Abdominal Fat and Sympathetic Overactivity

From Calorie Intake to Postmenopausal Hypertension

Heinz Rupp, Bernhard Maisch

Background: Epidemiologic studies have found an association between overweight and increased mortality arising primarily from cardiovascular disorders. A major determinant is a chronically raised sympathetic nervous system activity which can arise from calorie intake-dependent and -independent mechanisms. Calorie-dependent parameters reflecting sympathetic overactivity are an increased body fat mass and body mass index.

Visceral Fat: Although influenced by calorie intake to a certain extent, visceral fat accumulation is a mechanism which is determined also by estrogen deficiency (postmenopausal hypertension) or enhanced corticoid influences. It is hypothesized that excess catecholamines trigger various adverse processes which, if they persist, can lead or aggravate hypertension and insulin resistance. Visceral but not peripheral fat mass was correlated with atherogenic metabolites.

Excess Catecholamine Syndrome: The present focus on visceral fat accumulation strengthens the concept of an "excess catecholamine syndrome" of which the "metabolic syndrome" appears as one consequence. It is proposed to further assess the potential of transthoracic echocardiography as routine imaging method for the prediction of visceral fat accumulation and its adverse health consequences.

Key Words: Hypertension · Sympathoadrenergic stimulation · Central obesity

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Abdominales Fett und Sympathikusüberaktivität. Von der Kalorienaufnahme bis zur postmenopausalen Hypertonie


Schlüsselwörter: Sympathisches Nervensystem · Übergewicht · Adipositas · Viszerales Fett · Hypertonie · Insulinresistenz · Katecholamine

1Molecular Cardiology Laboratory, Department of Internal Medicine and Cardiology, Philipps University Marburg, Germany.
Introduction

Epidemiologic studies have found an association between overweight and increased mortality arising primarily from cardiovascular disorders. Since the proportion of overweight persons appears to increase steadily in societies with a sedentary lifestyle, therapy of overweight-linked diseases has become a major challenge. Until recently, anthropometric parameters with a prognostic value for cardiovascular morbidity and mortality remained ill-defined. A major progress in identifying overweight-associated cardiovascular disorders came from the determination of localized fat tissues with dual-energy X-ray absorptiometry, magnetic resonance imaging (MRI) and computed tomography (CT) [22]. Among the recent unexpected findings was the observation that pericardial fat accumulation was a stronger coronary risk factor than the other body fat distributions in nonobese men [40]. Moreover, epicardial fat was the strongest independent variable for the severity of coronary artery disease as determined by coronary angiography [14]. Persons with predominant visceral fat accumulation showed also higher epicardial adipose tissue thickness than subjects with predominant peripheral fat distribution [14]. A linear regression analysis showed a good correlation between epicardial adipose tissue and waist circumference and MRI abdominal visceral adipose tissue. Thus, transthoracic echocardiography could be an easy and reliable imaging method for visceral adipose tissue prediction [14].

The need arises, therefore, to better understand pathophysiologic mechanisms associated with the accumulation of different fat tissues. In the present review, evidence is summarized favoring a crucial link between visceral fat accumulation and sympathetic overactivity. Of particular interest, in this respect, is the postmenopausal status which is associated with central fat distribution. Mechanisms will be delineated which link visceral fat accumulation with the progression of hypertension and metabolic disorders. Evidence will be provided which strengthens the concept of the “excess catecholamine syndrome” [28, 29], which represents an early marker of adverse processes underlying the “metabolic syndrome” [27].

Calorie Intake and Sympathetic Overactivity

The sympathetic nervous system activity is modulated by various environmental factors arising from high food abundance and stress [8]. Of crucial importance appears to be calorie intake. Since basal metabolism is determined by sympathetic activity, a close link between calorie intake and energy expenditure is essential. In times of food shortage, the body responds with a reduction in sympathetic activity, heart rate and metabolism which ensures a prolonged survival. Candidates involved in the signaling are insulin and leptin [6, 9]. In rats with chronically implanted pressure transducers, heart rate was linearly correlated with an altered body weight arising from a restricted calorie intake or overfeeding (Rupp, unpublished). It can thus be concluded that a raised heart rate associated with an increased calorie intake represents the consequence of an important principle of energy conservation. Under conditions of a chronically enhanced calorie intake, sympathetic overactivity has, however, adverse effects.

In a number of studies, an increased body mass index (BMI) was associated with a raised sympathetic activity of skeletal muscle [33] and an impairment of reflex sympathetic restraint [11, 12]. Furthermore, kidney norepinephrine spillover was found increased in overweight persons [43]. Of importance is the finding that sympathetic activation occurs already at BMI values < 30 [33]. The view that a raised body weight per se is a crucial determinant of sympathetic overactivity is also supported by experimental data. In animal experiments, an increased calorie intake was associated with a parallel rise in heart rate and blood pressure [31]. The type of diet which raised the calorie intake was identified as a mixture of saturated fat and sucrose. Normotensive rats with implanted radiotelemetry pressure transducers were fed increasing amounts of coconut fat (8%, 16%, and 24%) corresponding to 20–47% of total calories from fat. Thereafter, increasing amounts of sucrose (16%, 32%, and 50%) and fructose (50%) were added to the 24% fat diet corresponding to 13–40% of total calories from sugar. In contrast to the fat diets, the 32% and 50% sucrose diets as well as the 50% fructose diets increased blood pressure and heart rate irrespective of the day-night cycle and the unaltered locomotor activity. Body weight was increased during the 32% and 50% sucrose feedings. The rise in heart rate and blood pressure occurred independently of day-night cycle (Figure 1). Thus, the dip during sleep which is required for maintaining normal vascular structure was prevented by overfeeding the rats. This “hyperkinetic hypertension” associated with body weight gain is a hallmark of a raised sympathetic nervous system activity.

A relationship between body weight increase and rise in sympathetic activity can be inferred also from the finding that younger hypertensive persons exhibit an in-