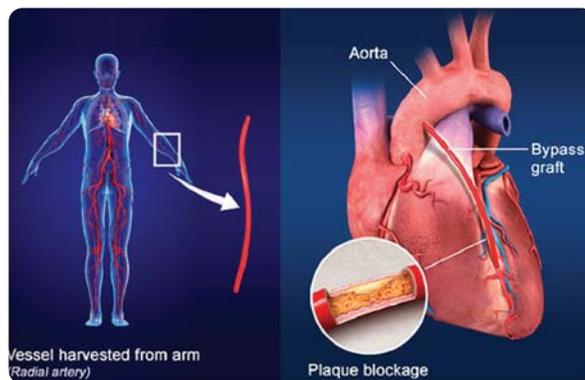


Preoperative Trimetazidine is Effective in Myocardial Preservation in Coronary Artery Bypass Graft Patients

Pre-operative trimetazidine therapy appears to have a positive effect on myocardial preservation in CABG patients, published in the journal *Cardiology*. Coronary artery bypass grafting (CABG) is a key and effective surgical treatment modality for coronary artery disease. Unfortunately, ischemia-reperfusion injury during and after CABG can lead to reversible and irreversible myocardial damage. Trimetazidine [1-(2,3,4-trimethoxybenzyl) piperazine dihydrochloride] is a metabolic anti-ischemic agent with demonstrated cardioprotective effects that does not alter cardiac hemodynamics. Accordingly, meta-analyses of randomized controlled trials (RCTs) have validated the beneficial cardioprotective effects of trimetazidine therapy in patients with stable angina pectoris and congestive heart failure (CHF). Although trimetazidine shows promise as an anti-ischemic agent, its effects with respect to myocardial preservation in CABG patients remain unclear. Now this study reports pre-operative trimetazidine therapy appears to have a positive effect on myocardial preservation in CABG patients. A systematic review and meta-analysis of RCTs was conducted to investigate the effectiveness of myocardial preservation of pre-operative trimetazidine therapy in CABG patients by assessing the post-operative levels of several blood-based biochemical



markers of myocardial injury, including creatine kinase (CK), creatine kinase-MB (CKMB), creatine phosphokinase (CPK), troponin T (TnT) and troponin I (TnI). The RCTs were classified into two subgroup analyses by the timing of sample collection. Six RCTs were finally included in the meta-analysis. The pooled effect sizes showed significantly lower post-operative levels of CK, CK-MB, TnT and TnI in the trimetazidine-treated CABG patients relative to control CABG patients. In both the ≤ 12 and >12 h post-CABG subgroup analyses, significant differences in CK, CK-MB, TnT and TnI were detected between the trimetazidine-treated CABG patients relative to control CABG patients. However, there were no significant

differences in the post-operative CPK levels between trimetazidine-treated CABG patients relative to control CABG patients. Significantly lower post-operative levels of CK, CK-MB, TnT and TnI were found in the trimetazidine-treated CABG patients relative to control CABG patients. Thus, this systematic review and meta-analysis of 6 placebo controlled RCTs investigated the effectiveness of preoperative trimetazidine therapy on myocardial preservation in CABG patients by assessing the postoperative levels of several blood-based biochemical markers of myocardial injury.

Olmесartan/Amlodipine: Blood Pressure Lowering and Beyond in Special Populations

Clinical studies and population-based analyses show that in patients with hypertension, the majority cannot control their blood pressure (BP) by treatment with a single antihypertensive agent. Combining agents from different antihypertensive classes with complementary modes of action significantly increases efficacy and is a treatment strategy recommended by European treatment guidelines, particularly in patients at high cardiovascular risk. The combinations of antihypertensive agents recommended by the European guidelines include an angiotensin receptor blocker (ARB) with a calcium channel blocker (CCB). The single-pill combination formulation of the ARB olmesartan medoxomil plus the CCB amlodipine is an effective and well-tolerated treatment that provides greater blood pressure lowering and control than the component monotherapies and



favors compliance by not increasing pill burden. Importantly, the efficacy and tolerability of olmesartan plus amlodipine is not affected by age, gender, hypertension severity, diabetes status, race or body mass index. Additional blood pressure lowering effects are observed with stepwise up-titration of olmesartan plus amlodipine with or without hydrochlorothiazide, with more patients achieving blood pressure goals. In addition, olmesartan plus amlodipine has demonstrated effects beyond BP lowering by showing beneficial effects on markers of inflammation, endothelial dysfunction and oxidative stress, as well as metabolic improvements and a reduction in new-onset diabetes

incidence in hypertensive patients with metabolic syndrome. These findings were published in the journal *Therapeutic Advances in Cardiovascular Diseases*.

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Risk of Stroke Better Predicted by Blood Pressure Pattern

Instead of relying on individual blood pressure readings, doctors should review the overall pattern to predict a patient's risk of stroke or early death, according to a new research. "Our study suggests that looking at someone's blood pressure over time and whether it increases slowly or steeply may provide additional information above only the level of blood pressure at a certain time," said researcher. High blood pressure is the number one risk factor for stroke. But, most studies assessing risk have looked only at measurements taken at a single point in time, the researchers said in background notes. For this new study, the researchers collected 20 years of data on the systolic blood pressure of more than 6,700 Dutch adults. Participants were ages 55 to 106 and living in a suburb of Rotterdam. The trial started in 1990, and five follow-up medical examinations were conducted over two decades. Those whose systolic blood pressure rose steeply from mid-life on and those whose high blood pressure dropped after age 65 had the highest risk of stroke or death from other blood pressure-related diseases up to age 80, the study found. Moderately high blood pressure was linked to the highest risk of stroke overall, but the lowest risk of death from heart attack, heart failure and kidney disease, the researchers said. This finding "further underlines the importance of treating people with a high blood pressure, even if it is only moderately elevated," said the researcher. People with normal blood pressure that gradually increased had the lowest risk of stroke and a low risk of death from other causes, the researchers found. Overall, the researchers team identified four blood pressure



patterns- most common was a gradual increase in blood pressure from normal systolic blood pressure (120 mm Hg) in middle age to high (160 mm Hg); normal blood pressure in middle age but a steep rise to very high (200 mm Hg); moderately high blood pressure (140 mm Hg) in middle age that did not change much and high blood pressure (160 mm Hg) in middle age, which decreased after 65. This pattern was more frequent in men, and these patients were more likely than some others to take blood pressure medication. Compared with people whose blood pressure increased gradually, people whose high blood pressure dropped after 65 had the highest risk of stroke (13.6 %). Next in line

were those whose blood pressure rose steeply (8% greater risk) and adults whose moderately high blood pressure stayed stable (a nearly 5% higher risk of stroke), the researchers found. "The highest risk of stroke and death was found in the class with a high mid-life blood pressure and the class that increased steeply in blood pressure," the researcher said. The report was published in the journal *Hypertension*. Other doctors agreed the findings support the need for regular blood pressure checks. "This study shows the importance of routine blood pressure checks and treatment of high blood pressure at early ages to maintain normal, or only modestly elevated, blood pressure," said Dr. Andrew Rogove, medical director of stroke at Northwell Health Southside Hospital in Bay Shore, N.Y. Regardless, "control of high blood pressure starting at an early age and continued throughout one's lifetime is important," he concluded.

Angiotensin Receptor Blockers are Effective in Long-Term BP Lowering in Patients with Essential Hypertension

Angiotensin receptor blockers (ARBs) are widely used in managing essential hypertension, with considerable evidence available on their short-term efficacy in lowering blood pressure (BP). Now, a study published in the *Journal of the American Society of Hypertension* reports that ARBs are effective in long-term BP lowering in patients with essential hypertension. The purpose of this study was to conduct a systematic review and meta-analysis assessing the long-term effects of ARBs as a class on BP control, myocardial infarction, hospitalization for heart failure, cerebrovascular events (ie, stroke), cardiovascular mortality, and all-cause mortality. The MEDLINE, EMBASE, PubMed, and the Cochrane Library databases were searched from inception to March 2015. Two evaluators independently reviewed studies for eligibility. Randomized controlled hypertension trials were included if they reported on ARB efficacy in either BP control (relative to placebo for periods ≥ 6 months) or cardiovascular/cerebrovascular outcomes (relative to non-ARB antihypertensive therapies for periods ≥ 24 months). Studies were pooled with a random-effects model using weighted mean differences (WMDs) and relative



risks for continuous and dichotomous outcomes, respectively. A total of 11 articles were included in the narrative synthesis, representing seven unique trials (16,864 participants). Six ARB agents were studied: candesartan, eprosartan, irbesartan, olmesartan, losartan (each represented by one trial arm), and telmisartan (represented by two arms). The ARB therapy significantly reduced mean systolic BP (WMD: -4.86; 95% CI: -6.19, -3.53 mm Hg) and diastolic BP (WMD: -2.75; 95% CI: -3.65, -1.86 mm Hg) compared to placebo. The risk of stroke was reduced by 21% in the ARB group compared with alternative anti-hypertensives (risk ratio: 0.79; 95% CI: 0.66, 0.96). Angiotensin receptor blockers did not, however, produce statistically significant reductions in the risk of myocardial

infarction, heart failure hospitalization, or mortality. The findings suggest that ARBs, as a class, are more effective than placebo therapy in long-term BP lowering in patients with essential hypertension. Long-term ARB treatment may also confer enhanced protection against stroke but no other cardiovascular outcomes relative to placebo.

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Statins: Beyond Treatment for Low-Density Lipoprotein Cholesterol

Statins may aid in extensive lipid changes beyond low-density lipoprotein cholesterol (LDL-C), according to new data published in the *Journal of the American College of Cardiology*. While statins have become a mainstay therapy for dyslipidemia and cardiovascular disease risk, little is known about the molecular effects on metabolic pathways. Researchers analyzed metabolic profiles in 4 population-based cohorts from the United Kingdom and Finland, based on serum nuclear magnetic resonance metabolomics at 2 time points (2.5 years and 23 years of follow-up). A total of 5590 patients were included—716 of whom started statin therapy and 4874 of whom were “persistent nonusers.” During follow-up, concentration changes in 80 lipid and metabolite measures were compared between the 2 groups. Remnant cholesterol was substantially lowered (80% relative to LDL-C), but triglycerides were only moderately lowered (25% relative to LDL-C). Omega-6 achieved the lowest levels of the fatty acids (68% relative to LDL-C) and other fatty acids were only “modestly affected.” Circulating amino acids, ketones, and glycolysis-related metabolites were not significantly affected. To better understand pharmacological effects of statins, researchers used Mendelian randomization to analyze a genetic variant,



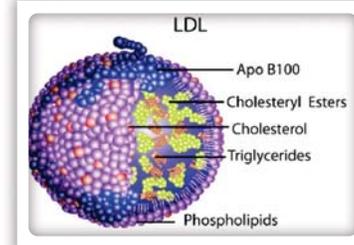
rs12916, known to mimic inhibition of Hydroxymethylglutaryl-CoA (HMG-CoA) reductase (HMGCR; the intended drug target) with the same 80 lipids and metabolites identified in the 4 original cohorts, but in a much larger population: 27 914 individuals from 8 cohorts. The authors wrote, “Although Mendelian randomization of drug targets has been used previously, our study was the first to our knowledge to combine the concept with observational results across a wide range of cardiometabolic biomarkers.” They discovered the metabolic changes associated with statins closely matched the association pattern with rs12916 in the HMGCR gene ($R^2=0.94$; slope 1.00 ± 0.03). “Starting statins was associated with minor lowering of large- and medium-sized VLDL [very-low-density lipoprotein] particle concentrations (11% to 20% relative to the LDL-C-lowering effect), whereas substantial lowering of the smallest VLDL particles (71% relative to LDL-C) was observed.” In addition, total cholesterol, non-HDL-C (high-density lipoprotein), and IDL-C (intermediate-density lipoprotein) were all lowered (92% to 100%), similar to LDL-C. In the future, molecular effects of drugs may be better understood via metabolic profiling and genetic proxies that mimic pharmacological action.

Statin Use, Intensity, and 3-year Clinical Outcomes among Older Patients with Coronary Artery Disease

Clinical trial evidence suggests that statin therapy reduces adverse clinical events and provides even greater benefit at high-intensity doses in coronary artery disease (CAD) patients. The researchers from Centers for Medicare and Medicaid Services linked detailed in-hospital data (2005–2009) on 15,729 Get With The Guidelines CAD patients ≥ 65 years prescribed statins to Centers for Medicare and Medicaid Services claims. High-intensity statin therapy was defined as discharge prescription of atorvastatin ≥ 40 mg, rosuvastatin ≥ 20 mg, or simvastatin 80 mg. They used Kaplan-Meier curves to calculate all-cause mortality, major adverse cardiovascular events (MACEs), and all-cause readmission at 3 years post-discharge; log-rank tests to compare survival via overall statin use and intensity; and Cox proportional hazards regression with inverse propensity weighting to evaluate adjusted rates of adverse events over 3 years post-discharge. Results of the study show that of 35,903 patients meeting inclusion criteria, 24,367 (67.9%) were discharged on statin. Of 15,729 patients with statin intensity information, 4488 (28.5%) received high-intensity therapy; these recipients were more often younger, male, and had acute myocardial infarction. After inverse propensity weighting adjustment, statin use was associated with significantly lower hazards of mortality (hazard ratio 0.89, 95% CI 0.84–0.93) and MACE (0.92, 0.88–0.96), but not readmission (1.01, 0.97–1.04). High-intensity (vs low/moderate) use was not associated with lower risk of all-cause mortality (1.07, 1.00–1.14), MACE (1.05, 0.99–1.11), or readmission (1.05, 1.00–1.10). Clinically relevant subgroups had similar results. The study concludes that in older hospitalized CAD patients, use of statin therapy at discharge was associated with improved long-term outcomes. Consistent with current American College of Cardiology/American Heart Association cholesterol guideline recommendations supporting moderate- rather than high-intensity statin therapy in CAD patients >75 years, high-intensity statin therapy was not associated with incremental benefit in this older population. The research was published in *American Heart Journal*



LDL Cholesterol Reductions Depend on Statin Choice and Dose



For patients with hypertriglyceridemia, low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) reductions depend of the choice and dose of statin, according to research published in *The American Journal of Cardiology*. The researchers used data from a meta-analysis of the VOYAGER study (Individual patient meta-analysis Of Statin Therapy in At-risk Groups: Effects of rosuvastatin, atorvastatin, and Simvastatin) to examine LDL-C and TG reductions in patients with baseline TG ≥ 177 mg/dL. Using 15 800 patient exposures to rosuvastatin, atorvastatin, and simvastatin, the least squares mean percentage change from baseline in LDL-C and TG were compared. Researchers found that the mean reductions in LDL-C varied from -26.9% to -55.5% . Significantly greater reductions in LDL-C were seen for 10 to 40 mg rosuvastatin vs equal or double doses of atorvastatin and simvastatin ($P<.05$). The mean reductions in TG varied from -15.1% to -31.3% . Significantly greater reductions were seen for rosuvastatin 10 mg vs atorvastatin 10 mg ($P<.05$); similar reductions were seen for 20 to 40 mg rosuvastatin vs equal doses of atorvastatin. Significantly greater reductions were seen for rosuvastatin 20 to 40 mg vs equal or double doses of simvastatin ($P<.05$). “In patients with hypertriglyceridemia, LDL-C reduction was substantial and dependent on the choice and dose of statin,” the researcher concluded.

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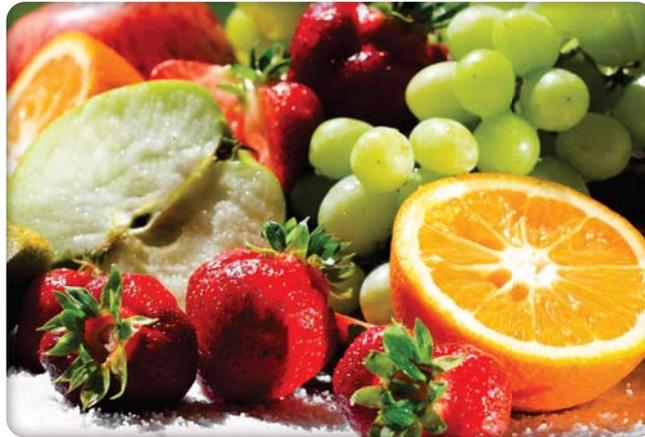
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Fresh Fruit Associated With Lower Risk of Heart Attack and Stroke

People who eat fresh fruit on most days are at lower risk of heart attack and stroke than people who rarely eat fresh fruit, according to new research published in the journal *the New England Journal of Medicine*. The findings come from a 7-year study of half a million adults in China, where fresh fruit consumption is much lower than in countries like the UK or US. Researchers from the University of Oxford and Chinese Academy of Medical Sciences conducted a large, nationwide study of 500,000 adults from 10 urban and rural localities across China, tracking health for 7 years through death records and electronic hospital records of illness. The present study was among people who did not have a history of cardiovascular diseases or anti-hypertensive treatments when first joined the study. Fruit is a rich source of potassium, dietary fiber, antioxidants, and various other potentially active compounds, and contains little sodium or fat and relatively few calories. The study found that fruit consumption (which was mainly apples or oranges) was strongly associated with many other factors, such as education, lower blood pressure, lower blood glucose, and not smoking. But, after allowing for what was known of these and



other factors, a 100g portion of fruit per day was associated with about one-third less cardiovascular mortality and the association was similar across different study areas and in both men and women. Study author said "The association between fruit consumption and cardiovascular risk seems to be stronger in China, where many still eat little fruit, than in high-income countries where daily consumption of fruit is more common." Also, fruit in China is almost exclusively consumed raw, whereas much of the fruit in high-income countries is processed, and many previous studies combined fresh and processed fruit. Co-author said "A recent Global Burden of Disease report put low fruit consumption as one of the leading causes of premature death in China. The senior author said "It's difficult to know whether the lower risk in people who eat more fresh fruit is because of a real protective effect. If it is, then widespread consumption of fresh fruit in China could prevent about half a million cardiovascular deaths a year, including 200,000 before age 70, and even larger numbers of non-fatal strokes and heart attacks."

Fasting before Cholesterol Tests not Necessary, New Study Says

For the first time, a group of international experts is recommending that fasting is no longer necessary before cholesterol and triglyceride testing. New research from Denmark, Canada and the United States involving more than 300,000 people suggests that fasting and not fasting before blood tests produce similar cholesterol and triglyceride levels. The findings were published in the *European Heart Journal*. According to a statement from the researchers, fasting can be difficult for many patients, particularly people with diabetes, the elderly, children and people with busy schedules. Non-fasting cholesterol testing can be extremely beneficial in these cases and can also save patients from extra follow-up visits with their doctor. Non-fasting tests also help clinics keep test results in order and doctors from spending extra time



looking at delayed tests. "This will improve patients compliance to preventive treatment aimed at reducing number of heart attacks and strokes, the main killers in the world," said the researcher. Fasting before cholesterol and triglyceride testing is required in all countries except for Denmark, which has successfully used non-fasting blood for cholesterol tests since 2009, according to the news release. This allows patients to come in for testing at any time of the day, regardless of if they have just eaten. It also stops patients from foregoing cholesterol and triglyceride testing due to inconvenience. That more patients will have their cholesterol and triglycerides measured will facilitate advice from their doctors on how best to prevent heart attacks and strokes in the future.

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