Nutrition, risk factors, prevention, and imaging: The 2018 Mario Verani Lecture

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Heart disease has been the leading cause of death in the United States since 1918. Cardiac mortality rates have dramatically decreased in this era of advanced medical and interventional therapies. However, this has been aptly described as ''mopping up the floor instead of turning off the faucet.'' With this recognition, prevention in cardiology is poised to become a central focus. Within prevention, dietary intervention is recognized as the single largest opportunity for improved cardiovascular outcomes, including improvement or elimination of cardiac risk factors, prevention of myocardial infarction, stroke and cardiovascular death, and reduction of plaque burden and myocardial ischemia. Cardiac imaging, particularly nuclear perfusion and coronary computed tomographic angiography, plays a critical role in early diagnosis and serial evaluation of myocardial ischemia and coronary artery disease. These techniques have the potential to help refine research protocols and evaluate their success by providing intermediate markers of improved myocardial blood flow and coronary plaque morphology. (J Nucl Cardiol 2019;26:86–91.)

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INTRODUCTION

Heart disease has been the leading cause of death in the United States since 1918, when it was supplanted for 1 year by the Spanish Flu epidemic. About 630,000 Americans died from heart disease in 2015, 366,000 from coronary artery disease. It is the leading cause of death for people of most racial/ethnic groups in the United States, including African Americans, Hispanics, and whites, with an estimated cost of over $200 billion annually, in health care services, medications, and lost productivity. After 4 decades of decline, heart disease deaths rose in 2015 by 1%. This trend has been attributed to the obesity epidemic.[1]

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OBESITY

The nutritional aspects of obesity revolve around the principle of balancing caloric intake with caloric expenditure. The increased availability of affordable palatable and high calorie foods along with decreased physical demands of many jobs have fueled the epidemic of obesity, and with this the consequent increases in hypertension and diabetes mellitus.[2]

Multiple nutritional studies have demonstrated weight loss, but they are typically temporary and not sustained. One prospective randomized trial[3] compared four diets for weight loss in moderately obese patients: Atkins (low carbohydrate), Ornish (vegetarian, low fat), Weight Watchers (calorie restriction), and Zone diets (macronutrient balance).

Adherence to each diet was moderate and decreased over time, with only about half of the original cohort remaining in each group. The Atkins and Ornish diets had the highest discontinuation rates (48% and 50%, respectively), compared with Zone and Weight Watchers (35% each). When evaluated for available data, each diet resulted in substantial weight loss, but at 1 year, the weight reduction occurred with the Ornish Diet.

Figure 1. Adapted from http://www.dresselstyn.com/site/study03/.

A second randomized trial[4] compared five dietary patterns over 6-month period standard (omnivore), semi-vegetarian (reduced animal products), pescovegetarian (vegetarian plus fish), vegetarian (includes dairy) and vegan (excludes all animal products). This showed 79% adherence and significant weight loss in each group, with the most sustained loss (− 3.1%, − 3.1, − 3.1, − 6.2, and − 7.5%, of weight) occurring in the vegetarian and vegan groups.

Ketogenic Diets

Beyond short-term weight loss, there is evidence that dietary patterns that focus on low intake of carbohydrates using high intake of animal fat and protein are associated with increased total mortality, if used for extended periods,[5] particularly post-myocardial infarction.[6] In one metanalysis of 4 low-carbohydrate prospective randomized studies,[7] these diets were associated with a 31% higher risk of all-cause mortality.

HYPERTENSION

As noted in prior guidelines,[8] lifestyle and non-pharmacologic intervention can result in significant reduction in systemic blood pressure in patients with systemic hypertension. This includes adherence to a DASH dietary pattern with a diet rich in fruits, vegetables, whole grains and low-fat dairy products with a reduced content of saturated in total fat, resulting in approximately an 11 mm Hg decrease in systolic blood pressure.

In a meta-analysis of 7 prospective randomized trials and 32 observational studies,[9] vegetarian diets resulted in an average of 5 mm Hg and 7 mm Hg reductions in systolic pressure, respectively. In the large Adventists Health Studies' prospective observational cohort, the incidence of hypertension was between 23% and 75% lower with progressively more vegetarian diets.[10] In the INTERMAP micronutrient studies,[11] this has been attributed to the antihypertensive effect of glutamic acid in vegetable protein.

CHOLESTEROL

While the beneficial effects of soluble fiber, monounsaturated and polyunsaturated fats, and deleterious effects of both trans- and saturated fats, on serum cholesterol have generally been agreed upon, the relationship between ingested cholesterol and serum cholesterol has become controversial in recent years,[12] with a focus short-term studies of risk factors rather than long-term outcomes.[13] Considering the saturation of the Niemann-Pick C1-Like 1 receptors in the small bowel, there is a progressively flat relationship between ingested cholesterol and serum cholesterol. Large increases in serum cholesterol are noted in ''hyperresponders,'' particularly those who have a lower cholesterol baseline degree of cholesterol consumption.[14] The relationship between ingested cholesterol and the consequent increase in serum cholesterol is essentially linear ($y = 0.0974x$) at lower levels.[15] In a metaanalysis of 224 studies of cholesterol ''real world'' dietary interventions,[16] there was a 2.2 mg/dL decrease in serum LDL for every 100 mg lowering of ingested cholesterol.

Therefore, the Institute of Medicine has recommended that ''saturated fatty acid, trans fatty acid, and cholesterol consumption be as low as possible while consuming a nutritionally adequate diet.''[17]

In terms of dietary patterns, the randomized prospective PORTFOLIO diet, high in plant sterols, soy protein, viscous fibers, and almonds, has been shown to reduce both low-density lipoprotein cholesterol (LDLc) and high-sensitivity C-reactive protein (hs-CRP) equally as did low-dose lovastatin therapy.[18]

Similarly, a metaanalysis of 30 observational studies and 19 clinical trials,[19] consumption of vegetarian diets compared with omnivorous diets in observational studies and clinical trials was associated with lower mean concentrations of total cholesterol (− 29.2 and − 12.5 mg/dL, $P < 0.001$), low-density lipoprotein cholesterol (− 22.9 and − 12.2 mg/dL, $P < 0.001$), and high-density lipoprotein cholesterol (− 3.6 and − 3.4 mg/dL,

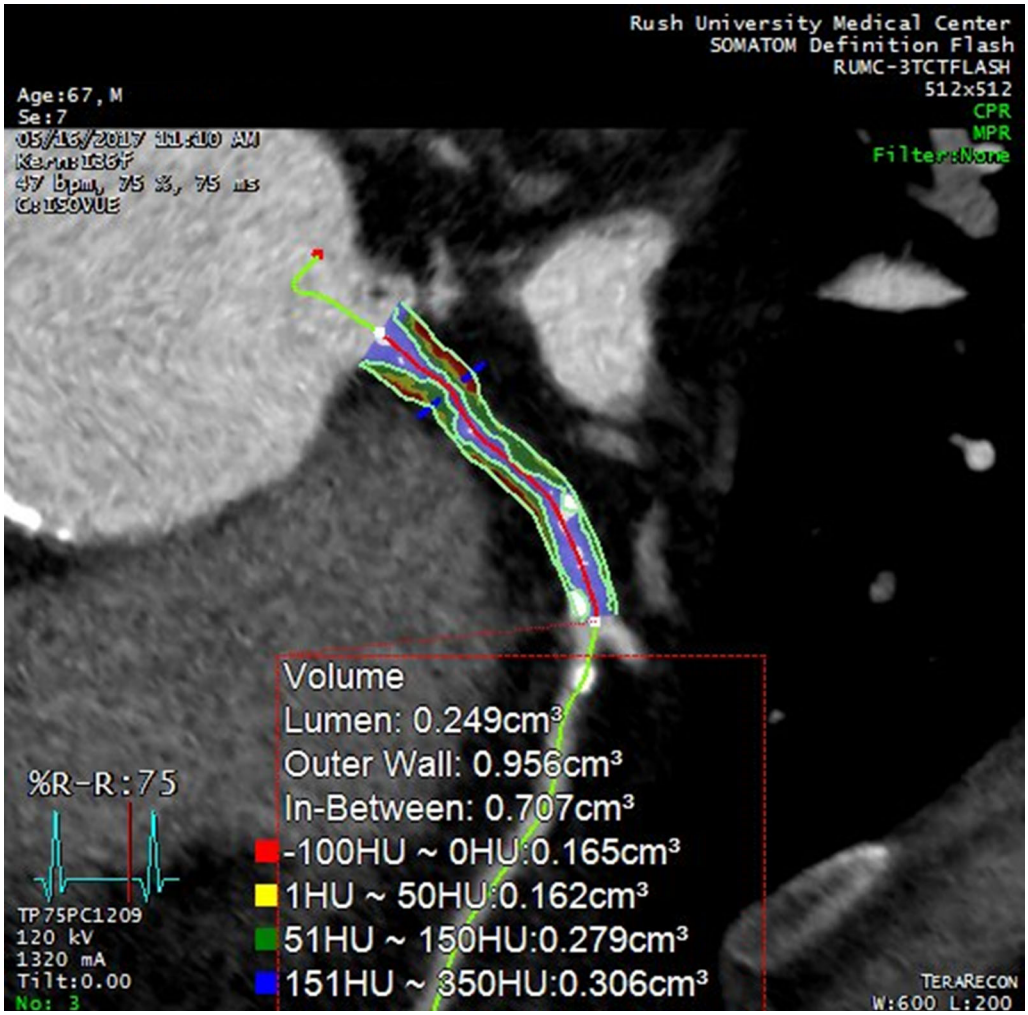

Figure 2. An example of plaque characteristics on a left main and proximal left anterior descending coronary stenosis, rendering volume of low-density, fibrotic and more dense and stable plaque.

$P < 0.001$), respectively. Triglyceride differences were − 6.5 ($P = 0.092$) in observational studies and 5.8 mg/dL ($P = 0.090$) in intervention trials.

DIABETES

Despite the focus on refined carbohydrates and fat consumption and consequent insulin resistance, recent literature in nutrition has focused on the role of red meat consumption on elevating the risk of type 2 diabetes mellitus.[20] This includes 3 metaanalyses[21–23] of prospective cohorts with strongly positive associations, which is only partially mediated by increased body weight.[23]

Further, glycemic control can be improved (or regained) with low a reduction of red meat consumption,[23] or a diet devoid of animal product and low in saturated fat.[20] When polyunsaturated vegetable fat is substituted for sugar, glycemic control is improved.[24]

CV EVENTS AND MORTALITY

Recent literature has focused on several eating patterns, food substances, micronutrients, and metabolic consequences in relationship to the development of cardiovascular events and mortality.

Sugar and artificially sweetened beverages have been correlated with increasing the development of type II diabetes mellitus, and therefore cardiovascular risk, with an increase in the frequency of diabetes by 20% with just one daily serving of these sweetened beverages.[25]

In several cohort studies, consumption of sugar has been associated with increased mortality. In the nurses'

health study a glycemic load resulted in a 22% increase in mortality while cholesterol consumption increased mortality by only 17%, and mortality was reduced by 16% with vegetable fiber consumption.[26]

In the REGARDS trial,[27] the Southern dietary pattern was identified as substantially increasing health risks including a 56% higher risk of heart disease and a 30% higher risk of stroke. This pattern consisted of more fried food, added fats, organ and processed meats and sugar sweetened beverages. It has been noted that consuming an unhealthy plant-based diet[28] with similar elements to the Southern diet including juices/sweetened beverages, refined grains, potatoes/fries and sweets results in increased coronary events exceeding the point estimate for that associated with consumption of animal products.

Correlation between dietary elements and cardiovascular mortality were also examined in a recent publication from the National Health and Nutrition Examination Surveys or NHANES,[29] indicating that high sodium content (> 2000 mg daily), red meat (> 14 g/day), sugar sweetened beverages, or processed red meat consumption, in any amount, were associated with cardiovascular death.

The Mediterranean diet was tested in the PREDIMED trial,[30] a prospective randomized study that was recently retracted and re-published after re-analysis with correction to the randomization process. This demonstrated a 30% reduction in the combined end point myocardial infarction, stroke and cardiovascular mortality. However, the benefit of this dietary pattern with either extra virgin olive oil or nuts was confined statistically to stroke reduction, with no improvement over the control diet for mortality or myocardial infarction. When the PREDIMED data was reanalyzed for the ''provegetarian'' food pattern (more vegetable consumption vs. less animal product consumption, and a significant mortality reduction (41%) was noted in the quintile with the highest vegetarian score.[31]

A comparison of plant and animal protein from the Adventist Health Study-2 cohort[32] similarly indicated that using meat for protein increased mortality by 61% while replacing meat with nuts and seeds reduce mortality by 40%.

The prospective cohort study of US healthcare professionals[33] with at least one risk factor, including over 130,000 nurses and physicians, indicated that replacement of animal protein with plant protein would reduce cardiovascular mortality and all-cause death, with poultry and fish increasing mortality by 6%, dairy by 8%, unprocessed red meat by 12%, eggs by 19%, and processed red meat by 34%. Overall plant protein reduced mortality by 10% for every 3% energy increment replacement for animal protein.

Intestinal microbiota and dietary phosphatidylcholine,[34] ingested with animal products, such as meat, eggs, and cheese for example, have been identified as a novel mechanism for the development of myocardial infarction, stroke and death, by accelerating arterial plaque formation along with increased platelet adhesiveness generated by trimethylamine-N-oxide (TMAO). In addition to ischemic events, TMAO has been correlated with mortality in congestive heart failure.[35]

The relative risk of processed versus unprocessed red meat associated with development of heart failure, coronary heart disease, hemorrhagic stroke, ischemic stroke and diabetes mellitus has been examined in a meta-analysis, indicating that TMAO, heme iron, nitrosamine, nitrates, nitrate and nitroso compounds, saturated fat, advanced glycation end products, and branched amino acids represent possible mediators.[36] Similarly, the NIH-AARP diet and health study found an association between all-cause mortality with the total and processed red meat attributable to nitrate intake and he iron.[37]

Sensitization to red meat measured by immunoglobulins against the mammalian oligosaccharide galactose-α-1,3-galactose has been associated with accelerated atherosclerosis and plaque instability.[38] This may represent another method to identify patients who should avoid consumption of mammalian meat due to risk of ischemic heart disease, a modifiable risk factor.

CORONARY IMAGING

Direct and indirect visualization of coronary plaque regression has been a long-sought target, using invasive coronary angiography,[39,40] intravascular ultrasonography [41] and positive emission tomography (PET) myocardial perfusion imaging,[42,43] after cholesterol lowering with cholesterol lowering medications or plant-based diet (Figure 1).

Serial perfusion imaging has been helpful to analyze reduction of ischemia after a variety of interventions, such as nitrates, exercise, ranolazine, and statins.[44] However, there is growing interest in serial plaque imaging with coronary computed tomography (CCTA). This technique can elucidate stenosis severity, number of coronary lesions, non-calcified plaque volume, high-risk plaque characteristics (positive remodeling, stippled calcification, low-density plaque volume, Figure 2) that correlate the risk of future coronary events, and yields quantitative parameters that can be used to detecting changes in plaque over time

with interventions such as cholesterol lowering diet or drugs.[45]

CONCLUSIONS

Nuclear cardiology has focused on detecting ischemia as a surrogate for the presence or absence of obstructive coronary disease, and rendering prognostic variables for optimal management of patients. As we move more into prevention, serial measurement of myocardial blood flow with PET and alteration in plaque burden and characteristics with CCTA will be the tools to help define the interventions, such as nutrition to improve cardiac risk and prevent ischemic events. We now have the tools to ''turn off the faucet instead of mopping up the floor'' and the means to verify how effective these tools can be.

Disclosure

There were no disclosures or relationships with industry.

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