with heart failure, and it is our hope that future consensus statements from our professional organizations should reflect these findings."

Dr. Naka goes on to say that even higher risk heart transplant recipients, including both obese and malnourished patients, often have much improved survival after transplantation. In fact, severe end-stage heart failure patients, who without a heart transplant have a life expectancy measured in months, may live 10 or 20 years longer.

Dr. Russo will present this study on Monday, March 26, at 9:00 a.m. in room Hall H.

Adverse Cardiovascular Effects of Air Pollution in Patients With Coronary Heart Disease (Presentation Number: 805-5)

Among the many damaging effects of traffic-derived air pollution, researchers have noted that exposure to air pollution may worsen symptoms of angina (chest pain) or even trigger acute myocardial infarction (heart attack) in people with existing heart conditions. Researchers from the University of Edinburgh in the United Kingdom and Umea University in Sweden conducted a controlled-exposure study of dilute diesel exhaust to determine the direct effects of air pollution on myocardial ischemia in patients with stable coronary heart disease.

In a double-blind, randomized cross-over study, 20 patients with prior myocardial infarction were exposed to dilute diesel exhaust (particle concentration 300 ìg/m3, similar to levels encountered in urban road traffic) or filtered air during periods of rest and moderate exercise in a controlled-exposure facility. During the exposure, myocardial ischemia was quantified by ST segment analysis using continuous 12-lead electrocardiography.

Overall, exposure to diesel exhaust caused a three-fold increase in maximal ST segment depression (-49 vs. -17 ìV) among participants. While exercise-induced ST segment depression was present in all patients, there was a marked increase in ischemic burden during exposure to diesel exhaust (-22 vs. -8 ìV). During periods of exercise, participants experienced a similar increase in heart rate regardless of exposure to either diesel exhaust or filtered air.

"While substantial evidence links exposure to air pollution with cardiovascular disease, these observations are limited by the effect of potential confounding environmental and social

factors," said David Newby, M.D., of the University of Edinburgh and lead investigator on this study. "In a carefully controlled study, we report that brief exposure to diesel exhaust at levels encountered in urban road traffic promotes myocardial ischemia in patients with existing heart conditions. Our findings strengthen the observation that exposure to combustion-derived air pollution is associated with adverse cardiovascular events, including acute myocardial infarction. Environmental health policy interventions targeting reductions in urban air pollution should be considered in order to decrease the risk of adverse cardiovascular events."

Dr. Nicholas L. Mills will present this study on Monday, March 26, at 7:30 a.m. in Room 265.

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The American College of Cardiology (www.acc.org) represents the majority of board certified cardiovascular physicians in the United States. Its mission is to advocate for quality cardiovascular care through education, research, promotion, development and application of standards and guidelines- and to influence health care policy. ACC.07 and the i2 Summit is the largest cardiovascular meeting, bringing together cardiologists and cardiovascular specialists to share the newest discoveries in treatment and prevention, while helping the ACC achieve its mission to address and improve issues in cardiovascular medicine.