Does Junk Food Lead to Heart Failure?
Importance of Dietary Macronutrient Composition in Hypertension

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Experimental and clinic studies show that chronic hypertension leads to myocardial pathology and systolic and diastolic dysfunctions that frequently progress to heart failure. Elevated afterload causes cardiomyocyte hypertrophy, which alters myocardial energy metabolism by increasing glucose metabolism and impairing mitochondrial oxidative capacity, increasing the production of reactive oxygen species and oxidative damage, and triggering remodeling of the myocardial extracellular matrix and the left ventricle (see Figure). Obesity is also a strong risk factor for both hypertension and heart failure and has been at epidemic proportions worldwide. The increase in obesity in Western societies over the last century is associated with greater consumption of highly processed carbohydrates (eg, sugar, white flour, and white potatoes) and saturated fats. At present, there is little information regarding the effects of dietary fat and carbohydrate composition on cardiac function and the development of heart failure in hypertension.

In the present issue of Hypertension, Majane et al present the novel finding that consuming a diet that is high in sugar and saturated fat results in relative modest obesity (10% increase in body mass) compared with a sugar-free, low-fat diet but greatly accelerates left ventricular dysfunction in a rat model of essential hypertension. Importantly, this effect occurred in the absence of an increase in blood pressure and with no signs of diabetes mellitus or systemic insulin resistance. Cardiac dysfunction was associated with 2 classic indicators of myocardial pathology that occur in response to hypertension: accelerated cardiomyocyte apoptosis and activation of matrix metalloproteinase 2. These important findings support the concept that, in essential hypertension, a high-saturated fat/high-sugar diet accelerates the progression from modest left ventricular concentric hypertrophy to frank pump dysfunction.

The effects of glycemic load and fat intake on the development of myocardial pathology and contractile dysfunction in patients with hypertension have not been reported. There is, however, a growing shift in the paradigm for the role of dietary macronutrient composition in the incidences of coronary heart disease. Recent epidemiological studies found no reduction in coronary heart disease associated with consumption of a low-fat/high-carbohydrate diet and reduced risk with consumption of a diet that is low in sugar and rapidly absorbed starches and high in polyunsaturated fatty acids. It is becoming increasing clear that consuming a diet with a high glycemic load typical of the “junk-food” diet is strongly associated with an increased risk for coronary heart disease.

Other recent reports from rodent models of chronic arterial pressure overload suggest that, in the absence of severe obesity, a low-carbohydrate/high-fat diet attenuates development of left ventricular hypertrophy and heart failure, whereas a high-sugar diet accelerates this process. The cardiac effects of dietary lipids and carbohydrates in hypertension are complex and poorly defined, and the optimal diet for prevention of cardiac dysfunction and heart failure in hypertension is not known. It is important to separate the adverse effects of dietary intake of sugar, refined starches, and saturated fat on the heart from the established detrimental impact of obesity on the cardiovascular system. In our recent work in the Dahl hypertensive rat, we observed less left ventricular dysfunction and chamber expansion with a high-fat/low-carbohydrate diet compared with a high-starch or high-sugar diet in the absence of any differences in fat or body mass, thus suggesting a direct pathological link between dietary glycemic index and cardiac pathology in hypertension. This suggests that the pathology observed by Majane et al may be because of the high intake of sugar and saturated fat and not the relatively modest level of obesity that was induced by the diet. Adverse effects of a high-sugar diet can clearly occur without obesity. The mechanism behind this observation may be the generation of NADPH and reactive oxygen species by accelerated flux of glucose into the oxidative pentose phosphate pathway, as suggested by the observation that treatment with the antioxidant Tempol prevented cardiac hypertrophy, left ventricular remodeling, contractile dysfunction, and myocardial lipid peroxidation in fructose-fed mice subjected to aortic constriction. Alternatively, it could be the result of flux through the hexosamine biosynthetic pathway or greater N-acetyl-glucosamine production.

We propose that prolonged intake of a typical junk-food diet triggers multiple steps that eventually converge to accelerate the onset of heart failure (see Figure). Excess caloric intake results in obesity that is closely linked to myocardial structural and functional changes, for example, increased left ventricular mass, that frequently result in heart failure. In support, a large community-based study found that obesity is an independent risk factor for the onset of heart failure. There is also a robust relationship between obesity and the
development of hypertension, that is, increased sympathetic activity likely plays a crucial role in obesity-induced hypertension and could raise arterial pressure by causing peripheral vasoconstriction and by increasing renal tubular sodium retention. Hypertension itself is also an independent risk factor for the onset of contractile dysfunction and heart failure. We further propose that excessive intake of high-glycemic foods and saturated fats perturbs normal myocardial metabolism and signaling, activating pathological processes (see Figure). For example, a high glycemic load enhances glucose uptake & mitochondrial function, pentose & hexosamine pathway flux, ROS production & oxidative damage, extracellular matrix and chamber remodeling, & cardiomyocyte apoptosis.

In summary, the results of the study by Majane et al suggest that high intake of sugar and saturated fat accelerates the development of cardiac pathology and pump dysfunction in hypertension despite no signs of diabetes mellitus and only a modest level of obesity. Thus, the combination of poor macronutrient intake and hypertension appears to form a potent mixture that severely impairs cardiac function. These findings raise the interesting possibility that dietary manipulation may represent a relatively cost-effective and easy adjunctive therapeutic option that could be offered to hypertensive and heart failure patients. However, additional clinical and basic studies are required to further test this hypothesis and to delineate underlying mechanisms that link high junk-food intake with reduced contractile and diastolic functions.

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**References**

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