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Original Article

High fat diet aggravates atrial and ventricular remodeling of hypertensive heart disease in aging rats

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KEYWORDS
SHR;
High-fat diet;
Hypertension;
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Remodeling

Background/Purpose: Left ventricular hypertrophy is a major cause of heart failure in aging population. This study is to determine whether an excess dietary fat is lipotoxic or lipoprotein to the hypertrophic aging heart.
Methods: At 44-week-old, a normal chow (12% fat) was replaced a high-fat diet (HFD; 45% fat) for randomly selective spontaneously hypertensive rats (SHR + HFD, n = 6) and Wistar-Kyoto rats (WKY + HFD, n = 6, normotensive control). Others (SHR, n = 11; WKY, n = 10) were continuously fed with normal diets. After 27 weeks, electrocardiogram, echocardiography, and femoral arterial catheterization were performed before rats being sacrificed for molecular biology analyses.
Results: HFD aggravated cardiac atrial, ventricular dilation and hypertrophy in SHR (LV mass: SHR + HFD 2026.0 ± 424.9 vs SHR 1449 ± 461.1 mg, unpaired *t* test $P < 0.05$). HFD caused significant atrial dilatation in both WKY (LA diameter, 5.38 ± 0.36 vs 4.11 ± 0.42 mm, $P < 0.001$) and SHR (6.13 ± 0.79 vs 4.69 ± 1.00, $P < 0.01$). Only in SHR, HFD induced significant left ventricular dilatation (LV diameter, 8.87 ± 1.25 vs 7.08 ± 1.00 mm, $P < 0.01$) and reduced ejection fraction (LVEF, 62.8 ± 11.6 vs 75.1 ± 9.2 mm, $P < 0.05$). The α-myosin heavy chain was significantly upregulated in atria and ventricles of HFD groups. HFD induced significant upregulation of PPARα, ACADM, and TNFα transcripts in atrial tissues ($P < 0.05$).

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Conclusion: Hypertensive heart disease in aging rats was aggravated by HFD with worse atrial, ventricular remodeling and associated with left ventricular systolic function impairment.

Introduction

Hypertension with left ventricular hypertrophy (LVH) is a major independent risk factor for cardiovascular-related morbidity and mortality in aging population.[1] Although LVH is an adaptive process that occurs in response to increased hemodynamic load, patients with hypertensive LVH are at risk of progressing to systolic heart failure.[2] Aging per se also attributes to structural and functional changes in the heart, such as left ventricular (LV) hypertrophy, left atrial (LA) enlargement, and impairment of LV systolic and diastolic function.

The pathogenesis of cardiac hypertrophy in obesity is complex and may intervene the presence of coexisting hypertension with plasma volume expansion, and activation of the sympathetic nervous system.[3] Increased accumulation of intracellular triglyceride and lipids metabolites leads to apoptosis of cardiomyocytes.[4,5] On the other hand, patients with cardiovascular diseases seem to have a better prognosis with overweight and obesity than leaner patients.[6]

Abundant evidence in both human and animal studies shows that aging increases high-fat diet (HFD)-induced metabolic derangement.[7–9] Aging and HFD are suggested to synergistically accentuating capacity to metabolize excess fat.[7] Aging per se promotes development of fat deposition, dyslipidemia, insulin resistance, and advanced liver inflammation.[8] A typical elderly person's intake consists of 33–36% fat of daily food energy in Western countries.[10] As the elderly often have teeth problem, and abnormal threshold of taste and smell, high fat foods become a feasible option. However, elevated fat intake may increase vulnerability of the elderly to diseases. Whether abundant dietary fat is lipotoxic or lipo-protective to the hypertrophic aging hearts remains uncertain.

We hypothesized that HFD accelerates cardiac remodeling and ventricular dysfunction in the aging, hypertensive heart. In the present study, we investigated whether HFD contributes to progress of hypertrophy in the aging hearts, using an aging Wistar rats and spontaneous hypertensive rats (SHR). In addition, we investigated the effect of an HFD on cardiac structure, function, electrocardiographic parameters, and markers of inflammation and metabolism in myocardial tissues.

Materials and methods

Animal care

Male spontaneous hypertensive rats (SHR) and normotensive Wistar-Kyoto (WKY) rats were purchased from the National Laboratory Animal Center (Taipei, Taiwan). All animals were housed in a temperature-controlled facility (21–22 °C) with a 12-h light/dark cycle, free access to water and a standard chow diet. All applicable institutional and governmental regulations concerning ethical use of animals conformed to the NIH guidelines and all animal procedures were approved by the Institutional Animal Care and Use Committee of Kaohsiung Medical University.

Experimental design and diet

After 44 weeks, some rats' diet was switched to a high-fat diet (HFD, fat content 45% of energy, ingredients in the Table 1). Age of 44 was chosen for that all SHR had developed hypertensive heart disease manifested with increased ventricular septal thickness, and atrial dilation. Weight gain and food intake were monitored once a week. The duration of HFD as 6 months was chosen along with rats aging to the end of this study. After 27 weeks, echocardiography was performed for all rats. Two days later, invasive blood pressure recording and electrocardiography were performed and then rats were sacrificed. Venous blood was drawn from the heart into EDTA-coated vials, and plasma was prepared and stored at −20 °C pending further analysis. Heart tissue samples were collected and frozen in liquid nitrogen for protein and mRNA analysis as described below.

Electrocardiography recording and analysis

As the rats were 71-wk-old, recordings were conducted on 10 WKY rats, 5 WKY + HFD rats, 11 SHR rats, and 4 SHR + HFD rats. Rats were anesthetized with 60 mg/kg intraperitoneal pentobarbital injection. The electro

Table 1 Composition and energy content of the high-fat diet and standard chow.

Content (Kcal%)	Diets	
	HFD	Chow
Fat %	45	12
Protein %	20	24
CHO %	35	64
Energy (Kcal/kg)	4730	3188
Protein ingredients	Casein, L-Cystine	—
Fat ingredients	Soybean oil, Lard	—
CHO ingredients	Corn Starch, Maltodextrin, Sucrose	—

CHO = carbohydrate; Chow = standard chow; HFD = high fat diet.

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